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Blood Research

2024 Korean Society of Hematology International Conference 65th Annual Meeting

Date : March 28 - 30, 2024
Venue : Grand Walkerhill Hotel, Seoul, Korea

Springer

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iCKSH 2024

2024 KOREAN SOCIETY OF HEMATOLOGY INTERNATIONAL CONFERENCE & KSH 65th ANNUAL MEETING

MARCH 28 - 30, 2024

GRAND WALKERHILL HOTEL, SEOUL, KOREA

ABSTRACT BOOK

The Korean Society of Hematology
대한혈액학회

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About Blood Research

Blood Research is a peer-reviewed open-access journal and delivers important clinical, translational and basic study results in hematology and related fields to the readers worldwide. The areas covered by **Blood Research** include topics ranging from basic laboratory research to clinical studies, translational studies and precision medicine in the field of hematology. Any physicians or researchers throughout the world are welcome to submit a manuscript related to topics in hematology written in English. Our readership consists of clinical hematologists, hematopathologists, clinical oncologists, scientists in related fields, laboratory technicians, nurses and students.

All of the submitted manuscripts undergo intensive peer review by at least two independent reviewers and are selected based on the importance of the topic, originality of the work, quality of the content, and the compliance to the journal's format.

Blood Research (p-ISSN 2287-979X, e-ISSN 2288-0011) started as the official journal of the Korean Society of Hematology in 1966. The journal had been developed and officiated into consolidated main journal in 2005 for 4 academic societies of the Koreans Society of Hematology, the Korean Society of Blood and Marrow Transplantation, the Korean Society on Thrombosis and Hemostasis, and the Korean Society of Pediatric Hematolog-Oncology. The Journal title changed from the Korean Journal of Hematology (p-ISSN 1738-7949, e-ISSN 2092-9129) to Blood Research as an international journal in the field of hematology in 2013.

Article Formats

Research, Review, Editorials, Perspective, Correspondance, Image

Blood Research is indexed and covered by ESCI, PubMed Central, Scopus, KCI, KoreaMed Synapse, and CrossRef.

Open Access Policy

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WELCOME MESSAGE

Dear Colleagues and Friends,

On behalf of the organizing committee, it is our great pleasure to invite you to participate in the 2024 Korean Society of Hematology (KSH) International Conference & 65th Annual Meeting, hosted by KSH, from March 28 to 30, 2024.

Held every year since 2018, the ICKSH congress shares up-to-date information and provides a unique opportunity for world-class leaders in the field to debate vital and contentious issues in Hematology.

Our programs will include topics such as benign hematologic diseases, various types of hematologic malignancies, coagulation/thrombosis related disorders and transfusion medicine through plenary lectures, as well as scientific and educational sessions.

In addition, a variety of stimulating social programs have been planned so participants can enjoy the fascinating Korean culture and share our warm spirit of friendship.

We welcome your support and look forward to seeing you at ICKSH 2024 in Seoul, Korea!

Seoklae Chae, MD., Ph.D.
Congress Chair
The Korean Society of Hematology

Seongsoo Jang, MD., Ph.D.
President
The Korean Society of Hematology

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PROGRAM AT A GLANCE Thursday, March 28, 2024

TIME	ROOM 1 (Vista Hall 1)	ROOM 2 (Vista Hall 2)	ROOM 3 (Grand Hall 1)	ROOM 4 (Art Hall)
08:00-09:00	Registration			
08:50-09:00	Opening Remark			
09:00-10:15	**JS01** Asian Hematology Session I - EBV-associated lymphoid malignancy	**ES01** Histiocytic neoplasm	**SS01** Exploring the utilization of innovative technologies	**SS02** The unmet needs in CML - Overcoming the obstacles of the road to cure
	Prospective studies for NK/T-cell lymphoma in Asia (Seok Jin Kim, Korea)	Histiocytic neoplasm in pediatrics (Kyung-Nam Koh, Korea)	Elucidating the 3D chromatin landscape of pediatric B-cell acute lymphoblastic leukemia using Micro-C (Kajsa Paulsson, Sweden)	Molecular mechanism of primary TKI resistance in CML (Jerald Radich, USA)
	Chronic active EBV disease: Our challenge to elucidate the pathogenesis (Ayako Arai, Japan)	Histiocytic sarcoma (Sung Nam Lim, Korea)	Integrated RNA and protein profiling of B-cell acute lymphoblastic leukemia at single-cell level (Sungyoung Choi, Korea)	Targeting leukemic stem cells in CML (Mhairi Copland, UK)
	NK lymphoma genomics (Weili Zhao, China)	Pathologic characteristics of histiocytic and dendritic cell neoplasms (Sun Och Yoon, Korea)	Leveraging dysregulated signaling networks for therapeutic benefit in myeloproliferative neoplasm (Stephen T. Oh, USA)	The role of NGS to detect TKI resistance (Saeam Shin, Korea)
10:15-10:30	Break			

PROGRAM AT A GLANCE Thursday, March 28, 2024

TIME	ROOM 1 (Vista Hall 1)	ROOM 2 (Vista Hall 2)	ROOM 3 (Grand Hall 1)	ROOM 4 (Art Hall)
10:30-11:15	**PL01** Somatic mutations and clonal dynamics in human blood cells (Peter J. Campbell, UK)			
11:15-12:00	**PS01** Lab-on-a-chip in hematology (Chong H. Ahn, USA)			
12:00-12:15	Break			
12:15-13:05	**SY01** Satellite Symposium 01 - MM Janssen | Pharmaceutical Companies of Johnson & Johnson Treatment of newly diagnosed multiple myeloma: Focus on daratumumab combination (Elena Zamagni, Italy)	**SY02** Satellite Symposium 02 - PNH AstraZeneca The ultimate value of C5 inhibitors in the evolving treatment landscape of PNH (Sung-Hyun Kim, Korea)	**SY03** Satellite Symposium 03 - AML astellas Treatment strategies for elderly AML with *FLT3*-mutation, entering the era of FLT3 Inhibitors (Naoko Hosono, Japan)	**SY04** Satellite Symposium 04 - Lymphoma Roche Advances in the treatment paradigm with bispecific antibodies (Wendy Osborne, UK)
13:05-13:50	Poster Viewing 1			
13:50-15:20	**OP01** Acute leukemia-1	**OP02** Lymphoma	**OP03** Hematopoietic stem cell transplantation & Cellular therapy	**OP04** Laboratory hematology
15:20-15:30	Break			

PROGRAM AT A GLANCE Thursday, March 28, 2024

TIME	ROOM 1 (Vista Hall 1)	ROOM 2 (Vista Hall 2)	ROOM 3 (Grand Hall 1)	ROOM 4 (Art Hall)
15:30-16:45	**JS02** EHA-KSH Joint Symposium - Multiple myeloma	**SS03** Wise perspective on new approaches in hemophilia	**SS04** For the next generation CAR-T cells	**SS05** Deepened understanding of AML using multi-omics approaches
	Dynamic assessment of risk in multiple myeloma (Meral Beksak, Türkiye)	Approaches to treat people with hemophilia: What's new and what's not? (Leonard A. Valentino, USA)	CD7 CAR-T therapy for treating hematological malignancies (Peihua Lu, China)	Navigating cancer complexities via single-cell omics and AI (Manoj Bhasin, USA)
	PET/CT for risk stratification in multiple myeloma (Joon Ho Moon, Korea)	Prospects and challenges of gene therapy for hemophilia (Alok Srivastava, India)	Development of a novel anti-CD19 CAR-T cells in B cell lymphoma (Dok Hyun Yoon, Korea)	Targeting the developmental heterogeneity of human acute myeloid leukemia (Shanshan Pei, China)
	Bone marrow inflammation in multiple myeloma (Tom Cupedo, The Netherlands)	Exploring personalized tailored hemophilia treatment: Tailoring treatment to individual needs (Jeong A Park, Korea)	CAR-T cells for treatment of T cell malignancies (Paul M. Maciocia, UK)	Mutational profile in Korean AML patients (Jae-Sook Ahn, Korea)
	Single-cell analysis in multiple myeloma (Sung-Soo Park, Korea)			
16:45-16:55	Break			

PROGRAM AT A GLANCE Thursday, March 28, 2024

TIME	ROOM 1 (Vista Hall 1)	ROOM 2 (Vista Hall 2)	ROOM 3 (Grand Hall 1)	ROOM 4 (Art Hall)
16:55-18:10	**SS06** **Insights into lymphoma pathobiology**	**SS07** **Profound understanding of diagnosis and therapy in MDS**	**SS08** **Leukemogenesis in children and adults**	**ES02** **Basics for trainees (Kor)**
	Germinal center in the genesis of lymphomas (Laura Pasqualucci, USA)	Molecular alterations and clinical implications in MDS (Yasushi Miyazaki, Japan)	*RUNX1*-FPDMM natural history study at NIH (Pu Paul Liu, USA)	Overview of lymphoma classification (Tae-Jung Kim, Korea)
	Genomics of follicular lymphoma: Clinical implications? (Robert Kridel, Canada)	Recent advances and future therapeutic strategies in MDS (Guillermo Garcia-Manero, USA)	Clinical impact of DDX41 mutations in myeloid neoplasms (Talha Badar, USA)	What's new in AML classification (Hee Sue Park, Korea)
	Distinct and overlapping features of nodal peripheral T-cell lymphomas exhibiting a follicular helper T-cell phenotype: A multicenter study emphasizing the clinicopathological significance of follicular helper T-cell marker expression (Jin Ho Paik, Korea)	Current diagnostic challenges in MDS (In-Suk Kim, Korea)	Discovery of new regulators in hematopoietic stem cells and malignancies (Dongjun Lee, Korea)	Recent update of MDS classification (Miyoung Kim, Korea)
18:10-18:30	Break			
18:30-19:30	Welcome Reception (Aston House)			

PROGRAM AT A GLANCE Friday, March 29, 2024

TIME	ROOM 1 (Vista Hall 1)	ROOM 2 (Vista Hall 2)	ROOM 3 (Grand Hall 1)	ROOM 4 (Art Hall)
08:00-09:00	Registration			
09:00-10:15	**JS03** ASH-KSH Joint Symposium - Ped-ALL	**ES03** Leaps and hurdles in transfusion medicine (Kor)	**SS09** Clonal hematopoiesis: What should we know?	**SS10** Predictive biomarkers in multiple myeloma
	Pediatric and AYA ALL: Lessons learned from Children's Oncology Group clinical trials (Sarah K. Tasian, USA)	Comprehensive overview of cell-based artificial platelet production (Seung Yeob Lee, Korea)	Clonal hematopoiesis and aging (Siddhartha Jaiswal, USA)	The impact of immune profiling of T-cell and plasma cells on non-cellular immune therapy in myeloma (Nizar Jacques Bahlis, Canada)
	Multicenter trials investigating childhood acute lymphoblastic leukemia in South Korea (Hyery Kim, Korea)	Anti-CD38 and anti-CD47 delay timely transfusion (Hyungsuk Kim, Korea)	Clonal hematopoiesis: Implications for cell therapy (Adam S. Sperling, USA)	Single-cell techniques to characterize immune microenvironment in MM (Niels Weinhold, Germany)
	Dissecting the developmental origins of acute leukemia (Charles G. Mullighan, USA)	Reappraisal of transfusion-transmitted infections (Dae-Hyun Ko, Korea)	Clonal hematopoiesis and metabolic diseases (Sung Hee Choi, Korea)	The power of ONE: Immunology in the age of single cell genomics (Ido Amit, Israel)
	Unveiling precision medicine: RNA and DNA sequencing in targeted therapy for Korean pediatric leukemia (Myungshin Kim, Korea)			
10:15-10:30	Break			

PROGRAM AT A GLANCE Friday, March 29, 2024

TIME	ROOM 1 (Vista Hall 1)	ROOM 2 (Vista Hall 2)	ROOM 3 (Grand Hall 1)	ROOM 4 (Art Hall)
10:30-11:15	**PL02** How to win: Competitive strategies in the hematopoietic stem cell niche (Margaret Goodell, USA)			
11:15-12:00	Poster Viewing 2			
12:00-12:15	Break			
12:15-13:05	**SY05** Satellite Symposium 05 - AML Bristol Myers Squibb™ Continued hope with ONUREG - A new maintenance therapy to treat AML (Esther Oliva, Italy)	**SY06** Satellite Symposium 06 - Lymphoma KYOWA KIRIN Mogamulizumab: A new era in MF/SS management - Clinical evidence and practical consideration (Francine Foss, USA)	**SY07** Satellite Symposium 07 - CML NOVARTIS TKI treatment pattern and new therapy of CML (Qian Jiang, China)	**SY08** Satellite Symposium 08 - Lymphoma HANDOK The optimal treatment strategy for transplant-ineligible relapsed/refractory DLBCL (Kwai Han Yoo, Korea)
13:05-13:20	Break			
13:20-14:50	**OP05** Acute leukemia-2	**OP06** Multiple myeloma	**OP07** Myeloid neoplasm & Bone marrow failure	**OP08** Thrombocytopenia & Supportive care
14:50-15:05	Break			

PROGRAM AT A GLANCE Friday, March 29, 2024

TIME	ROOM 1 (Vista Hall 1)	ROOM 2 (Vista Hall 2)	ROOM 3 (Grand Hall 1)	ROOM 4 (Art Hall)
15:05-16:20	**JS04** **Current interests in hematologic disease in Asia**	**SS11** **Quality-of-life revisited**	**SS12** **Novel approaches for diagnosis & treatment of acute lymphoblastic leukemia**	**ES04** **Monoclonal gammopathies of clinical significance**
	The journey of bone marrow transplantation at BachMai General Hospital (Han Viet Trung, Vietnam)	Palliative care for patients with leukemia (Min Sun Kim, Korea)	Novel approaches for diagnosis & treatment of acute lymphoblastic and myeloid leukemia (Michel Zwaan, The Netherlands)	AL cardiac amyloidosis (Darae Kim, Korea)
	Current situation of management of Non-Hodgkin lymphoma in the Republic of Armenia (Yervand Hakobyan, Armenia)	Long-term survivorship in hematologic malignancies (Shahrukh K. Hashmi, UAE)	The role of blinatumomab in the treatment of MRD negative B-ALL in adults (Mark R. Litzow, USA)	Nephrologist's perspective on monoclonal gammopathy of renal significance (Soon Hyo Kwon, Korea)
	The evolution of hemophilia treatment in Thailand (Darintr Sosothikul, Thailand)	The importance of monitoring symptoms and quality of life in routine hematology practice (Fabio Efficace, Italy)	Revised WHO classification of ALL: New era of genetic diagnosis (Ari Ahn, Korea)	Monoclonal gammopathies of neurological significance (Ju-Hong Min, Korea)
16:20-16:35	**Break**			

PROGRAM AT A GLANCE Friday, March 29, 2024

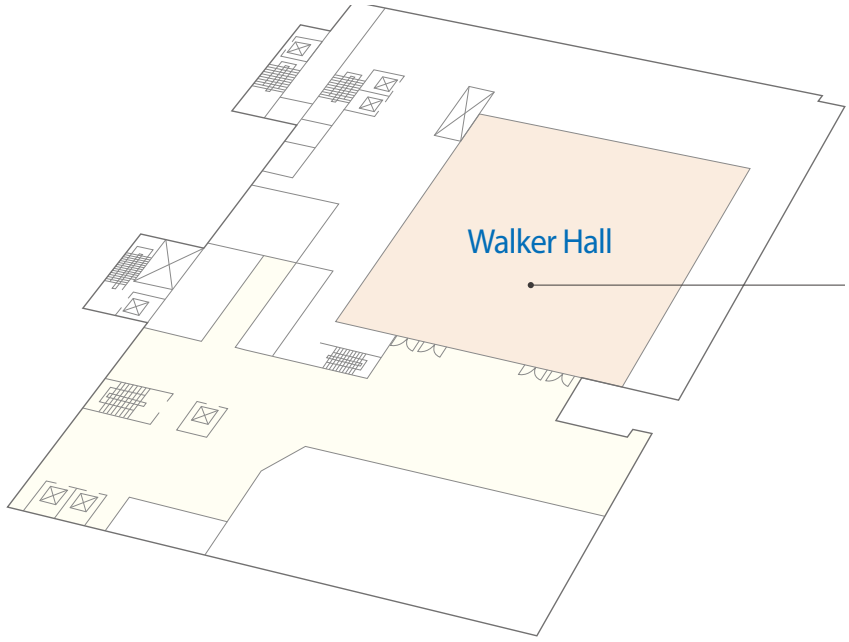
TIME	ROOM 1 (Vista Hall 1)	ROOM 2 (Vista Hall 2)	ROOM 3 (Grand Hall 1)	ROOM 4 (Art Hall)
16:35-17:50		**SS13** Advancing in knowledge of rare pediatric hematologic disorders	**JS05** Asian Hematology Session II - AML	**ES05** Principles of anticoagulation - All about blood clots (Kor)
		Clonal evolution of MDS/AML in patients with cancer predisposition syndromes (Kenichi Yoshida, Japan)	Epidemiology, risk stratification and treatment outcome in acute myeloid treatment: Taiwan experience (Hsin-An Hou, Taiwan)	Back to the basic: Coagulation pathway (Seonyang Park, Korea)
		Congenital and aquired thrombophilic conditions in children (Leonardo R. Brandão, Canada)	Advancement in leukaemia diagnostics: The role of next-generation sequencing (NGS) in acute myeloid leukaemia in Malaysia (Angeli Ambayya, Malaysia)	Pharmacology: Anticoagulants and reversal agents (Seo-Yeon Ahn, Korea)
		Management of rare pediatric lymphomas (Jae Wook Lee, Korea)	Determining fitness for treatments in older adults with AML (Byung Sik Cho, Korea)	Proper application of anticoagulation therapy on cancer associated thrombosis (Ho-Young Yhim, Korea)
17:50-18:30	Gala Reception (Vista Lobby)			
18:30-20:00	Gala Dinner (Vista Hall)			

PROGRAM AT A GLANCE Saturday, March 30, 2024

TIME	ROOM 1 (Vista Hall 1)	ROOM 2 (Vista Hall 2)	ROOM 3 (Grand Hall 1)	ROOM 4 (Art Hall)
07:30-08:00		Business Meeting		
08:00-09:00	Young Investigator Award Presentation			
09:00-10:15	**ES06** Essential knowledge for optimal hematologic consultation (Kor)	**SS14** Novel insights into pathogenesis of MPN	**SS15** Immunotherapies for lymphomas non-benefited from CAR-T cell therapy	**ES07** Basic genomics for clinical hematologists (Kor)
	Functional iron deficiency in cancer patients (Ik-Chan Song, Korea)	Myeloproliferative neoplasms and inflammation (Steffen Koschmieder, Germany)	Treatment options for relapsed/refractory Hodgkin lymphoma after brentuximab vedotin and PD-1 blockade (Alex F. Herrera, USA)	Genomic technologies for detecting structural variations in hematologic malignancies (Miae Jang, Korea)
	Assessment of neutropenia in hospitalized patients (Young Hoon Park, Korea)	Signaling contributing to the development of myelofibrosis: Beyond JAK/STAT (Douglas Tremblay, USA)	Aggressive B-cell lymphomas: Immuno-chemotherapies other than CAR-T cell therapies (Jason Westin, USA)	The role of NGS in hematologic malignancies (Young-Uk Cho, Korea)
	Perioperative consultation for the appropriate transfusion (Ka-Won Kang, Korea)	Clonal evolution in myelofibrosis (Sung-Eun Lee, Korea)	Extranodal NK/T cell lymphoma: The immunogenic tumor (Won Seog Kim, Korea)	Germline predisposition to hematologic malignancies (Sang Mee Hwang, Korea)
10:15-10:30	Break			
10:30-11:15	**PAP01** Plenary Abstract Presentation			
11:15-11:45	Award Ceremony & Closing			

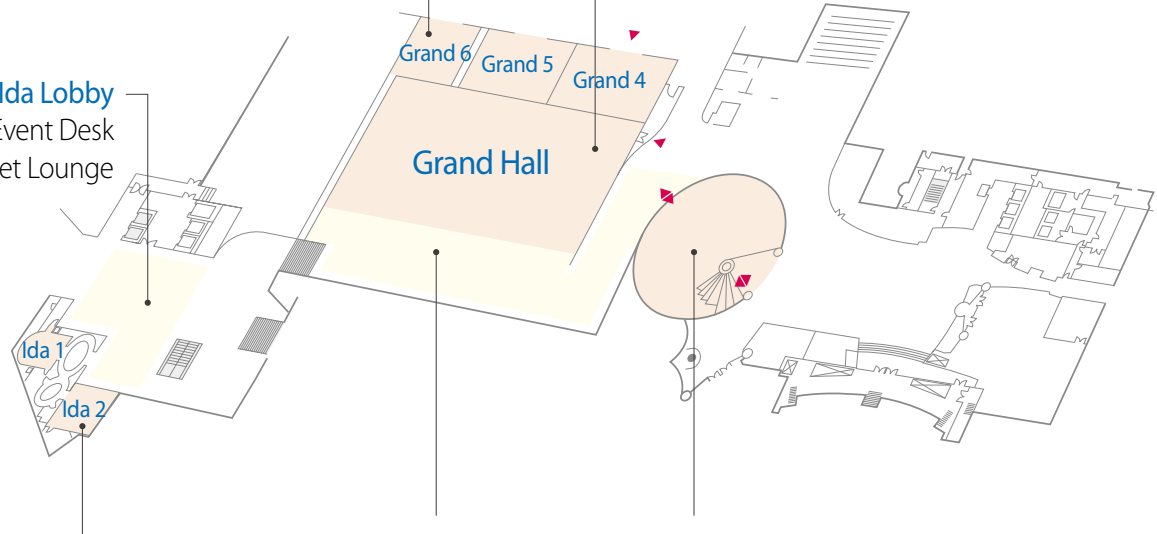
FLOOR PLAN

1F



Walker Hall
- Exhibition (Bronze)
- Posters
- Coffee Break

B1



Grand 4-6
- Small Meetings

Room 3
- Scientific Session

Ida Lobby
- Stamp Event Desk
- Internet Lounge

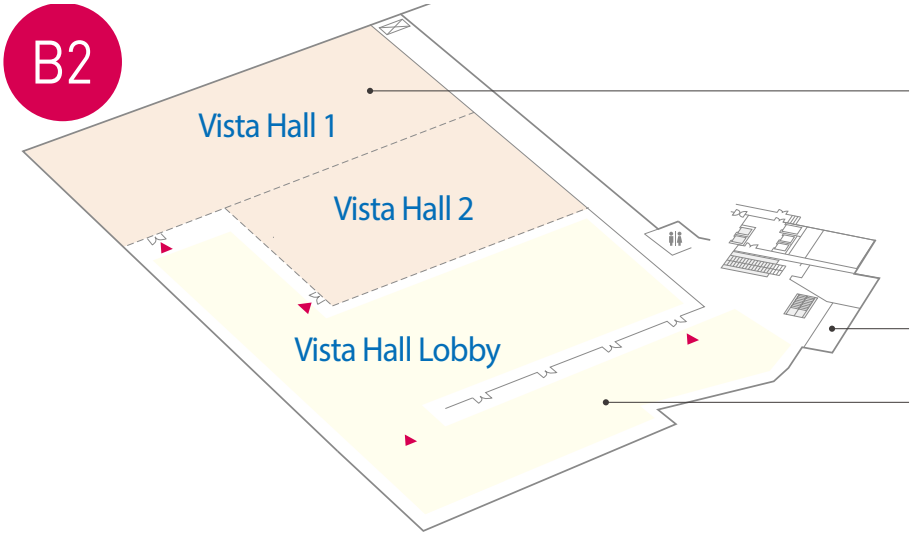
Ida 2
- Preview Room

Grand Hall Lobby
- Exhibition (Gold & Silver)
- Coffee Break

KSH Event Hall
- KSH Event Desk
- Photo Zone
- Coffee & Tea

FLOOR PLAN

B2

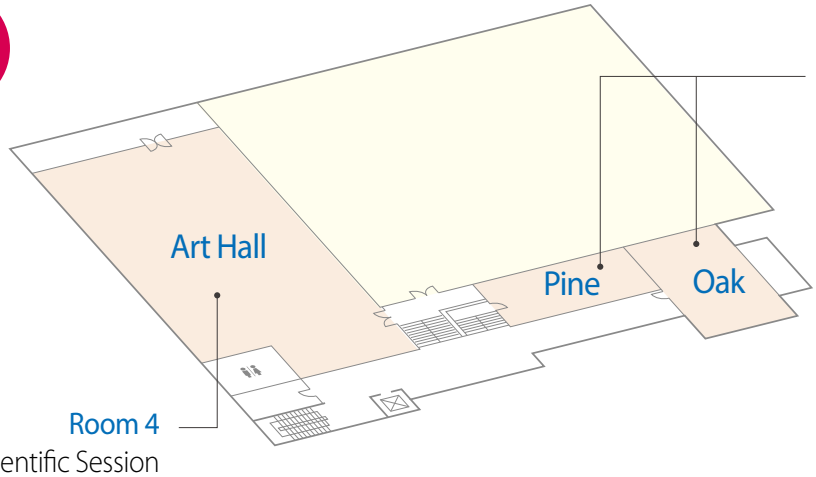


Room 1/Room 2
- Plenary Session
- Scientific Session
- Opening & Closing
- Gala Dinner (March 29)

ICKSH Secretariat

Vista Hall Lobby
- Exhibition (Diamond & Platinum)
- Coffee Break
- Registration
- Kit & Cloak Desk

4F



Pine/Oak
- Small Meetings

Room 4
- Scientific Session

GENERAL INFORMATION

REGISTRATION

All participants are required to visit the Self-registration Kiosk to pick up their badge. Scan the QR code and staff will assist you to receive your name tag. Badges must be worn during all scientific sessions and social programs.

>> Location: Vista Lobby (B2)

>> Operation Hours: March 28 (Thu) 07:00 – 18:00
March 29 (Fri) 07:00 – 18:00
March 30 (Sat) 07:00 – 12:00

>> On-Site Registration Fees

Category	Domestic	Overseas
Non-Member	KRW 300,000	USD 200
KSH Member	KRW 200,000	
Fellow/Nurse/Researcher	KRW 100,000	USD 100
Student/Resident	KRW 50,000	

+ Registration fees include: Participation in all scientific sessions, exhibitions, lunch box during satellite symposiums, coffee breaks, conference kit, welcome reception and gala dinner.

+ Conference kits will be distributed at the Kit Desk (B2).
Please scan your name badge to receive the kit.
Each kit includes a congress bag, program book, abstract book.

GENERAL INFORMATION

LUNCH AND COFFEE BREAKS

+ Satellite Symposia

Before the session begins, please pick up a lunch box at the entrance of the session room. Lunch boxes will be provided only to those who tag their name badges.

Satellite Symposium	SY01	SY02	SY03	SY04
Date/ Time	March 28 (Thu), 12:15-13:05			
Place	Room 1	Room 2	Room 3	Room 4
Sponsored by	janssen | PHARMACEUTICAL COMPANIES OF Johnson&Johnson	AstraZeneca	astellas	Roche
Satellite Symposium	**SY05**	**SY06**	**SY07**	**SY08**
Date/ Time	March 29 (Fri), 12:15-13:05			
Place	Room 1	Room 2	Room 3	Room 4
Sponsored by	Bristol Myers Squibb	KYOWA KIRIN	NOVARTIS	HANDOK

+ Coffee Breaks

Coffee and tea will be served during break times on each floor. Barista coffee and tea will be provided in the Grand Hall Lobby (KSH Event Hall, B1).

CERTIFICATES OF ATTENDANCE AND PRESENTATION

Your certificate of attendance can be downloaded from the ICKSH 2024 website after the conference.
The certificate of presentation can be issued after the conference by email. Please send a request to the secretariat (icksh@icksh.org) with your name, affiliation, and presentation code.

GENERAL INFORMATION

CME CREDIT INFORMATION (KOREAN PARTICIPANTS ONLY)

일자별 최대 취득가능 평점 안내

구분	3월 28일 (목)	3월 29일 (금)	3월 30일 (토)
대한의사협회 평점	6점	6점	2점
내과 전공의 평점	2점		

* 내과 전공의 평점은 대회 기간 동안 3시간 이상 출석해야 2평점 인정됩니다.

출결 체크

등록대에서 수령한 명찰에 인쇄된 바코드를 리더기에 태그해 주시기 바랍니다.
(매일 대회장 입장 시 1회, 퇴장 시 1회 (총 2회) 태그 필수)

부분 평점 인정 기준 안내

체류 시간	평점	체류 시간	평점
1시간 미만	평점 인정 불가	4시간 이상 - 5시간 미만	4평점
1시간 이상 - 2시간 미만	1평점	5시간 이상 - 6시간 미만	5평점
2시간 이상 - 3시간 미만	2평점	6시간 이상	6평점
3시간 이상 - 4시간 미만	3평점		

PARKING

Free parking is available for all attendees. Kindly state the name of the conference 'ICKSH 2024' when you exit.

SPEAKER AND CHAIR INFORMATION

PREVIEW ROOM

Please submit your file to the Preview Room no later than 2 hours before your scheduled session. Our staff will help you to upload the presentation file to the server. Afterwards, you can check to see that your files function correctly in the given environment.

>> Location: IDA 2 (B1)

>> Operation Hours: March 28 (Thu) 07:00 – 18:00
March 29 (Fri) 07:00 – 18:00
March 30 (Sat) 07:00 – 12:00

+ The Preview Room is only intended for submitting and checking files (No personal or other internet use).
+ It is not recommended that you connect your personal laptop directly to the podium because it may cause errors.
+ If you need to connect your personal laptop due to unavoidable circumstances, please notify the staff in the Preview Room in advance (You must have a USB-C type adapter for MacBooks).

INVITED/ORAL PRESENTATION

Speakers should be present in the session room 10 minutes prior to the session time. Please keep the allocated time to avoid time delays.

POSTER PRESENTATION

Poster presentation speakers should be present in front of their posters at the designated time. After onsite reviews, the scientific committee will select the Best Posters and winners should attend to receive the awards at the Closing Ceremony on March 30 (Sat). Snacks and drinks will be provided during the Poster Session.

>> Date & Time: March 28 (Thu) 13:05 – 13:50
March 29 (Fri) 11:15 – 12:00

>> Location: Walker Hall (1F)

CHAIR GUIDELINES

+ Chairs are kindly requested to be in the room at least 10 minutes before the session.
+ Please run the session as scheduled for smooth progress. (Please assist the presenter in completing the presentation within the allotted time frame.)

+ If a speaker is absent or late, our staff in the session room will notify the chairs in advance.

SOCIAL PROGRAM

ICKSH 2024 OPENING REMARK

We warmly welcome our participants from all around the world.

>> Date & Time: March 28 (Thu), 09:00

>> Location: Room 1+2 (Vista Hall, B2)

WELCOME RECEPTION

We would be delighted to have you at the Welcome Reception. Join us for a drink and have some fun!

>> Date & Time: March 28 (Thu), 18:30-19:30

>> Location: Aston House

GALA DINNER

Join us for an unforgettable evening of excellent cuisine, exciting performances, and networking opportunities. Stop in early and enjoy the cocktail reception in the lobby before the Gala Dinner!

>> Date & Time: March 29 (Fri), 18:30-20:00 (Cocktail Reception from 17:50)

>> Location: Room 1+2 (Vista Hall, B2)

AWARD CEREMONY & CLOSING

We will wrap up ICKSH 2024 by congratulating our award winners.

>> Date & Time: March 30 (Sat), 11:15-11:45

>> Location: Room 1+2 (Vista Hall, B2)

EVENTS

EARLY-BIRD EVENT

Gifts will be given daily to up to 100 session participants on a first-come, first-served basis.

>> Date & Time: March 28(Thu) – March 30(Sat)

>> Location: Each Session Room

BOOTH STAMP EVENT

If you visit exhibition booths and complete the stamp sheet, gifts will be given.

>> Date & Time: March 28(Thu) – March 30(Sat)

>> Location: IDA Hall Lobby (B1)

KSH INSTAGRAM FOLLOW EVENT (KOREAN PARTICIPANTS ONLY)

Visit Instagram, "Like" and Follow the KSH, and Win Gifts!

>> Date & Time: March 28(Thu) – March 30(Sat)

>> Location: Grand Hall Lobby (KSH Event Hall, B1)

ATTENDEES SURVEY

Please submit the survey every day after the conference ends. You can get a coffee gift card.

>> Date & Time: March 28(Thu) – March 30(Sat)

>> Location: IDA Hall Lobby (B1)

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EXHIBITION

B2

VISTA HALL

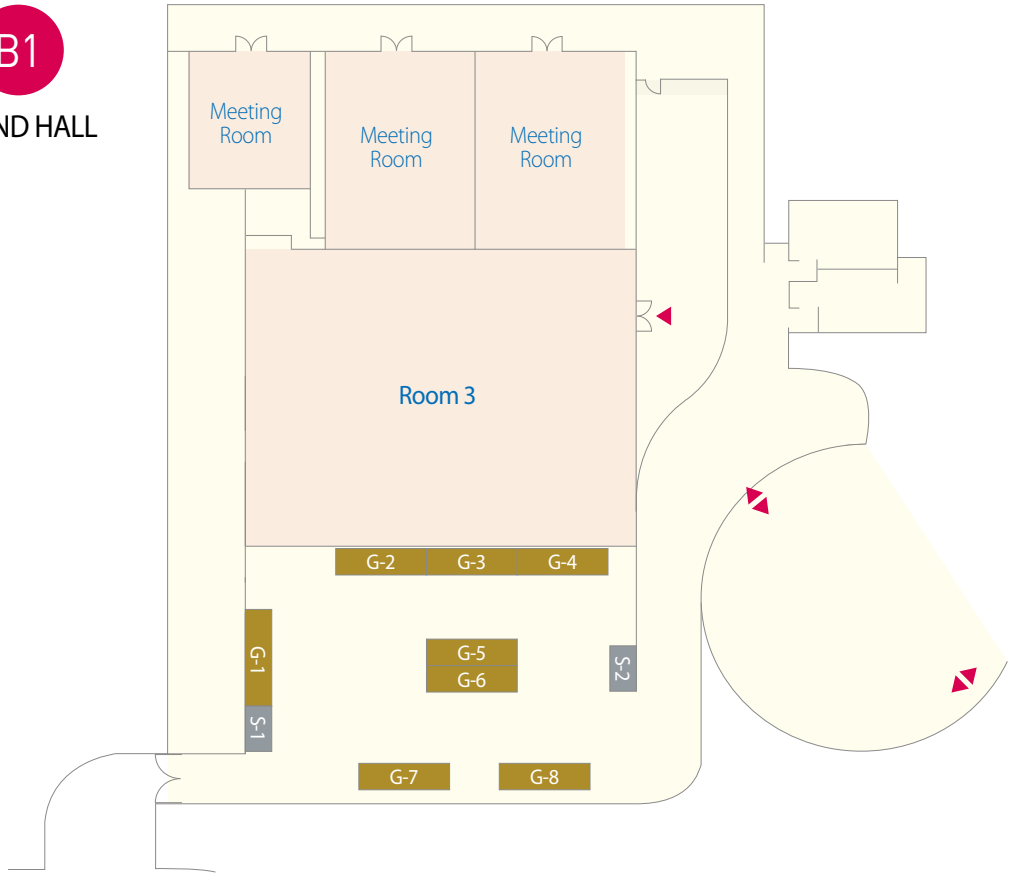
No.	Company Name
D-1	BMS Korea
D-2	Roche Korea
D-3	Handok Inc.
D-4	AstraZeneca Korea
D-5	JANSSEN KOREA
D-6	KYOWA KIRIN KOREA
D-7	Novartis Korea
D-8	Astellas Korea

No.	Company Name
P-1	GC Pharma
P-2	Takeda Korea

EXHIBITION

B1

GRAND HALL



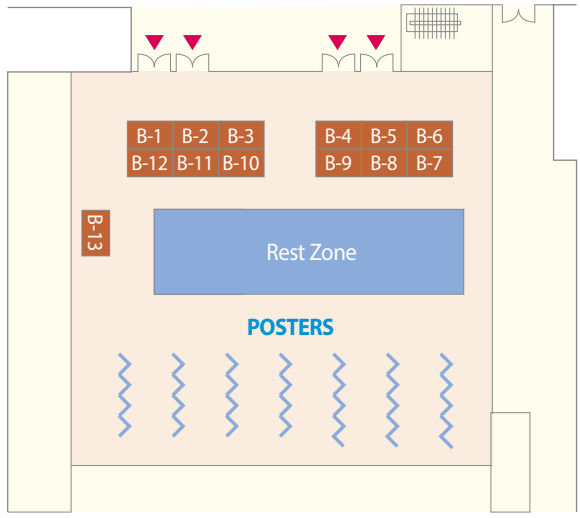
No.	Company Name
G-1	MSD Korea
G-2	YUHAN
G-3	Pfizer Korea
G-4	Otsuka
G-5	Sanofi-Aventis
G-6	abbVie
G-7	AMGEN
G-8	Celltrionpharm

No.	Company Name
S-1	QuantaMatrix
S-2	Samsung bioepis

EXHIBITION

1F

WALKER HALL



No.	Company Name
B-1	IL-YANG PHARM
B-2	roche - diagnostics
B-3	Sysmex Korea
B-4	BeiGene Korea
B-5, B-6	JW PHARMACEUTICAL
B-7	Antengene Medicine Co.,Ltd.

No.	Company Name
B-8	Boryung Pharmaceutical Co.,Ltd
B-9	RECORDATI KOREA
B-10	PharmaEssentia Korea
B-11	Samyang Holdings Corp.
B-12	Dong-A ST
B-13	SK Plasma

KEY SPEAKERS

MARCH 28 (Thu)

[PL01] Plenary Lecture 01
10:30 - 11:15 | Room 1+2

Somatic mutations and clonal dynamics in human blood cells

Peter J. Campbell
Wellcome Sanger Institute, UK

[PS01] Presidential Symposium
11:15 - 12:00 | Room 1+2

Lab-on-a-chip in hematology

Chong H. Ahn
University of Cincinnati, USA

MARCH 29 (Fri)

[PL02] Plenary Lecture 02
10:30 - 11:15 | Room 1+2

How to win: Competitive strategies in the hematopoietic stem cell niche

Margaret Goodell
Baylor College of Medicine, USA

ICKSH 2024

2024 KOREAN SOCIETY OF HEMATOLOGY
INTERNATIONAL CONFERENCE
& KSH 65th ANNUAL MEETING

DAILY PROGRAM

March 28 (Thursday)

March 29 (Friday)

March 30 (Saturday)

DAILY PROGRAM Thursday, March 28

08:50-09:00 **Opening Remark** — Room 1 Vista Hall 1

09:00-10:15 **[JS01] Asian Hematology Session I - EBV-associated lymphoid malignancy** — Room 1 Vista Hall 1

Chairs
Ki Seong Eom (College of Medicine, The Catholic University of Korea, Korea)
Dok Hyun Yoon (University of Ulsan College of Medicine, Korea)

JS01-1 Prospective studies for NK/T-cell lymphoma in Asia
Seok Jin Kim (Sungkyunkwan University School of Medicine, Korea)

JS01-2 Chronic active EBV disease: Our challenge to elucidate the pathogenesis
Ayako Arai (St. Marianna University School of Medicine, Japan)

JS01-3 NK lymphoma genomics
Weili Zhao (Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, China)

Discussion

09:00-10:15 **[ES01] Histiocytic neoplasm** — Room 2 Vista Hall 2

Chairs
Nack-Gyun Chung (College of Medicine, The Catholic University of Korea, Korea)
Hyoung Soo Choi (Seoul National University College of Medicine, Korea)

ES01-1 Histiocytic neoplasm in pediatrics
Kyung-Nam Koh (University of Ulsan College of Medicine, Korea)

ES01-2 Histiocytic sarcoma
Sung Nam Lim (Inje University College of Medicine, Korea)

ES01-3 Pathologic characteristics of histiocytic and dendritic cell neoplasms
Sun Och Yoon (Yonsei University College of Medicine, Korea)

09:00-10:15 **[SS01] Exploring the utilization of innovative technologies** — Room 3 Grand Hall 1

Chairs
Young Kyung Lee (Hallym University College of Medicine, Korea)
Yoon Hwan Chang (Seoul National University College of Medicine, Korea)

SS01-1 Elucidating the 3D chromatin landscape of pediatric B-cell acute lymphoblastic leukemia using Micro-C
Kajsa Paulsson (Lund University, Sweden)

SS01-2 Integrated RNA and protein profiling of B-cell acute lymphoblastic leukemia at single-cell level
Sungyoung Choi (Hanyang University College of Medicine, Korea)

SS01-3 Leveraging dysregulated signaling networks for therapeutic benefit in myeloproliferative neoplasm
Stephen T. Oh (Washington University School of Medicine, USA)

09:00-10:15 **[SS02] The unmet needs in CML - Overcoming the obstacles of the road to cure** — Room 4 Art Hall

Chairs
Chul Won Jung (Sungkyunkwan University School of Medicine, Korea)
Hawk Kim (Gachon University College of Medicine, Korea)

DAILY PROGRAM Thursday, March 28

SS02-1 **Molecular mechanism of primary TKI resistance in CML**
Jerald Radich (Fred Hutchinson Cancer Center, USA)

SS02-2 **Targeting leukemic stem cells in CML**
Mhairi Copland (University of Glasgow, UK)

SS02-3 **The role of NGS to detect TKI resistance**
Saeam Shin (Yonsei University College of Medicine, Korea)

10:15-10:30 **Break**

10:30-11:15 **[PL01] Plenary Lecture 01** — Room 1+2, Vista Hall 1+2

Chair Seoklae Chae (Dongguk University College of Medicine, Korea)

Somatic mutations and clonal dynamics in human blood cells
Peter J. Campbell (Wellcome Sanger Institute, UK)

11:15-12:00 **[PS01] Presidential Symposium** — Room 1+2, Vista Hall 1+2

Chair Seongsoo Jang (University of Ulsan College of Medicine, Korea)

Lab-on-a-chip in hematology
Chong H. Ahn (University of Cincinnati, USA)

12:00-12:15 **Break**

12:15-13:05 **[SY01] Janssen** — Room 1, Vista Hall 1

Chair Kihyun Kim (Sungkyunkwan University School of Medicine, Korea)

Treatment of newly diagnosed multiple myeloma: Focus on daratumumab combination
Elena Zamagni (IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy)

12:15-13:05 **[SY02] Astrazeneca** — Room 2, Vista Hall 2

Chair Jun Ho Jang (Sungkyunkwan University School of Medicine, Korea)

The ultimate value of C5 inhibitors in the evolving treatment landscape of PNH
Sung-Hyun Kim (Dong-A University College of Medicine, Korea)

12:15-13:05 **[SY03] Astellas** — Room 3, Grand Hall 1

Chair Hee-Je Kim (College of Medicine, The Catholic University of Korea, Korea)

Treatment strategies for elderly AML with FLT3-mutation, entering the era of FLT3 Inhibitors
Naoko Hosono (University of Fukui, Japan)

DAILY PROGRAM Thursday, March 28

12:15-13:05 **[SY04] Roche** — Room 4, Art Hall

Chair: Sung-Soo Yoon (Seoul National University College of Medicine, Korea)

Advances in the treatment paradigm with bispecific antibodies
Wendy Osborne (Newcastle University, UK)

13:05-13:50 **Poster Viewing 1** — Walker Hall

13:50-15:20 **[OP01] Acute leukemia - 1** — Room 1, Vista Hall 1

Chairs: Dae-Young Kim (Ewha Womans University College of Medicine, Korea)
Saeam Shin (Yonsei University College of Medicine, Korea)

OP01-1 The transcriptomic profiles of NPM1 mutated acute myeloid leukemia reveal distinct subtypes characterized by varying clinical outcomes
Joon Ho Moon (Kyungpook National University Hospital, Korea)

OP01-2 Leukemic stem cells in acute myeloid leukemia further refine treatment outcomes in ELN molecular risk groups
Ritu Gupta (All India Institute of Medical Sciences, India)

OP01-3 Azacitidine combined with novel flavonoid derivative GL-V9 demonstrated synergistic anti-leukemia effect in acute myeloid leukemia by targeting DDIT4/mTOR signaling
Jun Li (Institute of Hematology Southeast University, China)

OP01-4 Exploring the genetic landscape of B-ALL: Upregulation of cell adhesion pathway in the high risk adult as compared to pediatric B-ALL patients
Preity Sharma (All India Institute of Medical Sciences, India)

OP01-5 CD371 expression in B-lymphoblastic leukemia and its correlation with recurrent genetic abnormalities
Sweta Rajpal (ACTREC, Tata Memorial Centre, India)

13:50-15:20 **[OP02] Lymphoma** — Room 2, Vista Hall 2

Chairs: Ho Sup Lee (Kosin University College of Medicine, Korea)
Youngwoo Jeon (College of Medicine, The Catholic University of Korea, Korea)

OP02-1 Treatment patterns in patients with mantle cell lymphoma: Updated report of the Asia-Pacific multinational retrospective registry study
Dok Hyun Yoon (Asan Medical Center, Korea)

OP02-2 Pooled safety analysis of zanubrutinib monotherapy in Asian patients with B-cell malignancies
Won Seog Kim (Sungkyunkwan University School of Medicine, Korea)

OP02-3 Prognostic value of end-of-treatment [18F]FDG PET/CT in newly diagnosed patients with primary central nervous system lymphoma who respond to first-line treatment with high-dose methotrexate-based regimen
Hyungwoo Cho (University of Ulsan College of Medicine, Korea)

OP02-4 Efficacy of dexamethasone, L-asparaginase, ifosfamide, carboplatin, and etoposide in patients with relapsed/refractory peripheral T cell lymphoma
Tong Yoon Kim (College of Medicine, The Catholic University of Korea, Korea)

OP02-5 Characteristics and outcome of post-transplant lymphoproliferative disease in children treated with low-dose chemotherapy over 20 years in a single hospital
Hyery Kim (University of Ulsan College of Medicine, Korea)

DAILY PROGRAM Thursday, March 28

13:50-15:20 **[OP03] Hematopoietic stem cell transplantation & Cellular therapy** Room 3 Grand Hall 1

Chairs Sung-Hyun Kim (Dong-A University College of Medicine, Korea)
Jieun Uhm (Hanyang University College of Medicine, Korea)

OP03-1 Reduced GVHD incidence with post-transplantation cyclophosphamide in higher-risk myelodysplastic syndrome
Jin-Hee Han (University of Ulsan College of Medicine, Korea)

OP03-2 Effect of HLA mismatched on the prognosis of cord blood transplantation for childhood leukemia
Lu Liu (Children's Hospital of Soochow University, China)

OP03-3 Interleukin 6 polymorphisms 174 and 597: Impact on graft-versus-host disease after allogeneic hematopoietic stem cell transplantation in childhood
Bernd Gruhn (Jena University Hospital, Germany)

OP03-4 Reduced 8-Gray versus standard 13.2-gray total dose of total body irradiation based myeloablative conditioning for allogeneic hematopoietic cell transplantation in pediatric acute lymphoblastic leukemia
Jae Won Yoo (College of Medicine, The Catholic University of Korea, Korea)

OP03-5 High plasmacytoid dendritic cell dose infusion correlates with better plasmacytoid dendritic cell reconstitution and lower incidence of viral infection after transplantation: A single-center study
Di Yao (Children's Hospital of Soochow University, China)

OP03-6 BCMA-specific induced pluripotent stem cells and their specific regulatory pathways to differentiate into rejuvenated antigen-specific memory CD8+ T cells
Jooeun Bae (Dana Farber Cancer Institute, USA)

13:50-15:20 **[OP04] Laboratory hematology** Room 4 Art Hall

Chairs Sun-Young Kong (National Cancer Center, Korea)
Hyun-Young kim (Sungkyunkwan University School of Medicine, Korea)

OP04-1 Dynamic thrombocytopenia has a negative impact with distinctive genetic and immunologic features in patients with myelofibrosis
Tong Yoon Kim (College of Medicine, The Catholic University of Korea, Korea)

OP04-2 Ribosomal protein S4X functions as a novel suppressor for SCF complex-mediated ubiquitination of myeloid cell leukemia1 and beta-catenin
Satsuki Ryu (Tokushima Bunri University, Japan)

OP04-3 Targeted-NGS across the beta-globin gene cluster identifies multiple linkage disequilibrium patterns in north Indian non-transfusion dependent beta-thalassemia patients
Prashant Sharma (Research Block A, Postgraduate Institute of Medical Education and Research, India)

OP04-4 Novel insight into the role of HTLV-1 unspiced form of bZIP factor: Specific interaction with HS-1 associated protein X-1, preventing caspase9-dependent apoptotic pathway
Yuka Tanaka (Tokushima Bunri University, Japan)

OP04-5 Immune function of chimeric antigen receptor T cells quantitatively assessed via molecular imaging flow cytometry
Hiroshi Yasui (The Institute of Medical Science, The University of Tokyo, Japan)

15:20-15:30 Break

DAILY PROGRAM Thursday, March 28

15:30-16:45 **[JS02] EHA-KSH Joint Symposium - Multiple myeloma** — Room 1 Vista Hall 1

Chairs Jin Seok Kim (Yonsei University College of Medicine, Korea)
Meral Beksac (Ankara Liv Hospital, Türkiye)

JS02-1 Dynamic assessment of risk in multiple myeloma
Meral Beksac (Ankara Liv Hospital, Türkiye)

JS02-2 PET/CT for risk stratification in multiple myeloma
Joon Ho Moon (Kyungpook National University School of Medicine, Korea)

JS02-3 Bone marrow inflammation in multiple myeloma
Tom Cupedo (Erasmus MC Cancer Center, The Netherlands)

JS02-4 Single-cell analysis in multiple myeloma
Sung-Soo Park (College of Medicine, The Catholic University of Korea, Korea)

Discussion

15:30-16:45 **[SS03] Wise perspective on new approaches in hemophilia** — Room 2 Vista Hall 2

Chairs Eun Jin Choi (Daegu Catholic University School of Medicine, Korea)
Young Shil Park (Kyung Hee University College of Medicine, Korea)

SS03-1 Approaches to treat people with hemophilia: What's new and what's not?
Leonard A. Valentino (Rush University, USA)

SS03-2 Prospects and challenges of gene therapy for hemophilia
Alok Srivastava (Christian Medical College, India)

SS03-3 Exploring personalized tailored hemophilia treatment: Tailoring treatment to individual needs
Jeong A Park (Inha University College of Medicine, Korea)

15:30-16:45 **[SS04] For the next generation CAR-T cells** — Room 3 Grand Hall 1

Chairs Seok-Goo Cho (College of Medicine, The Catholic University of Korea, Korea)
Je-Jung Lee (Chonnam National University Medical School, Korea)

SS04-1 CD7 CAR-T therapy for treating hematological maligancies
Peihua Lu (Lu Daopei Hospital, China)

SS04-2 Development of a novel anti-CD19 CAR-T cells in B cell lymphoma
Dok Hyun Yoon (University of Ulsan College of Medicine, Korea)

SS04-3 CAR-T cells for treatment of T cell malignancies
Paul M. Maciocia (Cancer Research UK, UK)

15:30-16:45 **[SS05] Deepened understanding of AML using multi-omics approaches** — Room 4 Art Hall

Chairs Hyeoung-Joon Kim (Chonnam National University Medical School, Korea)
Myungshin Kim (College of Medicine, The Catholic University of Korea, Korea)

SS05-1 Navigating cancer complexities via single-cell omics and AI
Manoj Bhasin (Emory University, USA)

DAILY PROGRAM Thursday, March 28

SS05-2 Targeting the developmental heterogeneity of human acute myeloid leukemia
Shanshan Pei (Zhejiang University, China)

SS05-3 Mutational profile in Korean AML patients
Jae-Sook Ahn (Chonnam National University Medical School, Korea)

16:45-16:55 Break

16:55-18:10 **[SS06] Insights into lymphoma pathobiology** Room 1 Vista Hall 1

Chairs Gyeong-Sin Park (College of Medicine, The Catholic University of Korea, Korea)
Seok Jin Kim (Sungkyunkwan University School of Medicine, Korea)

SS06-1 Germinal center in the genesis of lymphomas
Laura Pasqualucci (Columbia University, USA)

SS06-2 Genomics of follicular lymphoma: Clinical implications?
Robert Kridel (University Health Network, Canada)

SS06-3 Distinct and overlapping features of nodal peripheral T-cell lymphomas exhibiting a follicular helper T-cell phenotype: A multicenter study emphasizing the clinicopathological significance of follicular helper T-cell marker expression
Jin Ho Paik (Seoul National University College of Medicine, Korea)

16:55-18:10 **[SS07] Profound understanding of diagnosis and therapy in MDS** Room 2 Vista Hall 2

Chairs Yoo Jin Kim (College of Medicine, The Catholic University of Korea, Korea)
Jun Ho Jang (Sungkyunkwan University School of Medicine, Korea)

SS07-1 Molecular alterations and clinical implications in MDS
Yasushi Miyazaki (Nagasaki University, Japan)

SS07-2 Recent advances and future therapeutic strategies in MDS
Guillermo Garcia-Manero (The University of Texas MD Anderson Cancer Center, USA)

SS07-3 Current diagnostic challenges in MDS
In-Suk Kim (Pusan National University School of Medicine, Korea)

16:55-18:10 **[SS08] Leukemogenesis in children and adults** Room 3 Grand Hall 1

Chairs Kyung Ha Ryu (Ewha Womans University College of Medicine, Korea)
Hoon Kook (Chonnam National University Medical School, Korea)

SS08-1 RUNX1-FPDMM natural history study at NIH
Pu Paul Liu (National Institutes of Health, USA)

SS08-2 Clinical impact of DDX41 mutations in myeloid neoplasms
Talha Badar (Mayo Clinic, USA)

SS08-3 Discovery of new regulators in hematopoietic stem cells and malignancies
Dongjun Lee (Pusan National University School of Medicine, Korea)

DAILY PROGRAM Thursday, March 28

16:55-18:10 **[ES02] Basics for trainees (Kor)** — Room 4, Art Hall

Chairs: Inho Kim (Seoul National University College of Medicine, Korea)
Jaewoo Song (Yonsei University College of Medicine, Korea)

ES02-1 Overview of lymphoma classification
Tae-Jung Kim (College of Medicine, The Catholic University of Korea, Korea)

ES02-2 What's new in AML classification
Hee Sue Park (Chungbuk National University College of Medicine, Korea)

ES02-3 Recent update of MDS classification
Miyoung Kim (University of Ulsan College of Medicine, Korea)

18:10-18:30 Break

18:30-19:30 **Welcome Reception** — Aston House

DAILY PROGRAM Friday, March 29

09:00-10:15 **[JS03] ASH-KSH Joint Symposium - Ped-ALL** — Room 1, Vista Hall 1

Chairs: Keon Hee Yoo (Sungkyunkwan University School of Medicine, Korea); Wendy Stock (University of Chicago, USA)

JS03-1 Pediatric and AYA ALL: Lessons learned from Childern's Onclogy Group clinical trials
Sarah K. Tasian (The Children's Hospital of Philadelphia, USA)

JS03-2 Multicenter trials investigating childhood acute lymphoblastic leukemia in South Korea
Hyery Kim (University of Ulsan College of Medicine, Korea)

JS03-3 Dissecting the developmental origins of acute leukemia
Charles G. Mullighan (St. Jude Children's Research Hospital, USA)

JS03-4 Unveiling precision medicine: RNA and DNA sequencing in targeted therapy for Korean pediatric leukemia
Myungshin Kim (College of Medicine, The Catholic University of Korea, Korea)

Discussion

09:00-10:15 **[ES03] Leaps and hurdles in transfusion medicine (Kor)** — Room 2, Vista Hall 2

Chairs: Duck Cho (Sungkyunkwan University School of Medicine, Korea); Jihyang Lim (College of Medicine, The Catholic University of Korea, Korea)

ES03-1 Comprehensive overview of cell-based artificial platelet production
Seung Yeob Lee (Jeonbuk National University Medical School, Korea)

ES03-2 Anti-CD38 and anti-CD47 delay timely transfusion
Hyungsuk Kim (Seoul National University College of Medicine, Korea)

ES03-3 Reappraisal of transfusion-transmitted infections
Dae-Hyun Ko (University of Ulsan College of Medicine, Korea)

09:00-10:15 **[SS09] Clonal hematopoiesis: What should we know?** — Room 3, Grand Hall 1

Chairs: Myung Geun Shin (Chonnam National University Medical School, Korea); Hyun Kyung Kim (Seoul National University College of Medicine, Korea)

SS09-1 Clonal hematopoiesis and aging
Siddhartha Jaiswal (Stanford University School of Medicine, USA)

SS09-2 Clonal hematopoiesis: Implications for cell therapy
Adam S. Sperling (Dana-Farber Cancer Institute, USA)

SS09-3 Clonal hematopoiesis and metabolic diseases
Sung Hee Choi (Seoul National University College of Medicine, Korea)

09:00-10:15 **[SS10] Predictive biomarkers in multiple myeloma** — Room 4, Art Hall

Chairs: Chang-Ki Min (College of Medicine, The Catholic University of Korea, Korea); Jeong Yeal Ahn (Gachon University College of Medicine, Korea)

SS10-1 The impact of immune profiling of T-cell and plasma cells on non-cellular immune therapy in myeloma
Nizar Jacques Bahlis (University of Calgary, Canada)

DAILY PROGRAM Friday, March 29

SS10-2 **Single-cell techniques to characterize immune microenvironment in MM**
Niels Weinhold (Heidelberg University, Germany)

SS10-3 **The power of ONE: Immunology in the age of single cell genomics**
Ido Amit (Weizmann Institute of Science, Israel)

10:15-10:30 **Break**

10:30-11:15 **[PL02] Plenary Lecture 02** — Room 1+2, Vista Hall 1+2

Chair Chuhl Joo Lyu (Yonsei University College of Medicine, Korea)

How to win: Competitive strategies in the hematopoietic stem cell niche
Margaret Goodell (Baylor College of Medicine, USA)

11:15-12:00 **Poster Viewing 2** — Walker Hall

12:00-12:15 **Break**

12:15-13:05 **[SY05] BMS** — Bristol Myers Squibb™ — Room 1, Vista Hall 1

Chair Je-Hwan Lee (University of Ulsan College of Medicine, Korea)

Continued hope with ONUREG - A new maintenance therapy to treat AML
Esther Oliva (Grande Ospedale Metropolitano Bianchi Melacrino Morelli, Italy)

12:15-13:05 **[SY06] Kyowa Kirin** — KYOWA KIRIN — Room 2, Vista Hall 2

Chair Won Seog Kim (Sungkyunkwan University School of Medicine, Korea)

Mogamulizumab: A new era in MF/SS management - Clinical evidence and practical consideration
Francine Foss (Yale University School of Medicine, USA)

12:15-13:05 **[SY07] Novartis** — NOVARTIS — Room 3, Grand Hall 1

Chair Dong-Wook Kim (Eulji University School of Medicine, Korea)

TKI treatment pattern and new therapy of CML
Qian Jiang (Peking University People's Hospital, China)

12:15-13:05 **[SY08] Handok** — HANDOK — Room 4, Art Hall

Chair Hyeon-Seok Eom (National Cancer Center, Korea)

The optimal treatment strategy for transplant-ineligible relapsed/refractory DLBCL
Kwai Han Yoo (Gachon University College of Medicine, Korea)

DAILY PROGRAM Friday, March 29

13:05-13:20 Break

13:20-14:50 **[OP5] Acute leukemia - 2** Room 1 Vista Hall 1

Chairs Jeong-Ok Lee (Seoul National University College of Medicine, Korea)
Sung Han Kang (University of Ulsan College of Medicine, Korea)

OP05-1 Efficacy and safety of low-dose venetoclax combined with voriconazole in patients with acute myeloid leukemia unfit for intensive chemotherapy
Meng Danchen (The First Affiliated Hospital of Anhui Medical University, China)

OP05-2 The microRNA miR-222 is overexpressed and regulates proliferation, differentiation and apoptosis pathways in paediatric acute myeloid leukemia
Christine Wilson (All India Institute of Medical Sciences, India)

OP05-3 Genetic characteristics and venetoclax efficacy in acute myeloid leukemia
Daehun Kwag (College of Medicine, The Catholic University of Korea, Korea)

OP05-4 Adverse clinical impact of RB1 gene deletions alone and with concurrent IKZF1 gene deletions in pediatric B-cell acute lymphoblastic leukemia
Gadha K Leons (All India Institute of Medical Sciences, India)

OP05-5 Prognostic impact of concurrent genetic deletions in IKZF1 and CDKN2 in adult patients with philadelphia chromosome-positive acute lymphoblastic leukemia
So Yeon Park (College of Medicine, The Catholic University of Korea, Korea)

OP05-6 Molecular map of T-lineage acute lymphoblastic leukemia: Clinical implications
Anita Chopra (All India Institute of Medical Sciences, India)

13:20-14:50 **[OP6] Multiple myeloma** Room 2 Vista Hall 2

Chairs Yeung-Chul Mun (Ewha Womans University College of Medicine, Korea)
Sung-Hoon Jung (Chonnam National University Medical School, Korea)

OP06-1 Carfilzomib, lenalidomide, dexamethasone in the real-world Asian relapsed and/or refractory multiple myeloma patients - KMM2201 study
Ji Hyun Lee (Dong-A University College of Medicine, Korea)

OP06-2 Real-world effectiveness of Ixazomib, lenalidomide, and dexamethasone (IRd) in Asian patients with relapsed/refractory multiple myeloma (RRMM)
Soo Chin Ng (Subang Jaya Medical Centre, Malaysia)

OP06-3 Efficacy and safety of carfilzomib, lenalidomide, and dexamethasone versus Ixazomib, lenalidomide, and dexamethasone in real world patients with relapsed/refractory multiple myeloma: KMM2004 study
Do Young Kim (Pusan National University School of Medicine, Korea)

OP06-4 Bortezomib maintenance therapy in transplant-ineligible newly diagnosed multiple myeloma have major response to induction chemotherapy (KMM 174)
Jung Yeon Lee (College of Medicine, The Catholic University of Korea, Korea)

OP06-5 Impact of pretransplant measurable residual disease(MRD) using multiparametric flow cytometry(mFCM) and imaging (PET-CT scan) before autologous stem cell transplantation(ASCT) in multiple myeloma : Insights from tertiary centre In India
Rudra Nrayan Swain (Post Graduate Institute of Medical Education and Research, India)

OP06-6 The efficacy of salvage second autologous hematopoietic stem cell transplantation in Korean patients with relapsed/refractory multiple myeloma in novel agent era: the KMM2301 study
Jongheon Jung (National Cancer Center, Korea)

DAILY PROGRAM Friday, March 29

13:20-14:50 **[OP7] Myeloid neoplasm & Bone marrow failure** Room 3 Grand Hall 1

Chairs Seong Hyun Jeong (Ajou University School of Medicine, Korea)
Ji Hyun Kwon (Chungbuk National University College of Medicine, Korea)

OP07-1 Efficacy & safety of momelotinib vs danazol in JAKi-experienced patients with myelofibrosis & anemia: Asian subgroup analysis of the MOMENTUM trial
Sung-Soo Yoon (Seoul National University College of Medicine, Korea)

OP07-2 Distinct molecular and cytogenetic profiles of myelodysplastic syndrome with bone marrow eosinophilia and basophilia
Yujin Jung (Seoul National University College of Medicine, Korea)

OP07-3 Clinical and molecular characteristics and prognostic significance of autoimmune disease in myelodysplastic syndrome
Yunsuk Choi (University of Ulsan College of Medicine, Korea)

OP07-4 Haploidentical HCT using ex vivo T cell-depleted PBSC as first-line therapy for pediatric patients with acquired SAA
Ho Joon Im (University of Ulsan College of Medicine, Korea)

OP07-5 STK10 mutation block erythropoiesis in acquired pure red cell aplasia via down-regulated the ribosome biosynthesis
Meng Danchen (The First Affiliated Hospital of Anhui Medical University, China)

13:20-14:50 **[OP8] Thrombocytopenia & Supportive care** Room 4 Art Hall

Chairs Junshik Hong (Seoul National University College of Medicine, Korea)
Seungmin Hahn (Yonsei University College of Medicine, Korea)

OP08-1 Clinical outcomes of TPO-receptor agonists in patients with steroid-refractory immune thrombocytopenia; Significant conditions of discontinuation with good response
Jae-Ho Yoon (College of Medicine, The Catholic University of Korea, Korea)

OP08-2 Efficacy and safety of avatrombopag in Chinese children with persistent and chronic primary immune thrombocytopenia: A multicenter observational retrospective study in China
Zhifa Wang (Beijing Children's Hospital, China)

OP08-3 Effect of anagrelide on health-related quality of life in patients with treatment-nave, high-risk essential thrombocythemia
Taekeun Park (Seoul National University College of Medicine, Korea)

OP08-4 Impact of hematopoietic stem cell transplantation on bone metabolism and growth in pediatric patients with thalassemia major
Yu Liu (Shantou University, China)

OP08-5 Effects of tertiary palliative care on the pattern of end-of-life care in patients with hematologic malignancies
Dong Hyun Kim (Seoul National University College of Medicine, Korea)

OP08-6 The clinical manifestation, prognostic factors, and outcomes of adenovirus pneumonia after allogeneic hematopoietic stem cell transplantation
Yuewen Wang (Peking University People's Hospital, China)

14:50-15:05 Break

DAILY PROGRAM Friday, March 29

15:05-16:20 **[JS04] Current interests in hematologic disease in Asia** — Room 1, Vista Hall 1

Chair: Byeong-Bae Park (Hanyang University College of Medicine, Korea)

JS04-1 The journey of bone marrow transplantation at BachMai General Hospital
Han Viet Trung (Bach Mai Hospital, Vietnam)

JS04-2 Current situation of management of non-Hodgkin lymphoma in the Republic of Armenia
Yervand Hakobyan (Armenian Hematology Association, Armenia)

JS04-3 The evolution of hemophilia treatment in Thailand
Darintr Sosothikul (Chulalongkorn University, Thailand)

Discussion

15:05-16:20 **[SS11] Quality-of-life revisited** — Room 2, Vista Hall 2

Chairs: Sung Yong Oh (Dong-A University College of Medicine, Korea)
Yong Park (Korea University College of Medicine, Korea)

SS11-1 Palliative care for patients with leukemia
Min Sun Kim (Seoul National University College of Medicine, Korea)

SS11-2 Long-term survivorship in hematologic malignancies
Shahrukh K. Hashmi (Mayo Clinic, UAE)

SS11-3 The importance of monitoring symptoms and quality of life in routine hematology practice
Fabio Efficace (Italian Group for Adult Hematologic Diseases, Italy)

15:05-16:20 **[SS12] Novel approaches for diagnosis & treatment of acute lymphoblastic leukemia** — Room 3, Grand Hall 1

Chairs: Hyoung Jin Kang (Seoul National University College of Medicine, Korea)
Ho-Jin Shin (Pusan National University School of Medicine, Korea)

SS12-1 Novel approaches for diagnosis & treatment of acute lymphoblastic and myeloid leukemia
Michel Zwaan (Princess Máxima Center for Pediatric Oncology, The Netherlands)

SS12-2 The role of blinatumomab in the treatment of MRD negative B-ALL in adults
Mark R. Litzow (Mayo Clinic, USA)

SS12-3 Revised WHO classification of ALL: New era of genetic diagnosis
Ari Ahn (College of Medicine, The Catholic University of Korea, Korea)

15:05-16:20 **[ES04] Monoclonal gammopathies of clinical significance** — Room 4, Art Hall

Chairs: Young Rok Do (Keimyung University School of Medicine, Korea)
Hyo Jung Kim (Hallym University College of Medicine, Korea)

ES04-1 AL cardiac amyloidosis
Darae Kim (Sungkyunkwan University School of Medicine, Korea)

ES04-2 Nephrologist's perspective on monoclonal gammopathy of renal significance
Soon Hyo Kwon (Soonchunhyang University College of Medicine, Korea)

ES04-3 Monoclonal gammopathies of neurological significance
Ju-Hong Min (Sungkyunkwan University School of Medicine, Korea)

DAILY PROGRAM Friday, March 29

16:20-16:35 **Break**

16:35-17:50 **[SS13] Advancing in knowledge of rare pediatric hematologic disorders** — Room 2, Vista Hall 2

Chairs: Ho Joon Im (University of Ulsan College of Medicine, Korea); Hye Lim Jung (Sungkyunkwan University School of Medicine, Korea)

SS13-1 Clonal evolution of MDS/AML in patients with cancer predisposition syndromes
Kenichi Yoshida (National Cancer Center Research Institute, Japan)

SS13-2 Congenital and aquired thrombophilic conditions in children
Leonardo R. Brandão (University of Toronto, Canada)

SS13-3 Management of rare pediatric lymphomas
Jae Wook Lee (College of Medicine, The Catholic University of Korea, Korea)

16:35-17:50 **[JS05] Asian Hematology Session II - AML** — Room 3, Grand Hall 1

Chairs: Sangkyun Sohn (Kyungpook National University School of Medicine, Korea); Byong Soo Kim (Korea University College of Medicine, Korea)

JS05-1 Epidemiology, risk stratification and treatment outcome in acute myeloid treatment: Taiwan experience
Hsin-An Hou (National Taiwan University, Taiwan)

JS05-2 Advancement in leukaemia diagnostics: The role of next-generation sequencing (NGS) in acute myeloid leukaemia in Malaysia
Angeli Ambayya (Ministry of Health, Malaysia)

JS05-3 Determining fitness for treatments in older adults with AML
Byung Sik Cho (College of Medicine, The Catholic University of Korea, Korea)

Discussion

16:35-17:50 **[ES05] Principles of anticoagulation - All about blood clots (Kor)** — Room 4, Art Hall

Chairs: Soo-Mee Bang (Seoul National University College of Medicine, Korea); Sung Hwa Bae (Daegu Catholic University School of Medicine, Korea)

ES05-1 Back to the basic: Coagulation pathway
Seonyang Park (Inje University College of Medicine, Korea)

ES05-2 Pharmacology: Anticoagulants and reversal agents
Seo-Yeon Ahn (Chonnam National University Medical School, Korea)

ES05-3 Proper application of anticoagulation therapy on cancer associated thrombosis
Ho-Young Yhim (Jeonbuk National University Medical School, Korea)

17:50-18:30 **Gala Reception** — VISTA Hall Lobby

18:30-20:00 **Gala Dinner** — Room 1+2, Vista Hall 1+2

DAILY PROGRAM Saturday, March 30

07:30-08:00 **Business Meeting** — Room 2, Vista Hall 2

08:00-09:00 **[YI] Young Investigator Award Presentation** — Room 1, Vista Hall 1

Chairs
Deog-Yeon Jo (Chungnam National University College of Medicine, Korea)
Je-Hwan Lee (University of Ulsan College of Medicine, Korea)

YI-1 Comparison of anti-thymocyte globulin (ATG) and post-transplant cyclophosphamide (PTCY) for the prevention of graft-versus-host disease in allogeneic hematopoietic stem cell transplant patients who achieved complete remission after induction therapy for acute myeloid leukemia
Hyunkyung Park (University of Ulsan College of Medicine, Korea)

YI-2 Evaluation of plasma cell sorting methods in multiple myeloma patients: Flow cytometry versus magnetic beads
Saeam Shin (Yonsei University College of Medicine, Korea)

YI-3 Comparative analysis of genes according to ropeginterferon alfa-2b treatment response in patients with polycythemia vera
Seug Yun Yoon (Soonchunhyang University College of Medicine, Korea)

YI-4 Single-cell transcriptome analysis to investigate the immune profile of T cells post-allogeneic hematopoietic stem cell transplantation and elucidate mechanisms underlying graft-versus-host disease
Jong Hyuk Lee (College of Medicine, The Catholic University of Korea, Korea)

YI-5 Characterization of cytotoxic CD4 T cells to promote cellular immunotherapy outcome in multiple myeloma
Hyunsoo Cho (Yonsei University College of Medicine, Korea)

YI-6 A study on the utility of next-generation sequencing-based assays for immunoglobulin gene rearrangement usage repertoire analysis and measu rable residual disease monitoring in B-cell acute lymphoblastic leukemia
Daehyun Chu (University of Ulsan College of Medicine, Korea)

YI-7 Clinical impact of NGS-based measurable residual disease as prognostic marker in pediatric acute myeloid leukemia
Hyun Jin Park (Seoul National University College of Medicine, Korea)

YI-8 Identification of relapse related clones using minimal residual disease monitoring by next-generation sequencing in Korean pediatric patients with acute myeloid leukemia
Jong-Mi Lee (College of Medicine, The Catholic University of Korea, Korea)

YI-9 The impact of the tumor immune microenvironment on the efficacy of CAR T-cell therapy or Bi-specific antibody therapy in relapsed or refractory diffuse large B-cell lymphoma
Hyungwoo Cho (University of Ulsan College of Medicine, Korea)

09:00-10:15 **[ES06] Essential knowledge for optimal hematologic consultation (Kor)** — Room 1, Vista Hall 1

Chairs
Jong Ho Won (Soonchunhyang University College of Medicine, Korea)
Deog-Yeon Jo (Chungnam National University College of Medicine, Korea)

ES06-1 Functional iron deficiency in cancer patients
Ik-Chan Song (Chungnam National University College of Medicine, Korea)

ES06-2 Assessment of neutropenia in hospitalized patients
Young Hoon Park (Ewha Womans University College of Medicine, Korea)

ES06-3 Perioperative consultation for the appropriate transfusion
Ka-Won Kang (Korea University College of Medicine, Korea)

DAILY PROGRAM Saturday, March 30

09:00-10:15 **[SS14] Novel insights into pathogenesis of MPN** — Room 2, Vista Hall 2

Chairs: Chul Won Choi (Korea University College of Mecine, Korea); Sung-Yong Kim (Konkuk University School of Medicine, Korea)

SS14-1 Myeloproliferative neoplasms and inflammation
Steffen Koschmieder (RWTH Aachen University, Germany)

SS14-2 Signaling contributing to the development of myelofibrosis: Beyond JAK/STAT
Douglas Tremblay (Mount Sinai School of Medicine, USA)

SS14-3 Clonal evolution in myelofibrosis
Sung-Eun Lee (College of Medicine, The Catholic University of Korea, Korea)

09:00-10:15 **[SS15] Immunotherapies for lymphomas non-benefited from CAR-T cell therapy** — Room 3, Grand Hall 1

Chairs: Jae-Yong Kwak (Jeonbuk National University Medical School, Korea); Deok-Hwan Yang (Chonnam National University Medical School, Korea)

SS15-1 Treatment options for relapsed/refractory Hodgkin lymphoma after brentuximab vedotin and PD-1 blockade
Alex F. Herrera (City of Hope, USA)

SS15-2 Aggressive B-cell lymphomas: Immuno-chemotherapies other than CAR-T cell therapies
Jason Westin (The University of Texas MD Anderson Cancer Center, USA)

SS15-3 Extranodal NK/T cell lymphoma: The immunogenic tumor
Won Seog Kim (Sungkyunkwan University School of Medicine, Korea)

09:00-10:15 **[ES07] Basic genomics for clinical hematologists (Kor)** — Room 4, Art Hall

Chairs: Hee-Jin Kim (Sungkyunkwan University School of Medicine, Korea); In-Suk Kim (Pusan National University School of Medicine, Korea)

ES07-1 Genomic technologies for detecting structural variations in hematologic malignancies
Miae Jang (Sungkyunkwan University School of Medicine, Korea)

ES07-2 The role of NGS in hematologic malignancies
Young-Uk Cho (University of Ulsan College of Medicine, Korea)

ES07-3 Germline predisposition to hematologic malignancies
Sang Mee Hwang (Seoul National University College of Medicine, Korea)

10:15-10:30 Break

10:30-11:15 **[PAP01] Plenary Abstract Presentation** — Room 1+2, Vista Hall 1+2

Chairs: Dong Yeop Shin (Seoul National University College of Medicine, Korea); Yoon Seok Choi (Korea University College of Medicine, Korea)

PAP01-1 A single-arm, open-label, multicenter study to assess molecular response of P1101 therapy in patients with polycythemia vera and elevated hematocrit: Results from 48 weeks core study
Sung-Eun Lee (College of Medicine, The Catholic University of Korea, Korea)

DAILY PROGRAM Saturday, March 30

PAP01-2 **Novel genomic variants influencing methotrexate delayed excretion in pediatric patients with acute lymphoblastic leukemia**
Jung Yoon Choi (Seoul National University College of Medicine, Korea)

PAP01-3 **Prognostic utility of minimal residual disease (MRD) after curative intent induction therapy for DLBCL: A prospective real-world ctdna study**
Sang Eun Yoon (Sungkyunkwan University School of Medicine, korea)

11:15-11:45 **Award Ceremony & Closing**

Room 1+2
Vista Hall 1+2

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& KSH 65th ANNUAL MEETING

POSTER LIST

POSTER LIST

PP01-1 **Genetic and epigenetic alteration of Wilms' tumor 1 (WT1) gene in acute myeloid leukemia**
Harsh Goel[1], Anita Chopra[1], Amar Ranjan[1], Jagdish Prasad Meena[2], Aditya Kumar Gupta[2], Ganesh Kumar Viswanathan[3], Sameer Bakhshi[4], Maroof Ahmad Khan[5], Pranay Tanwar[1*]
[1]*Laboratory Oncology , All India Institute of Medical Sciences, New Delhi , India*
[2]*Pediatric Oncology, All India Institute of Medical Sciences, New Delhi , India*
[3]*Hematology, All India Institute of Medical Sciences, New Delhi , India*
[4]*Medical Oncology, All India Institute of Medical Sciences, New Delhi , India*
[5]*Biostatistics, All India Institute of Medical Sciences, New Delhi , India*

PP01-2 **A prospective study to evaluate the prognostic implications and molecular mechanism of SLC40A1 gene in primary acute myeloid leukemia**
Harsh Goel[1], Pranay Tanwar[1*]
[1]*Laboratory Oncology, All India Institute of Medical Sciences, New Delhi, India*

PP01-3 **Using red ginger to prevent acute myeloid leukemia : A literature review**
Farah Maetam[1*], Rahma Yuantari [2]
[1]*Internal Medicine , Universitas Islam Indonesia, Yogyakarta, Indonesia*
[2]*Clinical Pathology, Universitas Islam Indonesia, Yogyakarta, Indonesia*

PP01-4 **Epigenetic modulation enhances the therapeutic potential of all-trans retinoic acid in acute myeloid leukemia**
Lukasz Szymanski[1*], Rafal Skopek[1], Malgorzata Palusinska[1], Karolina Maslinska-Gromadka[1], Leszek Kraj[1], Tino Schenk[2], Arthur Zelent[1]
[1]*Department of Molecular Biology, Institute of Genetics and Animal Biotechnology, Magdalenka, Poland*
[2]*Institute of Molecular Cell Biology, Center for Molecular Biomedicine Jena (CMB), Jena University Hospital, Jena, Germany*

PP01-5 **Loss of TET function results in myeloid malignancy associated with a heterochromatin-to-euchromatin transition**
Myunggon Ko[1,2*], Hiroshi Yuita[3], Isaac Lopez-Moyado[3,4], Hyeongmin Jeong[1], James Scott-Browne[5], Jungeun An[6], Toshinori Nakayama[7,8], Atsushi Onodera3[3,7,9], Anjana Rao[3,4]
[1]*Biological Sciences, Ulsan National Institute of Science and Technology, Ulsan, Republic of Korea*
[2]*Center for Genomic Integrity, Institute for Basic Science, Ulsan, Republic of Korea*
[3]*Signaling and Gene Expression, La Jolla Institute for Immunology, La Jolla, United States*
[4]*4SSanford Consortium , For Regenerative Medicine, La Jolla, United States*
[5]*Biomedical Research, National Jewish Health, Denver, United States*
[6]*Life Sciences, Jeonbuk National University, Jeonju, Republic of Korea*
[7]*Immunology, Chiba University, Chiba, Japan*
[8]*8AMED-CREST, AMED, Chiba, Japan*
[9]*Institute for Advanced Academic Research , Chiba University, Chiba, Japan*

PP01-6 **High expression of CXC-chemokine ligand 5 in bone marrow serum predicts favorable outcomes in children with acute myeloid leukemia**
Yongping Zhang[1], Hujun Li[1], Hui Zhang[1], Qi Ji[1], Li Gao[1], Yixin Hu[1], Shaoyan Hu[1*]
[1]*Hematology and Oncology, Children's Hospital of Soochow University, Suzhou, China*

PP01-7 **Gemtuzumab ozogamicin with half-dose CAG regimens as re-induction therapy for pediatric refractory/relapsed AML**
Liyan Fan[1], Li Gao[1], Shengqin Cheng[1], Yixin Hu[1], Peifang Xiao[1], Hailong He[1], Yi Wang[1], Shaoyan Hu[1*]
[1]*Hematology and Oncology, Children's Hospital of Soochow University, Suzhou, China*

PP01-8 **Fabrication of revesterol hybrid lecithin folic acid silver nanoparticles and its evaluation as anti-leukemia effect against benzene induced acute myeloid leukemia in rats**
Deeksha Chauhan[1*], Vikas Kumar[2]
[1]*Physics, RK College of Science, Uttarkhand, India*
[2]*Pharmaceutical Sciences, Sam Higginbottom University Of Agriculture, Technology & Sciences, Prayagraj, India*

POSTER LIST

PP01-9 **CYP2B6 polymorphism and leukaemia susceptibility in Asian populations: A systematic review and meta-analysis**
Novi Davitsen[1], Tohari Amin[1*], Alfatea Rahmi[2], Shinta Wardhani[3]
[1]*Internal Medicine Resident, Universitas Brawijaya, Malang, Indonesia*
[2]*Faculty of Medicine, Universitas Brawijaya, Malang, Indonesia*
[3]*Hemato-Oncology Divison of Internal Medicine Department, Universitas Brawijaya, Malang, Indonesia*

PP01-10 **Treatment behavior and outcomes of acute myeloid leukemia in the COVID-19 era**
Nayon Kim[1], Jeehyun Kong[1*]
[1]*Yonsei University Wonju College of Medicine, Wonju, Republic of Korea*

PP01-11 **Exploring neo-antigen and immunogenicity of acute myeloid leukemia (AML) using neo-ARSTM artificial intelligence tool**
Suyoung Choi[1,2,3], Joo-Young Kang[4], Jeong Suk Koh[5], Hyun-Jin Yang[5], Jeong-Yeon Park[6], Il-Oh Jeong[6], Jong Hui Hong[6], Jongsun Jung[6], Thi Thuy Duong Pham[1,2,3], Bu-Yeon Heo[1,2,3], Myung-Won Lee[4], Jung-Hyun Park[7], Yunsun Jang[7], Deog-Yeon Jo[4], Jaeyul Kwon[2,3,5,7,8], Ik-Chan Song[2,3,4]
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[2]*Department of Medical Science, College f Medicine, Chungnam National University, Daejeon, Republic of Korea*
[3]*Brain Korea 21 FOUR Project For Medical Science, Chungnam National University, Daejeon, Republic of Korea*
[4]*Department of Internal Medicine, College of Medicine, , Chungnam National University, Daejeon, Republic of Korea*
[5]*Genome Data Integration Centre, Syntekabio Inc., Daejeon, Republic of Korea*
[6]*Medical Science Study Centre, Syntekabio Inc., Seoul, Republic of Korea*
[7]*Translational Immunology Institute, College of Medicine, Chungnam National University, Seoul, Republic of Korea*
[8]*Department of Medical Education, College of Medicine, Chungnam National University, Daejeon, Republic of Korea*

PP01-12 **A paired sillico analysis of ALOX5AP gene expression/methylation and its prognostic impact among acute myeloid leukemia**
Pranay Tanwar[1*], Harsh Goel[1]
[1]*Laboratory Oncology, Dr BRA-IRCH, AIIMS, New Delhi, India*

PP01-13 **Investigation on novel ER transmembrane protein, SURF4, targeting cell death in myeloid leukemia**
Jayoung Kim[1], Dongjun Lee[1*]
[1]*School of Medicine, Convergence Medicine, Busan, Republic of Korea*

PP01-14 **Targeting estrogen-related receptor alpha as a novel treatment approach for acute myeloid leukemia with FLT3 mutation**
Wonhyoung Seo[1], Ik-Chan Song [2], Eun-Kyeong Jo[1*]
[1]*Department of Medical Science, Chungnam National University College of Medicine, Dajeon, Republic of Korea*
[2]*Department of Internal Medicine, Chungnam National University College of Medicine, Dajeon, Republic of Korea*

PP01-15 **Antithymocyte globulin (ATG) in allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia: Evaluating outcomes according to cytogenetic risk: Impact on chronic GVHD and cGRFS**
Hyeong Jun Kim[1], Mihee Kim[2], Seo-Yeon Ahn[2], Sung-Hoon Jung[2], Ga-Young Song[2], Deok-Hwan Yang[2], Je-Jung Lee[2], Mi Yeon Kim[3], Hyeo-ung-Joon Kim[2,3*], Ho-Young Lim[4], Jae-Sook Ahn[2,3]
[1]*Internal Medicine, Chonnam National University Hospital, Gwang-ju, Republic of Korea*
[2]*Hematology, Hematology-Oncology, Chonnam National University Hwasun Hospital, Jeollanam-do, Republic of Korea*
[3]*Hematology, Genomic Research Center for Hematopoietic Diseases, Chonnam National University Hwasun Hospital, Jeollanam-do, Republic of Korea*
[4]*Hematology, Hematology-Oncoloy, Jeonbuk National University Hospital, Jeonju, Republic of Korea*

PP01-16 **The oxysterols 27-hydroxycholesterol affects hematopoietic stem and progenitor cell pools**
Soo-Yeon Woo
Department of Convergence Medicine, Pusan National University School of Medicine, Yangsan, Republic of Korea

PP01-17 **From docking to overcoming resistance: Cannabidiol's potential in multidrug-resistant leukemia cancer K562/adr**
Krai Daowtak
Medical Technology, Faculty of Allied Health Sciences, Cellular and Molecular Immunology Research Unit, Naresuan University, Phitsanulok, Thailand, Phitsanulok, Thailand

POSTER LIST

PP01-18 **A real world analysis of impact of gilteritinib in relapse/refractory AML with FLT3-ITD mutation**
Hohyung Nam[1,2], Daehun Kwag[1,2], Gi June Min[1,2], Sung-Soo Park[1,2], Silvia Park[1,2], Jae-Ho Yoon[1,2], Sung-Eun Lee[1,2], Byung Sik Cho[1,2*], Ki-Seong Eom[1,2], Yoo-Jin Kim[1,2], Seok Lee[1,2], Chang-Ki Min[1,2], Seok -Goo Cho[1], Jong Wook Lee[1], Hee-Je Kim[1,2]
[1]*Department of Hematology, , Catholic Hematology Hospital, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea*
[2]*Leukemia Research Institute, College of Medicine, The Catholic University of Korea, Republic of Korea*

PP01-19 **Enhanced expression of glycolytic enzymes and succinate dehydrogenase complex flavoprotein subunit a by HMP promotes glycolysis and mitochondrial respiration in myeloblasts of acute myeloid leukemia**
Yunseon Jang[1], Jeong Suk Koh[2], Jung-Hyun Park[1], Suyoung Choi[3,4], Pham Thi Thuy Duong[3,4], Bu Yeon Heo[3,4], Sang Woo Lee[4], Jung Yeon Kim[5], Seok-Hwan Kim[5,6], Ik-Chan Song[1,2*]
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[2]*Department of Internal Medicine, Chungnam National University Hospital, Daejeon, Republic of Korea*
[3]*Brain Korea 21 FOUR Project for Medical Science, Chungnam National University School of Medicine, Daejeon, Republic of Korea*
[4]*Department of Medical Science, Chungnam National University School of Medicine, Daejeon, Republic of Korea*
[5]*Research Institute for Medical Science, Chungnam National University School of Medicine, Daejeon, Republic of Korea*
[6]*Department of Surgery, Chungnam National University Hospital, Daejeon, Republic of Korea*

PP01-20 **Risk stratification in AML through early bone marrow assessment during intensive chemotherapy**
Daehun Kwag[1,2], Gi June Min[1,2], Sung-Soo Park[1,2], Silvia Park[1,2], Jae-Ho Yoon[1,2], Sung-Eun Lee[1,2], Byung Sik Cho[1,2], Ki-Seong Eom[1,2], Yoo-Jin Kim[1,2], Seok Lee[1,2], Chang-Ki Min[1,2], Seok -Goo Cho[1], Chang-Ki Min[1,2], Jong Wook Lee[1], Hee-Je Kim[1,2*]
[1]*Hematology, Catholic Hematology Hospital, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea*
[2]*Leukemia Research Institute, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea*

PP01-21 **Genomic landscape of pediatric acute myeloid leukemia (AML)**
Jagdish Prasad Meena[1*], Riyaz Ahmad Mir[1], Harshita Makkar[1], Aditya Kumar Gupta[1], Sameer Bakhshi[1], Rakhee Yadav[1], Pranay Tanwar[1], Rachna Seth[1]
[1]*Division of Pediatric Oncology, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi, India, New Delhi, India*

PP01-22 **An artificial intelligence approach for measurable residual disease (MRD) detection in acute myeloid leukemia (AML)**
Pranay Tanwar[1*], Jaspreet Singh[2], Harsh Goel[1]
[1]*Laboratory Oncology Unit, Dr.B.R.A. Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi, India*
[2]*Laboratory Oncology Unit, ICMR-National Institute of Pathology, Sriramachari Bhawan, Safdarjung Hospital Campus , New Delhi, India*

PP01-23 **Glutathione S-transferases (GST) T1 polymorphism as the most susceptible to leukemia in Asians population: An updated meta-analysis and systematic review of multicenter study**
Tohari Tohari[1*], Muhammad Saifulhaq[1], Anindia Yolanda[2], Alfatea Rahmi[3], Shinta Wardhani[4]
[1]*Internal Medicine Resident, Universitas Brawijaya, Malang, Indonesia*
[2]*Emergency Department, Lavalette Hospital, Malang, Indonesia*
[3]*Medical student, Universitas Brawijaya, Malang, Indonesia*
[4]*Hematology Oncology Division of Internal Medicine Department, Universitas Brawijaya, Malang, Indonesia*

PP01-24 **GSTP1 val allele is associated with susceptibility to acute myeloid leukemia: A meta-analysis**
Raphael Enrique Tiongco[1], Neil David Cayanan[1], Miljun Catacata[1*], Michael John Dominguez[1,2]
[1]*College of Allied Medical Professions, Angeles University Foundation, Angeles City, Philippines*
[2]*School of Medicine, Angeles University Foundation, Angeles City, Philippines*

PP01-25 **Impaired CD45RO-CCR7+ naive CD8+T cells in AML are associated with lower overall survival**
Yongping Zhang[1], Hujun Li[1], Hui Zhang[1], Qi Ji[1], Shaoyan Hu[1*]
[1]*Hematology and Oncology, Children's Hospital of Soochow University, Suzhou, China*

PP01-26 **Dysregulation of immune regulators in AML bone marrow promotes dysfunction of CD8+ T cells**
Yongping Zhang[1], Hujun Li[1], Hui Zhang[1], Qi Ji[1], Shaoyan Hu[1*]
[1] *Hematology and Oncology, Children's Hospital of Soochow University, Suzhou, China*

POSTER LIST

PP01-27 **Acute promyelocytic leukemia with abundant small azurophilic granules: A case report**
Yeon Woo Seo[1], Sang Kyung Kim[1*]
[1]Laboratory Medicine, Daegu Catholic University School of Medicine, Daegu, Republic of Korea

PP01-28 **Exploring genomic complexity in acute myeloid leukemia through machine learning: Subtype identification, biomarker discovery, and prognostic models for personalized interventions**
Rifaldy Fajar[1*], Laura Barbara[2], Alessio Conta Rossi[3,2], Sofia Clara Binico[3,2], Erik Santa Andersson[4], Roland Helmizar[5]
[1]Information Engineering, Computer Science and Mathematics, University of L'Aquila, L'Aquila, Italy
[2]Computational Biology and Medicine Laboratory, University of L'Aquila, L'Aquila, Italy
[3]Hematology Research Unit, L'Aquila Hospital, L'Aquila, Italy
[4]Bioinformatics Research Group, Karlstad University, Karlstad, Sweden
[5]Internal Medicine, Baiturrahmah University, Padang, Indonesia

PP01-29 **The role of allogeneic stem cell transplantation in the aml patients who were treated with venetoclax and decitabine**
Ik Chan Song[1], Jeong Suk Koh[1], Wonhyoung Seo[1], Sora Kang[1], Chul Hee Kim[1], Myung-Won Lee[1], Hyewon Ryu[1], Hyo-Jin Lee[1], Hwan-Jung Yun[1], Deog-Yeon Jo[1*]
[1]Department of Internal Medicine, Chungnam National University Hospital, Daejeon, Republic of Korea

PP01-30 **Comparison of the current and 2022 system of the WHO classification of non-recurrent genetic abnormalities acute myeloid leukemia in the real-world setting**
Hye Seong Ryu[1], Young-Uk Cho[1*], Daehyun Chu[1], Taeguen Lee[1], Miyoung Kim[1], Seongsoo Jang[1]
[1]Laboratory Medicine, Asan Medical Center, Seoul, Republic of Korea

PP01-31 **Risk factors and infection patterns of febrile neutropenia after induction chemotherapy in patients with acute myeloid leukemia**
Made Sindy Astri Pratiwi[1], Made Priska Arya Agustini[1], Ni Made Renny Anggreni Rena[2*], I Made Bakta[2]
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PP01-32 **Survival analysis of acute myeloid leukemia patients at tertiary care hospital in Bali, Indonesia**
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PP01-33 **The efficacy of midostaurin in patients with FLT3-ITD mutated AML : A real-world setting in Korea**
Kyoung Il Min[1,2], Daehun Kwag[1,2], Jung Yeon Lee[1,2], Gi June Min[1,2], Sung-Soo Park[1,2], Silvia Park[1,2], Jae-Ho Yoon[1,2], Sung-Eun Lee[1,2], Byung Sik Cho[1,2], Ki-Seong Eom[1,2], Yoo-Jin Kim[1,2], Seok Lee[1,2], Chang-Ki Min[1,2], Seok -Goo Cho[1], Jong Wook Lee[1], Hee-Je Kim[1,2*]
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PP01-34 **Hypomethylating agent plus venetoclax treatment outcome in core binding factor acute myeloid leukemia**
Daehun Kwag[1,2], Gi June Min[1,2], Sung-Soo Park[1,2], Silvia Park[1,2], Jae-Ho Yoon[1,2], Sung-Eun Lee[1,2], Byung Sik Cho[1,2], Ki-Seong Eom[1,2], Yoo-Jin Kim[1,2], Seok Lee[1,2], Chang-Ki Min[1,2], Seok -Goo Cho[1], Jong Wook Lee[1], Hee-Je Kim[1,2*]
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PP01-35 **Gamma delta T-cell immune checkpoint receptor expression in acute myeloid leukemia**
Daehun Kwag[1,2], Byung Sik Cho[1,2*], Gi June Min[1,2], Sung-Soo Park[1,2], Silvia Park[1,2], Jae-Ho Yoon[1,2], Sung-Eun Lee[1,2], Ki-Seong Eom[1,2], Yoo-Jin Kim[1,2], Seok Lee[1,2], Chang-Ki Min[1,2], Seok-Goo Cho[1], Jong Wook Lee[1], Hee-Je Kim[1,2]
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PP01-36 **In vitro long-term culture conditions screening for primary AML sample**
Daehyeon Gwak[1,2], Dongchan Kim[1,2], Ja Min Byun[1,2,3], Junshik Hong[1,2,3], Sung-Soo Yoon[1,2,3], Dong-Yeop Shin[1,2,3*]
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PP02-1 **Impact of transfusion dependence on clinical and economic burden in patients with lower-risk myelodysplastic syndromes: A 28-year retrospective study**
Jun Ho Jang[1*], Ji-Hyun Kim[2], Kyungah Lee[3], Hyojin Kim[4], Fangyuan Wang[5]
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PP02-2 **Unlocking myelodysplastic syndrome insights: Meta-analysis and machine learning with MUHSeq tool for blood transcriptome analysis**
Mohammad Uzzal Hossain
Bioinformatics Division, National Institute of Biotechnology, Dhaka, Bangladesh

PP02-3 **Potential biomarkers for azacitidine resistance in myelodysplastic syndrome based on gene expression and DNA methylation profiles**
Da Yeon Kim[1,2], Eun Ju Kim[1,2,3,4*]
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PP02-4 **Chromosomal abnormalities in primary myelodysplastic syndrome**
Anila Rashid[1*], Mohammad Khurshid[1]
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PP02-5 **Subtype-specific germline DDX41 mutations and their distinct clinicopathological features in Korean patients with myelodysplastic syndrome and acute myeloid leukemia**
Daehyun Chu[1], Young-Uk Cho[1*], Taegeun Lee[1], Miyoung Kim[1], Sang-Hyun Hwang[1], Seongsoo Jang[1], Eul-Ju Seo[1]
[1]Laboratory Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

PP02-6 **Trafficking of NK-cells into bone marrow after hypomethylating agent treatment in mice and patients with high risk MDS or AML**
Junshik Hong[1,2*], Suji Min[1], Jihyun Park[1], Carly Fielder[3], Qianni Hu[3], Sung-Soo Yoon[1,2], Tae Kon Kim[3]
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PP02-7 **Reclassification of myelodysplastic neoplasms following updated WHO and ICC classification: A single center study**
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PP03-1 **Efficacy and 5 years survival of acute lymphoblastic leukemia (ALL) treated with bacterial L-asparaginase**
Natya Lakshita Ardhananeswari Riyanto
Faculty of Medicine, Universitas Islam Indonesia , Yogyakarta, Indonesia

PP03-2 **A pancytopenia preceeding a hypoplastic acute lymphoblastic leukemia**
Daniela Ratnani[1*], Lusi Oka Wardhani[1]
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PP03-3 **The association between GSTM1 and GSTT1 null genotype and susceptibility to leukemia in Asian population: A systematic review and meta-analysis**

Salsabila Farradisya[1], Alfatea Pintari Rahmi[1*], Evira Rahma Aya Sofia[1], Tohari Tohari[2], Shinta Oktya Wardhani[3]
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PP03-4 **IKZF1 deletion status and correlation with cytogenetics and measurable residual disease in adult B lineage acute lymphoblastic leukemia**

Prabhjot Kaur[1], Sudhanshi Raina[1], Anand Balakrishnan[1], Anshu Anshu[1], Shailja Rathore[1], Pramod Kumar[1], Parveen Bose[1], Jogeshwar Binota[1], Praveen Sharma[1], Shano Naseem[1], Arihant Jain[1], Alka Khadwal[1], Man Updesh Singh Sachdeva[1], Reena Das[1], Sreejesh Sreedharanunni[1*]
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PP03-5 **5-Methyl cytosine flow cytometry-based global methylation status and correlation with cytogenetics and measurable residual disease in adult B lineage acute lymphoblastic leukemia**

Prabhjot Kaur[1], Sudhanshi Raina[1], Arun Kumar[1], Parveen Bose[1], Jogeshwar Binota[1], Shano Naseem[1], Arihant Jain[1], Alka Khadwal[1], Man Updesh Singh Sachdeva[1], Sreejesh Sreedharanunni[1*]
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PP03-6 **Clinical impact of concurrent BTG anti-proliferation factor 1 (BTG1) and IKZF1 deletions in BCR::ABL1 negative B-cell acute lymphoblastic leukemia**

Sanjeev Kumar Gupta[1*], Gadha K Leons[1], Preity Sharma[1], Sameer Bakhshi[2], Ritu Gupta[1], Smeeta Gajendra[1], Deepam Pushpam[2]
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PP03-7 **Prognostic analysis of WT1 expression at diagnosis in pediatric acute lymphoblastic leukemia: A retrospective study from Seoul National University Children's Hospital**

Bo Kyung Kim[1], Hyun Jin Park[1], Jung Yoon Choi[1], Kyung Taek Hong[1], Juyeon Lee[1], Youngdai Kwon[1], Yoon Sunwoo[1], Hyoung Jin Kang[1*]
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PP03-8 **Key role of SOX4 and PI3K/AKT/mTOR pathway in relapsed pediatric precursor B cell acute lymphoblastic leukemia**

Jae Wook Lee[1*], Suejung Jo[1], Jae Won Yoo[1], Seongkoo Kim[1], Nack-Gyun Chung[1], Bin Cho[1]
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PP03-9 **Second hematologic malignancy risk following radioactive iodine therapy in thyroid cancer patients: A systematic review and meta-analysis**

Evira Rahma Aya Sofia[1*], Alfatea Pintari Rahmi[1], Salsabila Farradisya[1], Tohari Tohari[2], Shinta Oktya Wardhani[3]
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PP03-10 **Bioinformatics analysis of genomic alterations in pediatric acute lymphoblastic leukemia: Identifying prognostic markers and therapeutic targets**

Rifaldy Fajar[1*], Bona Francesco[2,3], Celeste Bonita Santana[3], Victor Zheyn[4], Betty Nakyama Baddeh[1,4], Claudia Mendosa[2,3], Andi Nursanti Andi Ureng[5]
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PP03-11 **Clinical implication of ponatinib salvage in adult patients with relapsed or refractory Philadelphia chromosome-positive acute lymphoblastic leukemia**

Jae-Ho Yoon[1], Daehun Kwag[1], Gi June Min[1], Sung-Soo Park[1], Silvia Park[1], Sung-Eun Lee[1], Byung-Sik Cho[1], Ki-Seong Eom[1], Yoo-Jin Kim[1], Hee-Je Kim[1], Chang-Ki Min[1], Seok-Goo Cho[1], Jong Wook Lee[1], Seok Lee[1*]

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PP03-12 **Minimal residual disease-based effect and safety of frontline ponatinib plus hyper-CVAD treatment for adults with newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia**

Seunghan Kim[1], Jae-Ho Yoon[1*], Daehun Kwag[1], Gi June Min[1], Sung-Soo Park[1], Silvia Park[1], Sung-Eun Lee[1], Byung-Sik Cho[1], Ki-Seong Eom[1], Yoo-Jin Kim[1], Hee-Je Kim[1], Chang-Ki Min[1], Seok-Goo Cho[1], Jong Wook Lee[1], Seok Lee[1]

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PP03-13 **The potential of extracellular vesicle derived microRNAs as a biomarker in acute lymphoblastic leukemia**

Jeong-An Gim[2], Kunye Kwak[1], Yong Park[1], Byung Soo Kim[1], Ka-Won Kang[1*]

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[2]Department of Medical Science, Soonchunhyang University, Asan, Republic of Korea

PP03-14 **An updated meta-analysis of the association of IKAROS zinc finger 1 rs4132601 T>G gene polymorphism with acute lymphoblastic leukemia risk**

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[3]Internal Medicine, Sipirok General Hospital, Sipirok, Indonesia

PP04-1 **Aberrant DNA methylation of tumor suppressor gene as one possible mechanism of its under-expression in chronic myeloid leukemia patients in India**

Asgar Ali[1], Sadhana Sharma[1*]

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PP04-2 **Biological potential and therapeutic effectiveness of Hinokiflavone for the treatment of chronic myeloid leukemia with their molecular mechanisms**

Dinesh Kumar Patel[1*], Kanika Patel[1]

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PP04-3 **Methylenetetrahydrofolate reductase A1298C gene polymorphism with risk of chronic myeloid leukemia: Updated meta-analysis**

William Djauhari[1], Batara Bisuk[2*]

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PP04-4 **Improvement of treatment-free remission rate following discontinuation of BCR::ABL1 tyrosine kinase inhibitors with longer treatment duration in chronic myeloid leukemia**

Sewon Lee[1], Yeung-Chul Mun[1], Hongtae Kim[2], Semin Lee[3], Seunghoon Kim[3], Sung-Ho Park[2], Sung-Hyun Kim[4], Young Rok Do[5], Soo-Hyun Kim[6], Kyung-Mi Kee[6], Yoon Sung Lee[7], Dong-Wook Kim[6,8*]

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PP04-5 **Association between waist circumference, body mass index, high-density lipoprotein cholesterol level, and risk of chronic myeloid leukemia**

Ka Young Kim[1], Daehun Kwag[1], Jung Yeon Lee[1], Gi-June Min[1], Sung-Soo Park[1], Silvia Park[1], Jae-Ho Yoon[1], Byung-Sik Cho[1], Ki-Seong Eom[1], Yoo-Jin Kim[1], Seok Lee[1], Chang-Ki Min[1], Hee-Je Kim[1], Seok-Goo Cho[1], Jong Wook Lee[1], Kyung Do Han[2], Sung-Eun Lee[1*]

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PP04-6 **Enumeration of CD26+ leukemic stem cells from peripheral blood using multiparametric flow cytometry: A potential tool for rapid diagnosis of chronic myeloid leukemia**

Praveen Sharma[1*], Namrata Kaul[1], Man Updesh Singh Sachdeva[1], Shano Naseem[1], Anshul Sabharwal[1], Sreejesh Sreedharanunni[1], Parveen Bose[1], Arun Kumar[1], Bhavishan Thakur[1], Pankaj Malhotra[2]

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PP04-7 **A successful leukapheresis in the management of chronic myeloid leukemia (CML) patients with pulmonary leukostasis: A case report and review of the literature**

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PP04-8 **The role of the microbiome gut axis in the development and relapse of chronic myeloid leukemia: Systematic review**

Daivan Febri Juan Setiya[1*], Dinda Ashilah Putri Kusnan[2], Ety Sari Handayani[3]

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PP04-9 **Impact of first-line and second-generation tyrosine kinase inhibitors on quality of life in chronic myeloid leukemia: Insights from a multi-center prospective study**

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PP04-10 **Paclitaxel and curcumin as dual-drug-loaded lipid nanocapsules exhibited protective effect against chronic myeloid leukemia via promotes apoptosis and suppress the BCR/ABL**

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PP04-11 **Predictive factors of patients with chronic phase chronic myeloid leukemia treated with tyrosine kinase inhibitor**

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PP04-12 **Low level mutations in the BCR-ABL1 kinase domain confers resistance to tyrosine kinase inhibitor in chronic myeloid leukemia patients**

Mohd Fadly Md Ahid[1*], Zahidah Abu Seman[2], Yuslina Mat Yusoff[2], Siti Shahrum Muhamed Said[3], Norazlina Azman[3], Julia Abdullah[2], Ermi Neiza Mohd Sahid[2], Nor Rizan Kamaluddin[2], Ezalia Esa[2]

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PP05-1 **In silico electrophysiological study reveals ibrutinib, an important therapeutic agent for B-cell lymphoma causes cardiac toxicity by inhibiting sodium current**

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PP05-2 **Subcutaneous epcoritamab plus lenalidomide in patients with relapsed/refractory diffuse large B-cell lymphoma from EPCORE NHL-5**

Won Seog Kim[1*], Irit Avivi[2], Po-Shen Ko[3], Carlos Grande Garcia[4], David Lavie[5], David Chism[6], Mostafa Seliem[7], Edwin E. Jeng[7], Neha Joshi[8], Satya Siddani[9], Wissam Assaily[10], Mariana Sacchi[11], Minh Dinh[7], Abraham Avigdor[12]
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[12]Division of Hematology and BMT , Sheba Medical Center, Ramat Gan and Tel Aviv University, Tel Aviv, Israel

PP05-3 **The clinical impact of PDGFR expression in patients with relapsed/refractory non-Hodgkin lymphoma treated with imatinib-combined chemotherapy: A pilot study**

Seom Gim Kong[1], Min-Jung Kim[2], Daejin Park[3], Hee Kyung Jang[4], Su-Jin Heo[5], Da Jung Kim[6], Jae-Cheol Jo[7], Jee-Yeong Jeong[2,8], Ho Sup Lee[6*]
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PP05-4 **Matching-adjusted indirect treatment comparison of axicabtagene ciloleucel and historical treatments in high-risk large B-cell lymphoma using Samsung Medical Center lymphoma registry**

Yeeun Choi[1], Sungho Bea[1], Ju Hwan Kim[1], Sang Eun Yoon[2], Won Seog Kim[2,3], Seok Jin Kim[2,3*], Ju-Young Shin[1,4,5]
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PP05-5 **The role of small bowel video capsule endoscopy in determining the treatment strategy for duodenal follicular lymphoma**

Gi June Min[1], Donghoon Kang[2], Tong Yoon Kim[3], Young-Woo Jeon[3], Yukyung Cho[2], Jae Myung Park[2], Joo Hyun O[4], Byung-Ock Choi[5], Gyeong-Sin Park[6], Seok-Goo Cho[1*]
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PP05-6

Mitigating cytokine release syndrome (CRS) in diffuse large B-cell lymphoma (DLBCL) with cycle 1 optimization: Preliminary results from EPCORE NHL-1

Won Seog Kim[1*], Julie M. Vose[2], Tatyana Feldman[3], Martine E.d. Chamuleau[4], Pieternella Lugtenburg[5], Pau Abrisqueta[6], Chan Y. Cheah[7], Ingrid Glimelius[8], Brian Hess[9], Wojciech Jurczak[10], Gerardo Musuraca[11], Adam J. Olszewski[12], Minh Dinh[13], Nurgul Kilavuz[14], Monica Wielgos-Bonvallet[14], Tommy Li[14], Zhu Li[14], Christian Eskelund[15], Umar Farooq[16], Tae Min Kim[17]

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PP05-7

Physician-reported treatment patterns and outcomes in marginal zone lymphoma in South Korea

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PP05-8

The long-term impact of rituximab-based chemoimmunotherapy in patients with DLBCL, real world outcomes using national health insurance database of South Korea

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PP05-9

Outcomes in refractory diffuse large B-cell lymphoma: Results from subgroup analysis of two prospective Korean cohort studies

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PP05-10

Trial in progress: A global phase 2 basket trial of nanatinostat in combination with valganciclovir in patients with EBV-positive (EBV+) relapsed/refractory lymphomas (NAVAL-1)

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PP05-11

Time to next treatment in patients with pre-treated cutaneous T-cell lymphoma receiving mogamulizumab or vorinostat: A MAVORIC post-hoc analysis

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PP05-12 **Characterization and outcomes in patients with mogamulizumab-associated skin reactions in the Mavoric trial**

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PP05-13 **Prognostic prediction of total metabolic tumor volume in lymphoma patients**

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PP05-14 **Treatment outcomes of aggressive B cell lymphoma: A single center review in Malaysia**

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PP05-15 **Prognostic role of 18F-FDG PET/CT in diagnosis and response evaluation of primary central nervous system lymphoma**

Hyungwoo Cho[1], Minyoung Oh[2], Ji Eun Park[3], Heounjeong Go[4], Chan Sik Park[4], Sang-Wook Lee[5], Sang Woo Song[6], Young Hyun Cho[6], Young-Hoon Kim[6], Seok Ho Hong[6], Jeong Hoon Kim[6], Dong Yun Lee[2], Jin-Sook Ryu[2], Dok Hyun Yoon[1*], Jae Seung Kim[2]
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PP05-16 **Association of interleukin-2 330 T/G gene polymorphism with the risk of non-Hodgkin lymphoma: A meta-analysis**

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PP05-17 **Nodal marginal zone lymphoma accompanied by in situ follicular neoplasia with t(14;18)(q32;q21)**

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PP05-18 **Clinicopathological and genetic landscape of plasmablastic lymphoma in Taiwan**

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PP05-19 **Report on initial results of treating diffuse large B-cell lymphoma with polatuzumab vedotin based regimen at Vinmec times city international hospital**

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PP05-20 **Emergence of EBV-positive diffuse large B-cell lymphoma five years later after a previous complete remission from EBV-positive classic Hodgkin lymphoma in an HIV-infected patient**

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PP05-21 **HIV-related lymphomas in Taiwan: A retrospective study of 63 cases showing a wide spectrum of histopathology**

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PP05-22 **Real-world experience with zanubrutinib treatment for patients with previously treated Waldenstrom macroglobulinemia**

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PP05-23 **Machine learning based prediction of 5-year survival outcome in patients with low grade B cell lymphoma**

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PP05-24 **Comparative analysis of the clinical outcomes and measurable residual disease in CLL patients treated with FCR chemoimmunotherapy followed by ibrutinib**

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PP05-25 **Challenges in overcoming advanced stage or relapsed refractory extra-nodal NK/T cell lymphoma, nasal type: Meta-analysis of individual patient data**

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PP05-26 **Epigenetic method for determining the subtype of mantle cell lymphoma**

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PP05-27 **Mutational profile of aggressive natural killer cell leukemia**

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PP05-28 **The role of hematopoietic stem cell transplantation in aggressive monomorphic epitheliotropic intestinal T-cell lymphoma**

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PP05-29 **Mosunetuzumab monotherapy continues to demonstrate durable responses in patients with relapsed and/or refractory follicular lymphoma after 2 prior therapies: 3-year follow-up from a pivotal phase II study**

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PP05-30 **Clinical profile and survival of non-Hodgkin lymphoma patients at tertiary hospital in Bali, Indonesia**

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PP05-31 **Double inhibition of EZH2 and EGFR/HER2: A new strategy for Burkitt lymphoma therapy**

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PP05-32 **Analysis of outcomes in patients with relapsed/refractory diffuse large B-cell lymphoma exhibiting CD20 loss**

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PP05-33 **The novel eIF4A inhibitor potently synergizes with BCL2 inhibitor in high grade B-cell lymphoma with MYC and BCL2 rearrangements through inhibition of UPR**

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PP05-34 **Clinical impact of sarcopenia for first-line chemotherapy in newly diagnosed NHL patients**

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PP06-1 **Decoding the genomic landscape of blastic plasmacytoid dendritic cell neoplasm (BPDCN): Insights into DNMT3A and TP53 mutations, MYC pathway activation, and therapeutic opportunitie**

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PP07-1 **Characteristics of regulatory T cell populations expressing checkpoint receptors PD-1 and TIM-3 in multiple myeloma patients**

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PP07-2 **Clinical characteristics of multiple myeloma at young age for early detection screening**

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PP07-3 **Longitudinal correlative profiles of responders, non-responders, and those with relapse on treatment with teclistamab in the MajesTEC-1 study**

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PP07-4 **JS-K, a nitric acid donor, mediated attenuation of autophagic flux alleviates multiple myeloma pathogenesis via induction of microRNA-144: A novel therapeutic approach**

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PP07-5 **Real-world effectiveness and safety of intravenous daratumumab in patients with multiple myeloma: A multi-center, observational study from Korea**

Youngil Koh[1], Sung-Soo Yoon[1], Je-Jung Lee[2], Kihyun Kim[3], Sung-Hoon Jung[2], Sung-Soo Park[4], Sang Eun Yoon[3], Youngju Park[5], Soomin Yoon[5], Chang-Ki Min[4*]
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PP07-6 **Enhancing the survival of patients with primary plasma cell leukemia and identification of prognostic factors: Insights from a comprehensive study (the KMMWP-2204 study)**

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PP07-7 **Fractures and mortality in multiple myeloma patients: A Korean population-based case-control study (the CAREMM-2105 study)**

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PP07-8 **Cardiovascular disease in long-term multiple myeloma survivors: A nationwide Korean case-control study (the CAREMM-2105 study)**

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PP07-9 **Favorable survival outcomes with delayed treatment in multiple myeloma patients with biochemical relapse**

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PP07-10 **The significance of galectin-3 level in plasma cell proliferations complicated by kidney damage**

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PP07-11 **A phase 3, two-stage, randomized study of mezigdomide, bortezomib, and dexamethasone (MeziVd) versus pomalidomide, bortezomib, and dexamethasone (PVd) in relapsed/refractory multiple myeloma (RRMM): SUCCESSOR-1**

Paul G. Richardson[1], Sorina N. Badelita[2], Britta Besemer[3], Jean-Samuel Boudreault[4], Ja Min Byun[5*], Claudio Cerchione[6], Moshe E. Gatt[7], Simon Gibbs[8], Junya Kuroda[9], Joaquin Martinez-Lopez[10], Chang-Ki Min[11], Robert Z. Orlowski[12], Hang Quach[13], Marc S. Raab[14], Katja Weisel[15], Xin Zhou[16], Michael Amatangelo[17], Yue Wang[17], Soo Jeong Hwang[17], Jessica Katz[17]

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PP07-12 **EXCALIBER-RRMM: A phase 3, 2-stage study of iberdomide, daratumumab, and dexamethasone (IberDd) versus daratumumab, bortezomib, and dexamethasone (DVd) in patients with relapsed/refractory multiple myeloma (RRMM)**

Sagar Lonial[1], Hang Quach[2], Meletios Dimopoulos[3], Paula Rodriguez Otero[4], Jesus Berdeja[5], Paul Richardson[6], Margee Kyada[7], Shuyu Chu[7], Min Chen[7], Patricia Abad[7], Juliane Morando[7], Kihyun Kim[9*], Niels Van De Donk[8]

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PP07-13 **Non-clinical test results of tetracyclic triterpene compound, a new effective drug candidate for multiple myeloma treatment**

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PP07-14 **Glutathione S-transferase M1 and T1 deletion mutation is associated with the risk of multiple myeloma development: A meta-analysis**

Arch Raphael Manalac[1*], Francheska Casupanan[1], Arlene Joy Canasa[1], Angela Mae Cuartelon[1], Justine Nicole Sison[1], Janina Carla Zapata[1], Raphael Enrique Tiongco[1]

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PP07-15 **MagnetisMM-3 trial: Updated long-term efficacy and safety of elranatamab in relapsed or refractory multiple myeloma**

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PP07-16 **Clinicopathological characteristics of monoclonal gammopathy of clinical significance in a single tertiary hospital**

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PP07-17 **Retrospective analysis of autologous stem cell transplantation treatment outcomes in patients with dialysis-dependent multiple myeloma (DDMM) : KMM2304 study**

Myung-Won Lee[1], Sung-Hoon Jung[2], Chang-Ki Min[3], Ho-Young Yhim[4], Dok Hyun Yoon[5], Sang Min Lee[6], Ho-Jin Shin[7], Jae-Cheol Jo[8], Jong-heon Jung[9], Yundeok Kim[10], Jae Hoon Lee[11], Ji Hyun Lee[12], Sunghyun Kim[12], Jieun Uhm[13], Kihyun Kim[14*]

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PP07-18 **Increase of regulatory T cells in multiple myeloma**

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PP07-19 **Distinct single-cell RNA sequencing-based transcriptional phenotype for AL amyloidosis**

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PP07-20 **Real-world outcomes of novel immunotherapy versus standard of care in patients with relapsed/refractory multiple myeloma (CAREMM-2305)**

Seung-Hwan Shin[1,6], Sung-Soo Park[2,6], Su-Ein Choi[3], Seung-Hoon Han[3], Jeong Yeon Lee[2,6], Seung-Ah Yahng[3,6], Young-Woo Jeon[4,6], Chang-Ki Min[2,6]

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PP07-21 **Exploration of clinical implication of circulating tumor DNA in multiple myeloma and its precursor diseases**

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PP08-1 **The TERT rs2736100 polymorphism as genetic predisposition of myeloproliferative neoplasms in Asian population: A systematic review and meta-analysis**

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PP08-2 **Molecular profile of myeloproliferative neoplasms**

Jiyeon Kim[1], Yu Jeong Choi[1], Haerim Chung[2], Hye Won Kook[2], Ji Eun Jang[2], Doh Yu Hwang[2], Seung-Tae Lee[1], Jong Rak Choi[1], June-Won Cheong[2], Saeam Shin[1*]

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PP08-3 **Targeting c-Abl in myeloproliferative neoplasms: Benzylisoquinoline derivatives and their inclusion complexes form by molecular docking/ ADMET profiles**

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PP08-4 **Combination of hydroxyurea and anagrelide as first-line treatment for patients with essential thrombocythemia**

Young Hoon Park[1*], Sewon Lee[1], Seonggyu Byeon[2], Hana Kim[2], Kyoo-Hyung Lee[1], Yeung-Chul Mun[1]

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PP08-5 **Risk of thrombosis, hemorrhage and leukemic transformation in patients with myeloproliferative neoplasms: A nationwide longitudinal cohort study**

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PP08-6 **Clinical features and outcomes of JAK2 unmutated erythrocytosis**

Jeong Suk Koh[1], Sora Kang[1], Myung-Won Lee[1], Hyewon Ryu[1], Ik-Chan Song[1], Hyo-Jin Lee[1], Hwan-Jung Yun[1], Deog-Yeon Jo[1*]

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PP08-7 **JAK2V617F, CALR and MPL mutation profiles in patients with myeloproliferative neoplasms, northeast Thailand**
Kanokon Chootawiriyasakul[1*], Chinadol Wanitpongpun[2], Prajuab Chaimanee[3], Pimjai Anata[3], Pinsuda Klangsang[1]
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PP08-8 **A pilot project to assess genotoxicity induced by hydroxyurea in patients with JAK2 positive polycythemia vera**
Senani Williams
Pathology, Faculty of Medicine, University of Kelaniya, Ragama, Sri Lanka

PP08-9 **Progression of carotid plaque burden in patients with polycythemia vera and essential thrombocythemia**
Seug Yun Yoon, Sun Young Jeong, Min-Young Lee, Kyoung Ha Kim, Namsu Lee, Jong-Ho Won[*]
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PP09-1 **Next generation sequencing is vital for accurate genotyping in inherited bone marrow failure syndromes**
Ganesh Kumar Viswanathan[1*], Jasmita Dass[1], Richa Chauhan[1], Rishi Dhawan[1], Mukul Aggarwal[1], Pradeep Kumar[1], Manoranjan Mahapatra[1]
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PP09-2 **The frequency of clonal T cells and its correlation with clinical and laboratory parameters in adult-onset aplastic anemia**
Sudhanshi Raina[1], Abhishek Asthul[1], Arihant Jain[1], Anand Balakrishnan[1], Praveen Sharma[1], Pramod Kumar[1], Prabhjot Kaur[1], Man Updesh Singh Sachdeva[1], Pankaj Malhotra[1], Alka Khadwal[1], Sreejesh Sreedharanunni[1*]
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PP09-3 **Establishing reference range for relative telomere length in normal Indian individuals**
Sudhanshi Raina[1*], Prabhjot Kaur[1], Pradeep Reddy[1], Shilpa Amatya[1], Anand N Balakrishna[1], Man Updesh Singh Sachdeva[1], Prateek Bhatia[1], Amita Trehan[1], Arihant Jain[1], Rekha Hans[1], Anup Ghosh[1], Pankaj Malhotra[1], Reena Das[1], Sreejesh Sreedharanunni[1]
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PP09-4 **Efficacy and safety of ATG + CsA + romiplostim for untreated aplastic anemia: A phase 2/3 clinical trial**
Jun Ho Jang [1], Masashi Sawa[2], Jong Wook Lee[3], Hirohito Yamazaki[4], Masahiro Kizaki[5], Yoshiaki Tomiyama[6], Koji Nagafuji[7], Kensuke Usuki[8], Jyh-Pyng Gau[9], Yasuyoshi Morita[10], Jih-Luh Tang[11], Hung Chang[12], Masayoshi Noshiro[13], Akira Matsuda[14], Keiya Ozawa[15], Kinuko Mitani[16], Yoshinobu Kanda[15], Jungah Hwang[17], Ki Hyon Kim[18], Shinji Nakoa[4*]
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PP09-5 **Efficacy and safety of romiplostim combined with cyclosporine A as a first-line treatment in patients with aplastic anemia: A phase 2/3 clinical trial**

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PP09-6 **Report of the first Delphi round of the ongoing Asian aplastic anemia recommendation development: An evidence- and opinion-based consensus**

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PP09-7 **Safety of SB12 (eculizumab biosimilar) in Asian and non-Asian patients with paroxysmal nocturnal hemoglobinuria: Subgroup analysis of a global phase III randomized controlled trial**

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PP10-1 **Red cell enzymopathies in Indians: Molecular specturm and diagnostic approach in unexplained hemolytic anemias**

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PP10-2 **Genotype analysis and clinical outcome in Indian patients with rare congenital anemias**

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PP10-3 **Molecular genetic spectrum of non-transfusion-dependent beta thalassemia: A study of primary and secondary phenotype modifiers in 258 north Indian cases**

Prashant Sharma[1*], Namrata Singh[1], Reena Das[1], Alka Rani Khadwal[2], Jasbir Kaur Hira[1], Sanjeev Chhabra[1], Amita Trehan[3], Richa Jain[3], Deepak Bansal[3], Pankaj Malhotra[2]

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PP10-4 **Blood count scattergrams are fingerprints of blood: Using AI to inform health status**

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PP10-5 **Evaluation of diagnostic utility of CD43 and CD200 in differentiating B-cell chronic lymphoproliferative disorders by flow cytometry**

Abhishek Purohit[1*], Gopal Krishana Bohra[2], Akanksha Garg[3], Parmod Kumar[3], Tejasvi Sharma[1], Shruti Vaswani[1], Sharumathi E[1]

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PP10-6 **Hit me, baby, one more time: The experience of learning phlebotomy using a hybrid-based approach**

Juan Pio Luis Bacani[1], Ryan Charles Bermas[1], Klouie Angeline Koh[1], Timotei James Morales[1], Christine Mae Naluz[1], Nicole Justine Padillo[1], Noel Mari Yamzon[1], Julie Ann Mercado[1*], Raphael Enrique Tiongco[1]

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PP10-7 **Low-cost LAMP-turbidimetric assay for detecting alpha(zero)-thalassemia (SEA deletion): Preventing and controlling Hb Bart's hydrops fetalis syndrome in Thailand**

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PP10-8 **Influencing of alpha-thalassemia-1 to HbE and HbA2 levels separated and quantified by capillary electrophoresis system in HbE heterozygotes: Simple and rapid screening using HbE levels alone**

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PP10-9 **Is digital morphology analyzer reliable for white blood cell differential in body fluids?: Performance assessment of sysmex DI-60**

Eunju Shin[1], Mina Hur[1*], Hanah Kim[1], Mi Hyun Hong[1], Hee-Won Moon[1], Yeo-Min Yun[1], Minjeong Nam[2], Seungho Lee[3]

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PP10-10 **Multiple primary cancers with hematologic malignancies and germline predisposition: A case series**

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PP10-11 **Development and clinical application of targeted NGS panels for hematological malignancies covering WHO/ICC 2022 guideline**

Young Eun Lee[1,4], Hye Ran Kim[3,4], Ha Jin Lim[1], Yong Jun Choi[1], Joo Heon Park[1], Hyun-Woo Choi[1], Hyun-Jung Choi[1], Seung-Jung Kee[1], Soo Hyun Kim[1], Jong Hee Shin[1], Myung Geun Shin[1,2,4*]

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PP10-12 **Parasite-derived particles: A new approach to diagnose malaria**
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PP10-14 **Automated blood cell counter-derived unghosted cells (UGC): Exploring a novel red cell research parameter for clinical insights and diagnostic significance in diverse clinico-pathological contexts**
Praveen Sharma[1*], Anita Giri[1], Prashant Sharma[1], Minakshi Gupta[1], Dikshat Gopal Gupta[2], Aashima Arora[4], Srinivasan Peyam[3], Alka Rani Khadwal[5], Reena Das[1]
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PP10-15 **Plasma soluble CSF1R is a promising prognostic indicator for pediatric Langerhans cell histiocytosis**
Ting Zhu[1,2,3,4], Chan-Juan Wang[2,3,4], Hong-Yun Lian[2,3,4], Hong-Hao Ma[2,3,4], Dong Wang[2,3,4], Tian-You Wang[2,3,4], Rui Zhang[2,3,4], Lei Cui[1,2,3,4], Zhi-Gang Li[1,2,3,4*]
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PP10-16 **Predictive value of the complete blood count in determining the length of hospital stay among Filipino patients with COVID-19: A single center study**
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PP10-17 **Unveiling the distinctive gene expression profile of Ph-like acute lymphoblastic leukemia**
Seoyoung Lim[1*], Yu Jeong Choi[2], Saeam Shin[2], Seung-Tae Lee[2], Jong Rak Choi[2]
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PP10-18 **Genetic differences in myelodysplastic syndrome and clonal cytopenia of undetermined significance**
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PP10-19 **Clinical and molecular spectrum of DDX41 variants in Korean patients with hematologic malignancies**
Boram Kim[1], Hee-Jin Kim[1], Chul Won Jung[2], Jun Ho Jang[2], Duck Cho[1], Sun-Hee Kim[1], Hyun-Young Kim[1*]
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PP10-20 **Clinical application of TRBC1 expression for diagnosis of T-cell lymphoma**
Sooho Yu[1], Boram Kim[1], Duck Cho[1], Hee-Jin Kim[1], Hyun-Young Kim[1*]
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PP10-21 **Hematological laboratory findings and its association with clinical spectrum of COVID-19 in pregnant women in Yogyakarta, Indonesia**
Isna Arifah Rahmawati[1*], Anita Rohmah[1,2]
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PP12-1 **Effect of omega 3 unsaturated fatty acid supplements on perioperative bleeding after spinal surgery**
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PP12-2 **Insulin resistance and increased risk of pulmonary embolism in leukemia, lymphomas and related disorders**
Javad Alizargar
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PP12-3 **Non-cirrhotic portal hypertension in a patient with essential thrombocythemia: A case report and literature review**
Novi Davitsen[1], Tohari Tohari[1*], Alfatea Rahmi[3], Shinta Wardhani[2]
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PP12-4 **Bernard Soulier syndrome caused by two novel heterozygous mutations in GP1BA gene: A case report and literature review**
Senlin Zhang[1], Jing Ling[1], Kai Cui[1], Junjie Fan[1], Shaoyan Hu[1*]
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PP12-5 **Paediatric thrombosis: A five-year experience from a tertiary care center of Pakistan**
Anila Rashid
Haematology, Aga Khan University Hospital, Karachi, Pakistan

PP12-6 **Cannabinoid receptor 2 signaling: Role in megakaryocyte development and neuro-immune regulation**
Ravi Kumar Gutti
Department of Biochemistry, University of Hyderabad, Hyderabad, India

PP12-7 **Plasma levels of three different types of direct oral anticoagulants measured with anti-factor Xa assay in patients with non-valvular atrial fibrillation: Comparison with heparin assays**
Suji Park[1], Min-Sun Kwak[1], Jae-Ryong Shim[1], Kwang-Sook Woo[1], Jong-Sung Park[2], Dae-Hyun Kim[3], Jin-Yeong Han[1*]
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PP12-8 **Evaluation of neutrophil extracellular traps as a novel circulating marker in acute ischemic stroke patients and the correlation with cytokines**
Suji Park[1], Jae-Ryong Shim[1], Dae Hyun Kim[2], Jin-Yeong Han[1*]
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PP12-9 **Thrombopoietin-independent generation of platelet-like particles from megakaryoblastic cells**
Duangdao Palasuwan[1*], Nuntiporn Nunthanasup[1], Nutpakal Ketprasit [1], Kasem Kulkeaw[2], Attakorn Palasuwan[1]
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PP12-10 **Evaluation of FVIII PK profile in Korean hemophilia a patients assessed with myPKFiT: A retrospective chart review**
Young Shil Park[1], Taiju Hwang[2], Sang Kyu Park[3], Ki-Young Yoo[4], Aeran Jung[5], Eun Jin Choi[6*]
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PP12-11 **Heparin-calibrated anti-factor Xa assay for the measurement of direct anticoagulant such as apixaban, rivaroxaban and edoxaban**
Hyunjung Kim[1*], Hyojin Chae[1], Yeongsic Kim[1], Hey Kyung Lee[1]
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PP12-12 **Beneficial role of moringa oleifera leaves extract in a rat model of deep vein thrombosis**
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PP12-13 **Acquired hemophilia A in an adult female without familial predisposition: A one-in-a-million rarity case report with review of the literature**

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PP12-14 **Treatment of bleeding episodes with efanesoctocog alfa in patients with severe haemophilia A in the phase 3 XTEND-1 study**

Angela C Weyand[1*], Sandrine Meunier[2], Kagehiro Amano[3], Linda Bystricka[4], Graham Neill[5], Lydia Abad-Franch[6], Annemieke Willemze[7], Alberto Tosetto[8], Sun A Lee[9]
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PP12-15 **Change in hemophilia joint health score (HJHS) during the phase 3 XTEND-1 study of efanesoctocog alfa in patients with severe hemophilia A**

Annette Von Drygalski[1*], Christoph Konigs[2], Chiai Nagae[3], Jennifer Dumont[4], Linda Bystricka[5], Annemieke Willemze[6], Elena Santagostino[7], Johannes Oldenburg[8], Sun A Lee[9]
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PP12-16 **Inflammation and hypercoagulability in type 2 diabetes mellitus with chronic kidney disease**

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PP12-17 **Diagnostic challenges and its clinical implications in women with inherited bleeding disorders**

Sehar Khaliq
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PP13-1 **The relationship between allogeneic hematopoietic stem cell transplantation recipients and COVID-19 vaccination: A literature review**

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PP13-2 **Risk factors for positive posttransplantation measurable residual disease in patients with acute lymphoblastic leukemia**

Yuewen Wang[1], Guomei Fu[1], Lanping Xu[1], Yu Wang[1], Yifei Cheng[1], Yuanyuan Zhang[1], Xiaohui Zhang[1], Yanrong Liu[1], Kaiyan Liu[1], Xiaojun Huang[1], Yingjun Chang[1*]
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PP13-3 **Effects of donor-specific anti-HLA antibodies(DSA) for primary graft failure of haploidentical hematopoietic stem cell transplantation in thalassemia major**
Jianyun Liao[1], Chaoke Bu[1], Lan He[1], Jujian He[1], Weiwei Zhang[1], Yuqian Xia[1], Yuelin He[1], Chunfu Li[1*]
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PP13-4 **Post-transplant complications revealed by mycophenolate mofetil related transporters and metabolic enzymes gene polymorphisms in pediatric patients with hematological disorders**
Qi Ji[1], Yixin Hu[1], Minyuan Liu[1], Lixia Liu[2], Jiayue Qin[2], Shaoyan Hu[1*]
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PP13-5 **Mesenchymal stem cells assisted successful treatment of pediatric patient with toxoplasma encephalitis after hematopoietic stem cell transplantation: A case report and literature review**
Qi Ji[1], Minyuan Liu[1], Hui Zhang[1], Shaoyan Hu[1*]
[1]*Hematology and Oncology, Children's Hospital of Soochow University, Suzhou, China*

PP13-6 **Avapritinib is effective and safe for preemptive treatment in pediatric acute myeloid leukemia with t(8;21) and KIT mutation after allogeneic hematopoietic stem cell transplantation**
Qingwei Wang[1], Li Gao[1], Senlin Zhang[1], Jun Lu[1], Bohan Li[1], Jie Li[1], Yanhua Yao[1], Yixin Hu[1], Peifang Xiao[1], Shaoyan Hu[1*]
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PP13-7 **Post-transplant serum ferritin level predicts severe acute graft-versus-host disease in umbilical cord blood transplantation for acute leukemia**
Zhiqi Zhang[1], Bohan Li[1], Lu Liu[1], Xiaohuan Du[1], Ruolan Xiong[1], Jie Li[1], Yanli Miao[1], Peifang Xiao[1], Shaoyan Hu[1*]
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PP13-8 **A prospective pilot study of graft-versus-host disease prophylaxis with postbiotics in allogeneic hematopoietic stem cell transplantation**
Seug Yun Yoon[1], Sun Young Jeong[1], Min-Young Lee[1], Kyoung Ha Kim[1], Namsu Lee[1], Jong-Ho Won[1*]
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PP13-9 **Efficiency of peripheral blood stem cell collection by Optia Spectra machine at hematologic department in Cho Ray Hospital**
Thao Nguyen Van[1], Nhu Cao Thi Bich[1*], Tung Tran Thanh[1], Cuong Bui Le[1], Dam Le Phuoc[1], Tung Nguyen Khac[1], Ut Nguyen Thi Be[1], San Le Thi[1], Anh Hoang Ngoc[1], Chau Le Thi Kim[1], Hanh Vo Thi Hong [1], Mai Nguyen Ngoc[1], Truc Tu Thi Thanh[1], Thoa Nguyen Thi[1]
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PP13-10 **Level of knowledge of Filipino nurses on care of patients undergoing hematopoietic stem cell transplant**
Cherry Ann Durante[1,2*], Raul Jr Durante[3]
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PP13-11 **The impact of cytomegalovirus reactivation on relapse in acute leukemia patients undergoing allogeneic stem cell transplantation**
Hyunkyung Park
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PP13-12 **The efficacy of haploid hematopoietic stem cell transplantation in the treatment of children with Diamond-Blackfan anemia**
Lu Liu[1], Bohan Li[1], Lin Wan[1], Qi Ji[1], Shaoyan Hu[1*]
[1]*Hematology and Oncology, Children's Hospital of Soochow University, Suzhou, China*

PP13-13 **Aerosolized pentamidine for pneumocystis jirovecii pneumonia prophylaxis in adult patients undergoing allogeneic hematopoietic cell transplantation**
Ga-Young Song[1], Mihee Kim[1], Seo-Yeon Ahn[1], Jae-Sook Ahn[1], Deok-Hwan Yang[1], Je-Jung Lee[1], Hyeoung-Joon Kim[1], Sung-Hoon Jung[1*]
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PP14-1 **Inflammation stimulates the stem system in a model of hematopoietic ectopic foci**
Dmitriy Karpenko[1*], Aleksei Bigildeev[1]
[1]*Laboratory of Epigenetic Regulation of Hematopoiesis, National Medical Research Center for Hematology, Moscow, Russian Federation*

PP14-2 **Administration of human tumor necrosis factor alpha to mice restores formation of ectopic foci of hematopoiesis lost by serial blood loss and results in the formation of foci of**
Aleksei Bigildeev[1*], Dmitriy Karpenko[1], Roman Mironov[2]
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[2]*Faculty of Biology, Department of Immunology, Lomonosov Moscow State University, Moscow, Russian Federation*

PP14-3 **Nes-GFP+ MSCs preserve functionality after bone marrow transplantation in a wild-type mice immunized vs-GFP**
Dmitriy Karpenko[1*], Nikolay Kapranov[2], Aleksei Bigildeev[1]
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PP14-4 **Thioredoxin-interacting protein regulates megakaryopoiesis and platelet counts**
Eunju Shin[1], Taeho Park[1,2], Ji-Yoon Noh[1,2*]
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[2]*Department of Functional Genomics, Korea University of Science & Technology, Daejeon, Republic of Korea*

PP14-5 **Understanding the role of hippo signaling pathway in hematopoiesis using hematopoietic-specific MST1/2 deficiency mice model**
Taeho Park[1,2], Inyoung Kim[3], So Hee Kim[1,2], Chuna Kim[1,2], Wantae Kim[3], Ji-Yoon Noh[1,2*]
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PP15-1 **Early intrathecal dexamethasone effectively alleviate immune effector cell-associated neurotoxicity syndrome**
Qi Ji[1], Yi Dong[1], Yongping Zhang[1], Xiaochen Wu[1], Zhenjiang Bai[2], Saihu Huang[2], Jian Pan[3], Shuiyan Wu[2], Jun Lu[1], Shaoyan Hu[1*]
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[3]*Institute of Pediatric Research, Children's Hospital of Soochow University, Suzhou, China*

PP15-2 **Non-viral engineering of off-the-shelf universal CAR T cells using CRISPR and transposons**
Jaitip Tipanee[1], Marinee Chuah[1], Thierry Vanden Driessche[1*]
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PP16-1 **Buffy coat pooled platelets: A cost-effective alternative to single donor apheresis platelets in hemato-oncology patients in Indian scenario - A randomized crossover trial**
Prateek Srivastava[1], Hari Krishan Dhawan[2*], Ratti Ram Sharma[2], Pankaj Malhotra[2], Shankar Prinja[2], Divjot Singh Lamba[2], Rekha Hans[2], Suchet Sachdev[2]
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PP16-2 **Strategies in blood supply management during the COVID-19 pandemic: Experiences of local blood bank managers**
Archie Policarpio[1,2], Raphael Enrique Tiongco[1,2*], Jennifer Santillan[1,3], Annalyn Navarro[1,2]
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PP16-3 **Blood supply in Central Luzon, Philippines in the context of the COVID-19 pandemic: A retrospective analysis**
Archie Policarpio[1,2], Raphael Enrique Tiongco[1,2*], Jennifer Santillan[1,3], Annalyn Navarro[1,2]
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PP16-4 **Motivators and barriers towards voluntary blood donation among Generation Z university students: Experience from a local higher education institution**
Engracia Arceo[1], Catherine Bacani[1], Miljun Catacata[1], Chastene Christopher Flake[1], Joey Kyle Mallari[1], Archie Policarpio[1], Madonna Sudio[1], Julie Ann Mercado[1*], Raphael Enrique Tiongco[1]
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PP16-5 **Suggestion for optimization of CD3+ T cell apheresis for CAR-T therapy: A retrospective analysis of parameters and predictive models**
Han Joo Kim[1], Kyong Suk Ryu[1], Dae-Hyun Ko[1*]
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PP16-7 **Serodetection of cytomegalovirus IgG antibody among blood donors: Preliminary findings from a teaching hospital in the Philippines**
Raphael Enrique Tiongco[1], Jharianne Javate[1], Gwyneth Magday[1], Erika Paniza[1], Patrick Pascual[1], Myka Santiago[1], Charis Yandan[1], Trisha Zapanta[1], Julie Ann Mercado[1*]
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PP16-8 **Educational outcomes and perceptional change of medical students after visiting blood donation centers**
Junseo Lee[1], Seryeong Kim[1*], Sun Young Jeong[2], Seug Yun Yoon[2], Namsu Lee[2], Jong Ho Won[2], Jeong Won Shin[3], Soon Hyo Kwon[2], Min-Young Lee[2], Kyoung Ha Kim[2]
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PP16-9 **Assessing centrifugal and membrane approaches in plasma exchange for kidney disease management: A comparative study**
Sindhu Bhargavi Akula[1], Divjot Singh Lamba[1*], Rekha Hans[1], Ratti Ram Sharma[1], Jasmine Sethi[1], Harbir Singh Kohli[1], Shankar Prinja[1]
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PP16-10 **Inconvinence and loss due to red cell transfusion dependence in patients with blood diseases and cancers: A patient-reported experience and outcomes study**
Eujin Na[1], Ja Min Byun[2], Dong-Yeop Shin[2], Youngil Koh[2], Inho Kim[2], Sung-Soo Yoon[2], Hye Yoon Park[3], Junshik Hong [2*]
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[3]*Department of Psychiatry, Seoul National University College of Medicine, Seoul, Republic of Korea*

PP16-11 **Temporal dynamics of platelet glycoprotein VI and reactive oxygen species: Insights from fresh and stored platelet concentrates**
Evana Kamarudin[1*], Razif Dasiman[1]
[1]*Medical Laboratory Technology, Universiti Teknologi MARA (UiTM), Puncak Alam, Selangor, Malaysia*

PP17-1 **How far we should care about education, wealth, and macroeconomic variables to prevent anemia prevalence among pregnant women?**
Ester Marnita Purba[1*], Rosinta Hotmaida P Purba[2], Ni Made Ratih Kusuma Dewi[3], Helen Try Juniasti[4]
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[3]*Economics, Astra Indonesia, Mataram, Indonesia*
[4]*Public Health, Cendrawasih University, Papua, Indonesia*

PP17-2 **V736A (rs855791) polymorphism in the TMPRSS6 gene is associated with iron deficiency anemia development in females: A meta-analysis**
Arch Raphael Manalac[1*], Francheska Casupanan[1], Arlene Joy Canasa[1], Angela Mae Cuartelon[1], Justine Nicole Sison[1], Janina Carla Zapata[1], Raphael Enrique Tiongco[1]
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POSTER LIST

PP17-3 **A meta-analysis on the association of gestational diabetes mellitus with tissue plasminogen activator**

Arch Raphael Manalac[1,2*], Henry Basilio[1,2], Glenford Monzon[1,2], Joyce Gomez[1,3], Justine Malonzo[1,4], Raphael Enrique Tiongco[1,2], Annalyn Navarro[1,2]

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[4]*Laboratory Department, Immaculate Concepcion Polyclinic and Hospital Inc., Tarlac City, Philippines*

PP17-4 **Association of temperature, rainfall, and humidity with the incidence of pregnancy-related anemia in Central Luzon, Philippines**

Miljun Catacata[1*], Ivy Cayabyab[1], Kristin Chernelle Dela Cruz[1], Mona Lisa Lacson[1,2], Arch Raphael Manalac[1], Julie Ann Mercado[1], Raphael Enrique Tiongco[1]

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PP17-5 **Diagnostic reliability of Mentzer index for beta-thalassemia trait: A systematic review and meta-analysis**

Jose Felipe Pajarillo[1,2], Daniel Frederick Mallari[1], Miljun Catacata[3*], Jay Andrea Vea Israel[4], Raphael Enrique Tiongco[1,3]

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PP17-6 **Hydroxyurea for improving leucocytosis with a splenectomized thalassemia patient in a resource limited setting**

Jungho Suh

Internal Medicine, Hebron Medical Center and KOICA, Phnom Penh, Cambodia

PP17-7 **Classification and prognostic stratification based on genomic features in myeloidysplastic neoplasms, myeloproliferative neoplasms and their overlapping conditions**

Jong-Mi Lee[1], Ginkyeng Lee[2], Byunggyu Bae[1], Yonggoo Kim[1], Myungshin Kim[1*]

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PP17-8 **Epidemiology and clinical aspects of hematology malignancies in Cote d'ivoire**

Boidy Kouakou[1*], Alexis D Silue[1], Ismael Kamara[1], Anicet Konan[1], Ruth Dieket[1], Clotaire D Nanho[1], Gustave K Koffi[1]

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PP17-9 **AI-powered precision: Elevating cell enumeration with innovative applications**

Kodchapan Junwong[1], Gunyarat Wongsa[1], Thanyaphon Sakhamula[1], Suthasinee Jitanun[3], Krai Dawtak[1,2], Nungruthai Nilsri[1,2*]

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[3]*Faculty of Sciences, Naresuan University, Phitsanulok, Thailand*

PP17-10 **Establishment of hereditary hemolytic anemia registry in Korea**

Hyoung Soo Choi[1*], Hee Won Chueh[2], Do Hyeon Lee[3], Ye Jee Shim[4], Hyery Kim[5], Hye Lim Jung[6], Namhee Kim[7], Sang Mee Hwang[8], Sang Hyuk Park[9], Ari Ahn[10], Myungshin Kim[10], Young Kyung Lee[11], Jin Yeong Han[12], Jung Ok Hah[13]

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POSTER LIST

PP17-11 **Pro-adrenomedullin and procalcitonin as biomarkers for predicting infections and response to antimicrobial therapy in febrile neutropenic children**

Jagdish Meena[1*], Harshita Makkar[1], Aditya Gupta[1], Ashutosh Halder[1], Rachna Seth[1]
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PP17-12 **Elevated IL-6 as a biomarker of immune reconstitution inflammatory syndrome in pediatric leukemia patients with invasive disseminated candidiasis**

Yoon Kyung Cho[1,2], Ye Ji Kim[1,2], Hyun Mi Kang[1,2], Jae Won Yoo[1], Jae Wook Lee[1], Nack-Gyun Chung[1], Dae Chul Jeong[1], Bin Cho[1*]
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PP17-13 **Unleashing the potential of exosomal MALAT1 lncRNA in liquid biopsy: A promising approach for wilms tumor**

Diwakar Sharma[1,3], Apoorv Singh[2], Christine Wilson[3], Priyanka Swaroop[2], Sachin Kumar[3], Devendra K. Yadav[2], Vishesh Jain[2], Sandeep Agarwala[2], Surender K. Sharawat[3], Mohammad Husain[1*]
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PP17-14 **Clinical characteristics and management outcomes of patients with tumors of the hematopoietic and lymphoid tissues at mittaphab hospital, Vientiane Capital, Lao PDR**

Phoutthasin Vongngakesone[1*], Phetsavanh Chanthavilay[1]
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PP18-1 **Do gender equality on mother bargaining power really matter on the prevalence of anemia among children?**

Rosinta Hotmaida P Purba[1*], Ni Made Ratih Kusuma Dewi[2], Ester Marnita Purba[3], Helen Try Juniasti[4]
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PP18-2 **Ginseng as an antidepressant to improve the quality of life in hematologic malignancies: A systematic review**

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PP18-3 **Long-term outcomes of coronavirus disease 2019 and risk factors for prolonged SARS-Cov-2 infection in lymphoma patients: Multicenter, retrospective cohort study**

Jung Ah Lee[1], Chang Hyup Kim[1], Min Han[1], Joon-Sup Yeom[1], Jun Yong Choi[1], Nam Su Ku[1], Su Jin Jeong[1], Jung Ho Kim[1], Jin Seok Kim[2], Haerim Chung[2], Hyunsoo Cho[2], Jin Young Ahn[1], Yu Ri Kim[3*]
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PP18-4 **Role of wearable technology and Geo-fencing device in management of physiological data and quality of life relation to myelodysplastic syndrome patients**

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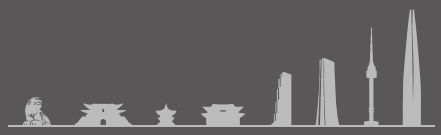

ICKSH 2024

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PLENARY LECTURE & PRESIDENTIAL SYMPOSIUM

PL01

Somatic mutations and clonal dynamics in human blood cells

Peter J. Campbell
Wellcome Sanger Institute, UK

All 40 trillion cells in an adult human can trace their lineage through a vast phylogenetic tree to the fertilised egg. Somatic mutations occur throughout development and adult tissue maintenance, with the individual cellular lineages on that tree acquiring new mutations at rates that are variable across tissue types. Every cell carries this mutational legacy written into its genome, whether it be a cell that founds a cancer, a cell that initiates a limb's development in embryogenesis, a stem cell responsible for tissue maintenance or a gamete that seeds the next generation. These mutations report the cellular dynamics of different organ systems, the mutagenic processes they are exposed to and the selective pressures that constrain cancer development. Directly studying somatic mutations in normal cells provides context to the patterns observed in cancer, enabling us to identify which processes are a general feature of that tissue type versus which are restricted to cancers. It also has the potential to reveal insights beyond cancer, including the contribution of somatic mutations to phenotypes of ageing, non-malignant disease processes and cellular dynamics in development and adult tissue maintenance.

PL02

How to win: Competitive strategies in the hematopoietic stem cell niche

Margaret Goodell

Baylor College of Medicine, USA

Clonal Hematopoiesis is the consequence of life-long competition among stem cells in the bone marrow, such that the progeny of "winning" stem cells become over-represented in the blood. Around 20 genes have been observed to be recurrently mutated among the winners, indicating that certain genetic variants confer a competitive advantage over many years. The mechanisms through which these variant stem cells triumph are generally poorly understood. Insights into successful strategies may have both prognostic and therapeutic value for CH-associated diseases including the development of hematologic malignancies.

The Goodell lab has studied the mechanisms through which variations in the function of DNMT3A, the most common driver of CH, promote winning, establishing the paradigm that enhanced self-renewal offers stem cells a profound advantage over many years. The lab has also studied the mechanisms of through which cells with PPM1D variants win, finding that a minor improvement in resistance to cell death makes stem cells victorious, at least in some contexts. Recently, the lab has considered intrinsic mechanisms that promote the advantage of additional variant genes, including the chromatin remodeler SRCAP. Surprisingly, all genes studied so far differ slightly in their potency, the molecular mechanisms that confer fitness, and the conditions under which they are most likely to "win". These mechanisms will be compared and discussed, in addition to the interplay between aging, clonal hematopoiesis, and leukemia development.

PS01

Lab-on-a-chip in hematology

Chong H. Ahn
University of Cincinnati, USA

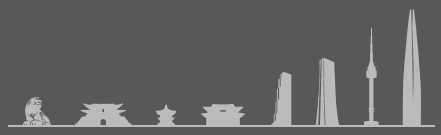
In recent years, tiny laboratories on a chip (Lab on a Chip, LOC), which can control or analyze a small volume of biochemical liquid sample or whole blood, have been newly developed on a polymer or glass chip. The LOC is usually composed of microchannels, microsensor and micro-reactors, thus it needs a small sample volume of around 1-100 uL and a short reaction time of 1-10 minutes, providing rapid sorting or analysis of the target molecules or cells in the sample.

Currently, the LOC has opened a new era for on-chip blood manipulation or analysis in a small volume, which includes on-chip blood test, blood/plasma separation, cell separation or sorting, analysis of circulation tumor cells (CTC) or immune cells, point-of-care test (POCT)for clinical diagnostics, and microfluidic flow cytometry.

In specific, the development of LOC as an integrated, automated, high-content hematology screening tool, which can perform sensitive bio-assays, is very desirable for the targeted anti-thrombotic and coagulation therapies, as well as for the reliable point-of-care clinical diagnostics. Our lab has developed a couple of on-chip blood/plasma separators which are integrated with a sample-to-answer LOC for the diagnosis of infectious or chronic diseases. The passive on-chip plasma separators offer a rapid extraction of plasma using capillary forces through the micro-channels or self-assembled bead columns embedded in a microfluidic platform.

A smart LOC for blood tests, on-chip blood/plasma separator, hematocrit sensor, and smartphone-based LOC for point-of-care test (POCT), which were developed in our lab, are presented in this talk. In addition, other LOCs or microfluidic devices developed for sorting cells in blood, separation of circulation tumor cells (CTC) or immune cells, and microfluidic flow cytometry are discussed.

The microfluidic LOC platforms and technologies can provide the innovative methods or tools desired for opening a new realm of hematology now and in the future.



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JOINT SYMPOSIUM

JS01-1

Prospective studies for NK/T-cell lymphoma in Asia

Seok Jin Kim

Sungkyunkwan University School of Medicine, Korea

Natural killer (NK)/T-cell lymphoma (NKTL) has been one of the main study topics of the Asian lymphoma study groups because NKTL is relatively more common in East Asian countries than Western countries. This disease entity is a rare but fatal subtype of non-Hodgkin lymphoma. The treatment outcomes for NKTL were improved by the development of non-anthracycline-based chemotherapy regimens incorporating etoposide and L-asparaginase. However, a substantial number of patients experience disease relapse or progression, and these patients have extremely poor survival outcomes. Thus, effective treatment strategies to prevent relapse are required. However, there is no consensus regarding the optimal therapy because there are little data about randomized studies. The novel agents with different mode of action such as immune checkpoint inhibitors could be used, but the efficacy of those drugs is still limited. Accordingly, prospective studies have been done to find more effective drugs and regimens for those patients with NKTL in Asia. This lecture summarizes recently reported prospective studies with novel agents for the treatment of NKTL.

Keywords: NK/T-cell lymphoma, Chemotherapy, Radiotherapy, Transplantation, Prognosis

JS01-2

Chronic active EBV disease: Our challenge to elucidate the pathogenesis

Ayako Arai

St. Marianna University School of Medicine, Japan

Chronic active Epstein-Barr virus disease (CAEBV) is a rare intractable disease that accompanies inflammation caused by persistent activation of EBV-infected T or NK cells and their clonal proliferation. The disease was officially defined as EBV-positive T- or NK-cell neoplasm in the WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues revised in 2017 (WHO 2017). The disease is classified into two subtypes: cutaneous CAEBV of which the lesion localizes on skin and systemic CAEBV which present systemic inflammation. Most patients had been reported from East Asia, but the number of reports from outside Asia has started to increase since the publication of WHO 2017.

To diagnose CAEBV, we must prove the infection of EBV in T or NK cells. Pathological diagnosis is not easy because the disease rarely forms solid tumors and frequently accompanies bleeding tendency due to thrombocytopenia, angiopathy, or disseminated intravascular coagulation. However, a method to separate lymphoid fractions from peripheral blood mononuclear cells followed by detecting EBV-DNA in each fraction enables the identification of EBV-infected cells easier and is now often used in the diagnosis of CAEBV.

Systemic CAEBV progresses to lethal course if not treated properly. It may result in hemophagocytic lymphohistiocytosis or treatment-resistant lymphoma. The only curative treatment strategy as of today is allogeneic hematopoietic stem cell transplantation (allo-HSCT). The three-year survival rate of allo-HSCT with non-myeloablative conditioning is approximately 70%. Disease activity of inflammation before the start of conditioning is a poor prognosis factor, and we need to develop a therapeutic drug to control disease activity and ultimately eliminate infected cells as soon as possible.

Almost all human adults on earth are infected by EBV, but it is not known why and how only certain people develop CAEBV. In recent years, attempts have been made to elucidate the pathogenesis of the disease from the perspective of viral and host factors. In this presentation, I would like to share with you the current results of our research.

JS01-3

NK Lymphoma Genomics: From Bench to Bedside

Weili Zhao

Ruijin Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, China

Natural-killer/T cell lymphoma (NKTCL) is the most common subtype of extranodal lymphoma with aggressive clinical behavior, which is prevalent in Asians and South Americans. System biology techniques provided novel insights into the pathogenesis, including molecular subtypes (TSIM, MB and HEA), immune subtypes (immune-inflamed, -deficient and -desert), EBV infection as well as immunometabolism features. With better understanding of its pathogenesis, clinical outcome of NKTCL patients has been significantly improved by asparaginase-based regimens and immune checkpoints inhibitors. Future investigations will be emphasized EBV-induced oncogenesis and targeted therapy to prevent tumorigenesis and cure relapsed/refractory patients.

JS02-1

Dynamic assessment of risk in multiple myeloma

Meral Beksac
Ankara Liv Hospital, Türkiye

Multiple myeloma is a biologically highly heterogeneous disease which is the underlying cause of major differences in clinical presentation and outcome. For decades multiple prognostic scores including ISS, R-ISS, R2-ISS, Mayo risk stratification or molecular expression profiling have identified standard or high risk subgroups. Widely applicable risk stratification tools are more informative if FISH or molecular profiles are integrated. The incidence or the predictive value the current staging systems are subject to the treatments patients receive. Furthermore current prognostication tools are not powerful for identifying high-risk, in particular functional high-risk patients—patients who do not necessarily display baseline high-risk features but typically show a suboptimal response to induction therapy or relapse early after treatment initiation. Such patients, display a particularly poor survival even in the context of novel therapies. Thus early recognition and management of this subset of patients, consitutes an unmet medical need. Current optimal myeloma treatment strategies requires risk stratification at diagnosis which will be summarized.

JS02-2

PET/CT for risk stratification in multiple myeloma

Joon Ho Moon
Kyungpook National University School of Medicine, Korea

JS02-3

Bone marrow inflammation in multiple myeloma

Tom Cupedo

Erasmus MC Cancer Center, The Netherlands

The non-malignant tumor microenvironment is an integral part of cancer pathobiology. Future development of successful anti-cancer therapies for currently incurable tumors will in part depend on our ability to unravel the biology of the malignant cells in the context of this nourishing environment. Multiple myeloma is a cancer of plasma cells that reside in the bone marrow, interacting with non-hematopoietic stromal cells and immune cells. Even though novel therapies have significantly increased progression-free survival, myeloma still is an incurable disease. We used single cell RNA-sequencing to transcriptionally define the stromal and immune microenvironments in the bone marrow of newly-diagnosed multiple myeloma patients. This led to the identification of inflammatory mesenchymal stromal cells, and their interaction with activated immune cells, as cornerstones of a tumor-supportive bone marrow environment that persists after successful first-line therapy. I will discuss the interplay between inflammatory stromal cells, the bone marrow immune system and multiple myeloma cells, with a focus on mechanistic understanding of tumor pathobiology and future clinical implications.

JS02-4

Single-cell analysis in multiple myeloma

Sung-Soo Park

College of Medicine, The Catholic University of Korea, Korea

Both the tumor and tumor microenvironment (TME) are crucial for pathogenesis and chemotherapy resistance in multiple myeloma (MM). Bortezomib, commonly used for MM treatment, works on both MM and TME cells, but innate and acquired resistance easily develop. By single-cell RNA sequencing (scRNA-seq), we investigated bone marrow aspirates of 18 treatment-naïve MM patients who later received bortezomib-based treatments. Twelve plasma and TME cell types and their subsets were identified. Suboptimal responders (SORs) to bortezomib exhibited higher copy number alteration burdens than optimal responders (ORs). Forty-four differentially expressed genes for SORs based on scRNA-seq data were further analyzed in an independent cohort of 90 treatment- naïve MMs, where 24 genes were validated. A combined model of three clinical variables (older age, low absolute lymphocyte count, and no autologous stem cell transplantation) and 24 genes was associated with bortezomib responsiveness and poor prognosis. In T cells, cytotoxic memory, proliferating, and dysfunctional subsets were significantly enriched in SORs. Moreover, we identified three monocyte subsets associated with bortezomib responsiveness and an MM-specific NK cell trajectory that ended with an MM-specific subset. scRNA-seq predicted the interaction of the GAS6-MERTK, ALCAM-CD6, and BAG6-NCR gene networks. Of note, tumor cells from ORs and SORs were the most prominent sources of ALCAM on effector T cells and BAG6 on NK cells, respectively. Our results indicate that the complicated compositional and molecular changes of both tumor and immune cells in the bone marrow (BM) milieu are important in the development and acquisition of resistance to bortezomib-based treatment of MM.

JS03-1

Pediatric and AYA ALL: Lessons learned from Children's Oncology Group clinical trials

Sarah K. Tasian

The Children's Hospital of Philadelphia, USA

Remarkable improvement in clinical outcomes for children and adolescents/young adults (AYAs) with acute lymphoblastic leukemia (ALL) has been achieved during the past 50 years with ten-year event-free and overall survival rates now exceeding 90%. These milestones have been facilitated via recognition of the central nervous system as a 'sanctuary site' requiring focused therapy, iterative testing of multi-agent chemotherapy regimens, advances in risk stratification based upon detailed genetic characterisation and therapeutic response assessment, intercalation of precision medicine therapies for biologically-relevant ALL subtypes, and improvements in supportive care measures. Collaborative clinical trials conducted by international pediatric oncology consortia have tested important hypotheses in their shared overarching goal of prioritizing development of most promising treatment strategies to increase cure rates and/or decrease toxicities, as well as potentially de-prioritize 'dead drugs.' This session will highlight recent achievements from the Children's Oncology Group and describe current therapeutic approaches for children and AYAs with newly-diagnosed T-ALL, newly-diagnosed B-ALL (including Ph+ and Ph-like), or relapsed B-ALL.

JS03-2

Multicenter trials investigating childhood acute lymphoblastic leukemia in South Korea

Hyery Kim
University of Ulsan College of Medicine, Korea

Acute Lymphoblastic Leukemia (ALL) is the most common cancer in children, representing a significant challenge in pediatric oncology worldwide. Recent advancements in the research and treatment of pediatric ALL have led to a notable increase in survival rates, largely attributed to innovative treatment protocols and multicenter clinical trials.

In this talk, an overview of the multicenter trials of ALL conducted in South Korea will be introduced, focusing on the evolution of treatment strategies and highlighting how collaborative efforts across various medical centers have contributed to optimizing protocols for ALL management in South Korea.

In Korea, medical expenses are covered through the National Health Insurance, in which over 97% of the population is enrolled. Consequently, there are limitations on medicine prescriptions and challenges in accessing clinical trials for new medications due to the unique medical environment. Therefore, a multicenter clinical study was mainly carried out to develop Korean standard guidelines for pediatric ALL based on the established protocols from major clinical working groups worldwide.

Since 2005, the pediatric acute lymphoblastic leukemia working group in Korea has undertaken collaborative efforts to find and apply the most optimal treatment approach on a nationwide level, with the aim of improving treatment outcomes for patients with high-risk, very high-risk, and relapsed ALL groups. The first multicenter prospective phase II trial was conducted in Korea from 2005 to 2014 with the objective of implementing the most efficacious treatment in three unique patient cohorts. Following that, a subsequent multicenter study was conducted from 2015 to 2018. The study sought to improve the survival rate by implementing additional treatment modifications into the protocol, as compared to the results of the original phase clinical trial. However, the first and second clinical trials were conducted only in three Korean hospitals, without the implementation of any protocols for the standard risk group or infant ALL. The third multicenter clinical trial was started in 2023, encompassing the involvement of five major hospitals in Korea. This study will include almost all cases of childhood ALL that occur in Korea, including cases classified as standard risk, high risk, very high risk, infant ALL, and relapsed ALL.

In addition to the regimen-based trials, a multicenter pharmacogenetic study was conducted between 2016 and 2019 to identify pharmacogenetic indicators specific to Koreans. As a result of the study, an initial dosage recommendation based on the pharmacogenetics of 6MP was implemented.

The measurement of minimal residual disease (MRD) is crucial in the treatment of childhood ALL. The next-generation sequencing-based MRD (NGS-MRD) test, implemented in Korea in 2020, has increased sensitivity and is better suited for nationwide multicenter studies. Starting in 2023, NGS-MRD testing in Korea has been expanded to encompass medical insurance coverage, enabling the implementation of a nationwide NGS-MRD-based guideline in the forthcoming trial.

The talk will also cover the current difficulties encountered in treating ALL in South Korea, including the handling of relapsed cases and the incorporation of innovative treatments into current protocols, with a focus on a multidisciplinary approach.

JS03-3

Dissecting the developmental origins of acute leukemia

Charles G. Mullighan

St. Jude Children's Research Hospital, USA

Genomic analysis has revolutionized our understanding of the biology of acute lymphoblastic leukemia, defining multiple new subtypes defined by distinct constellations of driver alterations, concomitant genetic alterations, and transcriptional profiles. Increasingly, these data are being incorporated into diagnostic, risk classification and treatment approaches. This talk will focus on two relatively neglected areas: acute leukemias of ambiguous lineage (ALAL), and T-lineage acute lymphoblastic leukemia (T-ALL). These subtypes have lagged behind discoveries in B-ALL and AML due to the lack of focused effort on cases that are difficult to classify, and/or the lack of genome-scale analysis approaches. Here we show that ALAL comprises diverse entities that include canonical subtypes of ALL as well as new entities that are often driven by deregulation of lineage or stage-inappropriate transcription factors in a subset of hematopoietic stem or progenitor cells. We have shown that with the deployment of large scale, integrated transcriptome and genome sequencing, childhood T-ALL may be classified into at least 15 types, with extensive heterogeneity within existing subtypes. Both these subtypes and subgroups therein have distinct biological, clinical and prognostic features. We show that there is interaction between genomic driver, cell of origin and concomitant genomic lesion in determining disease type and fate. These findings have profound implications for not only our understanding of disease ontogeny, but also clinical management.

JS03-4

Unveiling precision medicine: RNA and DNA sequencing in targeted therapy for Korean pediatric leukemia

Myungshin Kim

College of Medicine, The Catholic University of Korea, Korea

Precision application of risk-adapted and targeted therapies in pediatric leukemia necessitates swift and precise identification of the underlying genetic drivers and molecular subtypes. While chromosome analysis, fluorescence in situ hybridization, and reverse transcription PCR detect recurrent chromosome abnormalities, numerous genomic drivers remain undetectable through these means. Several novel genetic drivers have emerged through extensive genome and transcriptome profiling studies. Many of these drivers have already found their way into clinical practice, supported by robust data validating their diagnostic and prognostic significance.

RNA sequencing is a valuable tool for subtype determination through expression profiling and direct identification of oncogenic drivers, primarily fusion- and copy number changes. The integrated approach of utilizing both expression profiles and gene fusions from RNA sequencing enhances result confidence, potentially obviating the necessity for confirmation by separate assays. Additionally, mutation and copy number variations through DNA sequencing offer comprehensive genetic testing in leukemia.

In this talk, we are delving into the cutting-edge realm of precision medicine, utilizing RNA and DNA sequencing techniques to pave the way for targeted therapy advancements in Korean pediatric leukemia. I hope you explore the transformative potential of personalized treatment approaches in pediatric oncology.

JS04-1

The journey of bone marrow transplantation at BachMai General Hospital

Han Viet Trung
Bach Mai Hospital, Vietnam

Hematopoietic stem cell transplant (HSCT) is ofen the only curative option in many hematological malignant and nonmalignant conditions. HSCT was first described almost 70 years ago, and its use has expanded significantly over the last 30 years. Whereas HSCT has become the standard of care for many patients in developed countries, the significant economic investment, infrastructure, and health care provider training that are required to provide such a service have prohibited it from being widely adopted, particularly in developing countries. In VietNam, the first bone marrow transplant in Vietnam was performed in Blood Transfusion Hematology Hospital 1995, in BachMai General Hospital, we are learned experience from Japan and Ajou University Hospital, Suwon, Korea to setting up Hematopoietic stem cell transplant unit and was performed the first case in 2012. Over the past decade, we are performing more than 130 cases at our center, now we are performing 30-50 cases anually with excellent result.

JS04-2

Current situation of management of Non-Hodgkin lymphoma in the Republic of Armenia

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Armenian Hematology Association, Armenia

Background: Non-Hodgkin lymphoma (NHL) is a diverse group of blood cancers originating from lymphocytes, and its incidence and management have become a growing concern in the Republic of Armenia. This abstract provides an overview of the current landscape of NHL in Armenia, encompassing its prevalence, risk factors, diagnostic approaches, and treatment modalities. The Republic of Armenia, with its unique demographic and environmental factors, presents a distinct NHL profile within the larger context of global cancer epidemiology. The rising incidence of NHL in Armenia necessitates a comprehensive understanding of contributing factors, including genetic predisposition, infectious agents, and environmental exposures. The primary aim of this research was to comprehensively investigate the incidence patterns, diagnostics, treatment approaches, and mortality rates associated with Non-Hodgkin Lymphoma (NHL) in the Republic of Armenia. Methods: This retrospective cohort survey utilized data collected from multiple reliable sources, including ambulance cards, hospitalization journals, and clinical records sourced from the Registry of Blood Diseases at the Yeolyan Hematology and Oncology center. The study spanned from January 1, 2017, to December 31, 2022. The research encompassed a comprehensive analysis of the following key data points: age at diagnosis, gender, anatomical location, socioeconomic demographics, treatment protocols, side effects, viral characteristics and survival. Mortality data, including dates of death, were sourced from the United Information System of Electronic Healthcare in the Republic of Armenia to facilitate an analysis of survival. Results: The average annual incidence of Non-Hodgkin Lymphoma (NHL) in the Republic of Armenia during the period from 2017 to 2022 was 4.54 cases per 100.000 people. Comparing this data with earlier studies (1998-2004 and 1966-1971) revealed a significant increase in the NHL incidence rate, with a 1.5-fold and 4-fold rise, respectively. A notable surge was observed in 2019 compared to 2017, with rates of 5.9 cases per 100,000 people versus 3.3 cases per 100,000 people. The age-standardized risk of NHL was 4.8 among males and 3.9 among females. Incidence rates for both men and women were higher in the age group of 55 years and older. The analysis revealed that the proportion of Diffuse Large B-Cell Lymphoma (DLBCL) among NHL cases was 30%, with unclassified lymphomas accounting for 20-25%. Over a twelve-year period, 391 patients were diagnosed with DLBCL. The median age at the time of DLBCL diagnosis was 59.3 years (ranging from 21 to 82). Of these patients, 43.2% were female, and 68.5% were at stage IV of the disease. Thirty percent (118) of patients did not survive the study period. Of the 91 patients who received chemotherapy, 55.6% received rituximab-like therapy (R-CHOP or RB). Resistance to the first line of therapy was observed in 24.2% of patients, leading to their refusal of further treatment. In 23.1% of cases, it was not possible to determine remission or the cause of death. The study highlighted significant disparities in DLBCL treatment outcomes, particularly impacting patients in Armenia. These findings provide valuable insights into the changing epidemiological landscape of NHL in Armenia, specifically the notable increase in incidence rates. The focus on DLBCL survival and treatment underscores the challenges faced by patients and healthcare providers, emphasizing the need for further research and improved access to effective therapies. Conclusions: The results of this study reveal a concerning upward trend in Non-Hodgkin Lymphoma (NHL) incidence rates, with a several-fold increase observed during the analyzed period. Notably, risk factors include the male demographic and individuals aged 55 years and older. These findings underscore the urgency of targeted interventions and screening programs, particularly for these at-risk populations. One critical aspect highlighted in this research is the high rate of treatment refusal within the analyzed cohort, affecting 44.4% of all patients. This phenomenon is compounded by the fact that nearly half of these patients did not initiate any treatment. A significant contributor to these treatment refusals is the prevailing stigma surrounding cancer, leading to instances where patients remained unaware of their diagnosis, with treatment decisions being made by their relatives. Furthermore, financial and social factors played a substantial role in the high abandonment rates, reflecting the multifaceted challenges faced by patients in Armenia. These findings emphasize the urgent need for comprehensive healthcare interventions addressing not only medical aspects but also the socio-cultural and financial dimensions of NHL management. Reducing treatment refusal rates and improving access to care are critical steps in enhancing the overall prognosis and well-being of NHL patients in Armenia. As this research contributes valuable insights into the evolving landscape of NHL and its challenges in Armenia, it calls for collaborative efforts among healthcare providers, policymakers, and the broader communities to implement strategies that mitigate treatment barriers, reduce stigma, and ultimately improve the outcomes and quality of life for NHL patients in the Republic of Armenia.

Keywords: Non-Hodgkin lymphoma, Incidence rates, Causes of death, Rituximab-like therapy (R-CHOP or RB), Armenia

JS04-3

The evolution of hemophilia treatment in Thailand

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Hemophilia is an inherited bleeding disorder caused by deficiency of a specific coagulation factor. Efficient hemophilia care requires establishment and implementation of a well-coordinated plan guided by clearly defined principles and involvement of multiple stakeholders. Objectives: To gather insights about current diagnostic and treatment practices on hemophilia patients with the objective of understanding the clinical practices and limitations in Thailand. Findings: Nowadays, only 2166 Thai hemophiliacs have been registered to the national healthcare system which account for only 60% of expected cases. This underreport and underdiagnosis can be attributed to lack of appropriate facilities in smaller cities and rural areas. Most hemophilia cases are diagnosed by general practitioners, pediatricians or internists at rural hospitals and are referred to hemophilia specialists at the Hemophilia Treatment Centers (HTCs). The diagnosis is confirmed by factor assay along with prothrombin time (PT) and activated partial thromboplastin time (aPTT). Genetic testing was noted to be limited and available only at tertiary care centers. Once the diagnosis is confirmed, a prophylactic factor replacement therapy using clotting factor concentrates (CFCs) is generally offered, particularly for severe and moderate hemophiliacs with frequent bleeds. Recombinant and plasma-derived standard half-life (SHL) CFCs have been widely used in the country while the availability of extended half-life (EHL) CFCs is limited. Nevertheless, implementation of adequate prophylaxis remains a major challenge in Thailand due to a limited budget. A recent clinical study in Thailand using low-dose pharmacokinetics-guided EHL FVIII prophylaxis has shown benefits and practicability of this personalized regimen. The development of emicizumab over the past decade as non-factor replacement therapy for patients with hemophilia A (HA) has shown strong potential. Also, budget constraints are still a major limitation in the implementation of standard-dose emicizumab prophylaxis in real-world practice. Therefore, to be more economically compatible, the concept of reduced-dose or low-dose emicizumab prophylaxis has been introduced while the overall efficacy remains anticipated. Establishing accurate diagnosis and presence of inhibitors were additionally pointed as challenges. The National Hemophilia Foundation of Thailand, in cooperation with the Thai Hemophilia Patient Club, is actively promoting self-engagement and use of digital technology, i.e., smart watch monitoring to foster improvement of aerobic exercise capacity and muscle strength among Thai hemophiliacs. A study to evaluate the impact of increased physical activities monitored by these modalities during low-dose pharmacokinetics-guided EHL FVIII prophylaxis in Thai hemophiliacs showed improvements in clinical bleeding outcomes, quality of life and musculoskeletal status. Conclusion: Despite the challenges pertaining to infrastructure and cost of treatment, Thailand has progressed substantially over the past three decades in providing the ideal hemophilia care, as evidenced by an evolution in acquiring and sharing knowledge as well as collaborative efforts among multiple stakeholders.

Keywords: Hemophilia, Thailand, Coagulation factor, Clotting factor concentrates, Hemophilia A, Hemophilia B, Healthcare rationing

JS05-1

Epidemiology, risk stratification and treatment outcome in acute myeloid treatment: Taiwan experience

Hsin-An Hou

National Taiwan University, Taiwan

Acute myeloid leukemia (AML) is a heterogeneous clonal hematologic disease with great variability in the pathogenesis, clinical features and treatment outcome. It is the most common acute leukemia in adults with high mortality. In Taiwan, the revised WHO-2022 classification, International Consensus Classification and European LeukemiaNet (ELN)-2022 well risk stratify AML patients into distinct groups. The proposed refinement of ELN-2022 further improves risk stratification among AML patients. The population-based cohort study showed that there is an increased age-adjusted incidence of AML in past 20 years and the incidence increases with age with a median age at diagnosis of 60 years in Taiwan. Patients who were older, male, a prior cancer history and a higher Deyo-CCI score had a significantly higher risk of death. In contrast, patients with a higher socioeconomic status level and receiving treatment in a medical center had a lower risk of mortality than their respective counterparts. Since 2017 there has been an explosion of newly approved treatment options to tailor personalized treatment for AML. Although novel agents improve treatment outcome in adverse risk or unfit cohorts, high cost and limited availability of these compounds implement the barrier in clinical practice in Taiwan.

JS05-2

Advancement in leukaemia diagnostics: The role of next-generation sequencing (NGS) in acute myeloid leukaemia in Malaysia

Angeli Ambayya
Ministry of Health, Malaysia

Initially based on morphological evaluation, leukaemia diagnostics now revolunised into integrating multifaceted assays to fulfil the WHO classification and ELN prognostication systems. Over the last decade, next-generation sequencing (NGS) advancements have provided comprehensive insights into leukaemia's genomic and transcriptomic landscapes. The heterogeneity and complex molecular landscape of acute myeloid leukaemia (AML) explored using the NGS technology will be discussed in this talk. This study subjected a cohort of acute myeloid leukaemia-normal karyotype (AML-NK) patients to DNA and deep transcriptome sequencing to explore the underlying cryptic genomic abnormalities and their gene expression profiles. The AML-NK patients' DNA and transcriptome landscape were assessed at presentation and after completion of the chemotherapy regimen to assess their MRD profiles. Various customised bioinformatics pipelines and tools were utilised to elucidate the genetic profiles of AML-NK patients in this cohort. Ultimately, these findings have shed light on novel genomic aberrations and biomarkers that could be potential targets for prognostication and therapeutics in AML patients. As NGS technology is becoming increasingly available in Malaysia, the diagnosis, prognostication and treatment selection for AML are expected to significantly improve patient outcomes.

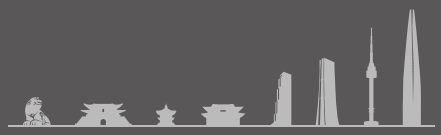
JS05-3

Determining fitness for treatments in older adults with AML

Byung Sik Cho

College of Medicine, The Catholic University of Korea, Korea

Acute myeloid leukemia (AML) is a disease of the elderly. Older adults with AML, usually defined as aged 60 years and older, have worse survival outcomes than younger AML patients due to their different biology, with more frequent unfavorable cytogenetics, a decline in performance status, and acquired comorbidities. Selected cases of older adults with AML can benefit from intensive chemotherapy despite the risk for increased toxicity from treatment. Combination therapy with hypomethylating agents and venetoclax has become the first recommended therapy in patients with AML unfit for intensive chemotherapy. Several prognostic models have been developed to identify patients at high risk of early death, treatment resistance, or poor survival after conventional intensive AML therapy. However, they were limited by low accuracy and the need for reassessment to reflect changes resulting from continuous improvement in supportive care. Chronological age, performance status, and comorbidities are employed commonly to determine fitness for intensive treatment. These variables are relatively easy to assess but are limited in capturing the heterogeneity of older patients with hematologic malignancies. Therefore, additional assessment tools are needed to better characterize fitness in the context of therapy and to capture the frailty. Among various frailty assessments, multi-parameter geriatric assessment (GA) offers more comprehensive evaluations, including functional ability, physical health, cognition, psychological health, nutritional status, and social support. Despite the growing evidence of GA to detect unrecognized vulnerabilities in patients with hematologic malignancies to predict treatment tolerance and survival, it is limited by lack of standardization and consensus regarding the prognostic value in older adults with AML. Today, I will discuss the latest advances in assessing the fitness of different treatment intensities using GA for older adults with AML. Validating fitness criteria would help guide treatment selection, supportive care interventions, fitness-based trials, interpreting trial outcomes, and facilitating drug labeling.



ICKSH 2024

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SCIENTIFIC SESSION

SS01-1

Elucidating the 3D chromatin landscape of pediatric B-cell acute lymphoblastic leukemia using Micro-C

Kajsa Paulsson
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Whereas the somatic genomics of childhood B-cell precursor (BCP) acute lymphoblastic leukemia (ALL) has been studied extensively, its 3D chromatin landscape remains poorly explored. Considering that chromatin architecture is directly involved in gene regulation, this is a hitherto untapped source of novel data for the development of targeted and personalized treatments. Micro-C, a variant of Hi-C, provides a high-resolution map of chromatin interactions at different levels, from A/B compartments and topologically associated domains (TADs) down to specific enhancer-promoter interactions that directly affect gene expression. Applying this technique to primary BCP ALL, we found substantial differences in chromatin interactions between genetic subtypes that explained differences in the expression of well-known leukemia-related genes such as FLT3 and IKZF1. BCP ALL with chromosomal gains, including the high hyperdiploid (51-67 chromosomes) subtype, had fewer TADs and weaker TAD boundaries, indicating that chromosomal copy number changes can affect chromatin organization, whereas ETV6::RUNX1-positive leukemias displayed a significantly higher proportion of the genome in the inactive B compartment. With single cell (sc) whole genome sequencing, scRNA-sequencing, scATAC-sequencing, and cytogenetic techniques, we further elucidate the differential chromatin landscape in pediatric BCP ALL and deepen our understanding of gene dysregulation in leukemogenesis.

SS01-2

Integrated RNA and protein profiling of B-cell acute lymphoblastic leukemia at single-cell level

Sungyoung Choi
Hanyang University College of Medicine, Korea

Simultaneous in situ detection of transcript and protein markers at single-cell level is essential for enhancing our comprehension of tumor heterogeneity and for predicting and monitoring treatment responses. However, the limited accessibility to advanced 3D imaging techniques has hindered its rapid implementation. In this study, we present a 3D amplified single-cell imaging technique that streamlines fluorescence signal detection from both individual protein and transcript markers at single-cell level with standard microscopy and off-the-self reagents. We validated the clinical utility of our technique by identifying BCR/ABL1 fusion transcript positive cells with or without CD19 protein expression, in patients with B-cell acute lymphoblastic leukemia. This result suggests that our method holds promise in supporting the prediction of responses to current standard CD19-directed therapies, such as blinatumomab or CAR-T cells.

SS01-3

Leveraging dysregulated signaling networks for therapeutic benefit in myeloproliferative neoplasm

Stephen T. Oh

Washington University School of Medicine, USA

Myeloid malignancies harbor distinct molecular drivers but share convergence of oncogenic signaling pathways and propagation by ripe pro-inflammatory niches. To delineate these hallmarks across the spectrum of myeloid disease states, we established the largest comprehensive atlas of myeloproliferative neoplasms (MPN) and secondary acute myeloid leukemia (sAML) through RNA-sequencing and mass cytometry (CyTOF) of 370 primary samples encompassing CD34+ hematopoietic stem/progenitor cells and CD14+ monocytes, revealing aberrant of PI3K/AKT/mTOR signaling and NFκB-mediated hyper-inflammation. As a central mediator of these hyperactive signaling pathways, ribosomal S6 kinases (RSKs) represent potentially attractive novel therapeutic targets warranting further evaluation.

Using both genetic approaches and a first-in-class oral RSK inhibitor, PMD-026, that is currently being evaluated in phase 1/1b clinical trials (NCT04115306) in breast cancer, we found that RSK1 (RPS6KA1) inhibition potently induced apoptosis and G2/M arrest in conjunction with suppression of PI3K/AKT/mTOR and NFκB signaling. Further NFκB cascade profiling following RSK1 perturbation revealed reduced phosphorylation of IKKα/β and p65/RELA and prevention of p65/RELA nuclear translocation. In cytokine CyTOF, PMD-026 nearly abrogated all induction of inflammatory cytokines including TNF, IL-6, IL-8, CCL3, and CCL4 in primary MPN monocytes to levels substantially below basal conditions.

Across in vivo models, PMD-026 ameliorated MPN disease features driven by MPL W515L including leukocytosis, splenomegaly, and bone marrow fibrosis, while prolonging survival, in conjunction with suppression of inflammatory cytokines including TNF, IL-6 and IL-1b. We then evaluated PMD-026 across multiple myelofibrosis (MF) and post-MPN sAML patient-derived xenograft (PDX) models encompassing various driver and multiple high-risk mutations. Treatment in PDX mice decelerated disease progression, extended survival, and reduced splenomegaly.

Taken together, our findings uncover a novel therapeutic avenue for a conserved RSK1 dependency in MPNs. The potent and consistent disease-ameliorating effects demonstrates promise for repurposing PMD-026 for the treatment of MPNs.

SS02-1

Molecular mechanism of primary TKI resistance in CML

Jerald Radich
Fred Hutchinson Cancer Center, USA

The advent of TKIs has radically changed the treatment of CML, with most patients treated in chronic phase enjoying a near normal lifespan. Early molecular response to TKI therapy is a very good predictor of long-term response, and thus, those patients with a poor early response are a population that might benefit from more frequent monitoring or changes in therapy, as they are more likely to have a suboptimal response and have a higher potential to evolution to advanced phase disease. Several lines of evidence suggest that 1) early response may be mediated by the immune system, and 2) molecular features of resistance overlap with those of progression. This talk will discuss these lines of evidence and offer some ideas for further study and treatments.

SS02-2

Targeting leukemic stem cells in CML

Mhairi Copland

University of Glasgow, UK

Chronic myeloid leukemia (CML) is a clonal myeloproliferative disorder, derived from a hematopoietic stem cell (HSC), which acquires the BCR::ABL1 fusion oncogene. Despite the success of tyrosine kinase inhibitors (TKIs) in treating CML, resulting in the majority of patients obtaining a major molecular response (MMR) on sustained therapy, there is strong evidence that these drugs are ineffective against the CML stem cell (LSC), leading to molecular disease persistence and recurrence, both on TKI therapy and after TKI cessation. TKI discontinuation studies, e.g. STIM, TWISTER and EUROSKI, demonstrate that less than 50% of optimally responding patients can safely stop their TKI without evidence of molecular recurrence.

Recent single-cell next generation sequencing studies have enabled elucidation of CML biology and cell interactions at an unprecedented level of detail; and have demonstrated that CML stem cells utilize multiple cell-intrinsic pathways, together with microenvironmental and immune cell interactions to evade current therapies. These studies highlight the heterogeneity of LSC in CML, and the differences in key pathways between normal HSC and LSC, including self-renewal, metabolism and autophagy, apoptosis, and interactions with the stem cell niche and immune system. Further specific clinically relevant targets, e.g. PPARγ, p53, c-MYC, BCL-2 and EZH2, have been identified on CML stem cells and therapeutic exploitation of these is likely to lead to improved therapies for patients with both chronic and blast phase CML in the future.

Overall, the long term goal is improved elimination of CML LSCs in both chronic and blast phase, leading to reduced resistance in blast phase and increased numbers of optimally responding chronic phase patients capable of permanently discontinuing TKI therapy – a further step on the pathway to cure for all CML patients.

SS02-3

The role of NGS to detect TKI resistance

Saeam Shin

Yonsei University College of Medicine, Korea

Chronic myeloid leukemia (CML) treatment outcome has significantly improved since the introduction of imatinib, a tyrosine kinase inhibitor (TKI). Imatinib showed good therapeutic response in most CML patients. Still, many patients in the accelerated and blast phases and some in the chronic phase do not respond to imatinib or show progression after response. Studies in CML and Ph-positive acute lymphoblastic leukemia patients resistant to imatinib reported that the change of a single amino acid by a mutation in the kinase domain site of the BCR::ABL1 fusion gene hinders the binding of imatinib and is the cause of the TKI resistance. Until now, the most widely used method to identify BCR::ABL1 mutations is direct sequencing. However, the limit of detection of the direct sequencing in the test method is 15~20%, which can be detected in the case with a high level of clonal mutations. Direct sequencing cannot detect low-level mutations or quantify the level of mutations. In addition, there is a limitation in distinguishing between compound mutations that cause multidrug resistance. Next-generation sequencing (NGS), which has recently been actively used in diagnostic areas, millions of sequence reads can be analyzed simultaneously, resulting in excellent sensitivity for detecting even low-level mutations. NGS can quantify the level of mutations so that the dynamics of resistance mutations during treatment can be tracked. In addition, NGS amplifies a single DNA molecule to obtain multiple sequence leads, making it easier to distinguish between compound and polyclonal mutation and possibly to reconstruct the tumor's clonal architecture. In this presentation, I would like to talk about the role of NGS in detecting TKI resistance mutations in CML patients.

SS03-1

Approaches to treat people with hemophilia: What's new and what's not?

Leonard A. Valentino

Rush University, USA

Hemophilia is due to the deficiency of thrombin generation[1] which leads to bleeding, oftentimes spontaneously and frequently into the joints and muscles causing pain, deformity and decreases in health-related quality of life[2, 3]. Preventation of bleeding by restoring the endogenous thrombin potential is the goal of modern hemophilia therapy[4]. This can be accomplished with replacement of the deficient coagulation factor VIII or IX administered as prophylaxis to prevent bleeding[5, 6] or with the use of newer agents which restore thrombin generation but do not replace the deficient FVIII or IX[7]. Irrespective of the modality chosen to prevent bleeding, assessment of thrombin generation is useful to guide therapy and optimize outcomes[8]. This presentation will review the approaches available to treat people with hemophilia and provide a perspective on the benefits and risks of newer agents that have or soon will be available in Korea.

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SS03-2

Prospects and challenges of gene therapy for hemophilia

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Christian Medical College, India

Hemophilia has been a good model for gene therapy given its easily identifiable monogenic pathology and remarkable improvement of bleeding profile even with modest elevation of circulating levels of clotting factor VIII or IX. Efforts initiated over two decades ago culminated in approval of two adeno associated virus (AAV) 5 vector-based liver directed gene therapy for hemophilia A and B in 2022. Several other AAV based gene therapy products targeting the hepatocyte are in advanced clinical trials. Within these successes their remain several challenges. Variable tropism of the different AAV vectors require high vector genome doses to achieve adequate gene transfer which often lead to immune responses causing transaminitis in a significant proportion of these patients associated with reduction or loss of expression of the transgene factor VIII / IX. This phenomenon is being managed through immunosuppression with different drugs with variable success. Two other challenges affect the utility of this approach. The first of these is the high prevalence of anti-AAV antibodies in the population ranging from 30-90% for the different AAV serotypes in different countries. There appears to be particularly high prevalence in countries with emerging economies. The other challenge is the current norm of offering this therapy only after the liver has reached near adult size by 12 years of age or older necessitating other effective modalities of treatment till then. This again becomes a major issue in countries with lack of access to good universal prophylaxis with hemostasis products.

Considering these limitations of the AAV vector-based approach to gene therapy for hemophilia, other strategies are also being explored. One of those is through lentiviral vectors – both in-vivo as well as ex-vivo gene transfers. The former has encouraging pre-clinical data from the IRCCS Ospedale San Raffaele in Milan, Italy but has not reached clinical trials yet. There are two ongoing clinical trials with the latter approach for hemophilia A. Both these products target the hematopoietic stem cells but with different end cells for expression. The clinical trial at the Medical College of Wisconsin, USA, targets the megakaryocytes with factor VIII expression being in platelets in people with hemophilia A with inhibitors. The first participant was treated more than a year ago and the clinical response is encouraging though being platelet targeted, FVIII levels cannot be measured in plasma. The second clinical trial with this approach is at the Christian Medical College, Vellore, India in collaboration with the Emory University, Atlanta, USA where expression is controlled by a CD68 promoter in an engineered transgene to allow efficient expression and secretion of F8. Clinically significant levels of circulating F8 have been documented in these patients. No major safety signals have emerged from either of these clinical trials. However, this ex-vivo approach requires harvesting of hematopoietic stem cells with ex-vivo manipulation for gene transfer and then an autologous stem cell transplantation. Though much more invasive, this has the advantage of allowing treatment of even very young children without any immunological barriers. Further studies are needed to evaluate their safety and efficacy.

It should be noted that the last decade as seen tremendous advances in treatment product options for hemophilia with many new advanced extended half-life factor concentrates as well novel non-factor hemostasis products which have enhanced protection from bleeding and significantly reduced treatment burden. Gene therapy will need to compete with these options. Regardless, these are exciting times for treatment of hemophilia with increasing options of products to choose from.

SS03-3

Exploring personalized tailored hemophilia treatment: Tailoring treatment to individual needs

Jeong A Park

Inha University College of Medicine, Korea

Hemophilia management has traditionally focused on preventing and controlling bleeding episodes through standardized prophylaxis and acute care approaches. Recent years have seen a paradigm shift towards personalized medicine, leveraging advancements in genetic testing, pharmacogenomics, and pharmacokinetics to tailor treatment to individual patient needs. With the rapid advancement of medical technologies, the landscape of hemophilia treatment has been dramatically and significantly broadening the array of therapeutic options available to patients. This evolution has paved the way for implementing personalized medicine strategies, which now extend beyond traditional treatments to include extended half-life (EHL) factor VIII and factor IX concentrates, factor VIII-mimicking monoclonal antibodies, agents that rebalance coagulation, and the promising horizon of gene therapy. These innovations not only offer more flexible treatment schedules but also aim to enhance overall patient well-being by maintaining increased trough levels and reducing the frequency of bleeding episodes. However, it remains uncertain which patients will derive the greatest benefit from these new treatment options, as long-term data are still limited. Additionally, it is still unclear how to effectively combine genetic data, pharmacogenetic insights, and pharmacokinetic profiles to optimize personalized prophylaxis in hemophilia treatment. This review explores the integration of these advanced diagnostic and therapeutic options within the framework of personalized medicine, highlighting their potential to tailor treatment plans to the individual characteristics and needs. By reviewing the latest research and clinical trial outcomes, we will assess the impact of these advancements on patient care, discuss the challenges and considerations in their application, and envisage the future directions of hemophilia management.

SS04-1

CD7 CAR-T therapy for treating hematological malignancies

Peihua Lu

Lu Daopei Hospital, China

In this representation, we will focus on CD7 CAR-T (NS7CAR-T)for treating refractory and relapsed (R/R) T-ALL/LBL (phase I/II clinical trials) and AML (phase I clinical trial).

We have developed a novel fratricide-resistant approach to derive "naturally selected" anti-CD7 CAR (NS7CAR)-T cells using lentiviral transduction of peripheral T-cells that could overcome CD7-directed fratricide without additional genetic modifications. NS7CAR-T cells remain CD7-positive but the number of available surface CD7 antigens is minimized via CAR-mediated CD7 epitope masking or by intracellular sequestration of the CD7 protein, thus precluding major fratricide.

CD7 CAR-T for treating R/R T-ALL/LBL

While the use of chimeric antigen receptor T (CAR-T) therapy in treating T-cell malignancies is still in the early-stage of clinical trials, it exhibits substantial potential and possibly offering long-term remission for patients with refractory/relapsed (R/R) T-cell malignancies, who generally have very limited effective treatment options.

A phase I/II clinical trial was conducted and enrolled pediatric and adult patients with R/R T-cell acute lymphoblastic leukemia and lymphoblastic lymphoma (T-ALL/LBL). (NCT04572308 & NCT04916860). Patients received one single dose of naturally selected anti-CD7 CAR (NS7CAR) T cells at three levels: a low dose (5×10^5/kg), a medium dose (1 to 1.5×10^6/kg), and a high dose (2×10^6/kg). Sixty patients received NS7CAR-T cell infusion. Post therapy, 94.4% of patients achieved deep CR within their bone marrow. Among the 32 patients presenting with extramedullary disease (EMD), 78% showed response, with 56% in CR and 22% in partial response. The median follow-up time was 368.5 days (range: 23-833). The 2-year OS and PFS were 63.5% (95%CI 47.7-79.4) and 53.7% (95%CI, 38.9-68.6), respectively with no significant discrepancies between pediatric and adult patients or across the varied dosage range. For the 47 CR patients, the PFS was significantly higher among the 37 patients who proceeded with consolidation allo-HSCT than the 10 patients who did not with 1-year PFS 67.2% (95%CI 51.9-82.4) vs. 15.0% (95%CI 0-40.2), $p<0.0001$. Of the 10 CR patients without consolidation transplants, 8 relapsed within 150 days, while 2 sustained their CR on day 128, and day 180, respectively. Cytokine release syndrome occurred in 91.7% of patients (grade 1/2 in 80.0%, grade 3/4 in 11.7%) and 5% of patients had neurotoxicity. NS7CAR-T therapy is effective in treating R/R T-ALL/LBL patients with promising long-term outcomes while maintaining a manageable safety profile.

CD7 CAR-T for treating R/R AML

R/R acute myeloid leukemia (AML) is associated with a relatively poor prognosis. Approximately 30% of AML patients express CD7 on their leukemic blasts and malignant progenitor cells. In a phase I clinical study (https://clinicaltrials.gov NCT04938115), we investigated the safety and efficacy of CAR-T therapy for treating CD7-positive AML patients. Between June 2021 and January 2023, we enrolled 12 patients with CD7-positive r/r AML and 10 patients were administered NS7CAR-T cell infusions, with 4 receiving dose level 1 (5×10^5/kg) and 6 receiving dose level 2 (1×10^6/kg). Before enrollment, patients had undergone a median of 8 (range: 3-17) prior lines of therapy. Seven patients had a history of transplant. At four weeks post NS7CAR-T cell infusion, 7/10 (70%) patients achieved complete remission (CR) in BM, and 6 of them attained minimal residual disease (MRD)-negative CR. Three patients showed no remission (NR), including 1 with EMD who had partial remission (PR) based on PET-CT evaluation on Day 35. The median observation time was 178 days (28-776 days). Among the 7 patients who achieved CR, 3 who relapsed from prior transplants underwent consolidative 2nd allo-HSCT about 2 months after CD7 CAR T-cell infusion. One patient remained leukemia-free survival on day 401, while 2 patients died on day 241 and day 776, respectively from transplant-related mortality. Among the other 4 patients without consolidative allo-HSCT, 3 relapsed on day 47, day 83, and day 89, respectively, and 1 patient died from lung infection. All the NR and relapsed patients were found CD7 loss. Post-infusion, the majority of patients (80%) experienced mild cytokine release syndrome (CRS), with 7 displaying grade I and 1 having grade II CRS, while 2 patients (20%) experienced grade III CRS. None of the patients had neurotoxicity. Our study highlights the NS7CAR-T therapy as a promising approach for achieving a favorable initial CR in CD7-positive AML patients, even in those who have undergone extensive prior treatments and experienced relapse post-transplant. The safety profile of NS7CAR-T therapy was manageable.

SS04-2

Development of a novel anti-CD19 CAR-T cells in B cell lymphoma

Dok Hyun Yoon

University of Ulsan College of Medicine, Korea

CAR T-cell therapy, an innovative cellular immunotherapy, signifies the intersection of genetic engineering, immunology, and cell biology. This approach has transformed the management of B-cell malignancies, achieving unprecedented response rates. Notably, four CD19 CAR T-cell therapies—tisagenlecleucel, axicabtagene ciloleucel, brexucabtagene autoleucel, and lisocabtagene maraleucel—have secured approval in the United States and the European Union, with tisagenlecleucel standing as the exclusive agent reimbursed in Korea. Despite its success, a subset of patients remain refractory or experiences relapse following CAR T-cell therapy, attributed to challenges such as antigen escape or tumor-mediated mechanisms impeding the local immune cell activity of CAR-T cells. Furthermore, the logistical intricacies and elevated costs associated with CAR T-cell therapy present additional hurdles. To surmount these limitations, novel CAR T-cell approaches are under exploration in Korea, encompassing gene silencing to downregulate checkpoint inhibitory molecules, a pioneering novel non-FMC63-based humanized CD19 scFv, bispecific CAR T-cell therapy, and groundbreaking transmembrane domains. This presentation will delve into these advancements and assess their potential impact.

SS04-3

CAR-T cells for treatment of T cell malignancies

Paul M. Maciocia

Cancer Research UK, UK

The introduction of CAR-T cell therapy has revolutionised the care of patients with relapsed and refractory B cell malignancies. Due to a lack of tumour-specific molecules, pan-B cell antigens are targeted. However, application of CAR-T to T cell malignancies is more challenging. Targeting a pan-T cell antigen such as CD4, CD5 or CD7 could lead to two main problems: loss of essential normal T cells and self-kill 'fratricide' of CAR-T. While B cell aplasia is well tolerated, T cell aplasia is highly immunosuppressive. Further, complex manufacturing strategies to prevent CAR-T fratricide by preventing target expression may be required. Some tumour-selective approaches have also been proposed (eg TRBC1, CD30 for T cell lymphoma; CD1a, CCR9 for T acute lymphoblastic leukaemia). Multiple approaches are now being tested in clinic, with highly promising data in T-ALL using anti-CD7 CAR-T. In this talk I will review progress in this new avenue for cellular therapies

SS05-1

Navigating cancer complexities via single-cell omics and AI

Manoj Bhasin
Emory University, USA

Single-cell and spatial profiling assists in unraveling the leukemia heterogeneity to better understand disease progression, outcomes, and novel targets. In this presentation, I will delve into our efforts to comprehensively map the heterogeneity of hematological cancers in both adult and pediatric populations using single-cell profiling. Our goal is to elucidate the intricate interplay between tumor characteristics and the tumor microenvironment, shedding light on their associations with adverse clinical outcomes. I will also discuss the development of a new pediatric single-cell atlas for exploring single-cell data related to pediatric cancers followed by the identification of a novel target for identifying and treating aggressive pediatric AML.

SS05-2

Targeting the developmental heterogeneity of human acute myeloid leukemia

Shanshan Pei

Zhejiang University, China

Single-cell multi-omic studies have clearly revealed the complex developmental heterogeneity of human acute myeloid leukemia (AML), posing immediate challenges to the development of molecular and cellular targeted therapies. Our understanding of the origin of developmental heterogeneity as well as the invention of targeting strategies however are significantly lacking. Our group at Zhejiang University along with Dr. Craig Jordan's group at University of Colorado have been focusing on the biological basis and therapeutic targeting of AML heterogeneity in recent years. Through analyzing AML patients treated with small molecule BCL-2 inhibitor venetoclax, we surprisingly uncovered a previously unrecognized form of pathogenesis characterized by monocytic disease progression. We demonstrate that this form of disease arises from a fundamentally different type of leukemia stem cell (LSC), which we designate as monocytic LSC (m-LSC), that is developmentally and clinically distinct from the more well- described primitive LSC (p-LSC). The m-LSC is distinguished by a unique immunophenotype, distinct transcriptional state, reliance on purine metabolism, and selective sensitivity to cladribine. Critically, in some instances, m-LSC and p-LSC subtypes can co-reside in the same patient with AML and simultaneously contribute to intra-patient heterogeneity, while in other cases, they exist independently in different patients, producing inter-patient heterogeneity. Simultaneous use of p-LSC targeting venetoclax combined with m-LSC targeting cladribine can eradicate disease subpopulations at different developmental stages, resulting in a deeper cure of disease. Thus, our findings demonstrate that the heterogeneity of human AML is rooted at the stem cell level and has direct clinical significance. We postulate that the development of the next generation of precision medicine for AML requires careful dissection of human AML heterogeneity at the LSC level and discovery of combinatory therapies tailored to eradicate varying LSC subtypes.

SS05-3

Mutational profile in Korean AML patients

Jae-Sook Ahn

Chonnam National University Medical School, Korea

Acute myeloid leukemia remains challenging hematologic malignancy due to its molecular heterogeneity. Understanding the unique mutational pattern within different patient populations is crucial for developing personalized treatment strategies. To gain this insight, we conducted retrospectively multicenter studies specifically targeting AML patients. Though these efforts, we unveiled the mutational profile prevalent this cohort.

Today, in this talk, my focus will be on the Korean dataset obtained from a recent multicenter, prospective study (KCT0004825). This study not only explores the intricate mutational patterns but also seeks to prospectively analyze and comprehend their dynamic impact on treatment responses and patient outcomes within the Korean AML population. By focusing on this dataset, I aim to emphasize the significant implications of these mutational profiles on crafting more precise and effective therapeutic approaches tailored to this specific demographic.

SS06-1

Germinal center in the genesis of lymphomas

Laura Pasqualucci
Columbia University, USA

SS06-2

Genomics of follicular lymphoma: Clinical implications?

Robert Kridel

University Health Network, Canada

Follicular lymphoma (FL) is the most common indolent non-Hodgkin lymphoma. It is generally characterized by a slowly progressive course with a continual remitting and relapsing disease cycle, typically persisting as a largely incurable malignancy.

The underlying molecular diversity of FL has not been as clearly conceptualized as in diffuse large B-cell lymphoma where cell-of-origin and genetic subtypes are becoming increasingly established for clinical decision-making. Recent studies have sought to understand the inter-patient heterogeneity in FL and the variability of responses to chemotherapy and targeted therapies. I will review novel insights into molecular clusters of FL that potentially identify patients with diverging clinical trajectories.

The targeting of the histone methyltransferase EZH2 is of interest as EZH2 gain-of-function mutations are observed in approximately 20% of patients. Consequently, inhibiting EZH2 has demonstrated efficacy, particularly in cases where these mutations are present. An underappreciated aspect is that EZH2 mutations are also associated with preferential response to chemotherapy. I will discuss recent studies that propose potential benefits in tailoring chemotherapy selection based on EZH2 mutation status.

While most FL patients have favourable outcomes, around 20% experience early progression or transformation, increasing the risk of lymphoma-related mortality. Understanding the molecular basis of early disease progression and histological transformation is crucial for predicting patient outcomes. This knowledge might lead to tailored therapeutic approaches based on risk assessment and specific pathobiological factors. Therefore, I will also focus on our current understanding of tumour evolution in FL and its association with disease progression and transformation.

SS06-3

Distinct and overlapping features of nodal peripheral T-cell lymphomas exhibiting a follicular helper T-cell phenotype: A multicenter study emphasizing the clinico-pathological significance of follicular helper T-cell marker expression

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SS06-3

Nodal peripheral T-cell lymphoma (PTCL) is a heterogeneous category including angioimmunoblastic T-cell lymphoma (AITL), PTCL of follicular helper T-cell (Tfh) phenotype (PTCL-Tfh), and PTCL, not otherwise specified (PTCL-NOS). We explored Tfh marker profiles in nodal PTCL. Nodal PTCLs (n = 129) were reclassified into AITL (58%; 75/129), PTCL-Tfh (26%; 34/129), and PTCL-NOS (16%; 20/129). Histologically, clear cell clusters, high endothelial venules, follicular dendritic cell proliferation, EBV+ cells, and Hodgkin-Reed-Sternberg (HRS)-like cells were more common in AITL than PTCL-Tfh (HRS-like cells, P = .005; otherwise, P < .001) and PTCL-NOS (HRS-like cells, P = .028; otherwise, P < .001). PTCL-NOS had a higher Ki-67 index than AITL (P = .001) and PTCL-Tfh (P = .002). Clinically, AITL had frequent B symptoms (versus PTCL-Tfh, P = .010), while PTCL-NOS exhibited low stage (versus AITL + PTCL-Tfh, P = .036). Positive Tfh markers were greater in AITL (3.5 ± 1.1) than PTCL-Tfh (2.9 ± 0.9; P = .006) and PTCL-NOS (0.5 ± 0.5; P < .001). Tfh markers showed close correlations among them and AITL-defining histology. By clustering analysis, AITL and PTCL-NOS were relatively exclusively clustered, while PTCL-Tfh overlapped with them. Survival was not different among the PTCL entities. By Cox regression, sex and ECOG performance status (PS) independently predicted shorter progression-free survival in the whole cohort (male, P = .001, HR = 2.5; PS ≥ 2, P = .010, HR = 1.9) and in 'Tfh-lymphomas' (ie, AITL + PTCL-Tfh) (male, P = .001, HR = 2.6; PS ≥ 2, P = .016, HR = 2.1), while only PS predicted shorter overall survival (OS) in the whole cohort (P = .012, HR = 2.7) and in 'Tfh-lymphomas' (P = .001; HR = 3.2). ICOS predicted favorable OS in 'Tfh-lymphomas' (log-rank; P = .016). Despite the overlapping features, nodal PTCL entities could be characterized by Tfh markers revealing clinicopathologic implications.

Keywords: Angioimmunoblastic T-cell lymphoma; Follicular helper T-cell; Peripheral T-cell lymphoma of follicular helper T-cell phenotype; Peripheral T-cell lymphoma, Not otherwise specified.

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SS07-1

Molecular alterations and clinical implications in MDS

Yasushi Miyazaki

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Myelodysplastic syndromes (MDS) is a group of clonal diseases which show ineffective hematopoiesis, dysplasia of hematopoietic cells, and tendency of leukemia transformation. Genome alterations accumulated in hematopoietic stem cells (HSC) / progenitor cells play important roles for the development of MDS. Several extrinsic factors are clearly shown as risk of MDS through epidemiological studies: benzene, chemotherapeutic agents, and Atomic bomb radiation. MDS caused by chemotherapeutic agents, called therapy-related MDS, seems to have different clinical and pathological features than de novo MDS in which aging is a major factor for its development. We analyzed MDS among A-bomb survivors to understand its clinical and etiological features, and found that it showed different clinical features, cytogenetic abnormalities, and genome alterations from those of de novo and therapy-related MDS. It is suggested that MDS among survivors has developed through unique steps of genome alterations.

Genetic alterations in MDS are important markers for the prediction of treatment response, and survival of patients. Recently, Molecular International Prognostic Scoring System (IPSS-M) was published, demonstrating the prognostic importance of genome alterations. We examined genome alterations before and after azacitidine treatment for higher-risk MDS, and found that the change in clone size can be a new marker for the prognosis of these patients.

Genome alterations are important information for etiology, clinical course, and treatment response and prognosis for MDS.

SS07-2

Recent advances and future therapeutic strategies in MDS

Guillermo Garcia-Manero
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SS07-3

Current diagnostic challenges in MDS

In-Suk Kim
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Myelodysplastic Syndromes (MDS) encompass a heterogeneous group of clonal hematopoietic disorders characterized by ineffective hematopoiesis, cytopenias, and an increased risk of progression to acute myeloid leukemia (AML). Over the years, advancements in molecular and cytogenetic technologies have significantly improved our understanding of MDS, yet several diagnostic challenges persist, posing hurdles to accurate and timely identification of these disorders.

This review synthesizes the current state of diagnostic challenges in MDS, focusing on key aspects that complicate the diagnostic process. Firstly, the inherent heterogeneity of MDS, both in terms of clinical presentation and underlying molecular abnormalities, complicates the establishment of clear diagnostic criteria. The evolving landscape of genetic and epigenetic markers associated with MDS further adds complexity, requiring continuous updates to diagnostic guidelines.

Secondly, the overlap of clinical features between MDS and other hematologic disorders, such as aplastic anemia and other myeloproliferative neoplasms, often leads to misdiagnosis and delays in appropriate management. The lack of specific biomarkers for MDS exacerbates this issue, necessitating a multidisciplinary approach that integrates clinical, morphological, and molecular information.

Furthermore, the identification of low-risk MDS cases, which may exhibit indolent disease courses, remains challenging. Distinguishing these cases from other causes of cytopenias or reactive conditions is crucial for guiding therapeutic decisions and avoiding unnecessary interventions.

In addition to diagnostic challenges, the review addresses the complexities associated with risk stratification, as current prognostic scoring systems may not fully capture the dynamic nature of MDS progression. The need for refined prognostic tools that incorporate molecular and functional parameters is underscored.

Finally, the advent of novel therapeutic agents demands a reevaluation of diagnostic criteria to ensure their applicability in the era of precision medicine. The review concludes by highlighting emerging technologies and approaches, such as liquid biopsy and single-cell sequencing, which hold promise in overcoming current diagnostic challenges and improving the accuracy of MDS diagnosis.

In summary, this comprehensive analysis sheds light on the multifaceted diagnostic challenges faced in the field of MDS, emphasizing the importance of ongoing research and collaborative efforts to refine diagnostic criteria, enhance risk stratification, and pave the way for more personalized therapeutic interventions.

SS08-1

RUNX1-FPDMM natural history study at NIH

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National Institutes of Health, USA

Familial platelet disorder with associated myeloid malignancy (FPDMM) is an autosomal dominant genetic disease caused by mutations in RUNX1, which is characterized by thrombocytopenia, platelet functional defects and predisposition to hematologic malignancies. The overall lifetime risk of hematologic malignancies in FPDMM patients is 35 - 40%, and the average age of malignancy onset is 33 years (range 6 – 77 years). Currently, we do not understand why hematopoietic malignancies develop in some FPDMM patients but not others. It is likely that RUNX1 germline mutations are not sufficient for leukemogenesis, and we need to identify cooperating mutations and study the mechanisms. Moreover, there are no biomarkers or assays to predict which patients will progress to malignancy. Likewise, there are no treatments and/or preventative measures that can reduce or stop disease progression. To address these questions, we launched a natural history study of RUNX1-FPDMM at NIH in 2019 to conduct longitudinal, systematic, and prospective phenotyping and genotyping of patients with the disease.

So far we have enrolled 388 participants, including 202 individuals with RUNX1 pathogenic and likely pathogenic variants from 94 independent families. 87% of the patients had thrombocytopenia and 100% had abnormal platelet aggregometry. Dysmegakaryopoiesis was found in 76% patients, and reduced cellularity for age was seen in 55% adults and 81% pediatric cases. 63% families have at least one family member who have developed hematologic malignancies. Moreover, 93% patients had allergic symptoms, and 80% had gastrointestinal symptoms. Genomic characterization showed that nearly half of the patients without heme malignancy harbor somatic mutations in CHIP or AML genes. The most mutated genes are TET2 and BCOR. More studies are needed to understand the significance and mechanism of interactions between somatic mutations and germline RUNX1 variants. Multiple genomic, epigenomic, and proteomic studies are ongoing, which may lead to the identification of biomarkers for disease progression. This actively accruing, longitudinal study will follow more patients with FPDMM, which will lead to better understandings of disease pathogenesis and clinical course and may inform preventive and therapeutic interventions.

SS08-2

Clinical impact of *DDX41* mutations in myeloid neoplasms

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DDX41 encodes a DEAD-Box helicase protein that is considered essential for cell growth and viability. Defects in DDX41 lead to loss of its tumor suppressor function due to altered splicing and RNA processing. Experimental knockout systems suggest that DDX41 may participate in the development of leukemogenesis. 70% of cases with DDX41m are associated with MDS/AML alone. More than 65% of familial cases harbor a heterozygous germ line frameshift mutation (p.D140Gfs*2). A somatic DDX41m of the second allele, can be acquired in 50% of cases, leading to hematological malignancy. Myeloid neoplasms with DDX41m are typically characterized by long latency, high-risk disease at presentation (MDS/AML) with normal cytogenetics and without any additional molecular markers. Recent reports suggests that sub-group of these patients have an indolent clinical course, and have a better long-term survival compared to favorable or intermediate risk AML. Distinct clinical/ pathologic features and favorable outcomes in MDS/AML, highlights the need for standardized classification and gene specific guidelines that could assist in management decisions in patients with DDX41m.

SS08-3

Discovery of new regulators in hematopoietic stem cells and malignancies

Dongjun Lee
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The functional distinction between stem and progenitor cells is well-established in several tissues, particularly in the blood. There, hematopoietic stem cells preserve self-renewal potential and reconstitution ability in the bone marrow niche. Bone marrow represents a unique setting in which to examine how stroma influences tissue function. It was the setting in which the experimental definition of a niche was first provided in mammalian stem cell biology and where clear evidence for non-cell autonomous oncogenesis was first defined. One hallmark of acute myeloid leukemia (AML) that is shared across genetic subtypes is that leukemic myeloblasts are arrested at an immature and self-renewing stage of development. Differentiation is associated with a reduction in leukemic cell burden and leukemia stem cells as well as improved survival.

1. In this study, we report that the endogenous endoplasmic reticulum transmembrane protein surfeit 4 suppresses cell death by negatively regulating the stimulator of interferon genes-signal transducer (STING) and activator of transcription 6 (STAT6) axis in myeloid leukemia. We investigated the function of SURF4 and reported that its inhibition promotes apoptosis via activation of the STING-STAT6 axis in leukemic cells. Moreover, silencing SURF4 inhibited cell growth and increased apoptosis in leukemic cells. In addition, we also observed the synergistic enhancement of apoptosis by paclitaxel in the absence of SURF4 in leukemic cells. SURF4 induced apoptosis via the accumulation of reactive oxygen species, which activated ER stress via the PERK-peIF2α-CHOP pathway. Reduced SURF4 expression was capable of triggering myeloid differentiation in vitro and in vivo in murine and human leukemic cell models.

2. Oxysterols are oxygenated derivatives of cholesterol and, compared to cholesterol, contain an additional hydroxy, epoxide, or ketone group in the sterol nucleus, and/or a hydroxyl group in the side chain. 27-hydroxycholesterol (27HC) is a side-chain oxysterol oxygenated at the 27-carbon atom of cholesterol. This oxysterol is produced via oxidation by sterol 27-hydroxylase (CYP27A1) and metabolized via 7α-hydroxylation for bile acid synthesis in the liver. The previous study demonstrated that treatment with the alternative ERα ligand 27HC induced ERα-dependent hematopoietic stem cell (HSC) mobilization. Here, we report that exogenous 27HC treatment exhibits impaired hematopoietic stem and progenitor cell (HSPC) numbers owing to significantly increased ROS levels and apoptosis in the HSPCs. However, 27HC did not influence the mature cell population. Thus, our study suggests that 27HC is indispensable for regulating pools of HSPCs and may serve as novel therapeutic targets for hematological malignancies.

SS09-1

Clonal hematopoiesis and aging

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A diverse set of driver genes, such as regulators of DNA methylation, RNA splicing, and chromatin remodeling, have been associated with pre-malignant clonal expansion of hematopoietic stem cells (HSCs), commonly referred to as 'clonal hematopoiesis'. The factors mediating expansion of these mutant clones remain largely unknown, partially due to a paucity of large cohorts with longitudinal blood sampling. To circumvent this limitation, we developed and validated a method to infer clonal expansion rate from single timepoint data called PACER (passenger-approximated clonal expansion rate). Applying PACER to 40,000 persons with clonal hematopoiesis accurately recapitulated the known fitness effects due to different driver mutations. We have also uncovered genetic and environmental determinants of clonal expansion rate using large datasets. PACER is an approach that can be widely applied to uncover the determinants of pre-malignant clonal expansion in blood and other tissues.

SS09-2

Clonal hematopoiesis: Implications for cell therapy

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Dana-Farber Cancer Institute, USA

Clonal hematopoiesis (CH) refers to the age-related accumulation of somatic mutations in blood cells, occurring even in individuals without circulating blood cancers. The existence of CH has been linked to a reduced overall survival rate, elevated risk of subsequent myeloid malignancies, and non-malignant inflammatory conditions like cardiovascular disease and chronic obstructive pulmonary disease. In patients with lymphoid malignancies, the concurrent presence of CH correlates with negative outcomes. Specifically, in cases of non-Hodgkin lymphoma (NHL) and multiple myeloma (MM), CH not only diminishes overall survival but also increases the risk of developing secondary myeloid leukemias, particularly when autologous transplantation is involved. CH is frequently observed in patients who have undergone chemotherapy, particularly in those with relapsed or refractory disease who have been treated with multiple cycles of cytotoxic agents. As a result, CH is commonly found in patients eligible for cell therapies and may significantly influence both the toxicity and effectiveness of these treatments. Importantly, the interaction between CH and subsequent therapies may heighten the risk of developing secondary malignancies in some patients.

SS09-3

Clonal hematopoiesis and metabolic diseases

Sung Hee Choi
Seoul National University College of Medicine, Korea

Clonal hematopoiesis has been reported its correlation with different settings of metabolic disorders such as atherosclerosis and cardiovascular diseases. We performed several research between CHIP and new onset diabetes, new onset cardiovascular diseases based on health examination cohort, and the complications of diabetes mellitus in hospital settings. We reported that the presence of CHIP is significantly associated with new onset type 2 diabetes in subjects with high LDL cholesterol. Synergistic effects of CHIP and high LDL cholesterol on the development of ASCVD in asymptomatic Korean adults. However, the presence of CHIP is negatively associated with Diabetic neuropathy without clear reason in patients with diabetes. Further investigation of CHIP in the area of metabolic diseases and finding the mechanism of CHIP and metabolic consequences will be interesting topic.

SS10-1

The impact of immune profiling of T-cell and plasma cells on non-cellular immune therapy in myeloma

Nizar Jacques Bahlis
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Targeted immunotherapy has significantly improved the outcome of patients with hematological malignancies by leveraging the power of the immune system to eliminate tumor cells. In multiple myeloma (MM), bispecific T-cell engagers (BsAb) targeting B-cell maturation antigen (BCMA), G protein-coupled receptor, class C, group 5, member D (GPRC5D), and Fc receptor-like 5 (FcRL5) have already demonstrated remarkable clinical activity in triple-class refractory patients. However, responses to BsAb are not universal, and resistance often emerges while on therapy. Mechanisms mediating resistance are tumor intrinsic or immune dependent. Reported tumor intrinsic factors include antigenic loss (biallelic or functional) through deletions or mutations of target genes, increased soluble BCMA (for BCMA targeting BsAb), high tumor burden, and extramedullary disease. Immune-mediated resistance are largely dependent on T-cell fitness and tolerant immune environment. Understanding these mechanisms will allow the design of optimized BsAb therapy and an informed approach to sequencing and combining these molecules with other anti-MM agents and immune therapies.

SS10-2

Single-cell techniques to characterize immune microenvironment in MM

Niels Weinhold
Heidelberg University, Germany

Single-cell sequencing technologies allow evaluation of changes in cell number and state, as well as interactions between myeloma cells and the immune microenvironment. I will show that significant changes in the microenvironment are already present in the precursor stages. However, cell proportions in the microenvironment are heterogeneous even within the same disease stage, highlighting the need for larger data sets and underscoring the existence of an individual immune phenotype. Next, I will briefly review results from recent single-cell studies of the microenvironment in high-risk disease and in patients who do not respond to immunotherapy. I will show that the microenvironment in focal lesions is different from that at the iliac crest, and that myeloma genotype and phenotype influence their environment or vice versa. I will discuss flow cytometry as an alternative or complementary approach to single-cell sequencing for cost-effective assessment of immune phenotypes in the microenvironment. Finally, I will show that it will be important to combine single-cell technologies with spatially resolved multiplex methods to better define the role of the microenvironment in myeloma development.

SS10-3

The power of ONE: Immunology in the age of single cell genomics

Ido Amit
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The immune system is a complex, dynamic and plastic network composed of various interacting cell types that are constantly sensing and responding to environmental cues. From very early on, the immunology field has invested great efforts to characterize the various immune cell types and elucidate their functions. However, accumulating evidence indicates that current technologies and classification schemes are limited in their ability to account for the functional heterogeneity of immune processes. Single cell genomics hold the potential to revolutionize the way we characterize complex immune cell assemblies and study their spatial organization, dynamics, clonal distribution, pathways, and crosstalk. This emerging field can greatly affect basic and translational research of the immune system. I will discuss how emerging single cell genomic studies are changing our perspective in cancer immunology. Finally, I will consider recent and forthcoming technological and analytical advances in single cell genomics and their huge potential impact on the future of immunology research and immunotherapy.

SS11-1

Palliative care for patients with leukemia

Min Sun Kim
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Despite advancements in oncology, patients with refractory leukemia face a grim prognosis, often succumbing to their disease. While innovative therapies offer a glimmer of hope for some, the reality for many is a challenging and often painful journey. In this context, palliative care emerges as a crucial intervention, aiming to optimize quality of life and alleviate the multifaceted burdens associated with this complex illness.

Studies reveal that patients with hematological malignancies are more likely to receive aggressive end-of-life interventions compared to those with solid tumors. This discrepancy stems from several key factors, including the curative potential of even advanced-stage hematological malignancies and the disease's inherent need for intensive treatment (transfusions, antibiotics, antifungals) until the end, hindering hospice transition.

To bridge this gap and optimize care for refractory leukemia patients, a proactive approach to palliative care is essential. This involves early integration of palliative care into the treatment landscape by primary care teams, strategic deployment of specialty palliative care teams at key junctures, and proactive identification of palliative care windows.

By prioritizing and integrating palliative care into the treatment path for refractory leukemia patients, we can empower them to navigate their illness with dignity, comfort, and hope. This approach recognizes the multifaceted nature of their suffering and offers a holistic support system that extends beyond traditional oncology interventions.

SS11-2

Long-term survivorship in hematologic malignancies

Shahrukh K. Hashmi
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In 2024, the survivorship care post treatment of hematologic malignancies has changed considerably in some countries, especially in developed countries. Focus on survivorship is critically important since we are curing more patients with chemotherapies, immunotherapies, stem cell transplants, CAR-T cells and gene therapies, but they are accumulating various non-hematologic complications collectively known as "late effects" which include heart disease, subsequent cancers, endocrinopathies, neurologic dysfunction, fertility loss etc…

The aspects of survivorship differ in different blood cancers, but survivorship has another often-overlooked angle – the AGE of the patient. The COG studies in pediatric cancers were instrumental in formulating policies and guidelines in pediatric leukemia survivors and in Hodgkin lymphoma survivors. In contrast the adult guidelines for survivors of hematologic malignancies took a decade or more to be assimilated. Age itself remains the greatest variable in determining the long-term survivorship outcomes. E.g. a B-cell ALL pediatric survivor may have a near normal long-term outcome if preventative screening is undertaken for the late effects, however, an elderly AML patient would not only have more late effects due to chemotherapy, but also a significantly decreased non-cancer related survival. The reason is mainly the exposure-outcome rule of epidemiology. I.e. those with more cumulative exposures (e.g. smoking + alcohol + chemotherapy ± radiation etc.) tend to have a multiplicative effect on the late effects which lead to a decreased survival.

But these late effects can be very different depending on the exposure of chemotherapies or radiation. E.g. in CML, continuous exposure to TKI may increase the risk of heart disease or dysrhythmias, whereas, in a Hodgkin lymphoma patient who received ABVD (bleomycin component) + brentuximab on relapse, and then an autologous transplant (which commonly utilizes BEAM conditioning) has a lot more risk of pulmonary toxicity due to multiple chemotherapies (bleomycin+brentuximab+carmustine) and is at risk of long term lung fibrosis much more than survivors of other hematologic malignancies.

Thus, the survivorship care plans for each patient need to be individualized and one size does NOT fit all when it comes to adhering to international or national guidelines. Cancer centers must invest resources (personnel, space etc.) to provide care to long term survivors of hematologic malignancies, as curing cancer is not enough. After all, it was never about the battle against cancer, but the whole purpose of clinicians' provision medical care has been a battle against suffering!

SS11-3

The importance of monitoring symptoms and quality of life in routine hematology practice

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Remarkable treatment advances have been made in recent years for patients with hematologic malignancies. Clinicians and patients now frequently face challenging choices regarding various treatments that are often similar with regard to safety or efficacy, and decision-making has grown in complexity. Within this evolving landscape, health-related quality of life (HRQoL) and symptoms data have become critical to make more informed treatment decisions. This presentation will discuss the added value of integrating patient-reported HRQoL data collection in routine practice and will provide real-world examples of its clinical utility. The patient's view is unique and can provide invaluable data that cannot be inferred by other types of traditional medical indicators or laboratory exams.

SS12-1

Novel approaches for diagnosis & treatment of acute lymphoblastic and myeloid leukemia

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Despite impressive improvements in outcome in pediatric acute leukemias over the past decades, both in pediatric ALL as well as in AML, medical need still exists for relapsed/refractory cases. However, rather than treating relapse our aim should focus on the prevention of relapse by further increasing the efficacy of upfront treatment. The third major goal is to reduce long-term side effects by replacing toxic therapy elements by less toxic but equally efficacious therapy elements.

In the past improvements were mainly achieved by finme tuning risk classification and available chemotherapy. However rthe afomentioned aims can best be achieved by studying the introduction of various recently developed drugs into pediatric leukemia treatment, especially when characterized by a different mode of action addressing the biology of the disease as well as a better safety profile. During the presentation I will review the development stage and available data for several of the more novel compounds described below, that may have entered or may enter treatment for newly diagnosed patients in the near future.

For BCP-ALL, this mainly concerns the introduction of blinatumomab and inotuzumab ozogamicin, as well as the recently developed menin inhibitor revumenib, which is mainly be of relevance for KMT2A-rearranged (infant) ALL. Other menin inhibitors are also under development, such as ziftomenib and JNJ-75276617.

Other targeted therapy options are mainly relevant in Philadelphia-chromosome positive leukemias, and in adult ALL the concept of chemo-free induction therapy is already under development consisting of combinations of tyrosine kinase inhibitors (TKIs) such as imatinib, dasatinib or ponatinib, in combination with with steroids or blinatumomab, and challenging the need for SCT in this disease. Similar studies are in development for newly diagnosed/relapsed Ph+-ALL in children. Moreover, patients with ABL-class fusions are also eligible for addition of TKIs.

Introducing CAR T-cell therapy as an alternative to SCT is an attractive therapy approach to avoid the long-term toxicities of SCT especially in case of TBI, which is needed in ALL in the conditioning regimen. Also for T-cell ALL, newer therapy options are available including CAR T-cell therapy, for example the allogenic off-the-shelf, fractricide-resistant CD7-targeted CAR-T cell therapy studies in the WU-CART-007 study.

For AML, immunotherapy is less well advanced, but next to various FLT3-inhibitors, which are now tested in upfront therapy protocols, newer options include targeting KMT2A and other rearrangements such as NUP98 fusions with menin inhibition, and targeting the rare but dismal group of CBFA2T3-GLIS2 abnormalities for example with Luveltamab tazevibulin, which is an anti-folate receptor targeted ADC originally developed for treatment of ovarian cancer. Newer options for immunotherapy include the development of CAR NK-cells, as well as bispecific CD123 targeting NK-cell engaging molecule, such as SAR443579.c. The current studies in adults with HMAs and venetoclax suggest that this may be vary efficacious but there is limited experience in pediatrics, mainly restricted tio relapsed/refractory patients. Further exploring the acitivity of low dose options and combining it with targeted agents (as triplets) certaibnly needs further study in children.

Taken together there are multiple novel options directed at changing therapy in pediatric leukemia, and clearly a new era with major changes in the existing chemotherapy-based protocols is on the horizon.

SS12-2

The role of blinatumomab in the treatment of MRD negative B-ALL in adults

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Treatment of B lineage acute lymphoblastic leukemia (B-ALL) has seen notable improvement in outcome in the past few years with the advent of use of pediatric intensive regimens for adolescents and young adults, use of measurable residual disease (MRD) for risk assessment and introduction of potent immunotherapeutic agents including blinatumomab (Blin), inotuzumab ozogamicin (IO) and chimeric antigen receptor T-cell (CAR-T) therapy. The TOWER randomized trial showed the benefit of Blin versus chemotherapy in patients with relapsed and refractory B-ALL and the INO-VATE randomized trial demonstrated the benefit of IO compared with chemotherapy also in the setting of relapsed/refractory B-ALL.[1,2] The ELIANA trial in children and the ZUMA-3 trial in adults of CAR-T therapy has shown the significant benefit of these modalities of therapy.[3,4] Blinatumomab has also shown significant benefit in converting patients who are MRD positive to MRD negative at a rate of 80%.[5]

These encouraging results have led to significant interest in moving these immunotherapeutic approaches to the front-line setting. At MD Anderson IO and Blin have been combined with the HyperCVAD and miniCVD regimens with achievement of a 100% complete remission (CR) rate, MRD negativity in 95% and a 3 year overall survival (OS) of 87% with HyperCVAD+IO+Blin and a CR rate of 90%, MRD negativity rate of 94% and OS of 48% at 5 years in patients with miniCVD+IO+Blin in Philadelphia chromosome negative (Ph neg) B-ALL.[6,7]

The German GMALL group has studied addition of 3 cycles of IO as induction therapy followed by standard chemotherapy in 43 patients with Ph neg B-ALL over 55 years of age and demonstrated a 100% CR rate, a 74% MRD negativity rate and OS at two years of 81%.[9]

The United States intergroup E1910 trial treated Ph neg B-ALL adults, ages 30-70, with 2 months of induction chemotherapy followed by an intensification cycle of high dose methotrexate and pegaspargase for CNS prophylaxis and then randomized patients who were in CR and MRD negative by flow cytometry to receive 4 cycles of consolidation chemotherapy followed by maintenance or 4 cycles of Blin interspersed with the same 4 cycles of consolidation chemotherapy followed by maintenance chemotherapy. Patients could proceed to allogeneic transplant at the discretion of the investigator. 488 patients were enrolled and 81% achieved a CR. 224 MRD negative patients were randomized, 112 to each arm of consolidation chemotherapy alone or Blin + chemotherapy. After a median follow up of 3.6 years the overall survival of patients on the Blin + chemotherapy arm was 83% versus 65% for the patients on the chemotherapy only arm (hazard ratio of 0.42, 95% CI: 0.24-0.75, log rank test, p=0.003).[9]

A US intergroup pilot trial led by the Alliance Cooperative Group treated newly diagnosed patients with B-ALL that was CD22+ with IO for one to three cycles depending on response. Those without cytoreduction received Blin. Patients who achieved a CR to InO received 2-3 more cycles of Blin. Twenty three patients with a median age of 71 years were treated and the cumulative CR rates was 97%. With a median follow up of 22 months the one year EFS and OS were 75% and 84%, respectively.[10]

The phase II, single arm D-ALBA trial combined dasatinib and Blin for newly diagnosed patients with Ph positive (Ph pos) B-ALL and 98% of the 63 patients enrolled achieved a CR. A 60% molecular response was achieved in patients after dasatinib induction and 2 cycles of blinatumomab. At a median follow up of 18 months the OS was 95% and DFS was 88%. Disease-free survival was lower in patients with an IKZF1 mutation in combination with other mutations.[11] The MD Anderson group has combined ponatinib with blinatumomab (up to 5 cycles) and achieved a CR in 97% of 35 patients. Ninety percent of patients achieved a complete molecular response (CMR) at any point in the study. The estimated EFS and OS are 80% and 90%, respectively.[12] The United States intergroup is currently conducting a phase III randomized trial of dasatinib or ponatinib (investigator choice) with HyperCVAD or blinatumomab in patients aged 18-70 with newly diagnosed Ph pos ALL. The results are eagerly awaited.

In conclusion, the addition of immunotherapeutic agents to frontline therapy of B-ALL has been shown to improve survival in phase II and III clinical trials. Earlier introduction of these agents in therapy will likely improve outcomes further and early studies suggest that these agents could likely replace or significantly reduce the use of chemotherapy, lessen toxicity and improve outcomes. The addition of CAR-T therapy in the frontline setting has the potential to enhance responses even further.

SS12-2

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SS12-3

Revised WHO classification of ALL: New era of genetic diagnosis

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Acute Lymphoblastic Leukemia (ALL) is diagnosed by a combination of morphology and immunophenotyping, while further classification is now largely by defined cytogenetic and/or molecular abnormalities. These genetic subtypes form the basis for the present classification, and may be associated with characteristic morphologic, immunophenotypic or clinical features with prognostic and/or therapeutic implications.
In this new era of genetic diagnosis, the identification of specific genetic abnormalities has led to the development of targeted therapies and precision medicine approaches. Drugs such as tyrosine kinase inhibitors and immunotherapies have demonstrated remarkable efficacy in treating subgroups of ALL patients, emphasizing the importance of tailored treatment strategies based on genetic profiling. This genetic diagnosis has also important implications for disease management, including minimal residual disease assessment. Furthermore, the revised classification has opened doors for the discovery of novel genetic mutations and therapeutic targets, driving ongoing research efforts to improve the outcomes of ALL patients. As our understanding of the genetic landscape of ALL continues to evolve, so too does the potential for more personalized and effective treatments.
In conclusion, a new era of genetic diagnosis, revolutionizing the way we approach the disease. By harnessing the power of genomics, clinicians and researchers are better equipped to diagnose, prognosticate, and treat ALL, ultimately offering hope for improved outcomes.

Table 1. WHO Classification of Hematolymphoid Tumors, 5th edition: B-ALL and T-ALL.

B-cell lymphoblastic leukaemias/lymphomas	
B-lymphoblastic leukaemia/lymphoma, NOS	(Same)
B-lymphoblastic leukaemia/lymphoma with high hyperdiploidy	B-lymphoblastic leukaemia/lymphoma with hyperdiploidy
B-lymphoblastic leukaemia/lymphoma with hypodiploidy	(Same)
B-lymphoblastic leukaemia/lymphoma with iAMP21	(Same)
B-lymphoblastic leukaemia/lymphoma with *BCR::ABL1* fusion	B-lymphoblastic leukaemia/lymphoma with t(9;22)(q34;q11.2); *BCR-ABL1*
B-lymphoblastic leukaemia/lymphoma with *BCR::ABL1*-like features	B-lymphoblastic leukaemia/lymphoma, *BCR-ABL1*-like
B-lymphoblastic leukaemia/lymphoma with *KMT2A* rearrangement	B-lymphoblastic leukaemia/lymphoma with t(v;11q23.3); *KMT2A*-rearranged
B-lymphoblastic leukaemia/lymphoma with *ETV6::RUNX1* fusion	B-lymphoblastic leukaemia/lymphoma with t(12;21)(p13.2;q22.1); *ETV6-RUNX1*
B-lymphoblastic leukaemia/lymphoma with *ETV6::RUNX1*-like features	*Not previously included*
B-lymphoblastic leukaemia/lymphoma with *TCF3::PBX1* fusion	B-lymphoblastic leukaemia/lymphoma with t(1;19)(q23;p13.3); *TCF3-PBX1*
B-lymphoblastic leukaemia/lymphoma with *IGH::IL3 fusion*	B-lymphoblastic leukaemia/lymphoma with t(5;14)(q31.1;q32.1); *IGH/IL3*
B-lymphoblastic leukaemia/lymphoma with *TCF3::HLF* fusion	*Not previously included*
B-lymphoblastic leukaemia/lymphoma with other defined genetic abnormalities	(Same)

T-lymphoblastic leukaemia/lymphoma	
T-lymphoblastic leukaemia / lymphoma, NOS	T-lymphoblastic leukaemia/lymphoma
Early T-precursor lymphoblastic leukaemia / lymphoma	Early T-cell precursor lymphoblastic leukaemia
(Entity deleted)	NK-lymphoblastic leukaemia/lymphoma

SS13-1

Clonal evolution of MDS/AML in patients with cancer predisposition syndromes

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Recent studies revealed that normal tissues acquire somatic mutations, including cancer driver mutations, caused by aging and exposure to environmental factors, leading to the clonal expansion of precancerous lesions. Cancer predisposition syndromes (CPSs) are heritable conditions that confer an increased risk of one or more types of cancer and are caused by germline mutations in tumor suppressor genes. Clonal evolution patterns and early cancer development in CPSs has not been fully elucidated. We investigated somatic mutation in blood cells in CPSs, such as Fanconi anemia, by whole-genome sequencing of single cell-derived colonies, which revealed unique patterns of genetic alterations in blood cells and clonal evolution in CPSs. In this symposium, I will talk about the recent progress of our understating of the clonal evolution of MDS/AML in patients with CPSs.

SS13-2

Congenital and acquired thrombophilia in children

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Background : The recognition of venous thromboembolism (VTE) in children is on the rise, particularly at pediatric referral centers. Throughout childhood, two age group categories are more commonly affected, infants and adolescents. In such instances, at least three different thrombosis risk factors are identified at VTE onset, making it challenging to ascertain the potential causal role that acquired/inherited thrombophilas may have in relation to the first/recurrent VTE.

Method : Our analysis will review the changing perceptions about the importance of inherited/acquired thrombophilia testing in VTE in children. Data will summarize international evidence- and consensus-based guidelines/guidance documents on this topic, from their inception until their last iteration, including reccommendations made by the American Society of Hematology, the International Society on Thrombosis and Haemostasis, the College of American Pathology, the British Societh of Haematology, and the American Society..of Pediatric Hematology Oncology.

Results : Over time, pediatric guidelines have de-emphasized the importance of universal thrombophilia testing, stressing their relevance only in certain specific scenarios where pre-emptive or post-VTE investigation may still merit consideration. Additionally, thrombophila testing pitfalls will be highlighted to maximize the chances of obtaining reliable laboratory results. Morever, progresses on the understanding of specific genotypes associated with greater thrombosis risks will be covered, as well as specific pediatric recommendations pertainig to anthiphospholipi syndrome/thrombosis storm. Finally, the performance of direct oral anticoagulants in such scenarios will be reviewed.

Conclusion : In summary, the role of acquired/inherited thrombophilia in children at risk or diagnosed with VTE has evolved, being still relevant in selective scenarios such as in non-catheter-related VTE or when a significant family or personal thrombosis history has been identified. It is vital to recognize the ideal timing for ordering laboratory investigation, testing pitfalls, and scenarios where ordering such tests is no longer acceptable.

Keywords : Thrombophilia, Congenital, Acquired, Children, Thrombosis

SS13-3

Management of rare pediatric lymphomas

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Primary mediastinal large B-cell lymphoma (PMLBL) is a rare subtype of B-cell Non-Hodgkin lymphoma (NHL) and predominantly affects adolescents and young adults. Although previously classified as part of diffuse large B-cell lymphoma, PMLBL is clinically and genetically more akin to nodular sclerosing Hodgkin lymphoma.

For adult PMLBL patients, combination chemotherapy consisting of etoposide, doxorubicin, and cyclophosphamide with vincristine and prednisone plus rituximab (DA-EPOCH-R) has shown long-term event-free survival surpassing 90% without the need for local irradiation. However, the optimum treatment strategy for children and adolescents with PMLBL remains unclear. One study found significantly higher EFS for 67 patients treated with DA-EPOCH-R compared with those treated on BFM NHL regimens. However, another international study of 46 patients showed a 4-year EFS of 69.6% for DA-EPOCH-R treated patients, an outcome clearly worse than was observed for adult patients. Key findings of the study included CNS relapses and cardiac toxicity, results that are uncommonly seen with other pediatric NHL regimens. Finally, a French study of rituximab combined with LMB-based chemotherapy without radiotherapy resulted in 5-year EFS of 95.2% in 21 PMLBL patients, emphasizing that rituximab combined with an intensive pediatric NHL chemotherapy backbone may result in favorable outcome for these patients.

PMLBL is known for high expression of programmed death-1 ligand and treatment with a checkpoint inhibitor (CPI) may be considered for relapsed/refractory disease. However, CPI use prior to or after allogeneic HSCT may result in a significant risk of GVHD-related mortality.

Hodgkin lymphoma (HL) has an overall favorable outcome in children and adolescents, but a minority of patients may show primary refractory disease, or disease relapse. Salvage treatment regimens for these patients may include bendamustine, gemcitabine, and vinorelbine combination. More recently, HL chemotherapy includes target agents such as brentuximab vedotin, as well as CPIs. Combinations of these agents with conventional chemotherapy, such as brentuximab vedotin and gemcitabine, or brentuximab vedotin and nivolumab bendamustine have shown efficacy for relapsed/refractory patients in clinical trials. Achievement of complete molecular response with these agents prior to consolidation with autologous/allogeneic HSCT may allow for optimum outcome in the subset of pediatric HL patients who fail first-line treatment.

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SS14-1

Myeloproliferative neoplasms and inflammation

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This lecture will focus on the role of inflammatory processes in Bcr-Abl negative Myeloproliferative neoplasms (MPNs). MPNs, including the classical subtypes polycythemia vera, essential thrombocythemia, and primary myelofibrosis, are chronic clonal malignancies originating from hematopoietic stem cells (HSCs) in the bone marrow (BM). Upon transformation by oncogenic driver mutations such as JAK2V617F, calreticulin (CALR), or TPO receptor (MPL) gene mutations, these HSCs acquire capabilities of cytokine-independent JAK-STAT activation, causing enhanced cellular proliferation with preserved differentiation into their mature progeny. This leads to myeloproliferation and an increase in one or more blood cell lineages in the peripheral blood (erythrocytosis, leukocytosis, thrombocytosis), which mainly determines the clinical MPN phenotype. In addition, the malignant HSCs are mobilized out of the BM into the periphery and home to the spleen and other organs, leading to splenomegaly and other signs of extramedullary hematopoiesis. At the same time, deregulated JAK-STAT signaling in the malignant cells induces secretion of inflammatory cytokines (e.g. interleukin-1 (IL1)-beta, IL-6, IL-8, and tumor necrosis factor), which, in turn, activates inflammatory programs in non-malignant hematopoietic bystander cells, augmenting the inflammatory milieu in the body. In addition, these cytokines activate similar inflammatory processes in the non-hematopoietic cells of the BM microenvironment (e.g. endothelial cells, mesenchymal stromal cells [MSCs]). The MSC population responds by producing an excess of fibrous material in the BM, leading to progressive myelofibrosis (MF). This entire process reinforces stimulation of the malignant clone at the expense of residual normal hematopoietic cells, causing anemia and thrombocytopenia. Clinically, patients with MPN typically suffer from inflammatory symptoms such as fatigue, night sweats, weight loss, pruritus and fever, and they are at an increased risk of vascular complications such as thrombosis and severe hemorrhage. Finally, the MPN-associated inflammation enables clonal evolution by promoting reactive oxygen species and by facilitating additional mutations (e.g. ASXL1, EZH2, IDH1/2, SRSF1, TP53), which significantly increases the risk of progression to acute leukemia. Treatment of patients with MPN has to take into account all of these symptoms, signs and complications, and may include anti-inflammatory drugs such as JAK inhibitors, cytoreductive drugs, antiplatelet agents or anticoagulants, but also immunotherapeutic approaches such as ropeginterferon-alpha or allogeneic stem cell transplantation.

SS14-2

Signaling contributing to the development of myelofibrosis: Beyond JAK/STAT

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Myelofibrosis is a chronic hematologic malignancy that can develop either de novo or secondary to an antecedent essential thrombocythemia or polycythemia vera. JAK-STAT pathway overactivation is fundamental to the development of myelofibrosis, as evidenced by the high prevalence of driver mutations and hyperactivation of this pathway even in patients negative for JAK2, CALR and MPL. Despite this, there are numerous lines of evidence to suggest that aberrancies in additional pathways outside of JAK-STAT are key to disease manifestations and leukemic potential of this chronic hematologic malignancy. For one, mutations in genes outside the JAK-STAT pathway are frequent in myelofibrosis, including those responsible for epigenetic modifications. These mutations create a perturbed epigenetic landscape that facilitates clonal selection and elaboration of inflammatory cytokines that are responsible for disease manifestations. In addition, overactivate NFκB signaling has been identified as a key pathway leading to dysregulate cytokine production. Additional inflammatory signaling including IL-4/IL-13, IL-8 and TGF- β have been implicated in the pathogenesis of myelofibrosis and its progression. Finally, MDM2, a negative regulator of p53, has been shown to be overexpressed in myelofibrosis and leads to downstream expansion of pro-survival signaling. Some of these signaling pathways are being therapeutically exploited to provide the next generation of myelofibrosis directed therapies that can potentially delay disease progression, which is currently not accomplished by presently available JAK inhibitors. This talk will highlight pathways outside of JAK-STAT signaling with a focus on the present and future clinical translations of these findings into improving the quality and quantity of life for myelofibrosis patients.

SS14-3

Clonal evolution in myelofibrosis

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Philadelphia-negative myeloproliferative neoplasms (MPNs) include 3 main diseases: polycythemia vera (PV), essential thrombocythemia (ET), and primary myelofibrosis (PMF). PV and ET can evolve to secondary myelofibrosis, known as post-polycythemia vera (PPV-MF) and post-essential thrombocythemia (PET-MF) myelofibrosis. Based on WHO's 2016 criteria, pre-fibrotic (pre-PMF) and overt fibrotic (overt PMF) stages can be identified. MPN patients are at increased risk for thrombotic and hemorrhagic events, but evolution into secondary myelofibrosis, myelodysplastic syndrome or acute myeloid leukemia may represent the main causes of death.

The identification of driver mutations in JAK2, CALR, and MPL has contributed to a better understanding of disease pathogenesis, implicating near-universal upregulation of JAK-STAT signaling, and has led to the development and therapeutic use of novel targeted treatments, such as JAK2 inhibitors. More recently, according to the implementation of next-generation sequencing techniques and sequential repetition of this analysis, more precise characterization of complex molecular patterns associated with disease evolution in MPN has been revealed. Although in some patients MPN clones remain very stable over time, other patients show clonal expansion and appearance of new mutations that may linked to the evolution of the disease. Indeed, a recent study reported that patients experiencing clonal evolution during follow-up had a poor prognosis. However, the mechanisms of particular clonal outgrowth are not fully elucidated. Recent data have been demonstrated aging, the bone marrow microenvironment, and other genetic factors such as germline predisposition, order of mutation acquisition, and variant allele frequency as key factors influencing clonal outgrowth.

Herein, I review our current knowledge of the initiating and additional mutations in MPNs, explaining routes of disease progression and evolution, and their relationship with clinical presentation. I then address the outcomes in the patients experiencing clonal evolution and which factors influence clonal outgrowth.

SS15-1

Treatment options for relapsed/refractory hodgkin lymphoma after brentuximab vedotin and PD-1 blockade

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Brentuximab vedotin (BV) and PD-1 blockade have become integral components of the classic Hodgkin lymphoma (cHL) treatment paradigm. However, as these agents are utilized in earlier lines of cHL therapy, an increasing number of patients with relapsed or refractory cHL exhibit resistance to these novel treatments. The approach to patients with cHL that is resistant to BV and PD-1 blockade is evolving, with therapeutic options ranging from new immunotherapies (e.g. CAR T-cells or bispecific immune cell engager therapies) or novel combinations that can re-sensitize patients to BV or PD-1 blockade and allow ongoing use of these well-tolerated therapies. This talk will examine the treatment approach to patients with relapsed/refractory cHL that has progressed after BV and PD-1 blockade.

SS15-2

Aggressive B-cell lymphomas: Immuno-chemotherapies other than CAR-T cell therapies

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SS15-3

Extranodal NK/T cell lymphoma: The immunogenic tumor

Won Seog Kim
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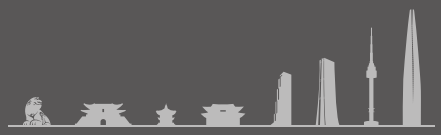

ICKSH 2024

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EDUCATION SESSION

ES01-1

Histiocytic neoplasm in pediatrics

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This lecture presents a comprehensive overview of pediatric histiocytic neoplasms, a group characterized by diverse clinical presentations and complex diagnostic challenges. Histiocytic and dendritic cell neoplasms, derived from common myeloid progenitors, have undergone significant classification updates, including the repositioning of these neoplasms after myeloid neoplasms and the addition of entities like Rosai-Dorfman disease (RDD) and ALK-positive histiocytosis.

A key focus will be on the molecular genetics underlying these neoplasms, particularly the frequent mutations in the MAPK pathway. This understanding has spurred the development of targeted therapies, such as BRAF and MEK inhibitors, revolutionizing treatment approaches. The lecture will delve into the diagnostic criteria for blastic plasmacytoid dendritic cell neoplasm (BPDCN), highlighting the role of immunophenotypic diagnostics and the recognition of clonal MPDCP in association with myeloid neoplasms.

Furthermore, I will discuss the diagnostic intricacies of conditions like Langerhans cell histiocytosis (LCH), Erdheim-Chester disease (ECD), and RDD. The broad histopathologic differential diagnosis of these neoplasms requires a meticulous approach, integrating clinical, radiological, and pathological data. An immunohistochemistry panel, including markers such as CD163, CD1a, langerin, S100, Factor XIIIa, OCT2, and BRAF V600E, is essential for definitive diagnosis in LCH and RDD, while ECD diagnosis necessitates genetic confirmation of MAPK pathway mutations.

Moreover, the lecture will explore the emerging therapeutic landscape for histiocytic neoplasms, including the use of cobimetinib, a MEK1 and MEK2 inhibitor, in patients regardless of tumor genotype. This therapy has shown promising results across various MAPK-pathway mutations, demonstrating the significant dependence of these neoplasms on MAPK signaling and their responsiveness to MEK inhibition.

In summary, this presentation aims to provide healthcare professionals with the latest insights into the classification, diagnostic challenges, and evolving therapeutic strategies for pediatric histiocytic neoplasms, highlighting the importance of molecular diagnostics and targeted therapies in this rapidly advancing field.

ES01-2

Histiocytic sarcoma

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Histiocytic sarcoma (HS) is an extremly rare neoplasia, of hematopoietic origin that accounts for less than 1% of hematologic malignancies. Previously known as "true histiocytic lymphoma", the tumor follows an aggressive clinical course. According with the World Health Organization classification HS is caracterized by the proliferation of malignant cells that have the morphological and immunohistochemical characteristics of mature histiocytes. HS can be diagnosed in all age group, but it is frequently seem in adults [1].

The term HS was first introduced by Mathe et al. [2] based on an analysis of 110 cases of "reticulosarcomas" that were grouped into two varieties: histoblastic and histiocytic types. They noted that both types had the same duration of evolution, but with the difference that the presence of cutaneous lesions was predominant in the histiocytic type.

HS can be localized or disseminated. The majorities of lesions are reported with presentation at extra-nodal sites, most frequently in the soft tissues and skin [3]. Other anatomical sites and can also be affected including the intestinal tract, the central nervous system, head and neck structures like tyroid and parotid among others [4-6]. Cases of HS associated with malignant leukemia or lymphoma have been also reported, but the nature of this association has not been established [7].

Recent studies have shown that HS has a prominent inflammatory background and is immunoreactive for CD45, CD163, CD68, and lysozyme. The differential diagnosis includes metastatic carcinoma, metastatic melenoma, and large cell non-Hosgkin lymphoma and should be excluded by immunhistochemistry. The CD163, a recently characterized hemoglobin scavenger receptor, appears to be a specific marker of histiocytic lineage and a promising diagnostic tool for HS [8].

Most patients presenting HS are being treated on an individual basis and the outcomes are still poor, particularly in those advanced or disseminated disease. The largest series published of HS treated with upfront surgery with the intent of diagnosis or treatment included 14 patients. All patients presented with a solitary mass with sizes ranging grom 1.8 cm to 12 cm. Seven tuors arose in soft tissue, 5 in the gastrointestinal tract, 1 in the nasal cavity, and 1 in the lung. Six patients were treated with postoperative radiation and 7 with chemotherapy (CHOP or PROMACE-MOPP). The follow up was available for 10 patients: 2 of them recurrent locally, and 5 patients developed distant metastasis [9].

The international Lymphoma Study Group stained 61 tumors of suspected histiocytic/dendritic cell type with a panel of 15 antibodies and found 18 malignant histiocytic tumors, with 15 cases of HS and 3 cases of malignant histiocytosis with disseminated disease. In this series there was a predominance of males, adults (median age: 46 years) and extranodal (72%) presentation. The following phenotype was observed: CD68 (100%), LYS (94%), CD1a (0%), S100 (33%), CD21/35 (0%). Nine patients (50%) had stage III or stage IV disease, and seven patients (58%) died of the disease [10].

Despite the rarity of the disease and paucity of data, radiotherapy has being used in some instances with a relative success in the local control. Median radiation doses, fractions of radiotherapy was 60 Gy and 30 fractions, respectively.

Chen et al. [11] recently published a case of a patient with oropharyngeal HS and regional lymph node involvement that was successfully treated with a combination of CHOP-E and adjuvant radiotherapy (50 Gy given in 25 fractions). The patient had no evidence of recurrent disease after 3 years of the end of the treatment.

Recent reveiws reported the use of thalidomide in patients with HS after systemic failure [12,13]. The potential mechanisms of antitumoral activity of thalidomie include inhibition of both vascular and fibroblast growth factors, cytokine regulation, apoptosis induction and oxidative DNA damage by free by free radicals. One review of the use of thalidomide in pediatric patients concluded that it should be used as a last resort when all other therapies fail [14].

Currently there is no standard treatment recommended for HS. The treatment protocols available in the literature are diverse, with most patients being treated on an individual basis. Although HS is considered a potentially fatal disease, some cases do not pursue such as an aggressive clinical course. Surgery and/or chemotherapy are the most commoly employed treatments, but radiotherapy also seems to be a treatment option in patients with localized disease. Futher research is still needed to explore the use of new treatment combinations in this entity.

ES01-2

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ES01-3

Pathologic characteristics of histiocytic and dendritic cell neoplasms

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Histiocytic and dendritic cell neoplasms comprise a diverse group of tumors originating from the mononuclear phagocyte system, which includes monocytes, macrophages, and dendritic cells. The 5th edition of the World Health Organization (WHO) classification has advanced in categorizing these tumors, reflecting a deeper understanding of their pathogenesis.

Here's an overview of the categories and subtypes: The category of 'plasmacytoid dendritic cell neoplasms' includes mature plasmacytoid dendritic cell proliferation associated with myeloid neoplasm and blastic plasmacytoid dendritic cell neoplasm. 'Langerhans cell neoplasms' encompass Langerhans cell histiocytosis (LCH) and Langerhans cell sarcoma. The 'other dendritic cell neoplasms' category comprises indeterminate dendritic cell tumor and interdigitating dendritic cell sarcoma. 'Histiocyte/macrophage neoplasms' include juvenile xanthogranuloma, Erdheim-Chester disease, Rosai-Dorfman Disease, ALK-positive histiocytosis, and histiocytic sarcoma. Additionally, 'follicular dendritic cell neoplasms' are classified as mesenchymal dendritic cell neoplasms within the stroma-derived neoplasms of lymphoid tissues, including follicular dendritic cell sarcoma, EBV-positive inflammatory follicular dendritic cell sarcoma, and fibroblastic reticular cell tumor.

Each subtype of histiocytic and dendritic cell neoplasms exhibits distinct morphological characteristics. The tumors also show a characteristic immunophenotypic profile, including markers such as CD68, CD163, CD1a, S100, CD207/langerin, Factor XIIIa, CD123, CD21, CD23, CD35, ALK, as well as hematolymphoid markers like CD45, CD4, and CD43. In situ hybridization for EBV-encoded small RNA (EBER) is characteristic of a specific subtype. Such immunoprofiling is instrumental in determining their cell of origin and specific subtype. Recently, it has been recognized that subtypes of histiocytic and dendritic cell neoplasms often exhibit genomic alterations, particularly in the mitogen-activated protein kinase (MAPK) pathway, including mutations in BRAF (especially BRAF p.V600E), MAP2K1, KRAS, or NRAS. In cases of ALK+ histiocytosis, a characteristic ALK gene translocation is observed.

The pathologic criteria for diagnosing these neoplasms are multifaceted, involving the assessment of morphological aspects, immunophenotypic profiles, and molecular genetics. This comprehensive approach is essential for accurately differentiating and classifying these neoplasms, in accordance with the updated WHO classification.

ES02-1

Overview of lymphoma classification

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We herein present of 4th edition of the World Health Organization (WHO) Classification of Haematolymphoid Tumours focusing on lymphoma and the introduction of upcoming 5th edition of classification. In addition to describing the classification's entities, we highlight the changes from the revised 4th edition. These include reorganization of entities using a hierarchical system, as used throughout the 5th edition of the WHO classification of tumors of all organ systems, modification of nomenclature for some entities, revision of diagnostic criteria or subtypes, deletion of certain entities, and introduction of new entities, as well as inclusion of tumor-like lesions. Furthermore, we will discuss the diagnostic importance of core needle biopsy in lymphoma diagnosis and the role of multidisciplinary approach in optimization of both clinical and pathological result.

ES02-2

What's new in AML classification

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The World Health Organization Classification of Hematolymphoid Tumors has served as an international diagnostic criterion for an extended period. However, in 2022, the International Consensus Classification (ICC) and the 5th edition of the WHO classification (WHO-HAEM5) introduced a similar yet distinct approach diagnostically, leading to confusion in practical applications.

Both classifications primarily utilize recurrent genetic abnormalities as the first criteria, maintaining the genetic disease definition from the WHO-HAEM4 classification, such as PMR::RARA, RUNX1::RUNX1T1, CBFB::MYH1, DEK::NUP214 fusion, and KMT2A rearrangement. However, a notable difference arises in blast percentage. The ICC requires a minimum of 10% blasts in bone marrow or peripheral blood, while WHO-HAEM5 does not set a blast cutoff. Both classifications stipulate at least a 20% blast percentage for defining AML with BCR::ABL1. Additionally, the ICC requires a blast percentage of at least 10% for NPM1 and CEBPA inframe bZIP mutations, whereas WHO-HAEM5 has no blast number cutoff for NPM1, but a 20% blast count is necessary for AML with CEBPA mutation. The newly introduced TP53 mutation is exclusive to the ICC, diagnosable when the blast count is over 20% and VAF is over 10%.

A significant alteration from AML with myelodysplasia-related changes (WHO-HAEM4) is the elimination of morphologic dysplasia and the transition to a cytogenetic or gene mutation-based definition. It is now termed AML, myelodysplasia-related (AML-MR) by WHO-HAEM5, defined by the ICC as AML with myelodysplasia-related gene mutations and AML with myelodysplasia-related cytogenetic abnormalities. Cytogenetics remain similar to WHO-HAEM4, but ICC includes trisomy 8 and del(20q), while WHO-HAEM5 includes del(11q), -13, or del(13q). Both include genetic mutations in ASXL1, BCOR, EZH2, STAG2, SF3B1, SRSF2, U2AF1, and ZRSR2, with ICC additionally incorporating RUNX1.

Finally, AML defined by differentiation (WHO-HAEM5) and AML not otherwise specified (ICC) are characterized by a lack of defining genetic abnormalities. In the therapy-related myeloid neoplasm category, WHO-HAEM5 terms it as myeloid neoplasm post cytotoxic therapy (MN-pCT), while in the ICC, therapy-related can be identified by describing it as "therapy-related," but it is not separately classified by AML subtype.

ES02-3

Recent update of MDS classification

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The World Health Organization (WHO) Classification of Haematolymphoid Tumours recently released its 5th edition and the International Consensus Classification (ICC) developed its classification scheme. Both classification systems provide definitions of clonal hematopoiesis, clonal hematopoiesis of indeterminate potential, and clonal cytopenia of undetermined significance. The WHO classification categorizes MDS into two categories – MDS with defining genetic abnormalities and MDS, morphologically defined. The former is further divided into (i) MDS with low blasts and isolated 5q deletion, (ii) MDS with low blasts and SF3B1 mutation, and (iii) MDS with biallelic TP53 inactivation. The latter is divided into (i) MDS with low blasts, (ii) MDS, hypoplastic, and (iii) MDS with increased blasts, which consists of MDS with increased blasts 1, MDS with increased blasts 2, and MDS with fibrosis. The ICC is similar but has a few differences. MDS is categorized as (i) MDS with mutated SF3B1, (ii) MDS with del(5q), (iii) MDS, NOS without dysplasia, (iv) MDS, NOS with single lineage dysplasia, (v) MDS, NOS with multilineage dysplasia, (vi) MDS with excess blasts, and (vii) MDS/AML. The differences between the WHO2016 classification and the two current classifications will be discussed in this lecture.

ES03-1

Comprehensive overview of cell-based artificial platelet production

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Artificial platelet production, particularly via cell-based methods, has emerged as a pivotal area in biomedical research, offering promising avenues for addressing the chronic shortages in blood transfusions and improving therapeutic outcomes in hemostatic disorders. This presentation reviews a comprehensive overview of the current state and advancements in the production of cell-based artificial platelets. The production process of artificial platelets is a complex interplay of biological, chemical, and engineering principles. Central to this process is the selection of appropriate progenitor cells, which are typically derived from megakaryocytes or pluripotent stem cells. The transformation of these cells into platelets or platelet-like particles is directed by a precisely structured sequence of biochemical signals, which closely mimic the physiological process of thrombopoiesis. Advances in bioreactor design have further enhanced the scalability and efficiency of the production. These bioreactors, often incorporating microfluidic systems, provide controlled environments that facilitate the maturation and release of platelets, closely resembling the natural shear stress and microenvironmental conditions found in bone marrow niches. A significant challenge in this domain is ensuring the functional equivalence of artificial platelets to their natural counterparts. This includes the ability to aggregate, adhere to vascular injury sites, and interact with clotting factors. Innovations in surface engineering and biomimetic approaches have been instrumental in enhancing these functional aspects. In conclusion, the production of cell-based artificial platelets stands at the forefront of translational medicine. While significant progress has been made, ongoing research and collaboration between biologists, chemists, and engineers are critical to overcoming existing challenges and fully realizing the potential of this innovative technology. The future of artificial platelet production holds immense promise, not only in revolutionizing transfusion medicine but also in opening new pathways for therapeutic interventions.

ES03-2

Anti-CD38 and anti-CD47 delay timely transfusion

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Various types of third-generation cancer immunotherapy agents have been developed, gaining significant attention in the fields of research and clinical practice. Cancer immunotherapy offers many advantages over conventional cancer treatments in terms of side effects, long-term effectiveness, the potential for achieving complete response, and the feasibility of combination therapy. However, in the case of drugs targeting CD38 and CD47, they have been identified to pose challenges regarding blood transfusion, causing false positive results during pre-transfusion compatibility testing, making it difficult to find suitable blood products or leading to delays in blood transfusion.

CD38 is a transmembrane protein antigen highly expressed on the surface of myeloma cells in patients with multiple myeloma, and it is best known as the primary target for monoclonal antibody therapy, daratumumab (Darzalex, Johnson & Johnson, New Brunswick, NJ, USA). CD38 is also expressed on the surface of immune cells such as lymphocytes and is known to have expression also on red blood cells (RBCs). As a result, when performing pre-transfusion testing on patients receiving daratumumab, the drug can attach to the RBCs used in the test, primarily in conditions where an indirect antiglobulin test is employed, leading to false positive results. The most challenging practical scenario involves panreactive false positive results exhibited during unexpected antibody screening or crossmatching, making it difficult to determine the presence of other RBC alloantibodies and hindering the selection of appropriate and safe blood products. To address this issue, the use of DTT treatment on RBCs is widely employed.

The CD47-signal regulatory protein α (SIRPα) checkpoint is a major mechanism used by macrophages to distinguish "self" from "non-self." In cancer cells, CD47 is known to be overexpressed as a means to evade macrophage phagocytosis. To block this mechanism, monoclonal antibodies targeting CD47 or drugs of the SIRPα-Fc fusion protein type have been developed and are being utilized in research for the treatment of solid and hematologic malignancies. The CD47 cell surface antigen is observed in various types of cells, including RBCs, where CD47 binds to the Rh complex and is expressed to a significant extent. For this reason, drugs with antibody-like properties that bind to CD47 and block the CD47-SIRPα pathway have been reported to interfere with pre-transfusion testing, similar to anti-CD38 drugs. However, a well-established method, such as DTT treatment of RBCs as in the case of CD38, to address interference in pre-transfusion testing related to CD47 has not been established. As it is difficult to confirm the presence of RBC alloantibodies, the current best practice is considered to be the implementation of extended antigen-matched RBC transfusion as an alternative. This session aims to provide a more detailed discussion of these topics.

ES03-3

Reappraisal of transfusion-transmitted infections

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The blood-derived blood products inherently cannot be free from the risk of infection, as they are biologic materials derived from the human body. To prevent this, many countries conduct screening tests for blood products intended for transfusion. However, due to technological limitations, it is still not possible to reduce the risk to zero. In this review, I aim to examine the current status of the risk of transfusion-transmitted infections and provide prospects for the future.

ES04-1

AL cardiac amyloidosis

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Amyloid light chain (AL) amyloidosis represents a complex and severe condition characterized by a systemic and progressive accumulation of amyloid proteins, particularly affecting individuals around the median age of 65, with a slight male predominance. This disorder, marked by clonal plasma cell dyscrasia, leads to the production of amyloidogenic immunoglobulin light chains, primarily of the λ subtype, which form insoluble fibrils depositing in various tissues and causing significant organ dysfunction. The heart, being the most frequently affected organ, showcases over three-quarters of patients presenting with cardiac symptoms at diagnosis, making cardiac involvement a critical factor in the disease's prognosis and the leading cause of mortality in AL amyloidosis, accounting for more than 61% of deaths.

The disease trajectory varies significantly with the extent of cardiac involvement, where patients with advanced cardiac disease have a median survival of merely four months, in contrast to a near five-year expectancy in less severe cases. Despite these daunting figures, advancements in therapeutic strategies and earlier detection have notably improved patient survival rates.

Cardiac manifestations are diverse, ranging from arrhythmias and heart failure to embolic events and conduction abnormalities, often culminating in life-threatening complications. The pathological hallmark in cardiac amyloidosis includes symmetrical thickening of the ventricular walls without dilation and a preserved ejection fraction until the advanced stages of the disease. The amyloid infiltration pattern in the heart is distinctive, with a reduction in longitudinal strain that is more pronounced than in other forms of heart failure, leading to a characteristic imaging pattern known as the "bull's-eye pattern."

Beyond the heart, AL amyloidosis affects multiple other organs, leading to a wide array of symptoms from nephropathy and hepatomegaly to neuropathy and macroglossia, further complicating the clinical picture and impacting patients' quality of life across various dimensions, including physical well-being, emotional health, and social functioning.

In summary, AL amyloidosis is a grave condition with a multifaceted impact on patients, predominantly dictated by the degree of cardiac involvement. Continuous advancements in medical research and treatment methodologies hold promise for better management and improved outcomes for those affected by this challenging disease.

ES04-2

Nephrologist's perspective on monoclonal gammopathy of renal significance

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Kidney disease frequently complicates multiple myeloma and other malignancies associated with monoclonal gammopathy. Nonetheless, kidney diseases related to dysproteinemia can also arise independently of overt multiple myeloma or hematologic malignancies.

Monoclonal Gammopathy of Renal Significance (MGRS) denotes a spectrum of disorders where a monoclonal immunoglobulin, produced by a benign or pre-malignant B cell or plasma cell clone, inflicts kidney damage. MGRS-associated renal diseases manifest in various forms, including immunoglobulin-associated amyloidosis, Monoclonal Immunoglobulin Deposition Diseases (MIDDs - light chain, heavy chain, and combined light and heavy chain deposition diseases), Proliferative Glomerulonephritis with Monoclonal Immunoglobulin Deposits (PGNMID), C3 glomerulopathy with monoclonal gammopathy, light chain proximal tubulopathy, among others. Although MGRS is a non-malignant or pre-malignant hematological condition, its renal implications are significant, often leading to progressive kidney damage and eventually end-stage kidney disease (ESKD).

This presentation will explore the diagnosis and management of MGRS, particularly focusing on the nephrologist's viewpoint.

ES04-3

Monoclonal gammopathies of neurological significance

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Monoclonal gammopathy is frequently found in the general population, which could be referred to as 'monoclonal gammopathy of undetermined significance' (MGUS) or related to hematological malignancies. MGUS is a premalignant disorder with a 0.5-1.5% per year risk of progression to multiple myeloma (MM) or other related hematological malignancies. In addition, this association of MGUS with peripheral neuropathy is not uncommon and monoclonal gammopathy is one of various disorders, which should be included in the differential diagnostic evaluation of peripheral neuropathy. Several clinical and laboratory features could differ between MGUS without neuropathy and MGUS with neuropathy. Therefore, it is important that MGUS should be monitored carefully whether neurological symptoms occur, particularly progressive sensorimotor deficits and ataxia.

ES05-1

Back to the basic: Coagulation pathway

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혈액응고는 섬유소원을 불용성의 섬유소로 변환시켜 손상된 혈관을 통한 출혈을 막는 과정이다. 이 과정은 extrinsic (tissue factor) pathway와 intrinsic (contact activation) pathway로 나누어 설명할 수 있다. 두 경로는 각각 FXa를 생성하고 FXa는 prothrombin을 thrombin으로 활성화시켜서 섬유소를 생성한다. 혈액응고는 phospholipid(PL) 표면에서 이루어지는데, tissue factor(TF)에 의한 응고 개시, intrinsic tenase complex에 의한 증폭, 그리고 혈소판 PL 표면에서의 전파 등 3단계로 이해할 수 있다.

혈관이 손상되면 TF가 혈액에 노출되면서 응고과정이 시작된다. 보효소인 TF는 FVII에 결합하고 FVII는 FVIIa로 활성화된다. Extrinsic tenase complex(FVIIa-TF, PL, Ca)는 FX과 FIX을 활성화시킨다. FXa는 보효소인 FVa와 결합하여 prothrombinase complex(FXa-FVa, PL, Ca)를 형성하고 prothrombin을 thrombin으로 활성화시킨다. 이때 생성되는 thrombin은 FVa 양이 적어 소량만 만들어진다.

Thrombin은 소량이지만 혈소판을 활성화하고 혈소판에서 FV를 분비시키고 활성화시킨다. 또한 thrombin은 FVIII을 활성화시키고 운반단백인 vWF로부터 분리시킨다. Thrombin은 FXI도 활성화한다. 활성화된 보효소인 FVIIIa는 FIXa과 결합하여 intrinsic tenase complex(FIXa-FVIIIa, PL, Ca)를 형성한다. Intrinsic tenase complex는 extrinsic tenase complex보다 50배 가량 더 강력하게 FX을 활성화시켜 대량의 thrombin을 생성한다(thrombin burst). Thrombin은 섬유소원에서 fibrinopeptide A와 fibrinopeptide B를 잘라내어 섬유소를 생성한다.

TF가 발현된 세포에서 FIXa는 혈중 억제인자들에 큰 영향을 받지 않고 혈소판 표면으로 이동하여 FVIIIa와 결합하고 FX을 활성화시킨다. Thrombin에 의해 활성화된 FXIa도 FIX를 활성화시켜 FXa 형성에 기여한다. Tissue factor pathway inhibitor(TFPI)는 FXa와 함께 TF-VIIa complex의 활성을 저해하고 FXa 생성을 정지시킨다. TF는 응고과정에 중요한 역할을 하지만 protease activated receptor(PAR) 등 수용체들과 반응하여 이루어지는 염증에서의 역할도 연구되고 있다.

강력한 응고제인 thrombin은 혈관내피세포 표면에서 thrombomodulin(TM) 및 endothelial cell protein C receptor(EPCR)와 결합하면 protein C를 활성화시켜 항응고작용을 나타낸다. Activated protein C(APC)는 EPCR에서 분리되면 보효소인 protein S와 함께 FVa와 FVIIIa를 불활성화한다. APC는 EPCR에서 분리되지 않으면 PAR-1과 반응하여 항염증 및 세포보호작용을 한다. Antithrombin은 thrombin 외에도 FXa, FIXa, FXIa, FXIIa, FVIIa 기능을 억제하여 응고과정을 조절한다.

Contact activation system은 혈액응고 뿐만 아니라 염증, 섬유소용해, 보체계 등과도 연관되어있다. 혈관내피세포가 손상되어 노출되는 collagen이나 채혈용기의 유리 등 음전하 물질은 FXII를 활성화시켜 intrinsic pathway를 활성화한다. FXIIa는 prekallikrein을 활성화시켜 kallikrein을 생성하고 kallikrein은 보다 많은 FXIIa를 생성한다. FXIIa는 FXI를 활성화시켜 응고를 촉진할 수도 있지만 지혈기전에서의 역할은 제한적이다. Kallikrein에 의해 high-molecular-weight kininogen으로부터 생성된 bradykinin은 염증반응에 관여한다. FXIIa는 plasmin 활성화를 통하여 섬유소용해를 촉진할 수도 있고 보체계의 C1r, C1s를 활성화시킬 수도 있다. 보체계 억제에 중요한 C1 inhibitor는 FXIIa의 주된 억제제이기도 하다.

ES05-2

Pharmacology: Anticoagulants and reversal agents

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ES05-3

Proper application of anticoagulation therapy on cancer associated thrombosis

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ES06-1

Functional iron deficiency in cancer patients

Ik-Chan Song
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In cancer patients, anemia is commonly observed due to anticancer chemotherapy or radiation therapy, as well as the inflammatory response caused by the cancer itself. In such cases, functional iron deficiency may occur, where there is sufficient stored iron, but a reduced functional utilization of iron needed for red blood cell production. Functional iron deficiency anemia is defined by a ferritin level between 30 and 500μg/dL with a transferrin saturation of less than 50%. Functional iron deficiency often arises following continued erythropoiesis stimulating agent (ESA) use, resulting in a blunted erythropoietic response to anemia. Although oral iron has been used more commonly, intravenous iron has superior efficacy and should be considered for supplementation in this setting. Recently, many studies have reported on the efficacy of ferric carboxymaltose in various conditions accompanied by iron deficiency. In the randomized clinical trial IVICA trial, which included 116 anemia colorectal cancer patients, preoperative administration of ferric carboxymaltose in higher Hb levels after surgery compared to oral ferrous sulfate. And a follow-up study indicated that patients who received ferric carboxymaltose had significantly improved quality of life scores, compared to patients who received oral iron. However, ferric carboxymaltose has been associated with severe phosphate deficiency that is often asymptomatic. Therefore, patients receiving ferric carboxymaltose should be closely monitored for hypophosphatemia.

ES06-2

Assessment of neutropenia in hospitalized patients

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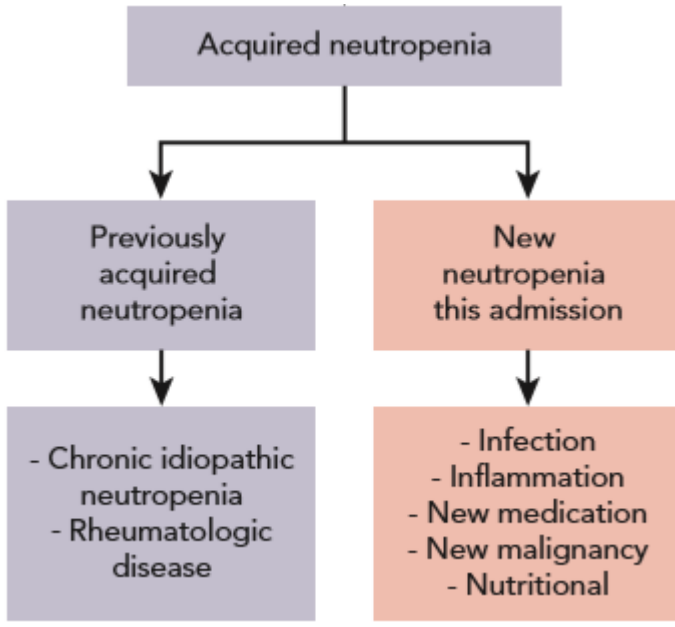
Neutrophils play an essential role in immune defenses by ingesting, killing, and digesting invading microorganisms, including fungi and bacteria. Neutropenia is a common clinical problem seen in clinical practice and the prevalence of neutropenia is reported from 0 to 10 percent in healthy, asymptomatic individuals, but is higher in individuals with certain medical conditions (eg, autoimmune, connective tissue diseases, and malignancies). The etiologies of neutropenia vary from transient suppression by self-limited viral illnesses to previously undetected congenital syndromes to serious systemic diseases. The clinical significance likewise ranges from a mild laboratory abnormality with no detectable consequence to a severe disorder characterized by recurrent, life-threatening infections. Especially, the hospitalized patient with neutropenia should be promptly assessed for potential medical emergencies and managed accordingly. Evaluation of neutropenia in the hospitalized patient should determine, when possible, whether neutropenia developed during the hospitalization or was present previously. Results of CBCs with differential counts from prior hospitalizations and the ambulatory setting are important for making these distinctions.



ES06-3

Perioperative consultation for the appropriate transfusion

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ES07-1

Genomic technologies for detecting structural variations in hematologic malignancies

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Sungkyunkwan University School of Medicine, Korea

Genomic structural variations in myeloid, lymphoid, and plasma cell neoplasms can provide key diagnostic, prognostic, and therapeutic information while elucidating underlying disease biology. A variety of molecular diagnostics plays a central role in the evaluation of hematologic malignancies. Traditional cytogenetic diagnostic assays such as chromosome banding and fluorescence in situ hybridization are essential components of the current diagnostic workup that guides clinical care for most hematologic malignancies. However, there are inherent limitations to each assay, including limited resolution for detecting small structural variations and low coverage that can only detect alterations in the target regions. Recently, rapid expansion and increasing availability of novel and comprehensive genomic technologies are leading to adoption in clinical laboratories for use in clinical management and translational research. This review aims to improve understanding of the clinical utility of structural variation in hematologic malignancies and to introduce various genomic technologies that enable more personalized tumor characterization and individualized treatment.

ES07-2

The role of NGS in hematologic malignancies

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University of ulsan College of Medicine, Korea

Genetic abnormalities have been classically identified through traditional cytogenetics, fluorescence in situ hybridization, and single polymerase chain reaction tests. Next-generation sequencing (NGS) allows simultaneous detection of dominant molecular alterations and minor clones in a high-throughput, efficient, and cost-effective manner. The ability to detect multiple targets in multiple samples dramatically reduces overall cost and test time compared to stepwise analysis using a single test. Over the past 15 years, NGS has rapidly evolved from a promising research tool to a core component of the clinical laboratory. Sequencing of tumor cells provides an important step to detect somatic driver mutations that not only characterize the disease but also influence treatment decisions. In hemato-oncology, NGS technology is used for accurate classification and diagnosis based on genetic alterations, risk stratification, treatment guidance, and even disease monitoring [1]. In the context of this advancement, the classification of blood cancers recently revised by the World Health Organization and the European Leukemia Net recommendations for the diagnosis and management of acute myeloid leukemia consider genetic abnormalities as a top priority for diagnosis and prognostication, monitoring measurable residual disease and treatment choice [2, 3]. Here, we will review the role, strengths, and limitations of various NGS approaches for the diagnosis, treatment, and follow-up of hemato-oncology patients.

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ES07-3

Germline predisposition to hematologic malignancies

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Recent advances in technology lead to high throughput sequencing, especially gene panel testing, of hematologic malignancies in clinical practice. Germline predisposition had been only considered in certain patients with prior personal history of multiple cancers or with family history. However, recent studies have shown that inherited hematologic malignancies are underappreciated and may be diagnosed at a later stage in life, without prior syndromic features, or without personal history or relevant family history. The diagnosis of germline predisposition may change choice of therapy, donor selection for hematopoietic stem cell transplantation, patient management and surveillance. This review will discuss approaches to diagnose various germline predisposition to hematologic malignancies and review current genomic testing for germline predisposition in hematologic malignancies.

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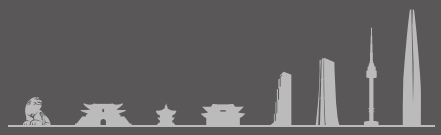

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SATELLITE SYMPOSIUM

SY01

Treatment of newly diagnosed multiple myeloma: Focus on daratumumab combination

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Despite advances in myeloma care, multiple myeloma (MM) remains an incurable disease, and almost all patients relapse after treatment. The use of effective combinations early in the treatment pathway may prolong remission and increase the chances of a positive long-term outcome. The European Hematology Association (EHA)-European Society for Medical Oncology (ESMO) guidelines recommend Daratumumab-based regimens as first-line treatment options for both transplant-eligible and transplant-ineligible patients with Newly diagnosed multiple myeloma. The use of Daratumumab combined quadruplet therapy for transplant-eligible patients has have demonstrated their clinical benefits, paving the way for their consideration in the treatment regimen. Its efficacy and safety in patients with Daratumumab/Bortezomib/Thalidomide/Dexamethasone (DaraVTd) were evaluated in the CASSIOPEIA trial, which included 1,085 patients. In Part 1, DaraVTd induction/consolidation improved depth of response, including increased rates of sCR, ≥CR, and MRD negativity, and prolonged progression free survival. MRD-negativity rates and sustained MRD-negativity rates were significantly higher after D-VTd induction/consolidation versus Bortezomib/Thalidomide/Dexamethasone (VTd). The most common grade 3 or 4 adverse events were neutropenia, lymphopenia, and stomatitis. Besides, the recent updates on Daratumumab/Bortezomib/Lenalidomide/Dexamethasone (from the Griffin/Perseus trial), Daratumumab/Carfilzomib/Lenalidomide/Dexamethasone (from the IFM 2018-04 trial), and Isatuximab/Carfilzomib/Lenalidomide/Dexamethasone (from the IsKia EMN24 trial) affirm the significant strides in treatment advancements. For transplant-eligible patients, the inclusion of a monoclonal antibody as part of a quadruplet therapy regimen is now being considered as a standard of care, reflecting a significant evolution in therapeutic approaches.

In South Korea, the VRd regimen is the standard of care, and access to Darzalex combination therapy is limited due to it being non-reimbursable yet. In this presentation, we aim to discuss the clinical usefulness of DVTd as an induction therapy, particularly focusing on patient populations where it can offer clinical benefits and, notably, greater clinical advantages compared to VRd, such as those with renal impairment or high risk.

SY02

The ultimate value of C5 inhibitors in the evolving treatment landscape of PNH

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Paroxysmal Nocturnal Hemoglobinuria (PNH) is a rare hematologic disorder distinguished by chronic intravascular hemolysis (IVH) resulting from a deficiency in glycosylphosphatidylinositol (GPI)-anchor protein synthesis caused by the PIG-A gene mutation [1-3]. With an incidence of 15.9 per million population, PNH presents a distinctive challenge in the field of hematologic diseases [4, 5]. Clinical manifestations encompass elevated lactate dehydrogenase (LDH), diminished hemoglobin levels [6], and associated complications such as thrombosis and pulmonary hypertension [7].

The primary therapeutic goal in PNH management is to control IVH, which is recognized as the main physiological threat, along with associated symptoms like anemia, fatigue, and low hemoglobin levels. This is crucial because IVH leads to a red blood cell destruction rate (200 mL of RBC/hour), approximately 10 times higher than that of extravascular hemolysis (EVH) [8]. Recognizing the criticality of timely diagnosis and proactive intervention is pivotal, as conventional treatments like oral iron supplementation, red blood cell transfusion, and antibiotic therapy have historically yielded high 5-year (35%) and 10-year (50%) mortality rates [9].

Thus, introducing C5 inhibitors has revolutionized the landscape of PNH treatment. A comprehensive analysis of real-world data from the Korean Health Insurance Review and Assessment Service, spanning from 2009 to 2020 and focusing on the first-generation monoclonal antibody C5 inhibitor, eculizumab, reveals notable outcomes. This study includes 80 patients with PNH and a high disease burden. The overall survival rates reached an impressive 96.2%, and LDH levels stabilized in most patients throughout the treatment duration. Furthermore, the introduction of eculizumab resulted in the resolution of complications related to PNH at the initiation of treatment. Specifically, 44.4% of patients with renal failure, 95.8% with smooth muscle spasm, 70.0% with thromboembolism, and 26.7% with pulmonary hypertension experienced resolution of these complications. This advancement in PNH treatment with C5 inhibitors not only contributes to an enhanced quality of life for patients but also underscores the long-term efficacy and safety of these interventions in managing PNH [10].

Afterward, ravulizumab, an enhanced C5 inhibitor designed to augment the therapeutic efficacy of the former, has emerged. Ravulizumab features a 4-fold longer half-life achieved through FcRn-mediated recycling in an acidic endosome environment. Clinical studies, namely 301 (NCT02946463) and 302 (NCT03056040), have demonstrated immediate, complete, and sustained C5 inhibition, along with excellent safety profiles and a significant reduction in breakthrough hemolysis (BTH) compared to eculizumab among both inhibitor-naïve patients and those switched from eculizumab [11-13]. Subsequently, an extension study (301) was conducted to compare the survival rates between ravulizumab and eculizumab. Over a period of up to 6 years, ravulizumab provided effective long-term control of IVH, as evidenced by the maintenance of LDH levels and a low incidence of major adverse vascular events, including thrombotic events. Furthermore, age- and sex-adjusted survival analysis revealed a significantly lower risk of death in patients treated with ravulizumab (hazard ratio [95% confidence interval] = 0.14 [0.06-0.32]) [14].

Recently, there has been a notable emergence of C3 inhibitors targeting the proximal complement system to address the unmet needs associated with C5 inhibitors, such as EVH [15, 16]. While offering the advantage of sustaining elevated hemoglobin levels [17], a documented risk of increased LDH levels, reaching up to 10~15 times the upper limit of normal (ULN) and resulting in massive BTH, has been reported [1, 6]. Consequently, despite the potential benefits of C3 inhibitors in hemoglobin preservation, the fundamental issue of IVH in PNH treatment remains. Thus, C5 inhibitors, ensuring long-term efficacy and safety, persist as the established standard care for PNH [10, 18, 19].

As the landscape of PNH treatment continues to evolve, a nuanced understanding of determinants beyond mere symptom improvement becomes imperative for enhancing patients' quality of life. A post hoc analysis of ravulizumab's 301 study underscores the statistically significant association between the reduction in absolute mean LDH levels and the improvement in patient-reported outcomes. Metrics such as Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) scores revealed rapid and sustained improvements in quality of life, even with modest increases in hemoglobin levels. Notably, patients with LDH levels < 1.5 x ULN consistently exhibited greater improvements in FACIT-F and EORTC QLQ-C30 scores across all time points compared to those with LDH levels ≥ 1.5 x ULN [20]. Additionally, the extension study 302 highlights PNH treatment preferences, revealing that 93% of eculizumab-experienced patients favor ravulizumab. The 11-item questionnaire emphasizes factors such as infusion frequency, planning activities, and overall quality of life. Notably, 43% identified infusion frequency as the most crucial factor. This patient-centric approach underscores the need to consider holistic aspects, indicating a step toward more personalized and impactful PNH care with ravulizumab [21].

SY02

In conclusion, PNH, a rare disease characterized by persistent IVH, poses a significant challenge. C5 inhibitors, notably eculizumab and ravulizumab, have revolutionized treatment. Eculizumab shows a remarkable 96.2% survival rate and complication resolution, while ravulizumab, with a 4-fold longer half-life, exhibits superior efficacy. Ravulizumab emerges as a valuable choice, providing sustained IVH control and positive impacts on patient-reported outcomes, emphasizing its potential as a preferred treatment. Despite C3 inhibitors' emergence, C5 inhibitors remain the standard care for PNH. The evolving treatment landscape underscores the importance of comprehensive outcomes beyond symptom relief, with ravulizumab demonstrating a significant association between reduced LDH levels and improved quality of life metrics. In summary, the continued importance of C5 inhibitors in the treatment of PNH underscores their pivotal role in the evolving landscape of PNH therapy. These inhibitors not only transform physiological outcomes but also significantly enhance overall well-being for patients.

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SY03

Treatment strategies for elderly AML with FLT3-mutation, entering the era of FLT3 Inhibitors

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FMS-like tyrosine kinase 3 (FLT3) mutations are found in 25-30% of patients with acute myeloid leukemia (AML) and are associated with leukemic cell proliferation through constitutive activation of receptor-type tyrosine kinases. While FLT3-ITD-positive AML generally responds to chemotherapy, the short duration of remission and high relapse rate leads to consideration of allogeneic transplantation.

FLT3 inhibitors are classified into two major types based on their inhibitory activity according to their structural formula: type 1 inhibitors (midostaurin, gilteritinib), which are effective for both FLT3-ITD and TKD mutations, and type 2 inhibitors (sorafenib, quizartinib), which are effective only for FLT3-ITD mutations. Although the use of FLT3 inhibitors has improved the prognosis of Fit patients with FLT3-mutated AML, in elderly patients who are not candidates for transplantation, the goals of treatment are prolonged survival and improved quality of life, which requires appropriate use of low intensity agents.

Azacitidine and venetoclax (AZA/VEN) are commonly used as initial induction therapy for unfit patients who are not eligible for intense chemotherapy, based on the results of the VIALE-A trial. Although AZA/VEN treatment in this trial also demonstrated a high remission rate in FLT3-mutated AML, unfortunately no survival advantage was found in the subgroup analysis. One reason for this has been indicated as the expansion of FLT3 mutated clones. When AZA/VEN therapy is used to prolong OS, any signs of increased leukemic cells after initial response should be checked for FLT3 mutations.

For FLT3-mutated AML that relapsed after initial therapy, monotherapy with gilteritinib or quizartinib has been shown to have better response rates and longer survival than salvage chemotherapy (FLAG, MEC, azacitidine, etc.). In a phase III study (ADMIRAL trial) comparing gilteritinib and salvage chemotherapy, the CRc rate was significantly higher in the gilteritinib group (34% vs. 15%) and the median overall survival was significantly longer than that in the salvage chemotherapy (9.3 months vs. 5.6 months; hazard ratio for death, 0.64). Long-term follow-up data from the ADMIRAL trial were also published, showing favorable tolerability and long-term safety. Because of the different adverse event profiles of AZA/VEN and gilteritinib, it is recommended that treatment strategies for older patients with AML be based on an evaluation of patient factors (organ function, cognitive function, and social support) and treatment goals.

In addition, the Beat AML S8 study of a triplet therapy (decitabine/VEN/gilteritinib) in newly diagnosed FLT3-mutated AML aged ≥60 years old showed a high response rate (CRc rate 61.1%) and did not reach median OS (median follow-up 19.7 months). In the future, the triplet therapy (AZA/VEN/gilteritinib) is expected to be used to achieve a deeper response and longer survival for elderly patients with FLT3-mutated AML who are ineligible for intensive chemotherapy, and the results of ongoing clinical trials (NCT05520567) are awaited.

SY04

Advances in the treatment paradigm with bispecific antibodies

Wendy Osborne
Newcastle University, UK

The development of bispecific antibodies for lymphoma has allowed our patients to have an "off the shelf" T cell engaging treatment. To maximise patient benefit, we need to optimise the delivery of these new drugs and understand optimal patient selection. More treatment options are now available for relapsed/refractory B cell lymphoma and the impact of one treatment on the subsequent efficacy of the next, will become a focus of research to further improve patient outcomes.

SY05

Continued hope with ONUREG - A new maintenance therapy to treat AML

Esther Oliva
Grande Ospedale Metropolitano Bianchi Melacrino Morelli, Italy

Acute myeloid leukemia (AML) generally affects older adults and has a poor prognosis. Although induction chemotherapy results in complete remission (CR) in many, relapse is common and overall survival is poor. Subcutaneous azacitidine as maintenance therapy has not shown clear advantage in improving outcomes in patients obtaining a CR. A phase 3, randomized, double-blind, placebo-controlled trial, compared Onureg, the oral formulation of azacitidine (CC-486, a hypomethylating agent that is not bioequivalent to injectable azacitidine) to placebo as maintenance therapy in patients with AML who were 55 years of age or older, in CR with or without complete blood count recovery, and were not candidates for hematopoietic stem-cell transplantation. Patients were randomly assigned to receive CC-486 (300 mg) or placebo once daily for 14 days per 28-day cycle. The primary end point was overall survival. Secondary end points included relapse-free survival and health-related quality of life (HRQOL).

472 patients underwent randomization; 238 were assigned to the CC-486 group and 234 to the placebo group. The median age was 68 years (range, 55 to 86). Median overall survival from the time of randomization was significantly longer with CC-486 than with placebo (24.7 months and 14.8 months, respectively; $P<0.001$). Median relapse-free survival was also significantly longer with CC-486 than with placebo (10.2 months and 4.8 months, respectively; $P<0.001$). Benefits of CC-486 with respect to overall and relapse-free survival were shown in most subgroups, including patients with FLT-3 mutations, defined according to baseline characteristics. Some cases with minimal residual disease (MRD) at randomization becane MRD negative during randomization. Modulation of dosing prevented overt relapse in some cases. The most common adverse events in both groups were grade 1 or 2 gastrointestinal events. Common grade 3 or 4 adverse events were neutropenia (in 41% of patients in the CC-486 group and 24% of patients in the placebo group) and thrombocytopenia (in 22% and 21%, respectively). HRQOL was preserved and comparable in both arms. In conclusion, CC-486 maintenance therapy was associated with significantly longer overall and relapse-free survival than placebo among older patients with AML who were in remission after chemotherapy. Side effects were mainly gastro-intestinal symptoms and neutropenia. HRQOL measures were maintained throughout treatment.

SY06

Mogamulizumab: A new era in MF/SS management - Clinical evidence and practical consideration

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SY07

TKI treatment pattern and new therapy of CML

Qian Jiang
Peking University People's Hospital, China

Background: Effective TKIs options are available in early lines of therapy for CML, but patients may experience intolerance or resistance to TKIs.

Methods: Review of TKI treatment pattern and the new therapy of CML from the last 3-5 years.

Results: CML patients with TKI treatment are faced with resistance or intolerance, or both. In China, patients resistant to TKIs are not uncommon, resulting in a substantial unmet clinical need.

There are currently a variety of drugs working to address this issue. Several studies show that asciminib(ABL001), the first BCR::ABL1 inhibitor that works by Specifically Targeting the ABL Myristoyl Pocket (STAMP), can quickly achieve a deep molecular response in CML-CP patients who have previously been resistant or intolerant to ≥2 types of TKIs. Olverembatinib (HQP1351), compared to the existing best available treatment, demonstrated superior efficacy and tolerability in patients with TKI-resistant CML-CP. Phase I study indicated that Tgrx-678 exhibited favorable clinical activity and tolerability in patients with TKI-resistant / refractory CML. Moreover, ponatinib has proven its efficacy as salvage therapy for patients intolerant, or resistant to at least 2 TKI in CP-CML.

Conclusions: New generation of TKIs, especially STAMP inhibitor hold promise in addressing CML resistance / intolerance after ≥2TKIs.

SY08

The optimal treatment strategy for transplant-ineligible relapsed/refractory DLBCL

Kwai Han Yoo
Gachon University College of Medicine, Korea

While initial chemoimmunotherapy cures most patients with diffuse large B-cell lymphoma (DLBCL), approximately 30%-40% will experience relapsed or refractory (R/R) disease. The standard approach for treating these individuals involved salvage chemotherapy, followed by an autologous stem-cell transplant (ASCT). However, approximately half of the patients cannot undergo ASCT due to various reasons such as age, comorbidities, or poor performance status, and it has significant therapeutic challenges with poor outcomes.

Tafasitamab is a monoclonal antibody targeting CD19, a protein ubiquitously expressed on the surface of B-cells. When paired with lenalidomide, an immunomodulatory agent, the synergy between the two drugs activates multiple immune pathways, leading to enhanced antitumor activity. This multimodal action facilitates direct tumor cell killing and primes the immune system to recognize and eliminate cancer cells more effectively. The L-MIND trial, a single-arm, multicenter study, demonstrated a significant improvement in overall response rates and progression-free survival among patients treated with tafasitamab plus lenalidomide, marking a notable advancement in the management of transplant-ineligible R/R DLBCL patients. Complementing these results, the RE-MIND2 study further solidified the position of tafasitamab and lenalidomide within the DLBCL treatment landscape by employing a real-world evidence approach.

While CAR T-cell therapy has proven effective for treating R/R DLBCL, and several bispecific T-cell engagers (BiTEs) are being introduced, accessibility of immunotherapy remains limited in many countries, including Korea. In this context, chemotherapy-free regimens, including tafasitamab plus lenalidomide, can serve as complementary alternatives to immunotherapy for transplant-ineligible patients with R/R DLBCL.

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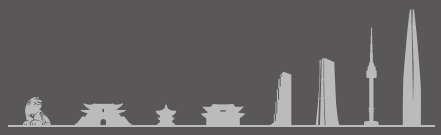

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ORAL PRESENTATION

PAP01-1

A single-arm, open-label, multicenter study to assess molecular response of P1101 therapy in patients with polycythemia vera and elevated hematocrit: Results from 48 weeks core study

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Background : Ropeginterferon alfa-2b(P1101) has shown greater effectiveness in achieving durable hematological and molecular remissions than hydroxyurea in patients with polycythemia vera (PV). However, there are limited data on the clinical relevance of MR during P1101 in Eastern Asians. Here, we evaluated clinical and molecular response, and the association between efficacy and MR.

Method : Patients were eligible if 19 years or older with PV diagnosed by WHO's 2016 criteria, requiring cytoreductive therapy and elevated hematocrit (>45%). Patients were treated with P1101 subcutaneously every 2 weeks, starting at a dose of 250 μg, followed by 350 μg in week 2, 500 μg in week 4, and thereafter until week 48. The JAK2 Val617Phe allele burden was assessed every 12 weeks (Core Study).

Results : A total of 99 patients were enrolled, and considering the full analysis definition, a total of 95 patients were included in this analysis: 52 (54.7%) patients was HU-naïve and 43 (45.3%) patients was HU-resistant/intolerant(R/I). The median age was 58 years (range, 26-81). During 48 weeks of treatment, CHR was achieved in 27%, 46%, 56%, and 63% at 12, 24, 36, and 48 weeks, respectively. In terms of molecular response (defined as 2009 ELN criteria), 32%, 36%, 49%, and 57% achieved the MR at 12, 24, 36, and 48 weeks, respectively. The Phi Coefficient for determining of association between CHR and MR was 0.61 ($P<0.0001$) at 48 weeks. In the safety profiles, there were 75 subjects (76%) with at least one treatment-emergent adverse events and 56 subjects (57%) with at least one treatment-related adverse events.

Conclusion : This study demonstrated that ropeginterferon alfa-2b therapy, with rapid dose optimization, induced hematological response, reduced JAK2 allele burden, and was well tolerated in Korean. Moreover, we clarified the association between efficacy and molecular response as assessed by a reduction in JAK2 allele burden.

Keywords : Polycythemia vera, Ropeginterferon alfa-2b, JAK2 mutation allele burden, Complete hematologic response, Molecular response

PAP01-2

Novel genomic variants influencing methotrexate delayed excretion in pediatric patients with acute lymphoblastic leukemia

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Background : Methotrexate (MTX) is the primary drug used in the treatment of pediatric acute lymphoblastic leukemia (ALL). However, some patients exhibit delayed excretion of high-dose (HD) MTX, which induces severe nephrotoxicity. We sought to identify relevant mutations associated with delayed excretion of HD MTX in pediatric patients with ALL.

Method : Whole exome sequencing of germline DNA was performed in 51 Korean pediatric acute ALL patients who received intravenous HD MTX 5g/m^2/dose as a 4 h infusion with oral 6-mercaptopurine and intrathecal MTX. Clinical data including serum MTX levels and toxicity markers were collected. A total of 341 HD MTX infusion data from 51 patients and 51 representative infusions showing maximum fold creatinine (maximum fold Cr) for each patient were analyzed. Correlations between serum MTX level at 24 h as peak level and toxicity markers were assessed. Analyses were performed to identify variants affecting delayed MTX excretion.

Results : The 24 h MTX level was strongly correlated with subsequent creatinine level. In 51 infusions showing max fold Cr, Grade 2 - 3 acute kidney injury was developed in 13 (25.5%) of the 51 infusions. One (2.0%) patient experienced grade 4 toxicity requiring dialysis. DE was developed in 25 (49%) of the 51 infusions showing max fold Cr. Moreover, rs2229866 in CNTN2, rs200687372 in MTMR9, rs777260512 in POLI, rs16954698 in PKD1L2, rs117765468 in NSMCE1, and rs1800956 in ENG were identified as candidate variants associated with delayed MTX excretion. In particular, ENG rs1800956 was significantly associated with delayed MTX excretion in all analyses.

Conclusion : This is the first whole-exome sequencing-based analysis of delayed MTX excretion in pediatric patients with ALL. Six candidate variants were identified, and ENG rs1800956 was identified as a novel and promising variant affecting delayed MTX excretion. Therefore, further analyses and validation are required.

Keywords : Methotrexate, Children, Acute lymphoblastic leukemia, Pediatric, Pharmacogenomics

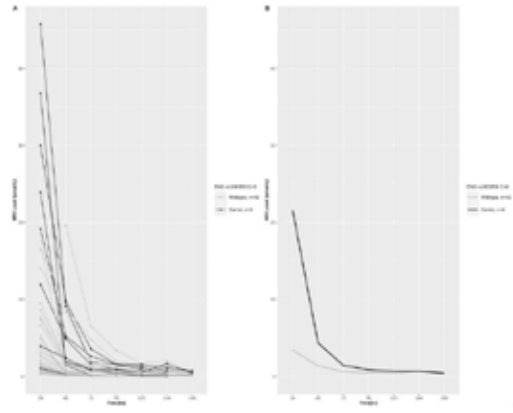

Figure 1. Longitudinal trajectories of serum MTX levels for *ENG* rs1800956. (A) Individual trajectories of each group. (B) Mean trajectories of each group.

PAP01-3

Prognostic utility of minimal residual disease (MRD) after curative intent induction therapy for DLBCL: A prospective real-world ctDNA study

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Background : We assessed longitudinally measured ctDNA levels in real-world DLBCL patients treated with anthracycline-based chemotherapies for the practical utility of ctDNA MRD assays in forecasting survival outcomes.

Method : We prospectively enrolled 99 ND-DLBCL patients undergoing anthracycline-based chemotherapy (RCHOP or E-EPOCH) for ctDNA profiling at 3 pre-defined milestones (Baseline, Interim after 3 cycles (C4D1), and end of treatment [EOT]). Three hundred

sixty-four samples were profiled in a blinded manner by phased variable enrichment and detection sequencing (PhasED-Seq, Foresight Diagnostics). MRD positive was determined when ctDNA levels exceeded an analytical detection threshold (~1:106 cfDNA molecules) corresponding to 98% specificity. MRD levels were compared to standardized responses by PET/CT (Lugano 2014), PFS, and OS.

Results : The median age was 58, and 67% had stage III-IV disease. 53% had IPI scores ≥3, and 6% had MYC and BCL2 translocations. The median follow-up was 44 months. We tested ctDNA performance at each landmark for predicting outcomes. When dividing pretreatment ctDNA levels at the median, ctDNA significantly predicted outcomes (PFS: p=0.004, OS: p=0.0004). At C4D1 and EOT, patients were categorized based on detectable or undetectable ctDNA-MRD. This stratification significantly correlated with outcomes at both C4D1 (PFS: p=0.0002, OS: p=0.0046) and EOT (PFS: p<0.0001, OS: p<0.0001). Additionally, while interim PET/CT scans were prognostic for PFS, they were not significantly prognostic for OS (PFS: p=0.02, OS: p=0.06). At EOT, PET/CT scans were prognostic for PFS and OS (PFS: p=0.011, OS: p=0.011). At both milestones, PET/CT appeared less discriminatory than ctDNA-MRD. A Cox proportional hazards model for OS revealed sustained prognostic value for ctDNA-MRD at interim and EOT, while PET/CT lost significance in predicting outcomes.

Conclusion : The higher predictive value and accuracy of detectable ctDNA-MRD compared with PET/CT suggest opportunities to integrate such assays in lymphoma response criteria, potentially informing future clinical decision-making.

Keywords : Diffuse large B cell lymphoma, ctDNA, Minimal residual disease

OP01-1

The transcriptomic profiles of NPM1 mutated acute myeloid leukemia reveal distinct subtypes characterized by varying clinical outcomes

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Background : Nucleophosmin (NPM1) mutations in acute myeloid leukemia (AML) are typically linked to a favorable survival outcome after standard therapy. Nonetheless, within the subset of NPM1-mutated AML cases, distinct clinical outcomes are observed, highlighting the existence of heterogeneity within this group. In this study, we employed RNA-seq-based gene expression profiling to delineate the molecular heterogeneity among patients with NPM1-mutated AML.

Method : The RNA-sequencing data of 77 patients diagnosed with NPM1-mutated AML from the University Health Network cohort in Toronto, Canada, were subjected to comprehensive analysis. Employing supervised clustering, candidate gene clusters were discerned based on FLT3-ITD and corresponding expression profiles. A Likelihood Ratio Test (LRT) was executed to identify differentially expressed genes (DEGs) within these candidate clusters. Epigenetic modifier genes (EMGs) of particular interest were then extracted from the DEG list and subjected to functional analysis using Enrichr.

Results : By employing clustering techniques, we identified six distinct clusters. Remarkably, one cluster from the FLT3-ITD negative subset exhibited a gene expression profile (GEP) like that of the FLT3-ITD positive group. Notably, epigenetic modifier genes (EMGs) demonstrated significantly disparate expressions among these delineated clusters. Upon examining the interplay between these EMGs and FLT3-ITD, IDH1 consistently exhibited higher expression in the cluster associated with poorer outcomes, irrespective of FLT3-ITD condition. In contrast, TET2 expression significantly increased within clusters associated with a favorable outcome, specifically within the FLT3-ITD positive group. A multivariate analysis underscored that elevated TET2 expression within the FLT3-ITD positive group correlated with a favorable response rate. Importantly, these findings were validated in the BeatAML cohort.

Conclusion : The observed differential expressions of TET2 and IDH1 across distinct clusters in NPM1-mutated AML underscore their potential as valuable prognostic markers and therapeutic targets. This highlights their prospective utility in guiding tailored treatments for NPM1-mutated AML.

Keywords : Acute myeloid leukemia, NPM1 mutation, Gene expression profile, RNA sequencing

OP01-2

Leukemic stem cells in acute myeloid leukemia further refine treatment outcomes in ELN molecular risk groups

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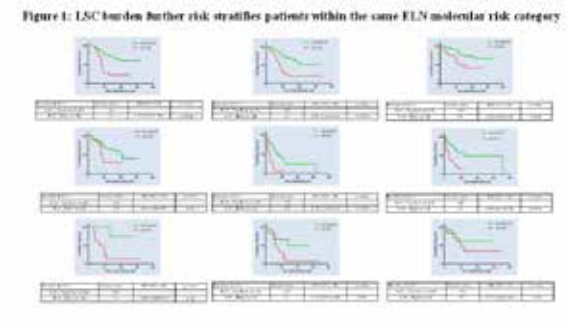
Background : Measurable residual disease (MRD) and molecular risk categories are the strongest predictors of survival in AML but a considerable fraction of MRD-negative and good molecular risk patients relapse. Leukemic stem cells (LSCs) have emerged as a major breakthrough in this context and are believed to be responsible for disease refractoriness and relapse. This study aimed to evaluate the impact of LSC burden on short-term outcomes in terms of conventional and deep responses after induction therapy and long-term treatment outcomes of relapse-free survival (RFS), event-free survival (EFS), and overall survival (OS).

Method : The diagnosis of AML was established as per the WHO 2016 guidelines. Molecular risk stratification was done as per the European Leukemia Net (ELN) guidelines. Enumeration of LSCs and MRD assessment was done using flow cytometry. The median LSC percentage was correlated with treatment outcomes.

Results : LSCs were identified in 83.8% of AML patients (n=161). Patients achieving complete remission (p=0.02) and MRD negativity (p=0.03) had lower median LSC% compared to those not achieving morphological remission or with MRD-positive status. Patients were divided into LSClow and LSChigh groups based on median LSC%. The LSCneg group had higher RFS, EFS, and OS compared to the LSClow (p=0.01) and LSChigh (p<0.0001) group of patients. LSCneg/low group had significantly higher RFS (ELNFAV: HR=3.39, p=0.0002; ELNINT: HR=2.60, p=0.09; ELNADV: HR=7.28, p=0.02), EFS (ELNFAV: HR = 3.29, p< 0.0001; ELNINT: HR=2.90, p<0.0001; ELNADV: HR=3.10, p=0.06) and OS (ELNFAV: HR=2.62, p=0.009; ELNINT: HR=4.55, p=0.0004; ELNADV: HR=1.76, p=0.46) compared to LSChigh across the ELN molecular risk groups (Figure 1).

Conclusion : The LSC burden at baseline is a biomarker of early treatment outcome and a predictor of relapse and survival outcomes. Furthermore, LSC burden further risk stratifies patients within the same ELN molecular risk category.

Keywords : Leukemic stem cells, Acute myeloid leukemia, Flow cytometry, Survival, MRD



OP01-3

Azacitidine combined with novel flavonoid derivative GL-V9 demonstrated synergistic anti-leukemia effect in acute myeloid leukemia by targeting DDIT4/mTOR signaling

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Background : Acute myeloid leukemia (AML) is a highly heterogeneous hematologic malignancy. GL-V9, derived from wogonin, hinders cancer cell growth. Azacitidine (AZA), an effective DNA hypomethylation agent against AML, is examined in combination with GL-V9 for enhanced anti-leukemia effects and potential mechanisms.

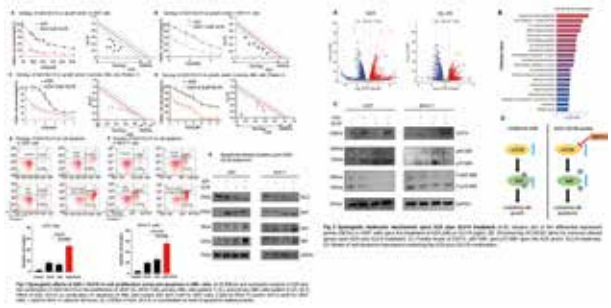
Method : We evaluated cell viability using CCK-8, apoptosis via Annexin-V/PI staining and flow cytometry. Gene expression was examined through RNA-sequencing, RT-qPCR, and Western Blot.

Results : Our results demonstrated significant cell proliferation arrest

in AML cell lines, treated with the combination of AZA and GL-V9, compared to the single drug (Fig. 1A&B). CalcuSyn analysis showed a strong synergistic effect for the combination (Fig. 1A&B). Similar results were also found in primary AML cells derived from 2 AML patients [patient 1 exhibited t(6;11) (q27;q23) chromosomal translocation, while Patient 2 presented with secondary AML) and featured ASXL1 and SRSF2 mutations] (Fig. 1C&D). Moreover, AZA plus GL-V9 induced a substantial increase in cell apoptosis in U937 and MV4-11 cells compared to the single drug (Fig. 1E&F). Consistently, the AZA+GL-V9 combination led to a notable increase in the protein level of Bax, BAD, BIM, and a decrease in BCL2 (Fig. 1G). To understand the underlying mechanisms of this synergy, we performed RNA-seq analysis in U937 cells, identifying 1385 and 586 DEGs (log2FC≥2.0, P<0.05) upon AZA or GL-V9 treatment, respectively (Fig. 2A). The mTOR signaling pathway exhibits prominent enrichment in the KEGG analysis of the overlapping DEGs between AZA and GL-V9 (Fig. 2B). DDIT4, a negative regulator of mTOR emerged as one of the top DEGs in response to both AZA and GL-V9 treatment. Importantly, the AZA+GL-V9 treatment exhibited a higher expression level of DDIT4 compared to either drug alone and suppressed the phosphorylation of p70 S6K (Fig. 2C).

Conclusion : These findings suggested that the combination may exert the anti-leukemia effect by targeting the DDIT4/mTOR signaling pathway (Fig. 2D).

Keywords : Azacitidine, GL-V9, Synergistic, AML



OP01-4

Exploring the genetic landscape of B-ALL: Upregulation of cell adhesion pathway in the high risk adult as compared to pediatric B-ALL patients

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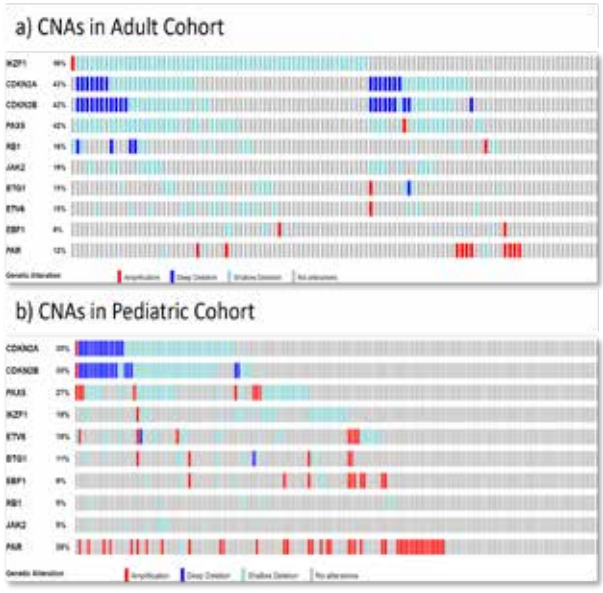
Background : Generally, paediatric B-ALL patients are seen to have better prognostic outcomes than adults. The 'MRplus' score (Gupta et al, 2021) based on Moorman's criteria and IKZF1plus criteria given by Stanulla et.al. categorizes B-ALL into three risk groups1. However, there is a lack of comparative data on prevalence of 'MRplus' score risk stratification in adult and paediatric B-ALL patients.

Method : The CNAs were detected by MLPA to categorize the cases based on MRplus score into favourable(MR0), moderate(MR1), and unfavourable(MR2) groups. RNA sequencing of 61 Pediatric(n=37) and adult(n=24) B-ALL cases were performed. DEGs were obtained using the 'DESeq2' R package and 'clusterProfiler' R package was utilized for GO pathway analysis.

Results : The study consists of 281 patients comprising 171(60.85%) pediatric and 110(39.15%) adult B-ALL cases. The median age of the adult cohort was 33.5 years(19–61), and the pediatric cohort was 7 years(8mth–18 years). CNAs were identified in 216(76.9%) cases in the overall cohort; 94(85.4%) cases in the adult group and 122(71.3%) cases in the pediatric group(p-value=0.006) (Fig.1). The adult cohort had 33(30%), 53(48.2%), 24(21.8%) cases and the pediatric cohort had 18(10.5%), 59(34.5%), 94(54.9%) cases with MR-2, MR-1, and MR-0 risk-groups respectively. The upregulation of cell-cell adhesion pathway was observed in MR-2 adult cohort in comparison to MR-2 pediatric cohort. MR-1 adult cohort also showed the involvement of adhesion pathways. On review of the DEGs, the increased expression(Log2Fold change>1.5) of genes associated with adhesion was observed. The top upregulated adhesion genes (GO) with their fold change in MR2 adults are PCDH15(7.7),THY1(5.9),HHLA(4.5),RND3(4.2),NEXMIF(3.7),CCL2(3.6),APBA1(3.1),BMP4(2.8),CX3CL1(2.6),COL16A1(2.6) and in MR1 adults are EDIL3(4.8),MUC4(4.6),SPP1(4.5),KRT18(4.2),FOXA1(3.5), LGALS2(3.5),NRP2(3.3), LAMB4(3.2), PCDH15(3.0), IL12B(2.9).

Conclusion : Compared to the paediatric cohort, the adult cohort exhibits a higher number of MR2(Poor risk) cases. The upregulation of the cell-cell adhesion pathway in MR2 adults may contribute to the poor prognosis of adult patients compared to paediatric patients.

Keywords : B-ALL, NGS, Adhesion pathway, Childhood leukemia, Risk-stratification



OP01-5

CD371 expression in B-lymphoblastic leukemia and its correlation with recurrent genetic abnormalities

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Background : CD371(CLL-1) is a transmembrane glycoprotein usually expressed on normal myeloid cells and most of the myeloid blasts. Aberrant expression of CD371 was observed in DUX4- rearranged B cell precursor ALL (BCP ALL). However, extensive data of CD371 expression in B-ALL and its expression pattern in patients with disease-defining recurrent genetic abnormalities is limited. With the advent of anti-CD371-immunotherapy, we aimed to assess the expression of CD371 in patients of all B-ALL and study its correlation with underlying genetic abnormalities.

Method : Expression of CD371 (fluorochrome-PE, clone- 50C1) was evaluated in consecutive B-ALL patients from January 2020 to December 2021 using 12-color MFC immunophenotyping on Dx-FLEX flow-cytometer. Data was analysed using Kaluza-softwareV2.1. CD371-expression was correlated with demographic details, cytogenetics, and molecular genetics data including DUX4 rearrangement.

Results : CD371 was assessed in 690 B-ALL patients (412 paediatric and 278 adult-B-ALL). CD371 was positive in 64 patients (9.28%) of B-ALL. Incidence of CD371 expressing B-ALL was higher in paediatric patients (59.3%, n-38). RNA-sequencing data was available in 484/690 patients and DUX4 rearrangement was detected in 14/484 (2.9%) patients. CD371 was positive in 12 of these 14 patients (85.7%, p-value <0.0001). CD371 was also detected in patients with other genetic abnormalities including 3/20 (15%) B-ALL with KMT2A-rearrangement (p-value 0.63), 7/99 (7.1%) B- ALL with BCR::ABL1 (p-value 0.61) and 1/180 (0.5%) patients of B-ALL with hyperdiploidy. Co- expression of CD371 and CD2 was noted in 5/14 patients (35%) with DUX4-rearrangement (p-value <0.0001).

Conclusion : Aberrant expression of CD371 was significantly associated with DUX4 rearranged B-ALL. However, it was also positive in other genetic abnormalities including KMT2A rearrangement and BCR::ABL1. This highlights the need for extensive study of CD371 expression in B-ALL with recurrent genetic abnormalities and underlines the utility of anti-CD371 immunotherapy in such patients.

Keywords : CD371, B-ALL

OP02-1

Treatment patterns in patients with mantle cell lymphoma: Updated report of the Asia-Pacific multinational retrospective registry study

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Background : We conducted a multinational, multicenter retrospective registry study to better define the treatment patterns and survival outcomes of newly diagnosed patients with mantle cell lymphoma (MCL) in the Asia-Pacific region.

Method : Data were collected from newly diagnosed MCL patients between January 2008 and September 2019 from 27 hospitals in Asian countries, including China, Malaysia, Japan, Singapore, South Korea, Taiwan, and Thailand. The first interim analysis with 191 patients was previously reported. An updated analysis of 381 patients was performed at the data cutoff date of June 20, 2023.

Results : The median age was 62 years (range, 26–90), and 282 patients were male (74.0%). The majority of the patients had stage 3 or 4 disease (n = 329, 87.1%). Based on the MIPI score, 20.7% (n = 139) were classified as high-risk. The most frequently administered 1st line regimen was R-CHOP or R-CHOP-like regimens (n = 177, 46.5%), followed by cytarabine-containing regimens (n = 113, 29.7%), including R-Hyper-CVAD (n = 78). The median progression-free survival (PFS) and overall survival (OS) was 40.6 months and 86.8 months, respectively (Figure). The role of upfront ASCT was evaluated in patients who are < 65 years old and achieved at least partial response to 1st line treatment (n = 181). There were no significant differences in PFS and OS between the ASCT and non-ASCT groups, with a 5-year PFS rate of 56.3% vs. 48.9% (P = 0.190) and a 5-year OS rate of 82.1% vs. 76.1% (P = 0.069), respectively.

Conclusion : Our study demonstrated that the majority of patients with MCL in the Asia-Pacific region were treated with rituximab-based regimens in the contemporary era. The rate of upfront ASCT was relatively low, and there was no significant difference in survival outcomes according to upfront ASCT. Our contemporary real-world analysis showed improved survival outcomes compared to previous studies.

Keywords : Mantle cell lymphoma, Real world, Treatment pattern, Asia-Pacific

OP02-2

Pooled safety analysis of zanubrutinib monotherapy in Asian patients with B-cell malignancies

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Background : In patients with B-cell malignancies, continuous treatment with the first-generation Bruton tyrosine kinase inhibitor (BTKi) ibrutinib is often limited due to toxicities that may be associated with inhibition of off-target kinases. Zanubrutinib is a potent and selective next-generation BTKi designed to maximize BTK occupancy and minimize off-target effects. Here, we present the pooled safety analysis of 406 Asian patients treated with zanubrutinib.

Method : A post hoc pooled safety analysis of Asian patients from 10 clinical trials of zanubrutinib was performed. The analyses included patients with CLL/SLL, MCL, WM, FL, DLBCL, and MZL. Treatment-emergent adverse events (TEAEs) were summarized using MedDRA preferred terms and adverse events of special interest (AESIs) using pre-defined grouped terms. Rates of TEAEs and exposure-adjusted incidence rates of AESIs were assessed.

Results : The analyses included 406 Asian patients (median age, 61 years) treated with zanubrutinib monotherapy. Median exposure to zanubrutinib was 25.0 months, with 38.7% of patients receiving treatment ≥36 months. Zanubrutinib discontinuation due to any TEAE occurred in 10.6% of patients; TEAEs leading to dose reduction occurred in 7.4%. Most common nonhematologic TEAEs of any grade were upper respiratory tract infection (38.2%), pneumonia (26.4%), and rash (21.2%). Pneumonia (16.0%) and anemia (8.1%) were the most common grade ≥3 TEAEs. Serious TEAEs occurred in 43.8% of patients, with pneumonia (14.5%) being the only serious TEAE in ≥10% of patients. There were no cases of grade ≥3 atrial fibrillation and flutter. Deaths attributed to TEAEs occurred in 4.9% of patients, with most (2.0%) due to infections. Cardiac disorder–related deaths were 1.0% (n=4).

Conclusion : Zanubrutinib AEs were mild-to-moderate in severity and only a minority lead to treatment discontinuation. The overall safety profile in the present analysis remains largely consistent with previous reports, suggesting that zanubrutinib is well tolerated in Asian patients with B-cell malignancies.

Keywords : Zanubrutinib, Safety, B-cell malignancies, BTKi, Asian

OP02-3

Prognostic value of end-of-treatment [18F]FDG PET/CT in newly diagnosed patients with primary central nervous system lymphoma who respond to first-line treatment with high-dose methotrexate-based regimen

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Background : The current standard tool for response evaluation in patients with primary central nervous system lymphoma (PCNSL) is brain MRI. However, brain MRI has limitations in distinguishing patients with radiologically unconfirmed complete response (CRu) from those with partial response (PR) or CR. This study analyzed the prognostic value of end-of-treatment [^{18}F]FDG brain PET/CT response assessment in PCNSL patients with CR, CRu, or PR at end-of-treatment MRI following first-line treatment.

Method : Patients with newly diagnosed PCNSL between August 2021 and October 2022 from Asan Medical Center, South Korea were registered and prospectively monitored. All patients received high-dose methotrexate-based chemotherapy as first-line treatment.

Results : In this prospective registry study, 28 patients diagnosed with PCNSL were initially enrolled. At the end-of-treatment response evaluation, 23 patients achieved CR/CRu/PR based on MRI and were included in this analysis. All patients achieved CR by PET (PET CR), among whom 14 CR, and 9 CRr or PR (CRu/PR) were observed based on MRI. The median age was 64 years (range, 46–78), and 10 patients (43.5%) were male. With a median follow-up duration of 12.6 months, 1-year PFS-rate and 1-year OS rate were 75.1% and 78.6%, respectively. There was no significant difference in PFS or OS between patients who achieved MR CR (n = 14) compared with who achieved MR CRu/PR (n = 9), with a 1-year PFS rate of 78.6% vs. 71.1% (P = 0.90) and 1-year OS rate of 78.6% vs. 83.3% (P = 0.50).

Conclusion : Our study demonstrated that survival outcomes of PCNSL patients who achieve end-of-treatment PET CR is excellent. This observation was consistent even among patients with residual disease on MRI (MR CRu/PR), which implies a possible role of PET in the response evaluation for this patient population.

Keywords : Primary CNS lymphoma, PET/CT, MRI

OP02-4

Efficacy of dexamethasone, L-asparaginase, ifosfamide, carboplatin, and etoposide in patients with relapsed/refractory peripheral T cell lymphoma

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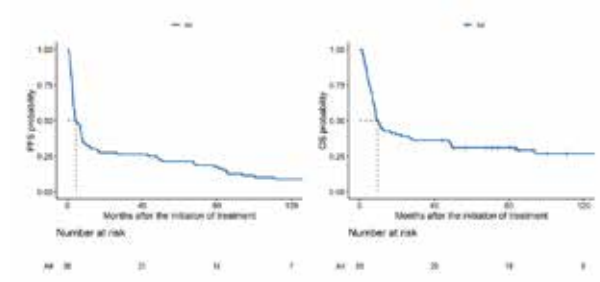
Background : Peripheral T-cell lymphomas (PTCL) are heterogeneous clinicopathologic entities derived from a mature, post-thymic T-cell. Despite the various trial attempt to overcome relapsed or refractory disease, outcomes are generally poor, with overall survival of less than one year. In this study, we analyzed efficacy of the L-asparaginase based chemotherapy (DLICE, Dexamethasone, L-asparaginase, ifosfamide, carboplatin, and etoposide) in patients with relapsed/refractory(R/R) PTCLs.

Method : A total of 80 adult patients were relapsed or refractory with PTCLs between November 2001 and March 2021 at Seoul and Yeoido St. Mary's Hospital were included in this study.

Results : A total of 80 patients with R/R PTCL were identified. The median age of those diagnosed with PTCL was 49.5(21-64). Among the patients with PTCL, 32 (40%) patients classified as PTCL not otherwise specified, followed by 26 (32.5%) with Extranodal NK/T cell lymphoma, 9 (11.2%) with angioimmunoblastic T cell lymphoma, and 8 (10%) with Anaplastic Large Cell Lymphoma. The median follow-up among patients with survival was 92 months. The median survival was 9.6 months and progression free survival accounted for 4.4 months. Overall response was 35% with 30% of complete response. In the multivariate analysis, refractory status (HR 2.03, p-value =0.013), High-intermediate risk in Prognostic Index for T-cell lymphoma (HR 2.24, p-value =0.004) account for inferior OS. 11 Patients (10 CR and one progressive disease) underwent autologous hematopoietic stem cell transplantation (HSCT), median survival were 49 months. 16 Patients (4 CR, 3 partial response, and 9 no response) underwent allogeneic HSCT median survival were not reached.

Conclusion : PFS achieved by DLICE chemotherapy was not long in patients with R/R PTCL but was effective in bridging therapy to the HSCT. Furthermore, Allogeneic-HSCT could be considered even in non-CR status. This study suggests that patients with R/R PTCLs have stagey with DLICE regimen as bridging therapy in planning HSCT.

Keywords : PTCLs, Relapse/Refractory, ICE, L-asparaginase



OP02-5

Characteristics and outcome of post-transplant lymphoproliferative disease in children treated with low-dose chemotherapy over 20 years in a single hospital

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Introduction : Post-Transplant Lymphoproliferative Disease (PTLD) is a critical issue after organ or stem cell transplantation, more common in children than adults, often linked to the Epstein-Barr virus (EBV). The primary treatment is reducing immune suppression, but its effectiveness varies based on factors like the disease's stage and type. A study from the Children's Oncology Group (COG) showed that children with EBV-positive PTLD treated with low-dose cyclophosphamide and prednisone after ISR had a 67% 2-year event-free survival rate and a 73% overall survival rate. This research was conducted at Korea's leading pediatric organ transplant center, aiming to explore the characteristics and outcomes of pediatric PTLD treatment.

Methods : This retrospective study at Asan Medical Center's Pediatric Oncology and Hematology Department involved children post-sol-

id organ and stem cell transplantation. Treatment for PTLD included weekly Rituximab for polymorphic or early-stage CD20-positive cases and multiagent chemotherapy for monomorphic cases. Initial treatment was COG ANHL0221, followed by CHOP with or without rituximab if unresponsive. The ANHL0221 protocol consisted of 6 cycles, every 3 weeks, with intravenous cyclophosphamide (600 mg/m2) on the first day of each cycle, oral intake of prednisone (1 mg/kg), or intravenous administration of methylprednisolone (0.8 mg/kg) every 12 hours from days 1 to 5 of each cycle.

Results : A total of 784 allogeneic hematopoietic stem cell transplantations, 22 lung transplantations, 500 liver transplantations, and 170 kidney transplantations were carried out between 1997 and 2022. During this time, a total of 16 patients undergoing allogeneic hematopoietic stem cell transplantation, 11 patients undergoing kidney transplantation, 7 patients undergoing liver transplantation, and 1 patient undergoing lung transplantation were assessed and treated for PTLD. The median time for PTLD diagnosis was 6 months (range, 0~120) after transplantation in all patients. PTLD tended to occur later in solid organ transplantation. Fever was the predominant first symptom in 62.9% of the 35 patients, while gastrointestinal bleeding was observed in 5 individuals with PTLD in the abdominal region. The median serum EBV titer at diagnosis was 3.2 log IU/mL, ranging from 0 to 5.6. There was no evident correlation between EBV titer and PTLD diagnosis in all patients. The pathology exhibited a polymorphic type, with a total of 11 patients. There were cases of monomorphic types, with 8 patients diagnosed with diffuse large B-cell lymphoma (DLBCL), 1 patient with Hodgkin lymphoma, 1 patient with MALT lymphoma, 1 patient with peripheral T-cell lymphoma, 1 patient with Burkitt lymphoma, 1 patient with precursor B-cell leukemia, and 3 patients with plasmacyte-type pathology. Treatment comprises immune suppression reduction in 3 patients, administration of the POG9317 regimen in 2 patients, weekly rituximab up to 4 cycles in 12 patients, ANHL0221 in 8 patients, and rituximab followed by the ANHL0221 or COPAD regimen in 3 patients. Five patients necessitated further treatment following the initial treatment. If persistent lesions were seen on a PET scan, CHOP therapy was administered 2–6 times, depending on the response. As a result, 80% of the patients attained complete remission (CR) following the initial treatment. There were a total of seven deaths. Two of these deaths resulted from infections contracted while receiving POG9317, one from progressive PTLD in a kidney transplant recipient with EBV+ DLBCL in the duodenum, and the remaining four deaths were due to transplantation-related complications, initial refractory malignancy, or subsequent MDS. The rate of survival without any events for a period of 2 years (remaining alive with a functioning original allograft and no PTLD) was 75.7%, and the overall rate of survival was 75.1%. These results were obtained after a median follow-up period of 49 months. Adverse effects observed following the ANHL0221 treatment encompassed temporary hyperglycemia and neutropenic fever.

Conclusions : Due to the small numbers, we were unable to determine the significance of tumor histology, stage of disease, allograft type, or early response to treatment on outcome. These data suggest rituximab combined with low-dose chemotherapy is safe and effective in treating pediatric with EBV (+) PTLD in children.

Keywords : PTLD, EBV, Rituximab, Chemotherapy

OP03-1

Reduced GVHD incidence with post-transplantation cyclophosphamide in higher-risk myelodysplastic syndrome

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Background : Post-transplantation cyclophosphamide (PTCy) is increasingly utilized to prevent GVHD in allogeneic HCT. We previously assessed its feasibility in higher-risk MDS patients. This study aims to evaluate efficacy and safety of PTCy-based allogeneic HCT in higher-risk MDS with an extended cohort, alongside comparing outcomes against ATG-based GVHD prophylaxis.

Method : Patients with higher-risk MDS underwent HCT with busulfan-based conditioning. GVHD prophylaxis in the PTCy group comprised 50 mg/kg/day of PTCy on days 3 and 4 and cyclosporine/MMF. The historical control ATG group received HCT with ATG, methotrexate, and cyclosporine. ATG dosage varied by donor types.

Results : A total of 152 patients who participated in the prospective study involving PTCy were compared with a historical cohort of 145 patients receiving ATG. PTCy participants were younger (median age 59 vs. 53 years), had a higher rate of 4-day busulfan conditioning (32.9% vs. 11.7%), and experienced more recent allogeneic HCT, resulting in a longer follow-up duration. Engraftment took longer in the PTCy group: median 15 days for neutrophils and 25 days for platelets, compared to 11 days and 15 days in the ATG group, respectively. The PTCy group showed significantly lower rates of grade II-IV and III-IV acute GVHD (26.9% vs. 9.9% and 25.5% vs. 7.2%), and moderate to severe chronic GVHD (38.0% vs. 25.5%). Patients in the

PTCy group displayed a trend towards lower non-relapse mortality (29.7% vs. 19.1% at 2-year), and higher cumulative incidence of relapse (16.6% vs. 27.8% at 2-year) without statistical significance. The estimated 2-year overall survival and event-free survival did not significantly differ between the two groups.

Conclusion : In conclusion, PTCy in allogeneic HCT for higher-risk MDS lowered acute and chronic GVHD rates without notable impacts on relapse or non-relapse mortality compared to ATG-based GVHD prophylaxis. Further research is warranted to understand its clinical implications.

Keywords : Post-transplantation cyclophosphamide, ATG, Myelodysplastic syndrome, GVHD

OP03-2

Effect of HLA mismatched on the prognosis of cord blood transplantation for childhood leukemia

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Background : To investigate the effect of the numbers and sites of high-resolution human leukocyte antigen (HLA) mismatch on the prognosis of umbilical cord blood transplantation in children with leukemia.

Method : Clinical data and high-resolution HLA-A, HLA-B, HLA-C, HLA-DRB1 and HLA-DQB1 locus gene information were collected in the children who underwent the first hematopoietic stem cell transplantation using a single unrelated cord blood unit in our hospital from 2016 to 2023. Cox proportional hazards model and Fine-Gray proportional hazards model were employed for multivariate analysis of events.

Results : A total of 100 children with leukemia were enrolled in this study. Two pieces of genetic information of five loci (HLA-A, HLA-B, HLA-C, HLA-DRB1, and HLA-DQB1) were analyzed. The numbers of HLA mismatches between donors and recipients were 0-3 and each locus at most 1 mismatched. A lower incidence of acute graft-versus-host disease (GVHD) (8.3% vs 36.4% ,P=0.046)and a higher incidence of relapse(51.4%vs 15.8%,P=0.003) were associated with HLA10/10 versus 7-9/10 matched patients , but there were no significant differences in non-relapse mortality (NRM) and overall survival (OS) between the two groups. HLA-DRB1 mismatch was associated with a higher incidence of grade II-IV aGVHD(44.8% vs17.5%,P=0.01), a lower incidence of relapse(0 vs 31.2%,P=0.028), a higher NRM(34.7% vs 0 ,P=0.008) and a worse OS(76.3% vs 100%,P=0.036) compared with HLA-DRB1matched. The incidence of grade II-IV aGVHD was higher in HLA-A locus mismatching than in HLA-A locus matched(38.6%11.2%,P=0.024). The relapse rate of HLA-B locus mismatch was lower than that of matched HLA-B locus(0 vs 41.2%,P=0.047). No HLA loci mismatched were associated with cGVHD and delayed engraftment.

Conclusion : The numbers and sites of HLA mismatched in cord blood transplantation in children with leukemia affect the incidence of complications and prognosis after cord blood transplantation.

Keywords : HLA matching, Umbilical cord blood transplantation, Acute leukemia, Children, NF-B

OP03-3

Interleukin 6 polymorphisms 174 and 597: Impact on graft-versus-host disease after allogeneic hematopoietic stem cell transplantation in childhood

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Background : The investigation of non-HLA immunogenetics, particularly of cytokines, could identify predictors of an unfavorable outcome after allogeneic HSCT. In this study, we examined the impact of single nucleotide polymorphisms (SNPs) within the promotor region of interleukin 6 (IL6) on the development of graft-versus-host disease (GVHD) after pediatric allogeneic HSCT.

Method : We included 320 pediatric patients who underwent an allogeneic HSCT and their respective donors. We used TaqMan real-time polymerase chain reaction to analyze the SNPs IL6-174 (G/C) and IL6-597 (G/A). We investigated the influence of the IL6-174 and IL6-597 polymorphisms on the occurrence of GVHD.

Results : GG polymorphism at position 174 of the recipient IL6 gene was associated with a higher frequency of acute GVHD (GG vs. GC/CC; 36% vs. 24%; P=0.024). Patients with IL6-597 GG genotype developed acute GVHD more frequently than individuals with an A allele (GG vs. GA vs. AA; 39% vs. 24% vs. 19%; P=0.013). IL6-174 GG homo-

zygous recipients had a more frequent occurrence of chronic GVHD (GG vs. GC/CC; 22% vs. 14%; P=0.049). We observed a significant increased risk of chronic GVHD in recipients with IL6-597 GG genotype (GG vs. GA vs. AA; 23% vs. 13%; P=0.012). Polymorphisms of donors did not affect the incidence of acute and chronic GVHD. In multivariate analysis, the IL6-174 and IL6-597 SNPs were independent significant risk factors for acute GVHD (P=0.030; P=0.007, respectively) as well as for chronic GVHD (P=0.045; P=0.015, respectively). In addition, older age at time of transplantation turned out to be a significant risk factor for chronic GVHD (P=0.003).

Conclusion : Our study identified the IL6-174 and IL6-597 GG genotypes of pediatric allogeneic HSCT recipients as genetic risk factors for the development of acute and chronic GVHD. These findings could implicate the adjustment of prophylactic measures to reduce the occurrence of acute and chronic GVHD.

Keywords : Interleukin 6, Single nucleotide polymorphism, Allogeneic hematopoietic stem cell transplantation, Childhood, Graft-versus-host disease

OP03-4

Reduced 8-gray versus standard 13.2-gray total dose of total body irradiation based myeloablative conditioning for allogeneic hematopoietic cell transplantation in pediatric acute lymphoblastic leukemia

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Background : Myeloablative total body irradiation (TBI) is an important component of conditioning for hematopoietic cell transplantation (HCT) in children with acute lymphoblastic leukemia (ALL). However, high-dose TBI is associated with acute and long-term toxicities. We aimed to compare the outcomes of HCT following a total TBI dose of reduced 8Gray (Gy) versus standard 13.2Gy in pediatric ALL.

Method : Ninety-one children with high-risk ALL in remission who underwent HCT between 2014 and 2023 were analyzed. Donors were unrelated donors and haploidentical family donors (HFD). Conditioning regimens consisted of TBI at a total dose of 8Gy in combination with busulfan and fludarabine (8Gy TBI/BuFlu, n=27), and 13.2Gy in combination with cyclophosphamide (13.2Gy TBI/Cy, n=64). Post-transplant cyclophosphamide (PTCy) and low-dose antithymocyte globulin were used for in vivo T cell depletion in the former and latter groups, respectively.

Results : The median age at transplant was 11 years (range, 2-25). Patients in the 8Gy TBI/BuFlu group had a significantly higher proportion of second or third remission, a prior history of transplant, and HFD compared to the 13.2Gy TBI/Cy group. The 13.2Gy TBI/Cy group showed significantly shorter median times to neutrophil engraftment (12 days in 13.2Gy TBI/Cy vs. 14 days in 8Gy TBI/BuFlu, p<0.01). There were no differences between two groups in the cumulative incidences of acute and severe chronic GVHD. Comparable relapse rates were observed in two groups (21.1% in 8Gy TBI/BuFlu vs. 46.2% in 13.2Gy TBI/Cy, p=0.89). With a median follow-up period of 52.3 months (range, 3-108), leukemia-free survival and overall survival (OS) were similar between two groups (OS: 81.7% in 8Gy TBI/BuFlu vs. 72.3% in 13.2Gy TBI/Cy, p=0.80).

Conclusion : We observed that a reduced dose of 8Gy TBI combined with busulfan and fludarabine conditioning with PTCy showed comparable outcomes in pediatric ALL. These results suggest that 8Gy TBI may be sufficient for pediatric patients transplanted in remission.

Keywords : Total body irradiation, Hematopoietic cell transplantation, Post-transplant cyclophosphamide, Acute lymphoblastic leukemia, Pediatrics

OP03-5

High plasmacytoid dendritic cell dose infusion correlates with better plasmacytoid dendritic cell reconstitution and lower incidence of viral infection after transplantation: A single-center study

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Background : Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) infections are major complications following allogeneic hematopoietic stem cell transplantation (allo-HSCT). Plasmacytoid dendritic cells (pDC)

are widely known for their capacity to produce type I interferon (IFN-I) in response to viruses, which activates virus-specific T cells to eliminate viral infection. In this study, we sought to investigate the association between the pDC dose in grafts and CMV and EBV infections after allo-HSCT.

Method : Eighty patients receiving allo-HSCT at our center were included in the discovery cohort to investigate the effects of pDC dose infusion on CMV and EBV infections within 100 days following allo-HSCT. Circulating pDC concentration on day 30 after allo-HSCT was examined to explore the possible correlation between the pDC dose infusion and pDC reconstitution.

Results : In the discovery cohort, 54 patients (68%) developed CMV viremia, and multivariate analysis suggested that high pDC dose infusion was an independent protective factor for CMV viremia (hazard ratio [HR], 0.456; 95% confidence interval [CI], 0.247-0.843; P=0.012). Furthermore, 41 patients (51%) in the discovery cohort developed EBV viremia, and multivariate analysis suggested that high pDC dose infusion was an independent protective factor for EBV viremia (HR, 0.499; 95% CI, 0.257–0.967; P=0.040). An association between pDC dose infusion and viral infection was also observed in the validation cohort. Additionally, patients who developed CMV or EBV viremia in the validation cohort had a lower circulating pDC concentration than patients without viremia, and patients with a higher pDC dose infusion had a higher circulating pDC concentration on day 30 after allo-HSCT (Pearson r = 0.72; P<0.001).

Conclusion : A high pDC dose infusion might be a protective factor against CMV and EBV infections following allo-HSCT, possibly by enhancing pDC reconstitution early after allo-HSCT, and may be a promising therapeutic intervention for viral infections and other transplantation outcomes in allo-HSCT.

Keywords : Allogeneic hematopoietic stem cell transplantation, Plasmacytoid dendritic cell, Cytomegalovirus, Epstein-Barr virus, Children

OP03-6

BCMA-specific induced pluripotent stem cells and their specific regulatory pathways to differentiate into rejuvenated antigen-specific memory CD8+ T cells

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Background : A major hurdle in cancer therapy, particularly adoptive T cell therapy, is T cell exhaustion and a failure to maintain immunogenic responses against cancer cells. Here, we report an approach to revitalize fully functional memory T cells specific to an antigen through induced Pluripotent Stem Cells (iPSC) technology targeting multiple myeloma.

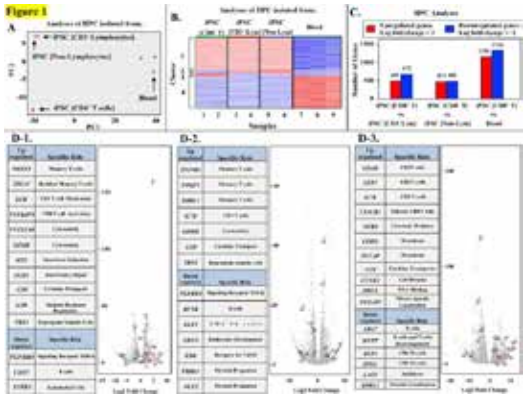
Method : Heteroclitic $BCMA_{72\text{-}80}$ (YLMFLLRKI)-specific IFN-γ producing $CD8^+$ cytotoxic T lymphocytes (CTL) were reprogrammed into iPSC with self-renewal and pluripotency potential, followed by differentiation into highly functional $CD8^+$ CTL to myeloma, and further characterized for their potential to differentiate into BCMA-specific memory T cells.

Results : Mirroring differentiation by blood stem cells, the resulting HPC ($CD34^+CD43^+/CD14^-$ $CD235a^-$) developed from individual iPSC clones (n=20) demonstrated unique cellular pathways leading to a specific lineage. Our RNAseq analyses revealed unique transcriptional profiles of the iPSC committed to $CD8^+$ T cells, which include upregulation of transcriptional regulators controlling CD4/CD8 T cell differentiation ratio, memory CTL formation, NF-kappa-B/JNK pathway activation, and cytokine transporter/cytotoxic mediator development, as well as downregulation of regulators controlling B and T cell interactions, $CD4^+$ Th cells, and inhibitory receptor development (Figure, Table attached). BCMA-specific T cells differentiated from the iPSC were characterized as displaying mature and rejuvenated $CD8\alpha\beta^+$ T cell phenotype with BCMA (YLMFLLRKI) peptide specificity without inhibitory checkpoint expression. Furthermore, the T cells differentiated were fully functional to induce anti-tumor activities, evidenced by high levels of cell proliferation, Th1-specific cytokine (IFN-g, IL-2, and TNF-a) production, and robust cytotoxicity against myeloma cells by presenting a single unique T cell receptor clonotype.

Conclusion : We identified specific regulatory pathways used by iPSC-derived HPC to yield fully functional BCMA-specific memory $CD8\alpha\beta^+$ T cells, which provides not only a promising immunotherapy for multiple myeloma, but also a method that can be applied to other cancers.

Keywords : Induced pluripotent stem cells, Rejuvenate T cells, Regenerative Medicine, Immunotherapy, Novel approach

Figure 1



Supplemental Table 1.

Upregulated Genes	Aliases	Function, Expression	References
Cell Fate Decision, Early T cell Development			
TBX3	T-box transcription factor 3	Cell fate decision toward mesendoderm	Khan et al. 2020 Weidgang et al. 2003
HOXA11	Homeobox A11	Early stages of T cell development	Shelton et al. 2019 Pineault et al. 2019
CD8+ T Cell Regulation, Differentiation and Activation, CD8+ Memory T Cell Formation			
IRF4	Interferon Regulatory Factor 4	Differentiate cytotoxic effector CD8+ T cells, Form CD8+ memory T cells	Ahmed-Ismich et al. 2019 Huber et al. 2014
PIK3CD	Phosphatidylinositol-4, Phosphate 3-Kinase Catalytic Subunit	Differentiate Effector/Memory T cells, Regulate CD4/CD8 T cell differentiation ratio	Singh et al. 2018 Rodriguez-Rodado et al. 2003
KLF15	Kruppel Like Factor 15	Develop innate CD8+ T cells	Jo et al. 2020
IL-12B	Interleukin 12B	Inhibit B cells differentiation, Augment CD8+ T cell Activation, Differentiate Th1 cells	Kim et al. 2008 Johnston et al. 2013 Henry et al. 2008
MAPK4	Mitogen-Activated Protein Kinase 4	Activate TCR-induced T cells	Marques et al. 2014
Immunogenic Signal Transduction			
IFLN 1/2	Interleukin 1/2	Innate immune defense	Chen et al., 2020 Yi et al. 2017
TRIM6	Tripartite motif-containing protein 6	Activate type I interferon signaling pathway	Van Tol et al. 2020 Rajsbaum et al. 2014
EDA2R	Ectodysplasin A2 Receptor	Activate NF-kappa-B and JNK pathways	Verhelst et al. 2015 Sinha et al. 2002

Supplemental Table 2

Downregulated Genes	Aliases	Function, Expression	References
Cell Differentiation and Cell Cycle Regulation			
RPS6KA2	Ribosomal Protein S6 Kinase A2	Mediate mitogenic activation of transcription factors and cellular differentiation	Tai et al. 2020
CDK3	Cyclin Dependent Kinase 3	Regulate G0-G1 and G1-S cell cycle transitions	Ren et al. 2004
YPEL4	YIPPEE LIKE 4	Epithelioid conversion of fibroblasts	Farfler et al. 2001
Lineage-Specific Immune Cell Differentiation			
BATF2	Basic Leucine Zipper ATF-Like Transcription Factor 2	Differentiate lineage-specific cells in immune system	Kuyama et al. 2019
BTN3A1	Butyrophilin Subfamily 3 Member A1	Regulate proliferation of activated T cells and release of cytokines	Smith et al. 2010
USP44	Ubiquitin Specific Peptidase 44	Promote Treg Function, Regulate spindle assembly checkpoint and mitotic checkpoint	Stemmler et al. 2007 Yang et al. 2020
CD70	CD27L, TNSF7	Regulate activation of B-cells and Natural Killer cells	Al Sayed et al. 2013 Arens et al. 2004
ZXDA	Zinc Finger X-Linked Duplicated A	Cooperate with CIITA to promote transcription of MHC class I and class II	Al-Kandari et al. 2007
Regulation of Early Embryonic and Stem Cells Development			
FGFR1	Fibroblast Growth Factor Receptor 1	Regulate embryonic development, neural outgrowth, cell differentiation and migration	Bottos et al. 2021
NPM2	Nucleoplasmin-2	Regulate chromatin reprogramming during fertilization and early embryonic development	Chen et al. 2019
GGN	Gametogenetin	Localize proliferating germ cells and regulates spermatogenesis	Zhang et al. 2005
SPAG11	Sperm Associated Antigen 1	Regulate fertilization and cytoplasmic assembly of the ciliary dynein arms	Chagot et al. 2019
CATSPER2	Cation Channel Sperm Associated 2	Facilitate calcium-dependent responses essential for fertilization	Luo et al. 2019
Regulation, Organization and Development of Central Nervous System			
N4BP3	NEDD4 Binding Protein 3	Develop anterior structures including eye, brain and cranial cartilage	Kiem et al. 2017
P2RY14	Purinergic Receptor P2Y14	Regulate stem cell compartment and neuroimmune function	Kook et al. 2017
NLGN2	Neuroligin 2	Form, maintain, and remodel synapses of the central nervous system	Ali et al. 2020
SHC2	SHC Adaptor Protein 2	A signaling adaptor that couples activated growth factor receptors to signaling pathway in neurons	Terui et al. 2005
GRASP	General Receptor for Phosphoinositides 1 Associated Scaffold Protein	Mediate intracellular trafficking and macromolecular organization of metabotropic glutamate receptors at synapses	Pandey et al. 2020
AMIGO2	Adhesion molecule with Ig Like Domain 2, Alivin-1, AL1I	Enable depolarization-dependent neuronal survival; mediates tumoral survival, angiogenesis, and metastasis	Ono et al. 2003 Park et al. 2015
TBC1D32	TBC1 Domain Family Member 32	Mediate Shh responses in the developing neural tube	Wang et al. 2018
CACNA1A	Calcium Voltage-Gated Channel Subunit Alpha 1 A	Regulate neurotransmitter release, hormone release, or muscle contraction via calcium channels	Gandini et al. 2021
SLC6A9	Solute Carrier Family 6 Member 9	Regulate Glycine in NMDA receptor-mediated neurotransmission	Marques et al. 2020
Formation and Regulation of Vascular System, Cytoskeletal Arrangement and Angiogenesis			
HEYL	Hes Related Family BHLH Transcription Factor with YRPW Motif Like	Develop cardiovascular system	Kathiriya et al. 2004
NEURL	Neuralized E3 Ubiquitin Protein Ligase 1	Promote endocytosis and neurite growth	Zhang et al. 2017
RAB39B	RAB39B Member RAS Oncogene Family	Involve in vesicular trafficking	Lesage et al. 2015
ANK1	Ankyrin 1	Links integral membrane proteins and underly spectrin-actin cytoskeleton	Li et al. 2020
PSD	Pleckstrin and Sec7 Domain Containing	Induce cytoskeletal remodeling	Macia et al. 2019
LRRK1	Leucine Rich Repeat Kinase, KIAA1790	Regulate bone mass	Si et al. 2018
RUNX2	Runt-Related Transcription Factor 2	Osteoblastic differentiation and skeletal morphogenesis, regulatory factors involved in skeletal gene expression	Komori et al. 2017
CXCL5	C-X-C Motif Chemokine Ligand 5	Recruit neutrophils, promote angiogenesis and remodel connective tissues	Korbecki et al. 2021
Promotion of Inflammation, Mediation of Cellular Stress Response and Homeostasis			
SEMA7A	Semaphorin 7A	Promote inflammation and focal adhesion complex formation, Activate kinase PTK2/FAK1 and MAPK/MAPK3	Suzuki et al. 2007
JDP2	Jun Dimerization Protein 2	Mediate cellular stress response and apoptosis, Repress transactivation mediated by Jun family of proteins	Kimura et al. 2008 Jin et al. 2002 Wuputra et al. 2021
PLA2G6	Phospholipase A2 Group VI	Mediate cellular membrane homeostasis, mitochondrial integrity and cell stress	Larsson et al. 1998 Larsson et al. 1999 Gino et al. 2018
MAP3K9	Mitogen-Activated Protein Kinase Kinase Kinase 9	Mediate mitochondrial death signaling pathway, including release cytochrome c, leading to apoptosis	Xu et al. 2001
PIPOX	Pipecolic Acid and Sarcosine Oxidase	Protect against oxidative stress	Patterson et al. 2017 Natarajan et al. 2017
TNFRSF6B	TNF Receptor Superfamily Member 6b	Protect against apoptosis, neutralize cytotoxic ligands TNFSF14/LIGHT, TNFSF15, TNFSF6/FASL	Hsieh et al. 2017 Zampino et al. 2020

OP04-1

Dynamic thrombocytopenia has a negative impact with distinctive genetic and immunologic features in patients with myelofibrosis

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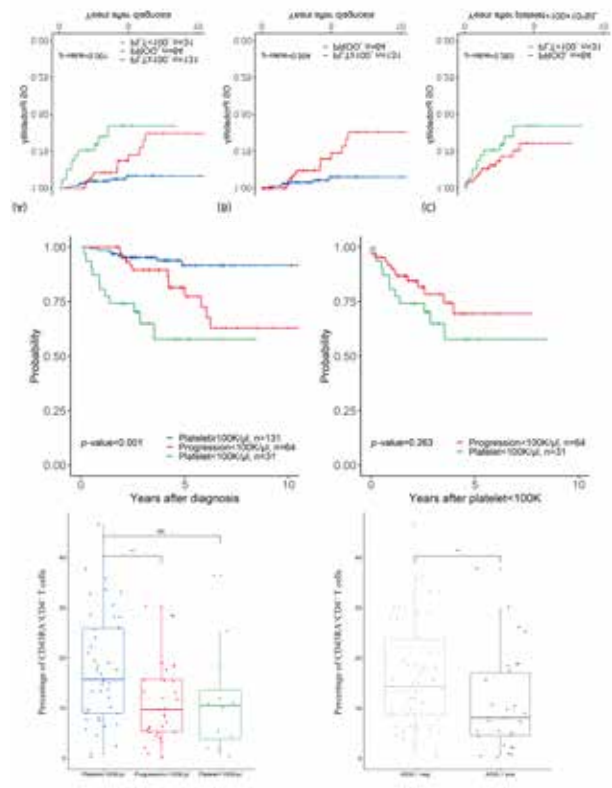
Background : Myelofibrosis (MF) can be categorized as primary myelofibrosis (PMF), which occurs independently, or secondary myelofibrosis (SMF), which progresses from other blood disorders, such as polycythemia vera and essential thrombocythemia. Some cases of MF show cytopenic features, which have been associated with poor outcomes; however, the underlying mechanisms of this association are unclear. We evaluated the association between prognosis and temporal progression to thrombocytopenia in patients with MF and aimed to identify genetic and immunologic features associated with progression to thrombocytopenia and poor prognosis.

Method : A total of 226 patients diagnosed with myelofibrosis and treated at Seoul St. Mary's Hematology Hospital from December 2001 to August 2021 who were performed DNA samples for NGS and FACS were included

Results : In total, 226 patients with SMF or PMF were included in this study and categorized into three groups: platelet count of 100×10^9/L or more (PLT≥100 group; n = 131), progression to thrombocytopenia (PROG group; n = 64), and platelet count less than 100×10^9/L (PLT<100 group; n = 31). Survival analysis revealed a 4-year overall survival of 57.7%, 89.4%, and 93.9% for the PLT<100, PROG, and PLT≥100 groups, respectively. Time-dependent covariate analysis between the PLT≥100 and PROG group revealed the progression of thrombocytopenia showed an inferior overall survival (P=0.004). Multivariate analysis indicated that progression to thrombocytopenia and ASXL1 and IDH1 mutations are associated with poor overall survival. Flow cytometry revealed a lower prevalence of $CD45RA^+CD4^+$ T cells in the PROG group than in the PLT>100 group. Furthermore, the PROG group exhibited a greater ASXL1 mutation rate than the other groups, and patients with ASXL1 mutation had fewer $CD45RA^+CD4^+$ T cells than the other patients.

Conclusion : Our study demonstrated that dynamic thrombocytopenia, as a time-dependent variable, has prognostic value for patients with MF, and ASXL1 mutation and low $CD45RA^+CD4^+$ T cell levels correlate with the progression to thrombocytopenia

Keywords : Myelofibrosis, Thrombocytopenia, Time dependent



OP04-2

Ribosomal protein S4X functions as a novel suppressor for SCF complex-mediated ubiquitination of Myeloid cell leukemia1 and Beta-catenin

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Background : The rise of myeloid cell leukemia1 (MCL1) and β-catenin protein level leads to chemoresistance and correlates with poor prognosis in patients with hematological malignancies. It has been well known that MCL1 and β-catenin are ubiquitinated and destabilized by SCF E3 ubiquitin ligase complex (named after its main components, Skp1, Cullin1, and F-box protein). We found that ribosomal protein S4X(RPS4X) interacted with Cullin1, one of the essential components of the SCF complex. Therefore, we focused on the molecular significance of the interaction between RPS4X and Cullin1 into the stability of MCL1 and β-catenin.

Method : Interaction between RPS4X and Cullin1 was investigated in mammalian cells and binding domains were also detected. To clarify the effects of RPS4X in the SCF complex-mediated ubiquitination for MCL1 and β-catenin respectively, the ubiquitination levels of MCL1 and β-catenin were investigated by immunoprecipitation(IP) assay. Moreover, to examine whether RPS4X affected the formation of SCF complex, we tested the interaction between RPS4X and components of SCF complex.

Results : Association of RPS4X with Cullin1 was confirmed in mammalian cells by IP assay. C-terminus domain of RPS4X bound to the N-terminus of Cullin1. Furthermore, we found that RPS4X regulated the formation of the SCF complex by preventing the association between Cullin1 and Skp1. Indeed, the levels of ubiquitinated-MCL1 and -β-catenin were reduced by expressing RPS4X in cells. Interestingly, we also defined that RPS4X inhibited the association of MCL1 as well as β-catenin with F-box protein. These results suggested that RPS4X provides a dual effect in the depression of SCF complex-mediated ubiquitination for target proteins.

Conclusion : These findings could contribute to the elucidation of chemoresistance mechanisms by high levels of MCL1 and β-catenin protein in hematological tumors.

Keywords : MCL1, Beta-catenin, RPS4X, Ubiquitination, SCF complex

OP04-3

Targeted-NGS across the beta-globin gene cluster identifies multiple linkage disequilibrium patterns in north indian non-transfusion dependent beta-thalassemia patients

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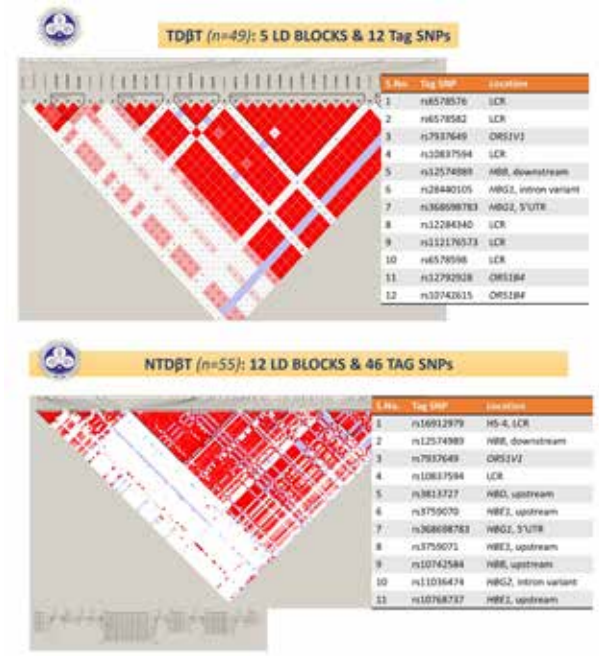
Background : Phenotypes of non-transfusion dependent β-thalassemia (NTDβT) are determined by HBB and α-globin genotypes and fetal hemoglobin levels. Haplotyping of β-globin gene cluster's locus control region (β-LCR's) is often attempted to discover single nucleotide polymorphisms (SNPs) with high linkage disequilibrium (LD) that may modulate the HbF-to-HbA switch and thereby, disease severity. Tag-SNPs are representative polymorphisms that "tag" a particular haplotype and help test associations of a marker locus with qualitative/quantitative traits, without having to genotype all of its SNPs. We attempted to identify haplotypes and Tag-SNPs across the β-LCR in genetically similar north Indian NTDβT patients.

Method : NTDβT patients (n=51) harbouring HBB:c.92+5G>C and β^0/β^+ variant underwent targeted NGS of the β-globin gene cluster using Agilent's HaloPlexHS™ target-enrichment kit, with variant calling using Agilent's SureCall™ pipeline. Haplotypes were constructed using HaploView™ v4.2 (Broad Institute). Patients were divided into mild (n=28) and moderate (n=23) severity using the Mahidol scoring system.

Results : 135 SNPs were identified across 95 kbp region. Haplotypes were constructed using common SNPs (MAF >0.05, Hardy-Weinberg p-value>0.01). In mild NTDβT, 94 qualifying polymorphisms were segregated into 8 LD-blocks with 30 Tag-SNPs. Moderate NTDβT generated five LD blocks containing 62 SNPs and 27 tag-SNPs. Mild NTDβT group's largest LD-block 2 spanned a >22-kb region with 14 tag SNPs while the moderate group's LD block 1 had 13 tag SNPs. These two largest blocks covered the ε, $^{G}\gamma$, $^{A}\gamma$, δ and β globin genes. Five tag SNPs were common to both severity groups. HBG1-HBD ($^{A}\gamma$-δ) intergenic region containing the non-coding gene BGLT3 contained two tag-SNPs: rs7483789 in mild and rs7480197 in moderate NTDβT.

Conclusion : NGS-based haplotyping identifies multiple LD-patterns in genetically-similar north Indian NTDβT patients. This suggests a diversified genomic structure in this group and should aid future comparisons of NTDβT patients with divergent phenotypes across various regions.

Keywords : Linkage disequilibrium, Next-generation seqeuencing, Haplotype, SNP analysis/discovery, Association study



OP04-4

Novel insight into the role of HTLV-1 unspiced form of bZIP factor: Specific interaction with HS-1 associated protein X-1, preventing caspase9-dependent apoptotic pathway

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Background : Human T-cell leukemia virus type-1 (HTLV-1) infection causes adult T-cell leukemia (ATL). The HTLV-1 bZIP factor (HBZ) gene was identified and this protein expression is consistently observed in all ATL cells. It has been also reported that there are two different HBZ transcripts, unspliced form (HBZ-US) and spliced isoform (HBZ-SI). In almost all reports, the functional significance of HBZ-SI is focused, but not HBZ-US. In this study, we noted that HBZ-US interacted specifically with HS1-associated protein X-1 (HAX-1), known as a potent antiapoptotic protein through inhibition of caspase-9, which is an initiator caspase in apoptotic pathway.

Method : Interaction of HAX-1 with HBZ-US or HBZ-SI was investigated in mammalian cells. Subcellular distribution, when coproduction of HAX-1 together with HBZ-US or HBZ-SI in cells were examined confocal microscopic. Also, we investigated whether HBZ-US regulated the HAX-1 ubiquitination and the effect on apoptosis induced by staurosporine (STS), which is known to induce the intrinsic caspase-9-dependent apoptotic pathway.

Results : HAX-1 specifically associated with HBZ-US, but not HBZ-SI. When HBZ-US-GFP and mCherry-HAX-1 were co-expressed in cells, the localization of HBZ-US-GFP which alone was localized to the nucleus was partially shifted to the cytoplasm. The ubiquitination level of HAX-1 was significantly reduced by the expression HBZ-US in cells. Unexpectedly, this ubiquitination level was suppressed by HBZ-SI as well as HBZ-US, raising the possibility there was another pathway of suppressing HAX-1 ubiquitination. Furthermore, we found that HBZ inhibited the STS induced apoptosis. Our current study is focused on the functional difference between HBZ-US and HBZ-SI in anti-apoptotic activity through the HAX-1-mediated pathway.

Conclusion : Our results suggested the functional difference might exist between HBZ-US and HBZ-SI in pathogenesis of HTLV-1. To elucidate the function of HBZ-US will help us to understand the development of ATL.

Keywords : HTLV-1, ATL, HBZ, HAX-1, Apoptosis

OP04-5

Immune function of chimeric antigen receptor T cells quantitatively assessed via molecular imaging flow cytometry

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Background : Chimeric antigen receptor (CAR) T cells are genetically synthesized to reprogram T cells for antigen recognition and intracellular signaling to destruct tumor cells. A sensitive and reproducible assay to evaluate CAR T-cell function is essential to research and develop novel therapies, optimize manufacturing, and evaluate efficacy in clinical and non-clinical settings. However, conventional methods, such as cytotoxicity assays and in-vitro cytokine production, require a long cell culture processing time with a less quantitative and more time-consuming variability. In this study, we constructed the quantitative assay to analyze the change in localization of CAR molecules using molecular imaging flow cytometry (MI-FCM) to evaluate the immune functionality of CAR T-cells since aggregation of CAR molecules are observed after antigen recognition.

Method : Anti-CD19 CAR T-cells were generated by isolating human peripheral blood mononuclear cells from nine healthy donors. Next, each lot of CAR T-cells was co-cultured with CD19-expressing K562 cells and then evaluatinged cytotoxicity using a luciferase assay. Lastly, intensity, area, and distribution of CAR expression on CD4-positive or CD8-positive CAR T-cell in each lot of CAR T-cells with or without stimulation with CD19 antigen was quantitatively analyzed using MI-FCM evaluating correlation with cytotoxic activity.

Results : Stimulated with CD19 antigen, the area of CAR expression on CD4-positive or CD8-positive CAR T-cells significantly decreased without particular change of intensity in each lot of CAR T-cells. Importantly, the proportion of decrease of CAR expression area distributing a single spot among CD8-positive CAR T-cells was very strongly positively correlated with killing activity, while the proportion among CD4-positive CAR T-cells was significantly positively correlated.

Conclusion : These results suggest that quantifying the CAR localization in CAR T-cells by MI-FCM could be useful for evaluating their immune function.

Keywords : CAR T cell therapy, Immune functionality, Molecular imaging flow cytometry

OP05-1

Efficacy and safety of low-dose venetoclax combined with voriconazole in patients with acute myeloid leukemia unfit for intensive chemotherapy

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Background : Venetoclax combined with hypomethylating agents is the standard regime for elderly patients with acute myeloid leukemia unfit for intensive induction therapy. Nevertheless, many patients struggle with finances and forgo treatments due to the high costs of venetoclax. Concurrent application of venetoclax and CYP3A4 inhibitors such as voriconazole in low-income patients may be a feasible strategy to reduce the dose of venetoclax.

Method : We conducted a single-institutional, non-randomized, open-label, prospective study. Between June 2020 and March 2023, 57 AML patients newly diagnosed in our institution were enrolled. Twenty-three patients received low-dose venetoclax plus voriconazole plus azacitidine (cohort 1), whereas another 34 patients received standard dose venetoclax plus azacitidine (cohort 2). The efficacy of the two regimes between cohorts was analyzed and compared, the peak venetoclax concentration (C_{max}) and side effects of the patients were also detected.

Results : Totally, there were 35 males and 22 females, with a median age of 67 years old. 86% (49/57) of patients were adverse/intermediate risk in the whole cohort. The baseline characteristics were all balanced differently between the two cohorts. Venetoclax C_{max} were 1930±225 ng/mL and 2371±274 ng/mL, there was no significant difference between the two cohorts (P=0.3138). The overall response rates were 91% (21/23) and 85% (29/34) in cohort 1 and cohort 2, respectively (P=0.0834). At a median of 16 months of follow-up, the median progression-free survivals were 16 and 12 months in two cohorts, respectively (P=0.2651) with a hazard ratio of 0.6507. The median overall survivals were not reached and 14 months in the two cohorts, respectively (P=0.4636) with a hazard ratio of 0.7466. The most common hematological adverse events were neutropenia, thrombocytopenia, and anemia, whereas the most frequent non-hematological adverse events include infections, vomiting, diarrhea, and hypokalemia.

Conclusion : The combination of low-dose venetoclax and voriconazole is well-tolerated and effective in unfit AML patients.

Keywords : Venetoclax, Low-dose, Voriconazole, Unfit, Acute myeloid leukemia

OP05-2

The microRNA miR-222 is overexpressed and regulates proliferation, differentiation and apoptosis pathways in paediatric acute myeloid leukemia

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Background : Knowledge about the molecular pathobiology of paediatric acute myeloid leukemia (pAML) is limited. microRNA-222 (miR-222) is dysregulated across several cancers and we aim to delineate its role in pAML.

Method : Six AML cell lines (Kasumi-1, THP1, HL-60, KG1, MOLM-13, MOLM-14) were cultured in RPMI-1640 media. Bone-marrow (n=26) and peripheral-blood (n=46) from paediatric AML patients were included. Expression was quantified using qPCR. Downstream targets were predicted using TargetScan and 3'UTR was cloned into pmirGLO vector. Interaction was then studied using dual-luciferase assay. Cell cycle analysis was performed by quantifying 7-AAD, apoptosis by annexin-PI method and myeloid differentiation by quantifying CD11b expression using flow cytometry. Immunofluorescence was performed to observe p27 protein levels. Overall Survival (OS) was analysed using the log-rank test.

Results : miR-222 was consistently overexpressed in all AML cell lines ($p<0.0001$) as well as marrow ($p<0.001$), and peripheral-blood samples ($p=0.0005$) from pAML patients. High miR-222 expression had lower OS ($p=0.0072$) in pAML. Downregulation of miR-222 led to cell-cycle arrest of THP1 and KG1 cells ($p<0.0001$ & $p=0.002$), while promoting apoptosis ($p=0.0017$ & $p=0.0003$) and cellular differentiation of THP1 cells ($p=0.0019$). The cell cycle inhibitor protein p27 was predicted as the target of miR-222. Co-transfection of p27-3'UTR and miR-222 mimic in HEK293T cells decreased luciferase activity ($p<0.0473$) demonstrating in vitro interaction. Inhibiting miR-222 led to an increase in p27 protein level. Additionally, a decrease in levels of anti-apoptotic protein BCL-2, BCLXL, and MCL1, and an increase of monocyte marker CD11b was observed upon miR-222 downregulation.

Conclusion : miR-222 is overexpressed and associated with inferior OS in pAML. miR-222 is potentially involved in underlying regulatory pathway for cell survival while inhibiting apoptosis and cell differentiation in AML

Keywords : AML, microRNA, Proliferation, Differentiation, Apoptosis

OP05-3

Genetic characteristics and venetoclax efficacy in acute myeloid leukemia

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Background : Despite Venetoclax (VEN) becoming a mainstay for unfit acute myeloid leukemia (AML) patients, there is a dearth of predictive genetic data for treatment response in first-line and salvage settings. Therefore, we conducted an analysis in patients treated with VEN plus hypomethylating agent (HMA) at our institution to narrow this clinical need.

Method : We analyzed patients receiving a combination of HMA five days with VEN from January 2020 to June 2023. Genetic data at the time of relapse were collected for patients experiencing relapse. A total of 364 patients were included, comprising 152 newly diagnosed (ND) and 212 relapse/refractory (R/R) cases. We compared the overall response (complete remission (CR), CR with incomplete hematologic recovery, and morphologic leukemia-free state) to treatment based on chromosomal abnormalities or molecular genetic alterations in these patient groups.

Results : Genetic abnormalities below a significance level of 0.10 when assessing treatment efficacy through logistic regression in all, ND, and R/R AML patients, were summarized in the Figure. In all patients, complex karyotype, *SETBP, TET2, TP53* mutations significantly diminished the response to HMA+VEN, while core binding factor (CBF)-β or *IDH1/2* mutations showed improvement. Borderline significance was observed for reduced response in CBFα AML and increased efficacy in *K/NRAS* mutations. In ND AML, CBFβ predicted a favorable response, while *SH2B3* and *TET2* mutations linked to diminished response. A borderline increase was noted in *IDH1/2* mutations, and a decrease in *JAK2* mutations. In R/R AML, *CBFβ, IDH1/2*, and *STAG2* mutations significantly favored response, while CBFα and *TP53* significantly reduced response. *PHF6* mutation showed borderline significance, indicating a trend towards increased response.

Conclusion : We noted improved HMA+VEN treatment efficacy in CBFβ AML and *IDH1/2* mutated groups across all treatment settings, while patients with *TET2* and *TP53* mutations showed less favorable outcomes. Building on this, establishing a decision-making model for VEN administration in treatment seems promising.

Keywords : Acute myeloid leukemia, Genetics, Venetoclax, Efficacy

A. Total patients (N = 364)

Genetics	Odds ratio for overall response (95% CI)	p
CBFα	0.39 (0.14-1.04)	0.0607
CBFβ	> 100 (NA)	<0.001
Complex karyotype	0.57 (0.34-0.99)	0.0441
K/NRAS mutated	1.71 (0.91-3.40)	0.0966
IDH1/2 mutated	2.27 (1.23-4.45)	0.0081
SETBP1 mutated	< 0.01 (NA)	0.0454
TET2 mutated	0.46 (0.24-0.87)	0.0166
TP53 mutated	0.35 (0.15-0.76)	0.0078

0.01 0.1 1 10 100

B. Newly diagnosed (N = 152)

Genetics	Odds ratio for overall response (95% CI)	p
CBFβ	> 100 (NA)	0.0189
IDH1/2 mutated	2.34 (0.89-7.36)	0.0892
JAK2 mutated	0.15 (0.01-1.18)	0.0720
SH2B3 mutated	< 0.01 (NA)	0.0312
TET2 mutated	0.26 (0.10-0.65)	0.0041

0.01 0.1 1 10 100

C. Salvage (N = 212)

Genetics	Odds ratio for overall response (95% CI)	p
CBFα	0.16 (0.02-0.65)	0.0090
CBFβ	>100 (NA)	0.0064
IDH1/2 mutated	2.22 (1.02-5.28)	0.0449
PHF6 mutated	5.00 (0.87-94.35)	0.0753
STAG2 mutated	>100 (NA)	0.0401
TP53 mutated	0.19 (0.04-0.63)	0.0059

0.1 1 10 100

OP05-4

Adverse clinical impact of *RB1* gene deletions alone and with concurrent *IKZF1* gene deletions in pediatric B-cell acute lymphoblastic leukemia

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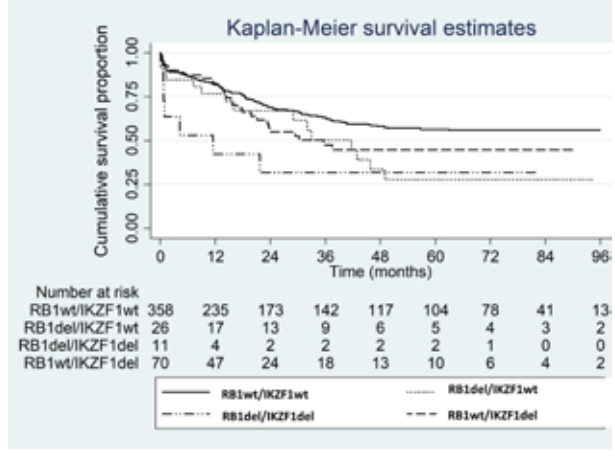
Background : There is a need for newer biomarkers to improve the risk-stratification of B-ALL. The aim of the study was to estimate the prevalence and effect of RB transcriptional corepressor1(RB1) deletion in childhood B-ALL, when present alone or along with IKAROS family zinc finger1(IKZF1) deletion.

Method : The pediatric B-ALL cases were analyzed for RB1 and IKZF1 deletions using multiplex ligation-dependent probe amplification(MLPA).

Results : The study includes 517 pediatric B-ALL patients, with a median age of 7 years(1-18). This comprised 470 BCR::ABL1 negative and 47 BCR::ABL1 positive patients. Overall, 41/517 patients(7.9%) exhibited RB1 deletions (RB1del); 36/470(7.7%) in BCR::ABL1 negative, and 5/47(10.6%) in BCR::ABL1 positive. Furthermore, IKZF1 deletions(IKZF1del) were identified in 99 patients(19.1%); 70/470(14.9%) in BCR::ABL1 negative; 29/47(61.7%) in BCR::ABL1 positive. Concomitant RB1 and IKZF1 deletions(RB1del/IKZF1del) were found in 14(2.7%) cases, while RB1 deletions without IKZF1 deletions(RB1del/IKZF1wt) were observed in 27 cases. These were compared with 85 cases having IKZF1 deletions without RB1 deletion(RB1wt/IKZF1del) and 391 cases lacking both RB1 and IKZF1 deletions(RB1wt/IKZF1wt). The post-treatment outcome was available in 465 cases. The group with both RB1 and IKZF1 deletions(RB1del/IKZF1del) showed the worst post-induction remission rate(54.6%;p=0.019) compared to 76.9% in RB1del/IKZF1wt, 80% in RB1wt/IKZF1del, and 86% in RB1wt/IKZF1wt. Additionally, median event-free survival(EFS) and median overall survival(OS) were the least in the RB1del/IKZF1del group(8.9 months;p=0.0002 and 11.5 months;p=0.007 respectively) compared to RB1del/IKZF1wt(28.5, 41.7 months), RB1wt/IKZF1del(22.6, 35.6 months), and RB1wt/IKZF1wt(41.4 months, median OS not reached) (Fig.1).

Conclusion : RB1 deletions were seen in 7.9% and IKZF1 deletions were observed in 19.1% of B-ALL. The B-ALL patients with concomitant RB1/IKZF1 deletions(2.7%) had much poorer outcomes than cases without any of these deletions or having RB1 deletions or IKZF1 deletions alone. Thus, the presence of RB1 deletions and IKZF1 deletions, particularly if present together, can be used as a predictive marker for poor outcome in B-ALL.

Keywords : Pediatric B-ALL, RB1 gene, IKZF1 gene, Childhood leukemia, Risk-stratification



OP05-5

Prognostic impact of concurrent genetic deletions in *IKZF1* and *CDKN2* in adult patients with philadelphia chromosome-positive acute lymphoblastic leukemia

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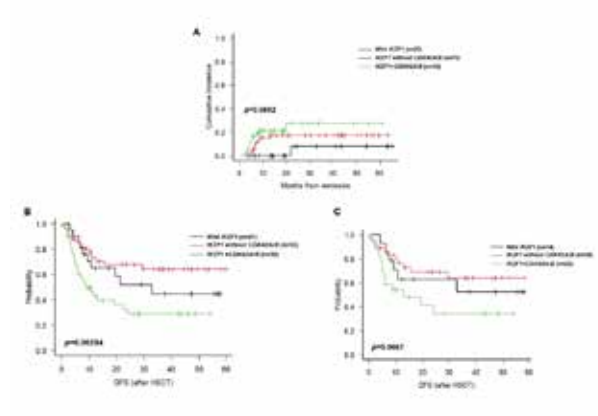
Background : Many studies have discovered various gene aberrations in acute lymphoblastic leukemia (ALL). Deletion of IKZF1 is frequently observed in Ph-positive ALL and IKZF1-plus is defined as a poor subgroup when CDKN2, PAX5, or PAR1 deletions are combined. Most results were from Western pediatric data and new gene mutations are being detected but their clinical correlation is controversial.

Method : We identified the deletions in 11 genes by MLPA and 73 gene mutations by NGS in 146 consecutive patients with Ph-positive ALL. All were treated with hyper-CVAD and imatinib-based therapy. Among them, 112 underwent allo-HCT (95 in CR1, and 17 ≥CR2) and 72 of them were in complete molecular response (CMR, undetectable BCR::ABL1 transcript).

Results : We identified IKZF1del in 119 (81.5%) patients, CDKN2del in 56 (38.3%), and PAX5del in 54 (37.0%) followed by EBF1del (n=22), RB1del (n=19), JAK2del (n=14), and ETV6del (n=12). Frequently observed mutation was SETD2 (n=9), RUNX (n=8), and IKZF1 (n=7). CDKN2del was the only aberration associated with poor outcome. Among the 56 with CDKN2del, 49 (87.5%) had concurrent IKZF1del, and this group showed the worst outcome. We made three subgroups to assess the prognostic impact: Group-3 (concurrent IKZF1del and CDKN2del), Group-2 (IKZF-1del without CDKN2del), and Group-1 (no IKZF1del). Although post-induction CMR rate was not different (33.3%, 26.5%, and 33.3%, p=0.929), relapse before allo-HCT was more frequent in Group-3 (27.6% vs. 17.3% vs. 8.0%, p=0.065). After allo-HCT, 3-year DFS was significantly inferior in Group-3 (28.9% vs. 64.2% vs. 44.6%, p=0.002). Multivariate analysis showed Group-3 and pre-HCT CMR were significant factors for survival. Even in pre-HCT CMR subgroup, Group-3 exhibited significantly inferior DFS (34.4% vs. 60.1%, p=0.023).

Conclusion : Our data showed concurrent IKZF1del and CDKN2del was significantly associated with poor outcomes in Ph-positive ALL. No other mutations were observed significant, but large data analysis is needed to find clinical relevance.

Keywords : Acute lymphoblastic leukemia, IKZF1, CDKN2



OP05-6

Molecular map of T-lineage acute lymphoblastic leukemia: Clinical implications

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Background : T-acute lymphoblastic leukemia (T-ALL) is a heterogeneous malignancy characterized by the abnormal proliferation of T-cell precursors. Despite advances in immunophenotypic classification, understanding the molecular landscape and its impact on patient prognosis remains a challenge. The aim of the study was to identify the gene expression profiles of different immunophenotypic subtypes of T-ALL and to determine their prognostic relevance.

Method : In this study, we conducted RNA sequencing on 35 T-ALL samples to unravel the transcriptomic profile of T-ALL subtypes. Subsequently, we validated the prognostic relevance of 23 targets in an independent cohort of 99 T-ALL patients.

Results : Unsupervised clustering analysis revealed distinct gene clusters aligning with immunophenotypic subtypes, providing insights into the molecular heterogeneity of T-ALL. The identified signature genes exhibited associations with clinicopathologic features. RAG1 expression was higher in children <12 years of age. XIST and KDM6a expression was higher in females. We found a significant association between immature T-ALL immunophenotype with high expression of BAALC, MEF2C, LYL1, HHEX and low expression of

EZH2. RAG1 and FAT1 expression was higher in cortical T-ALL. DOT1L expression was higher in mature T-ALL. ETP-ALL immunophenotype was associated with high levels of BAALC, MEF2C, LYL1, LYN, XIST and lower levels of ST20 and EML4. MRD positivity was associated with high PCAT18, HHEX, and MEF2C expression. Prednisolone resistance was associated with MEF2C expression. Survival analysis uncovered several independent predictors of patient outcomes. Higher expression of MEF2C, BAALC, HHEX, and LYL1 genes emerged as robust indicators of poor OS, EFS, and RFS. Conversely, higher LMO2 expression correlated with adverse EFS and RFS. Increased expression of lncRNA ST20, coupled with RAG1, demonstrated a favorable prognostic impact on OS, EFS, and RFS.

Conclusion : Several novel associations of gene expression patterns with clinicopathological features and prognosis were identified, which may help understand T-ALL's molecular pathogenesis and provide novel prognostic markers.

Keywords : T-ALL, RNAseq, Outcome, Gene expression profile

OP06-1

Carfilzomib, lenalidomide, dexamethasone in the real-world asian relapsed and/or refractory multiple myeloma patients - KMM2201 study

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Background : The survival of multiple myeloma (MM) has been improved dramatically owing to the development of new class of drugs. Carfilzomib, in combination with lenalidomide and dexamethasone (KRd) significantly improved the survival of relapsed and/or refractory multiple myeloma (RRMM) patients. However, the real-world outcome of KRd in a large cohort of Asian MM patient is still lacking. The aim of this study was to analyze the effectiveness, especially focused on clinical trial eligibility and high-risk clinical factors, and adverse event (AE) profile of KRd regimen in the real-world Korean RRMM patients.

Method : Retrospective data of 364 RRMM patients who have received KRd regimen between February, 2018 and October, 2020, was collected from 21 centers participating in the Korean multiple myeloma working party (KMMWP).

Results : Forty-nine percent of patients were trial ineligible. Overall response rate was 90% among the response evaluable patients, including a very good partial response, a complete response (CR) and a stringent CR of 25%, 32% and 6%. Among the 62 patients who were evaluated for minimal residual disease (MRD) by EuroFlow standard operation procedure, 36% (22 of 62) were Flow MRD-negative. With a median follow-up duration of 34.8 months (range, 0.00-61.5), the median progression-free survival (PFS) and overall survival (OS) was 26.4 months (95% confidence interval, CI, 23.1-29.7 months), and not reached. High-risk cytogenetics at diag-

nosis of MM, EMD, doubling of M protein, and symptomatic MM at the time of KRd treatment affected poorly on PFS by univariate and multivariate analysis. Hematologic toxicities were more commonly observed than non-hematologic AEs. The most common grade 3 or higher toxicities were neutropenia, followed by infections, fatigue, and acute kidney injuries. Grade 3 or higher cardiovascular AEs were observed in less than 5 percent of the patients

Conclusion : KRd for real-world Korean RRMM patients was highly effective with a tolerable AE profile.

Keywords : Relapsed and/or refractory multiple myeloma, Asian, Carfilzomib, Lenalidomide, Dexamethasone

OP06-2

Real-world effectiveness of Ixazomib, lenalidomide, and dexamethasone (IRd) in Asian patients with relapsed/refractory multiple myeloma (RRMM)

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Background : Randomized clinical trials have shown IRd to be efficacious and safe in Asian patients with RRMM[1]; however, real-world data are limited.

Method : This multicenter, observational, cohort study was conducted in 16 sites across South Korea (KOR), Malaysia (MY), and Thailand (TH). Patients treated with IRd during 2016–2023 were enrolled; data were collected by retrospective chart review and 6-months prospective follow-up. Patients with RRMM aged ≥20 years who received 1–3 prior lines of therapy, with ECOG performance status 0–2 were included. Co-primary endpoints were median time to next treatment (TTNT) and overall response rate (ORR).

Results : Overall, 104 patients were enrolled (69 KOR, 27 MY; 8 TH). Median age at treatment initiation was 64.0 years (range 42.0–83.0). At diagnosis, 54.8% were International Staging System Stage II/III. 13.5% had high risk cytogenetic abnormalities (data available for 60.6%). Majority had 1 prior therapy (70.2%), 20.2% had 2; 47.1% had prior autologous stem-cell transplantation. Median number of IRd cycles was 13 (range 1–50) and median ixazomib treatment duration was 14.8 months (95% CI 11.3, 23.0). Median TTNT was 32.1 months (95% CI 22.5–not reached [NR]) but varied across countries (Table 1). ORR was 72.1% (KOR 79.7%, MY 48.2%, TH 87.5%). Median progression-free survival was 27.7 months (95% CI 19.5–NR). Median overall survival was NR. In elderly patients (≥65 years; 49% of patients), median TTNT was 35.7 months (95% CI 28.8, NR); ORR 80.4% (95% CI 66.9, 90.2). AEs occurred in 90.4% and serious AEs in 29.8% of all patients; 18.3% discontinued due to AEs. Common Grade ≥3 adverse drug reactions were pneumonia (9.6%), neutropenia (7.7%), and gastroenteritis (2.9%).

Conclusion : ORR, TTNT, and PFS of IRd in this Asian real-world study are comparable to TOURMALINE-MM1 and other real-world studies. IRd has a manageable safety profile.

Keywords : Relapsed/refractory multiple myeloma, Lxazomib, Real-world, Asia, Effectiveness

Table 1: Effectiveness outcomes

	South Korea (n=69)	Malaysia (n=27)	Thailand (n=8)	Total (N=104)
Primary outcomes				
Time to next treatment*, months, median (95% CI)	31.6 (18.2, NR)	27.4 (8.7, 41.8)	NR (6.2, NR)	32.1 (22.5, NR)
Overall response rate**, n (%) [95% CI]	55 (79.7) [68.3, 88.4]	13 (48.2) [28.7, 68.1]	7 (87.5) 47.4, 99.7]	75 (72.1) [62.5, 80.5]
Stringent complete response, n (%) [95% CI]	1 (1.5) [0.04, 7.8]	0 [0, 12.8]	0 [0, 36.9]	1 (1) [0.02, 5.2]
Complete response, n (%) [95% CI]	18 (26.1) [16.3, 38.1]	5 (18.5) [6.3, 38.1]	4 (50.0) [15.7, 84.3]	27 (26.0) [17.9, 35.5]
Very good partial response, n (%) [95% CI]	14 (20.3) [11.6, 31.7]	2 (7.4) [0.9, 24.3]	3 (37.5) [8.5, 75.5]	19 (18.3) [11.4, 27.1]
Partial response, n (%) [95% CI]	22 (31.9) [21.2, 44.2]	6 (22.2) [8.6, 42.3]	0 [0, 36.9]	28 (26.9) [18.7, 36.5]
Secondary outcomes				
Duration of treatment, months, median (95% CI)	14.3 (10.4, 25.4)	13.2 (4.5, 27.1)	47.3 (5.6, 50.5)	14.8 (11.3, 23.0)
Overall survival, months, median (95% CI)	NR (NR, NR)	NR (33.0, NR)	NR (20.8, NR)	NR (58.0, NR)
Progression-free survival, months, median (95% CI)	27.7 (22.5, NR)	16.9 (7.0, NR)	NR (1.7, NR)	27.7 (19.5, NR)

*Time to next treatment was defined as the time from the initiation of IRd-based regimen after enrollment to the initiation of subsequent MM therapy, and was censored for enrolled patients who were alive but did not receive subsequent therapy based on date that the subject's information was last available, or for deceased patients who did not receive subsequent therapy based on the date of death.

**ORR was defined as the sum of stringent complete response, complete response, very good partial response, and partial response.

CI, confidence interval; ixazomib, lenalidomide, and dexamethasone (IRd); MM, multiple myeloma; NR, not reached.

OP06-3

Efficacy and safety of carfilzomib, lenalidomide, and dexamethasone versus ixazomib, lenalidomide, and dexamethasone in real world patients with relapsed/refractory multiple myeloma: KMM2004 study

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Background : The recent influx of novel agents with different mechanisms of action has led to rapid changes in treatment strategies of RRMM. The approval of KRd in 2018, followed by IRd in 2020, has raised questions about the most effective treatment strategies for patients with RRMM.

Method : We retrospectively reviewed the medical records of RRMM patients treated with KRd(112) or IRd(70) at 17centers in South Korea 2020-2021.

Results : Median age(65 vs 66 yrs, p=0.38) and R-ISS at diagnosis(I: 13.3 vs 21.7%, II: 54.3 vs 48.3% and III: 32.4 vs 30.0%, p=0.38) were not different between the two groups. Patients with high risk cytogenetics were more likely to be treated with KRd(43.8 vs 18.0%, p=0.003) and the time from diagnosis to XRd treatment was longer in the IRd(20.5 vs 33.7mo, p=0.08). Patients in the KRd received 13 cycles of treatment and patients in the IRd received 15 cycles of treatment (median, p=0.1), with more dose modifications in the IRd(30.1 vs 41.1%, p=0.023). ORR was not significantly different at 89.1 vs 87.0% (p=0.67), but CRR was better in the KRd(45.5 vs 30.4%, p=0.046). Median PFS(19.1 vs 28.4 mo, p=0.08) showed a trend towards better in the IRd and median OS(31.6 vs not reached, p=0.02) was better in the IRd. In the safety analysis, hematologic toxicity, infection, and cardiac events were more frequent in the KRd, and GI toxicity and skin rash were relatively more frequent in the IRd.

Conclusion : Our data showed the treatment outcomes of KRd and IRd in the real-world. Contrary to predictions based on clinical trials, the IRd showed better survival data. Clinicians tended to choose KRd in the high risk and it actually showed a deeper response. In contrast, the IRd did not acheieve a deeper response, but the treatment response was found to be sustainted for a longer period of time.

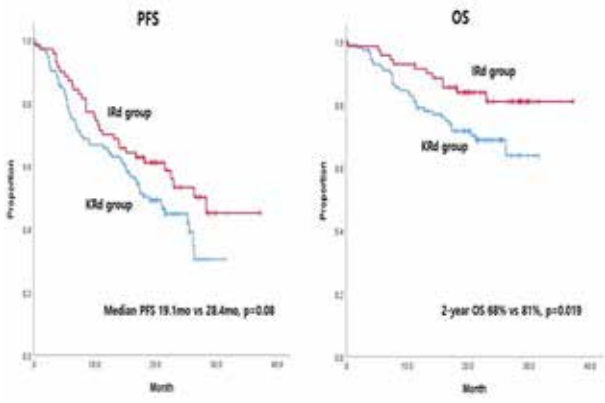

Table 1.

Characteristics	KRd Group (n=112)	ASPIRE (n=396)	IRd Group (n=70)	TOURMALINE (n=360)	P value
Age					
Median (range)	65 (41-81)	64 (38-87)	66 (45-86)	66 (38-91)	0.382
≥65 yr	57 (50.9)	185 (46.7)	42 (60.0)	192 (53)	0.220
Plasmacytoma (at XRd)	24/106 (22.6)		14/70 (20.0)		0.677
GFR<30	9 (8.4)		5 (7.5)	5 (1)	0.058
B2MG elevation	31/54 (57.4)	319 (80.6)	20/33 (60.6)		0.769
FISH High risk group (at Dx.)	35/80 (43.8)	48/195 (24.6)	9/50 (18.0)	75/274 (27.4)	0.003
Trial feasibility	93 (83.0)		61 (87.1)		0.455
Time to Dx. To XRd	20.5 (2.9-124.5)	36 (4.8-236)	33.7 (1.5-88.2)	44.2 (3-281)	0.077
VGPR or better	78/110 (70.9)	277 (69.9)	40/69 (58.0)	173 (48)	0.075
ORR	98/110 (89.1)	87.1	60/69 (87.0)	282 (78)	0.666
PFS (median, mo)	19.1	26.5	28.4	20.6	0.08
OS (median, mo)	NR	48.3	NR	53.6	0.019

OP06-4

Bortezomib maintenance therapy in transplant-ineligible newly diagnosed multiple myeloma have major response to induction chemotherapy (KMM 174)

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Background : Maintenance therapy (MT) post-induction in newly diagnosed multiple myeloma (NDMM) patients represents an important treatment strategy to delay the disease progression and relapse. Bortezomib or lenalidomide MT improve long-term outcomes in transplant-eligible NDMM patients. However, there is less evidence to support bortezomib MT in transplant-ineligible NDMM.

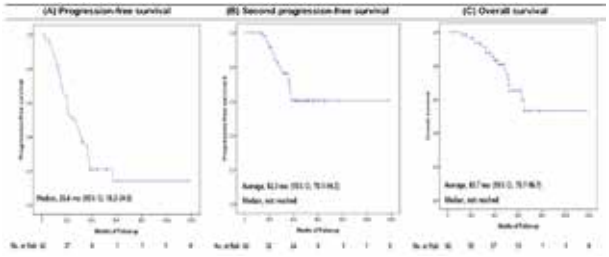
Method : A prospective multicenter study was performed in 14 medical centers in Korea. A total of 62 transplant-ineligible NDMM patients who received bortezomib MT after achieving better than partial response to induction chemotherapy between 2017 and 2021 were analyzed. Bortezomib MT was defined as (1.3mg/m^2) once

a week for 3 weeks (Day 1, 8, 15) at 28-day intervals, administered subcutaneously. It is administered until the disease progression or unacceptable toxicity occurs, and completed after up to 24 months. Response criteria were defined according to the International Myeloma Working Group 2014 consensus. Progression free survival (PFS) and overall survival (OS) were the primary and secondary end-points.

Results : Of the total 62 patients, the median age was 71.5 years (range, 56-83) and the sex ratio was 1.5. According to the International staging system (ISS) at diagnosis, 23 patients (37.1%) were stage II and 23 (37.1%) were stage III. Bortezomib-Melphalan-Prednisolone (VMP) regimen (88.7%) was most commonly used as induction therapy. In bortezomib MT, median treatment cycle was 10 (range, 1-26) and median treatment duration was 8.6 months (range, 0.9-25.4). During bortezomib MT, 67.7% had one or more adverse event, 20.9% had grade 3 or higher adverse events, and 6.4% discontinued treatment due to toxicity. Median PFS was 26.6 months (95% CI, 18.2-34.9) and average OS was 83.7 months (median, not reached). The median follow-up duration was 44.5 months (range, 7.0-117.6).

Conclusion : These prospective multicenter data showed that bortezomib MT is feasible, safe, and effective for transplant-ineligible NDMM patients. More research is warranted to further assess the role of bortezomib MT.

Keywords : Bortezomib, Multiple myeloma, Maintenance therapy, Survival



OP06-5

Impact of pretransplant measurable residual disease(MRD) using multiparametric flow cytometry(mFCM) and imaging (PET-CT scan) before autologous stem cell transplantation(ASCT) in multiple myeloma : Insights from tertiary centre in India

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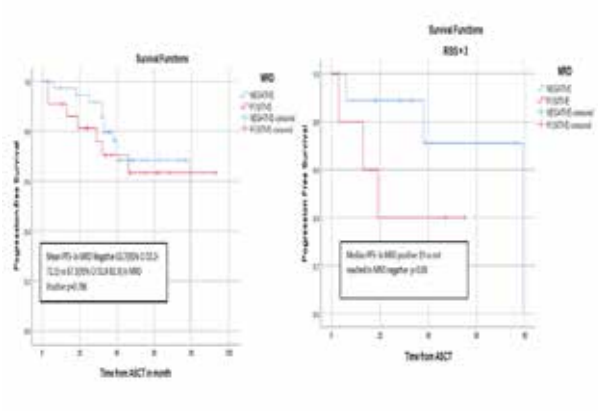
Background : Although significance of MRD in multiple myeloma(MM) has been studied quite extensively , its relevance and impact before ASCT on outcome yet not been elucidated

Method : MM patients who underwent (ASCT) at our centre from January 2027 to December 2021 and had pretransplant measurable residual disease (MRD) assessment by mFCM at 0.001%(10^{-5}) cutoff and imaging by PET CT were included. Data were retrospectively retrieved from the medical record department, encompassing baseline characteristics, risk stratification, and outcome measures such as the incidence of relapse and progression-free survival(PFS). The cohort was stratified into two groups based on pretransplant MRD status and similarly categorized for PET positivity and negativity. Descriptive statistical analysis was conducted, for characteristics and outcomes within each subgroup, Kaplan-Meier survival analysis was performed.

Results : A total of 85 multiple myeloma (MM) patients underwent autologous stem cell transplantation (ASCT), with 60 included in the study based on pretransplant measurable residual disease (MRD) data. The median age was 55 years, and the female-to-male ratio was 1.1, evenly distributed among MRD-positive and MRD-negative groups. Risk stratification revealed 26.6% R-ISS III and 38.3% ISS III. Baseline data showed 31.2% with renal impairment, and 88% had bone involvement. Most received bortezomib-based induction; lenalidomide was in 59%, and three received daratumumab. Pretransplant, 63% had no MRD, and 39% had negative PET scans. At a median follow up 39 months, 31% relapsed in MRD-positive vs. 28% in MRD-negative(p=0.610) . For PET-positive patients achieving MRD negativity, estimated PFS at 3 years was 71.8%, similar to MRD-positive 60.2% (p=0.176). R-ISS III patients not achieving MRD negativity had 40% PFS at 3 years, contrasting with 70% for MRD negativity (p=0.063).

Conclusion : The findings underscore the potential impact of achieving MRD negativity, particularly in specific subgroups, on long-term outcomes in MM patients undergoing ASCT

Keywords : Autologous, Mesurable residual disease, PET CT, Multiple Myeloma transplant, India



OP06-6

The efficacy of salvage second autologous hematopoietic stem cell transplantation in Korean patients with relapsed/refractory multiple myeloma in novel agent era: The KMM2301 study

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Background : Autologous stem cell transplantation (ASCT) has been contributed to improve prognosis in patients with multiple myeloma (MM). Second salvage ASCT (SAT) have demonstrated clinical benefits, but many studies were performed before the introduction of novel agents.

Method : In this retrospective study, we enrolled 51 patients who received SAT for relapsed/refractory MM after novel agent-based induction therapy. Response status and survival outcomes including overall survival (OS) and progression-free survival (PFS) were analyzed. Additionally, we compared outcomes of SAT to the results of salvage KRd without SAT.

Results : Median duration from 1st ASCT to relapse was 26.9 months, and 34% of patients showed CR before SAT. CR rate increased to 58% after SAT. Median PFS and OS after SAT were 16 and 73 months, respectively. When we compared outcomes according to the duration of response (DOR) after the 1st ASCT (<18 vs. ≥ 18 months), it showed significant results for PFS (median 5 vs. 22 months, p=0.009) and OS (median 14 vs. 103 months, p=0.001). Line of treatment (LOT) for SAT (2nd vs. ≥3rd line) was also significant factors for PFS (median 22 vs. 7 months, p<0.001) and OS (median 103 vs. 15 months, p<0.001). Multivariate Cox analysis demonstrated LOT was significant for PFS (HR 0.235, p=0.004) and OS (HR 0.205, p=0.008). DOR after 1st ASCT was significant for OS (HR 3.59, p=0.013). When we compared results of SAT (n=33) to outcomes of KRd without SAT (n=113) as a 2nd line treatment, SAT presented a tendency to better 3-year PFS (48.4% vs. 38.9%, p=0.109) and significantly superior OS (93.3% vs. 77.8%, p=0.006) compared to KRd without SAT.

Conclusion : In conclusion, SAT may have a role in novel agent era, especially for feasible patients who presented sufficient DOR after 1st ASCT and received SAT as an early LOT.

Keywords : Salvage, Autologous, Stem cell, Transplantation ,Myeloma

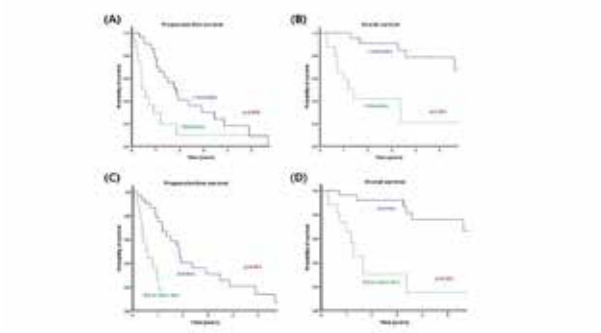

Fig. Kaplan-Meier curves of progression-free survival (A) and overall survival (B) in patients who received 2nd salvage autologous stem cell transplantation (SAT) according to the duration of response after the 1st autologous stem cell transplantation, and progression-free survival (C) and overall survival (B) according to the line of treatment in which SAT was performed.

OP07-1

Efficacy & safety of momelotinib vs danazol in JAKi-experienced patients with myelofibrosis & anemia: Asian subgroup analysis of the MOMENTUM trial

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Background : Momelotinib (MMB), a Janus kinase 1/2 and activin A receptor type 1 inhibitor, showed clinical activity on myelofibrosis symptoms, anemia, and spleen in the MOMENTUM trial (NCT04173494). This post hoc analysis (funded by GSK) investigated the efficacy and safety of MMB in the Asian subpopulation of MOMENTUM.

Method : Eligibility: Primary or post-essential thrombocythemia/polycythemia vera myelofibrosis; DIPSS High/Intermediate-2/Intermediate-1; Total Symptom Score (TSS) ≥10; hemoglobin <10g/dL; prior JAKi; palpable spleen ≥5cm. Randomization: 2:1 to MMB 200mg once daily (QD) plus danazol (DAN) placebo (MMB group) or DAN 600mg QD plus MMB placebo (DAN group) for 24 weeks (W), after which patients could receive open-label MMB/DAN. Primary endpoint: W24 TSS response rate (≥50% reduction from baseline). W24 key secondary endpoints: transfusion independence rate; mean TSS change from baseline; splenic response rate (≥25/35% volume reduction from baseline); rate of 0 transfusions.

Results : Seventeen Asian patients with myelofibrosis enrolled from Korea (n=11), Singapore (n=4), and Taiwan (n=2). MMB vs DAN: 11/17 and 6/17 were in each group, 54.5% (6/11) and 0.0% (0/6) were female, primary myelofibrosis was in 54.5% (6/11) and 50.0% (3/6), median hemoglobin 7.9g/dL and 7.4g/dL, platelets 87.0x10^9/L and 89.5x10^9/L. Prior JAKis: 100% (17/17) ruxolitinib, 9.09% (1/11) fedratinib in MMB group only. TSS response rate at W24 was 36.4% (4/11) with MMB and 0.0% (0/6) with DAN. Secondary outcome results were consistent with the intent-to-treat population (Table 1). MMB vs DAN: grade ≥3 TEAEs in 36.4% (4/11) and 66.7% (4/6); one grade ≥3 anemia in MMB; no grade ≥3 thrombocytopenia. MMB vs DAN: treatment interruption and/or dose reduction in 18.2% (2/11) and 16.7% (1/6). DAN: two patients discontinued study treatment (Table 1).

Conclusion : In the Asian sub-population of MOMENTUM, MMB improved myelofibrosis-associated symptoms, anemia measures, and spleen response, and generally favorable safety vs DAN in JAKi-experienced patients with symptomatic myelofibrosis and anemia.

Keywords : Momelotinib, Janus kinase inhibitor, Myelofibrosis, Anemia,Asia

Table 1. Summary of efficacy outcomes and treatment-emergent adverse events during the randomized study period

Efficacy outcomes at Week 24			
Efficacy endpoints	**MMB (n=11)**	**DAN (n=6)**	**Difference (95% CI)***
TSS response rate, n (%)	4 (36.4)	0.0	33.3 (-20.0, 86.7)
TI rate, n (%)	7 (63.6)	0.0	100.0† (58.4, 141.6)
SRR (≥25% reduction), n (%)	7 (63.6)	1 (16.7)	33.3 (-20.0, 86.7)
Least squares mean TSS change from baseline (SE)	-9.52 (2.8)	-9.19 (4.1)	-0.34‡ (-10.9, 10.3)
SRR (≥35% reduction), n (%)	4 (36.4)	0.0	33.3 (-20.0, 86.7)
Rate of zero transfusions, n (%)	8 (72.7)	0.0	100.0 (100, 100)
Treatment-emergent adverse events during the 24-week randomization period			
	MMB (n=11)	**DAN (n=6)**	**Total (N=17)**
TEAE	11 (100)	6 (100)	17 (100)
Grade ≥3 TEAE	4 (36.4)	4 (66.7)	8 (47.1)
TEAE related to study treatment	7 (63.6)	2 (33.3)	9 (52.9)
Grade ≥3 TEAE related to study treatment§	2 (18.2)	1 (16.7)	3 (17.6)
TEAE leading to the permanent discontinuation of the study treatment	0 (0)	2 (33.3)	2 (11.8)
TEAE leading to treatment interruption and/or dose reduction	2 (18.2)	1 (16.7)	3 (17.6)
Serious TEAE	3 (27.3)	3 (50.0)	6 (35.3)
Serious TEAE related to the study treatment§	1 (9.1)	1 (16.7)	2 (11.8)
Fatal TEAE‖	1 (9.1)	1 (16.7)	2 (11.8)

CI, confidence interval; DAN, danazol; MMB, momelotinib; SE, standard error; SRR, splenic response rate; TEAE, treatment-emergent adverse event; TI, transfusion independence; TSS, total symptom score. *Differences in TSS response rate, SRRs and rate of zero transfusions were based on a stratified Cochran-Mantel-Haenszel test; †Non-inferiority proportion difference; ‡Least squares mean difference; §TEAE assessed as related to the study treatment by investigator; ‖Fatal TEAEs were transformation to acute myeloid leukemia in the MMB group and acute myeloid leukemia in the DAN group

Method : Bone marrow eosinophilia or basophilia was defined as a differential count of eosinophils or basophils more than 5% or 1% in bone marrow. Total 74 patients diagnosed with MDS were enrolled. Genomic DNA was extracted from diagnostic bone marrow aspirate or peripheral blood samples. Additional targeted NGS sequencing was done with 54 genes associated with hematologic malignancies in bone marrow eosinophilia (MDS-EOS, n = 14), bone marrow basophilia (MDS-BASO, n = 6) and neither bone marrow eosinophilia nor basophilia (MDS-/-, n=55).

Results : Beside ASXL1 mutation (33.8%), the frequently mutated genes included U2AF1(20.3%), TP53(16.2%), SRSF2(12.2%), BCR(10.8%) and DDX41(10.8%). Four genes including ATM, TP53, FLT3 and CEBPA had significantly higher mutation frequencies in MDS-EOS compared with MDS-/-. ASXL1 and U2AF1 had significantly higher mutation frequencies in MDS-BASO compared with MDS-/-. MDS-EOS had significantly higher mutation frequencies in DNA repair genes including ATM, PPM1D and TP53 than MDS-/-. The levels of VAF detected in the DNA repair gene mutation showed significant correlation with marrow eosinophil fraction. Chromosome 7 abnormalities and a complex karyotype with more than three abnormalities were associated with MDS-EOS. In Kaplan-Meier analysis, MDS-EOS had a poorer prognosis than MDS-/-.

Conclusion : This study showed that MDS patients with bone marrow eosinophilia have high frequencies of DNA repair genes mutation as well as chromosome 7 abnormalities and a complex karyotype. Moreover, MDS with bone marrow eosinophilia showed a poor prognostic value. Association of bone marrow eosinophilia with DNA repair genes mutation could inspire future genetic studies.

Keywords : Myelodysplastic syndrome, Eosinophil, Basophil, NGS

OP07-2

Distinct molecular and cytogenetic profiles of myelodysplastic syndrome with bone marrow eosinophilia and basophilia

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Background : Myelodysplastic syndromes (MDS) is sometimes associated with bone marrow eosinophilia. Although eosinophilia in MDS has been reported as a poor prognostic factor, the details of the molecular pattern are unclear. This study investigated the molecular and cytogenetic characteristics of bone marrow eosinophilia and basophilia in MDS.

OP07-3

Clinical and molecular characteristics and prognostic significance of autoimmune disease in myelodysplastic syndrome

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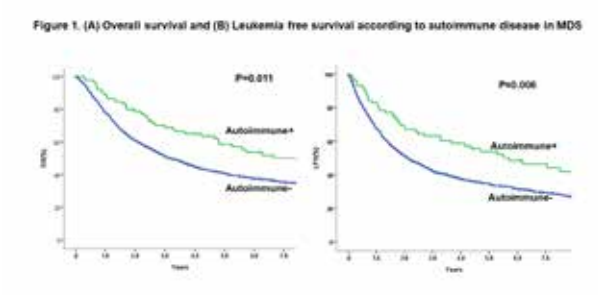
Background : The myelodysplastic syndromes (MDS) tend to present with heterogeneous autoimmune diseases and inflammatory manifestations. The pathobiology and prognostic impact of AD associated with MDS were not fully demonstrated. Therefore, we aimed to investigate the clinical and cytogenetic characteristics and prognostic significance of concomitant autoimmune disease in MDS.

Method : We retrospectively analyzed 1456 patients diagnosed with MDS at Asan Medical Center, Seoul, Korea, between 1989 and 2021. Next-generation sequencing (NGS) was performed in 446 patients.

Results : Of all patients, 90 (6.2%) had AD with MDS. Among AD, Behcet disease (20%), RA (18.9%), and ILD (14.4%) were frequently noted. Median hemoglobin level at the time of MDS diagnosis was significantly lower in patients without AD than in those with AD (8.2 vs. 9.4 g/dL, respectively, P=0.017). The MDS risk groups stratified by the R-IPSS system were similarly distributed between AD and no AD groups. In the AD group, common cytogenetic abnormalities were trisomy 8 (22.2%), complex karyotypes (5.6%), and der (1;7) (4.4%) other than normal karyotype (46.7%). In NGS data, BCORL1 (9.8% vs. 1.2%, P=0.006) and DNAH9 mutations (11.9% vs. 0%, P=0.014) are more frequently found in patients with AD than those without AD. Although the statistical difference was not significant, SETD2 (4.9% vs. 0.7%, P=0.069) and WT1 mutations (7.3% vs. 1.7%, P=0.055) tended to be more frequent in the AD group than no AD group. The patients with AD showed significantly higher overall survival (58.7% vs. 40.7% at 5 years, P=0.011) and leukemia-free survival rates (53.9% vs. 34.7% at 5 years, P=0.006) than those without AD.

Conclusion : The concomitant AD in MDS had unique clinical characteristics and a more favorable prognosis. Cytogenetic abnormalities of trisomy 8, der (1;7) and complex karyotypes and somatic mutations such as BCORL1, DNAH9, SETD2, and WT1 mutations are associated with MDS with AD.

Keywords : Myelodysplastic syndrome, Autoimmune disease, Prognosis, Cytogenetics, Next generation sequencing



OP07-4

Haploidentical HCT using ex vivo T cell-depleted PBSC as first-line therapy for pediatric patients with acquired SAA

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Background : Currently, HCT using an HLA-haploidentical family donor (HFD) is considered a viable therapeutic option for patients with acquired severe aplastic anemia (SAA) who have failed immunosuppressive therapy (IST) and cannot find a suitable matched donor. However, the upfront use of haploidentical HCT (haplo-HCT) for patients with treatment-naïve SAA requires more evidence. In this study, we evaluated the outcome of ex vivo T cell-depleted haplo-HCT as first-line therapy in pediatric patients with acquired SAA.

Method : Between October 2009 and November 2023, 40 pediatric patients with acquired SAA received ex vivo T cell-depleted haplo-HCT as initial therapy. None of the patients had undergone previous IST or transplantation. Five patients received CD3-depleted PBSC and 35 received TCRαβ-depleted graft.

Results : Of 40 patients, 39 achieved neutrophil engraftment at a median of 10 days (range, 9–12 days) posttransplant. One patient, who failed to achieve primary neutrophil engraftment, received two more rounds of haplo-HCTs and eventually achieved stable engraftment. Two patients experienced graft rejection within 30 days post-transplant and additional one patient developed late graft failure. All the 3 patients were successfully rescued with subsequent haplo-HCT. The CI of acute GVHD (aGVHD) ≥ grade 2 and ≥ grade 3 were 38% and 11%, respectively. No patient developed grade 4 aGVHD. Chronic GVHD occurred in 2 patients, one with mild and the other with moderate severity. Three patients died of transplant-related causes and all 37 survivors remained transfusion-independent. With a median follow-up of 6.7 years (range, 1.1–14.2), failure-free survival and overall survival were 85% ± 5.6% and 93% ± 4.2%, respectively.

Conclusion : In this study, HLA-haploidentical HCT with ex vivo T cell-depleted PBSC as first-line therapy showed a favorable outcome in pediatric patients with acquired SAA. Future study is warranted to verify the feasibility of this approach and evaluate the long-term complications such as infertility and second malignancies.

Keywords : Aplastic anemia, Hematopoietic cell transplantation, Haploidentical, Pediatric patients

OP07-5

STK10 mutation block erythropoiesis in acquired pure red cell aplasia via down-regulated the ribosome biosynthesis

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Background : The underlying mechanisms of acquired pure red cell aplasia (PRCA) remain obscure, and the role of gene mutation in the pathogenesis of acquired PRCA has not been elucidated yet. Herein, we identify gene mutations in acquired PRCA patients and their role in the pathogenesis.

Method : We performed whole exome sequencing in thirty newly diagnosed patients with acquired PRCA. The candidate genes with high frequency in acquired PRCA but low frequency in 1000 genomes which may affect protein function were selected. The erythroid and megakaryocytic differentiation was evaluated in the gene-silenced K562 cell lines. STK10 gene was selected which affects the erythropoiesis. The RNA sequencing in STK10 silenced K562 cells was performed. Next, ribosome RNA synthesis was detected, and ribosome proteins and p53 signaling pathway were also detected by western blotting.

Results : STK10 gene mutation is common in acquired PRCA patients, the mRNA/protein expression of STK10 was reduced and p53 increased in the bone marrow of the patients in which the gene mutated. The silence of the STK10 gene through the lentiviral vector harboring short hairpin RNAs in K562 cells could inhibit erythropoiesis after being induced by Hemin. Whereas, megakaryocytic differentiation was not impaired in STK10-silenced K562 cells. KEGG enrichment analysis of RNA sequencing in STK10-silenced K562 cells differentially expressed ribosome biosynthesis pathway and p53 signaling pathway were affected. 28S and 18S in ribosome RNA synthesis impaired in these STK10 silenced K562 cells through RNA electrophoresis. Further, through the western blotting test in STK10-silenced K562 cells, we found ribosome proteins expression down-regulated and p53, phosphor-p53, and p21 expression up-regulated due to STK10 mutated.

Conclusion : STK10 gene mutation is common in patients with acquired PRCA. The underlying research revealed that STK10 gene mutation could affect the ribosome biosynthesis pathway and down-regulated the ribosome protein level, contributing to abnormal erythropoiesis.

Keywords : Pure red cell aplasia, Mutation, Erythropoiesis, STK10, Ribosome biosynthesis

OP08-1

Clinical outcomes of TPO-receptor agonists in patients with steroid-refractory immune thrombocytopenia; Significant conditions of discontinuation with good response

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Background : The treatment strategy for immune thrombocytopenia (ITP) has evolved significantly, with thrombopoietin-receptor agonists (TPO-RA) like Revolade and Romiplate showing remarkable efficacy in steroid-refractory chronic ITP. This study analyzes real-world outcomes and identifies discontinuation conditions for TPO-RA with good platelet response.

Method : We analyzed 91 consecutive patients with steroid-refractory ITP treated with Revolade (n=59) or Romiplate (n=32) first from 2016 to 2021. Among them, 26 were treated with both by switching due to no response (NR), loss of response (LOR), adverse events (AE), or patient refusal. We evaluated autoimmune disease and markers such as ANA titer> 1:320, RA factor, Coombs test, ANCA, platelet, thyroid and antiphopholipid antibodies to define high autoimmune burden. TPO-RA was started at platelet count <20K, and obligatory discontinuation was done every 6 months.

Results : Overall response rate to initial treatment was observed in 77 (84.6%) – 51 out of 59 (86.4%) after Revolade and 29 out of 32 (90.6%) after Romiplate. Totally 14 Revolades (8 NR, 3 LOR, 3 AE) switched to Romiplate, and 12 Romiplates (3 NR, 5 LOR, 4 refusal) switched

to Revolade. After switching, 9 (64.3%) and 11 (91.7%) responded, respectively, so overall response was observed in 85 (93.4%) after TPO-RA. We discontinued TPO-RA in 34 (37.3%) patients with maintaining platelet count >50K at least 6 months to 3 years F/U, and the significant condition for final discontinuation was maximum platelet response >100K (OR 4.46, p=0.005), low autoimmune burden (OR 2.8, p=0.065), and early TPO-RA start <1 year (OR 2.34, p=0.083).

Conclusion : Our real-world data confirmed the efficacy of TPO-RA in steroid-refractory ITP and suggested possibility of discontinuation in good responders with early TPO-RA treatment and low autoimmune disease burden. This emphasizes the potential for personalized treatment strategies in managing ITP.

Keywords : ITP, Thrombocytopenia, TPO-RA, Revolade, Romiplate

	High Autoimmune burden (n=30)	Others (n=61)	P
Response > 30K	24 (80.0%)	53 (86.9%)	0.392
NR+LOR	**14 (46.7%)**	**15 (24.6%)**	**0.034**
No response (NR)	6 (20.0%)	8 (13.1%)	0.392
Loss of response (LOR)	**8 (33.3%)**	**7 (13.2%)**	**0.039**
Final discontinuation	**7 (23.3%)**	**27 (46.6%)**	**0.052**
	PLT Max < 100K (n=25)	**PLT Max > 100K (n=52)**	**P**
Loss of response (LOR)	**8 (32.0%)**	**7 (13.5%)**	**0.054**
Final discontinuation	**6 (24.0%)**	**27 (51.9%)**	**0.020**
	TPO-RA<1 year (n=41)	**TPO-RA>1 year (n=50)**	**P**
Response > 30K	37 (90.2%)	41 (82.0%)	0.499
NR+LOR	12 (29.2%)	17 (34.0%)	0.428
No response (NR)	5 (12.2%)	10 (20.0%)	0.499
Loss of response (LOR)	7 (17.1%)	7 (14.0%)	0.636
Final discontinuation	**20 (48.8%)**	**14 (28.0%)**	**0.032**

OP08-2

Efficacy and safety of avatrombopag in Chinese children with persistent and chronic primary immune thrombocytopenia: A multicenter observational retrospective study in China

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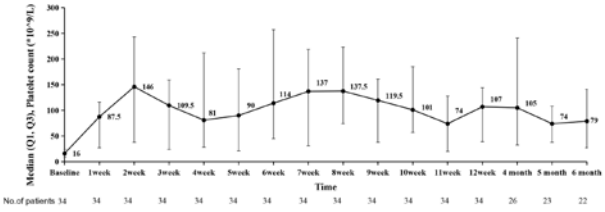
Background : Avatrombopag (AVA), a novel thrombopoietin receptor agonist, is the most recently approved TPO-RA for the treatment of immune thrombocytopenia (ITP) in adults, but there is still a lack of efficacy and safety evidence in children with ITP. Objectives: This study aims to demonstrate the efficacy and safety of AVA in children with ITP.

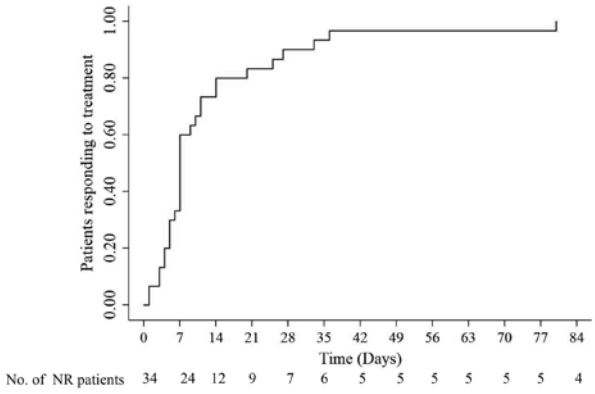
Method : A multicentre, retrospective, observational study was conducted in P/CITP children who had not responded to or had relapsed to previous treatment and switched to AVA for at least 12 weeks.The outcomes were the responses at 4th, 12th and sustained response at 12th, 24th week, the bleeding and the concomitant ITP medications control and safety.

Results : There were 34 (18 males) patients with median age of 6.3 (1.9, 15.3) years were enrolled. At week 4 of AVA, overall response (OR) was achieved in 27/34 (79.4%) and complete response (CR) in 23/34(67.7%) patients with the median response time was 7 (1, 27) days. At 12th week, OR was achieved in 30/34 (88.2%), CR in 26/34 (76.5%) patients, and 15 patients sustained response. At 24th week, 12/22(54.55%) patients who followed up to 24 weeks achieved sustained response. At 12th week, the use of concomitant ITP medications and bleeding decreased, 9 patients need rescue therapy, and 21(61.8%) patients have 59 AEs, 17(29.8%) were CTCAE grade 1 and the rest were grade 2.

Conclusion : Our study showed that AVA could achieved a rapid and sustained response in children with P/CITP as a second-line treatment, with good clinical bleeding control and reduction of concomitant ITP medications, without significant adverse effects, could be the second-line TPO-RAs option for children with ITP.

Keywords : Avatrombopag(AVA), Primary immune thrombocytopenia, Children, PITP, CITP





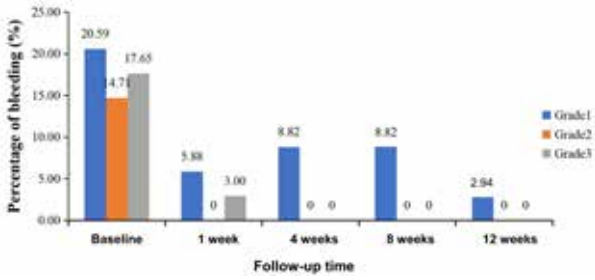


TABLE 1 The characteristics of baselines.

Contents	Number (%) or median (range)
Number of patients (*n*)	34
Male gender, *n* (%)	18 (52.9)
Age at AVA initiation, median (range), years	6.3 (1.9, 15.3)
Weight, median (range), kg	28 (16, 39)
Type of ITP	
PITP, *n* (%)	7 (20.6)
CITP, *n* (%)	27 (79.4)
Pervious treatment with other TPO-RAs	14 (41.2)
Duration of follow-up, median (range), days	149 (84552)
Concomitant ITP medication at baseline	9 (26.47%)
Bleeding (WHO bleeding scale grade 1–3)	18 (52.94%)
Platelet count at baseline, median (range), $\times 10^9$/L	15 (1, 28)
Pervious treatment types before ELT (type)	4 (1, 6)

TABLE 2 Rapid response (within 4 weeks) and sustained response (12th week and 24th week) of AVA.

Efficacy	Number (%) or median (range)
Rapid response	
OR	27 (79.4)
CR	23 (67.7)
R	4 (11.8)
NR	7 (20.6)
Time to response	7 (1, 27)
Proportion of patients required rescue therapy within 4 weeks	
Yes	2 (5.9)
No	32 (94.1)
Proportion of patients who responded at least once within 12 weeks	
OR	30 (88.2)
CR	26 (76.5)
R	4 (11.8)
NR	4 (11.8)
Sustained response at 12th week	15 (44.1)
Time to response within 12 weeks	7 (1, 80)
Proportion of patients required rescue therapy within 4–12 weeks	9 (26.47)
Bleeding (WHO bleeding scale) at 12th week	
Grade 1	1 (2.94)
Grade 2–4	0
Concomitant ITP medication discontinued during AVA treatment within 12 weeks	6 (17.65)
Proportion of patients required rescue therapy within 12 weeks	
Yes	9 (26.47)
No	25 (73.53)
Proportion of patients who achieved sustained response in 22 patients who followed up 24 weeks	12 (54.55)

TABLE 3 Adverse events.

AE	Number (%)
Upper respiratory infection	22 (39.34)
Gastrointestinal symptom	7 (11.47)
Pneumonia	1 (1.64)
Fever	12 (19.67)
COVID-19	6 (9.83)
Headache	4 (6.55)
Elevated WBCs	1 (1.64)
Elevated alkaline phosphatase	1 (1.63)
Hives	2 (3.27)
Alopecia	1 (1.69)
Nose bleeding	2 (3.27)

OP08-3

Effect of anagrelide on health-related quality of life in patients with treatment-naïve, high-risk essential thrombocythemia

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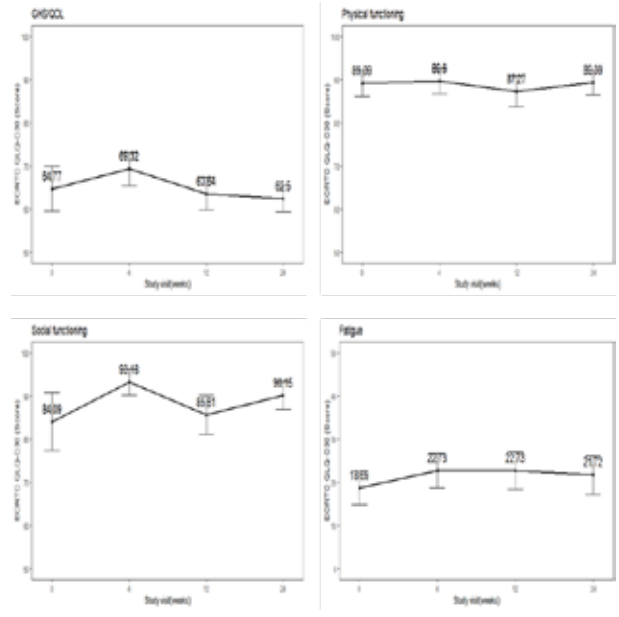
Background : Anagrelide has proved the efficacy and safety as first-line treatment in treatment-naïve, high-risk essential thrombocythemia (ET) patients. However, concern about frequent adverse events remains. The effect of anagrelide on patient-reported outcomes (PROs) is presented here with the health-related quality of life (HRQOL) analyses from NCT03232177 trial. In addition, we further investigated the association between the adverse events of anagrelide and the single nucleotide polymorphisms (SNPs) of cytochrome P450 1A2 (CYP1A2) gene, encoding anagrelide metabolizing enzyme.

Method : The NCT03232177 trial [PMID: 36505839] was a multi-center, prospective observation study to examine the efficacy and safety of first-line anagrelide treatment in high-risk Korean ET patients. HRQOL was evaluated at baseline and week 4, 12 and 24, using the European Organisation for Research and Treatment of Care (EORTC) Quality of Life Questionnaire-Core 30 (QLQ-C30). The data were analyzed descriptively. Genotyping of SNPs of the CYP1A2 gene was performed using TaqMan assay and direct sequencing. We evaluated the association of SNP genotypes and adverse event to find possible predictive biomarkers of anagrelide for the occurrence of adverse events.

Results : The completion rate for all HRQOL questionnaires was 31.4% (22/70). The mean HRQOL scores showed no significant differences or clinical deteriorations in entire domains over time. For global health status (GHS)/QOL domain, mean scores at baseline and week 24 were 64.77 and 62.5, which showed no significant differences. Among CYP1A2 gene SNPs, rs762551 (-164 A>C) homozygous mutant genotype (CC) showed a trend toward differences in adverse events (p=0.09, OR 6.60). However, no other SNPs showed statistically significant association with the adverse events of anagrelide.

Conclusion : Anagrelide is a good treatment option as first-line regimen for high-risk Korean patients with ET, without significant deterioration of HRQOL indices. A SNP of CYP1A2 gene could be a potential predictor for the occurrence of adverse events in patients who are treated with anagrelide.

Keywords : Essential thrombocythemia, Anagrelide, Quality of Life, CYP1A2, SNP marker



OP08-4

Impact of hematopoietic stem cell transplantation on bone metabolism and growth in pediatric patients with thalassemia major

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Background : Children with thalassemia major (TM) face growth delays from chronic anemia and iron overload due to transfusions. Hematopoietic stem cell transplantation (HSCT) offers a potential cure, but its effect on bone metabolism and growth remains poorly understood.

Method : A total of 159 TM patients received HSCT in 2019. Despite recommendations for post-HSCT growth and bone health monitoring, only 22 patients consistently followed up, having bone metabolism and growth metrics assessed over two years and their clinical data were retrospectively analyzed.

Results : The cohort comprised 11 girls and 11 boys with a median age of 7 ± 3 years at HSCT. Most patients (n=20) underwent haploidentical HSCT, while two received transplants from an HLA-matched sibling and an unrelated donor, respectively. Serum 25(OH) D3 levels significantly increased post-HSCT, from 22.16 ± 6.38 ng/ml pre-HSCT to 26.89 ± 10.20 ng/ml at 1-year and 29.54 ± 9.17 ng/ml at 2-year (*p=0.02, one-way ANOVA). Conversely, alkaline phosphatase levels significantly decreased over time (p=0.01, from 106.7 ± 78.47 IU/ml to 71.43 ± 50.56 IU/ml and 65.97 ± 30.83 IU/ml, one-way ANOVA). Serum ferritin also decreased significantly (*p=0.01, from 3497 ± 1686 ng/ml to 3211 ± 2060 ng/ml and 1942 ± 1543 ng/ml, one-way ANOVA). The number of patients with severe growth impairment (less than 2 standard deviations of normal children) increased from 6 to 9 at 2 years post-HSCT. Growth impairment was significantly associated with post-HSCT steroid use (*p=0.01, Chi-square test).

Conclusion : HSCT may improve bone health by decreasing iron overload and optimizing the Vitamin-D absorption. However, HSCT may not improve overall growth impairments of TM patients, probably due to the use of steroids. These findings underscore the necessity of diligent monitoring and management of bone health and growth in TM patients post-HSCT, with particular attention to the implications of steroid therapy on growth outcomes.

Keywords : Hematopoietic stem cell transplantation, Thalassemia major, Bone metabolism, Growth , Pediatrics

OP08-5

Effects of tertiary palliative care on the pattern of end-of-life care in patients with hematologic malignancies

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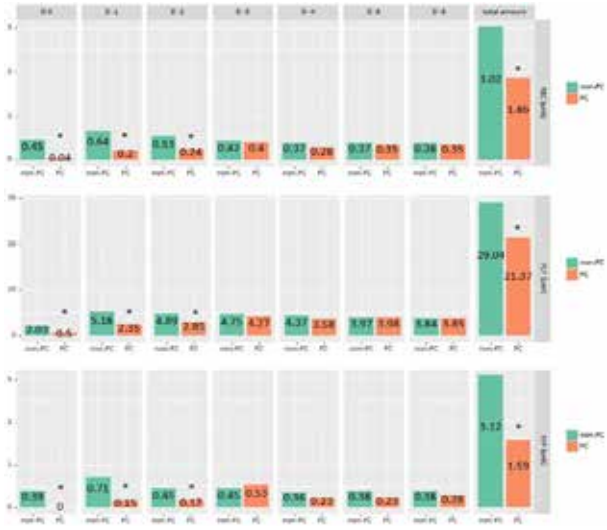
Background : Patients with hematologic malignancies (HMs) often face challenges in accessing palliative care (PC) and receiving quality end-of-life (EOL) care. This study aimed to examine the status of EOL care and the effects of tertiary PC on EOL care in patients with HMs.

Method : We included patients with HMs who were admitted to a university-affiliated hospital and died during hospitalization between January 2018 and December 2021. We investigated the receipt of PC consultations, patient characteristics, and quality of the EOL care indicators including documentation on advance care planning and EOL healthcare utilization.

Results : A total of 487 patients were included in the analysis, with 156 (32%) undergoing PC consultation. A higher proportion of patients who received PC completed advance statements (34% vs. 18.4%, $P < 0.001$) and life-sustaining treatment documents (96.8% vs. 86.7%, $P = 0.001$). Patients who received PC was significantly less frequently admitted to the ICU (25% vs. 56.8%, $P < 0.001$) and received less CPR (3.8% vs. 22.4%, $P < 0.001$), mechanical ventilation (18.6% vs. 53.2%, $P < 0.001$), and renal replacement therapy (14.7% vs. 39.6%, $P < 0.001$). Moreover, 10.9% of the PC group died in the ICU compared with 50.8% of the non-PC group ($P < 0.001$). The PC group had lower blood transfusion rates during the last 3 days of life than the non-PC group (red blood cell, 30.8% vs. 56.2%, $P < 0.001$; platelet, 51.3% vs. 68.9%, $P < 0.001$; fresh frozen plasma, 9% vs. 28.7%, $P < 0.001$). Moreover, the PC group had lower daily transfusion amounts than the non-PC group during the last 3 days of life.

Conclusion : Tertiary PC aims to reduce aggressive EOL care through patient-centered goal-of-care discussions. Therefore, there is an imperative need for concerted efforts toward the seamless integration of PC.

Keywords : Hematologic malignancy, End-of-life care, Palliative care, Consultation



	Non-PC group N = 331	PC group N = 156	All N = 487	P-value
Advance statement, n (%)	61 (18.4)	53 (34.0)	114 (23.4)	< 0.001
Time between advance statement and death, median, days (IQR)	10 (1-37)	9 (3-23)	9 (2-30)	0.798
LST implementation documentation, n (%)	287 (86.7)	151 (96.8)	438 (89.9)	0.001
Patient-determined	57 (19.9)	52 (34.4)	109 (24.9)	0.001
Family-determined	230 (80.1)	99 (65.6)	329 (75.1)	
Time between LST implementation documentation and death, median, days (IQR)	1 (0-3)	4 (2-9)	1 (0-5)	< 0.001
Aggressive care within last 30 days, n (%)				
ED visit	145 (43.8)	64 (41.0)	209 (42.9)	0.631
ICU care	188 (56.8)	39 (25.0)	227 (46.6)	< 0.001
CPR	74 (22.4)	6 (3.8)	80 (16.4)	< 0.001
Mechanical ventilator	176 (53.2)	29 (18.6)	205 (42.1)	< 0.001
Hemodialysis	131 (39.6)	23 (14.7)	154 (31.6)	< 0.001
Chemotherapy, n (%)				
Within last 30 days	179 (54.1)	85 (54.5)	264 (54.2)	1.000
Within last 14 days	117 (35.3)	49 (31.4)	166 (34.1)	0.452
Within last 7 days	73 (22.1)	22 (14.1)	95 (19.5)	0.052
Within last 3 days	42 (12.7)	10 (6.4)	52 (10.7)	0.053
Active procedures at imminently dying state (within 3 days before death), n (%)				
Blood test	327 (98.8)	127 (81.4)	454 (93.2)	< 0.001
Imaging study	306 (92.4)	98 (62.8)	404 (83.0)	< 0.001
Levin tube insertion	230 (69.5)	53 (34.0)	283 (58.1)	< 0.001
Intravenous antibiotics	311 (94.0)	139 (89.1)	450 (92.4)	0.088
High-flow nasal cannula	103 (31.1)	40 (25.6)	143 (29.4)	0.258
Blood transfusion				
Within last 7 days, n (%)				
RBC	265 (80.1)	114 (73.1)	379 (77.8)	0.107
PLT	273 (82.5)	124 (79.5)	397 (81.5)	0.504
FFP	119 (36.0)	30 (19.2)	149 (30.6)	< 0.001
Within last 3 days, n (%)				
RBC	186 (56.2)	48 (30.8)	234 (48.0)	< 0.001
PLT	228 (68.9)	80 (51.3)	308 (63.2)	< 0.001
FFP	95 (28.7)	14 (9.0)	109 (22.4)	< 0.001
Comfort care within last 3 days of life, n (%)				
Opioid administration	221 (66.8)	130 (83.3)	351 (72.1)	< 0.001
Antipsychotics administration	96 (29.0)	41 (26.3)	137 (28.1)	0.606
Place of death, n (%)				< 0.001
ICU	168 (50.8)	17 (10.9)	185 (38.0)	
General ward	163 (49.2)	139 (89.1)	302 (62.0)	

PC, palliative care; IQR, interquartile range; LST, life-sustaining treatment; ED, emergency department; ICU, intensive care unit; CPR, cardiopulmonary resuscitation; RBC, red blood cell; PLT, platelet; FFP, fresh frozen plasma.

OP08-6

The clinical manifestation, prognostic factors, and outcomes of adenovirus pneumonia after allogeneic hematopoietic stem cell transplantation

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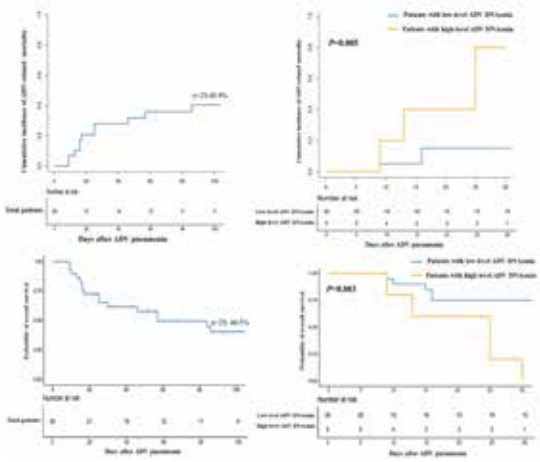
Background : Adenovirus (ADV) infection is one of the important opportunistic viral infections after allo-HSCT. ADV pneumonia is one of the most severe types of ADV infection in HSCT recipients with high mortality. We aimed to identify the clinical manifestation, prognostic factors, and outcomes of ADV pneumonia after allo-HSCT.

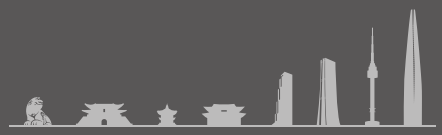
Method : Twenty-nine patients who underwent allo-HSCT at the Peking University Institute of Hematology and met the criterion of ADV pneumonia after allo-HSCT were retrospectively enrolled. ADV was detected with real-time quantitative polymerase chain reaction. This work was supported by the National Key Research and Development Program of China (2022YFC2502606), Peking University People's Hospital Research and Development Funds (RZ2022-02), Natural Science Foundation of Beijing (Z230016) and Tongzhou District Distinguished Young Scholars (JCQN2023009).

Results : The median time from allo-HSCT to the occurrence of ADV pneumonia was 99 days (range 17-609 days). The most common clinical manifestations were fever (86.2%), cough (34.5%) and dyspnea (31.0%). The 100-day cumulative incidence of ADV-related mortality was 40.4% (95%CI 21.1%-59.7%) and the probability of OS at 100 days after ADV pneumonia was 40.5% (95% CI 25.2%-64.9%). The 30-day cumulative incidence of ADV-related mortality for the patients with low-level (<10^6 copies/ml in plasma) and high-level (≥ 10^6 copies/ml in plasma) ADV DNAemia was 15.0% (95% CI 0-31.1%) versus 80.0% (95% CI 37.5%-100%) (P=0.005), respectively. In multivariate analysis, high-level ADV PCR positivity in plasma (HR 6.394, 95% CI 1.426-28.666, P=0.015) was the only risk factor associated with ADV-related mortality and OS at 100 days after ADV pneumonia (HR 5.447, 95% CI 1.549-19.157, P=0.008).

Conclusion : We firstly reported the clinical manifestations, prognostic factors, and outcomes of ADV pneumonia after allo-HSCT and we further confirmed that this is a life-threatening post-transplant complication.

Keywords : Adenovirus pneumonia, Posttransplantation, Allogeneic hematopoietic stem cell transplantation





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POSTERS

PP01-1

Genetic and epigenetic alteration of Wilms' tumor 1 (WT1) gene in acute myeloid leukemia

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Background : Acute myeloid leukemia is a genetically complex hematologic malignancy characterized by abnormal differentiation and clonal proliferation of myeloid progenitor cells in the bone marrow with diverse genetic and epigenetic alterations. Wilms tumor 1 (WT-1) gene is a critical regulator of malignant hematopoiesis, which encodes a zinc-finger transcription factor that can either activate or repress genes to regulate cell growth, apoptosis, and differentiation.

Method : In the present study, we aim to investigate the RNA expression, methylation levels, and molecular functions of the WT-1 gene in 112 AML cases (112 at diagnosis [day 0] and 105 after completion of induction chemotherapy [day 28] and 20 non-malignant samples were recruited as controls. WT-1 gene expression and promoter methylation status were assessed during both intervals (day-0 & day-28) by performing RT-PCR.

Results : Of the 112 subjects studied, 73 were male (65.17%) and 39 were females (34.83%), out of these 97 (86.60%) cases showed overexpression of WT-1 gene at the time of diagnosis as compared with cases in complete remission (CR) remission or control samples (p= <0.001). Moreover, Robust hypermethylation of WT1 promoter was observed in 77 (68.75%) AML cases at the time of diagnosis as compared with patients in complete remission (CR) remission or control samples (p= <0.001). In all AML patients, WT-1 expression and methylation levels were inversely correlated with normal hematopoiesis and positively associated with age, high marrow blast counts, M4 subtype, adverse risk cytogenetic, and inferior outcome compared to patients with low WT-1 methylation and expression levels.

Conclusion : Overexpression and Hypermethylation of the WT-1 gene positively associates with the leukemic burden in most cases of AML. Thus, this gene can be considered a promising molecular marker for early diagnosis, and MRD detection, and a target for developing novel therapeutic approaches against AML.

Keywords : AML, WT1

PP01-2

A prospective study to evaluate the prognostic implications and molecular mechanism of *SLC40A1* gene in primary acute myeloid leukemia

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Background : Iron metabolism is altered in a variety of cancers; however, little is understood about the biology of iron metabolism and how it responds to AML. Ferroportin, encoded by the gene SLC40A1, is the only protein responsible for cellular iron export. However, the expression, molecular mechanism of SLC40A1 gene, and their molecular interaction remain unknown in AML.

Method : In this study, we aimed to characterize the molecular functions, clinical and prognostic value of SLC40A1 gene in AML. We investigated the expression level and DNA methylation status of SLC40A1 gene in AML (n=173) and control (n=70) cases using RT-PCR. Then, we did correlation analysis to find the potentially associated gene linked with the SLC40A1 gene based on their expression levels using Linked Omics database. Moreover, we also explored the molecular mechanisms of SLC40A1 in AML by performing gene set enrichment analysis (GSEA) analysis.

Results : Higher expression and lower methylation level of SLC40A1 gene was observed in AML (n=173) cohorts as compared with normal cases (n=70) and closely associated with poor overall survival (P <0.05). In correlation analysis SLC40A1 gene was positively correlated with the DNAJC6 gene, followed by PLS1, and CAPRIN2 genes while negatively correlated with MSLN, MYH11,and PLCD3 (P <0.001). Gene enrichment analysis revealed SLC40A1 gene was enriched in various biological process including endothelium development, spleen development, cell differentiation, while in molecular function SLC40A1 gene was enriched in transmembrane transporter activity, protein binding, and catalytic activity. Moreover

in KEGG pathway enrichment SLC40A1 gene was enriched in hematopoietic stem cell differentiation, ferroptosis, and signaling pathways regulating pluripotency of stem cells. In Spite of this we also found SLC40A1 gene and their positively correlated with different immune checkpoints including CD160, CD274, CD40,and CD44.

Conclusion : SLC40A1 may serve as a potential prognostic biomarker and therapeutic target for the effective management of AML.

Keywords : AML, SLC40A1

PP01-3

Using red ginger to prevent acute myeloid leukemia : A literature review

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Background : Acute myeloid leukemia (AML) is a serious disease of abnormal myeloid cells that form in large numbers in the bone marrow. This type of leukemia has a worldwide incidence of 4.2 per 100.000 population. Red ginger is an herb that is commonly found in Asia, especially in Indonesia and Malaysia. It has many good effects on the body. Nevertheless, red ginger is still not widely used as medicine compared to white ginger which is commonly found in traditional medicine. This article aims to look over the effect of red ginger on AML.

Method : A literature review was using Pubmed to search the data. The term used are red ginger and prevention of AML. The terms were found in four articles in the last ten years that related to literature. This literature review covers animal experiments and in vitro studies through the published article.

Results : Red ginger is an herb that contains substances that are used in prevention of leukemia, supported by the research. Red ginger (zingiber officinale var. rubrum) contains quercetin, 6-gingerol and 6-shogaol. In vitro study of P39 cells obtained from leukemia patients concluded that quercetin was able to stop the cancer cell cycle at the G1 phase, preventing cancer cells from growing abnormal myeloid cells in HL- 60 cells in cancer patients. In vitro studies showed that 6-shogaol induces apoptosis by inhibiting BCL-2. The component of red ginger act as antioxidants by donating electron to free radical for protect the normal cell conduced in the experimental studies.

Conclusion : Red ginger, a natural herbal most found in Asia, contains vanilloid and flavonoid that have an important effect to be antitumor activity and antioxidant activity in white blood cells malignant.

Keywords : Red ginger, Antitumor activity, Acute myeloid leukemia, Antioxidant

PP01-4

Epigenetic modulation enhances the therapeutic potential of all-trans retinoic acid in acute myeloid leukemia

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Background : Epigenetic dysregulation has been strongly associated with the development and progression of AML. While ATRA has demonstrated significant effects in APL-AML) treatment, its clinical efficacy in non-APL AMLs has been limited. This limited response can be attributed to the epigenetic silencing of genes targeted by or involved in the ATRA pathway, rendering them unresponsive to the drug. Consequently, our research aims to overcome the epigenetic barriers in AML by combining ATRA with small molecules that possess epigenetic modulating properties.

Method : HEK-293 cells were transduced with p-GreenFire- RARE-Tk-Luc construct to examine the activation of the RA-pathway in response to ATRA and 650 epigenetic compounds. The effect of selected compounds on cell viability, differentiation, and ERK1/2, AKT1, MAPK9, p38, and MAPK9 phosphorylation was evaluated in HL-60, NB4, KG1a, BMNC, and primary AML cells. RNAseq and CUT&Tag were performed on ex vivo AML samples following exposition to selected compounds.

Results : We have identified 11 promising compounds. When combined with ATRA a dual PI3K-HDAC inhibitor, and a pan-PKC inhibitor, demonstrated 4-5 fold increase in RARE activity, indicating a synergistic effect. Selected compunds were noncytotoxic to HL60, BMNC, and primary MSC. Dual PI3K-HDAC inhibitor with ATRA reduced the viability of KG1α by more than 95%. Moreover, dual PI3K-HDAC in-

hibitor and a pan-PKC inhibitor, with ATRA, lead to a 2-4 fold increase in the differentiation of HL60 cells and AML cells (M1, M2, and M4) compared to ATRA with the LSD1 inhibitor TCP and untreated cells. PI3K-HDAC inhibitor combined with ATRA significantly reduced p-MAPK and p-p38 levels while increasing the phosphorylation of p53 in HL-60 cells.

Conclusion : The combination of ATRA with specific dual PI3K-HDAC and pan-PKC inhibitors holds promise as a potential therapeutic approach for AML. Nevertheless, further investigations, including studies utilizing patient-derived xenograft models, are warranted to validate the efficacy and feasibility of this proposed treatment strategy.

Keywords : AML, Epigenetics, ATRA, RARE

PP01-5

Loss of *TET* function results in myeloid malignancy associated with a heterochromatin-to-euchromatin transition

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Background : The three mammalian TET proteins act as 5-methylcytosine oxidases and are pivotal for DNA demethylation. Loss of TET function is prevalent across a wide range of cancers. However, how TET loss contributes to oncogenesis remains unclear.

Method : To define the consequences of complete TET deficiency in vivo, we induced deletion of all three Tet genes in the mouse genome. Employing various cellular and molecular techniques, including next-generation sequencings, we analyzed hematopoiesis from hematopoietic stem/progenitor cells and hematological neoplasia and aimed to define the underlying mechanism.

Results : The Tet1/2/3 triple knockout mice developed lethal acute myeloid leukemia by 4-5 weeks. Single-cell RNA sequencing demonstrated the appearance of novel myeloid cell populations displaying an elevated expression of all members of the stefin/cystatin gene cluster on mouse chromosome 16. In patients with AML, high stefin/cystatin gene expression correlated with unfavorable clinical outcomes. Notably, increased expression of the clustered stefin/cystatin genes was associated with a compartment switch of heterochromatin to euchromatin with a readthrough transcription downstream of the clustered stefin/cystatin genes and other highly expressed genes, with minor alterations in DNA methylation.

Conclusion : Our findings underscore the demethylation-independent roles of TET enzymes in suppressing oncogenesis by modulating transcriptional elongation and three-dimensional genome organization.

Keywords : TET proteins, Myeloid malignancy, Readthrough transcription, Heterochromatin-to-euchromatin transition, Stefins

PP01-6

High expression of CXC-chemokine ligand 5 in bone marrow serum predicts favorable outcomes in children with acute myeloid leukemia

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Background : Cytokines in the bone marrow microenvironment play a key role in regulating the proliferation and activation of acute myeloid leukemia cells, and researches have shown that cytokine expression levels are strongly associated with AML patients' survival and prognosis. CXC-chemokine ligand 5(CXCL5), a major chemokine in the micro-environment, has subsequently been demonstrated to have significant predictive value in patients with various types of cancer in an increasing number of studies. However, the impact of BM serum CXCL5 on survival of pediatric AML patients is unknown.

Method : We used targeted proteomic techniques to identify the relative expressions of 180 cytokines in the bone marrow plasma of

newly diagnosed AML patients and age-matched healthy donors in this research. In AML patients, correlation analysis was performed on clinical features, prognosis, and BM serum CXCL5 expression.

Results : The relative expression of CXCL5 in bone marrow serum was found to be an independent predictor for OS, EFS, and RFS in children with AML using multivariate regression analysis. CXCL5 levels in bone marrow serum were considerably lower in newly diagnosed AML than in healthy controls. Pediatric AML patients with high BM serum CXCL5 expression had a substantially better prognosis than those with low expression. CXCL5 expression levels in bone marrow serum can assist with the NCCN risk classification[1] . The time-dependent ROC curve and calibration curve demonstrated that the nomogram model based on expressions of cytokines like CXCL5 had a powerful predictive value for 2-year EFS in AML patients. We also constructed a risk-score model based on cytokines' expression characteristics, which have an elevated prognostic and predictive value for survival of pediatric AML patients.

Conclusion : Overall, our findings suggest that CXCL5 in bone marrow serum capabilities as an independent predictor of pediatric AML. Children with AML who have higher CXCL5 expression in their bone marrow serum have a favorable prognosis.

Keywords : CXCL5, Pediatric, Acute myeloid leukemia, Prognosis, Prediction model

PP01-7

Gemtuzumab ozogamicin with half-dose cag regimens as re-induction therapy for pediatric refractory/relapsed AML

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Background : Hematopoietic stem cell transplantation (HSCT) is an effective approach for treating refractory/relapsed acute myeloid leukemia (AML). Reducing tumor burden prior to transplantation has been shown to effectively decrease post-transplant relapse. We have used conventional chemotherapy in several courses for three pediatric patients with refractory/relapsed acute myeloid leukemia (AML) but have not achieved remission. We then adopted a new chemotherapy regimen and secured the opportunity of hematopoietic stem cell transplantation for three children.

Method : The combination of gemtuzumab ozogamicin with half-dose CAG was administered to reduce tumor burden. Subsequently, a sequential regimen of cladribine and cytarabine (Ara-C) was used as a bridge to total body irradiation (TBI), followed by cyclophosphamide for myeloablative conditioning (MAC), and finally, allogeneic hematopoietic stem cell transplantation (allo-HSCT) was performed.

Results : Among the three pediatric patients with refractory/relapsed AML, one achieved complete remission (CR), although the other 2 cases did not achieve CR, but the tumor load was significantly reduced. Of the two cases that did not get CR, one was given GO only once because of the high cost of treatment. In the other case, the CD33 expression was less than 50%. All three patients received hematopoietic stem cell transplantation and achieved long-term disease-free survival.

Conclusion : GO combined with various chemotherapy agents is an alternative to classic chemotherapy drugs for pediatric refractory/relapsed AML to improve the remission rate and reduce tumor burden in resistant AML patients, thereby providing a conducive setting for HSCT.

Keywords : Hematopoietic stem cell transplantation, Pediatric, Gemtuzumab ozogamicin, CAG regimens, Acute myeloid leukemia

PP01-8

Fabrication of revesterol hybrid lecithin folic acid silver nanoparticles and its evaluation as anti-leukemia effect against benzene induced acute myeloid leukemia in rats

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Background : Acute myeloid leukemia (AML) is a type of cancer that affects the bone marrow and blood. It is characterized by the rapid growth and accumulation of abnormal white blood cells, called myeloblasts, in the bone marrow. These abnormal cells interfere with the production of normal blood cells, including red blood cells, white blood cells, and platelets. Revesterol (flavonoids) mostly used in the

various herbal formulation used in the treatment of hemorrhage or blood purifier. The aim of the study, to fabricated the nanoparticle of revesterol and evaluated against the benzene induced acute myeloid leukemia in the rats.

Method : In this study, we fabricated the Revesterol hybrid lecithin folic acid silver nanoparticles (L-RT-FA-AgNPs). Long term administration of benzene was used for the induction of acute myeloid leukemia in the mice and mice were divided into different groups and orally treated with the revesterol and L-RT-FA-AgNPs. The Antioxidant, hematological, cytokines, apoptotic and inflammatory parameters were estimated.

Results : L-RT-FA-AgNPs remarkably suppressed the weight of liver and spleen tissue. L-RT-FA-AgNPs significantly altered the hematological parameters such as WBC (54.8%), RBC (63.2%), lymphocytes (43.2%), eosinophils (41.3%), neutrophils (42.5%), monocytes (38.6%), monocytes (38.9%) and basophils (40.6%), respectively. L-RT-FA-AgNPs boosted the level of GSH (35.6%), SOD (56.9%), CAT (38.3%), GPx (26.9) and suppressed level of MDA (45.8%) level. L-RT-FA-AgNPs remarkably suppressed the level of cytokines and inflammatory parameters. L-RT-FA-AgNPs exhibited the antiapotosis effect via reversing the level of apoptotic parameters like caspase-3, 9, Bcl-2 and BAX. L-RT-FA-AgNPs also restored the level of T cells and various subtypes like CD80+ and CD86+.

Conclusion : The results suggest that the L-RT-FA-AgNPs exhibited the protective effect against the benzene induced leukemia via alteration of immune modulation, antioxidative stress, inflammatory and antiapoptosis mechanism.

Keywords : Acute myeloid leukemia, Benzene, Leukemia, Apoptosis, Inflammation

PP01-9

Cyp2b6 polymorphism and leukaemia susceptibility in Asian populations: A systematic review and meta-analysis

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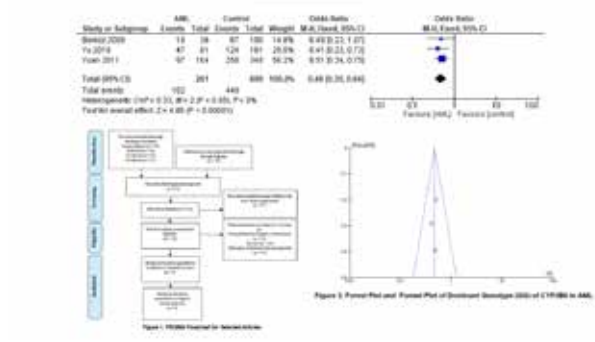
Background : Acute leukemia is a life-threatening blood cancer, that has a complex etiology that involves genetic factors. The CYP2B6 gene polymorphism has garnered interest as a potential contributor to leukemia susceptibility. This study focuses on Asian populations where genetic diversity is high. The research aims to provide insights into the genetic aspects of leukemia in Asians, potentially guiding future studies and personalized treatment approaches for this population.

Method : A systematic search of databases was carried out in PubMed, ScienceDirect, Cochrane, and ProQuest until the end of October 2023, using specific keywords ("polymorphism" OR "polymorphisms" OR "variant" OR "mutation" OR "genotype" OR "allele" OR "SNP") AND ("Cytochrome P-450 CYP2B6" OR "Cytochrome P450 CYP2B6" OR "P-450 CYP2B6, Cytochrome" OR "CYPIIB6" OR "Cytochrome P450 2B6" OR "P450 2B6, Cytochrome") AND ("leukemia" OR "Leukaemias"), and studies in English or Indonesian were included. The Newcastle-Ottawa scale assessed study quality and statistical analysis involved calculating Odd Ratio (OR) and 95% Confidence Intervals (CIs) using Review Manager software.

Results : A total of 4 studies, including 281 AML patients, 185 ALL patients, 153 CML patients, and 709 control subjects. There was a significant association between the CYP2B6 variant and an increased risk of AML and ALL under the dominant model (GG), with very low heterogeneity (I^2=0%); OR=0.48; 95% CI: 0.35–0.64; P<0.00001 and OR=0.41; 95% CI: 0.29–0.58; P<0.00001, there was insignificant association between the dominant and heterogeneity allele of CYP2B6 in CML (OR=0.74; 95% CI: 0.44–1.22; P=0.24 and OR=0.72; 95% CI: 0.43–1.21; P=0.22).

Conclusion : The CYP2B6 gene polymorphism plays a crucial role in the development of acute leukemia, potentially affecting susceptibility and prognosis. Further research with larger and more diverse study populations is needed to confirm these findings and explore the role of other genes in leukemia etiology.

Keywords : CYP2B6 gene polymorphism, Gene variant, Leukaemia



PP01-10

Treatment behavior and outcomes of acute myeloid leukemia in the COVID-19 era

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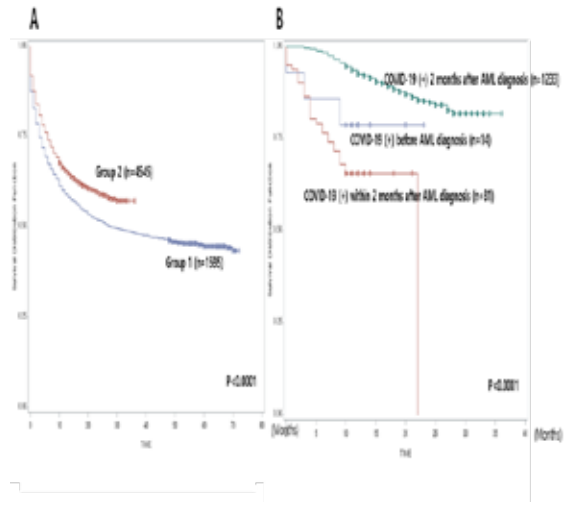
Background : Cancer patients, including those with AML, are vulnerable to respiratory viral infections, including COVID-19. However, during the COVID-19 pandemic, accessing medical care was a huge challenge in South Korea. On the other hand, the emphasis on personal hygiene might have had positive effect on immune compromised AML patients. Therefore, we aim to examine how COVID-19 affected treatment behaviors or prognosis of AML patients using the database of the National Health Insurance Service (NHIS) in South Korea

Method : We identified 1595 newly diagnosed with adult AML between 01Jan2017 to 31Dec2018 (Group 1; pre COVID-19 era), and 4545 between 01Mar2020 to 28Feb2022 (Group 2; COVID-19 era). Medication history, COVID-19 infection and death date were extracted.

Results : Clinical characteristics were described in table 1. Age, sex, and patient ratio who were treated with hypomethylating agent(HMA) were not different between two groups. However, the less patients received induction chemotherapy and more underwent allogeneic HSCT in group 2 compared to group 1. Among patients who received induction cytotoxic chemotherapy, 51% continued to consolidation therapy in group 2, but only 33.4% did in group 1 (p<0.001). The median time from diagnosis to induction (0 vs 0 days) and induction to 1st consolidation (52 and 53 days), or median consolidation cycle (both 2 cycles) were not different between two groups. Hypomethylating agent was given in 10.2% of all AML patients. The median treated HMA cycles and the median days between HMA cycle was not different group 1and 2. In COVID-19 pandemic era, 28.8% infected COVID-19, and they were youger (56 years) than patients who did not infected(63 years). The better survival outcome was observed in group 2 than group 1(Figure 1A). COVID-19 pandemic era, the timing of COVID-19 infection differentiated OS(Figure1 B).

Conclusion : COVID-19 pandemic did not seemed to affect treatment behavior or outcomes of AML in South Korea.

Keywords : Acute myeloid leukemia, COVID-19



	Group 1 (Pre COVID-19 era) n=1595	Group 2 (COVID-19 Pandemic era) n=4545	P
Age at diagnosis, median years (Range)	61 (19-95)	61 (19-100)	0.215
Sex M/F, n(%)	901 (56.5)/694 (43.5)	2515(55.3)/2030(44.7)	0.425
No treatment, n(%)	921 (57.7)	2948 (64.9)	<0.001
Induction chemotherapy, n(%)	520(32.6)	1137(25.0)	<0.001
Hypomethylating agent, n(%)	156 (9.8)	471 (10.4)	0.508
Allogeneic HSCT n(%)	222 (13.9)	772 (17.0)	0.004
COVID-19 infection n(%)	309 (19.3)	1311 (28.8)	<0.001
Mean frequency of hospitalization due to any infection (Range)	2.28 (1-37)	1.9 (1-14)	0.014
COVID 19 infection n(%)	307 (19.3)	1311 (28.8)	<0.001
Death, n(%)	891 (55.8)	1941 (42.7)	<0.001

PP01-11

Exploring neo-antigen and immunogenicity of acute myeloid leukemia (AML) using neo-arstm artificial intelligence tool

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Background : Neoantigen is formed through the production of proteins altered by non-synonymous mutations and are specific to cancer cells. This characteristic makes them applicable for specific therapeutic interventions targeting cancer cells through the immune system. However, research and understanding to reach such therapeutic approaches in Acute Myeloid Leukemia (AML) are still lacking.

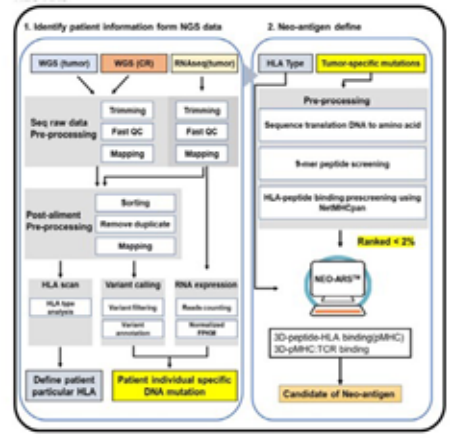
Method : Leukemic blast DNA from bone marrow mononuclear cells (BMMC) at diagnosis was compared with Germline DNA from BMMC at time of complete remission (CR) using whole exome sequencing (WES) for the identification of patient-specific tumor mutations and MHC alleles. In addition, RNA sequencing (RNAseq) was performed to determine the level of expression of the genes with leukemic-specific mutations. Of all possible neopeptides-MHC class I (pMHC) combinations, neoantigen candidates were identified using a physics-informed deep learning algorithm NEO-ARS™. For the peptides assumed to be neoantigen, IFN-γ ELIspot experiments were performed using peripheral blood mononuclear cells from human leukocyte antigen (HLA)-matched donor of allogeneic hematopoietic stem cell transplantation. Peptides confirmed as immunogenic were subjected to in silico three-dimensional image simulations to model their binding to T-cell receptors (TCR)

Results : With this approach, we prioritized a list of 6 neoantigen peptide-HLA candidates from 2 AML patients each (peptide lengths of 9 amino acids) across the available HLA class I alleles for that patient. IFN-γ ELISpot assay, the first patient (HLA-A*02:01), peptide #1(2068.3), #2(2163.3), #4(2006.6) and #6(1886.6) had higher spot forming units (SFU) than DMSO (1393.3) alone (P<0.0001). In the second patient (HLA-A*11:01), peptide #3(1165, P<0.01), #4(1043.3, P<0.05) and #5(1813.3, P<0.001) had higher spot forming units than DMSO (653.3) alone. The 3D modeling of the binding motif of peptide #6 in the second patient revealed reduced TCR-facing solvent-accessible surface areas in the sequence of the neopeptide.

Conclusion : The neoantigens predicted by NEO-ARSTM showed a good immunogenicity against T cells in ELIspot assay. Thus, Neo-ARSTM have the potential to be used efficiently in novel therapies such as customized cancer immune therapy for the patients with AML in the future.

Keywords : Neoantigne, Aml, Peptide binding

Figure 1. Neo-antigen prediction using Neo-ARS



PP01-12

A paired sillico analysis of ALOX5AP gene expression/methylation and its prognostic impact among acute myeloid leukemia

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Background : Acute myeloid leukemia (AML) is malignant proliferation of myeloid blast in bone marrow. The enzyme Arachidonate 5-Lipoxygenase-activating protein (ALOX5AP) has been recognized as an oncogene that has been linked to carcinogenesis including chemotaxis promotion and leukocyte activation. In this work, "In-sillico analysis" of clinical and prognostic impact of the ALOX5AP gene in patients with AML was conducted by determining its expression, methylation patterns, and molecular mechanism.

Method : In this study, we examined the ALOX5AP gene's expression and DNA methylation state in 173 AML patients and 70 control cases from data downloaded from TGCA. The correlations between ALOX-5AP gene expression was anlysed in single-cell datasets(GSE). The ALOX5AP was further analysed through Linked Omics database to

find its association with DEGs. Finally, we investigated the molecular mechanisms of ALOX5AP in AML using gene set enrichment analysis (GSEA).

Results : The ALOX5AP was significantly overexpressed but methylation level was low in AML (n=173) compared to control (n=70) ($p < 0.05$). However,gene expression was negatively correlated with methylation status ($p < 0.0342$) and was associated with poor overall survival (OS) ($p < .0024$). ALOX5AP expression was shown to be significantly greater in M5 subtypes, females, older AML cases, and AML patients with FLT3-ITD mutations. AML single-cell datasets proved that ALOX5AP expression was associated with metastasis, differentiation, proliferation, inflammation, and angiogenesis. In correlation analysis ALOX5AP gene was positively correlated with the NCF1 gene, followed by SIRPB1, IL1RN genes while negatively correlated with UBFD1, KDM5B, ($p < 0.001$). Gene enrichment analysis revealed ALOX5AP was enriched in granulocyte activation, phagocytosis, interleukin-1 production, neutrophil-mediated immunity, while in molecular function ALOX5AP was enriched in cytokine binding, pattern recognition receptor activity. It was also enriched in the Chemokine signalling pathway, Toll receptor signalling pathway, and Ras pathway activation in KEGG pathway enrichment.

Conclusion : The ALOX5AP is gives critical stimulus to AML and carries potential of futureprognostic biomarker

Keywords : AML, ALOX5AP, In sillico

PP01-13

Investigation on novel ER transmembrane protein, SURF4, targeting cell death in myeloid leukemia

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Background : One hallmark of acute myeloid leukemia (AML) that is shared across genetic subtypes is that leukemic myeloblasts are arrested at an immature and self-renewing stage of development. Differentiation is associated with a reduction in leukemic cell burden and leukemia stem cells as well as improved survival. In this study, we report that SURF4 inhibits apoptosis and suppresses myeloid differentiation by negatively regulating the STING and STAT6 functions in myeloid leukemic cells.

Method : Suppression of SURF4 was performed by SURF4-shRNA on leukemic cells. Apoptosis was detected on leukemic cells stained with annexin V and 7AAD using by flow cytometry. Western blot and qRT-PCR revealed expression of gene and protein. Leukemic cells were subcutaneous injected in mouse for development of tumor. And bioinformatics tools reveled the expression of SURF4 in AML patients.

Results : Silencing SURF4 inhibited cell growth and increased apoptosis in leukemic cells. In addition, we also observed the synergistic enhancement of apoptosis by paclitaxel in the absence of SURF4 in leukemic cells. SURF4 induced apoptosis via the accumulation of ROS, which activated ER stress via the PERK-peIF2α-CHOP pathway. Reduced SURF4 expression was capable of triggering myeloid differentiation in vitro and in vivo in murine and human leukemic cell models. Moreover, we found that IL4-dependent pSTAT6 and/or STING activation-induced apoptosis was increased in SURF4-silenced leukemic cells. Single-cell RNA-sequencing analysis revealed that the expression of SURF4 was significantly increased in patients with AML, suggesting that it is involved in the pathogenesis of hematological malignancies.

Conclusion : We demonstrated that the novel endogenous ER transmembrane protein, SURF4, inhibits cell death and suppresses myeloid differentiation by negatively regulating STING and STAT6 functions in myeloid leukemic cells. We propose that the inhibition of SURF4 may be used as a potential therapeutic strategy for the treatment of hematological malignancies.

Keywords : SURF4, Acute myeloid leukemia, Apoptosis, STING, STAT6

PP01-14

Targeting estrogen-related receptor alpha as a novel treatment approach for acute myeloid leukemia with FLT3 mutation

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Background : The FLT3 (fms-like tyrosine kinase) class III tyrosine kinase receptor is only found in normal hematopoietic cells and helps them stay alive, differentiate, and proliferate. However, FLT3 muta-

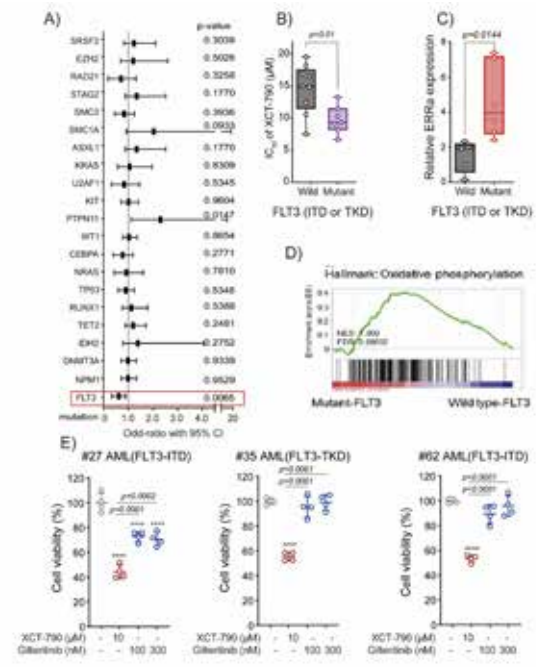
tions like FLT3-ITD (internal tandem duplication) and FLT3-TKD (tyrosine kinase domain) have been found in approximately 30% of AML patients and have been associated with a poorer prognosis. In the United States, FLT3 inhibitors like midostaurin and gilteritinib have been approved, and FLT3 mutation-targeted therapy has been developed. However, resistance to FLT3 inhibitors has grown, so novel approaches are needed to treat AML with the FLT3 mutation. Estrogen-related receptor-α (ERRα) is the orphan nuclear receptor for which no ligand has been identified. ERRα has been reported to affect AML disease progression by regulating mitochondrial function, and the ERRα inhibitor, XCT-790, has demonstrated anti-leukemic effects. However, the cytotoxicity of XCT-790 against primary AML cells varied depending on mutation profiles. To improve the cytotoxicity of ERRα inhibition, it is necessary to discover the relationship between ERRα and AML-related mutations.

Method : We conducted correlation assays among ERRα expression, IC_{50} value of XCT-790 against primary AML cells, and clinical information of AML patients. First, the relative ERRα expression in primary AML cells was obtained by qRT-PCR and XCT-790 cytotoxicity against primary AML cells was confirmed. Then, using clinical information of AML patients, mutations showing a relationship with the IC_{50} value of XCT-790 were identified and assessed using gene set enrichment analysis.

Results : AML patients with the FLT3 mutation had higher ERRα expression and XCT-790 efficacy. In TCGA-LAML, AML patients with the FLT3 mutation showed increased expression of oxidative phosphorylation-related genes compared to the normal FLT3 group. This was also detected in the high-ERRα expression group. Finally, XCT-790 demonstrated cytotoxicity against gilteritinib-resistant AML cells.

Conclusion : ERRα inhibition provides an attractive treatment option for refractory AML with the FLT3 mutation.

Keywords : Estrogen-related receptor alpha, Acute myeloid leukemia,FLT3 mutation



The relationship between AML-related mutations and ERRα. (A) Simple logistic regression between IC_{50} value of XCT-790 and mutation profile of AML. **(B)** The comparison IC_{50} values of XCT-790 according to FLT3 mutation (n= 7 and 9 for patients with mutation (9.786μM) and for patients with wild type (14.64μM), respectively). *P*-values were calculated by two-sided *t*-test. **(C)** The different expression of ERRα according to FLT3 status. *P*-value was calculated by two-sided *t*-test. **(D)** GSEA against oxidative phosphorylation. Genes were ranked based on fold changes between vehicle and FLT3 mutation (ITD or TKD) and wild type FLT3 patients in TCGA-LAML. **(E)** The comparison of cytotoxicity between XCT-790 and gilteritinib in primary AML cells with the FLT3 mutation.

PP01-15

Antithymocyte globulin (ATG) in allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia: evaluating outcomes according to cytogenetic risk: Impact on chronic GVHD and cGRFS

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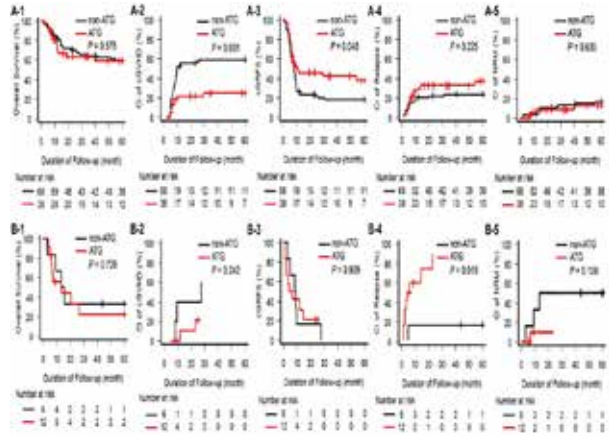
Background : Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is crucial for acute myeloid leukemia (AML) treatment, but graft-versus-host disease (GVHD) and relapse concerns persist. Antithymocyte globulin(ATG) has demonstrated promise in preventing GVHD during allo-HSCT. However, concerns about relapse remain.

Method : This retrospective single-center study aims to evaluate the prognostic implications of ATG based on cytogenetic risk stratification in 123 AML patients undergoing transplantation from an HLA-matched sibling.

Results : After a median follow-up of 48 months, the ATG group in the non-high cytogenetic risk group demonstrated a significant decrease in the 1-year cumulative incidence (CI) of chronic GVHD compared to the non-ATG group (21.7% vs. 54.4%, p = 0.001, Figure A-2). Additionally, the 1-year Chronic GVHD-free and relapse-free survival (cGRFS) was higher in the ATG group of the non-high cytogenetic risk group (45.8vs. 26.5%; p = 0.048, Figure A-3). Moreover, there were no significant differences in 1-year CI of relapse and 1-year non-relapse mortality (NRM) within the non-high cytogenetic risk group (ATG vs. non-ATG; p>0.05, Figure A-4,5). In the subgroup analysis of patients with high cytogenetic risk, although there was no statistical significance, the ATG group showed a trend towards decreased 1-year CI of chronic GVHD and higher cGRFS compared to the non-ATG group (p>0.05, Figure B-2,3). However, the ATG group exhibited a significantly higher 1-year CI of relapse compared to the non-ATG group (60.0% vs. 16.7%, p = 0.019, Figure B-4).

Conclusion : In conclusion, our study findings indicate that ATG was effective in preventing chronic GVHD and demonstrated higher cGRFS in AML patients undergoing matched sibling donor HSCT. However, AML patients with high cytogenetic risk should carefully consider the use of ATG due to the associated higher risk of relapse. Further investigations are warranted to validate these findings and determine the appropriate dosage of ATG for high cytogenetic risk AML patients.

Keywords : Antithymocyte globulin (ATG), Allogeneic hematopoietic stem cell transplantation , Acute myeloid leukemia, Graft-versus-host disease



PP01-16

The oxysterols 27-hydroxycholesterol affects hematopoietic stem and progenitor cell pools

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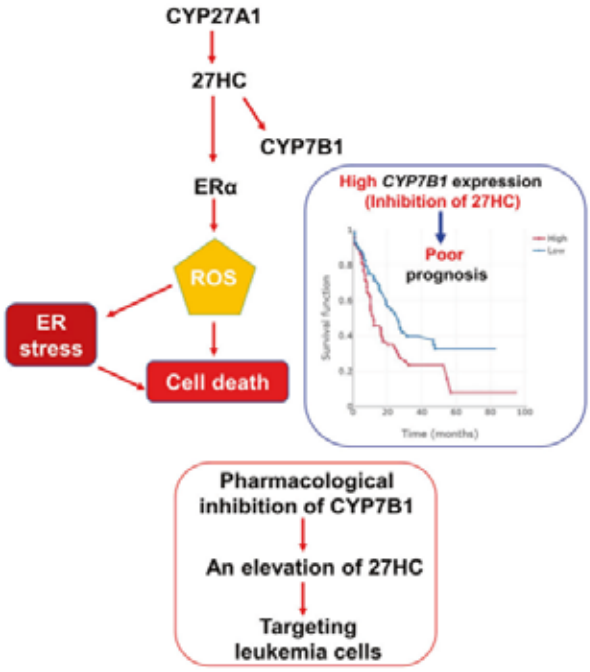
Background : Oxysterols are 27-carbon derivatives of cholesterol. Oxysterols are essential component of cell-membrane and acts as metabolic intermediates to synthesize bile acid and steroid hormone. Also, oxysterols function as transcription factor of Liver X receptor to regulate cholesterol metabolism and several signaling pathway. However, if elevated levels of oxysterols in the blood, oxysterols accumulate in blood vessel and cause human pathologies, such as atherosclerosis, Alzheimer's disease, Parkinson's diseases. In addition, accumulation of oxysterol in various tissue is connected with carcinogenesis and cancer progression. 27-hydroxy cholesterol(27HC) is a side chain oxysterol oxygenated at the 27 the carbon atom of cholesterol by the sterol hydroxylase CYP27A1. And 27HC is metabolized by oxysterol hydroxylase CYP7B1. 27HC acts as ligand for the nuclear receptor liver X receptor and estrogen receptor alpha (ERα). By proinflammatory processes mediated by ERα, 27HC promotes variety of cancer, metastasis and cause atherosclerosis progression. Circulating levels of 27HC in healthy humans is the most abundant oxysterol. Studies of 27HC in hematopoietic stem cell have been reported to induce hematopoietic stem cell mobilization and extramedullary hematopoiesis during pregnancy. However, what is influence of 27HC in hematopoiesis remains unknown.

Method : Mouse bone marrow cells and human leukemia cells were analyzed using fluoscence-activated cell sorting (FACS) after treatment of 6.2μM 27HC.

Results : We show that exogenous 27HC treatment lead to apoptosis of hematopoietic stem and progenitor cell (HSPC) population due to increased reactive oxygen species (ROS) level and ER stress. Furthermore, exogenous 27HC treatment suppresses leukemic cell growth and promote apoptosis via increase ROS level. Moreover, 27HC metabolizing enzyme CYP7B1 was highly expressed in AML patients and high CYP7B1 expressed AML patients exhibited shorter survival compared with low CYP7B1 expressed AML patients.

Conclusion : Our studies suggest that 27HC regulate HSPCs pool and have potential of novel therapeutic target for hematological malignancies.

Keywords : 27-hydroxycholesterol, Oxysterol, Hematopoietic stem cell, Acute myeloid leukemia



PP01-17

From docking to overcoming resistance: Cannabidiol's potential in multidrug-resistant leukemia cancer K562/ADR

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Background : Multidrug-resistant (MDR) leukemia poses a formidable challenge in the realm of cancer treatment, necessitating the exploration of innovative therapeutic agents. Cannabidiol (CBD), a non-psychoactive compound derived from the Cannabis sativa plant, has demonstrated auspicious anti-cancer properties. This study delves into the efficacy of cannabidiol (CBD) in surmounting MDR resistance in leukemia, with a specific focus on drug-resistant leukemic cells (K562/ADR).

Method : Various parameters, including the cytotoxicity of CBD, apoptosis assay, and the expression of apoptosis-related proteins, were meticulously evaluated. The study also assessed P-glycoprotein (P-gp) activity by monitoring the kinetics of P-gp-mediated efflux of pirarubicin (THP). Furthermore, molecular docking analysis was conducted to scrutinize drug–protein interactions

Results : The results revealed a dose- and time-dependent escalation in the cytotoxicity of CBD, resulting in growth inhibition in K562/ADR cells and heightened sensitivity to doxorubicin (DOX), suggesting its potential as a reversal agent. CBD exhibited an upregulation of cleaved caspase-3 and Bax, accompanied by the downregulation of anti-apoptotic Bcl-2, indicative of apoptosis induction. Moreover, CBD demonstrated a reduction in the expression of P-gp protein and its gene transcript levels. Additionally, CBD inhibited P-gp-mediated efflux, leading to increased intracellular drug accumulation in drug-resistant cells. Molecular docking studies provided valuable insights into the binding affinity of CBD to P-gp, highlighting its robust interaction with both the substrate and ATP binding sites of P-gp.

Conclusion : These findings substantiate the potential of CBD as a viable candidate for targeting P-gp, reversing drug resistance, and augmenting the efficacy of anticancer therapies.

Keywords : Cannabidiol, Multidrug-resistant leukemia, Molecular docking, Leukemia, K562/ADR

PP01-18

A real world analysis of impact of gilteritinib in relapse/refractory AML with FLT3-ITD mutation

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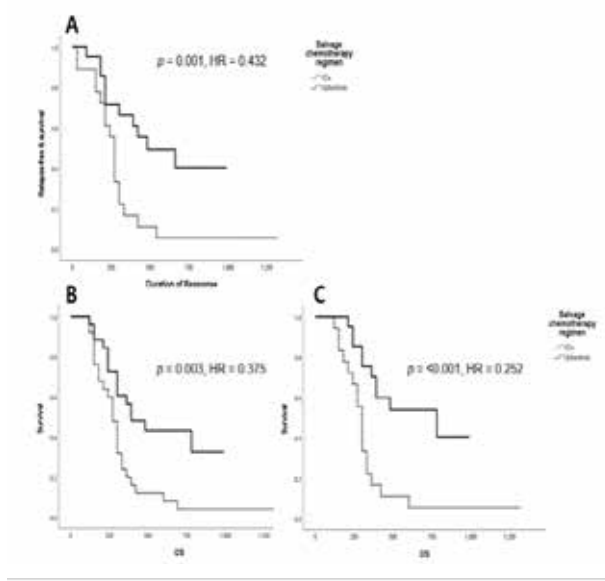
Background : In-frame internal tandem duplications of FMS-like tyrosine kinase-3 (FLT3-ITD mutation) is known for its negative effects on survival and failure of the initial therapy of acute myeloid leukemia. Gilteritinib is a highly-selective, oral FLT3 inhibitor, showing single-agent activity in patients with relapsed or refractory AML with the FLT3-ITD mutation.

Method : This study aims at evaluating over gilteritinib against conventional intensive chemotherapies (ICs) such as FLANG or MEC in the real world. A total of 51 patients, who were diagnosed as AML with refractoriness to standard chemotherapies or relapsed from June 2010 to April 2023 was included in this study. Medical records, bone marrow studies, complete-blood-counts, in case of extramedullary relapses, CT and MRI scans as well as PET-CT scans were evaluated.

Results : 54.9 percent of all study patients was male, 76.5 percent experienced a complete response more than once, and 88.5 percent received a hematopoietic stem cell transplantations (HSCTs) after salvage chemotherapies more than once. In addition, all patients who reached CR after salvage chemotherapies successfully underwent salvage HSCTs. Gilteritinib showed better OS and DoRs compared with ICs ($p = 0.003$, HR = 0.375; $p = 0.001$, HR = 0.432). Furthermore, gilteritinib also showed improved OS from salvage HSCTs compared with ICs for patients who achieved CR after salvage chemotherapies. ($p < 0.001$, HR = 0.252; $p = 0.003$, HR = 0.310)

Conclusion : In R/R settings, salvage chemotherapy regimens are limited. Gilteritinib not only showed significantly longer survival and duration of response among patients with R/R FLT3-ITD mutated AML, but also ensured following salvage HSCTs.

Keywords : R/R AML, FLT3-ITD mutation, Gilteritinib



	No. (%)
Age at salvage chemotherapy (median)	46 (years)
Sex	
Male	28 (54.9)
Female	23 (45.1)
Regimen	
Intensive chemotherapy	25 (49)
Gilteritinib	26 (51)
NGS data	
None	36 (70.6)
NPM1	7 (13.7)
CEBPA	3 (5.9)
DNMT3A	5 (9.8)
OS (median)	290 (days)
Duration of Response (median)	245 (days)
HSCT after Salvage chemotherapy	
Never	5 (9.6)
More than once	46 (88.5)
Achieving CR after Salvage chemotherapy	
Never	12 (23.5)
More than once	39 (76.5)

PP01-19

Enhanced expression of glycolytic enzymes and succinate dehydrogenase complex flavoprotein subunit a by HMP promotes glycolysis and mitochondrial respiration in myeloblasts of acute myeloid leukemia

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Background : Rapid growth and uncontrolled proliferation of undifferentiated myeloid cells are characteristic features of acute myeloid leukemia (AML). Metabolic reprogramming has been observed in the bone marrow of AML patients, as leukemia cells require increased ATP supplementation to support disease progression. In this study, we propose that human mesothelial protein (HMP) acts as a metabolic modulator in myeloid cells in AML.

Method : HMP is well-known as a marker of solid tumors, promoting cancer cell proliferation and survival. We analyzed alterations in HMP expression in myeloblast subpopulation, which is characterized by SSC-A^{low} and CD45^{dim}, obtained from AML patients using flow cytometry. And, we investigated metabolic changes in leukemia cells by comparing the oxygen consumption rate (OCR) of bone marrow samples derived from adult AML patients.

Results : HMP was overexpressed in approximately 36% of AML patients. Importantly, we observed a higher OCR in the HMP-positive group compared to the HMP-low or non-expressing group. Additionally, treatment with recombinant human HMP protein enhanced OCR and increased the expression of glycolytic enzymes and mitochondrial complex II protein in KG1α AML cells. Notably, targeting HMP by siRNA in KG1α cells showed a reduction of glycolysis-related gene expression and had no effect on mitochondrial complex.

Conclusion : HMP provokes metabolic changes in leukemia cells, enabling them to acquire a rapid supply of ATP for proliferation in AML. Targeting HMP represents a potential approach for mitigating the progression of AML by inhibiting glycolysis and mitochondrial respiration in myeloid cells.

Keywords : HMP, AML, SDHA, Glycolysis, Mitochondria

PP01-20

Risk stratification in AML through early bone marrow assessment during intensive chemotherapy

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Background : The current treatment strategy for 7+3 chemotherapy in AML involves assessing bone marrow (BM) on days 14-21. Previously, we found the prognostic value of earlier (on chemo-day 7, C7) BM evaluation. In this study, we aimed to further expand our previous findings to create a prediction model for induction response using C7 bone marrow results.

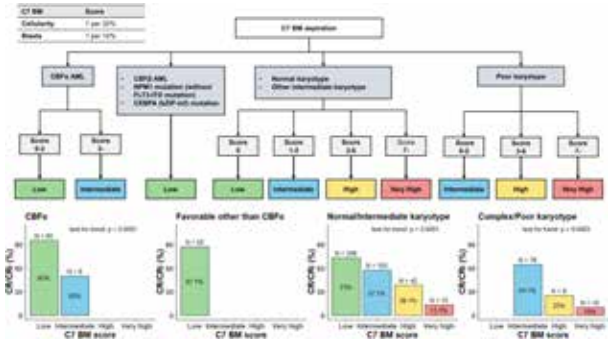
Method : We analyzed 794 patients from 2002 to 2022, documented with C7 BM results following 7+3 chemotherapy, without any intensification chemotherapy before response evaluation. Utilizing C7 BM aspiration results and patients' information, we developed a predictive model for forecasting complete remission (CR) or CR with incomplete hematologic recovery (CRi) after 7+3 induction.

Results : In the previous study, we found the diminished prognostic value of C7 BM in core binding factor (CBF) AML, so we initially elucidated its significance in non-CBF AML patients. Among them, both C7 BM cellularity and blast percentage emerged as significant independent factors of CR/CRi. Logistic regression models revealed similar increased odds for induction failure with a 20% increase in cellularity and a 10% increase in blast, leading us to introduce a scoring system (1 point for each: cellularity per 20%, blast per 10% increment). Subsequently, we assessed the significance of this scoring system across

genetic subtypes, applying a score cut-off associated with a 1.3-fold increase in induction failure risk for each subtypes. The final prediction model is summarized in the Figure. In this model, we could predict induction response effectively within the poor/intermediate genetic risk group. In the favorable genetic group, overall favorable responses were observed. However, within some CBFα AML cases, we could distinguish a subgroup with reduced induction response.

Conclusion : We have proposed effective model for stratifying induction failure risk through C7 BM. With this model, diverse augmentative treatment strategies can be devised based on the identified risk groups.

Keywords : Acute myeloid leukemia, Intensive chemotherapy, Early evaluation, Bone marrow, Response prediction



PP01-21

Genomic landscape of pediatric acute myeloid leukemia (AML)

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Background : Despite the advancements in treatment, the outcome of acute myeloid leukemia (AML) is dismal. Intermediate risk AML (IR-AML) is a heterogenous and poorly understood group. Next-generation sequencing technologies have expedited the discovery of novel genetic lesions in AML. The primary objective of this study was to investigate the mutational and methylation profile in pediatric AML with normal karyotype and lacking recurrent cytogenetic abnormalities in IR-AML by whole exome sequencing (WES). Secondary objectives were to determine post-induction remission status and survival outcomes.

Method : In this study, conducted from August 2021 to July 2023, bone marrow aspirates /or peripheral blood were collected at diagnosis of AML. Samples of patients with normal karyotypes were processed for WES and treated for bisulfite conversion, followed by genome-wide methylation microarray.

Results : A total of 61 patients were enrolled. The cytogenetic analysis revealed a normal karyotype in 20 patients. The DNA was sequenced to identify mutations in exonic regions (n=20). Common mutations were FLT3 (29.5%), CEPBA (12%), and WT (12%). The methylation analysis was performed by Infinium HumanMethylation850 (EPIC array) (n=13). HPCAL, FAM87B, VPS72, LINC00115, FAM41, SMAD11, and AGRN genes were differentially methylated in IR-AML. 1973 promoter sites had differential methylation levels, C12orf79 had a 3-fold hypermethylation, MLLT1 had a 1.8-fold hypermethylation, and EBNA1BP2 had a 6-fold hypermethylation. The differentially methylated CpG sites were most enriched in the Integrin signaling pathway, PDGF signaling pathway, and Nicotinic acetylcholine receptor signaling pathway. In our cohort, 78.6 % of patients achieved CR post-induction-1. At 24 months, the event-free survival and overall survival were 45% and 58%, respectively.

Conclusion : We identified significant genes with differential methylation that may have influenced the prognosis for AML and may represent novel therapeutic targets. Additionally, gene-specific molecular studies can shed light on the detailed function of these new genes in pediatric patients with IR-AML.

Keywords : Acute myeloid leukemia, Intermediate risk, Mutation, Methylation, Survival

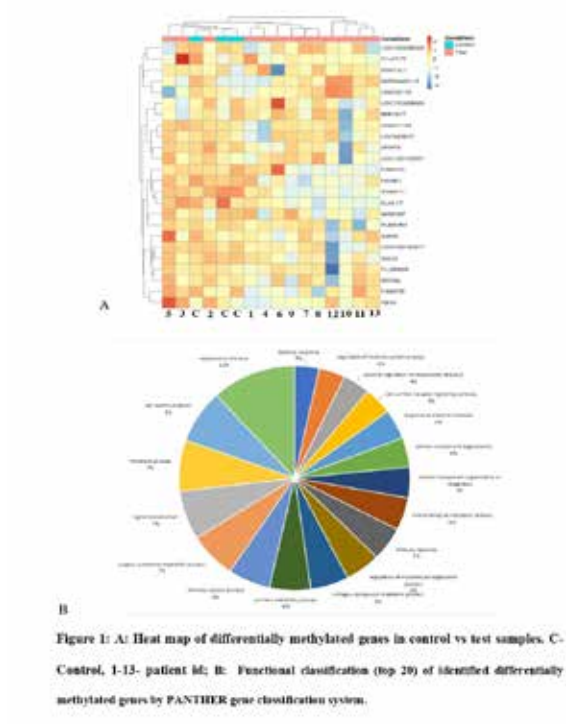

Figure 1: A: Heat map of differentially methylated genes in control vs test samples. C-Control, 1-13- patient id; B: Functional classification (top 20) of identified differentially methylated genes by PANTHER gene classification system.

Site	Promoter	CpG
SHPK	*FAM87B*	*ATAD3C*
HPCAL1	*RN7SL657P*	*TMEM240*
ZFPM1	*TMEM240*	*MIB2*
ZNF1	*RPL7P7*	*MMP25B*
LPIN2	*C1orf200*	*ARHGEF16*
VPS72	*UBE2V2P3*	*RNF207*
RNF122	*PRAMEF20*	*PIK3CD*
IL1RL1	*C1orf134*	*KIF1B*
LOC101927630	*FAM231B*	*CROCC*
MIR4706	*MIR3972*	*HTR6*

Table: Top 10 uniquely differentially methylated genes (based on p-value <0.05)

clustering algorithms, and deployment of the developed model.

Results : Our algorithm generated the cluster model of data consisting of 8 clusters with total number of items was: 100000. Cluster 0 was the largest cluster with 64017 items, with PCT averaging 56.33% smaller, PC5.5 averaging 54.79% smaller, and APC75 averaging 51.52% smaller, respectively. Cluster 6 was the smallest, consisting of 3 items, where the average size of KO/BV was 20,160.60% larger, APC75 was 12,976.84% larger, and PB/BV4 was 5,893.50% larger. We also observed our algorithm could identify MRD cases in AML relatively quickly with consistent accuracy. Furthermore, it may be completely integrated with current clinical laboratory alongside standardization of gating technique.

Conclusion : Our clustering algorithm shows great promise as next-generation automated MFC analysis tool for the future diagnosis and management of AML.

Keywords : Acute myeloid leukemia, Multicolor flow cytometry, Measurable residual disease, Artificial intelligence

PP01-22

An artificial intelligence approach for measurable residual disease (MRD) detection in acute myeloid leukemia (AML)

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Background : Acute myeloid leukemia (AML) is a heterogeneous disease distinguished by aberrant proliferation of myeloid progenitors and consequent bone marrow failure. Multiparameter flow cytometry (MFC) is critical in detecting MRD in patients with AML. Nevertheless, there are limitations to the current MFC interpretation, including the need for manual gating, and increased false negative MRD rates as a result of clonal development. Using newly emerging artificial intelligence (AI) technology, we aim to develop an automated MFC data interpretation algorithm for detecting MRD in AML.

Method : Thirty AML patients treated at Medical Oncology Department (DR BRA IRCH) of AIIMS, New Delhi were included in this study. In each enrolled patient's bone marrow aspirate we did MFC using a myeloid panel of antibodies. To create an automated MFC interpretation for MRD diagnosis, we employed an AI-based clustering approach. The data files were saved as .csv and imported to RapidMiner Studio for machine learning based modelling. Further, the imported data sets were used for training and validation sets, make any necessary data corrections, followed by simulation of

PP01-23

Glutathione s-transferases (GST) t1 polymorphism as the most susceptible to leukemia in asians population: An updated meta-analysis and systematic review of multicenter study

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Background : Previous studies have investigated the association of glutathione S-transferases (GST)M1, T1, and P1 polymorphism and their combination with susceptibility to leukemia yet the results were not specifically clear, especially in the Asian population. Profound analysis is needed to appraise and eliminate the possibility of bias and false positive tests. This study aimed to exclusively determine which of the three gene polymorphisms is most related to the risk of leukemia in the Asian population.

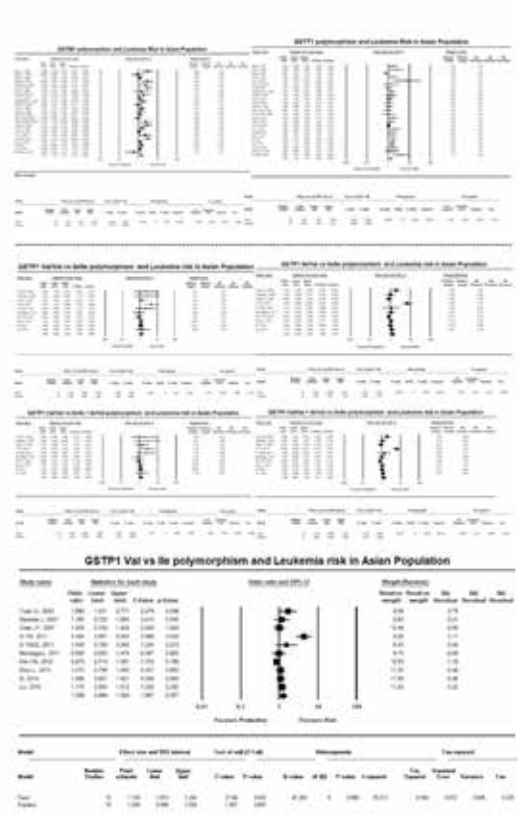
Method : A meta-analysis was designated with pooled odds ratios

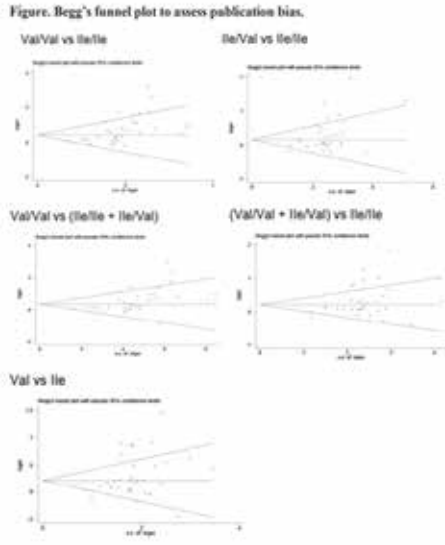
(ORs) and 95% confidence intervals (CIs) to examine the relationship between single and combined effects of the three GST-genes polymorphisms with susceptibility to leukemia. Subgroup analyses, meta-regressions, and sensitivity analyses were additionally performed with the false-positive report probability (FPRP) and Bayesian false discovery probability (BFDP) to appraise the credibility of the statistic result.

Results : A total of 25 case-control studies were included after screening 282 titles and abstracts. Single GSTM1, GSTT1, and GSTP1 Ile105Val polymorphisms increased the risk of leukemia. While the combined GSTM1 and GSTT1, GSTM1 and GSTP1, and GSTT1 and GSTP1 polymorphisms, positive results were also noted. Nevertheless, no significant relationship was obtained between the combined effects of these three polymorphisms with leukemia risk in the overall analysis. Furthermore, when only selecting Hardy–Weinberg equilibrium (HWE) and medium- and high-quality studies, we settled on similar results. Yet, when the FPRP and BFDP values were applied to assess the reliability of positive results, only the GSTT1 null genotype exhibited a significant relationship with the risk of leukemia in the Asian population. Meta-regressions identified smoking as a potential moderator of the risk of leukemia.

Conclusion : This study vigorously indicates a significantly increased risk of leukemia in the Asian population for GSTT1 polymorphism.

Keywords : GSTM1, GSTT1, GSTP1 Ile105Val, Leukemia, Polymorphisms





PP01-24

GSTP1 val allele is associated with susceptibility to acute myeloid leukemia: A meta-analysis

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Background : Acute myeloid leukemia (AML) is a complex hematologic malignancy that is linked to genetic and environmental factors. The glutathione S-transferase (GST) is a family of enzymes that play an essential role in carcinogen detoxification. It is hypothesized that lower levels of this enzyme may result in decreased detoxification

activity and increased cancer risk. Polymorphisms in the GST gene may alter enzyme expression, leading to leukemogenesis linked to AML. However, this relationship is still unclear, prompting us to do a meta-analysis to obtain more precise estimates.

Method : The literature search included 14 eligible articles in which GSTP1 polymorphism and its genotypes were determined in cases and controls. Pooled odds ratios (ORs) and 95% confidence intervals (95% CIs) were estimated in standard allelic, co-dominant, dominant, and recessive genetic models using Review Manager 5.4.

Results : Overall, analysis showed a significant association between the GSTP1 polymorphism and susceptibility to AML, favoring the development of AML in the presence of the variant allele. Significant associations were noted for the HWE-compliant studies. Further stratification of the studies into sub-groups (based on ethnicity and study population) showed significant associations only for the non-Asian cohort, favoring the development of AML in the presence of the mutant variant.

Conclusion : Results of the meta-analysis suggest that the GSTP1 polymorphism may affect the risk of AML development. Further large and well-designed genetic studies are needed to confirm this conclusion.

Keywords : GSTP1, Val, Acute myeloid leukemia, Meta-analysis

PP01-25

Impaired CD45RO-CCR7+ naive CD8+ T cells in AML are associated with lower overall survival

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Background : In the bone marrow (BM) micro-environment of AML, various immune cells and regulatory factors results in the dysfunction of T cells. Primarily, naïve CD8+ T cells, upon activation by antigen presentation from APCs, differentiate into effector cells and memory cells. While numerous studies have been conducted on the mechanisms and intervention strategies related to the exhaustion or senescence, the role of naïve CD8+ T cells in AML remains unclear.

Method : Collecting fresh BM samples from newly-diagnosed pediatric AML patients. Adapting flow-cytometry, transcriptome sequencing and in vitro culture models to identify the functional status of CD45RO-CCR7+CD8+T (CD8+Tnaïve-like) cells. Conducting correlation analysis with chemotherapy assessment and overall survival (OS) to elucidate the role of CD8+Tnaïve-like cells in AML.

Results : Compared to healthy donors, 56 pediatric AML patients showed a significantly lower proportion of CD8+Tnaïve-like cells in BM (HDs, 60%; AML, 45%; $p<0.05$). CD8+Tnaïve-like cells in AML exhibited significantly higher expression of inhibitory molecules VISTA and CTLA-4 (HDs, < 5%; AML, 10% to 20%; $p<0.05$). In vitro, the CD69-CD25- non-activated fraction of CD8+Tnaïve-like cells was significantly higher in AML (HDs, 20%; AML, 60%; $p<0.05$). GSEA revealed significantly activated bile-acid metabolism pathway but down-regulated MTORC1 signaling in CD8+Tnaïve-like cells in AML. CD8+T naïve-like cells' proportions before and after the first induction chemotherapy showed an increase in 11 complete remission (CR) patients, but a decrease in 4 non-CR patients. Using the 60% (mean of HDs) of CD8+Tnaïve-like cells' proportion as the cutoff-point, the 47 AML patients were divided into high and low expression groups (high : 10 cases; low : 37 cases). The 2-year OS was significantly lower in the high group (about 70%) compared to the low group (95%) ($p=0.026$,).

Conclusion : In pediatric AML patients, CD45RO-CCR7+ naïve CD8+ T cells exhibited impaired activation and memory-formation, and serve as a risk factor for 2-year OS.

Keywords : Pediatic, AML, Naive CD8+ T cells, Overall survival

PP01-26

Dysregulation of immune regulators in AML bone marrow promotes dysfunction of CD8+ T cells

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Background : Acute myeloid leukemia (AML) originates in the bone marrow, evading immune recognition and destruction. The bone marrow microenvironment (BME), comprising diverse immune cells and regulators, profoundly influences AML development. However, the impact of immune regulators in the BME, particularly on T-cell anti-AML immunity, remains inadequately understood.

Method : Using proteomics techniques, quantification of immune regulatory factors such as cytokines and chemokines in bone marrow plasma was performed. Bioinformatics analysis was utilized to identify pathways through which immunoregulatory factors affect

CD8+T cell signaling and function. An in vitro T cell exhaustion model was constructed to validate the aforementioned findings.

Results : Using proteomics techniques, we uncovered a substantial presence of immune-suppressive regulatory factors in AML bone marrow serum. Interestingly, the classical NF-κB pathway, vital for immune regulation, displayed significant downregulation, implying T-cell dysfunction. In our investigation, we identified dysfunctional CD8+ T cells in the primary AML bone marrow, characterized by heightened expression of co-inhibitory receptors and pro-dysfunctional transcription factors. Transcriptome sequencing further linked AML CD8+ T cells' dysfunction to reduced transcriptional activity of NF-κB p65 in the classical NF-κB signaling pathway. Intriguingly, in vitro inhibition of NF-κB p65 and its phosphorylation led to elevated expression of exhaustion markers, such as PD-1, LAG-3, and TIM-3 on primary CD8+ T cells. Most notably, the stimulation of the classical NF-kB signaling pathway effectively restored activation and effector function-related pathways in dysfunctional AML CD8+ T cells.

Conclusion : Immune regulators in the bone marrow microenvironment play a vital role in maintaining dysfunctional AML CD8+ T cells. These findings provide a novel strategy to investigate the potential mechanisms and interventions for T-cell dysfunction.

Keywords : Immune regulators, AML, CD8+ T cells, Dysfunction, NF-kB

PP01-27

Acute promyelocytic leukemia with abundant small azurophilic granules: A case report

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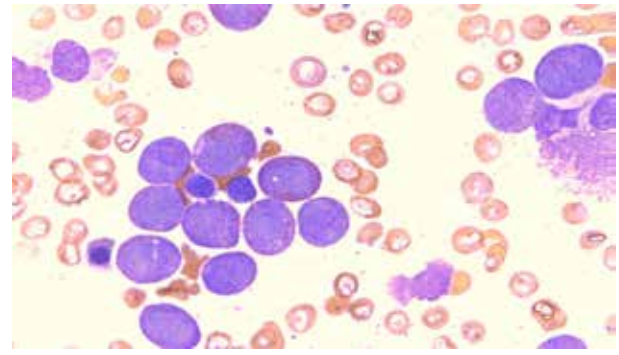
Early diagnosis of acute promyelocytic leukemia (APL) is important because all-trans retinoic acid (ATRA) therapy is uniquely effective in t(15;17) APL. However, numerous morphologic variations of APL makes prompt diagnosis difficult. This case report delves into the diagnostic intricacies encountered in a 42-year-old man with a personal history of hepatocellular carcinoma and hypertension. The patient presented with a life-threatening episode of actively bleeding epistaxis, along with a three-week history of unexplained bruising and recurrent epistaxis. Initial complete blood count (CBC) revealed pancytopenia, with white blood cell count (WBC) of 0.6x10^9/dL, hemoglobin of 7.9x10^9/dL, and platelet count of 14x10^9/dL. Bone marrow examination showed 86.94% consisted of unclassified promyelocytes characterized by abundant small azurophilic granules and occasional prominent nucleoli but no Auer rods, posing a diagnostic challenge between APL and acute basophilic leukemia. Immunophenotyping became imperative, demonstrating the expression of CD45, CD13, CD33, myeloperoxidase (MPO), CD64, and CD117 by gated medium to large mononuclear cells. Confirmation of APL was achieved through PML::RARA rearrangement positivity in AML leukemia PCR and a characteristic chromosomal study (46,XY,t(15;17)(q24;q21)[15]/46,XY[5]). Next-generation sequencing (NGS) did not detect hematologic neoplasm genes. Prompt initiation of treatment with ATRA and idarubicin yielded favorable outcomes. Follow-up bone marrow studies revealed a substantial decrease in blasts (2.67%) and severely decreased cellularity. Follow-up chromosomal study showed normal and PML::RARA quantification PCR showed weakly positive, with PML:RARA/ABL1 ratio of 0.0078. There was no evidence of PML::RARA rearrangement in FISH. The patient is currently undergoing consolidation therapy with sustained ATRA use.

Keywords : Acute promyelocytic leukemia, Azurophilic granules



PP01-28

Exploring genomic complexity in acute myeloid leukemia through machine learning: Subtype identification, biomarker discovery, and prognostic models for personalized interventions

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Background : Acute Myeloid Leukemia (AML) is characterized by genomic complexity, necessitating a nuanced approach for precise diagnostics and targeted therapies. This research aims to utilize advanced machine learning algorithms to unveil distinct genomic subtypes within AML, identify novel biomarkers, and refine prognostic models for more tailored and effective interventions.

Method : A cohort of 150 AML patients, each with detailed clinical annotations, was assembled. Leveraging multi-omics data from the Genotype-Tissue Expression (GTEx) project, we integrated genomic, transcriptomic, and epigenomic information. Cutting-edge machine learning algorithms, including Random Forest and t-SNE, were employed for unsupervised clustering to delineate genomic subtypes based on molecular signatures. Feature importance analysis, utilizing methods such as SHAP (SHapley Additive exPlanations), and rigorous cross-validation ensured the reliability and generalizability of the identified subtypes. Pathway enrichment analysis was conducted to elucidate the biological significance of each subtype.

Results : Our analysis uncovered 23% variability in gene expression patterns, delineating five distinct genomic subtypes within AML. Each subtype exhibited unique molecular signatures associated with specific biological pathways, providing a deeper understanding of the disease heterogeneity. Prognostic models based on these subtypes demonstrated an outstanding accuracy of 85%, surpassing conventional diagnostic approaches. Notably, 15 novel biomarkers specific to each subtype were identified, holding promise as potential targets for personalized therapeutic strategies.

Conclusion : This study demonstrates machine learning's effectiveness in uncovering AML's genomic complexity, identifying distinct subtypes with unique molecular signatures. Integrating multi-omics data from the GTEx project enhances our understanding of AML heterogeneity and establishes a foundation for personalized treatments. The identified genomic subtypes and 15 novel biomarkers offer insights for tailored interventions, marking a significant advance in AML management. These findings pave the way for further research, underlining the potential clinical application for improved AML patient outcomes.

Keywords : Genomic subtypes, Machine learning algorithms, Biomarker discovery, Prognostic models, Acute myeloid leukemia (AML)

PP01-29

The role of allogeneic stem cell transplantation in the AML patients who were treated with venetoclax and decitabine

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Background : Venetoclax combined with decitabine is one of standard treatment regimen for elderly acute myeloid leukemia (AML) patients. However, the outcomes of allogeneic hematopoietic stem cell transplantation (allo-HSCT) following treatment with venetoclax and decitabine are not well-established.

Method : We analyzed retrospectively the medical record of newly diagnosed AML patients who were treated with venetoclax and decitabine in Chungnam National University Hospital from March 2020 to June 2023. The primary endpoint was the overall survival (OS) of patients who underwent allo-HSCT compared to those who did not. And, secondary endpoints were relapse rate, event-free survival, and non-relapse mortality.

Results : A total of 50 AML patients received venetoclax with decitabine throughout the study period. Median age was 73 years, ranged from 45 to 84. Male to female ratio was 3:2. The Median follow-up duration was 8.2 months, ranged from 0.7 to 36.7 months. Among these patients, 34 (68%) patients had been achieved complete remission (CR) after venetoclax and decitabine treatment. And 15 (30%) patients underwent allogeneic HSCT. The median number of cycles of venetoclax plus decitabine before allo-HSCT was 3. Patient who underwent allo-HSCT exhibited a better overall survival compared to those who did not (median OS: not reached in allo-HSCT group vs 13.4 months in no-HSCT group, p=0.006). There was no treatment-related mortality in patient who underwent allo-HSCT. Among patients who achieved CR, the 2-year relapse rate was 34.6% in allo-HSCT group vs 100% in no-HSCT group (p=0.269). Among patients who underwent allo-HSCT, the 1-year event-free survival was 70.7%, and the 2-year event-free survival was 53%. And there was no non-relapse mortality.

Conclusion : Allo-HSCT in patients treated with venetoclax and decitabine may lead to an improvement in overall survival. However, given the high relapse rate even after allo-HSCT, further treatment will be necessary to mitigate post-transplant relapse in the future.

Keywords : Acute myeloid leukemia, Allogeneic HSCT, Venetoclax, Decitabine

PP01-30

Comparison of the current and 2022 system of the WHO classification of non-recurrent genetic abnormalities acute myeloid leukemia in the real-world setting

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Background : This study aimed to compare the current and 2022 system of the WHO classification of non-recurrent genetic abnormalities (GA) AML using the interanl cohort data.

Method : For this analysis, 311 AML cases without recurrent GA according to the WHO 2017 classification were selected from the internal cohort from January 2018 to June 2023.

Results : According to WHO 2022, 226 (72.7%) patients were diagnosed as AML, myelodysplasia-related (AML-MR) and 61 (19.6%) patients were diagnosed as AML, defined by differentiation (AML-DIFF). AML with defining genetic abnormalities (AML-GA) included 17 cases (5.5%), of whom 6 had AML with CEBPA mutation, 6 with NUP98 rearrangement, 3 with NPM1 mutation and 2 with BCR::ABL1 fusion. The remaining cases were four cases of AML associated with Down syndrome and three cases that could not be classified due to lack of karyotype data. Former provisional entity of AML with mutated RUNX1 was mainly classified as AML-MR (72.2%, 26/36) according to the co-occurrence with defining somatic mutations. Former therapy-related AML was also mainly classified as AML-MR (80.0%, 16/20), with almost all cases having defining cytogenetic abnormalities. Myelodysplasia-related AML has increased significantly from 147 AML-MRC as defined by WHO 2017 to 226 AML-MR as defined by WHO 2022. The increase was caused by mutations in the MR-defining genes solely in 43.4% (98/226), followed by MR-defining cytogenetic abnormalities solely in 34.1% (77/226), and co-occurrence of genetic and cytogenetic abnormalities in 20.8% (47/226). Genetic mutations and cytogenetic abnormalities were sufficient for AML-MR classification in almost all patients regardless of medical history. Additionally, 7.5% (11/147) of patients with prior AML-MRC were not classified as AML-MR. Of these, 10 were classified as AML-GA and only 1 was classified as AML-DIFF. The morphologically defined group was reduced from 137 AML-NOS to 61 AML-DIFF.

Conclusion : The updated WHO classification resulted in reclassification of AML cases without recurrent GA.

Keywords : Acute myeloid leukemia, WHO classification, Recurrent genetic abnormalities, AML-MRC, AML-NOS

PP01-31

Risk factors and infection patterns of febrile neutropenia after induction chemotherapy in patients with acute myeloid leukemia

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Background : Febrile neutropenia (FN) is a serious cause of mortality in acute myeloid leukemia (AML) with mortality rate of 10-30%. FN often occur after receiving induction chemotherapy in AML. Patients with FN are susceptible to various infections but the pathogens are often unknown. It is important to predict FN and identify the specific pathogen of infection. This study aims to identify risk factors and infection patterns of FN after induction chemotherapy in AML patients.

Method : This research was retrospective cohort study located at Prof. I.G.N.G Ngoerah General Hospital, Bali. The samples were AML patients aged ≥18 years treated with induction chemotherapy cytarabine plus daunorubicin in 2018-2022. The risk factors assessed were age, gender, body mass index, ECOG status, comorbidity, and pre-treatment blood count. The patients who had FN would be assessed for the incidence of infection through microbiological examination.

Results : This study included 92 patients aged 19 to 76 years old. There were 68 patients (73.9%) had FN. ECOG status ($p<0.01$), comorbidity ($p=0.042$), and haemoglobin level ($p=0.028$) were significant based on bivariate analysis. A multivariate analysis then showed ECOG status ($p<0.01$; OR 54.261; 95% CI 10.704–275.055) and low haemoglobin level ($p=0.040$; OR 5.301; 95% CI 1.082–25.964) as significant risk factors. The most common site of infection was the respiratory tract (63.75%), followed by genitourinary (15%), and skin (8.75%). Most specimens were obtained from sputum (35%), blood (26.25%), and urine (15%). Streptococcus sp., Staphylococcus sp., and Escherichia coli were top three most common pathogen found.

Conclusion : This study showed that ECOG status and low haemoglobin level were associated with FN after induction chemotherapy of AML. Patients with FN should be aware of various infections. The identification of risk factors and infections of FN will facilitate consideration of further treatment in AML.

Keywords : Acute myeloid leukemia, Febrile neutropenia, Infection

PP01-32

Survival analysis of acute myeloid leukemia patients at tertiary care hospital in Bali, Indonesia

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Background : Acute Myeloid Leukemia (AML) is a hematological malignancy caused by abnormal differentiation and proliferation of myeloid precursor cells. Research in United States showed new cases of AML in 2018 reached 1.3% with an incidence of 4.3 cases per 100.000 people. Although there are developments in AML treatments that improve outcomes, the prognosis in elderly patients is still poor. The estimated 5-year survival rate for AML is 30%. There are various factors that affect patient survival rates. This study aims to investigate the predictive factor and survival of AML patients at Tertiary Care Hospital in Bali, Indonesia.

Method : This research is a retrospective cohort study, with data collected from medical records at Prof I.G.N.G Ngoerah Denpasar General Hospital in Bali, Indonesia. The sample includes all adult patients who diagnosed with AML between January 2018 until June 2022. The dependent variable in this study is patient survival, while independent variables include age, gender, BMI, comorbid, clinical symptoms, type of AML, ECOG score, received chemotherapy or not, and complete blood count at diagnosis. Statistical analysis was performed using SPSS ver.25, employing the log-rank test and Kaplan-Meier method to generate survival curves. A p-value of ≤0.05 was considered statistically significant.

Results : The study involved 138 participants, comprising 84 patients who died during the follow-up period and 54 remaining alive. The median age of patients was 52 years, ranging from 19 to 92 years. The most common cause of death was septic shock (25.3%). 1-year overall survival (OS) was 39.1% with average OS was 6.3 months. Malnutrition (p=0.040), not receiving chemotherapy (0.024), severe anemia (p=0.004), and trombositopenia (p=0.041) are predictive factor that can shorten patient survival.

Conclusion : Prognostic factors strongly influence patient survival and are the basis for considering therapy selection.

Keywords : Acute myeloid leukemia, Survival, Predictive factor

PP01-33

The efficacy of midostaurin in patients with FLT3-ITD mutated AML : A real-world setting in Korea

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Background : Midostaurin has demonstrated efficacy in patients with FLT3-ITD mutated acute myeloid leukemia (AML). This retrospective, single-center study aims to investigate survival outcomes with midostaurin within a real-world context.

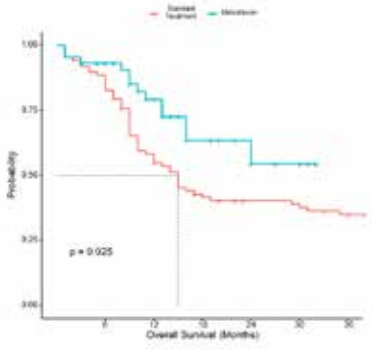
Method : A total of 131 patients with FLT3-ITD mutated AML, from January 2017 to March 2023, were included in this study. Among them, 44 patients underwent first-line intensive chemotherapy with midostaurin, while 87 patients received the standard treatment course. Midostaurin was administered at a dose of 50mg orally twice daily on days 8-21 following 7+3 chemotherapy. Patients who achieved complete remission received two cycles of consolidation therapy with high-dose cytarabine on days 1, 3, and 5, followed by midostaurin from days 8-21. Hematopoietic stem cell transplantation (HSCT) was pursued whenever feasible.

Results : Both groups exhibited balance in terms of age, gender, FLT3-ITD length, and mutation burden. The median follow-up duration of survivors in our study was 16 months. The midostaurin group demonstrated significantly prolonged overall survival compared to the standard treatment group (hazard ratio for death, 0.65; p=0.031). Factors such as sex, FLT3-ITD mutation burden, FLT3-ITD mutation length, and MRD status did not influence survival outcomes in the Cox-hazard proportional model. Attaining complete remission emerged as the most influential factor affecting survival, with a hazard ratio for death of 0.29. However, complete remission rates were comparable between the two groups, at 54.5% for the midostaurin group and 54.0% for the standard group. The incidence of HSCT was similar in both groups (70.5% vs. 74.7%, p=0.756). Although the incidence of relapse after transplantation was slightly lower in the midostaurin group, the difference was not statistically significant (23.1% vs. 36.7%, p=0.324).

Conclusion : In this real-world retrospective analysis, the combination of midostaurin with standard chemotherapy emerges as a

significant factor in extending overall survival in AML patients with FLT3-ITD mutation.

Keywords : Acute myeloid leukemia, FLT3-ITD, Midostaurin, Efficacy, Real-world



Variables	Overall, N = 131[1]	none, N = 87[1]	mido, N = 44[1]	p-value[2]
Gender				0.4
F	71 (54%)	45 (52%)	26 (59%)	
M	60 (46%)	42 (48%)	18 (41%)	
Age, yrs	49 (40, 59)	50 (40, 59)	48 (41, 58)	>0.9
ITD length, bp	48 (28, 63)	46 (26, 60)	52 (32, 65)	0.6
Unknown	17	13	4	
ITD burden, %	26 (13, 40)	27 (15, 41)	25 (9, 39)	0.3
Unknown	16	13	3	
Regimen				<0.001
1. IDA/ARA 3/7	74 (56%)	70 (80%)	4 (9.1%)	
3. DNV(90)/ARA 3/7	17 (13%)	14 (16%)	3 (6.8%)	
4. DNV(60)/ARA 3/7	40 (31%)	3 (3.4%)	37 (84%)	

[1] n (%); Median (IQR)
[2] Pearson's Chi-squared test; Welch Two Sample t-test

PP01-34

Hypomethylating agent plus venetoclax treatment outcome in core binding factor acute myeloid leukemia

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Background : While Core Binding Factor (CBF) AML typically responds well to cytarabine-based intensive chemotherapy, there are several cases unfit for such standard treatments. In these situations, hypomethylating agent+venetoclax (HMA+VEN) may be considered. However, data on the treatment outcomes for this group with HMA+VEN are limited. Therefore, we analyzed the outcomes of HMA+VEN treatment for CBF AML patients.

Method : In this study, we analyzed 31 CBF AML patietns who received HMA+VEN treatment. Among these patients, 14 were newly diagnosed (ND), and 17 were relapsed/refractory (R/R) cases. We grouped these 31 patients into CBFα and CBFβ groups and examined their initial response, best response, and overall survival outcomes following HMA+VEN treatment.

Results : Among the 14 ND patients, 7 each had CBFα and CBFβ AML, while among the 17 R/R patients, 10 were CBFα and 7 were CBFβ AML. Significant age differences were observed between ND and R/R patients (median 69 years vs. 59 years, $p < 0.01$). For response evaluation, as we found identical response rates between ND and R/R patients, we examined whole patients for comparing differences in response between CBF types. In initial response, significant differences were observed with CBFβ showing a remarkable overall response of 85.7% compared to 23.5% for CBFα ($p < 0.001$). In terms of best response, the overall response acquisition rates were 41.2% for CBFα and 92.9% for CBFβ, also demonstrating a significant difference ($p = 0.007$). Although no significant differences were observed in overall survival, there was a borderline significant survival difference between CBFα and CBFβ in R/R patients (median 10.0 months vs. 25.5 months, $p = 0.069$).

Conclusion : We confirmed that HMA+VEN is a feasible treatment option for CBFβ AML, both in ND and R/R settings. However, the treatment efficacy of HMA+VEN significantly declined in CBFα AML, and its application in these cases should be approached with caution.

Keywords : Venetoclax, Hypomethylating agent, Core binding factor, Acute myeloid leukemia, Treatment outcome

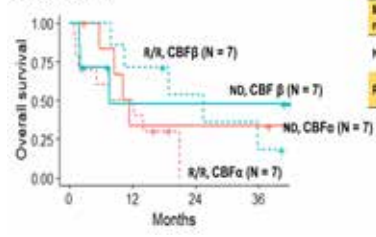
A. Initial response

	CBFα (N = 17)	CBFβ (N = 14)	p
Overall response	4 (23.5)	12 (85.7)	< 0.001
CR	1 (5.9)	1 (7.1)	
CRi	2 (11.8)	9 (64.3)	
MLFS	1 (5.9)	2 (14.3)	
NR	11 (64.7)	1 (7.1)	
Death in aplasia	2 (11.8)	0	

B. Best response

	CBFα (N = 17)	CBFβ (N = 14)	p
Overall response	7 (41.2)	13 (92.9)	0.007
CR	2 (11.8)	5 (35.7)	
CRi	2 (11.8)	7 (50.0)	
MLFS	3 (17.6)	1 (7.1)	
NR	6 (35.3)	1 (7.1)	
Death in aplasia	2 (11.8)	0	

C. Overall survival



Median OS, months (95% CI)	CBFα	CBFβ	p
ND	10.9 (8.5-NR)	7.7 (2.0-NR)	0.849
R/R	10.0 (1.8-NR)	25.5 (10.6-NR)	0.069

PP01-35

Gamma delta T-cell immune checkpoint receptor expression in acute myeloid leukemia

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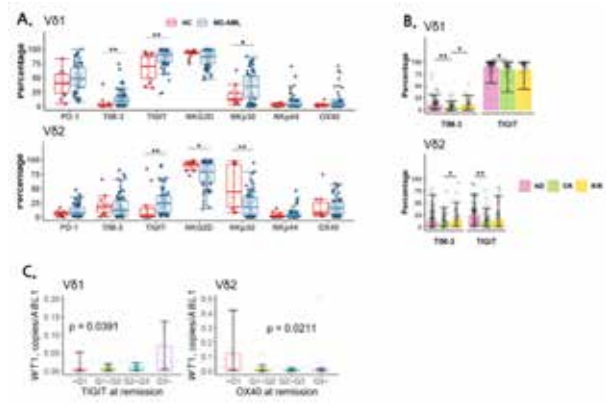
Background : γδ T-cells, a T-cell rare subpopulation, hold potential immunotherapeutic applications across various tumors. Due to the limited data on the bone marrow (BM) immune environment concerning this subset in acute myeloid leukemia (AML), we conducted an analysis of their expression of immune checkpoint (IC) receptors.
Method : Eighty-nine BM samples from AML patients at the time of diagnosis (ND), during complete remission (CR), and in cases of relapse/refractory (R/R) post-intensive chemotherapy, and 13 BM samples rom healthy controls (HC) were obtained. Multiparameter flow cytometry on BM mononuclear cells was conducted to assess IC receptor expression within the γδ T cell subset, specifically on the Vδ1 and Vδ2 subtypes.

Results : In the comparison of IC receptor expression between HC and ND-AML patients (Figure A), a significant increase in TIGIT expression was observed in both Vδ1 ($p = 0.0062$) and Vδ2 ($p = 0.0063$) subtypes, along with an increase in TIM-3 in Vδ1 ($p = 0.0014$) subtypes. Notably, NKG2D and NKp30 decreased significantly in ND-AML patients in Vδ2 subtypes, while NKp30 increased in Vδ1 subtypes. Analysis based on disease status revealed a trend of decreasing at CR and increasing at R/R for TIM-3 and TIGIT in both Vδ1 and Vδ2 subtypes (Figure B). When examining the association between IC receptor expression in CR and minimal residual disease levels measured by the Wilms Tumor gene 1 (WT1) transcript, TIGIT in Vδ1 subtypes and OX40 in Vδ2 subtypes showed a significant positive correlation with WT1 levels in CR samples (Figure C), indicating their potential association with MRD.

Conclusion : We revealed that γδ T cells in AML show altered IC receptor expression. TIGIT and TIM-3 shows the trend of increase in ND-AML, decrease at CR, and rise at R/R. The IC receptor expression on this subset may be associated with the depth of response level in AML.

Keywords : Gamma delta, T-cell , Acute myeloid leukemia, Immune checkpoint , Receptor



PP01-36

In vitro long-term culture conditions screening for primary AML sample

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Background : AML cell lines have been invaluable tools in many AML research, offering a continuous and reproducible source of cells for various experiments. However, cell lines are usually derived from a small population of cells, leading to a loss of heterogeneity observed in primary cells. And, cell lines can undergo genetic and phenotypic changes over time due to continuous passaging. Thus, this study aimed to evaluate culture conditions allowing long-term culture and phenotypic maintenance of primary AML cells in vitro.

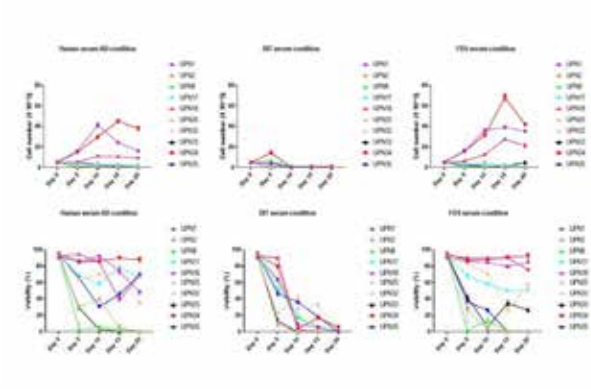
Method : Primary leukemic samples preparation and culture- All primary leukemic samples were collected from AML patients' peripheral blood (leukapheresis sample). Mononuclear cells (MNCs) were isolated by Ficoll gradient centrifugation, and the cell count was measured using a trypan blue. Hematoxylin and Eosin staining- Primary AML cell samples were stained according to the manufacturer's protocol. Flow cytometry- Cells were stained with the CD34-APC and CD38-FITC anti-human monoclonal antibodies.

Results : To establish primary AML long-term culture conditions, we selected samples from 10 AML patient samples with >85% viability upon thawing. Using FACS, we observed that Primary leukemic

samples were phenotypically heterogeneous as previously reported. Using H&E staining, we also observed that the primary leukemia samples were morphologically heterogeneous. According to the different culture conditions, primary AML samples were counted every 5 days. As a result, several primary samples still proliferated in a human serum AB-containing media condition until 15 days. However, the addition of a small molecule (HSC-expanding capacity SR1 or UM729) on the human serum AB-containing media did not make an increase of cell number and viability during culture.

Conclusion : This study identifies the challenge of establishing optimal culture conditions for the long-term maintenance of primary AML cells in vitro. We identified RPMI1640 with human serum AB and cytokines conditions conducive to sustained proliferation. These findings contribute valuable insights toward enhancing the primary AML research.

Keywords : Primary leukemic sample, Culture conditions, Acute myeloid leukemia, In vitro long-term culture



PP02-1

Impact of transfusion dependence on clinical and economic burden in patients with lower-risk myelodysplastic syndromes: A 28-year retrospective study

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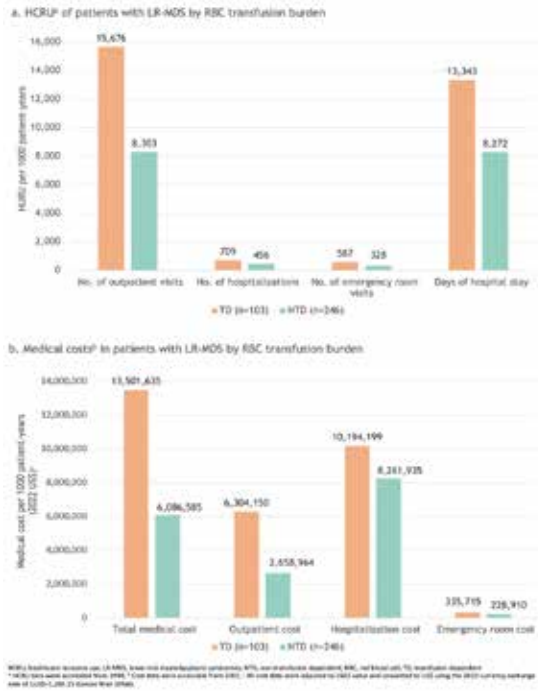
Background : Erythropoiesis-stimulating agents (ESAs) have limited efficacy in reducing red blood cell transfusion dependence (RBC TD) in myelodysplastic syndromes (MDS), which may increase mortality and leukemic progression. This study investigated the impact of TD on lower-risk MDS (LR-MDS) patients' response to ESAs, prognosis, healthcare resource use (HCRU), and medical costs, using a 28-year hospital database.

Method : Data were collected from 1994 to 2022. Patients with very low-, low-, or intermediate-risks were categorized as having LR-MDS. TD was defined as any 16-week period with ≥ 2 units of packed RBC transfusion per 8 weeks, with no 56 consecutive days without transfusion. The study explored response to ESAs and patients' attainment of transfusion independence (TI). Overall survival (OS), AML-free survival (AFS), HCRU, and medical costs were compared between TD and non-TD (NTD) patients.

Results : Among 349 LR-MDS patients, 103 (29.5%) experienced TD, of which 51 with baseline erythropoietin levels ≤ 500U/L were virtually eligible for ESAs, and 20 used darbepoetin-α. Seventeen (85%) had no initial response at 8 weeks of treatment, and 19 (95%) eventually discontinued darbepoetin-α treatment without re-initiation. Eight patients (40%) achieved ≥8-week TI within 24 weeks of darbepoetin-α treatment, but only 4 remained responders between week-24 and 48. Median OS (58.4 vs. 103.1 months; P=0.014) and AFS (52.7 vs. 102.7 months; P=0.003) were significantly shorter in the TD group compared to the NTD group. Moreover, RBC TD was associated with substantial HCRU and medical costs (Figure).

Conclusion : ESAs are limited option to treat RBC TD in LR-MDS. Since RBC TD is associated with shorter OS and AFS as well as substantial HCRU and medical costs, it highlights the unmet needs for alternative therapeutic options for TD LR-MDS patients. Abstract presented at ASH 2023 (Jang JH, et al. Blood. 2023;142[Suppl1]. 1869). © American Society of Hematology (2023). Adapted with permission.

Keywords : Lower-risk myelodysplastic syndromes,Transfusion dependence, Retrospective observational study, Prognosis, Healthcare resource use



PP02-2

Unlocking myelodysplastic syndrome insights: Meta-analysis and machine learning with MUHseq tool for blood transcriptome analysis

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Background : The myelodysplastic syndrome (MDS) represents a heterogeneous group of clonal hematologic stem cell disorders with the characteristic of ineffective hematopoiesis leading to low blood counts. RNA-Seq data combined with machine learning has shown promise in locating putative biomarkers and improving diagnostic precision. We investigated the gene expression profiles of CD34+ cells from MDS patients of multiple databases in order to clarify the distinct biological traits and enriched pathways linked to distinct MDS subtypes.

Method : In this study, a machine learning model employing an optimized random forest algorithm was applied to identify MDS from RNA-Seq data. Data retrieval, preprocessing, feature selection, model training, performance assessment, and hyperparameter adjustment were all steps in the process. A dataset consisting of RNA-Seq data from 580 subjects—345 of whom had myelodysplastic syndrome and 235 of whom did not—was used.

Results : After conducting an analysis of gene expression data obtained from individuals with myelodysplastic syndrome, we identified 72,678 differentially expressed genes (DEGs), which comprised 28,341 downregulated and 44,337 upregulated genes. Protein-protein network analysis and functional enrichment revealed RUNX1, GATA2, DKC1, IDH2, and CTC1 as potential myelodysplastic syndrome diagnostic biomarkers. Using sophisticated feature selection methods such as LassoCV and REFCV, we refined our original dataset of 13,249 genes to 43, which served as the basis for the training of classifiers based on machine learning. Support vector machine outperformed the other models tested, including deep learning, naive Bayes, random forest, logistic regression, and k-nearest neighbors. It achieved 0.65 accuracy (95%CI: 0.64-0.66), 0.70 AUC-ROC (95%CI: 0.67-0.77), and 0.35 MCC (95%CI: 0.67 - 0.78).

Conclusion : The MUHseq tool was developed as a result of the model's implementation and may be accessed at https://github.com/Uzzal/MUHSeq. Our current research findings may contribute to the discovery of putative genes for non-invasive clinical diagnostics for people with Myelodysplastic Syndrome (MDS) disease.

Keywords : Myelodysplastic syndrome, Hematopoiesis, Biomarkers, Gene expression, Machine learning

PP02-3

Potential biomarkers for azacitidine resistance in myelodysplastic syndrome based on gene expression and DNA methylation profiles

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Background : Myelodysplastic syndrome (MDS) comprises a group of heterogeneous hematopoietic disorders that present genetic mutations and/or cytogenetic changes and, in the advanced stage, exhibit wide-ranging gene hypermethylation. Patients with higher-risk MDS are typically treated with repeated cycles of the hypomethylating agents, azacitidine. However, some patients fail to respond to this therapy, and less than 50% show hematologic improvement. In this context, we herein focused on the potential use of epigenetic data in clinical management to aid in diagnostic and therapeutic decision-making.

Method : First, we used the F-36P MDS cell line to establish an azacitidine-resistant F-36P cell line. We performed gene expression profiling of azacitidine-resistant and parental F-36P cells, then used biological and bioinformatics approaches to analyze candidate azacitidine resistance-related genes and pathways. Subsequently, we analyzed differential DNA methylation patterns in the established cells and MDS patient samples, and tested their association with resistance to azacitidine.

Results : Eighty candidate genes were identified and found to encode proteins previously linked to cancer, chronic myeloid leukemia, transcriptional misregulation in cancer, etc. Interestingly, 24 of the candidate genes had promoter methylation patterns that were inversely correlated with azacitidine resistance, suggesting that DNA methylation status may contribute to azacitidine resistance. Especially, the DNA methylation status and/or the mRNA expression levels of the four genes (AMER1, HSPA2, NCX1, and TNFRSF10C) may provide benefit in predicting AZA responsiveness in MDS.

Conclusion : Based on these results, we are seeking to develop a diagnostic gene chip for azacitidine resistance in MDS patients, which could greatly benefit newly diagnosed MDS patients and those undergoing azacitidine treatment.

Keywords : Myelodysplastic syndrome, Azacitidine, Resistance, DNA methylation, Biomarkers

PP02-4

Chromosomal abnormalities in primary myelodysplastic syndrome

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Background : Myelodysplastic syndrome (MDS) is a group of disorder characterized by peripheral blood cytopenias in the presence of hypercellular/normocellular bone marrow with dysplastic features and increased risk of leukemic transformation.This study was undertaken to determine the frequency of cytogenetic abnormalities in patients diagnosed as primary myelodysplastic syndrome using conventional karyotyping

Method : The study was conducted at Aga Khan University hospital, Pakistan from January 2018 to October 2023 Patients of all ages and either gender who fulfilled WHO criteria for MDS were included. Cytogenetic analysis was conducted at the time of diagnosis. Patients who had secondary MDS were excluded from analysis. Chromosome identification and karyotype description was done according to the International System for Chromosome Nomenclature (ISCN, 1995) and described as frequency percentage

Results : Out of the 122 cases of MDS, 71 patients had their karyotype done at the time of diagnosis, including 42 males (59.2%) and 29 females (40.8%) with median age of 60 years. Forty one (57.7%) showed normal karyotype and 30 (42.3%) showed clonal karyotypic abnormalities at diagnosis. Out of which 14 (19.7%) had single, 11 (15.5%) had complex and 6 (8.5%) had double cytogenetic abnormalities. The common abnormalities found were: trisomy 8 in 7 cases (9.9%), -7/del (7q) in 3 cases (4.2%), -Y and complex 5q in 2 cases (2.8%) each, complex trisomy 8, del 11q , inversion 9, trisomy 19 and del 20q were found in 1 case (1.4%) each. Other abnormalities were found in 11 cases (15.5%)

Conclusion : Trisomy 8 was the most common disorder/abnormality found in this study population followed by the complex cytogenetics.

Keywords : Primary myelodysplastic syndrome, Karyotyping, Hematological malignancy, Cytogenetic abnormality

PP02-5

Subtype-specific germline DDX41 mutations and their distinct clinicopathological features in Korean patients with myelodysplastic syndrome and acute myeloid leukemia

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Background : While the prior studies have focused primarily on the clinical features and mutation profiles in DDX41-mutated cases, there has been little detailed information on pathologic findings in those pa-

tients. We investigated to characterize the detailed pathologic features of DDX41-mutated myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML).

Method : Internal next-generation sequencing database of myeloid neoplasms was queried to locate cases with pathogenic/likely pathogenic germline DDX41 mutations.

Results : The total number of study patients was 91 including 65 MDS and 26 AML. The most common germline mutation in DDX41 was Y259C (31.9%), followed by A500fs (23.1%), V152G (17.6%), splicing mutations (11.0%), E7* (7.7%) and miscellaneous mutations (8.8%). The main subtype of AML patients were AML not otherwise specified as defined by WHO 2017 classification (71.4%, 15/21). AML with DDX41 germline mutation was mutually exclusive with both AML with recurrent genetic abnormalities and AML with FLT3 and IDH1/2 mutations. Within the MDS, We divided patients into two groups based on the type of germline DDX41 mutation (missense and disruptive mutations). Patients with AML were highly enriched in disruptive mutation group (88.5%, 23/26) and those with MDS were slightly enriched in missense mutation group (69.2%, 45/65). Within MDS, germline DDX41 mutations were associated with excess blasts (EB) subtype (76.9%) and higher-risk (78.5%) and was mutually exclusive with SF3B1 mutation. MDS with missense DDX41 was significantly associated with MDS-EB-1 compared to disruptive DDX41 (P=0.015). On the contrary, MDS with disruptive DDX41 was significantly associated with MDS-EB-2 compared to missense DDX41 (P<0.001). In addition, cases harboring Y259C showed a lower level of granulopoiesis (P=0.003), higher frequency of bone marrow eosinophilia (P=0.035) and a trend for lower cellularity compared to those with V152G.

Conclusion : Our study indicates that type of germline DDX41 mutations may dictate the path of disease, ranging from lowering cellularity to blast proliferation.

Keywords : DDX41, Germline, Myelodysplastic syndrome, Acute myeloid leukemia

PP02-6

Trafficking of NK-cells into bone marrow after hypomethylating agent treatment in mice and patients with high risk MDS or AML

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Background : We tried to elucidate dynamic changes of immune cells profile and gene expression after hypomethylating agent (HMA) treatment in mice and patients with myelodysplastic syndrome (MDS) or acute myeloid leukemia (AML).

Method : A scRNAseq on consecutive BM samples from a high-risk MDS patient treated with azacitidine was conducted: Cell clusters were categorized based on immune-cell types, assessed changes in immune-cell proportions following treatment, and conducted a differentially expressed genes (DEG) analysis. Mouse myeloid leukemia C1498 cells were transplanted into the tail vein of 6-to-8-week aged syngeneic C57/BL6 mice. C1498 bearing mice were intraperitoneally treated with decitabine or vehicle for 5 consecutive days. In addition, changes in immune-cell proportions before vs. after HMA treatment and its association with HMA response were evaluated from sequential BM aspirates from HR-MDS or AML patients.

Results : In the scRNAseq, the NK-cell cluster exhibited the most significant increase in the relative proportion up to HMA response, whereas the effector T-cells showed only a modest increase of proportion upon response. DEG revealed an overexpression of CXCR4 in the NK-cell cluster at the timepoint of response, suggesting the recruitment of NK cells to BM. While HMA inhibited in vivo AML proliferation, the quantity of NK1.1+ cells were significantly increased in BM of HMA-treated mice than vehicle controls. In addition, CXCR4 expression in NK1.1+ cells from BM of HMA-treated mice were significantly up-regulated, compared with vehicle controls. The NK depletion in HMA-treated AML mice decreased anti-leukemic effect. The trafficking of NK cells to BM after HMA response were reproduced in serial BM aspirates from patients with HR-MDS/AML.

Conclusion : HMAs may boost NK cell recruitment to the bone marrow via CXCR4 overexpression, leading to anti-leukemic effects. This suggests a potential immunological mechanism for HMA efficacy in myeloid malignancies.

Keywords : Myelodysplstic syndrome, NK-cells, Cancer immunology, Bone marrow niche, Hypomethylating agent

PP02-7

Reclassification of myelodysplastic neoplasms following updated WHO and ICC classification: A single center study

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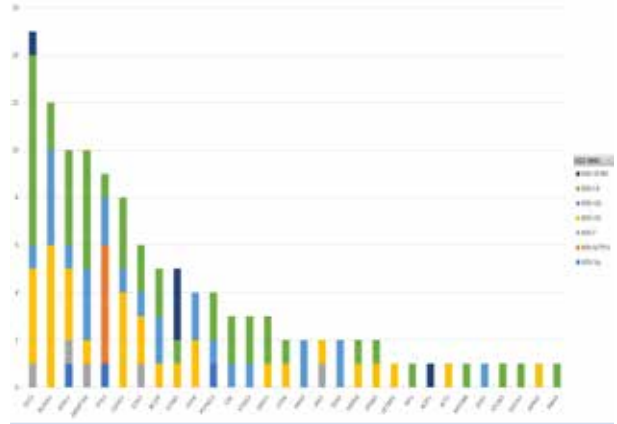
Background : Myelodysplastic neoplasms (MDS) are clonal hematopoietic disorders characterized by ineffective hematopoiesis and varying risks of progression to acute myeloid leukemia (AML). The advent of molecular genetic profiling has been instrumental in redefining MDS subtypes, facilitating the integration of genetic anomalies with traditional clinical and morphologic criteria. In this study, we analyzed the clinical and molecular characteristics in MDS patients, focusing on reclassification according to the latest WHO and ICC criteria.

Method : Patients diagnosed with MDS from July 2018 to October 2023 were included. Data on demographics, hematological and genetic data obtained from targeted sequencing panels, were analyzed. Reclassification was conducted based on the 2017 WHO criteria and the updated 2022 WHO and international consensus classification (ICC) to evaluate the impact of these revised diagnostic standards.

Results : The median age was 68, ranging from 35 to 85 years, with a male predominance (47 males, 30 females). Genetic analysis revealed variants in 70.1% of subjects, predominantly in TET2 and RUNX1 genes. The median value of the detected variants was 2 (1-8). Notable shifts in MDS subtypes were observed under the revised WHO classification, with reassignments from MDS-SLD (N=17) to MDS-LB (N=13) or MDS-h (N=4), and from MDS-MLD (N=24) to MDS-LB (N=19), MDS-SF3B1 (N=3), and MDS-biTP53 (N=2). MDS with defining genetic abnormalities such as MDS-SF3B1 and MDS-biTP53 according to the WHO classification, and MDS/AML with TP53 mutation or MR gene mutations as per the ICC guidelines, showed the diversity within the MDS categories.

Conclusion : The reclassification of MDS subtypes under the revised WHO and ICC guidelines, particularly in the presence of genetic aberrations, emphasizes the importance of incorporating genetic testing into diagnostic processes. This underscores the imperative of integrating genetic test results into diagnostic classifications to refine the prognostic stratification and inform therapeutic management.

Keywords : Myelodysplastic neoplasms, Classification, WHO, ICC



2017 WHO	2022 WHO	2022 ICC
MDS-SLD (N=17)	MDS-LB (N=13) MDS-h (N=4)	MDS-SLD (N=17)
MDS-MLD (N=24)	MDS-LB (N=19) MDS-*SF3B1* (N=3) MDS-biTP53 (N=2)	MDS-MLD (N=19) MDS-*SF3B1* (N=3) MDS with mutated *TP53* (N=2)
MDS-EB1 (N=18)	MDS-IB1 (N=17) MDS-biTP53 (N=1)	MDS-EB (N=17) MDS with mutated *TP53* (N=1)
MDS-EB2 (N=15)	MDS-IB2 (N=13) MDS-*biTp53* (N=2)	MDS/AML (N=5) MDS/AML with mutated *TP53* (N=4) MDS/AML with MR gene mutation (N=6)
MDS-EB1-F (N=2)	MDS-f (N=2)	MDS-EB (N=2)
MDS-del(5q) (N=1)	MDS-5q (N=1)	MDS-del(5q) (N=1)

PP03-1

Efficacy and 5 years survival of acute lymphoblastic leukemia (ALL) treated with bacterial l-asparaginase

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Background : Acute lymphoblastic leukemia (ALL) is an uncommon hematologic cancer that causes aberrant precursor cells for lymphoid tissues, accounting for around 30% of pediatric cancers, but it also makes up 1% of adult cancer diagnoses. Trials of pediatric or pediatric-inspired regimens incorporating asparaginase have been conducted in the adolescent and young adult (AYA) and adult populations due to the success of asparaginase-containing regimens in the treatment of pediatric ALL and the poor outcomes with conventional cytotoxic regimens in adults.

Methods: This is a study literature using Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement as a guideline. Literature were identified through database searches on Google Scholar, PubMed, ProQuest and ScienceDirect by taking data from last five years. Seven study were identified and the terms used are efficacy, 5 years survival, acute lymphoblastic leukemia (ALL), children, adult, bacterial L-asparaginase. Only quantitative and RCT research related to the topic included to the study.

Result: Acute lymphoblastic leukemia (ALL) cells do not express asparagine synthetase or express it only minimally, which makes them completely dependent on extracellular asparagine for survival. This dependency makes ALL cells vulnerable to treatment with L-asparaginase. Efficacy dan 5 year survical rate of treatment use is 43-63% in adult and 80-90% in children. Side effect occcurance usually worse the outcome. Meanwhile, severe and occasionally life-threatening toxicities of asparaginase therapy, which at least in the pediatric population has been clearly associated with a higher risk of leukemic relapse.

Conclusion: Efficacy dan 5 year survical rate of L-apsaraginase in ALL adult and children patient is varies where as children has efficacy and 5 year survival rate better than adult patients.

Keywords : Efficacy, 5 years survival, Acute lymphoblastic leukemia (all), Bacterial l-asparaginase

PP03-2

A pancytopenia preceeding a hypoplastic acute lymphoblastic leukemia

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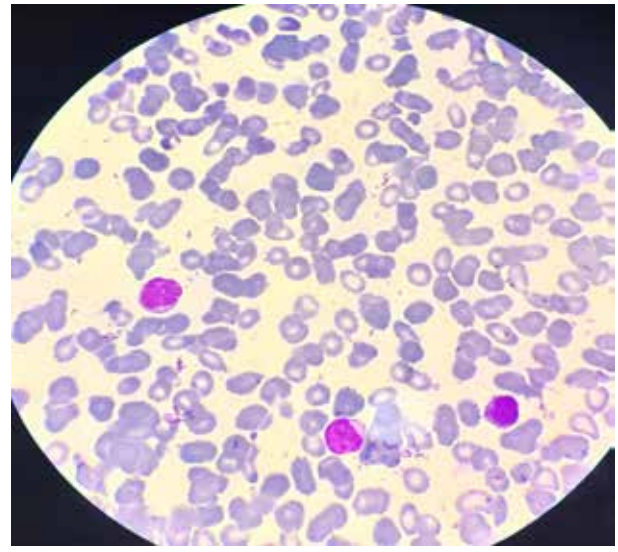
Background : Acute lymphoblastic leukemia (ALL) cases usually present with leukocytosis and hyperplastic marrow, but in 8-12% cases present with pancytopenia and 2% cases present with hypocellular marrow, therefore these particular cases are hard to be differed between ALL from myelodysplastic syndrome (MDS).

Method : We reported an ALL case with pancytopenia in peripheral blood and hypoplastic bone marrow.

Result : A case of a 42-year old male patient initially brought to the hospital with the chief complaint of fever and seizure. In physical examination, he had pallor in conjunctiva, nail beds and palms. Complete blood count showed a severe pancytopenia, whereas from blood smears examination he was suspected with MDS. Bone marrow aspiration was carried out on day fourth and the bone marrow smear was hypoplastic with 24.5% lymphoblast and he had been diagnosed with ALL-L2. On the fifth day, the patient had a complaint about abdominal pain, and abdominal Xray showed a small-bowel obstruction. Seizure can be caused by a febrile neutropenia, as patient with neutropenia and leucopenia are susceptible for infection. In this case, the patient progressed to septic shock and passed away on the fifth day.

Conclusion : We concluded patient ALL with pancytopenia has a high risk for infection which may shorten the survival. We presented this case therefore we could increase awareness of acute leukemia in patient with pancytopenia and hypoplastic marrow.

Keywords : Acute lymphoblastic leukemia, Pancytopenia, Hypoplastic marrow, Small-bowel obstruction



PP03-3

The association between GSTM1 and GSTT1 null genotype and susceptibility to leukemia in Asian population: A systematic review and meta-analysis

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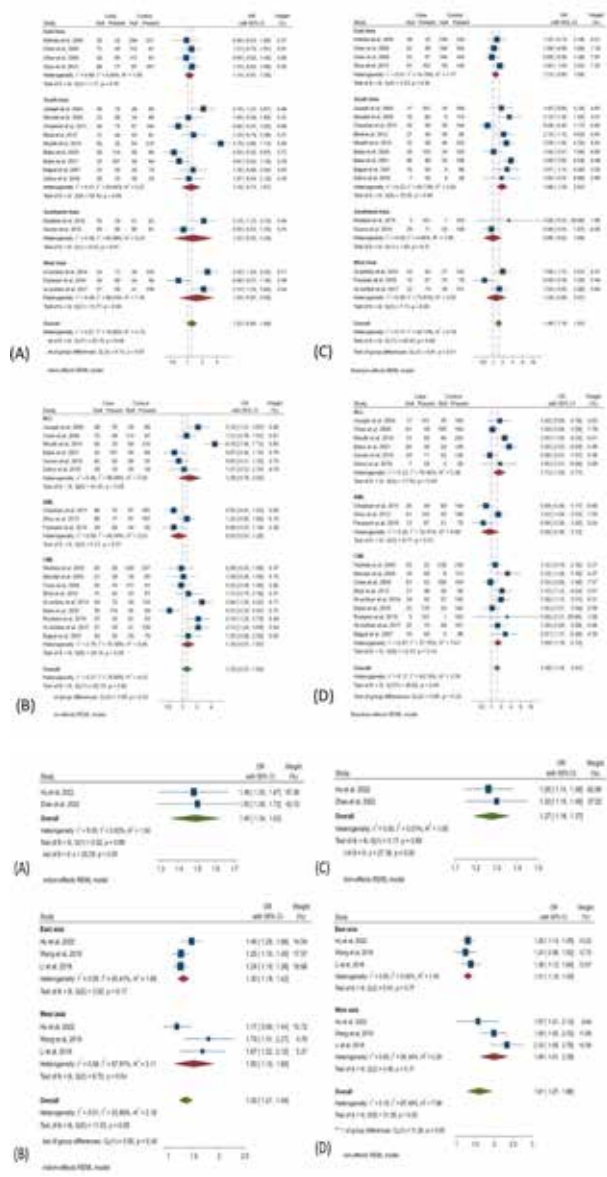
Background : Leukemia is a blood-related malignancy from hematopoietic stem or progenitor cell mutations. GSTs are one of the enzymes that play an important role in the progression of leukemia. The association between GSTM1 and GSTT1 null genotypes and leukemia has been extensively researched, but a complete analysis among Asians has not been conducted. This study aimed to confirm and quantify meta-analytic findings on the risk of GSTM1 and GSTT1 mutation for leukemia among the Asian population.

Method : A comprehensive literature search from PubMed, ScienceDirect, and Cochrane Central databases from the year 2000 up to October 2023, using keywords ((glutathione S-transferase M1) OR (GSTT1) OR (glutathione S-transferase M1) OR (GSTM1)) AND ((mutation) OR (polymorphism) OR (variant)) AND ((leukemia) OR (leukemia)). Case-control and meta-analysis studies targeting the Asian population were retrieved using specific inclusion criteria. The association between GSTM1 and GSTT1 mutation and leukemia was tested using STATA 17 in different subgroups based on leukemia type, region, and ethnicity to estimate the pooled odd ratios (OR) and 95% confidence interval (95% CI).

Results : A total of 17 case-controls and 4 meta-analyses were included after screening 269 titles and abstracts. We found significant associations with increased susceptibility to leukemia for GSTM1 (OR 1.22; 95% CI 0.93-1.60) and GSTT1 (OR 1.49; 95% CI 1.16-1.91) null genotype in the overall analysis. Further subgroup analysis by leukemia type and region suggests that GSTM1 and GSTT1 null genotypes were significantly associated with susceptibility to acute lymphoblastic leukemia and chronic myeloid leukemia, especially in South Asia. Additionally, meta-meta-analysis in this study confirms the association of GSTM1 (OR 1.49; 95% CI 1.34-1.63) and GSTT1 (OR 1.27; 95% CI 1.18-1.37) and susceptibility to leukemia in Asian ethnicity.

Conclusion : Our findings indicated that GSTM1 and GSTT1 null genotypes might serve as potential genetic biomarkers of leukemia in the Asian population.

Keywords : Asian, Glutathione s-transferase, GSTM1, GSTT1, Leukemia



PP03-4

IKZF1 deletion status and correlation with cytogenetics and measurable residual disease in adult B lineage acute lymphoblastic leukemia

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Background : IKZF1-deletion/IKZF1^{del} is recognized as a poor-risk genetic abnormality in pediatric B-lineage acute lymphoblastic leukemia (B-ALL), but its influence in adult B-ALL is not completely understood. We report the association of IKZF1^{del} and IKZF1^{plus} status with cytogenetic abnormalities/CG and measurable residual disease/MRD in a cohort of adult-B-ALL.

Method : Multiplex ligation-dependent probe amplification/MLPA (MRC, Holland) was used to study the copy number variations/CNV in 94 consecutive cases of adult-B-ALL. Final probe ratios of 0, 0.40-0.65, 1.3-1.65, and 1.75-2.15 were used to detect homozygous deletion, heterozygous deletion, heterozygous gain, triplication/homozygous gain respectively with a focus on IKZF1 gene. IKZF1^{plus} was diagnosed if IKZF1^{del} was associated with the deletion of one or more of CDKN2A/B, PAX5, or PAR1. The findings were correlated with CG abnormalities and flow-cytometry-based MRD status.

Results : The demographic profile of patients is summarized in Table 1. Overall, IKZF1^{del} was seen in 32/94(34%) cases, being more frequent in BCR::ABL1-positive (15/35;42%) than BCR::ABL1-negative 17/59(28.8%) patients. However, IKZF1^{plus} was diagnosed in 15(16%), more frequently in BCR::ABL1-negative cases [10(16.9%) vs. 5(14.2%)] especially in diploid/low-hyperdiploid cases (8/42;19%). None of the high-hyperdiploid (n=3)/near-triploid(n=3)/high-hypodiploid(n=1) B-ALLs showed IKZF1^{del}. The most frequent associated deletions in IKZF1^{del} were CDKN2A^{del}+CDKN2B^{del} (n=5). IKZF1^{del} were more frequent in MRD-positive cohort (33.3% vs. 26.6%) especially in BCR::ABL1-negative patients (36.3% vs. 10.5%). The frequency of IKZF1^{plus} was significantly higher in BCR::ABL1-negative MRD-positive patients compared to BCR::ABL1-negative MRD-negative patients (36.2% vs. 5.2%; p=0.047).

Conclusion : There are limited studies on the role of IKZF1^{del} and IKZF1^{plus} in adult B-ALLs compared to pediatric B-ALL. Our research reveals that among BCR::ABL1-negative adult B-ALLs, 28% exhibit IKZF1^{del}, while 15.9% display IKZF1^{plus}; in BCR::ABL1 positive cases, the frequencies are 42% and 16.9% respectively. Among BCR::ABL1-negative patients, IKZF1^{plus} was significantly more frequent in MRD-positive compared to the negative group. Overall, our findings suggest testing for IKZF1^{del} in adult B-ALLs, especially BCR::ABL1-negative cases.

Keywords : B-ALL, MLPA, IKZF1, IKZF1plus, Measurable residual disease

Table 1: Demographic profile and laboratory findings of Adult B-ALL patients (n=94)

Age – median (Inter-quartile range) years	26 (17-40)	
Males: females	55:39	
Hemoglobin (g/dL) median (Inter-quartile range)	7.3 (5.6-8.9)	
Total leukocyte count (x10^9/L) median (Inter-quartile range)	19.05 (6.57-99.05)	
Platelet counts (x10^9/L) median (Inter-quartile range)	28.5 (15.5-75.2)	
Cytogenetics (n;%)		
BCR::ABL1	35 (37.2%)	
Low hyperdiploidy	16 (17%)	
High Hyperdiploidy	3 (3.1%)	
Near triploidy	3 (3.2%)	
TCF3::PBX1	3 (3.2%)	
PAX1::CRLF2	2 (2.1%)	
MEF2D rearrangement	1 (1.1%)	
High hypodiploidy	1 (1.1%)	
IGH::CRLF2	1 (1.1%)	
Genetic abnormality in MLPA	n (%)	
IKZF1 deletions in the whole cohort	32 (34%)	
Type and distribution of *IKZF1* deletion		
Deletion Exons 4-7	8 (25%)	
Deletion Exons 2-7	7 (21.8%)	
Deletion Exons 1-8	4 (12.5%)	
Deletion Exons 5-7	2 (6.25%)	
Deletion Exons 4-5	2 (6.25%)	
Deletion Exons 1-2	2 (6.5%)	
Others	6 (18.7%)	
Monoallelic versus Biallelic	20 (62.5%) and 12 (37.5%)	
IKZF1 deletions in the subgroups	n (%)	
IKZF1 deletions in *BCR::ABL1* positive cohort	15/35 (42%)	P=0.17
IKZF1 deletions in *BCR::ABL1* negative cohort	17/59 (28%)	
$IKZF1^{plus}$ in the whole cohort	15 (15.9%)	
$IKZF1^{plus}$ in the subgroups	5 (33.3%)	
$IKZF1^{del}$+$CDKN2A^{del}$+$CDKN2B^{del}$	4 (26.6%)	
$IKZF1^{del}$+$CDKN2A^{del}$+$CDKN2B^{del}$+$PAX5^{del}$	2 (13.3%)	
$IKZF1^{del}$+$CDKN2A^{del}$	2(13.3%)	
$IKZF1^{del}$+PAR^{del}	1 (6.6%)	
$IKZF1^{del}$+PAX^{del}	1 (6.6%)	
$IKZF1^{del}$+$CDKN2A^{del}$+$CDKN2B^{del}$+$PAX5^{del}$+PAR^{del}		
$IKZF1^{plus}$ in *BCR::ABL1* positive cohort	5 (14.2%)	P=1.0
$IKZF1^{plus}$ in *BCR::ABL1* negative cohort	10 (16.9%)	
Measurable residual disease/MRD in the whole cohort (n=48)		
Positive	18 (37.5%)	
Negative	30 (62.5%)	
IKZF1 deletions in MRD positive cohort (n=18)	6 (33.3%)	P=0.75
IKZF1 deletions in MRD negative cohort (n=30)	8 (26.6%)	
IKZF1 deletions in *BCR::ABL1* negative MRD positive cohort (n=11)	4 (36.3%)	P=0.15
IKZF1 deletions in *BCR::ABL1* negative MRD negative cohort (n=19)	2 (10.5%)	
$IKZF1^{plus}$ in *BCR::ABL1* negative MRD positive cohort (n=11)	4 (36.3%)	P=0.047
$IKZF1^{plus}$ in *BCR::ABL1* negative MRD negative cohort (n=19)	1 (5.2%)	

PP03-5

5-Methyl cytosine flow cytometry-based global methylation status and correlation with cytogenetics and measurable residual disease in adult B lineage acute lymphoblastic leukemia

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Background : Methylation-induced epigenetic repression of tumor suppressor genes has prognostic relevance in B-acute lymphoblastic leukemia/B-ALL. Global methylation status is also targetable by hypomethylating agents like decitabine. While most previous studies have employed complex molecular techniques, the current study intends to study global methylation status by a relatively simpler flow-cytometry/FCM technique.

Method : FCM was used to study the global DNA methylation profile in 70 cases of adult B-ALL. Cells were surface stained for CD45, CD19, CD10, CD3. After cellular permeabilization, cells were stained with anti-5-methyl cytosine antibodies (5MC) and further with secondary fluorescent antibody conjugate with Alexa fluor 488. The median fluorescence intensity of expression of 5-MC (5-MC-MFI) was studied on B ALL blasts and compared to T cells within the sample. The MFI of expression on blasts and T cells was compared in two groups (Group-1) BCR::ABL1 negative and (Group-2) BCR::ABL1 positive by Man Whitney U test.

Results : The demographic profile of patients is summarized in Table 1. Overall, 5-MC-MFI was significantly lower on blasts compared to T lymphocytes ($p<0.0001$). 5-MC-MFI on blasts was significantly higher in group-1 compared to group-2 ($p=0.029$). Similarly, 5-MC-MFI on T cells was significantly higher in group-1 compared to group-2 ($p<0.0001$). In 33 patients with measurable residual disease/MRD data, 5-MC-MFI on blasts at diagnosis was significantly lower in the MRD-positive cohort compared to the negative group ($p=0.003$). It was significantly lower in the MRD-positive cohort compared to the negative group even after the exclusion of BCR::ABL1 positive patients ($p=0.011$).

Conclusion : 5-MC-based FCM results showed significantly poor global methylation (hypomethylation) in blasts and T lymphocytes of BCR::ABL1 positive B-ALL cases compared to BCR::ABL1 negative cases. MRD positive group showed significant hypomethylation compared to MRD negative group irrespective of BCR::ABL1 status. FCM-based global methylation status can be explored as a routine test to identify poor-risk B-ALL patients.

Keywords : B-ALL, Flow-cytometry, 5-Methyl cytosine, Hypomethylation, Measurable residual disease

Table 1: Demographic profile and laboratory findings of Adult B-ALL patients (n=70)

Age – median (range) years	27 (12-70)	
Males: Females	41:29	
Hemoglobin (g/L) median (range)	73 (27-134)	
Total leukocyte count (x10^9/L) median (range)	21.8 (0.5-386)	
Platelet counts (x10^9/L) median (range)	33 (4-322)	
Cytogenetics (n;%)		
BCR::ABL1	28 (40%)	
Low hyperdiploidy	8 (11.4%)	
High Hyperdiploidy	2 (2.8%)	
IGH::CRLF2	3 (4.2%)	
ETV6::RUNX1	1 (1.4%)	
TCF3::PBX1	1 (1.4%)	
MEF2D rearrangement	1 (1.4%)	
Low hypodiploidy	1 (1.4%)	
Near tetraploidy	1 (1.4%)	
Measurable residual disease/MRD (n=33)		
Positive	10 (30.3%)	
Negative	23 (69.6%)	
Median fluorescence intensity of 5-MC	Median (Inter quartile range)	*P* value
Blasts	56384 (13246-481449)	<0.0001
T cells	282170 (48827-1039313)	
BCR::ABL1 Negative blasts	73869 (36896-143549)	0.029
BCR::ABL1 positive blasts	42130 (24792-76951)	
BCR::ABL1 Negative T cells	425568 (246564-511565)	<0.0001
BCR::ABL1 positive T cells	184144 (127031-243430)	
Blasts at diagnosis in MRD-positive group	27346(23967-51006)	0.003
Blasts at diagnosis in MRD negative group	115699(47478-252854)	
Blasts at diagnosis in MRD-positive group (*BCR::ABL1* negative)	26103 (21992-49760)	0.011
Blasts at diagnosis in MRD negative group (*BCR::ABL1* negative)	121053 (51737-276355)	

PP03-6

Clinical impact of concurrent BTG anti-proliferation factor 1 (BTG1) and IKZF1 deletions in BCR::ABL1 negative B-cell acute lymphoblastic leukemia

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Background : Recently, BTG anti-proliferation factor1(BTG1) deletions in childhood B-ALL have been reported to have worse outcome when present concomitantly with IKAROS family zinc finger1 (IKZF1) deletions, compared to IKZF1 deletions alone. So, we aimed

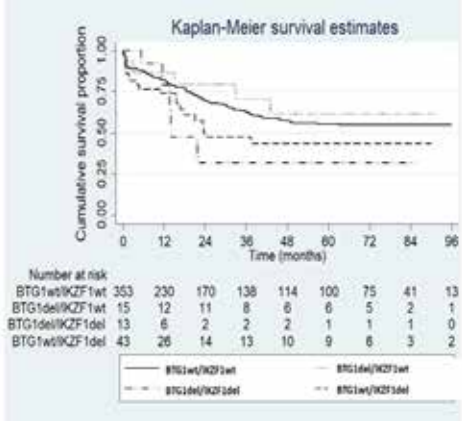
to establish the prevalence of BTG1deletions, its co-existence with IKZF1 deletions and clinical correlation in our pediatric B-ALL cohort.

Method : We retrospectively analyzed the baseline genetic work-up data from untreated B-ALL cases for BTG1 and IKZF1deletions. Multiplex ligation-dependent probe amplification (MLPA) was done using SALSA MLPA kits P335and P202 (MRC-Holland) for BTG1and IKZF1 deletions. Event free survival (EFS), overall survival (OS) were noted.

Results : The study included 470 pediatric BCR::ABL1 negative B-ALL patients with median age 6 years (1-18); M:F ratio::2:1. Out of 470, 30(6.4%) cases had BTG1 deletions(BTG1del). The IKZF1 deletions(IKZF1del) were detected in 70(14.9%) patients. Fifteen(3.2%)cases had concomitant BTG1 and IKZF1 deletions(BTG1del/IKZF1del). The remaining 15 cases were BTG1del/IKZF1wt and 55 were BTG1wt/IKZF1del.The post-therapy follow-up was available in 424 patients.The post-induction remission rate(84.6% vs 72.1%;p=0.112),median EFS (20.7 vs 18.6 months) and median OS (14.0 vs 23.9months;p=0.216) in the BTG1del/IKZF1del were comparable to BTG1wt/IKZF1del respectively. So, the patients with co-existent BTG1 and IKZF1 deletions had outcomes comparable to those having IKZF1 deletions alone. Their outcomes were however worse than the groups with BTG1del/IKZF1wt (93.3% remission,-medianEFS 34.7months and medianOS not reached) and BTG1wt/IKZF1wt (85.3% remission, medianEFS 41.4months and medianOS not reached). (Fig.1)

Conclusion : BTG1 deletions were seen in 6.4%, IKZF1 deletions in 14.9%, and concomitant BTG1/IKZF1 deletions in 3.2% of the studied B-ALL cohort. The patients with concomitant BTG1/IKZF1 deletions had outcomes comparable to those with IKZF1 deletions alone. However, the outcomes in these groups were worse than the groups without any deletions of BTG1 & IKZF1; and, BTG1 deletions alone in absence of IKZF1 deletions.

Keywords : Acute lymphoblastic leukemia , BTG1, IKZF1, Childhood leukemia, B-ALL



PP03-7

Prognostic analysis of WT1 expression at diagnosis in pediatric acute lymphoblastic leukemia: A retrospective study from Seoul National University Children's Hospital

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Background : Pediatric acute lymphoblastic leukemia (ALL) is the most common malignancy in children. Recent global efforts have focused on genomic analysis in ALL, with ongoing debates surrounding the role of the Wilms tumor gene (WT1) in leukemia and its prognostic significance. Concurrently, research on the importance of minimal residual disease (MRD) in ALL has gained prominence, and the prognostic significance of MRD is increasing in pediatric ALL. In this study, we aim to analyze the prognostic effects of WT1 in pediatric ALL.

Method : From 2016 to 2023, we conducted WT1 testing on pediatric ALL patients diagnosed at Seoul National University Children's Hospital during initial bone marrow examinations. The quantification of WT1 mRNA expression levels was performed using real-time PCR, with WT1 copies expressed per 10,000 ABL copies. Statistical analysis was carried out using SPSS, including log-rank tests and Kaplan-Meier survival curves.

Results : A total of 162 pediatric ALL patients were analyzed, with a median age at diagnosis of 6.7 years (range, 0.1-18.2 years). The disease distribution comprised 147 cases of B cell ALL, 13 cases of T cell ALL, and 2 cases of acute leukemias of ambiguous lineage. The median WT1 value at diagnosis was 62.3 WT1/10,000 ABL (range, 0.2-16302.0). There were no significant differences in relapse rates (WT1 ≥1000 13.5% vs. WT1 <1000 10.4%, p=0.566), event-free survival (78.4% vs. 88.0%, p=0.136), and overall survival (89.2% vs. 93.6%, p=0.325) between the WT1 ≥ 1000 and <1000 groups.

Conclusion : According to this study, the expression level of WT1 in pediatric ALL does not appear to be statistically related to prognosis. However, given the limitations of this relatively small-scale study, future research should focus on large-scale analyses of WT1 expression in diverse patient populations. Additionally, further investigations are warranted to elucidate the role of WT1 in pediatric ALL.

Keywords : Pediatric acute lymphoblastic leukemia, Wilms tumor 1 gene, Prognosis

PP03-8

Key role of SOX4 and PI3k/AKT/mTOR pathway in relapsed pediatric precursor B cell acute lymphoblastic leukemia

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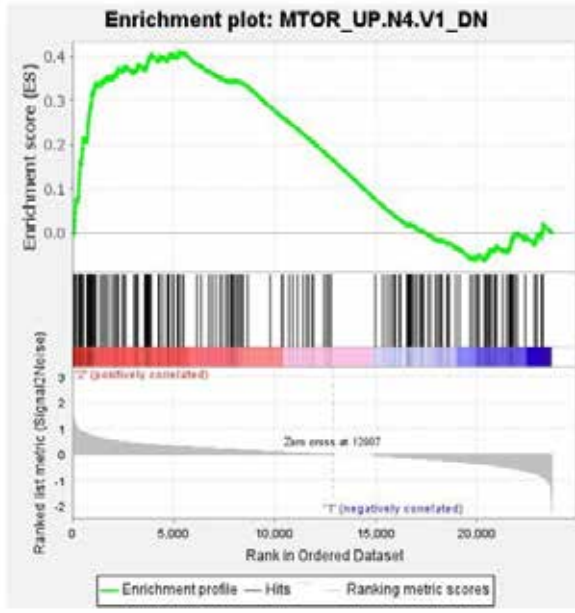
Background : The pathogenesis of pediatric acute lymphoblastic leukemia (ALL) relapse remains unclear. We undertook mRNA sequencing in paired relapse-complete remission (CR) bone marrow samples of 6 precursor B cell (Pre-B) ALL patients to clarify the major mechanisms underlying disease relapse.

Method : Median age at diagnosis of the 6 patients (male 4) was 7.0 years (range: 4.5 – 12.0). Initial risk group classification was as follows: standard (N=1), high (N=2), very high (N=3). Key genetic features at diagnosis included BCR::ABL1 (N=1), and IKZF1 deletion (N=1). From total RNA, libraries were prepared using the NEBNext Ultra II Directional RNA library prep kit, and mRNA was isolated by poly(A) RNA selection. High-throughput sequencing was performed as paired-end sequencing using NovaSeq 6000. Gene expression levels were estimated using FPKM values by Cufflinks.

Results : Initial interrogation of 991 genes with significant difference in gene expression at relapse compared to CR showed enrichment of genes in the transcriptional misregulation in cancer pathway. A subset analysis of 45 genes related to cell cycle, cell death and cell differentiation with significant difference in expression at relapse versus CR in all 6 patients also showed that these genes were involved in the following pathways: transcriptional misregulation in cancer, IL-17 signaling, B cell receptor signaling (KEGG pathway analysis). Among the 45 genes, SOX4 encoding SRY-box transcription factor 4 showed the highest fold-change increase in gene expression at relapse in the 6 patients. STRING analysis confirmed a SOX4-CD24 protein-protein interaction. Gene set enrichment analysis showed significant enrichment for mTOR pathway expression at relapse compared to CR ($P < 0.001$), consistent with SOX4 upregulation.

Conclusion : SOX4 overexpression and subsequent activation of the PI3K/AKT/mTOR pathway may have a key pathogenic role in relapsed pediatric Pre-B ALL.

Keywords : Acute lymphoblastic leukemia, Relapse, mRNA sequencing, Children, SOX4



PP03-9

Second hematologic malignancy risk following radioactive iodine therapy in thyroid cancer patients: A systematic review and meta-analysis

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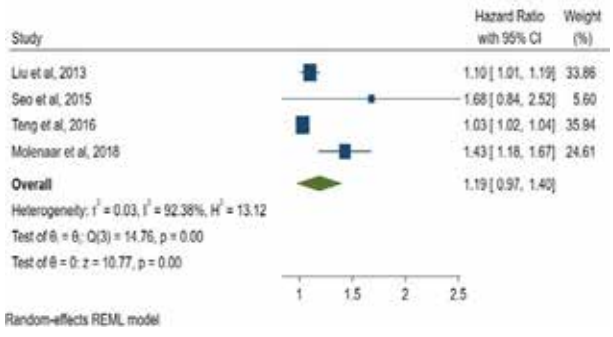
Background : Radioactive iodine (RAI) is widely used for the diagnosis and treatment of thyroid cancer patients. However, RAI usage is also related to the risk of developing second primary malignancies (SPMs) including hematologic malignancies. Despite being an essential concern in the survival of thyroid cancer patients, studies related to second hematologic malignancies (SHMs) were still minimal. Our objective was to determine whether RAI therapy increased the risk of SHMs in patients with thyroid cancer, compared to those not treated with RAI.

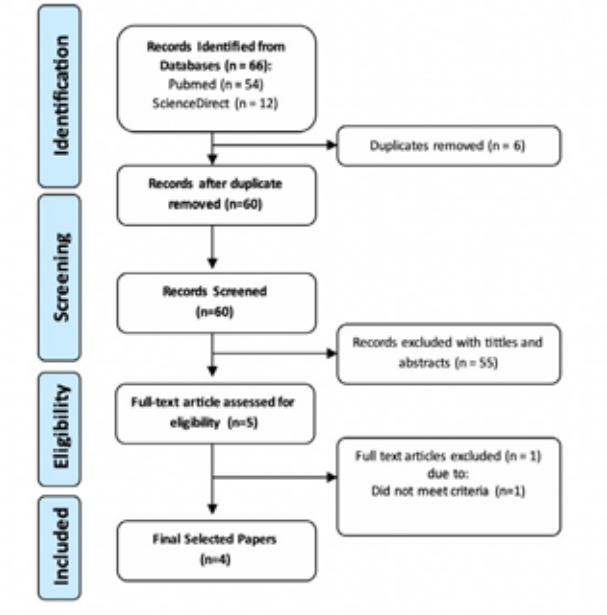
Method : We performed a comprehensive literature search from PubMed, ScienceDirect, and Cochrane Central databases from the year 2000 up to December 2023, using keywords (leukemia) AND (thyroid cancer) AND (radioactive iodine). We collected cohort studies with the presentation of hazard ratio comparing SHMs risk in thyroid cancer patients treated with RAI to those not treated with RAI. The analysis was conducted using STATA 17 to estimate the pooled hazard ratios (HR) and 95% confidence interval (95% CI).

Results : A total of 4 cohort studies were included after screening 60 titles and abstracts. We found that RAI therapy significantly increased the risk of SHMs in thyroid cancer patients (HR 1.19; 95% CI 0.97-1.40) in the overall analysis.

Conclusion : Our findings indicated that thyroid cancer patients who received RAI therapy are at a higher risk of developing SHMs compared to those not treated with RAI.

Keywords : Leukemia, Radioactive iodine, Second hematologic malignancy, Second primary malignancy, Thyroid cancer





PP03-10

Bioinformatics analysis of genomic alterations in pediatric acute lymphoblastic leukemia: Identifying prognostic markers and therapeutic targets

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Background : Pediatric acute lymphoblastic leukemia (ALL) presents a significant clinical challenge due to its heterogeneity and variable treatment responses. This study aims to investigate the genomic alterations contributing to treatment resistance and relapse in pediatric ALL. Through a detailed analysis of The Cancer Genome Atlas (TCGA) dataset, we focus on identifying somatic mutations with potential prognostic implications.

Method : We conducted a thorough examination of genomic data from pediatric ALL patients within the TCGA dataset. Integrating information from whole-genome sequencing and RNA-seq, we employed advanced bioinformatics tools to identify somatic mutations. Statistical analyses, including Bayesian inference, were utilized to discern significant mutations. Pathway enrichment analysis provided insights into the biological relevance of the identified genomic alterations. Notably, the TCGA dataset facilitated a robust and comprehensive exploration of the genomic landscape in pediatric ALL.

Results : Our analysis revealed a recurrent mutation in the NR3C1 gene, encoding the glucocorticoid receptor, in 15% of pediatric ALL cases (95% CI: 10-20%). Patients with NR3C1 mutations exhibited significantly lower event-free survival ($p < 0.05$), indicating a potential association with treatment resistance. Furthermore, a novel fusion event involving the PAX5 and ETV6 genes was identified in 8% of cases (95% CI: 4-12%), suggesting a potential link to early relapse. Pathway analysis identified dysregulation of the JAK-STAT signaling pathway in a subset of patients, offering potential therapeutic targets.

Conclusion : This comprehensive analysis of the TCGA dataset con-

tributes valuable insights into the genomic landscape of pediatric ALL. The identification of NR3C1 mutations and PAX5-ETV6 fusion events as potential prognostic markers underscores the importance of precision medicine in tailoring therapies. Dysregulation of the JAK-STAT pathway provides further avenues for targeted interventions, offering potential improvements in risk stratification and personalized treatment approaches for pediatric ALL patients.

Keywords : Pediatric acute lymphoblastic leukemia, Genomic alterations, Bioinformatics analysis, Prognostic markers, Precision medicine

PP03-11

Clinical implication of ponatinib salvage in adult patients with relapsed or refractory Philadelphia chromosome-positive acute lymphoblastic leukemia

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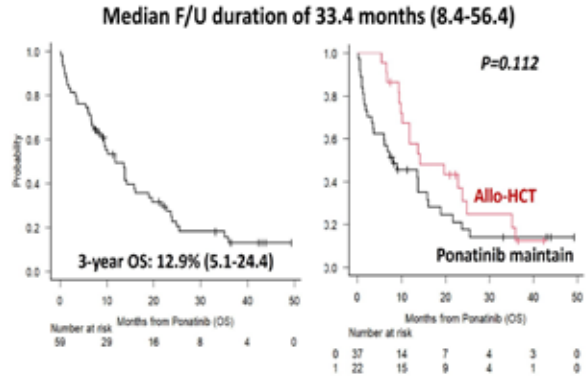
Background : The treatment strategy for Ph-positive ALL is based on tyrosine kinase inhibitors (TKI) and multiagent chemotherapy followed by allogeneic hematopoietic cell transplantation (allo-HCT). After relapse, next generation TKIs were evaluated in a few clinical trials. Ponatinib showed exceptionally good remission rate and MRD response, but long-term outcome was not good than expected. We tried to suggest Korean real-world data of ponatinib salvage in relapse or refractory (R/R) Ph-positive ALL.

Method : We analyzed 66 consecutive patients with R/R Ph-positive ALL treated with ponatinib from 2017 to 2022. Among them, 29 patients were primary refractory to imatinib and Dasatinib, 30 were relapsed patients after allo-HCT, and the rest 7 were ponatinib switching due to Dasatinib intolerance during preemptive therapy after allo-HCT. Final analysis was done in 59 patients excluding 7 preemptive switching. Ponatinib was initiated at a dose of 30mg (n=51) and 45mg (n=8).

Results : Out of the 59 patients, 4 were not evaluable due to early death and 55 were finally evaluated for response. Complete remission was achieved in 27 (49.1%) patients, and among them, complete molecular response was observed in 14 (51.9%), and major molecular response was in 5 (18.5%), and 8 (29.6%) were poor molecular responders. Twenty-two patients finally underwent allo-HCT but 14 subsequently relapsed at a median 158 days (range 26-517 days). Estimated 3-year OS was 12.9% and the outcome of patients who underwent allo-HCT was still poor with 3-year OS of 19.6%. For the 7 patients with preemptive ponatinib after Dasatinib intolerance, all except 1 relapsed patient are alive with maintaining complete molecular response.

Conclusion : Our data confirmed acceptable remission rate of ponatinib in R/R Ph-positive ALL, but long-term survival outcome was dismal even after allo-HCT. Ponatinib is not suitable for R/R setting and its frontline use should be the standard therapy for Ph-positive ALL.

Keywords : Acute lymphoblastic leukemia, Relapse, Refractory, Ponatinib, Salvage



PP03-12

Minimal residual disease-based effect and safety of frontline ponatinib plus hyper-CVAD treatment for adults with newly diagnosed Philadelphia chromosome-positive acute lymphoblastic leukemia

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Background : In adult patients with Philadelphia chromosome(Ph)-positive acute lymphoblastic leukemia(ALL), combination of tyrosine kinase inhibitor(TKI) and multi-agent chemotherapy is recommended as a standard frontline-therapy. Ponatinib plus hyper-CVAD was approved as a frontline-therapy for adult Ph-positive ALL in Korea since Sep 2023, we evaluated the effect and safety of the treatment in number of Korean patients.

Method : For adult patients diagnosed with Ph-positive ALL, two weeks of hyper-CVAD and ponatinib 45mg/day were administered for remission induction. Bone marrow biopsy was done after neutrophil and platelet recovery. By evaluating real-time quantitative PCR(5-log sensitivity) of BCR::ABL1 transcript, we assessed minimal residual disease(MRD)–based effect after the first cycle of treatment, while monitoring treatment-related toxicity. After assessment of the MRD, we restarted ponatinib at the dose of 15mg when achieving CMR(undetectable level of BCR::ABL1 transcript), while 30mg was administered if CMR achievement failed.

Results : From September to December 2023, ten consecutive patients(median age 41 years old, range 31-54) with Ph-positive ALL were treated with frontline ponatinib plus hyper-CVAD. Average time of recovery from cytopenia after treatment was 18 days, while average time of hopitalization was 29 days. After the first cycle of treatment, all patients(100%) achieved complete remission. 9(90%) of them had major molecular response(MMR, reduction of BCR::ABL1 ≤ 0.1%), while 4(40%) of them had CMR. There was no clinically significant adverse event(CTCAE Grade 4, 5) during treatment, while one patient had acute multifocal ischemic stroke with left sided weakness and facial palsy after treatment, which was self-resolved. Another two patients reduced dose(ponatinib 30mg) due to tinnitus and ear fullness.

Conclusion : Frontline ponatinib plus hyper-CVAD was effective for achieving complete remission with favorable molecular response compared to our previously published Imatinib or Dasatinib data. There was no significant drug-related adverse event that led to discontinuation. This analysis would be extended as Phase 2 observational study targeting 33 patient's accruals.

Keywords : Ph-positive ALL, Minimal residual disease, Ponatinib, Hyper-CVAD, Toxicity

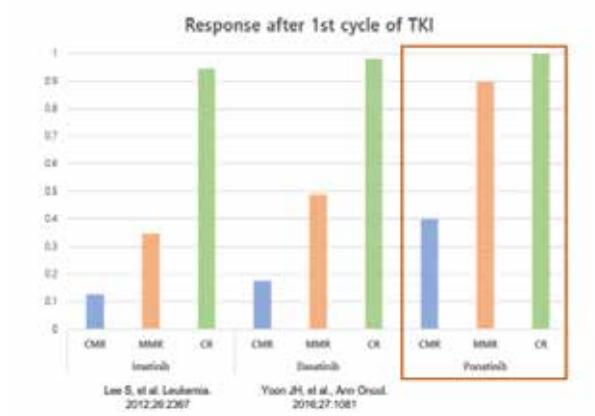

Figure 1. Response after 1st cycle of TKI (Imatinib, Dasatinib, Ponatinib)

	Induction	Consolidation
Multi agent chemotherapy	Hyper-CVAD (1cycle)	MTX/ARA, Hyper-CVAD alternative (2-6 cycles) / (2-4cycles) → Allo-HSCT
Ponatinib	45mg x 14d	30mg/d → 15mg/d after CMR

Table 1. Treatment schedule

Ponatinib	CMR	4/10 (40%)
	MMR	5/10 (50%)
	CR	10/10 (100%)
Imatinib (Lee S, et al. 2012)	CMR	12/85 (12.9%)
	MMR	33/85 (34.7%)
	CR	90/95 (94.7%)
Dasatinib (Yoon JH, et al. 2016)	CMR	9/51 (17.6%)
	MMR	25/51 (49.0%)
	CR	50/51 (98.0%)

Table 2. Response after 1st cycle of TKI (Imatinib, Dasatinib, Ponatinib)

Parameter		N (%)				
Toxicity (CTCAE Gr)	Total	1	2	3	4	5
Infection	5	0 (0)	1 (5.9)	4 (23.5)	0 (0)	0 (0)
Bacteremia	2	0 (0)	0 (0)	2 (11.8)	0 (0)	0 (0)
Disseminated zoster	1	0 (0)	0 (0)	1 (5.9)	0 (0)	0 (0)
Pneumonia	2	0 (0)	1 (5.9)	1 (5.9)	0 (0)	0 (0)
Hepatobiliary		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Increased Amylase/Lipase	1	0 (0)	0 (0)	1 (5.9)	0 (0)	0 (0)
Increased Transaminase	2	1 (5.9)	0 (0)	1 (5.9)	0 (0)	0 (0)
Cardiac		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hypertension	1	0 (0)	0 (0)	1 (5.9)	0 (0)	0 (0)
VTE (Stroke)	1	0 (0)	1 (5.9)	0 (0)	0 (0)	0 (0)
GI		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Constipation	1	0 (0)	1 (5.9)	0 (0)	0 (0)	0 (0)
Dyspepsia	1	0 (0)	0 (0)	1 (5.9)	0 (0)	0 (0)
Enterocolitis	1	0 (0)	0 (0)	1 (5.9)	0 (0)	0 (0)
Nausea	1	0 (0)	0 (0)	1 (5.9)	0 (0)	0 (0)
Others		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Folliculitis	1	0 (0)	0 (0)	1 (5.9)	0 (0)	0 (0)
Headache	1	0 (0)	1 (5.9)	0 (0)	0 (0)	0 (0)
Tinnitus	1	0 (0)	0 (0)	1 (5.9)	0 (0)	0 (0)

Table 3. Treatment related toxicities during and after treatment

PP03-13

The potential of extracellular vesicle derived micrornas as a biomarker in acute lymphoblastic leukemia

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Background : Extracellular vesicle (EV)-derived microRNAs (miRNAs) could be more valid as biomarkers because they are highly protected from degradation. In this study, we isolated miRNA in EVs from acute lymphoblastic leukemia (ALL) cell lines using a high-purity EV isolation method and attempted to validate its potential as a biomarker.

Method : Human ALL cell lines (primary cell line: CLL-119 and CRL-3273, chemo-resistant cell line: CRL-2264/CRL-2265 derived from CLL-119 and CRL-3274 derived from CRL-3273) were purchased from the American Type Culture Collection and cultured with EV-depleted fetal bovine serum according to protocol. EVs were isolated using size-exclusion chromatography, and sequencing was performed using Illumina HiSeq 2500. All data processing and visualization were conducted using R 4.0.3.

Results : A total of 122 EV-derived miRNAs were identified in all samples. We selected commonly downregulated or upregulated miRNAs by confirming changes in miRNA levels in CRL-2264 and CRL-2265 compared to CLL-119, as well as in CRL-3273 and CRL-3274 (miR-1226-5p and miR-760 were downregulated and miR-29b-3p was upregulated). To evaluate the potential of selected miRNAs as biomarkers, we investigated the correlation of these miRNAs and their correlated RNA with survival in patients with ALL using information from the cBioPortal and the GSE5314 database. In the miRNA-mRNA network analysis, higher expression of DDX24 in relation to downregulated miR-760 and lower expression of RGS1 in relation to upregulated miR-29b-3p were correlated with poor survival of ALL patients.

Conclusion : In conclusion, the results of this study demonstrated that EV-derived miRNAs may serve as prognostic biomarkers in ALL. However, further studies are needed to validate these EV-derived miRNAs in other cohorts.

Keywords : Acute lymphoblastic leukemia , Extracellular vesicle, Microrna

PP03-14

An updated meta-analysis of the association of IKAROS ZINC Finger 1 rs4132601 T>G gene polymorphism with acute lymphoblastic leukemia risk

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Background : Acute Lymphoblastic Leukemia (ALL) is one of the most common malignancy in childhood and its pathogenesis remains inconclusive. However, researchers strongly believe that genetic mutation plays major role on its progression. Moreover, several studies had discovered that mutations in the IKAROS Family Zinc Finger 1 (IKZF1) gene were related to malignancies' event in hematology. There are various studies carried out to examine the relationship between IKZF1 gene polymorphism and ALL risk, but the results remain doubtful and indeterminate. Therefore, this study was conducted to clarify the connection between ALL susceptibility and IKZF1 rs4132601 T>G Gene Polymorphism.

Method : This Meta-analysis was in accordance with the PRISMA guidelines. The literature was taken from Pubmed and Google Scholar, with August 2022 as the latest edition that was computed, and it is limited to English only. Total 8 studies were included in this review. A Review Manager 5.4 was utilized to analyze the data.

Results : 8 studies were incorporated. From the analysis, IKZF1 rs4132601 T>G gene polymorphism were associated with an increase of Acute Lymphoblastic Leukemia risk (G vs T, OR 95%CI = 1.41 [1.26-1.57] p< 0.00001; TG vs TT + GG, OR 95%CI = 1.24 [1.07-1.43] p= 0.005; GG vs TT + TG, OR 95%CI = 1.74 [1.37-2.22] p< 0.00001) and a decrease of Acute Lymphoblastic Leukemia risk (T vs G, OR 95%CI = 0.71 [0.64-0.79] p< 0.00001; TT vs TG+GG, OR 95%CI =0.68 [0.58-0.78] p< 0.00001)

Conclusion : There was correlation between IKZF1 rs4132601 T>G gene polymorphism and Acute Lymphoblastic Leukemia risk

Keywords : Acute lymphoblastic leukemia, Gene polymorphism, IKZF1

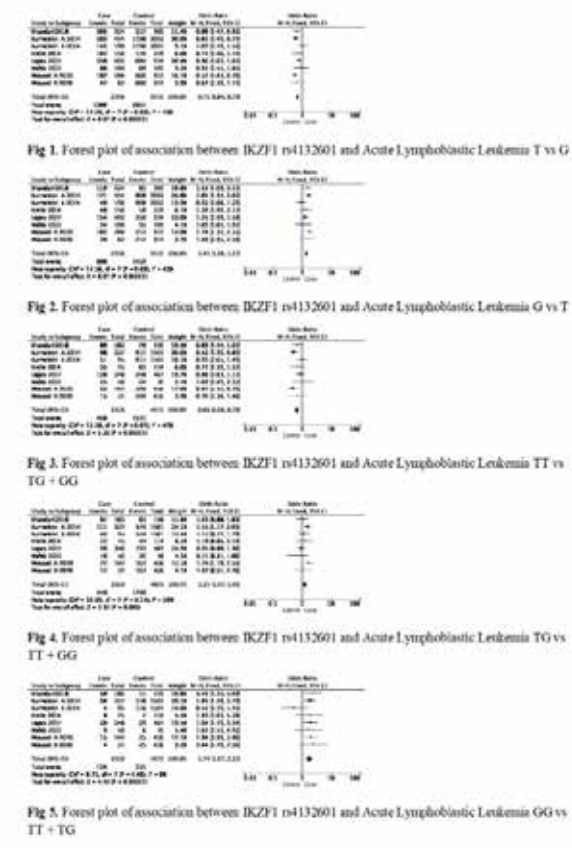

Fig 1. Forest plot of association between: IKZF1 rs4132601 and Acute Lymphoblastic Leukemia T vs G

Fig 2. Forest plot of association between: IKZF1 rs4132601 and Acute Lymphoblastic Leukemia G vs T

Fig 3. Forest plot of association between: IKZF1 rs4132601 and Acute Lymphoblastic Leukemia TT vs TG + GG

Fig 4. Forest plot of association between: IKZF1 rs4132601 and Acute Lymphoblastic Leukemia TG vs TT + GG

Fig 5. Forest plot of association between: IKZF1 rs4132601 and Acute Lymphoblastic Leukemia GG vs TT + TG

PP04-1

Aberrant DNA methylation of tumor suppressor gene as one possible mechanism of its under-expression in chronic myeloid leukemia patients in India

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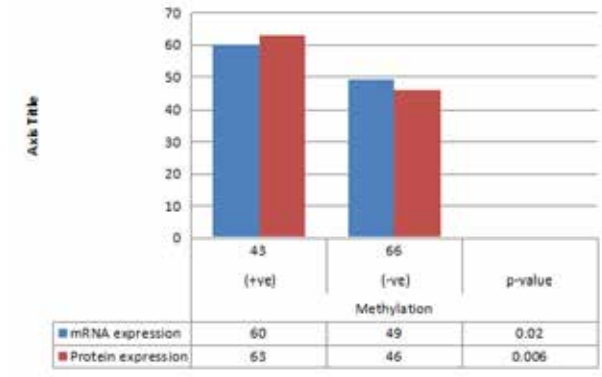
Background : Chronic myeloid leukemia starts in certain blood-forming cells of the bone marrow and it constitute about 30% to 60% of all adult leukemia in India. The BCR-ABL1 fusion oncogene involved in the pathogenesis of the disease. It translated into the BCR-ABL oncoprotein that activates number of pathways which affect the growth and survival of hematopoietic cells. However, the molecular mechanisms that initiate leukemogenesis are still unclear to date. Phosphatase and tensin homolog (PTEN) is frequently deleted in various tumors. It is down regulated by BCR-ABL in CML stem cells and its deletion is associated with acceleration of disease. However, it is unknown whether PTEN functions as a tumor suppressor in human Philadelphia chromosome–positive leukemia induced by the BCR-ABL oncogene in human.

Method : The study was design on 109 cases for detection of promoter methylation mutation and protein expression of PTEN gene. The methylation status was performed by methylation specific PCR. Sanger sequencing were applied for mutations detection across all the nine exons, while protein expression was evaluated by western blot respectively. Clinicopathologic parameters were finally correlated with above findings.

Results : Marginally high percentage (61%) cases were shown positive hypermethylation, in addition 72% cases shown loss of protein expression than control samples. The novel PTEN mutations were observed in 8.3%. Further, all mutated cases shown loss of PTEN expression, while 7/9 cases shown positive promoter methylation. Moreover, out of total methylated positive samples, 79% shown loss of PTEN expression and it was significantly correlated (p=0.06).

Conclusion : We found that promoter methylation is significantly correlated with loss of PTEN expression (61% vs 72 % respectively). This shows the possibility of involvement of PTEN hypermethylation in CML development. This further suggested that PTEN expression may be plays an important role in the susceptibility of the disease progression with valuable prognostic information to aid treatment strategies.

Keywords : PTEN, BCR-ABl, Chronic myeloid leukemia, Hypermethylation, Real time PCR



Clinicopathologic parameters		No. of samples	Methylation status of *PTEN*		mRNA expression of *PTEN*		Protein Expression of PTEN	
			+ve (%)	-ve (%)	+ve (%)	-ve (%)	+ve (%)	-ve (%)
		(n=109)	43	66	60	49	63	46
Age	=50	60	23	37	35	25	37	23
	=50	49	20	29	25	24	26	23
Sex	Male	75	27	48	42	33	44	31
	Female	34	16	18	18	16	19	15
Cryptogenic Test	Ph(+)(9;22)	102	40	62	54	48	57	45
	Ph(-)(9;22)	7	3	4	6	1	6	1
BCR-ABL fusion transcript	BCR-ABL (+ve)	103	40	63	56	47	59	44
	BCR-ABL (-ve)	6	3	3	4	2	4	2
PTEN Mutation	Mutation (+ve)	9	5	4	4	5	4	5
	Mutation (-ve)	100	38	62	56	44	59	41
Phase at Diagnosis	Chronic Phase	89	36	53	49	40	52	37
	Accelerated Phase	20	7	13	11	9	11	9
Smoking history	Smokers	64	21	43	38	26	40	24
	Non-smokers	45	22	23	22	23	23	22
Treatment	Glevec	103	40	63	57	46	60	43
	Other	6	3	3	3	3	3	3
WBC	=11 103/ul	101	41	60	54	47	57	44
	=11 103/ul	8	2	6	6	2	6	2
Hemoglobin	=12 mg/dl	79	30	49	50	29	52	27
	=12 mg/dl	30	13	17	10	20	11	19

Method : Biological potential of Hinokiflavone in the medicine for the treatment of myeloid leukemia have been investigated in the present work through scientific data analysis of different scientific research work. Biological potential of Hinokiflavone for their antitumor effect in chronic myeloid leukemia (CML) cells have been investigated with their possible molecular mechanisms in order to know the therapeutic effectiveness of Hinokiflavone on chronic myeloid leukemia. Biological potential of hinokiflavone on the viability of K562 cells has been investigated. However, other pharmacological activities of Hinokiflavone have been also investigated in the present work.

Results : Biological potential of Hinokiflavone for their effectiveness against chronic myeloid leukemia has been investigated through measurement of cell viability and was found to have significant effectiveness. Scientific data analysis revealed that Hinokiflavone has significant potential on the viability of K562 cells which was further found to be effective via different signaling pathway. Scientific data analysis revealed its biological potential as a potential therapeutic agent for the treatment of chronic myeloid leukemia.

Conclusion : Scientific data revealed the biological potential of Hinokiflavone against myeloid leukemia in medicine.

Keywords : Hinokiflavone, Chronic myeloid leukemia, Flavonoid, Phytochemical

PP04-2

Biological potential and therapeutic effectiveness of Hinokiflavone for the treatment of chronic myeloid leukemia with their molecular mechanisms

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Background : Flavonoids class phytochemical are important natural compounds commonly called secondary metabolites and found to be present in different types of plants and their derived products. Flavonoid class phytochemical is having important biological function mainly due to their anti-oxidant, anti-inflammatory, anti-bacterial, and anti-viral activities. Chronic myeloid leukemia is a type of tumor mainly occurred through hematopoietic stem cells. Hinokiflavone is an important class of bioflavonoid found to be present in the Rhus succedanea, Garcinia multiflora and Dacrydium balansae.

PP04-3

Methylenetetrahydrofolate reductase A1298C gene polymorphism with risk of chronic myeloid leukemia: Updated meta-analysis

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Background : Chronic myeloid leukemia (CML) has increased in incidence and prevalence in recent years. The etiology of CML is uncertain and therefore studies in genetics might provide insights into how the disease behaves. There is a concept that the pathogenesis of CML is correlated to folate metabolism. Folic acid metabolism is contributed by several enzymes, one of the most prominent has been attributed to 5,10-methylenetetrahydrofolate reductase

(MTHFR). Several studies discovered the association between MTHFR A1298C gene polymorphism and CML risk, however, published results were indeterminate. Therefore, this study was conducted to investigate the connection between CML susceptibility and MTHFR A1298C gene polymorphism.

Method : This Meta-analysis was following the PRISMA guidelines. The literature was taken from Pubmed and Google Scholar, with December 2019 as the latest edition that was computed, and it is limited to English only. A total of 6 studies were included in this review. A Review Manager 5.4 was utilized to analyze the data.

Results : 6 studies were incorporated. From the analysis, MTHFR A1298C gene polymorphism was associated with an increase of CML (C vs A, OR 95%CI = 1.48 [1.29-1.71] p< 0.00001; CC vs AA + AC, OR 95%CI = 2.64 [1.90-3.66] p<0.00001) and a decrease of CML (A vs C, OR 95%CI = 0.67 [0.58-0.78] p<00001; AA vs AC + CC, OR 95%CI =0.69 [0.57-0.84] p= 0.0001)

Conclusion : There was a correlation between MTHFR A1298C gene polymorphism and CML.

Keywords : Chronic myeloid leukemia, Folate metabolism, Gene polymorphisms, MTHFR A1298C

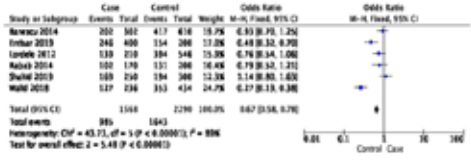

Fig 1. Forest plot of association between MTHFR A1298C gene polymorphism and CML risk A vs C

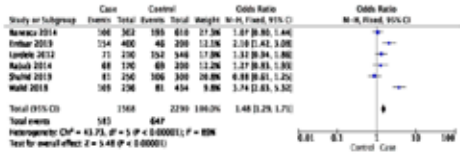

Fig 2 Forest plot of association between MTHFR A1298C gene polymorphism and CML risk C vs A

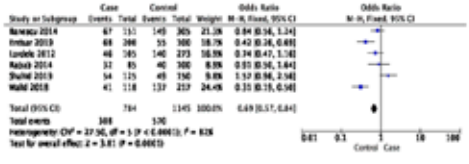

Fig 3. Forest plot of association between MTHFR A1298C gene polymorphism and CML risk AA vs AC + CC

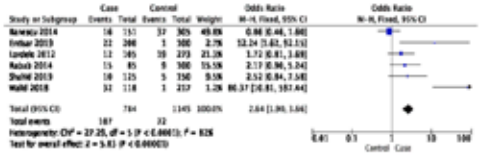

Fig 4. Forest plot of association between MTHFR A1298C gene polymorphism and CML risk CC vs AA + AC

PP04-4

Improvement of treatment-free remission rate following discontinuation of BCR::ABL1 tyrosine kinase inhibitors with longer treatment duration in chronic myeloid leukemia

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Background : To investigate a safer condition of treatment free remission (TFR) in chronic myeloid leukemia (CML), we conducted a study to discontinue BCR::ABL1 tyrosine kinase inhibitor (TKI) treatment with the longer duration of treatment duration and molecular response.

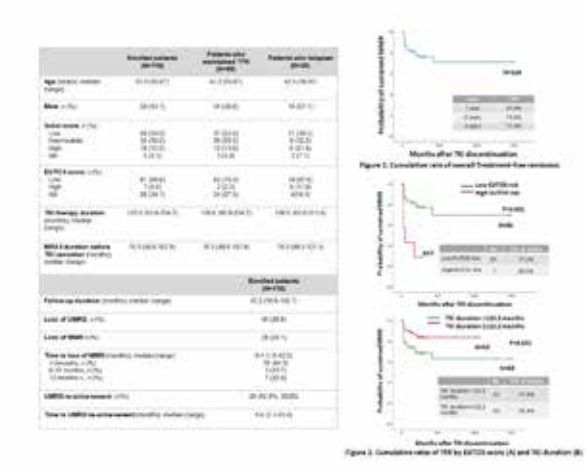
Method : We enrolled newly diagnosed chronic-phase CML (CP-CML) patients who initially received TKIs and maintained MR4.5 for at least 4 years. In the case of relapse, defined as loss of major molecular response (MMR), the last TKI therapy was reintroduced, and molecular responses were monitored monthly until the achievement of MMR.

Results : Prior to discontinuation, all 116 CP-CML patients received TKIs for a median of 122.2 months (range, 63.6-224.7), and the duration of sustained MR4.5 was 75.0 months (range, 48.6-157.9). Of them, 85 were treated with imatinib, and 31 used one of 2G TKIs as first-line TKI. At the time of discontinuation, 93 (80.2%) were using first-line TKI, while 13 (11.2%) and 10 (8.6%) patients were taking second- and third-line TKI, respectively. All reasons for changing TKI before treatment discontinuation were intolerance. With a median

follow-up of 42.2 months (range, 10.9-150.7), 28 (24.1%) patients lost their response at a median of 8.4 months (range, 1.8-42.0), and the TFR rates at 12, 24, and 48 months were 81.9%, 76.0%, and 71.0%, respectively. No progression toward advanced-phase CML occurred. The TKI treatment duration of 10 years or more was the only significant predictor for TFR (P<0.027).

Conclusion : This study suggests that TFR success rate can be improved in patients who receive longer treatment duration. However, safer indications ensuring over 90% TFR success rate at 5 years have not yet been determined.

Keywords : Chronic myeloid leukemia, Tyrosine kinase inhibitor, Treatment free remission



PP04-5

Association between waist circumference, body mass index, high-density lipoprotein cholesterol level, and risk of chronic myeloid leukemia

Ka Young Kim[1], Daehun Kwag[1], Jung Yeon Lee[1], Gi-June Min[1], Sung-Soo Park[1], Silvia Park[1], Jae-Ho Yoon[1], Byung-Sik Cho[1], Ki-Seong Eom[1], Yoo-Jin Kim[1], Seok Lee[1], Chang-Ki Min[1], Hee-Je Kim[1], Seok-Goo Cho[1], Jong Wook Lee[1], Kyung Do Han[2], Sung-Eun Lee[1*]

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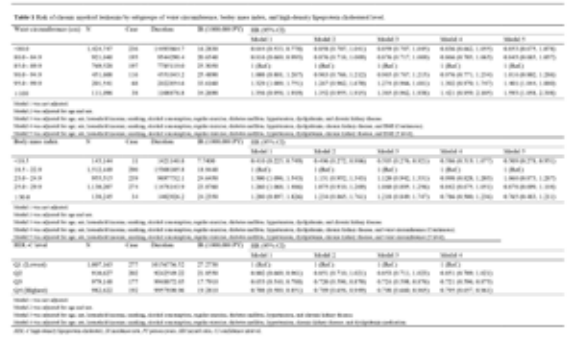
Background : Advances in the treatment of chronic myeloid leukemia (CML) have resulted in increased prevalence. However, a more comprehensive understanding of its pathogenesis and epidemiology is necessary. Recent studies suggested the association between altered lipid metabolism and carcinogenesis, prompting an investigation of the relationship between metabolic disorders and incidence of CML. Thus, we conducted a study to examine the association between waist circumference, body mass index (BMI), high-density lipoprotein cholesterol (HDL-C), and the incidence of CML.

Method : Using data from the Korean National Health Insurance Service from 2009 to 2017, a competing risks regression was conducted to examine the hazard ratios of CML in 3,879,560 individuals aged 20 years and above.

Results : During a mean of 10.13±1.24 years of follow-up, there were a total of 848 cases of CML, including 539 male and 309 female patients. 1) Individuals in the group with a waist circumference equal to or greater than 100cm had the greatest risk of CML (adjusted hazard ratio [aHR], 95% CI = 1.593, 1.058-2.398), compared to those with a waist circumference from 80 to less than 85cm. 2) Those with a BMI less than 18.5 showed the lowest incidence of CML ([aHR], 95% CI = 0.509, 0.278–0.931) in comparison to the reference population with a BMI between 18.5 and 22.9. 3) Individuals in the highest quartile of HDL-C had the lowest risk of CML ([aHR], 95% CI = 0.795, 0.657–0.961) compared to those in the lowest HDL-C quartile.

Conclusion : A large waist circumference was significantly associated with increased risk of CML, whereas a low BMI and high HDL-C were associated with a reduced risk of CML. This suggests that a large waist circumference may be an independent risk factor of CML, whereas a low BMI and high HDL-C may be association with a protective effect against CML.

Keywords : Chronic myeloid leukemia, Metabolic syndrome, Korean national health Insurance service, Risk factors



PP04-6

Enumeration of CD26+ leukemic stem cells from peripheral blood using multiparametric flow cytometry: A potential tool for rapid diagnosis of chronic myeloid leukemia

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Background : The potential utility of CD26+ leukemic stem cells (LSCs) as a diagnostic marker in chronic myeloid leukemia (CML) has recently been investigated. In this study, we employed flow cytometric immunophenotyping to evaluate the diagnostic relevance of CD26+ CML LSCs, its role in follow up and correlation between peripheral blood (PB) and bone marrow (BM) CD26+ CML LSCs.

Method : Patients aged >12 years with a clinical suspicion and morphological diagnosis of CML were included. PB and BM samples were utilized for CD26+ LSC enumeration. A pre-titrated antibody cocktail was prepared, containing CD45, CD34, CD38, and CD26 monoclonal antibodies. Peripheral blood from patients with diseases other than CML, BCR::ABL1 negative (such as non-CML MPNs, Acute Leukemias, MDS/MPNs, and Reactive bone marrows) served as controls. Reverse Transcriptase (RT-PCR) was performed to determine the BCR::ABL1 transcript type in all cases. FISH was also conducted in a subset of cases to analyze BCR::ABL1 positivity in sorted CD26+ leukemic stem cells.

Results : A total of N=151 samples were tested (112 PB and 41 BM) from 111 patients, comprising newly diagnosed CML (N=77), CML on follow-up (N=15) and non-CML control group (N=21). CD26+ LSCs were observed in 100% of patients with a documented molecular genetic BCR::ABL1 fusion. The median count of CD26+ LSCs was 0.125% (range 0.002%–26.79%). None of the patients in the control group (N=21) displayed the presence of CD26+ LSCs. Also, a strong correlation (r=0.917) was seen between the reported CD26+ CML LSCs in PB and BM.

Conclusion : Due to its consistent positivity in all CML cases and its cost-effectiveness combined with rapidity, the detection of CD26+ LSCs by flow cytometry shows promise as a potential surrogate for molecular genetic techniques for diagnosis of CML. Further research is needed to elucidate the role of CD26+ LSCs in monitoring residual disease and evaluating the 'stem cell response.'

Keywords : CML, CD26, Leukemic stem cells, Myeloproliferative neoplasm, TKI

PP04-7

A successful leukapheresis in the management of chronic myeloid leukemia (CML) patients with pulmonary leukostasis: A case report and review of the literature

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Background : Leukemia is a hematological malignancy characterized by the production of abnormal white blood cells (leukocytes) in the bone marrow, with impaired normal hematopoiesis and cytopenia. Hyperlekocytosis is one of the most common complications of leukemia that leads to leukostasis. Leukostasis is an emergency condition where there is blockage of small blood vessels due to malignant blast cells which will cause ischemia in tissues or organs which will increase morbidity and mortality

Method : We report a successful leukapheresis in the management of chronic myeloid leukemia (CML) patients with pulmonary leukostasis

Results : 48-year-old female patient with chief complaint of shortness of breath on activity since 1 week before admission. Headache since 3 months before. Loss of weight of 15 kg in the last 1 year. previous history of hyperleukocytosis. On examination, it was found that SaO2 was 93% room air, conjunctival anemia, no rales and wheezing, tribe's space dullness, splenomegaly Schaffner 5/8, Hb 8.4, leukocytes 585,000, hematocrit 22.2%, platelets 610,000, peripheral blood smear showed leukocytes. the number is greatly increased, blast cells (+), shift to the left, chest X-ray showed suspect leukostasis lung, abdominal ultrasound shows Hepatosplenomegaly, suggesting hematologic disease, Cholelithiasis multiple (> 10

seeds), the largest size is 9 cm and bone marrow aspiration indicates chronic phase CML

Conclusion : The patient was given therapy with Hydroxyurea and underwent leukapheresis. The results after the therapy showed that Pulmo's chest radiology was within normal limits, and no infiltrate was seen

Keywords : CML, Leukapheresis, Leukostasis, Pulmonary leukostatics

PP04-8

The role of the microbiome gut axis in the development and relapse of chronic myeloid leukemia: Systematic review

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Background : Chronic Myeloid Leukemia (CML) is a form of leukemia involving genetic changes in blood cells. Despite advances in therapy, disease progression and the risk of relapse remain challenges. Recent research highlights the Microbiome Gut Axis (MBGA) as a key factor in treatment response and relapse risk. Further understanding of the interaction between gut microbiota and the immune system is needed to unlock innovative treatment strategies and relapse prevention in CML.

Method : Journals were selected from the PubMed, Google Scholar, and ResearchGate database using keywords "Chronic Myeloid Leukemia," "Microbiome Gut Axis," and "Leukemia Treatment." Selected journals emphasize the role of gut microbiota in treatment response and relapse risk. The PICO eligibility criteria guided the selection process, focusing on CML patients, MBGA intervention, without specific comparisons, and outcomes related to disease development and relapse risk in CML.

Results : Gut microbiota shapes an immunosuppressive microenvironment, fostering tumor progression and relapse. Studies associate gut microbiota with hematological cancer development and treatment, highlighting the potential benefits of microbes in relapse prevention. A complex microbial ecosystem's impact on cancer is revealed, and specific taxa influencing leukemia risk are identified. Emphasis is placed on gut microbiota's role in relapse predisposition, and microbial classes and families with protective effects on leukemia are highlighted, unveiling a reciprocal relationship between gut microbiota and leukemia.

Conclusion : MBGA has the potential to influence treatment response and relapse risk in CML. Alterations in gut microbiota can be targeted to enhance treatment effectiveness and prevent relapse. Further research is needed to gain a deeper understanding of the mechanisms of MBGA interaction in the context of CML.

Keywords : Chronic myeloid leukemia, Microbiome gut axis, Gut microbiota, Hematological cancer treatment, Relapse

PP04-9

Impact of first-line and second-generation tyrosine kinase inhibitors on quality of life in chronic myeloid leukemia: Insights from a multi-center prospective study

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Background : The introduction of tyrosine kinase inhibitors (TKIs) has revolutionized the treatment landscape of chronic myeloid leukemia (CML). However, the influence of these novel targeted therapies on the quality of life (QoL) of CML patients remains a critical area for investigation. This prospective, multi-center study aims to assess and compare the QoL outcomes among CML patients receiving first-line TKIs (imatinib) versus second-generation TKIs (dasatinib or nilotinib).

Method : We conducted a collaborative, longitudinal study involving 3 major medical centers and a total of 120 adult CML patients newly diagnosed within the last six months. Patients were stratified into two groups based on their prescribed TKI: Group A (imatinib) and Group B (dasatinib or nilotinib). QoL assessments were performed at baseline, 3 months, 6 months, and 12 months using disease-specific instruments, including the EORTC QLQ-CML24 and FACT-Leu. Clinical parameters, including molecular response rates and adverse events, were recorded. Statistical analyses included repeated measures ANOVA and logistic regression to identify predictors of QoL outcomes.

Results : At baseline, both groups demonstrated impaired QoL, with mean EORTC QLQ-CML24 scores of 50.2 (Group A) and 49.8 (Group B). Over the study period, Group B exhibited a more rapid improvement in symptom burden, with a statistically significant increase in physical well-being at 6 months ($p < 0.05$). Notably, patients in Group B achieved higher rates of major molecular response at 12 months (78% vs. 62% in Group A, $p = 0.03$), correlating with improved overall QoL.

Conclusion : This multi-center study provides specific insights into the differential impact of first-line and second-generation TKIs on QoL in CML patients. Our findings suggest that the early use of second-generation TKIs may result in more favorable QoL outcomes and improved molecular responses. Tailoring treatment strategies across diverse clinical settings is crucial in the management of CML.

Keywords : Chronic myeloid leukemia (CML), Quality of life (QoL), Prospective study, Tyrosine kinase inhibitors (TKIs), Multi-center analysis

PP04-10

Paclitaxel and curcumin as dual-drug-loaded lipid nanocapsules exhibited protective effect against chronic myeloid leukemia via promotes apoptosis and suppress the BCR/ABL

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Background : Chronic Myeloid Leukemia (CML) is primarily an adult-onset leukemia, it can occur at any age, the incidence of CML tends to increase with age, and it is more commonly diagnosed in adults. CML is characterized by the uncontrolled growth of myeloid cells in the bone marrow and their accumulation in the blood. The current study was fabricating the Drug laoded nanocasules (DNC) of Paclitaxel and Curcumin and investigated the ability to suppress the CML cell proliferation.

Method : A risk-based approach was to use to develop the DLN of paclitaxel and curcumin and optimize the quality attributes. Also used the I-optimal response surface design for validation the formulation. The DNC was investigated against the different celllines such as TCCY-T315I (human imatinib-resistant) or K562 (human wild-type) and the Ba/F3-(T315I/E279K/Y253H) (mouse BCR/ABL point mutation-transfected cells) for cell proliferation and also estimated the mRNA expression.

Results : The optimized (DNCs), loaded with two drugs, exhibited a diameter of 171.3 nm, a polydispersity index of 0.281, and achieved a high encapsulation efficiency exceeding 90%, along with a drug loading capacity of 11.12%. Employing the microdialysis bag method for in vitro drug release studies, it was observed that over 70% of the medication was released within an 8-hour timeframe. DNCs remarkably suppressed the phosphorylation of BCR/ABL and their subsequent molecular signals such as MAPK and AKT activation. DNC induces the release cleaved caspase-3 and cleaved PARP induced apoptosis and suppressed the cell viability of these cells. DNC appeared to be more sensitive to imatinib resistant (T315I, Y253H, and E279K) than wild-type BCR/ABL cells, suggesting the beneficial effect to overcome imatinib-resistant serves issues in CML.

Conclusion : The findings indicate that Drug laoded nanocasules (DNC) inhibit the function of BCR/ABL and its downstream molecular signaling pathways, such as AKT and MAPK.

Keywords : Chronic myeloid leukemia, Dual-drug-loaded lipid nanocapsules , Apoptosis, Cytotoxicity

PP04-11

Predictive factors of patients with chronic phase chronic myeloid leukemia treated with tyrosine kinase inhibitor

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Background : Chronic Myeloid Leukemia (CML) is a hematological malignancy caused by an abnormality of the Philadelphia chromosome. Along with the development of CML treatment, the discovery of tyrosine kinase inhibitors (TKI) paved the way for CML patient and lead to longer survival rate. It is very important to know whether the treatment response is successful or not as well as the predictive factors that can improve the therapeutic response of CML patients treated with TKI.

Method : This study is an observational cohort study conducted for 12 months long and involving 40 CML patients treated with TKI, both hematological and molecular therapy response were evaluated in this study. We analyzed some predictive factors such as relationship between early clinical and laboratory symptoms before the treatment by TKI and treatment response and the relationship between Eutos, Sokal and Hasford scores and treatment response.

Results : A total of 40 chronic phase CML patients, consist of 25 men (62.5%) and 15 women (37.5%) with mean age of 37 years. Complete Hematologic Response (CHR) after 3 months of TKI therapy was achieved by 15 patients (37.5%). The number of patients who achieved 6-months CHR increased to 19 patients (47.5%). Among 37 samples who performed quantitative examination on fusion of the breakpoint cluster region (BCR) gene on chromosome 22 gene in band q11 and Abelson murine leukemia (ABL1) gene on chromosome 9 band q34 (BCR-ABL), 20 patients (54%) achieved major molecular response (MMR), and the remaining 17 (45.9%) had not yet achieved MMR. We found significant relationship between basophils and quantitative BCR-ABL levels ($p<0.01$). We didn't find any relationships between these three scores (Eutos, Sokal and Hasford) with treatment response, both hematological and molecular treatment response.

Conclusion : We found that basophil percent at 3 months after treatment is predictive factor and significantly associated with quantitative BCR-ABL levels.

Keywords : Chronic myeloid leukemia, Predictive factors, Treatment response

PP04-12

Low level mutations in the BCR-ABL1 kinase domain confers resistance to tyrosine kinase inhibitor in chronic myeloid leukemia patients

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Background : BCR-ABL1 kinase domain (KD) mutations are a well-known cause of resistance to tyrosine kinase inhibitors (TKIs) in patients with chronic myeloid leukemia (CML) and can lead to treatment failure. Rapid therapeutic assessment and individualization based on mutation status are crucial for optimal patient management. However, current methods for mutation detection are laborious, time-consuming and have limited sensitivity.

Method : Our study aims to investigate the landscape of BCR-ABL1 KD mutations in Malaysian CML patients with imatinib-resistance. A cohort of 84 CML patients who do not respond to TKI and 18 CML patients achieving stable optimal responses to TKI was enrolled in this study. Sequencing of patients' cDNA was performed using Sanger sequencing (SS) and next generation sequencing (NGS).

Results : In total, 12 different BCR-ABL1 KD mutations were identified by SS in 22.6% (19/84) of patients who were resistant to TKI treatment. Interestingly, NGS analysis of the same patient group revealed an additional four different BCR-ABL1 KD mutations in 27.4% (23/84) of patients. These mutations are M244V, A344V, E355A, and E459K with variant read frequency below 15%. All of the mutations detected by both SS and NGS are frequently involved in acquired resistance to TKIs in CML patients. On the other hand, no mutation was detected in 18 patients with optimal response to TKI therapy.

Conclusion : In conclusion, our study has demonstrated that resistance to TKIs is associated with the acquisition of additional mutations in BCR-ABL1 KD after treatment with TKIs. Moreover, the use of NGS is advised for accurately determining the mutation status of BCR-ABL1 KD, particularly in cases where the allele frequency is low, and for identifying mutations across multiple exons simultaneously. Therefore, the utilization of NGS for the identification of BCR-ABL1

KD mutations is essential for guiding treatment decisions and predicting response to therapy.

Keywords : Chronic myeloid leukemia, BCR-ABL1 kinase domain mutation, Tki resistance, Next generation sequencing, Sanger sequencing

PP05-1

In silico electrophysiological study reveals ibrutinib, an important therapeutic agent for B-cell lymphoma causes cardiac toxicity by inhibiting sodium current

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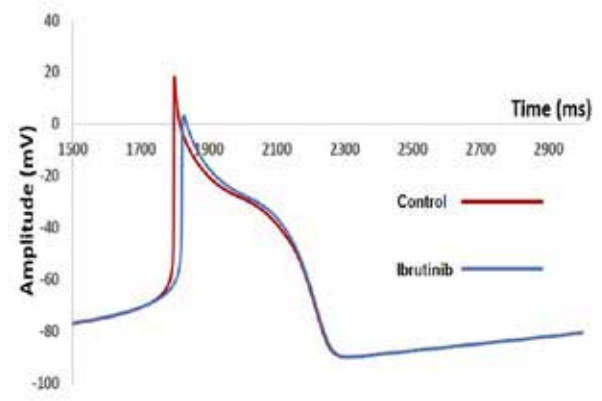
Background : Ibrutinib is a small-molecule drug that acts as an irreversible inhibitor of Bruton's tyrosine kinase and is used as an important therapeutic agent for B-cell lymphoma. Cardiotoxicity due to the use of Ibrutinib is still under clinical investigation. The purpose of this study is to clarify the propensity of Ibrutinib concentration to modulate cardiac electrophysiological properties.

Method : The electrophysiological setup of the sinoatrial node (SAN) comprises the inward rectifier ion channels, voltage-gated sodium channel, voltage-gated potassium channel, L-type calcium channel, calcium-dependent potassium channel, funny current channel, and calcium diffusion mechanisms. Concentration-dependent Ibrutinib (0.1 µmol/L to 10 µmol/L) profile for 200 ms is induced to alter the conductance of voltage-gated sodium ion channel (Nav1.5) and then incorporated into the SA node electrophysiology.

Results : First, we reproduced the current-voltage curve profile of the Nav1.5 ion channel regarding multiple doses of Ibrutinib under the voltage clamp protocol. It showed a continuous decrease of inward current because of multiple doses of Ibrutinib. At the highest concentrations (10 µmol/L), the peak of the inward current reduced to 26% of its control value. The current-voltage curve is shifted to a 20% more positive side and the half-activation potential is increased by 28%. Then, the altered inward current is incorporated into the whole-cell model to investigate the AP firing patterns. For 10 µmol/L of Ibrutinib, the repolarization phase of AP was prolonged and the frequency of the firing pattern was reduced. Figure 1 shows the AP for both the control and Ibrutinib injections.

Conclusion : Our study suggests that Ibrutinib at a higher concentration reduces the frequency rate of the spontaneous AP firing by suppressing the Nav1.5 current. Therefore, the dosage of Ibrutinib should be controlled to avoid cardiac toxicity. Further clinical trials are essential to analyze its' subcellular mechanisms.

Keywords : Ibrutinib, Lymphoma, Cardiac toxicity, Electrophysiology



PP05-2

Subcutaneous epcoritamab plus lenalidomide in patients with relapsed/refractory diffuse large B-cell lymphoma from EPCORE NHL-5

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Background : Epcoritamab, a subcutaneous CD3xCD20 bispecific antibody, is approved in the US for adults with R/R DLBCL NOS, including DLBCL arising from indolent lymphoma and high-grade B-cell lymphoma after ≥2 lines of systemic therapy. We present results from the phase 1b/2 EPCORE NHL-5 (NCT05283720) study arm 1 evaluating epcoritamab+lenalidomide for R/R DLBCL, representing the first data of a bispecific antibody plus lenalidomide in this population.

Method : Adults with CD20+ R/R DLBCL (ECOG 0-2) received subcutaneous epcoritamab (cycles 1-3: QW, cycles 4-12: Q4W) and oral lenalidomide (days 1-21: QD) for twelve 28-day cycles. Primary G-CSF prophylaxis was not mandatory. Patients received ≥1 prior systemic therapy containing an anti-CD20 antibody. The primary endpoint was dose-limiting toxicities (DLTs). Secondary endpoints included investigator-assessed ORR and time-to-response (TTR). Safety endpoints included severity/incidence of adverse events (AEs), including AEs of special interest (CRS, ICANS, and clinical tumor lysis syndrome).

Results : As of May 22, 2023, 26 patients (DLBCL, n=24 [92%]; follicular lymphoma grade [G] 3b, n=2 [8%]) received epcoritamab+lenalidomide. Fifteen patients (58%) received 1 prior line of anticancer therapy; 6 (23%) received prior CAR T; 2 received HSCT. One DLT (neutropenia) was observed; G3-4 treatment-emergent AEs (TEAEs; ≥10%) are shown (Table). TEAEs led to epcoritamab discontinuation in 1 patient (3.8%; thrombocytopenia). No G5 TEAEs were considered related to epcoritamab. CRS was predominantly low grade and occurred mostly after first full dose (C1D15). Preliminary biomarker analysis showed pharmacodynamic profiles consistent with the epcoritamab MOA. One patient experienced ICANS (G3), which resolved after 2 days. Among response-evaluable patients (n=24), ORR was 75% (CR: 58%; PR:17%); 3 PRs were ongoing at data cutoff (Table). Median TTR was 1.8 months. Fifteen patients (58%) remain on epcoritamab+lenalidomide. Follow-up is ongoing.

Conclusion : Epcoritamab+lenalidomide showed promising antitumor activity in patients with R/R DLBCL with a manageable safety profile and no new safety signals.

Keywords : Epcoritamab, Lenalidomide, R/R DLBCL

Table. Antitumor activity and safety of epcoritamab in patients with R/R DLBCL

Response	Response-evaluable patients (N=24)
Median duration of epcoritamab exposure, mo (range)	3.8 (0-7.5)
Median duration of lenalidomide exposure, mo (range)	4.0 (0.1-8.2)
Overall response rate, n (%; 95% CI)	18 (75.0) 95% CI: 53.3, 90.2
Complete response	14 (58.3)
Partial response	4 (16.7)
Stable disease	1 (4.2)
Progressive disease	3 (12.5)
Not evaluable	2 (8.3)
Median time to complete response, mo (range)	1.9 (1.6-3.6)
Median time-to-response, mo (range)	1.8 (1.0-2.8)
Safety	**All patients (N=26)**
Grade ≥3 TEAEs (≥10%)	
Neutropenia	15 (58)
Anemia	4 (15)
Thrombocytopenia	4 (15)
Febrile neutropenia	3 (12)

Data cutoff date: May 22, 2023. Response assessments were based on Lugano 2014 response criteria by investigator assessment.
DLBCL, diffuse large B-cell lymphoma; R/R, relapsed/refractory; TEAE, treatment-emergent adverse event.

PP05-3

The clinical impact of PDGFR expression in patients with relapsed/refractory non-hodgkin lymphoma treated with imatinib-combined chemotherapy: A pilot study

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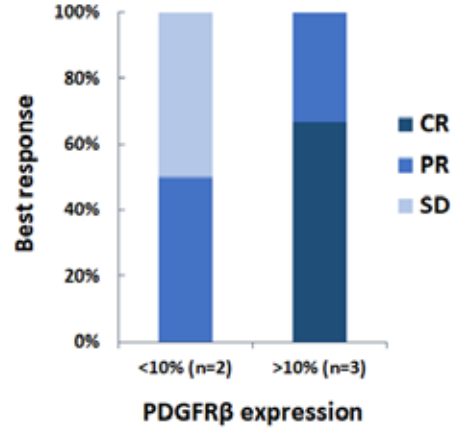
Background : Platelet-derived growth factor receptor (PDGFR) is considered one of the main targets for the treatment of relapsed/refractory non-Hodgkin lymphoma (NHL). We investigated PDGFR expression and response to imatinib-ESHAP treatment to determine whether PDGFR expression could be a major target of imatinib in relapsed/refractory NHL. Additionally, we evaluated PDGFR signaling and the effect of imatinib in lymphoma cell line.

Method : We evaluated PDGFRα, β, and c-kit expression in tumor tissues of relapsed/refractory NHL. In addition to ESHAP, imatinib was administered at a dose of 200 mg or 400 mg per day for 21 days, and the best response was confirmed. In addition, we confirmed PDGFR signaling in Pfeiffer cells expressing PDGFRα and confirmed the cytotoxic response to imatinib administration.

Results : From February 2017 to February 2021, 6 patients were recruited and received a total 27 cycles of imatinib and ESHAP. In 4 patients (66.7%), PDGFRβ expression of more than 10% was confirmed. There was no expression of PDGFRα and c-kit. In patients with PDGFR-β expression of less than 10%, partial response and stable disease were observed in one patient each. Among the patients whose PDGFR-β expression was more than 10%, complete response and partial response were observed in 2 and 1 patients, respectively, and 1 patient died before evaluation. In Pfeiffer cells, p-PDGFRα, p-AKT, and p-ERK were significantly increased by PDGF-AB treatment. When Pfeiffer cells were treated with imatinib, p-PDGFRα and p-AKT were decreased, but p-ERK was increased and maintained for 16 hours. Administration of PD98059, a MEK inhibitor, with imatinib inhibited p-ERK and increased cytotoxicity. A synergistic cytotoxic effect was confirmed when imatinib, PD98059 and rituximab were administered together.

Conclusion : In patients with relapsed/refractory NHL with PDGFR expression, imatinib may be considered, and combination treatment with MEK inhibitors or rituximab can be expected.

Keywords : Platelet-derived growth factor receptor, Non-Hodgkin lymphoma, Imatinib mesylate, MEK inhibitor, Rituximab



PP05-4

Matching-adjusted indirect treatment comparison of axicabtagene ciloleucel and historical treatments in high-risk large B-cell lymphoma using Samsung Medical Center lymphoma registry

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Background : Axicabtagene ciloleucel (Axi-cel), a novel CAR T-cell therapy, demonstrated efficacy in the ZUMA-12 trial for high-risk large B-cell lymphoma (LBCL) patients. However, being a single-arm trial, ZUMA-12 has inherent limitations in delivering pertinent impli-

cations for medical practitioners. We aimed to assess the effectiveness of Axi-cel through comparison of an external control group and a single-arm clinical trial.

Method : We performed a retrospective study using the data of Samsung Lymphoma Cohort Study III (NCT03117036, Samsung Medical Center-Lymphoma Cohort Study (SMC-LCS III) between March 2017 to June 2023 and ZUMA-12 published data between February 2019 to October 2020. By using SMC-LCS III as an external comparator, we conducted matching-adjusted indirect treatment comparison (MAIC). We measured overall survival (OS) and progress free survival (PFS) associated with Axi-cel by comparing published summary data from ZUMA-12 trial and individual patient data from SMC-LCS III.

Results : Patients of the external comparator were selected from the SMC-LCS III according to the inclusion criteria of ZUMA-12: 1) high-grade B-cell lymphoma with MYC and BCL2 and/or BCL6 translocations, or diffuse large B-cell lymphoma (DLBCL) not otherwise specified with an IPI score of ≥3 at initial diagnosis; 2) patients had any PET-positive lesions (Deauville score of 4 or 5) after two cycles of chemoimmunotherapy consisting of an anti-CD20 antibody, and an anthracycline-containing regimen. Based on the inclusion criteria, 45 patients with high-risk LBCL were identified from SMC-LCS III (median age 61) and 40 were identified from summary data of ZUMA-12 trial (median age 64). After weighting, use of Axi-cel was associated with a decreased risk of death with HR of 0.34 (95% CI 0.14-0.84); disease progression with HR of 0.25 (95% CI 0.13-0.50).

Conclusion : In this retrospective external comparator study, Axi-cel therapy reduced the risk of death and disease progression compared with the conventional first-line chemotherapy among patients with high-risk LBCL.

Keywords : Matching-adjusted indirect treatment comparison, Axi-cel, External comparator study, High-risk large B-cell lymphoma, Registry

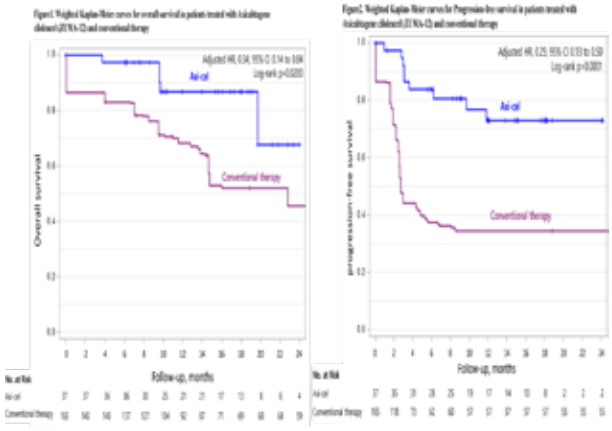

Table.1 Characteristics of the patients in the ZUMA-12 and SMC-LCS at baseline, before and after weighting

	Before weighting			After weighting		
	ZUMA-12 trial (Axicabtagene ciloleucel) N=40	SMC-LCS (Conventional therapy) N=45	aSD	ZUMA-12 trial (Axicabtagene ciloleucel) N=40	SMC-LCS (Conventional therapy) N=165	aSD
Age, median (range), years	61 (23 - 86)	64 (34 - 83)		61 (23 - 86)	63 (34 - 83)	
Age ≥ 65 years, n(%)	15 (38)	22 (49)	0.22	15 (38)	62 (38)	0
Male sex, n(%)	27 (68)	24 (53)	0.31	27 (68)	112 (68)	0
Histological disease type per investigator,n(%)						
DLBCL not otherwise specified	22 (55)	36 (80)	0.55	22 (55)	91 (55)	0
HGBL, Double-hit lymphoma	18 (45)	9 (20)	0.55	18 (45)	74 (45)	0
ECOG performance status score of 1, n (%)	25 (63)	17 (38)	0.51	25 (63)	105 (63)	0
Disease stage, n (%)						
1 or 2	2 (5)	3 (7)	0.08	2 (5)	8 (5)	0
3 or 4	38 (95)	42 (93)	0.08	38 (95)	157 (95)	0
IPI total score, n (%)						
1 or 2	9 (23)	1 (2)	0.67	9 (23)	38 (23)	0
3 ≤	31 (77)	44 (98)	0.65	31 (77)	127 (77)	0
Deauville five-point scale, n (%)						
4	19 (48)	36 (80)	0.71	19 (48)	79 (48)	0
5	21 (52)	9 (20)	0.73	21 (52)	86 (52)	0
Bone marrow assessment, n (%)						
Lymphoma present	10 (25)	11 (24)	0.02	10 (25)	35 (21)	0.1
Double- or triple-hit status by FISH per central laboratory and IPI total score, n (%)						
Double- or triple-hit and IPI ≥3	4 (10)	9 (20)	0.28	4 (10)	44 (27)	0.45
Double- or triple-hit only	6 (15)	1 (2)	0.48	6 (15)	38 (23)	0.20
IPI ≥3 only	27 (68)	35 (78)	0.23	27 (68)	83 (50)	0.37

PP05-5

The role of small bowel video capsule endoscopy in determining the treatment strategy for duodenal follicular lymphoma

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Background : Duodenal follicular lymphoma (DFL) is a rare type of non-Hodgkin lymphoma that arises in the duodenum. Because of its indolent nature and generally favorable prognosis when compared with other lymphomas, DFL treatment options range from watch and wait to radiotherapy or systemic chemotherapy.

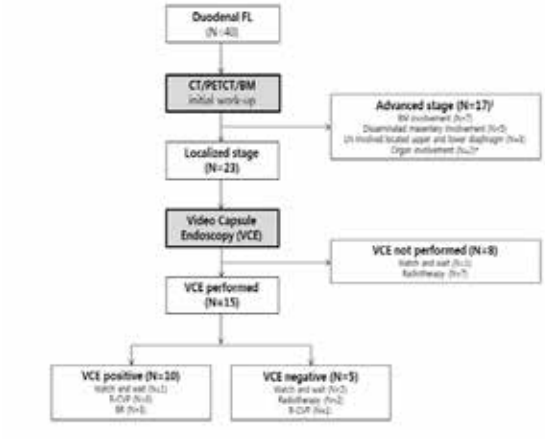
Method : This single-center study involved the retrospective analysis

of clinical and imaging data from 40 patients diagnosed with DFL at Seoul St. Mary's Hospital between 2015 and 2022.

Results : Imaging workup and bone marrow biopsies revealed that 22 patients presented with DFL only in the gastrointestinal tract (stage I), one in local lymph nodes (stage II_1), three in distant lymph nodes (stage II_2), one in the pancreas (stage $II_2E_{pancreas}$), and 13 in extranodal regions (stage IV). Of the 23 patients with localized (stages I and II_1) DFL, 15 underwent video capsule endoscopy (VCE) for comprehensive small bowel evaluation, which revealed that in 10 patients (66.7%), the lesions extended beyond the duodenum. Of the 10 patients, one elected the watch and wait strategy, whereas nine underwent systemic chemotherapy. Of the eight patients who did not undergo VCE, seven underwent radiotherapy, and one observation. Overall, nine of 23 patients (39.1%) received systemic treatment based on positive VCE results. Of the 17 advanced-stage patients (stages II_2 and IV), only one accepted radiotherapy, whereas 16 underwent systemic chemotherapy. The enrolled DFL patients' treatment algorithms for either localized or advanced stages are presented in Figure 1. During follow-up (median: 48.4 months, range: 12.4–96.2 months), only two relapse events occurred in the advanced stage, and there were no lymphoma-associated deaths.

Conclusion : Our findings indicate that DFL tends to be indolent, with favorable outcomes. When diagnosing DFL, it is recommended to proactively conduct VCE to determine small bowel involvement, which may influence treatment decisions.

Keywords : Duodenal follicular lymphoma, Video capsule endoscopy, Chemotherapy



PP05-6

Mitigating cytokine release syndrome (CRS) in diffuse large B-cell lymphoma (DLBCL) with cycle 1 optimization: Preliminary results from EPCORE NHL-1

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Background : The subcutaneous CD3xCD20 bispecific antibody epcoritamab is approved for the treatment of adults with different types of relapsed/refractory (R/R) large B-cell lymphoma after ≥2 lines of systemic treatment in various geographies, including the US, Europe, and Japan. In the phase 1/2 trial EPCORE™ NHL-1 (NCT03625037) dose-expansion cohort, CRS occurred in 49.7% of patients and was primarily low grade (G; 31.8% G1, 15.3% G2, 2.5% G3). Here we report a cycle (C) 1 optimization strategy designed to mitigate CRS.

Method : Adults with R/R CD20+ DLBCL and ≥2 prior treatment lines received epcoritamab (0.16/0.8-mg step-up and 48-mg full doses) in 28-d cycles until progressive disease or unacceptable toxicity (QW, C1–3; Q2W, C4–9; Q4W, C≥10). For CRS mitigation, patients received dexamethasone 15 mg, diphenhydramine, and acetaminophen prior to each dose and dexamethasone prophylaxis (D2–4, D9–11, D16–18, D23–25) in C1. Adequate hydration and holding antihypertensives 24 h before treatment were also recommended. Proactive hospitalization was not required. The primary endpoint was CRS rate (any grade and G≥2).

Results : As of April 21, 2023, 24 patients were treated in this C1 optimization cohort (median age, 65 y; primary refractory, 75%; median follow-up, 1.3 mo). The most common treatment-emergent AEs (TEAEs) were infections (38%; COVID-19, 8%), fatigue (21%), CRS (17%), and headache (17%). All CRS events were G1 and resolved (median time to resolution, 3.5 d); most occurred after the first full dose (C1D15), and none led to epcoritamab discontinuation. One patient received tocilizumab. No patients experienced ICANS, clinical tumor lysis syndrome, or fatal TEAEs. Median circulating IL-6 level at C1D16 was lower in the C1 optimization cohort (6.92 pg/mL) vs expansion (21.24 pg/mL). T-cell activation was not compromised.

Conclusion : Rate and severity of CRS were reduced in an optimization cohort in which dexamethasone prophylaxis and hydration were recommended.

Keywords : Clinical trials, Non-Hodgkin lymphoma, B-cell lymphoma, Aggressive lymphoma, Bispecific antibody therapy

PP05-7

Physician-reported treatment patterns and outcomes in marginal zone lymphoma in South Korea

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Background : Due to the rarity of marginal zone B-cell lymphoma (MZL), its management remains largely understudied. Only 1 chemoimmunotherapy—cyclophosphamide, vincristine, and prednisone plus rituximab (R-CVP)—is reimbursed in the first-line setting in South Korea. This study assessed physician-reported treatment patterns and outcomes in patients with advanced-stage MZL.

Method : Twelve South Korea–based hematologists were surveyed in 2023. They had at least 5 years of experience managing at least 10 patients with MZL per year and spent at least 4 days per week directly involved in patient care. Based on their clinical practice and experience, physicians responded to questions on the proportion of patients prescribed first-, second-, and third-line treatments and the most prescribed treatments for nodal MZL (NMZL), extranodal MZL (EMZL), and splenic MZL (SMZL). Medians were reported.

Results : Among patients with advanced-stage MZL, 90% received first-line systemic treatment, most commonly R-CVP (NMZL, 70%; EMZL, 80%; SMZL, 75%). Approximately 25% of patients with advanced-stage MZL who received first-line systemic treatment had relapse or recurrence; of these patients, at least 75% received second-line treatment. Choice of second-line and third-line treatments was more varied. The most prescribed second-line systemic treatments were bendamustine with rituximab (EMZL, 25%; NMZL, 12%); ifosfamide, carboplatin, and etoposide (NMZL, 25%; SMZL, 20%); and dexamethasone, cytarabine, and cisplatin (DHAP) (SMZL, 20%). DHAP was the most common regimen for SMZL. Approximately 30% of patients who received second-line treatment received third-line treatment, with the most frequently reported treatment being DHAP (NMZL, 20%; EMZL, 25%; SMZL, 10%).

Conclusion : This survey provided valuable insights about treatment patterns and outcomes in patients with advanced MZL. While the choice of first-line treatment was relatively consistent, more guid-

ance is needed on the selection of subsequent treatments.

Keywords : Marginal zone lymphoma, Treatment patterns, Advanced-stage

PP05-8

The long-term impact of rituximab-based chemoimmunotherapy in patients with DLBCL, real world outcomes using National Health Insurance Database of South Korea

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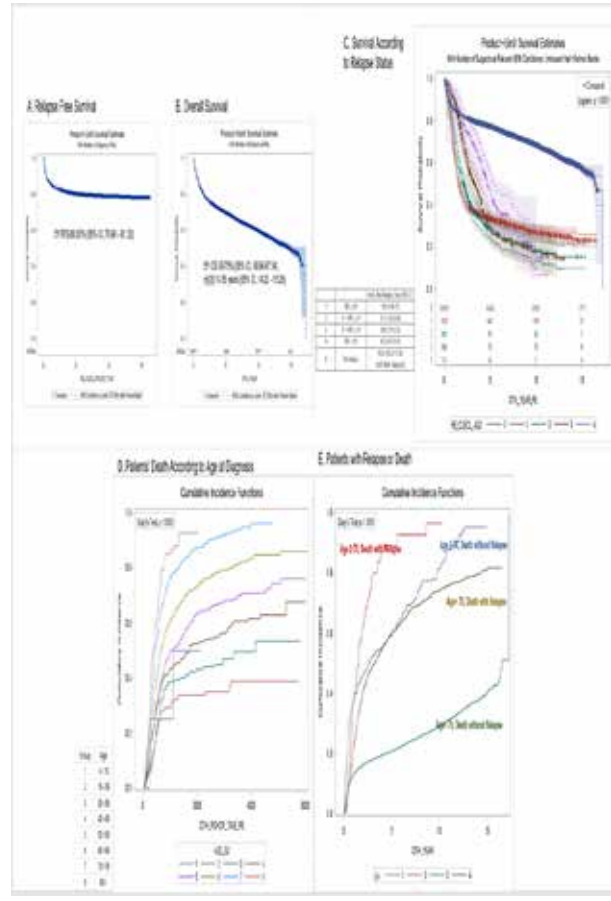
Background : We analyzed the long-term impact of rituximab (R) based chemoimmunotherapy (CIT) in patients with DLBCL.

Method : From 2005 to 2018, de novo DLBCL patients who were completed at least 3 cycles of R-CIT as an induction therapy were extracted from National Health Insurance Database of South Korea. Time to next treatment was used as a surrogate marker of relapse-free survival (RFS).

Results : From 2005 to 2021, total 20,038 patients were diagnosed as de novo DLBCL. Among the newly diagnosed de novo DLBCL, 13,577 (67.8%) patients were completed R-CIT. The mean age of these patients at diagnosis was 58 years (SD 14.84), with patients between 50 and 79 years of age accounting for 68.9% of all patients. The median follow-up duration for the eligible patients was 12.4 years. A total of 2724 (20.1%) patients relapsed during this time and 5-year RFS was 80.65% (Figure A). Patients relapsing after 5 years accounted for 4.7% of all relapses. The 5-year survival rate was 69.75% and the median survival was 14.85 years (Figure B). The survival after relapse increased significantly with the later time of recurrence (Figure C). Among the patients who died during follow-up, more patients died from causes other than relapse (n=3143) than from recurrence (n=1896). The cumulative mortality rate of patients tended to increase with age at diagnosis (Figure D). Patients older than 70 had a higher cumulative mortality rate than patients younger than 70 who relapsed, even though they did not relapse (Figure E).

Conclusion : R-CIT seems to have contributed to prolonged survival and RFS. However, there are still unmet need to overcome the poor prognosis associated with early relapse. Given that DLBCL patients are often elderly at diagnosis, we have to develop supportive measures to reduce the non-relapse related mortality as well as safe salvage therapies to improve survival after relapse.

Keywords : DLBCL, Rituximab, Relapse, Survival



		Total (N=13,577)
Age	mean(SD)	58.02 (14.86)
	0-14	21
	15-29	636
	30-39	994
	40-49	1966
	50-59	3196
	60-69	3382
	70-79	2783
	80-	599
Sex		
	Male	7463
	Female	6114
Total # of R-CHOP		
	3	1122
	4	1280
	5	1267
	6	7898
	7	503
	8	1507
Unerlying Disease		
	DM	7165
	HTN	7450
	Hyperlipidemia	9903
	IHD	3940
	Stroke	1946
Death		5039
Death	with relapse	1896
	without relapse	3143
Relapse		2724
	RFS ≤ 1Y	1836
	1Y < RFS ≤ 2Y	362
	2Y < RFS ≤ 5Y	396
	RFS > 5Y	130
No event		7710
Median duration of follow-up		12.4 Years

PP05-9

Outcomes in refractory diffuse large B-cell lymphoma: Results from subgroup analysis of two prospective Korean cohort studies

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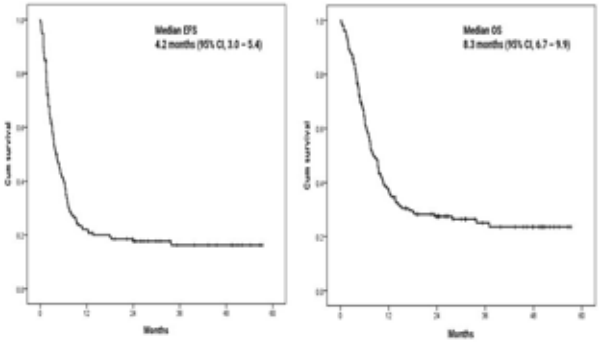
Background : The superiority of second-line chimeric antigen receptor T-cell therapy over standard of care (SoC) followed by autologous stem cell transplantation (ASCT) for relapsed or refractory diffuse large B-cell lymphoma (RR-DLBCL) have been demonstrated in several large-scaled phase III studies. To further define outcomes of RR-DLBCL patients who had been treated with SoC, we have carried out subgroup analysis of two prospective Korean cohort studies.

Method : The primary data consist of patients from two prospective cohort studies that include over 1,500 DLBCL patients treated with R-CHOP (#NCT01202448 and #NCT02474550). RR-DLBCL was defined as 1) no response from R-CHOP; 2) relapse within 12 months after the completion of R-CHOP; 3) received systemic treatment for RR-DLBCL except radiation or intrathecal therapy. The primary endpoint of the study was event-free survival (EFS) defined as the time from beginning of the second-line treatment to the earliest date of disease progression, new treatment, or death from any cause.

Results : A total of 159 patients met the criteria for RR-DLBCL after a median time to progression of 5.9 months (95%CI 5.5-6.3). The median age was 62 (range, 21–86), and 106 (68.4%) patients were male. SoC regimens included platinum-based combinations (n=120, 77.4%), high-dose MTX combinations (n=13, 8.4%), ifosfamide/etoposide combinations (n=11, 7.1%), and bendamustine-rituximab (n=6, 3.9%). The overall response rate was 35.5% (55/155), and the CR rate was 18.1% (28/155). The estimated median EFS was 4.2 months (95%CI 3.0-5.4). The median OS was 8.3 months (95%CI 6.7-9.9). Among 93 patients who were 65 years-old or younger, 30 patients (32.3%) could proceed to ASCT, and their median EFS was 7.1 months (95%CI, 4.3–9.9) and the median OS was not reached.

Conclusion : In line with previous studies, the outcomes of current analysis showed devastating outcomes of RR-DLBCL patients when they were treated with SoC. Therefore, these patients should promptly be approached to novel therapies.

Keywords : Diffuse large B-cell lymphoma, Refractory, Relapse, Standard of care



PP05-10

Trial in progress: A global phase 2 basket trial of nanatinostat in combination with valganciclovir in patients with EBV-positive (EBV+) relapsed/refractory lymphomas (NAVAL-1)

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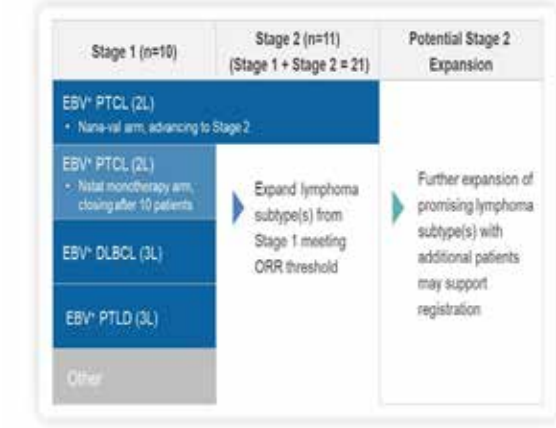
Background : Epstein-Barr virus-positive (EBV+) lymphomas are a heterogeneous group of malignancies that harbor latent EBV within the lymphoma cells, and the outcomes in EBV+ lymphoma patients are typically inferior compared to EBV– lymphomas of the same subtype. As there are no approved targeted treatments specific for EBV+ lymphomas and the poor prognosis of relapsed/refractory (R/R) disease, treatment of R/R EBV+ lymphoma is an unmet medical need. The all-oral combination of nanatinostat (Nstat), a potent Class-I HDACi, and valganciclovir (VGCV), a pro-drug of ganciclovir (GCV), is a novel mechanism to kill EBV+ tumor cells through inducing the expression of the lytic BGLF4 protein kinase to activate the nucleoside analog GCV, resulting in termination of DNA replication and apoptosis. The combination of Nstat+VGCV was generally well-tolerated and showed promising preliminary activity in a Phase 1b/2 study of patients with R/R EBV+ lymphoma (NCT03397706), with an ORR/CR of 40%/19% in efficacy-evaluable patients. Patients with T/NK-NHL had an ORR/CR of 60%/27%; in EBV+ DLBCL,NOS, the ORR/CR was 67%/33%. In addition, the degree of EBER-ISH positivity(%) was not related to the clinical response, with the majority of patients having a baseline EBER-ISH below 50% (Haverkos 2021).

Method : NAVAL-1 is an international, open-label, multicenter, single-arm, basket design trial(Simon, 1989). 3 subtypes of R/R EBV+

lymphomas are represented: EBV+ DLBCL, NOS, PTCL(including PTCL-NOS, AITL) and PTLD. Eligible patients have R/R EBV+ lymphoma after ≥2 prior systemic therapies(≥1 prior systemic therapy for PTCL), with no curative therapy available, measurable disease according to Lugano 2007, and adequate hematopoietic, hepatic and renal function. Patients will receive Nstat 20 mg daily, 4 days weekly with VGCV 900 mg daily, 7 days weekly to evaluate overall response rate, overall and progression-free survival, time to progression, safety, and pharmacokinetics.

Results : Enrollment began in May 2021 with more than 75 study sites worldwide. NCT No.: NCT05011058.

Keywords : EBV lymphoma, EBV positive T cell lymphoma, Peripheral T cell lymphoma (PTCL), Diffuse arge B-cell lymphoma (DLBCL), Post-transplant lymphoproliferative disorders (PTLD)



PP05-11

Time to next treatment in patients with pre-treated cutaneous T-cell lymphoma receiving mogamulizumab or vorinostat: a MAVORIC post-hoc analysis

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Background : CTCL is a rare group of NHL of T-cell origin, characterized by relapsing/remitting behavior and progressive resistance to treatments, with a median time to next treatment (TTNT) in mycosis fungoides (MF) and Sézary syndrome (SS) of 5.4 months (mo) (Hughes CF, et al. Blood, 2015). In the phase 3 MAVORIC study, mogamulizumab (MOGA) was superior to vorinostat (VORI) in progression-free survival (median 7.7 vs 3.1 mo, P<0.0001) and confirmed overall response rates (28% vs 4.8%, P<0.0001) in previously treated patients with MF/SS (Kim YH, et al. Lancet Oncol 2018). This post-hoc analysis examines TTNT to further explore the patient clinical experience.

Method : Previously treated patients with MF/SS (n=372) were randomized 1:1 to receive MOGA (1.0 mg/kg, administered once weekly for the first 28-day cycle, then on Days 1 and 15 of subsequent cycles) or oral VORI (400 mg daily). Patients on VORI were permitted to crossover to MOGA upon approval (eg disease progression or intolerable toxicity). TTNT was defined as time to any significant therapy. The length of TTNT was assessed overall and by disease stage grouping (IB/II and III/IV) and disease type (MF and SS).

Results : Median TTNT for the full ITT population was longer with MOGA at 11 mo (95% CI, 8.8–12.6) compared to VORI at 3.5 mo and consistently longer for MOGA vs VORI across disease stage grouping or by disease type (Table). In subjects who crossed over to MOGA, median TTNT was 10 months (95%CI, 8.0–12.6).

Conclusion : TTNT in MF/SS represents a measure of clinical benefit and disease control in patients who may have progressed based on strict protocol definitions of progression. This post hoc analysis shows prolonged TTNT across disease stages and types, and supports a clinical benefit for MF and SS patients who receive MOGA.

Keywords : Cutaneous T-cell lymphoma (CTCL), Mycosis fungoides (MF), Sezary syndrome

Table. TTNT, Overall and By Disease Stage and Type

Median TTNT (mo), 95% CI	N	MOGA	N	VORI	*P*-value (stratified log-rank)
Intent-to-treat population	186	11.0 (8.8–12.6)	186	3.5 (3.1–4.3)	<0.0001
Stage IB/II	68	7.0 (4.9–10.1)	72	3.3 (2.8–4.9)	0.0664
Stage III/IV	118	12.9 (10.6–16.7)	114	3.5 (2.8–4.7)	<0.0001
MF	105	8.8 (6.1–11.5)	99	4.1 (3.1–5.2)	0.0038
SS	81	12.9 (10.7–16.7)	87	3.3 (2.6–3.8)	<0.0001

PP05-12

Characterization and outcomes in patients with mogamulizumab-associated skin reactions in the Mavoric trial

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Background : In the MAVORIC trial of mogamulizumab (Moga) vs vorinostat (Vori) in patients (pts) with relapsed/refractory mycosis fungoides (MF) or Sézary syndrome (SS) (NCT01728805), moga-associated rash (MAR) was the second most common TEAE in the Moga treatment arm. This analysis describes drug rash (DR) characteristics in pts receiving Moga.

Method : 372 pts randomized 1:1 to receive intravenous Moga (1.0 mg/kg once weekly for Cycle 1 (28 days); days 1 and 15 of subsequent cycles) or oral Vori (400 mg daily). Pts with Grade 1 DR continued Moga, with topical steroids as needed. Pts with Grade ≥2 DR temporarily stopped Moga and used topical steroids. Systemic steroids were prohibited. Treatment resumed if DR resolved to Grade

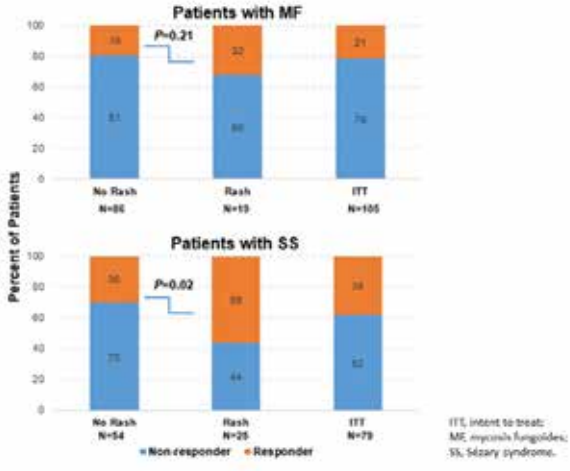
≤1 within 2 weeks. This analysis included 44 Moga pts with DR. Central review assessed DR as granulomatous, histiocytic spongiotic, lichenoid, eosinophilic, psoriasiform, or a combination.

Results : MAR displayed heterogeneous histopathology with no predominant feature. More pts with SS (56.8, 25/44) experienced DR vs MF pts (43.2%, 19/44). Median (Q1, Q3) Moga exposure was 344 days (162, 652) in SS DR pts and 185 days (85, 463) in MF DR pts. Proportion of SS responders with DR was significantly higher than those without DR (P=0.02; Figure); proportion of MF responders with DR did not differ from those without DR (P=0.21). Median (Q1, Q3) time to onset of DR was 106 days (36, 254). Initial DR occurred after response to Moga in 70% (14/20) of pts who experienced both. 35 pts (80%) resumed Moga treatment upon DR resolution, with median (Q1, Q3) duration of exposure to Moga after DR of 183 days (58, 332).

Conclusion : MAR was heterogenous in pts with SS and MF. Most (80%) pts continued Moga for >6 months following resolution of DR suggesting that appropriate evaluation, identification, and management prevents premature discontinuation.

Keywords : Cutaneous T-cell lymphoma (CTCL), Mavoric, Mogamulizumab, Mycosis fungoides, Sezary syndrome

Figure. Correlation of Drug Rash and Response to Mogamulizumab



PP05-13

Prognostic prediction of total metabolic tumor volume in lymphoma patients

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Background : Total metabolic tumor volume (TMTV) is a novel parameter derived from PET-CT data (1). TMTV has been demonstrated to outperform basic quantitative PET-CT measurements in predicting progression-free survival (PFS) and overall survival (OS) in various subtypes of lymphoma (2). In this retrospective study, we aimed to determine prognostic factors affecting the survival of Hodgkin (HL) and non-Hodgkin lymphoma (NHL) patients.

Method : A total of 87 patients diagnosed with HL (n:30) and NHL (n:57) between 2010 and 2021 were included in this study. The TMTV was calculated by summing the product of the two largest diameters of the uptake areas and SUVmax values, for each PET-CT scan. Patients' baseline, interim and end-of-treatment TMTV, baseline TMTV differences with interim (I\B) and end-of-treatment (Eot\B) TMTV, volume changes based on the percentage of TMTV between the baseline and interim (ΔTMTVi) and between baseline and end-of-treatment (ΔTMTVeot) values were calculated.

Results : Optimal baseline TMTV cut off was 3745,38 mm^2xSUVmax in NHL patients. NHL and HL patients with low baseline TMTV showed longer OS (p=0,054; p=0.65, respectively) (Figure 1). No correlation was found between baseline TMTV and PFS in HL and NHL patients (p=0,28; p=0,53, respectively). I\B correlated with PFS in HL patients (p=0,04). Eot\B correlated with OS in HL patients (p=0,01) and correlated with PFS in NHL patients (p=0,02) (Figure 2). In HL and NHL patients, PFS was found to be shorter in patients with ΔTMTVeot below the cut off value (p<0,001).

Conclusion : Baseline TMTV was statistically significant at the borderline of significance for predicting OS in NHL patients. Essentially, Eot\B was found to be effective in predicting OS for HL patients and PFS for NHL patients. Although interim PET-CT provides guidance in determining treatment options, our study did not demonstrate its impact on PFS or OS. Combining developing artificial intelligence methods and TMTV may reveal this effect.

Keywords : Total metabolic tumor volume, Hodgkin lymphoma, Non-Hodgkin lymphoma, Progression-free survival, Overall survival

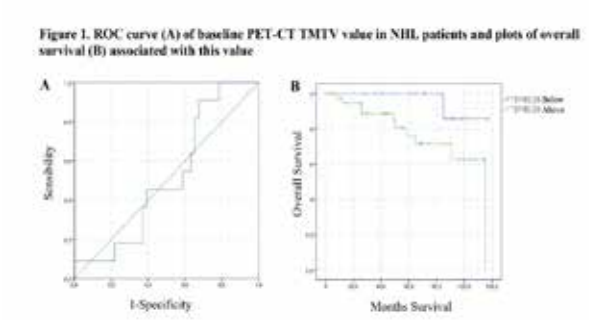

Figure 1. ROC curve (A) of baseline PET-CT TMTV value in NHL patients and plots of overall survival (B) associated with this value

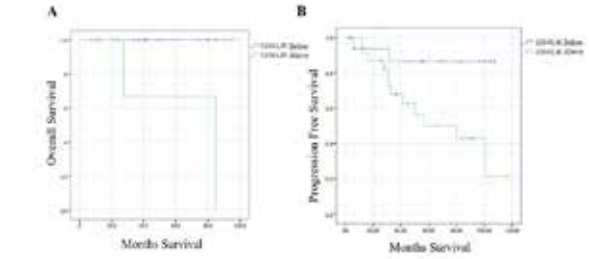

Figure 2. Prediction of EoCB PET-CT TMTV value for overall survival in HL patients (A) and disease-free survival in NHL patients (B)

PP05-14

Treatment outcomes of aggressive B cell lymphoma: A single center review in Malaysia

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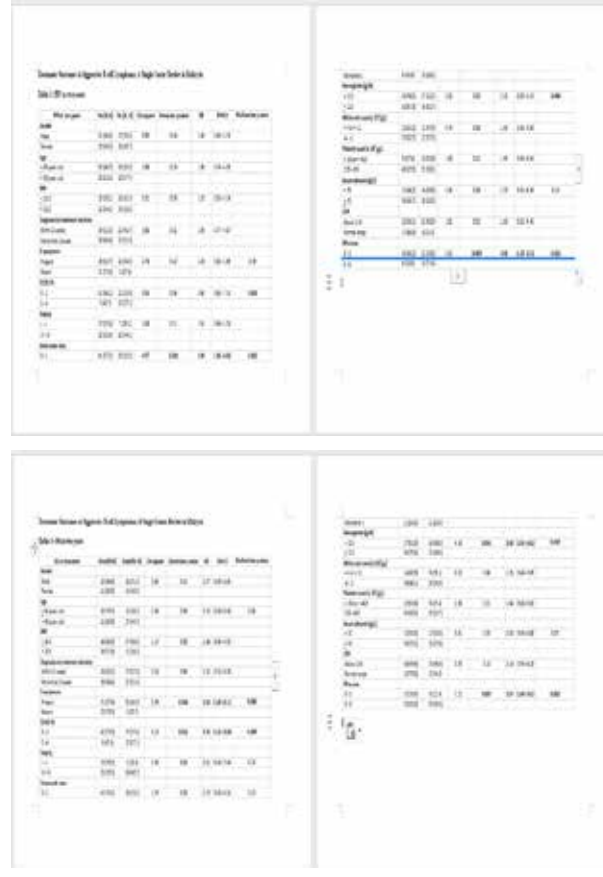
Background : Aggressive B cell lymphoma accounts for majority of non-Hodgkin lymphoma encountered in Malaysia and worldwide. The treatment response varies among treatment centers.

Method : This retrospective study was performed to assess the treatment outcomes for patients diagnosed with aggressive B cell lymphoma at the Sarawak General Hospital, Malaysia between January 2020 and October 2021. Major inclusion criterion was adult patients (> 18 years old) with the diagnosis of Burkitt lymphoma (BL), high grade B cell lymphoma (HGBCL), primary mediastinal B cell lymphoma (PMBCL) or diffuse large B cell lymphoma (DLBCL) who received intensive chemotherapy within the study period. Patients who refused chemotherapy or elected for palliation were excluded. Primary end points were progression-free survival (PFS) and overall survival (OS).

Results : There were 83 patients in the study. Majority of the study cohort was male patients (57.8%), with mean age of 56.3 years. DLBCL was the most frequent lymphoma recorded (84.3%). Majority of them presented in advanced stage of disease (68.7%). The median time of diagnosis to treatment duration was 13 days. All patients received R-CHOP or R-CHOP-like immunochemotherapy as front line treatment. The 2-year PFS and OS were 60.2% and 65.1%, respectively. Performance status, pre-treatment hemoglobin level (< 12 g/dL) and international prognostic index (IPI) score were the significant prognostic factors for both PFS and OS in the multivariate analysis.

Conclusion : In addition to the IPI score, our study showed that pre-treatment hemoglobin level can be used as additional prognostic marker for patients with aggressive B cell lymphoma

Keywords : Aggressive B cell lymphoma, Treatment, Prognosis



PP05-15

Prognostic role of 18F-FDG PET/CT in diagnosis and response evaluation of primary central nervous system lymphoma

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Background : 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG-PET/CT) has become a standard tool for assessing treatment response in non-Hodgkin lymphoma. However, its prognostic utility in primary central nervous system lymphoma (PCNSL) remains controversial.

Method : We conducted a retrospective analysis of 268 consecutive patients diagnosed with diffuse large B-cell lymphoma (DLBCL) of the CNS between January 2006 and August 2020. Among them, 105 patients underwent baseline 18F-FDG-PET/CT, 97 had interim scans, and 110 had post-treatment scans. Quantitative analysis of baseline PET/CT images included measurement of maximal standardized uptake value (SUVmax), metabolic tumor volume (MTV), and total lesion glycolysis (TLG).

Results : The median age of patients was 61 years (range: 19-84 years). Treatment regimens included high-dose methotrexate alone (HD-MTX, n=58) or methotrexate, procarbazine, and vincristine with or without rituximab (MPV ± R, n=47), followed by autologous stem cell transplantation (ASCT, n=48) or non-myeloablative high-dose chemotherapy (n=57). With a median follow-up duration of 37.7 months, the median progression-free survival (PFS) and overall survival (OS) were 27.5 and 34.0 months, respectively. Baseline 18F-FDG-PET/CT revealed visually detectable tumor uptake in all patients. The average SUVmax at baseline was 15.3 ± 5.7 (median 15.1), while the mean MTV and TLG were 12.6 ± 13.9 and 135.0 ± 152.7, respectively. Patients with a baseline MTV of ≥17.0 had significantly shorter PFS (20.0 months vs. 74.0 months, p=0.003). Although post-treatment MRI did not show statistically significant differences in PFS (p=0.130) or OS (p=0.540), post-treatment PET (positive vs. negative) was significantly associated with PFS (median: 9 months vs. 46 months, p=0.001) and OS (median: 21 months vs. 62 months, p=0.002).

Conclusion : In patients with PCNSL, baseline MTV and post-treatment PET are significant prognostic markers, offering valuable insights into disease progression and survival outcomes. These findings underscore the potential clinical utility of 18F-FDG-PET/CT in risk stratification and treatment response for PCNSL.

Keywords : PET, PCNSL, Prognosis

PP05-16

Association of interleukin-2 330 T/G gene polymorphism with the risk of Non-Hodgkin lymphoma: A meta-analysis

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Background : Non-Hodgkin Lymphoma (NHL) risk factors are still in extensive investigation, it is the most frequent hematologic malignancy worldwide and has increased in incidence for the past 10 years. Interleukin-2 (IL-2) signals and regulates the activities of the immune system, particularly the T-cells and natural killer cells. Growing body of research suggests a role for IL-2 gene polymorphism in malignant transformation. Extensive research had been conducted to discover the relationship between IL-2 330T/G gene polymorphism and NHL risk, but the results remained contradictory. Therefore, this study was carried out to investigate the connection between NHL susceptibility and Interleukin-2 330T/G Gene Polymorphism.

Method : This Meta-analysis was following the PRISMA guidelines. The literature was taken from Pubmed and Google Scholar, with November 2020 as the latest edition that was computed, and it is limited to English only. A total of 3 studies were included in this review. A Review Manager 5.4 was utilized to analyze the data.

Results : 3 studies were incorporated. From the analysis, IL-2 330T/G gene polymorphism was associated with an increase of NHL (G vs T, OR 95%CI = 1.51 [1.29-1.78] p< 0.00001; GG vs TT + TG, OR 95%CI = 1.77 [1.29-2.45] p=0.0005) and a decrease of NHL (T vs G, OR 95%CI = 0.66 [0.56-0.78] p<00001; TT vs TG + GG, OR 95%CI =0.57 [0.45-0.72] p<0.00001)

Conclusion : There was a correlation between IL-2 330T/G gene polymorphism and NHL

Keywords : Non-Hodgkin lymphoma, Gene polymorphisms interleukin-2

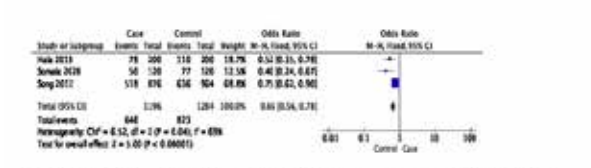

Fig 1. Forest plot of association between IL-2 330T/G gene polymorphism and NHL risk T vs G

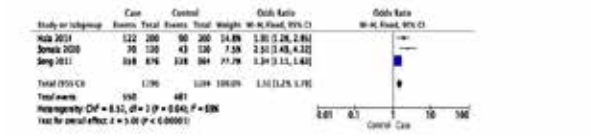

Fig 2 Forest plot of association between IL-2 330T/G gene polymorphism and NHL risk G vs T

Fig 3. Forest plot of association between IL-2 330T/G gene polymorphism and NHL risk TT vs TG + GG

Fig 4. F Forest plot of association between IL-2 330T/G gene polymorphism and NHL risk GG vs TT + TG

PP05-17

Nodal marginal zone lymphoma accompanied by in situ follicular neoplasia with t(14;18)(q32;q21)

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Background : Nodal marginal zone lymphoma (NMZL) is a primary nodal lymphoma of small, mature B cells derived from marginal zone B cells, without involvement of extranodal sites or the spleen. This entity comprises around 1.5 - 1.8% of all lymphoid neoplasms.[1] In situ follicular neoplasia (ISFN) is a monoclonal proliferation of BCL2 positive B cells confined to follicle centers which are also positive for t(14;18)(q32;q21). [2]. We have a case report of a 64-year-old male patient with NMZL accompanied by ISFN with t(14;18)(q32;q21) at Blood transfusion and Hematology hospital (BTH).

Method : Case report

Results : This patient's lymph node architecture is completely effaced by a small lymphoid proliferation with a diffuse growth pattern. The neoplastic cells have minimally cleaved/indented nuclei along with scant to moderate amount of cytoplasm; cells containing more abundant or pale-staining cytoplasm. These cells express CD20 and BCL2 and no expression of CD5, CD10, BCL6, CD23 and Cyclin D1. There are some residual secondary follicles with a few follicle centers that are strongly positive for CD10 and BCL2 with low proliferation index (Ki67 around 10%). This patient did not have splenomegaly or any other lesions of other sites ISFN is a monoclonal proliferation of BCL2 positive B cells confined to follicle centers which are also positive for t(14;18)(q32;q21). It is detected in 2 - 3% of randomly selected reactive lymph node biopsies. It can be seen in lymph nodes with other lymphoid neoplasms such as Follicular lymphoma (FL), Mantle cell lymphoma, marginal zone lymphoma and Diffuse large B-cell lymphoma.

Conclusion : Therefore, we should always be careful to combine all the datas to avoid misdiagnoses and to establish a good diagnois as we can so that we will have an appropriate treatment protocols for our patient.

Keywords : Nodal marginal zone lymphoma, In situ follicular neoplasia, t(14;18)(q32;q21)

PP05-18

Clinicopathological and genetic landscape of plasmablastic lymphoma in Taiwan

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Background : Plasmablastic lymphoma (PBL) is an aggressive large B-cell lymphoma with a terminal B-cell differentiation phenotype and is frequently associated with immunodeficiency. We aimed to investigate the clinicopathological and immunophenotypic features, genetic alterations, and mutational landscape of PBL in Taiwan
Method : We investigated 26 cases from Taiwan. Seven (28%) patients were HIV-positive and 21 (81%) presently extranodally.

Results : There were two morphological groups: one with purely monomorphic large cells (85%) and the other comprising large cells admixed with plasmacytic cells (15%). Phenotypically, the tumors expressed MYC (8/10; 80%), CD138 (20/26; 77%), and MUM1 (20/20; 100%), but not CD20 (n=26; 0%). Fourteen (54%) cases were positive for EBV by in situ hybridization; and the EBV-positive cases were more frequently HIV infected (p=0.036), with extranodal presentation (p=0.012) and CD79a expression (p=0.012), but less frequent light chain restriction (p=0.029). Using fluorescence in situ hybridization, we identified 13q14 deletion, MYC rearrangement, and CCND1 rearrangement in 74%, 30%, and 5% cases, respectively, without any cases having rearranged BCL6 or IGH::FGFR3 fusion. In the 15 cases with adequate tissue for whole exome sequencing, the most frequent recurrent mutations were STAT3 (40%), NRAS (27%), and KRAS (20%).

Conclusion : Most PBL cases in Taiwan were HIV-unrelated. Around half of the cases were positive for EBV, with distinct clinicopathological features. Deletion of chromosome 13q14 was frequent. Our cases showed recurrent mutations involving JAK-STAT, RAS-MAPK, epigenetic regulation, and NOTCH signaling pathways, findings similar to that from the West.

Keywords : Plasmablastic lymphoma, JAK-STAT, RAS-MAPK, NOTCH, Epigenetic

PP05-19

Report on initial results of treating diffusion large B-cell lymphoma with polatuzumab vedotin based regimen at Vinmec Times City International Hospital

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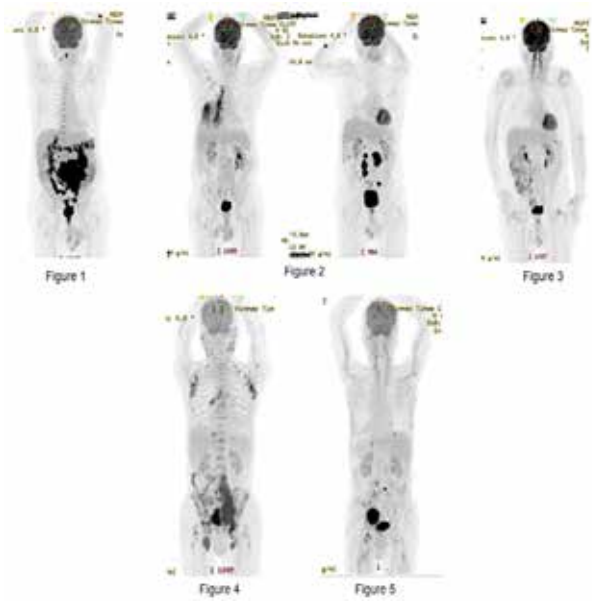
Background : Diffuse large B-cell lymphoma (DLBCL) is a prevalent and rapidly progressing lymphoma. Despite the efficacy of R-CHOP treatment, a substantial percentage of patients, particularly the elderly, experience relapse or are refractory to therapy, leading to poor outcomes. The introduction emphasizes the need for alternative treatments, introducing polatuzumab vedotin as a novel therapy targeting CD79a, a crucial component of the B-cell receptor.

Method : The study presents two cases of elderly DLBCL patients, refractory to initial treatment, who received polatuzumab vedotin as part of their therapy at Vinmec Times City International Hospital. 2 elderly patients exhibited primary refractory disease and were subjected to the Pola-R-Bendamustine and Pola-R regimens, respectively. The methods section details the patients' clinical presentations, diagnostic procedures, and the administration of polatuzumab vedotin in conjunction with other agents.

Results : In the first case, an 82-year-old patient achieved complete remission after the Pola-R-Bendamustine regimen, demonstrating the efficacy of polatuzumab vedotin in overcoming primary refractory DLBCL. The second patient, aged 90 years old, exhibited disease progression involving the central nervous system after initial treatment, but achieved remission with the Pola-R regimen. The results suggest that incorporating polatuzumab vedotin into the treatment regimen is a safe and potentially effective strategy for managing relapsed/refractory DLBCL.

Conclusion : With restrictions in two patients, we suggest that Pola-BR shows promise as a novel combination for relapsed/refractory DLBCL patients. It appears to be safe for elderly patients and effective in cases of central nervous system involvement. Longer-term observation and additional studies are required to ascertain the optimal efficacy of Polatuzumab vedotin in conjunction with various treatment regimens for different subgroups of B-cell lymphoma.

Keywords : Polatuzumab vedotin, Diffusion large B-cell lymphoma, Relapsed/refractory, PET/CT, Complete remission



Results : A 40-year-old male presented with multiple nodules in four limbs, fever, and perianal abscess with pain in June 2023. Biopsy of the subcutaneous tumor in the left elbow showed DLBCL of non-germinal center phenotype. The tumor cells were diffusely positive for EBV by in situ hybridization (ISH), but negative for HHV8 by immunohistochemistry. Tracing back his history, he was diagnosed with HIV infection in February 2018 and was treated with antiretroviral therapy (ART). He developed CHL in October 2018, with the Hodgkin and Reed-Sternberg cells also positive for EBV by ISH. He obtained a complete remission of the stage III CHL after chemotherapy with ABVD. After the diagnosis of stage IV EBV+DLBCL, he is currently under 2nd course of R-ESHAP regimen.

Conclusion : Distinct lymphoma types occurring in patients with the setting of IDD are rare. New lesions in lymphoma patients during the follow-up period are usually considered relapses. Some clinicians would assume the new lesions represent recurrence of the same tumor and would go ahead for treatment as such, without doing biopsy. Our case illustrates the importance of performing biopsy for a newly emerged tumor and the rare occurrence of sequential EBV+CHL and EBV+DLBCL in an HIV-infected patient.

Keywords : EBV, HIV, Immunodeficiency, Immune deficiency and dysregulation, Lymphoma

PP05-20

Emergence of EBV-positive diffuse large B-cell lymphoma five years later after a previous complete remission from EBV-positive classic Hodgkin lymphoma in an HIV-infected patient

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Background : Immune deficiency and dysregulation (IDD)-associated lymphoproliferative disorders (LPD) form a heterogenous group, both clinicopathologically and etiologically. Human immunodeficiency virus (HIV) infection is one of the four major background for IDD-LPDs. We present an HIV patient who had developed diffuse large B-cell lymphoma (DLBCL) five years after a complete remission of classic Hodgkin lymphoma (CHL) nearly 5 years ago. We emphasize the importance of biopsy for a new (nodal) lesion in lymphoma patient as the lymphoma type might be different, needing different treatment regimen.

Method : We retrospectively review the clinical and pathological findings of an HIV-infected lymphoma patient.

PP05-21

HIV-related lymphomas in Taiwan: A retrospective study of 63 cases showing a wide spectrum of histopathology

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Background : Immune deficiency and dysregulation (IDD)-associated lymphoproliferative disorders are clinicopathologically and etiologically heterogeneous diseases. Human immunodeficiency virus (HIV) infection is one of the major causes of IDD-related lymphomas in the West, yet the spectrum of HIV-related lymphomas in Taiwan

has not been reported.

Method : We retrospectively investigated patients with HIV-related lymphomas from five medical centers in Taiwan by reviewing the medical charts and histopathology with immunohistochemical study and in situ hybridization.

Results : We identified 63 patients including 61 males and 2 females with a median age of 38 (range, 22-62). The diagnoses included classic HL (n=1), marginal zone lymphoma (MZL; n=2), follicular lymphoma (FL; n=2, including 1 each of low-grade FL and follicular large B-cell lymphoma), plasmablastic lymphoma (n=2), Burkitt lymphoma (BL; n=15; 24%), diffuse large B-cell lymphoma (DLBCL; n=40; 63%), and angioimmunoblastic T-cell lymphoma (n=1). Nearly half of the tumors (49%; 31/63) investigated were positive for EBV by in situ hybridization, including BL (9/15; 60%) and DLBCL (19/40; 48%). One DLBCL case was double positive for EBV and HHV8. Of the 12 cases of BL with successful florescent in situ hybridization assays, only half of cases were MYC rearranged. 54% (21/39) of DLBCL cases were of germinal center B-cell phenotype, without double or triple hit lymphoma cases.

Conclusion : The spectrum of HIV-associated lymphomas in Taiwan is wide. BL and DLBCL were the most common types, accounting for 87% of all cases. There was a relatively low rate of MYC rearrangement in our BL cases. Our results support the notion that HIV testing is required in all lymphoma patients, even in low grade tumors, as the underling HIV infection status may help guide the clinicians for appropriate management of such patients.

Keywords : HIV, Lymphoma, Immunodeficiency associated lymphoma, EBV

PP05-22

Real-world experience with zanubrutinib treatment for patients with previously treated Waldenstrom Macroglobulinemia

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Background : Waldenstrom macroglobulinemia (WM) is defined as lymphoplasmacytic lymphoma (LPL) associated with immunoglobulin M (IgM) monoclonal gammopathy, irrespective of the M protein size. The treatment of goal of WM is to control disease without compromising quality of life by treatment-related adverse events. Zanubrutinib, a second generation covalent BTK inhibitor, constitute the incumbent stand of care irrespective of line of therapy based on the recent success of ASPEN trial. Recognizing the lack of real-world data on zanubrutinib treatment for previously treated WM patients, we carried out this study.

Method : We conducted a retrospective cohort study of previously treated WM patients and identified 12 patients undergoing zanubrutinib treatment. All patients started on 160mg bid schedule. The efficacy and safety of zanubrutinib treatment was investigated. The response was evaluated according to the 6th International Workshop on WM. Major response was defined as composite of complete response (CR) + very good partial response (VGPR) + partial response (PR). Overall response rate (ORR) was defined as minor response (MR) or better response.

Results : The median age at WM diagnosis was 65, while the median age at zanubrutinib start was 71 years old. There were 8 males and 4 females. There were 2 patients with underlying arrhythmias and 2 with hypertension. All but 2 were previously treated with chemoimmunotherapy, and there were 4 patients previous exposure to bortezomib. The median time from last line of therapy to zanubrutinib was 4 months (range 0-72 months). The reason for starting zanubrutinib were neuropathy (2), anemia (1), kidney-related (4), extramedullary manifestation (1), Bing Neel Syndrome (2), and physician's decision (2). During the median follow-up of 17 months, 6 (50%) achieved VGPR, 5 (41.7%) achieved PR and 1 (8.3%) achieved MR.

Conclusion : Real-world data are consistent with previously published data from trials. (Part of this study was presented at IMS 2023)

Keywords : Zanubrutinib, Waldenstrom macroglobulinemia

PP05-23

Machine learning based prediction of 5-year survival outcome in patients with low grade B cell lymphoma

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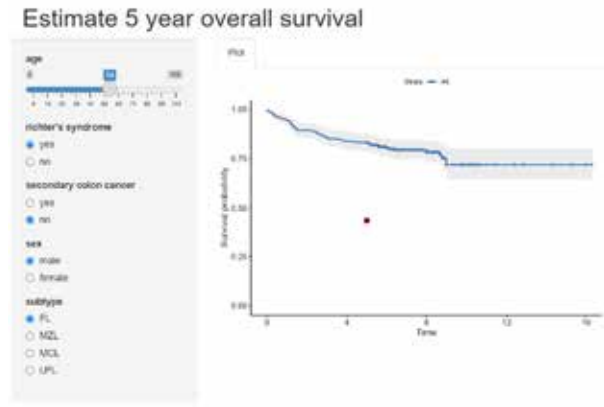
Background : The development of treatment increased long-term survival in patients with low-grade B cell lymphoma (LGBCL), including marginal zone lymphoma (MZL), mantle cell lymphoma (MCL), lymphoplasmacytic lymphoma (LPL), and follicular lymphoma (FL). However, there is a lack of prediction data for the survival rates of individuals. This study finds the risk factors for survival outcomes and models the prediction of survival outcomes by machine learning methods.

Method : We evaluated 2816 adult patients diagnosed with LGBCL between January 2000 and September 2023 at Yeoido, Seoul, Bucheon, Incheon, Daejeon, Eunpyeong, and Uijeongbu St. Mary's Hospital. Patients who had Less than five years of follow-up without death were excluded from the study. There were 1283 patients included in the study. Among them, 681 were used for modeling, and 602 cohorts were used for testing.

Results : Among the 625 patients, 263 were FL, MZL were 206 patients, 126 were MCL, and 30 were LPL. The median follow-up was 6.3 years. 5-year overall survival was 83.3% in FL, 85% in MZL, 40% in LPL, and 45.2% in MCL. Richter syndrome affects inferior survival outcomes (p<0.001). Patients with secondary colon cancer showed inferior outcome(p=0.025), other risk factors were shown as follows: male sex, diagnosed age, and subtype. We compared the machining learning algorithms with XGBoost, randomforest, and linear regression. Best accuracy algorithm was randomforest. The random forest model showed that accuracy was 71.6%. For example, in a male patient with FL diagnosed age at 54 years with Richter syndrome, predicted 5 years OS were 43.2%.

Conclusion : Our study suggests that secondary colon cancer and Richter's syndrome could increase mortality in LGBCL patients. Further, we tried to determine individuals' survival rates using machine-learning methods. We developed a web-based risk score system using the suggested model to enhance model usage in the clinic. Further, prospective studies are warranted to validate the conclusion.

Keywords : Low grade B cell lymphoma, Machine learning , Richter syndrome, Prediction



PP05-24

Comparative analysis of the clinical outcomes and measurable residual disease in CLL patients treated with FCR chemoimmunotherapy followed by Ibrutinib

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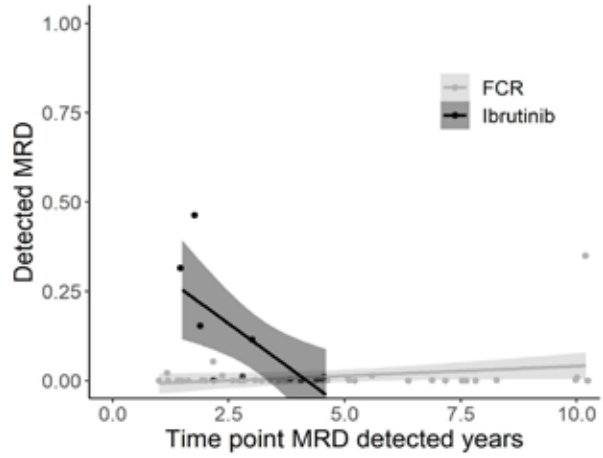
Background : The introduction of anti-CD20 monoclonal antibodies in alkylator-based chemotherapy has markedly improved progression-free survival (PFS) and overall survival (OS) among patients with CLL. In Korea, disease prognosis is known to be worse compared to that in Western Countries in the past. However, the efficacy of the sequential strategy, FCR chemotherapy followed by Bruton's tyrosine kinase, needed to be reevaluated. In this study, we analyzed of both FCR and ibrutinib groups and clinical characteristics affecting the survival outcome, further tracking the minimal residual disease in the patients with complete remission.

Method : We retrospectively reviewed the data of patients with CLL who were diagnosed and treated with the FCR chemoimmunotherapy regimen, in Seoul and Yeouido St. Mary's Hospitals between April 2008 and January 2023.

Results : This study included 145 patients who received FCR. Among the treated patients, ibrutinib was administered to 22 relapsed patients. The 5-year OS of all patients was 83.8%. The 5-year PFS was 82.5% in the FCR group, and the 2-year PFS was 70.5% in the ibrutinib group. In multivariate analysis of the FCR group, Rai stage IV and TP53 mutation detection showed associations with worse OS. However, the ibrutinib group showed different survival outcomes in the univariate analysis. MRD assessment for patients who achieved CR was evaluated in 40 patients in the FCR group and 11 in the ibrutinib group. Increment in MRD showed a linear positive gradient(MRD =0.00006 x years after chemotherapy, p=0.018) in the FCR group and a linear negative gradient (MRD=-0.09473 years after chemotherapy, p=0.013) in the ibrutinib group.

Conclusion : We showed the usefulness of sequential standard therapy and gradually caught up with Western survival data. Furthermore, a different perspective on MRD trends by treatment modality is needed.

Keywords : CLL, Minimal residual disease, RFC, Ibrutinib



PP05-25

Challenges in overcoming advanced stage or relapsed refractory extra-nodal NK/T cell lymphoma, nasal type: Meta-analysis of individual patient data

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Background : Extranodal NK/T-cell lymphoma (ENKTCL) is a non-Hodgkin T-cell lymphoma known for locally destroying nasal structures and systemically inducing inflammatory cytokines. Concurrent radiation and non-anthracycline-based chemotherapy have improved survival in patients with localized stages. However, survival outcomes in advanced-stage and relapsed or refractory (R/R) lym-

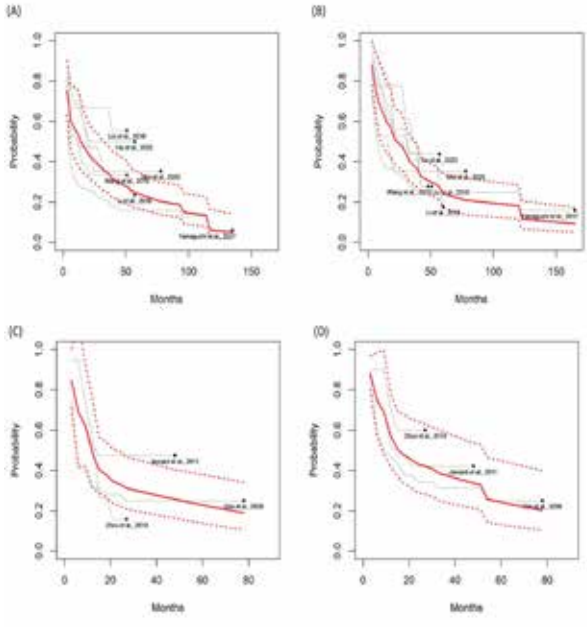
phoma have varied across studies.

Method : Our analysis integrated prognostic factors in advanced or R/R ENKTCL using a digital extractor on Kaplan-Meier graphs, addressing the scarcity of published prospective trials for these patients. The meta-analysis applied random effects models to calculate hazard ratios and 95% confidence intervals for survival prognostic factors.

Results : We observed that patients with advanced ENKTCL treated with L-asparaginase had a median progression-free survival (PFS) of 14.3 months and overall survival (OS) of 19 months. In R/R ENKTCL treated with L-asphalt regimen, PFS was 11.7 months, and OS was 15.4 months. Additionally, overall survival in advanced-stage ENKTCL was better in the asparaginase group than in the non-asparaginase group, with the Peg-asparaginase group showing superior outcomes compared to the L-asparaginase group. Epstein-Barr Virus (EBV)-DNA positivity in the bloodstream before treatment was associated with inferior outcomes in advanced-stage ENKTCL, and patients with R/R ENKTCL with EBV viremia also showed inferior post-treatment outcomes.

Conclusion : Our study indicates that chemotherapy containing L-asparaginase or peg-asparaginase can improve survival in advanced or R/R ENKTCL. However, there is a need for future strategies to effectively suppress EBV viremia.

Keywords : Extra-nodal NK/T cell lymphoma, Advanced, Relapsed/Refractory, Estimate individual patient data, Meta-analysis



PP05-26

Epigenetic method for determining the subtype of mantle cell lymphoma

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Background : The main subtypes of mantle cell lymphoma (MCL) are classical (cMCL) and nonnodal leukemic (nnMCL). They are characterized by distinct clinical course and differ in therapy approaches. Recently, it was shown that MCL subtypes can be determined by measuring the degree of methylation of three CpGs (cg03425785, cg07769421 and cg23892310) using NGS sequencing. Here we suggest to use new Sanger sequencing-based technique to measure methylation of those CpGs for determination of MCL subtype.

Method : Peripheral blood (PB) samples (n = 39), BM (n = 37), or lymph node (LN) biopsy (n = 19) were obtained at the onset of the disease in patients with MCL (n = 59). DNA was isolated from all tissue and cell samples. Bisulfite conversion followed by amplification of genomic regions containing CpGs cg03425785, cg07769421 and cg2389231018 were performed for 18 patients with MCL (PB, n = 11; BM, n = 6; LN, n = 1). The PCR products were purified and sequenced by Sanger method. The degree of methylation of all CpGs contained in the PCR product was determined according to a previously developed method (DOI: 10.1089/dna.2019.5310). To classify MCL subtypes, only data from the three above-mentioned CpGs were used.

Results : Lymphocytosis was observed in 5 of 11 studied PB samples. The developed method correctly determined the MCL subtype in 80% (in 4 cases). An increased content of lymphocytes was observed in two BM samples. In one of them, where lymphocytosis was the highest (76%), the method correctly identified the MCL subtype (C1). In the only sample where the DNA source was a LN biopsy, the MCL subtype was identified correctly (C1).

Conclusion : The epigenetic approach has shown promise, but it needs improvement. One possible refinement is DNA isolation from cell fraction enriched by tumor cells.

Keywords : Mantle cell lymphoma, MCL, CpG, 5mC, Epigenetic method

PP05-27

Mutational profile of aggressive natural killer cell leukemia

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Background : Aggressive NK-cell leukemia (ANKL) is an extremely rare disease with systemic neoplastic proliferation of mature NK-cells that involves multi-organs and shows fulminant course. It is prevalent in young adults in Asia. Although previous studies have found some mutations of genes involved in JAK-STAT pathway, RAS-MAPK pathway and in other epigenetic regulators, no common mutational profile has been yet established in ANKL. This study explored the mutational profiles of ANKL.

Method : In 23 patients diagnosed with ANKL from 2006 to 2022 at a single tertiary hospital in South Korea, DNA was extracted from their bone marrow aspirate slides and targeted sequencing of 282 hematologic cancer panel genes was performed.

Results : The mean age of the patients was 41.57 years. Male were 78.3% (18/23) and female were 21.7% (5/23), showing a male predominance. The mean depth of targeted sequencing was 711.40×. The median number of mutated genes per sample was 8. Mutations in the JAK-STAT pathway were identified in 43.48% (10/23) of ANKL patients, from which JAK3 (13.04%) was the most frequently mutated gene. Mutations in epigenetic modifier genes were identified in 82.61% (19/23). KMT2D (34.78%) and KMT2C (26.09%) were the most frequently mutated epigenetic modifiers. RAS-MAPK pathway mutations were identified in 13.04% (3/23), from which the most frequently mutated gene was MAP2K1 (8.70%). Additional frequently mutated genes included APC (30.43%), FAT1 (30.43%), FAT3 (26.09%) and TP53 (21.74%).

Conclusion : JAK-STAT pathway mutations can result in constitutive activation of JAK-STAT signaling, leading to cell proliferation in ANKL. Mutations in epigenetic modifiers can allow NK-cells to adapt to aging and changing environments, leading to progression of malignancy. We hope this will contribute to elucidating the molecular mechanisms of ANKL.

Keywords : Aggressive NK-cell leukemia, JAK-STAT pathway, Epigenetic modifiers, NK-cell lymphoma, Targeted sequencing

PP05-28

The role of hematopoietic stem cell transplantation in aggressive monomorphic epitheliotropic intestinal T-cell lymphoma

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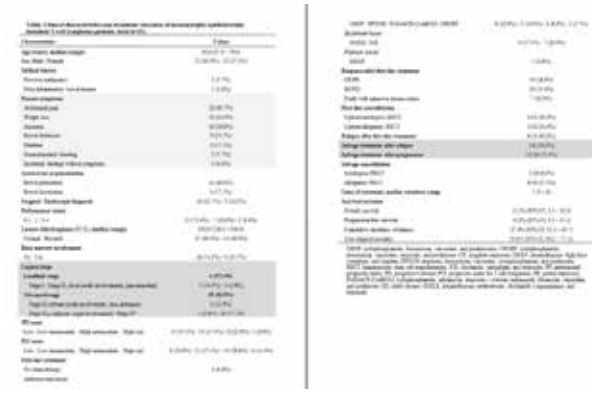
Background : Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL) is a rare yet aggressive subtype of primary gastrointestinal T-cell lymphoma. Due to the absence of characteristic symptoms in MEITL, diagnosis can be challenging, and the low response rate to conventional chemotherapy leads to an abysmal prognosis.

Method : This single-center study involved a retrospective analysis of clinical and imaging data from 35 patients diagnosed with MEITL at Seoul St. Mary's Hospital between 2012 and 2023.

Results : The study included 22 males and 13 females (median age: 59 years; range 37 – 79). Many patients showed acute symptoms of abdominal pain (n=23, 65.7%) related to bowel perforation (n=21, 60.0%). Most patients (30/35, 85.7%) underwent surgical intervention to diagnose MEITL; five patients were diagnosed by endoscopic evaluation. Of the 32 patients receiving first-line therapy, 4 died before assessment, 10 achieved complete remission (CR), 6 showed relapse, and 18 showed progressive disease (PD). Seven of 10 patients received upfront hematopoietic stem cell transplantation (HSCT), either autologous (auto-HSCT, n=4) or allogeneic (allo-HSCT, n=3). All four patients on auto-HSCT died after relapse. All three patients who received allo-HSCT are currently maintaining CR. Three of 6 relapsed patients and 13 of 18 PD patients received salvage therapy; one patient on salvage auto-HSCT with cytokine-induced killer cell infusion has remained alive without relapse since. Salvage allo-HSCT was performed on 6 of 16 patients; among them, 2 achieved CR, 2 died after relapse, and 2 died due to septic shock while in CR. The remaining patients receiving salvage therapy without HSCT died mostly from PD. The median overall survival was 12.1 months after a median follow-up of 33.2 months (7 living patients). One-year and 2-year OS were 47.9% and 23.3%, respectively.

Conclusion : MEITL is an aggressive disease resistant to conventional therapy. Therefore, intensive chemotherapy followed by upfront allo-HSCT needs consideration after diagnosis.

Keywords : Monomorphic epitheliotropic intestinal T-cell lymphoma, Intestinal perforation, Intestinal obstruction, Hematopoietic stem cell transplantation



PP05-29

Mosunetuzumab monotherapy continues to demonstrate durable responses in patients with relapsed and/or refractory follicular lymphoma after 2 prior therapies: 3-year follow-up from a pivotal phase II study

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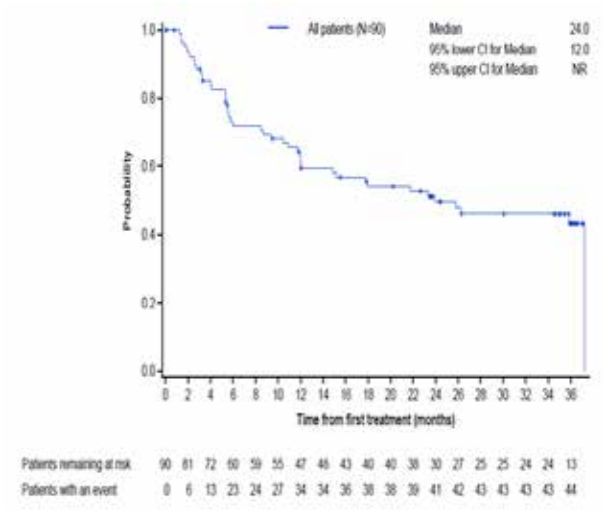
Background : Mosunetuzumab is a CD20xCD3 T-cell engaging bispecific antibody that redirects T cells to eliminate malignant B cells. In a pivotal Phase II study (NCT02500407), mosunetuzumab demonstrated a high complete response (CR) rate with a manageable safety profile in patients with relapsed/refractory (R/R) follicular lymphoma (FL) and ≥2 prior lines of therapy (Budde et al. Lancet Oncol 2022). Mosunetuzumab is a fixed-duration treatment that can be administered in an outpatient setting. Here, we present updated data for patients with R/R FL and ≥2 prior lines of therapy, after 3 years of follow-up.

Method : Eligible patients with R/R FL Grade (Gr) 1–3a and ≥2 prior therapies received intravenous mosunetuzumab in 21-day cycles with step-up dosing in Cycle (C) 1 (C1 Day [D] 1, 1mg; C1D8, 2mg; C1D15/C2D1, 60mg; C3D1 and onwards, 30mg). Hospitalization for treatment was not required. Patients achieving a CR by C8 completed treatment without additional cycles; patients with a partial response or stable disease received a total of 17 cycles. The primary endpoint was CR rate as determined by an Independent Review Committee (as best response; Cheson 2007 criteria). Duration of response (DOR), duration of complete response (DOCR), progression-free survival (PFS), event-free survival (EFS), and safety were secondary endpoints. Time to next treatment (TTNT), response to retreatment, biomarkers of minimal residual disease (MRD), and circulating B-cell counts were exploratory endpoints.

Results : 70 patients (78%) achieved an OR; 54 patients (60%) achieved CR as best response.

Conclusion : In this updated analysis, with a median follow-up of 37.4 months, durable responses continued to be observed with fixed-duration mosunetuzumab in patients with R/R FL. The manageable safety profile was consistent with previous reports. Evidence of B-cell recovery was observed after a median of 18 months following the end of treatment.

Keywords : Bispecific, Mosunetuzumab, Follicular lymphoma



Efficacy endpoints assessed by investigators	All patients N=90
	n=70
Median DOR, months (95% CI)	35.9 (20.7–NR)
30-month DOR rate, % (95% CI)*	56.6 (44.2–68.9)
	n=54
Median DOCR, months (95% CI)	NR (33.0–NR)
30-month DOCR rate, % (95% CI)*	72.4 (59.2–85.6)
Median PFS, months (95% CI)	24.0 (12.0–NR)
36-month PFS rate, % (95% CI)	43.2 (31.3–55.2)
Median OS, months (95% CI)	NR (NR–NR)
36-month OS rate, % (95% CI)	82.4 (73.8–91.0)

PP05-30

Clinical profile and survival of Non-Hodgkin lymphoma patients at tertiary hospital in Bali, Indonesia

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Background : Non-Hodgkin lymphoma (NHL) is a heterogeneous group of lymphoproliferative diseases that originate from B lymphocytes, T lymphocytes, or Natural Killer (NK) cells. NHL ranks seventh among all cancers and ninth among the causes of cancer-related deaths. The aim of this study is to describe the clinical profile and survival of NHL patients undergoing chemotherapy at tertiary hospital in Bali, Indonesia.

Method : We retrospectively studied all NHL patients (>18 years age) diagnosed and underwent chemotherapy at tertiary hospital in Bali, Indonesia, from January 2020 until August 2023. The data was collected from electronic medical record. Survival analysis was analyzed using Kaplan Meier and cox proportional hazard mode using SPSS 25.0 software.

Results : There were 138 cases of NHL during the period from January 2020 to August 2023. The mean age of the subjects at diagnosis was 54.7 ± 14.8 years, with the majority (59.4%) being male. At the time of diagnosis, 37% of patients were classified in clinical stage II, with 83.3% of subjects having an initial hemoglobin level of ≥10 g/dL and 61.6% having an International Prognostic Index score ≤2. Based on histopathological findings, the majority of patients (81.9%) exhibited intermediate-grade characteristics. A total of 50.7% of patients underwent chemotherapy with the CHOP regimen, while the remainder received the R-CHOP regimen. The median survival of NHL patients was 26 months, with a 3-year survival rate of 42%. Cox Regression analysis results indicated that the initial hemoglobin level played a role as a predictor of death within 3 years in NHL patients undergoing chemotherapy (HR 2.07; p=0.03).

Conclusion : The median survival of NHL patients was 26 months, with a 3-year survival rate of 42%. The initial hemoglobin level was identified as a factor influencing this survival outcome.

Keywords : Clinical profile , Non-Hodgkin lymphoma, Survival

PP05-31

Double inhibition of EZH2 and EGFR/HER2: A new strategy for burkitt lymphoma therapy

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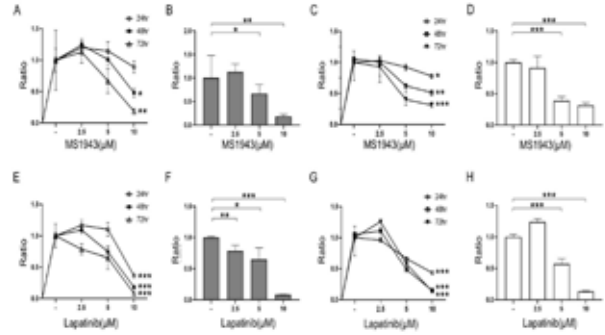
Background : Burkitt's lymphoma (BL), a rapidly proliferating B-cell lymphoma with MYC gene translocation, demands novel treatments. Targeting EZH2, a key epigenetic regulator, using inhibitors and degraders like MS1943, and addressing the HER2/neu-EGFR signaling pathway with Lapatinib, offers a promising strategy. Our findings reveal that combining MS1943 and Lapatinib synergistically enhances apoptosis and anti-tumor activity in BL, suggesting a potent and innovative approach for its treatment.

Method : Cell lines and cell culture: BL cell lines ramos and daudi were used. Drug preparation: Lapatinib (HER2/neu-EGFR inhibitor) and MS1943 (EZH2 degrader) were purchased from MedChemExpress (NJ, USA). Cell Counting Kit-8 (CCK-8) assay: Cell growth was assessed using the CCK-8 (Dojindo, Rockville, MD, USA) assay Western blotting: One million ramos or daudi cells were lysed in 2× laemmli sample buffer (Bio-Rad) with β-mercaptoethanol. RNA extraction and cDNA synthesis: The 5×10^5 cells treated with or without drugs same as described. Total RNA was extracted using TRIzol reagent (Invitrogen). Real-time reverse transcription PCR (RT-PCR) & Cell cycle analysis : the Annexin V-PI Apoptosis Kit (BioVision, London, UK)

Results : This study investigates the effects of combining MS1943, an EZH2 degrader, with Lapatinib, an EGFR/HER2 inhibitor, on Burkitt's lymphoma (BL) cells. Results show this combination inhibits cell growth and proliferation, induces cell cycle arrest, and activates the unfolded protein response (UPR) pathway. It also significantly increases apoptosis and necrosis rates, particularly in daudi cells, through the caspase pathway, with elevated caspase-3, PUMA, and PARP levels. The treatment also upregulates p53 and Bax expressions, highlighting its potential as an effective BL therapy.

Conclusion : The study indicates that combining MS1943 and Lapatinib effectively induces apoptosis in Burkitt's lymphoma, showing promising clinical potential with synergistic anti-proliferative and caspase pathway activation effects, warranting further clinical validation.

Keywords :PROTAC, EZH2, Lymphoma, HER2/neu-EGFR



PP05-32

Analysis of outcomes in patients with relapsed/refractory diffuse large B-cell lymphoma exhibiting CD20 loss

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Background : Despite advances in therapy, approximately 30% of diffuse large B-cell lymphoma (DLBCL) patients experience relapse/refractory (R/R) disease, and some of these patients are confirmed to have lost CD20 expression. In this study, we aimed to analyze the incidence and prognosis of CD20-negative R/R DLBCL.

Method : We retrospectively analyzed data from November 2004 to July 2022. Inclusion criteria included patients: (1) diagnosed with CD20+ DLBCL receiving first-line R-CHOP; (2) with R/R disease; and (3) histologically confirmed prior to second-line chemotherapy. Overall survival (OS) was defined as the time from the first relapse to death, while relapse-free survival (RFS) was defined as the time from the first relapse to death or the initiation of the next treatment. Both OS and RFS were estimated using Kaplan-Meier analysis.

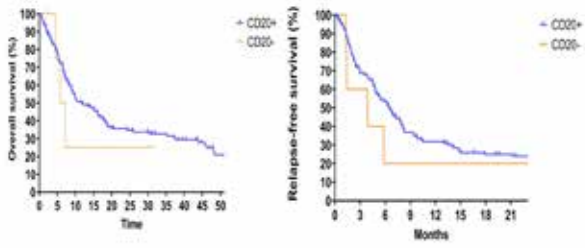
Results : Out of a total of 1142 DLBCL patients, 386 (33.8%) relapsed, and the number of patients who met the inclusion criteria was 127.

At diagnosis, the median age was 62 years, 58.3% of patients had stage 3 or 4, 19.7% had germinal center B-cell (GCB) type, and 55.1% had non-GCB subtype. Median time from diagnosis to first relapse was 405 days. Of the 127 patients, 5 patients (3.9%) lost CD20 expression at first relapse. The median OS in the CD20+ group was 11.6 months compared to 6.5 months in the CD20- group, but there was no statistical significance (p=0.6). The estimated RFS in the CD20+ group was 6.5 months compared to 3.9 months in the CD20- group, but there was no significance (p-val=0.45).

Conclusion : CD20-negative R/R DLBCL occurred in less than 5% of patients and survival was numerically lower than that observed in CD20-positive relapsed/refractory DLBCL. Further research with a larger cohort is needed to validate the prognosis of these patients. Subsequently, it is important to evaluate the efficacy of chemotherapy, including CD20-targeted therapy, in this patient population.

Keywords : DLBCL, CD20

Figure 1. Kaplan-Meier estimates of overall survival and relapse-free survival in relapsed/refractory DLBCL



PP05-33

The novel eIF4A inhibitor potently synergizes with BCL2 inhibitor in high grade B-cell lymphoma with MYC and BCL2 rearrangements through inhibition of UPR

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Background : Double hit lymphoma(DHL) is defined to be a chromosomal break with MYC gene combined with BCL2 or BCL6. MYC is an oncogene which proliferation the cells and BCL2 inhibit cell death. If eIF4A inhibitor preferentially inhibit the translation of oncogenes such as cMyc and venetoclax inhibit the BCL2 in DHL, then the combination of eIF4A inhibitor and BCL2 inhibitor will be highly effective for DHL and potentially safe for animals and humans

Method : We tested the anti-lymphoma effect of CR-1-31-B, in combination with Venetoclax in lymphoma cell lines using flow cytometry. We performed cell apoptosis assays in increasing concentrations of Venetoclax, CR-1-31-B and a combination of the two drugs at 48 hours. To better understand molecular mechanisms underlying the observed synergistic effect in DLBCL-DHL, RNA-seq profiling was performed on cells treated with single drugs and their combinations, respectively.

Results : Venetoclax and CR1-31-B exhibited concentration and time dependent cytotoxicity in lymphoma cell lines at low nanomolar concentrations. Overall, the combination of eIF4A inhibitor and BCL2 inhibitor showed synergy in all kinds of DLBCL cell lines. Especially DHL cell lines were more sensitive to the drug combination and showed enhanced synergy compared to the non-DHL cell lines($p<0.0001$). We analyzed RNA-seq profiling of cells treated with single drugs and their combinations and found that the transcriptional signature of the synergistic combination was unique relative to that of either constituent monotherapy. Gene set enrichment analysis was performed in the DHL and non-DHL group. The analysis demonstrates that known Unfolded protein response(UPR) part and metabolism, are enriched in DHL groups.

Conclusion : These findings suggest that the combination of eIF4A inhibitor and BCL2 inhibitor have potent pharmacological activity in DHL lines, it was closely related with UPR. These combination is promising and novel treatment for high-grade B-cell lymphoma with MYC and BCL2 rearrangements.

Keywords : Lymphoma, MYC, eiF4A, Double hit

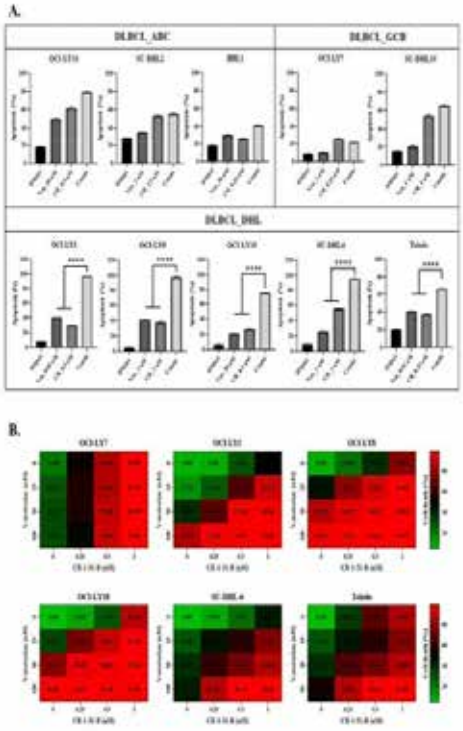

Figure 1. (A) Venetoclax and CR-1-31B cooperatively induce cell apoptosis of DLBCL cells. A. Venetoclax cooperated with CR-1-31B to promote DHL cells death at 48 h. (B) Synergy effect heat maps for venetoclax combined with CR-1-31B. Representative heat maps for indicated combinations of the DHL and non-DHL cell lines.

Table 1. The IC50 values of Venetoclax and CR-1-31B in lymphoma cell lines at 48 hours

		Venetoclax (nM)	CR-1-31-B (nM)
DLBCL (ABC)	OCI-LY10	35.85	-
	SU-DHL-2	-	289.9
DLBCL (GCB)	OCI-LY7	-	318.1
	SU-DHL-10	-	962.7
DLBCL (DHL)	OCI-LY1	52.01	1313
	OCI-LY8	66.95	1116
	OCI-LY18	17.703	894.8
	SU-DHL-6	179.5	1227
	Toledo	21.07	204.5

Abbreviation: DLBCL, diffuse large B-cell lymphoma, GCB, germinal center B-cell, ABC, activated B-cell like, DHL; double hit lymphoma

PP05-34

Clinical impact of sarcopenia for first-line chemotherapy in newly diagnosed NHL patients

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Background : Sarcopenia has been known as a poor prognostic factor in cancer patients. It has been demonstrated that muscle mass decreases and fat mass increases during chemotherapy. In this study, we investigated the clinical outcomes of sarcopenia in newly diagnosed NHL patients and analyzed the changes of sarcopenia status during chemotherapy.

Method : The 87 patients with newly diagnosed NHL from April 2020 to August 2023 were enrolled. We measured skeletal muscle index (SMI), SMI-Z score, phase angle (PhA), and extra-celluar water to total body water ratio (ECW/TBW) by bioelectrical impedance analysis (BIA). Each parameter was measured at the time of diagnosis and after 3 cycles of chemotherapy. The primary endpoint was progression-free survival (PFS).

Results : In our study, almost of patients had diffuse large B cell lymphoma (77 patients, 88.5%). Twenty-nine (33.3%) patients had sarcopenia, defined as SMI-Z<-1. The median follow-up period was 21.3 months. The estimated 2-year PFS (61.1% vs. 82.1%) (p=0.042) and OS rate (66.3% vs. 90.4%) (p=0.020) were inferior in sarcopenia group (Figure 1) The estimated 2-year PFS (81.8% vs. 53.8%) (p=0.018) and OS rate (86.4% vs. 66.3%) (p=0.014) were improved in high PhA group. Also, the estimated 2-year PFS (81.6% vs. 57.6%) (p=0.007) and OS rate (86.0% vs. 69.9%) (p=0.030) were improved in low ECW/TBW group. The sarcopenia group exhibited higher frequency of grade 3/4 neutropenia (86.2% vs 58.6%, p=0.009). During chemotherapy, the average of SMI decreased by 0.15(kg/m2) and the average of body fat mass increased by 1.58kg.

Conclusion : Sarcopenia is associated with inferior PFS, OS and higher frequency of neutropenia in newly diagnosed NHL patients. The muscle mass decreases and body fat mass increases after chemotherapy. Measuring sarcopenia through BIA is helpful in predicting the prognosis and managing NHL patients

Keywords : Sarcopenia, Lymphoma

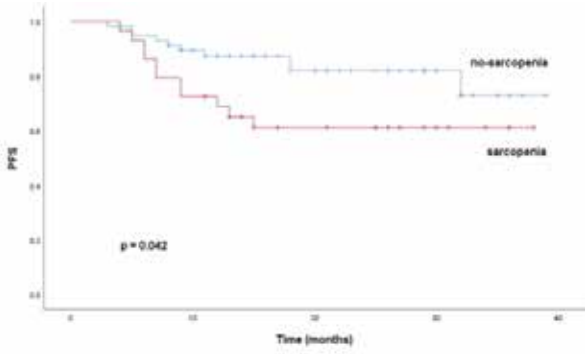

Figure 1A

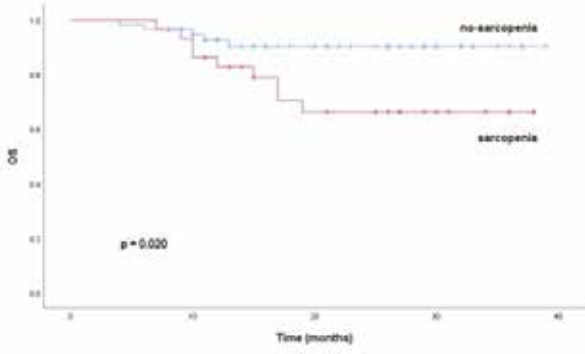

Figure 1B

PP06-01

Decoding the genomic landscape of blastic plasmacytoid dendritic cell neoplasm (BPDCN): Insights into *DNMT3A* and *TP53* mutations, MYC pathway activation, and therapeutic opportunitie

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Background : Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is an aggressive and rare hematologic malignancy with limited treatment options and poor outcomes. This study aims to comprehensively characterize the genomic landscape of BPDCN, identify key molecular drivers, and explore potential therapeutic targets to enhance precision medicine strategies.

Method : A targeted sequencing approach was employed to analyze genomic DNA from a cohort of 25 BPDCN patients, focusing on key genes implicated in hematologic malignancies. Integration of RNA sequencing data provided insights into the transcriptomic profile, while flow cytometry and immunohistochemistry facilitated precise determination of the immunophenotype. Clinical parameters, treatment responses, and outcomes were meticulously documented. Statistical analyses, including Kaplan-Meier survival curves and Cox proportional hazards modeling, were conducted to assess the impact of specific genomic alterations on patient prognosis.

Results : Our study uncovered recurrent mutations in the DNA methyltransferase gene DNMT3A (72% prevalence) and the tumor suppressor TP53 (58% prevalence) in BPDCN, underscoring their potential role as pivotal drivers in disease pathogenesis. Additionally, a distinct gene expression signature characterized by upregulated MYC pathway components was identified in 80% of cases. Strikingly, patients harboring TP53 mutations exhibited a significantly shorter overall survival (HR 2.5, CI 95%, p = 0.018), emphasizing the prognostic relevance of this genetic alteration. Furthermore, targeted therapy simulations suggested potential efficacy of hypomethylating agents in DNMT3A-mutated cases.

Conclusion : To conclude, our study unravels essential genomic insights into Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN), pinpointing DNMT3A and TP53 mutations as key drivers. The distinctive MYC-associated signature contributes to our understanding. These findings advance molecular classification and set the stage for personalized therapeutic strategies, marking a significant step in precision medicine for this aggressive hematologic malignancy.

Keywords : Blastic plasmacytoid dendritic cell neoplasm (BPDCN), Genomic landscape, *DNMT3A* mutation, *TP53* mutation, Therapeutic targets

PP07-1

Characteristics of regulatory T cell populations expressing checkpoint receptors PD-1 and TIM-3 in multiple myeloma patients

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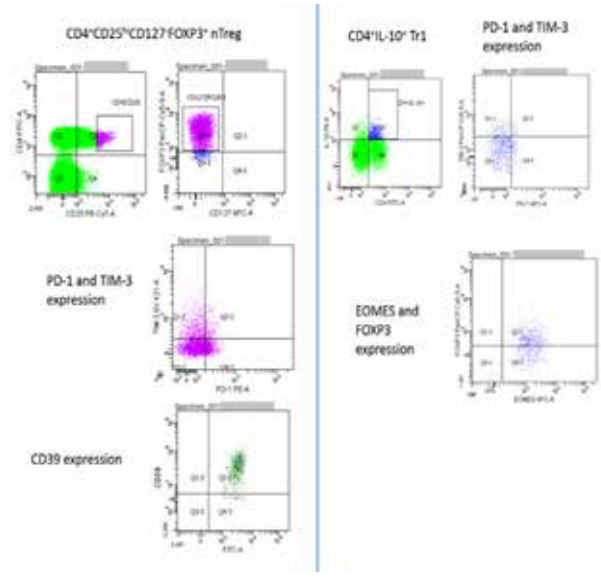
Background : Regulatory T cells (Tregs) are able to up-regulate checkpoint receptors. However, the significance of such expression are poorly studied. Presumably, unresponsiveness to anti-PD-1 therapy in solid tumors is mediated by PD-1-expressing Tregs. The objective of the study was to investigate quantitative and functional features of $CD4^+CD25^{hi}CD127^-FOXP3^+$ natural Tregs (nTregs) and IL-10-producing type 1 regulatory T cells (Tr1) expressing PD-1 and TIM-3 inhibitory receptors in multiple myeloma (MM) patients.

Method : Peripheral blood (PB) and bone marrow (BM) samples were obtained from 36 MM patients and 13 healthy individuals. Frequencies of $CD4^+CD25^{hi}CD127^-FOXP3^+$ nTregs and $CD4^+IL\text{-}10^+$ Tr1 expressing inhibitory receptors PD-1 and TIM-3, ectonucleotidase CD39, and intranuclear expression of transcription factor EOMES were assessed with flow cytometry.

Results : Relative counts of circulating nTregs did not differ in healthy controls and MM patients (at medians 3.1-3.7 % of $CD4^+$ T cells). Frequencies of PD-1-/TIM-3-expressing nTregs in PB of MM patients were significantly higher comparing with healthy donors (at medians 8.2 % and 9.4 % versus 2.0 % and 2.9 %, respectively). Simultaneously, bone marrow samples of MM patients contained higher counts of PD-1-/TIM-3-expressing nTregs (at medians about 18%). Higher frequencies of PD-1-/TIM-3-expressing nTregs up-regulate CD39, associated with suppressive activity, comparing to PD-1-/TIM-3-negative subset. Interestingly, proportions of circulating and BM Tr1 in MM patients were 13.2 % and 19.0 %, respectively, which markedly higher comparing to nTregs. Circulating and BM Tr1 expressed PD-1 and TIM-3 (at medians 20 %, 18 % and 24 %, 28 %, respectively). Natural Tregs were almost EOMES-negative, while more than 90% of Tr1 were EOMES-positive and ~50 % co-express FOXP3.

Conclusion : Frequencies of Tr1 in MM patients are higher comparing with nTregs. Moderate counts of Treg populations up-regulate PD-1 and TIM-3 in MM, which seemed to retain high suppressive potential. The study was funded by the Russian Science Foundation project N 23-25-00399.

Keywords : Multiple myeloma, Regulatory T cells, Type 1 regulatory T cells, PD-1, TIM-3



PP07-2

Clinical characteristics of multiple myeloma at young age for early detection screening

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Background : Multiple myeloma (MM) is a blood cancer and occurs in 65-year-old patients. However, about 10% of the MM cases occur in young patients under 50 years of age. There are differences clinical characteristics on both. Hence, the literature review is intended to identify these characteristics so that maybe as an early detection screening that increases young patients' prognosis.

Method : The search for literature is carried out using PubMed in the last 10 years. Old MM is over 50 years while young MM is under 50 years. Clinical characteristics referred to the results of laboratory examination and prognosis.

Results : The results obtained from laboratory examinations in old and young MM patients are quite similar. However, in young patients ISS 1 (International Staging System) is higher so the disease is less severe compared to older patients. Approximately 19-45% of patients less than 50 years of age show high levels of MM light chains and the IgA of young patients appears to be lower. There was an increase in serum LDH concentration in 49% of MM patients aged less than 40 years old. 72 patients with MM aged less than 40 years had a relatively high incidence of hypercalcemia and renal impairment. Therefore young patients appear to have a high prevalence of extramedullary disease. Study found that patients aged 21-40 years had a higher prevalence of high-risk cytogenetics compared with old patients. MM at young age is more aggressive but responds better to therapy.

Conclusion : In young patients higher ISS 1, higher MM light chain, higher cytogenetic risk, lower IgA levels, and more aggressive but responds better to therapy compared to older age. Young patients also have high incidence of hypercalcemia and renal impairment and elevated serum LDH levels.

Keywords : Multiple myeloma, Young adults

PP07-3

Longitudinal correlative profiles of responders, non-responders, and those with relapse on treatment with teclistamab in the MajesTEC-1 study

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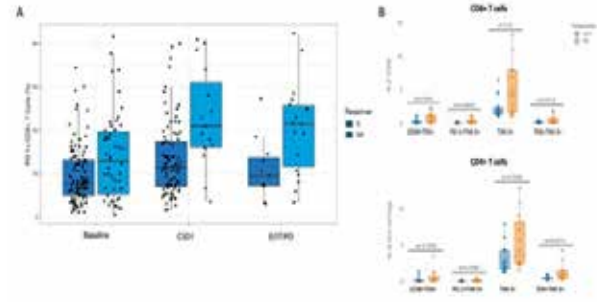
Background : Teclistamab is the only approved BCMA × CD3 bispecific antibody for the treatment of triple-class exposed RRMM. To better understand mechanisms of resistance and relapse in MajesTEC-1, we assessed longitudinal BCMA expression and immune profiles.

Method : Bone marrow and peripheral blood samples of RRMM patients (N=165) were analyzed at baseline, on-treatment, and progression, using flow cytometry for BCMA expression and immune cell populations. Bone marrow aspirates were analyzed by CyTOF and sBCMA was analyzed in serum samples by electrochemiluminescence ligand binding

Results : Patients who responded to teclistamab had a greater recovery of CD3+ T cells in the periphery and bone marrow during the first treatment cycles, which was sustained over time compared with non-responders. Greater activation during the first cycle was observed in responders, indicated by a transient increase in CD38 on CD8+ T cells. In contrast, an exhausted T-cell phenotype in the blood and bone marrow was observed longitudinally in non-responders versus responders, indicated by increasing and sustained levels of activation and exhaustion markers including persistence of CD38+ T cells and expression of LAG-3, PD-1 (Fig 1A), PD-1/LAG-3, and PD-1/TIM-3 on CD4+ or CD8+ T cells. Higher levels of Tregs (including CD38+ T regs) were also sustained in the periphery in non-responders. Among patients who initially responded, then relapsed on teclistamab, there were no significant changes in the frequency of BCMA+ plasma cells, , or sBCMA levels at PD relative to baseline, suggesting complete BCMA loss was not a mechanism of relapse. In contrast, higher proportions of peripheral CD4+ and/or CD8+ T cells expressing CD38, TIM-3, PD-1, and PD-1/TIM-3 were observed at relapse versus baseline.

Conclusion : Patients responding to teclistamab exhibited a differential immune profile in early cycles compared with non-responders. These results suggest the importance of immune fitness and T-cell function in achieving and maintaining a response to teclistamab.

Keywords : Clinical research, Multiple myeloma, Bispecific, Correlative study , Immune profiles



PP07-4

JS-k, a nitric acid donor, mediated attenuation of autophagic flux alleviates multiple myeloma pathogenesis via induction of microRNA-144: A novel therapeutic approach

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Background : The rise in relapse rate of Multiple myeloma (MM) demands novel and effective treatment regimen. Previously, our group reported that microRNAs hamper the pathogenesis of MM by targeting Versican (VCAN). The maintenance of stability of microRNAs is quite challenging, hence, an alternative approach is employed. A small molecule, JS-K, an arylating nitric oxide donor, is tested as a mean to regulate microRNAs and modulating cellular mechanisms to combat MM.

Method : MM cell line (RPMI8226) was treated with JS-K to screen a panel of microRNAs (miR-144, miR-199 and miR-203) and to assess various cancer hallmarks. Cell viability was investigated by MTT assay while PI staining was done for cell cycle analysis. The apoptosis was assessed by Annexin-V-FITC/PI staining and JC-1 mediated determination of mitochondrial membrane potential. Further, CFSE is used to evaluate cell proliferation. The consequence of JS-K on autophagy was determined by transcript analysis of autophagy associated molecules (HMGB1, LC-3, beclin and p62).

Results : Treatment of myeloma cells by JS-K exhibited significant cell death in dose-dependent manner and 0.55μM & 0.65μM were identified as inhibitory concentration 30 (IC30) & IC50. JS-K treatment resulted in significant upregulation of miR-144 in MM cells. The treatment arrested myeloma cells at Sub-G0/G1 phase. The treatment with JS-K significantly predisposed myeloma cells to intrinsic apoptotic pathway assessed by depolarisation of mitochondrial membrane. Myeloma cell proliferation reduced significantly in treated cells. Moreover, autophagic flux was found to be diminished in myeloma cells treated with JS-K.

Conclusion : A small molecule, JS-K mediated induction of miR-144 could be of translational significance for myeloma therapeutics. The anti-myeloma efficacy of JS-K could be attributed by inhibition of autophagic flux with simultaneous induction of apoptosis. This maiden study, thus, signifies plausible utilization of JS-K as a therapy for providing better clinical outcome in MM in future.

Keywords : Multiple myeloma, JS-k, Apoptosis, Autophagy, Cancer therapeutics

PP07-5

Real-world effectiveness and safety of intravenous daratumumab in patients with multiple myeloma: A multi-center, observational study from Korea

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Background : Daratumumab is a first-in-class monoclonal antibody binding specifically to CD38-expressing tumor cells and induce cell death. In Korea, daratumumab first received regulatory approval in 2017 as a monotherapy for patients with MM who have received at least three prior lines of therapy (LOT), including a proteasome inhibitor and an immunomodulatory agent, based on results from the SIRIUS trial. This study provides a valulable real-world evidence on daratumumab treatment for patients in Korea.

Method : This study is a multicenter, prospective, observational study to evaluate safety and effectiveness of treatment of daratumumab from September 2018 to February 2021 in Korea.

Results : A total of 125 patients were enrolled. Among 118 patients evaluated for clinical effectiveness, the ORR was 52.5%; better than VGPR was observed in 23 (19.5%) patients; PR was observed in 39 patients (33%). The median PFS was 4.1 months. Among all patients, 702 AEs were reported in 121 patients (96.8%); Fever was the most frequently observed AE (24.0%), followed by dyspnea (20%), chills (16.8%), decreased neutrophil count (14.4%) and anemia (14.4%). 164 treatment-emergent AEs (TEAE) were reported in 77 patients (61.6%); Dyspnea was the most frequently observed TEAE (15.2%), followed by chills (14.4%) and fever (10.4%). 175 grade 3–4 AEs were reported in 65 patients (52.0%), of which 8.8% were treatment-related. The most frequent grade 3–4 AEs were decreased neutrophil count (12.8%), anemia (8.8%) and febrile neutropenia (8.0%). The most frequent grade3-4 TEAEs were decreased neutrophil count (2.4%), pneumonia (1.6%) and febrile neutropenia (1.6%).

Conclusion : Almost all patients enrolled in this study (96.8%) received 3 or more prior LOT. The ORR observed in this study was higher than previously observed in the SIRIUS study (52.5 vs 29.2%). The median PFS in this study was comparable with the SIRIUS study (4.1 months vs 3.7 months). There were no unexpected safety results from this observation.

Keywords : Multiple myeloma, Daratumumab, Real-world, Effectiveness, Safety

PP07-6

Enhancing the survival of patients with primary plasma cell leukemia and identification of prognostic factors: Insights from a comprehensive study (the KM-MWP-2204 study)

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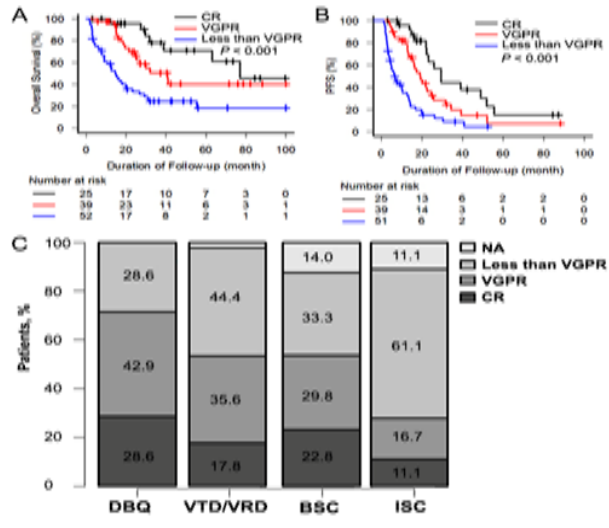
Background : Primary plasma cell leukemia (pPCL) is a rare and aggressive subtype of plasma cell disorder. Despite advancements in treatment, such as novel therapies and autologous stem cell transplantation, pPCL continues to pose significant clinical challenges. This retrospective study evaluated the optimal first-line treatment and prognostic factors in patients diagnosed with pPCL based on the revised criteria.

Method : A total of 127 patients diagnosed with pPCL were eligible.

Results : 25 patients who achieved a complete response (CR) after induction therapy showed significantly improved progression free survival (PFS) and overall survival (OS) than other patients. Moreover, multivariate analysis identified achieving CR after frontline therapy as independent predictor of OS. When evaluating response rates according to the induction therapies such as daratumumab-based quadruplets, bortezomib and thalidomide or bortezomib and lenalidomide combinations, bortezomib-based combinations, or immunomodulatory drugs based combinations, CR rate was the highest in daratumumab-based quadruplets than other induction therapy. In addition, 33 patients underwent ^{18}F-FDG PET/CT prior to initial treatments, and 11 showed more than 3 focal lesions. However, there was no difference of survival outcomes according to the PET/CT postivity.

Conclusion : In conclusion, achieving CR after induction therapy was crucial for improving survival outcomes, and daratumumab-based quadruplets may be reasonable choice as an induction therapy for pPCL.

Keywords : Primary plasma cell leukemia, Induction therapy, Prognosis



PP07-7

Fractures and mortality in multiple myeloma patients: A Korean population-based case-control study (the CAREMM-2105 study)

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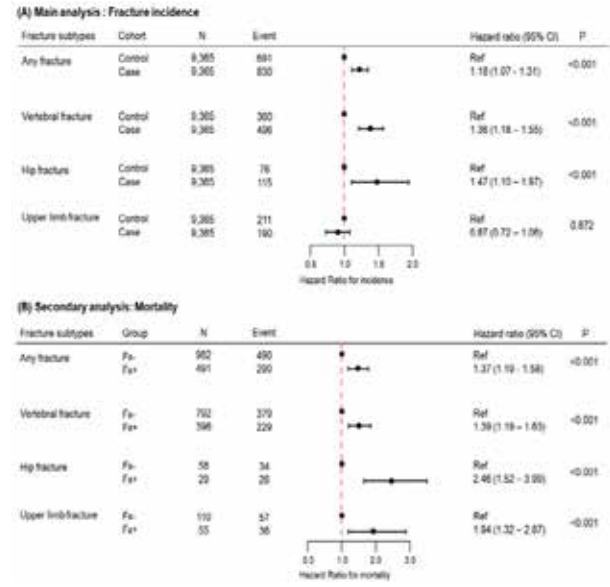
Background : Multiple myeloma (MM) is a malignant hematological disorder. It significantly affects bone health and increases vulnerability to fractures, which compromise the quality of life and increase mortality rates. This study investigated the incidence of fractures in MM patients using a recent extensive cohort and explored the relationship between fractures and mortality to elucidate their impact on survival.

Method : Data from the Korean National Health Insurance Service database were used to establish a population-based cohort of 13,925 patients diagnosed with MM between January 2010 and December 2020. A control group comprising 111,400 individuals from the general population was also selected. To compare fracture incidence between MM patients and the general population, we created matched case and control cohorts using 1:1 propensity score matching. We calculated the cumulative incidence of fractures by considering death as a competing risk factor. The fractures were categorized into vertebral, hip, and upper limb fractures, and their incidence at each location was compared. A survival analysis was conducted, considering the occurrence of fractures and specific fracture types.

Results : Among the 13,925 MM patients analyzed, the observed hazard ratios (HRs) for fractures during the study period were: any fracture- 1.18 (95% confidence interval [CI]:1.07-1.31); vertebral fractures- 1.36 (95% CI:1.18-1.55); and hip fractures- 1.47 (95% CI:1.10-1.97). HRs for mortality were as follows: any fracture- 1.37 (95% CI:1.19-1.58); vertebral fractures- 1.39 (95% CI:1.19-1.63); hip fractures- 2.46 (95% CI:1.52-3.99); and upper limb fractures- 1.94 (95% CI:1.32-2.87). All results were statistically significant ($p < 0.001$), thereby confirming that MM patients have a significantly higher risk of fractures than the general population.

Conclusion : MM patients experiencing fractures within 1 year of diagnosis exhibit increased mortality compared with those without fractures. Clinicians are encouraged to closely monitor these risks and incorporate targeted bone health strategies and patient education programs into their care approaches.

Keywords : Multiple myeloma, Fracture, Mortality, Bone health, Quality of life



PP07-8

Cardiovascular disease in long-term multiple myeloma survivors: A nationwide korean case-control study (the CAREMM-2105 study)

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Background : Multiple myeloma (MM), prevalent among older adults, is associated with significant cardiovascular (CV) risks due to its treatment side effects and patient comorbidities. While recent advancements have notably improved MM survival rates, there is a conspicuous lack of data regarding the long-term CV impact on survivors.

Method : This analysis used comprehensive data from South Korea's National Health Insurance Service, covering approximately 50 million individuals from 2009 to 2020. Participants were selected through 1:1 propensity score matching from an initial cohort of 37,883 MM patients and 378,830 controls, ensuring comparability between the groups. A 5-year landmark analysis included 6,949 patients from each group. The primary focus was on assessing the incidence of CV events in MM survivors who had surpassed 5 years post-diagnosis.

Results : The MM and control groups were comparable in mean age (62.2 ± 11.1 years and 62.8 ± 10.6 years, respectively), gender, age distribution, and comorbidities. An 8-year cumulative incidence of CV events was 5.8% in the MM group and 6.4% in the control group, with no statistically significant difference. The cause-specific hazard ratio for CV events in MM patients versus controls was 0.898, within a 95% confidence interval of 0.714 to 1.131.

Conclusion : The study reveals no substantial long-term difference in CV risks between MM survivors and a matched control group. These findings suggest that the long-term CV outcomes for MM patients might not be as adversely affected as previously assumed. These results underscore the need for continued research into cardiovascular management in multiple myeloma survivorship.

Keywords : Multiple myeloma, Cardiovascular disease, Mortality, Survivors

PP07-9

Favorable survival outcomes with delayed treatment in multiple myeloma patients with biochemical relapse

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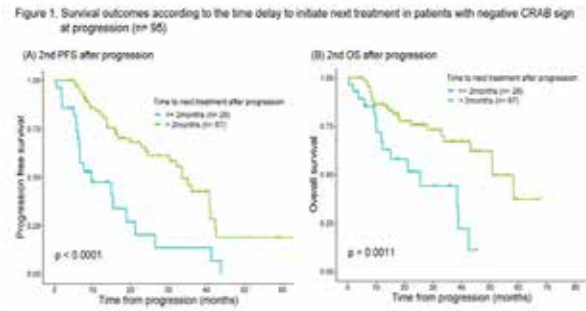
Background : Despite recent advances, multiple myeloma (MM) remains an incurable disease, and initial remission is to be followed by relapse, demanding additional therapy. However, since the patients with biochemical relapse are asymptomatic and do not require immediate treatment, it's a challenge for clinicians to decide the optimal timing for moving onto second-line therapy. We investigated the prognostic relevance of treatment free interval in patients with relapsed/refractory multiple myeloma (RRMM).

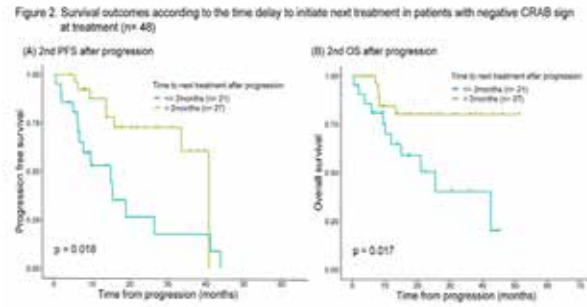
Method : The Medical records of RRMM patients from 2 centers in South Korea between 2013 and 2022 were retrospectively reviewed. A cut-off duration of 2 months was used to define whether treatment free interval was extended or not.

Results : Among 143 patients with RMM, a total of 45.5% was male and 54.5% was female, and the median age at the initial diagnosis was 65.8. All patients received either carfilzomib or ixazomib based therapy for second-line treatment. At the time of biochemical relapse, 95 patients showed negative CRAB signs, and 48 patients did not experience CRAB signs until the initiation of next treatment. In the group of negative CRAB signs at relapse, the patients with the time delay to initiate next treatment longer than 2 months had a prolonged progression-free survival (PFS) and overall survival (OS) compared to those with the delay interval shorter than 2 months (median PFS: 11.54 vs. 6.46 months, p<0.0001; median OS: 16.11 vs. 11.28 months, p=0.0011) (Fig.1). The group of patients which had both negative CRAB signs at treatment and the extended delay interval also showed a better PFS and OS (median PFS: 9.57 vs. 8.19 months, p=0.018; median OS: 14.86 vs. 13.81 months, p=0.017)

Conclusion : The present study suggested that the treatment delay in RMM patients with negative CRAB signs is shown to be associated with better survival outcomes.

Keywords : Multiple myeloma, Biochemical relapse, CRAB signs, Delayed treatment





mination of the level of galectin-3 in blood serum was carried out by the CMIA method on ARCHITECT 12000SR analyzer.

Results : The median level of galectin-3 in MM patients-16.2 ng/ml, MGUS-18.0 ng/ml, p=0.24. Kidney damage associated with MGUS at the time of diagnosis was detected in 22 (28.6%) cases, in patients with newly diagnosed MM in 41 (47.7%). In MM and MGUS patients with kidney damage, a significant increase in the galectin-3 level was revealed in relation to patients with preserved renal function, in whom the galectin-3 level corresponded to normal rates. (p=0.006, p=0.0001 respectively). The level of produced galectin-3 correlated with the level of β2-microglobulin (p<0.001), which is associated with the severity of renal dysfunction and tumor burden. In MM patients with β2-microglobulin >3 mg/l, galectin-3 levels were significantly higher (p=0.005) than in patients with normal indices, in MGUS patients (p=0.0001). Patients with secretion of light chains of immunoglobulins were significantly more likely to have higher than normal levels of galectin-3 (with MM - p = 0.002), with MGUS - p=0.0001), in relation to patients with other variants of immunoglobulin secretion.

Conclusion : Galectin-3 is promising for use as a biomarker of tumor damage to the kidneys in patients with plasma cell proliferations.

Keywords : Galectin-3, Kidney damage, Multiple myeloma, Monoclonal gammopathy of undetermined significance

PP07-10

The significance of galectin-3 level in plasma cell proliferations complicated by kidney damage

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Background : Galectin-3 is an expressed lectin in the human body that promotes inflammation and fibrotic changes and it is a biomarker for certain types of heart disease, autoimmune diseases, viral infections, etc. The study of galectin-3 level in plasma cell proliferations - MM and MGUS with kidney damage has not been sufficiently investigated.

Method : The study included 163 patients, 86 MM (median age of 64 years) and 77 MGUS patients (median age of 62 years). The observation period was 2018-2023. The criterion for exclusion was the presence in patients of DM and pathology of the cardiovascular system in the decompensation stage. Deter-

PP07-11

A phase 3, two-stage, randomized study of mezigdomide, bortezomib, and dexamethasone (MeziVd) versus pomalidomide, bortezomib, and dexamethasone (PVd) in relapsed/refractory multiple myeloma (RRMM): SUCCESSOR-1

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Background : Mezigdomide (MEZI) is a novel, potent oral cereblon E3 ligase modulator (CELMoD™) with enhanced antimyeloma effects compared with IMiDs®. Preclinically, MEZI has shown potent synergy with Vd, and preliminary phase 1/2 results showed encouraging efficacy and safety of MeziVd in RRMM.

Method : This multicenter, open-label, phase 3 trial comprises 2 stages. Stage 1: 140 patients will be randomized 1:1:1:1 to 1.0, 0.6, or 0.3mg MEZI plus Vd or PVd to select optimal MEZI dose based on efficacy, safety, pharmacokinetic, pharmacodynamic, and exposure-response analyses. Stage 2: 620 patients will be randomized 1:1 to MeziVd or PVd for efficacy and safety analyses. Key eligibility criteria include ≥18 years, 1-3 prior lines of antimyeloma treatment, prior lenalidomide exposure, minimal response or better to ≥1 prior treatment, no prior pomalidomide exposure, no proteasome inhibitor refractoriness, and documented progressive disease (PD) during or after last regimen. MeziVd arm treatment includes 21-day cycles with MEZI on D1–14; 1.3mg/m^2 subcutaneous bortezomib on D1,4,8,11 of C1–8, and on D1, 8 of ≥C9; 20mg oral dexamethasone on D1,2,4,5,8,9,11,12 of C1–8, and D1,2,8,9 of ≥C9. PVd arm treatment includes 21-day cycles with 4mg oral pomalidomide D1–14 plus Vd as in the MeziVd arm. Treatment continues until PD or unacceptable toxicity. Primary efficacy endpoint is progression-free survival. Planned interim analyses include MEZI dose selection, and PFS futility and superiority. Secondary endpoints include recommended MEZI dose plus Vd, overall survival, overall response rate, time to and duration of response, time to progression, safety, and quality of life. Patients will be stratified by age, number of prior lines of treatment, and ISS stage at screening.

Results : Enrollment began September 2022 and is ongoing.

Conclusion : SUCCESSOR-1 (NCT05519085) will compare the efficacy and safety of MEZI versus pomalidomide in RRMM.

Keywords : Clinical trial, Phase 3, Trial in progress, CELMoD, RRMM

PP07-12

Excaliber-RRMM: A phase 3, 2-stage study of iberdomide, daratumumab, and dexamethasone (IberDd) versus daratumumab, bortezomib, and dexamethasone (DVd) in patients with relapsed/refractory multiple myeloma (RRMM)

Sagar Lonial[1], Hang Quach[2], Meletios Dimopoulos[3], Paula Rodriguez Otero[4], Jesus Berdeja[5], Paul Richardson[6], Margee Kyada[7], Shuyu Chu[7], Min Chen[7], Patricia Abad[7], Juliane Morando[7], Kihyun Kim[9*], Niels Van De Donk[8]

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Background : Iberdomide (IBER) is a novel, potent oral cereblon E3 ligase modulator (CELMoD™) with enhanced tumoricidal and immune-stimulatory effects compared with IMiD® agents. IBER has synergy with dexamethasone (DEX), daratumumab (DARA), and bortezomib (BORT) in-vitro. In a phase 1/2 trial, IberDd demonstrated efficacy and manageable safety profile in patients with RRMM.

Method : This multicenter, open-label study comprises 2 stages: Stage 1, ≥200 patients will be randomized 1:1:1:1 to 1.0, 1.3, 1.6mg IBER +DARA +DEX or to DVd to identify optimal IBER dose; Stage 2, ~664 patients will be randomized 1:1 to selected IberDd dose or DVd. Patients will be stratified by number of prior treatment lines, age, and ISS stage at study entry. Primary efficacy endpoint is progression-free survival (PFS). Secondary endpoints include overall survival, duration of response, time to progression, overall response rate, residual disease negativity rate, safety, and quality of life. Treatment in the IberDd arm consists of 28-day cycles with IBER on D1–21; 1800mg DARA on D1,8,15 and 22 of C1–2, D1 and 15 of C3–6, and D1 of ≥C7; 40mg DEX on D1,8,15 and 22. Treatment in the DVd arm consists of 21-D cycles for C1–8 and 28-D cycles for ≥C9; 1800mg DARA on D1,8 and 15 for C1-3, D1 for ≥C4; 1.3mg/m^2 BORT on D1,4,8 and 11 for C1-8; and 20mg DEX on D1,2,4,5,8,9,11 and 12 for C1-8. Treatment will continue until PD or unacceptable toxicity. Key eligibility criteria include ≥18 years, 1–2 prior lines of antimyeloma, partial response or better to ≥1 prior treatment, documented PD during/after last regimen. Prior anti-CD38 treatment is allowed in Stage 2.

Results : Enrollment is ongoing.

Conclusion : EXCALIBER-RRMM (NCT04975997) will compare efficacy and safety of IberDd versus DVd in patients with early RRMM.

Keywords : RRMM, Clinical trial, Phase 3, CELMoD, Trial in progress

PP07-13

Non-clinical test results of tetracyclic triterpene compound, a new effective drug candidate for multiple myeloma treatment

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Background : Multiple myeloma (MM) is an incurable hematologic cancer that originates in plasma cells and occurs primarily in older patients over 60. This study screened for hit compounds for MM treatments targeting mitochondria and apoptosis proteins. Further, non-clinical testing, including molecular docking analysis, was performed.

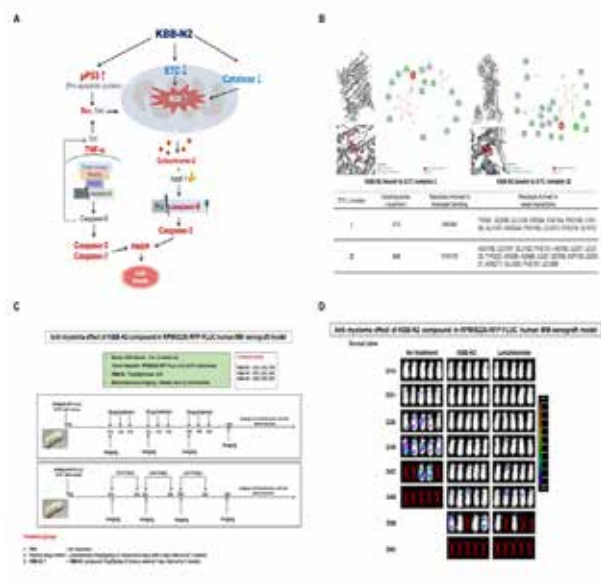
Method : Based on our previous studies, candidate compounds targeting mitochondria were screened (www.medchemexpress.com). Apoptosis mechanisms were investigated in vitro. Complex immunocompromised mice were established by injecting RPMI8226-RFP-FLuc cells through the tail vein. Efficacy of the KBB-N2 activity was assessed following intraperitoneal and tail vein infusions for three days a week at daily intervals. Toxicity, pharmacokinetics, and molecular docking analyses were performed according to the established protocols.

Results : The primary mechanism of action of KBB-N2 in MM cells was inhibiting the activity of the mitochondrial electron transport (ETC) complex, resulting in the generation of excess intracellular reactive oxygen species (ROS), which led to tumor cell death by ROS-mediated apoptosis. In addition, exposure to KBB-N2 inhibited the activity of catalase, a powerful antioxidant enzyme in MM cells. KBB-N2 activity involves PARP cleavage and caspase activation in the apoptotic pathway. Furthermore, KBB-N2 inhibited cell growth and exerted cytotoxicity. KBB-N2 induced apoptosis by activating the P53 apoptosis pathway in MM cells. In vivo, all untreated tumor-bearing mice showed rapid tumor growth and severe plasmacytomas, which led to death within seven weeks. Mice treated with KBB-N2 had significantly inhibited tumor growth and longer survival times. The molecular docking assay revealed the optimal docking conformation binding energy of KBB-N2 with docking scores

(kcal/M) of -7.3 and -9.8 for ETC complexes I and III, respectively.

Conclusion : The triterpene compound, KBB-N2, was identified as a hit compound and may act as a targeted agent for MM treatment. The antimyeloma activity of KBB-N2 involves interference with the ETC complex and leads to MM cell death.

Keywords : Triterpene, Anti-myeloma effect, Multiple myeloma



PP07-14

Glutathione S-transferase M1 and T1 deletion mutation is associated with the risk of multiple myeloma development: A meta-analysis

Arch Raphael Manalac[1*], Francheska Casupanan[1], Arlene Joy Canasa[1], Angela Mae Cuartelon[1], Justine Nicole Sison[1], Janina Carla Zapata[1], Raphael Enrique Tiongco[1]

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Background : Several studies suggest that the deletion mutations M1 and T1 of the glutathione s-transferase (GST) gene are associated with cancer development. However, limited studies on its association with multiple myeloma (MM) development are available. Hence, we performed this meta-analysis to obtain more precise estimates by pooling together individual studies that had been conducted.

Method : Relevant studies were searched from database websites and screened. Data from the resulting studies were pooled in a customized spreadsheet and analyzed using the Review Manager software. Odds ratios (ORs) and 95% confidence intervals (CIs) were interpreted accordingly.

Results : A total of 118 studies resulted from the search. Four studies involving 1131 participants (446 cases and 685 controls) were included in the meta-analysis. Both M1 and T1 deletion mutations showed significant association with MM development. Based on the overall and post-outlier findings, the M1 deletion mutation is associated with a lower risk of MM development. In contrast, the T1 deletion mutation is more associated with an increased risk of MM development. These findings are supported by the high degree of association and robustness of the pooled outcomes.

Conclusion : Overall, the presence of the M1 and T1 deletion mutation is significantly associated with the risk of developing MM. However, further studies are needed to verify these claims, especially their applicability in various ethnic settings.

Keywords : GST, GSTT1, GSTM1, Multiple myeloma, Meta-analysis

PP07-15

MagnetisMM-3 trial: Updated long-term efficacy and safety of elranatamab in relapsed or refractory multiple myeloma

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Background : Elranatamab, a humanized, bispecific antibody, targets B-cell maturation antigen (BCMA) on myeloma cells and CD3 on T cells. In the phase 2 registrational MagnetisMM-3 trial (NCT04649359) of elranatamab monotherapy, patients (pts) with relapsed or refractory multiple myeloma (RRMM) who had not received prior BCMA-directed therapy (n=123) achieved an ORR of 61%.

Method : Eligible pts had previously received ≥1 proteasome inhibitor, immunomodulatory drug, and anti-CD38 antibody. Pts received elranatamab subcutaneously (step-up doses of 12 and 32 mg and then 76 mg once weekly). The primary endpoint was objective response rate (ORR) assessed by blinded-independent central review per IMWG criteria. Minimal residual disease (MRD) status was assessed using NGS (10^{-5} sensitivity).

Results : Median follow-up was 17.6 months (data cutoff: Sept 11, 2023). Confirmed ORR was 61.0% (95% CI, 51.8-69.6); ≥CR was 37.4%. In evaluable pts (n=30), 90.0% achieved MRD negativity. Probability of maintaining a response at 18 mos was 68.8%. Median PFS was 17.2 mos and median OS was 21.9 mos (not yet mature with >50% of pts censored). Common AEs (any grade ≥25%, grade 3/4 ≥10%) were infections (69.9%, 40.7%), cytokine release syndrome (57.7%, 0%), neutropenia (49.6%, 49.6%), anemia (48.8%, 37.4%), diarrhea (44.7%, 3.3%), fatigue (36.6%, 4.1%), decreased appetite (33.3%, 0.8%), pyrexia (32.5%, 4.1%), thrombocytopenia (31.7%, 23.6%), cough (27.6%, 0.8%), lymphopenia (26.8%, 25.2%), hypokalemia (26.8%, 11.4%), nausea (26.8%, 0%), injection site reaction (26.8%, 0%), and leukopenia (16.3%, 13.0%).

Conclusion : Extended follow-up from the ongoing MagnetisMM-3 trial of elranatamab in pts with RRMM demonstrated sustained clinical efficacy and no new safety signals.

Keywords : BCMA-Directed therapy, Elranatamab, Relapsed or refractory multiple myeloma, Bispecific antibody

PP07-16

Clinicopathological characteristics of monoclonal gammopathy of clinical significance in a single tertiary hospital

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Background : Monoclonal gammopathy of clinical significance (MGCS) refers to a group of nonmalignant heterogeneous diseases that have clinical symptoms due to monoclonal protein. MGCS is subgrouped into renal, cutaneous, and neurologic significance based on the site of clinical manifestation. MGCS can present in multiple systemic manifestations, and some patients have overlapping symptoms in multiple organs, leading to subgroups based on the predominant symptom. We investigated the clinicopathological characteristics of MGCS.

Method : We retrospectively evaluated 121 patients with monoclonal gammopathy (MG) who did not meet diagnostic criteria for plasma cell myeloma, Waldenström macroglobulinemia, or other lymphoproliferative disorders. We excluded patients with a history of hemodialysis, kidney transplantation, or malignancy among those diagnosed with MG. Patients with estimated glomerular filtration rate (e-GFR)

Results : Among the 121 patients with MG, the largest subgroup was 64 (52.9%) suspected MGRS, of which kidney biopsy was performed in 29 (24.0%) patients and 15 (12.4%) patients were diagnosed with MGRS. Among the MGRS, 12 renal immunoglobulin light chain amyloidosis, 1 thrombotic microangiopathy, 1 proliferative glomerulonephritis with monoclonal immunoglobulin deposits, and 1 C3 glomerulonephritis were diagnosed. Nine (7.4%) patients were diagnosed to monoclonal gammopathy of neurological significance that consists of 5 polyneuropathy, organomegaly, endocrinopathy, M-protein, skin changes (POEMS) syndrome and 4 anti-myelin-associated glycoprotein (MAG) peripheral neuropathy. Four (3.3%) cases of monoclonal gammopathy of cutaneous significance included cryoglobulinemia, necrobiotic xanthogranuloma, Schnitzler syndrome, and scleromyxedema. A total of 44 (36.4%) patients did not show clinical symptoms.

Conclusion : The diagnosis of MGCS was made in 23.1% (28/121) of the patients with MG. Treatments may need to be tailored to the clinical symptoms and in-depth differential diagnosis process could improve the early diagnosis of MGCS.

Keywords : Monoclonal gammopathy of clinical significance, Monoclonal gammopathy of renal significance, Monoclonal gammopathy of cutaneous significance, Monoclonal gammopathy of neurological significance

PP07-17

Retrospective analysis of autologous stem cell transplantation treatment outcomes in patients with dialysis-dependent multiple myeloma (DDMM) : KMM2304 study

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Background : Autologous stem cell transplantation performed after remission-inducing chemotherapy can improve the survival of multiple myeloma patients, but little research has been done on the effectiveness and safety of autologous stem cell transplantation in the dialysis-dependent multiple myeloma (DDMM) patient group.

Method : The patients receiving dialysis who were diagnosed with multiple myeloma from January 2001 to December 2022 in Korea were enrolled in this study. We retrospectively analyzed the treatment effectiveness and toxicities of the group that underwent autologous stem cell transplantation in DDMM patients with transplantable age of less than 70 years.

Results : Fifty-five DDMM patients with a median age of 56 (38-69 years) were enrolled from nine Korean institutions. Forty-one male (74.5%) and fourteen female (25.5%) patients were enrolled. In twenty-eight patients (50.9%), the stage (R-ISS) at first diagnosis was stage III, accounting for half of all patients. High-risk cytogenetic abnormalities included 17p deletion in four patients (7.3%), 4;14 chromosome translocation in six patients (10.9%), and 1q gain in sixteen patients (29.1%). Patients most often received the VTD regimen as a remission induction chemotherapy (30 patients, 54.5%), and most patients received reduced doses of melphalan as conditioning chemotherapy. (Table 1) The most common side effects were hematological toxicities, with grade 3 or higher thrombocytopenia occurring in twenty-four patients (43.6%) and grade 3 or higher neutropenia occurring in twenty-one patients (38.1%). There were no treatment-related deaths among DDMM patients included in this study. (Table 3) The median progression-free survival rate was 39.7 months (95% CI, 29.1-50.3), and the median OS was 67.2 months (95% CI, 52.8-81.6). (Figure 1)

Conclusion : In patients with dialysis-dependent multiple myeloma (DDMM) under the age of 70, autologous stem cell transplantation improves the treatment response rate and survival outcome with tolerable treatment-related toxicities.

Keywords : Multiple myeloma, Dialysis, Autologous stem cell transplantation

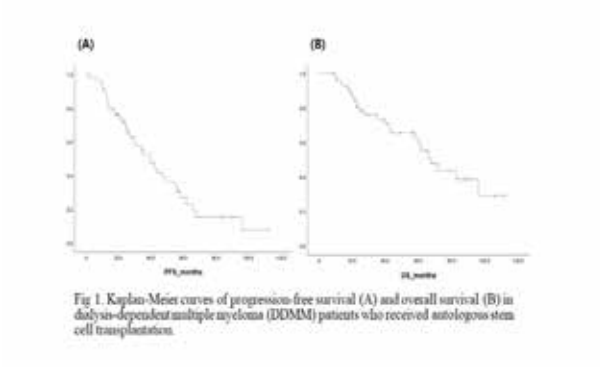

Fig 1. Kaplan-Meier curves of progression-free survival (A) and overall survival (B) in dialysis-dependent multiple myeloma (DDMM) patients who received autologous stem cell transplantation.

Table 1. Baseline characteristics

Baseline characteristics	Total patients (n=55)
Median age, years (range)	56 (38-69)
Sex, n (%)	
Male	41 (74.5)
Female	14 (25.5)
ECOG performance status score, n (%)	
0	3 (5.5)
1	38 (69.1)
2	8 (14.5)
3	3 (5.5)
Unknown	3 (5.5)
Type of heavy chain, n (%)	
IgG	20 (36.4)
IgA	9 (16.4)
IgD	5 (9.1)
Light chain disease	20 (36.4)
Unknown	1 (1.8)
Revised International Stage System, n (%)	
I	2 (3.6)
II	21 (38.2)
III	28 (50.9)
Unknown	4 (7.3)
High-risk cytogenetic abnormalities, n (%)	
del(17p)	4 (7.3)
t(4;14)	6 (10.9)
t(14;16)	2 (3.6)
gain(1q)	16 (29.1)
Extramedullary disease, n (%)	1 (1.8)
Kidney biopsy, n (%)	13 (23.6)
Cast nephropathy	7 (12.7)
Light chain deposit disease	4 (7.3)
Progressive GN with IgG deposition	1 (1.8)
Others	1 (1.8)
RRT type, n (%)	
Hemodialysis	54 (98.2)
Peritoneal dialysis	1 (1.8)
Induction chemotherapy, n (%)	
Td, CTd	15 (27.3)
VelDex	4 (7.3)
VTD	30 (54.5)
VCD	1 (1.8)
VMP	2 (3.6)
VRd	2 (3.6)
D-VTD	1 (1.8)
Conditioning chemotherapy, n (%)	
MEL140	28 (50.9)
MEL200	13 (23.6)
MEL160	1 (1.8)
< MEL140	9 (16.4)
BuMEL	2 (3.6)
BuCy	1 (1.8)

in anti-tumor immune reaction interacting with various other immune cells. Especially, myeloma has been associated with immune abnormalities in number and function of B, T and NK cells. Moreover, although it has recently attracted attention as a therapeutic target for drugs, reports concerning Tregs are insignificant. In this study, we aimed to present the expression level of Treg in myeloma compared with that of the normal control group.

Method : Peripheral blood samples from 90 healthy adult and bone marrow aspiration samples from 10 initial diagnosed myeloma patients were collected. Eight-color flow cytometry was performed using a Duraclone IM Treg tube kit: CD45RA-FITC, CD25-PE, CD39-PC5.5, CD4-PC7, FoxP3-A647, CD3-AA750, Helios-PBe, CD45-KrO.

Results : The average age of 10 myeloma patients was 68 years, and the ratio of male to female was 6:4. Marrow aspirates contain a median of 41.8% plasma cells and 12.8% lymphocytes. A gating strategy was established based on the $CD3^{+}CD4^{+}FoxP3^{+}CD25^{+}$ immunophenotypic characteristics on Treg. Proportion of Treg in myeloma averaged 4.8% of CD3+CD4+ T cells, which was statistically significantly higher than the average of 1.8% in normal control ($p<0.001$).

Conclusion : Treg expression are elevated in myeloma and it can thwart protective anti-tumor immunity. Further research into the tumor microenvironment, not just tumor clones, should need be expanded.

Keywords : Multiple myeloma, Regulatory T cells , Flow cytometry, CD25+, FoxP3+

PP07-18

Increase of regulatory T cells in multiple myeloma

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Background : Regulatory T cells (Tregs) are a small subset of CD4+ T cells that regulate immune homeostasis and self-tolerance. In tumor microenvironment, Tregs play a significant role

PP07-19

Distinct single-cell RNA sequencing-based transcriptional phenotype for AL amyloidosis

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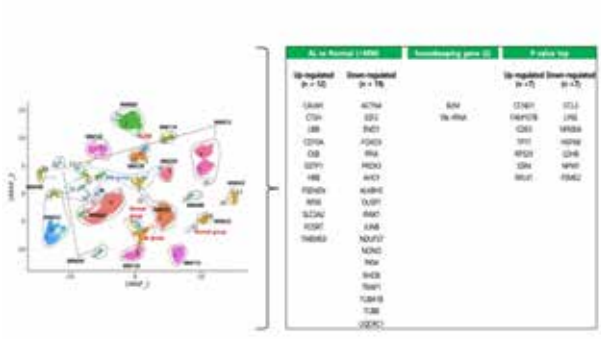
Background : AL amyloidosis, characterized by the deposition of amyloid fibrils derived from monoclonal light chains, often results in multi-organ dysfunction. Timely diagnosis is crucial for effective management. The gold standard for AL amyloidosis diagnosis involves the demonstration of amyloid deposits by biopsy, usually in affected organs. Despite their potential co-occurrence between multiple myeloma (MM) and AL amyloidosis, distinguishing AL amyloidosis within the context of MM poses diagnostic challenges.

Method : By single-cell RNA sequencing (scRNA-seq), we investigated bone marrow aspirates of 8 treatment-naïve AL amyloidosis, 18 treatment-naïve MM. Publicly available scRNA-seq data of BM-MNCs from 23 healthy donors were used as normal control.

Results : Utilizing single-cell RNA sequencing, we identified 37 distinct subtypes of plasma cells, with the majority being MM-specific and showing patient-specific independence. In contrast, control and AL groups exhibited a more convergent pattern, comprising 1-2 plasma cell subsets. We discovered gene expression differences among plasma cells in control, AL, and MM groups. Through comparative analysis of up-regulated and down-regulated genes, we identified 2,342 potential candidates specific to AL amyloidosis, of which 1,598 were up-regulated and 744 were down-regulated. Focusing on tier-1 genes with possible driver mutations and confirming gene nature related to protein metabolism disorders, we selected 54 genes unique to AL amyloidosis compared to MM or healthy controls. To develop a transcriptional biomarker panel for AL amyloidosis, we further refined the selection to 31 genes that facilitated panel construction, including two housekeeping genes and 14 genes with the highest statistical significance for panel development QC. Ultimately, we assembled a transcriptome panel consisting of 47 genes, specific to the diagnosis of AL amyloidosis.

Conclusion : This panel has the potential to aid in the identification of patients with asymptomatic plasma cell dyscrasia who should undergo amyloidosis tissue testing. However, its validation status necessitates further assessment in a validation cohort.

Keywords : AL amyloidosis, Myeloma, Single cell, Biomarker, Sequencing



PP07-20

Real-world outcomes of novel immunotherapy versus standard of care in patients with relapsed/refractory multiple myeloma (CAREMM-2305)

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Background : To address the unmet medical need for relapsed/refractory patients with multiple myeloma (MM), novel immunotherapies have been evaluated in prospective trials and have shown outstanding results compared to standard of care (SOC). Given the lack of real-world data for T-cell redirecting therapies and antibody-drug conjugates, we analyzed the outcomes of heavily pretreated patients with MM who received novel immunotherapy compared to SOC in real-world population.

Method : From February 2021 to January 2023, 479 patients who progressed after at least one line of prior anti-myeloma agents received novel immunotherapy or SOC at our hospital.

Results : In our cohort, 75 (15.7%) and 404 (84.3%) patients received novel immunotherapy and SOC, respectively. Most baseline characteristics were well balanced between the two groups, except for significantly lower lactate dehydrogenase (LDH; 250 vs 396; $P < 0.001$) and more lines of prior anti-myeloma therapy (4.0 vs 3.0; $P < 0.001$) in the novel immunotherapy group. Patients in the novel immunotherapy group received were bispecific antibodies in 31 (41.3%), antibody-drug conjugate in 30 (40.0%), CAR-T cells in 5 (6.7%), and others in 3 (4.0%). Median progression-free survival was significantly longer in the novel immunotherapy than in the SOC group (21.3 months vs. 9.5 months; $P = 0.021$ in overall cohort and 22.3 months vs. 4.5 months; $P < 0.001$ in the propensity-matched cohort), but median overall survival was not significantly different between the two groups (30.3 months vs. 29.5 months; $P = 0.570$ in the overall cohort and 30.3 months vs. 29.5 months; $P = 0.380$).

Conclusion : Our current study showed a survival benefit of novel immunotherapy compared to SOC in patients who progressed after at least one line of prior anti-myeloma agents in real-world practice. This research was supported by a grant (RS-2023-00216446) from the Ministry of Food and Drug Safety in 2023.

Keywords : CAR-T, Bi-specific antibody, Antibody-drug conjugate, Multiple myeloma

PP07-21

Exploration of clinical implication of circulating tumor DNA in multiple myeloma and its precursor diseases

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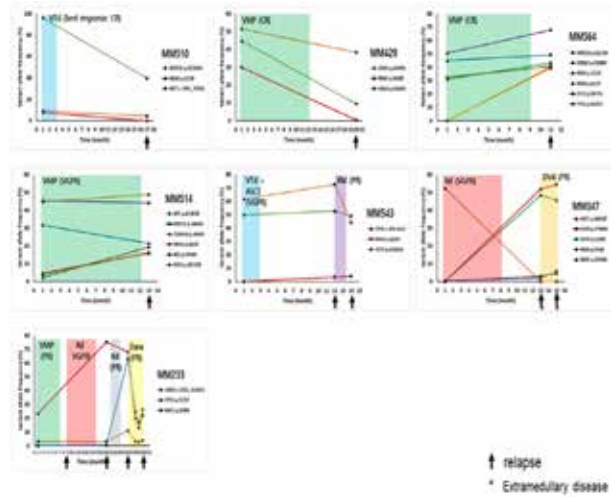
Background : Genetic alterations are pivotal in the development and therapeutic resistance of multiple myeloma (MM). Typically obtained from invasive bone marrow (BM) samples, the MM genetic profile poses challenges due to biopsy invasiveness. To overcome these limitations, we explored the clinical potential of liquid biopsy using circulating tumor DNA (ctDNA) derived from minimally invasive peripheral blood (PB) sampling in MM.

Method : Utilizing custom NGS panels (OncoChase, ConnectaGen, Seoul, Korea) targeting 156 cancer-related genes, we analyzed ctDNA samples from 106 patients with monoclonal gammopathy of undetermined significance (MGUS, n=7), smoldering MM (SMM, n=6), or MM (n=89) through targeted deep sequencing. In a subset (n=7) of MM patients, ctDNA was tracked at MM diagnosis and relapse.

Results : The cohort exhibited 226 somatic mutations (174 SNVs and 52 indels), with mutation frequency increasing from MGUS (average 1.3) to SMM (average 1.7) to MM (average 2.1). Shared mutations were prevalent in MM (68.9%) compared to MGUS (25.0%) in paired BM and ctDNA analysis. Recurrent mutations, particularly RAS/RAF activating mutations (KRAS, NRAS, or BRAF) and TP53, were significantly enriched in MM genomes. Specific mutations correlated with MM-related presentations: hypercalcemia and TET2 (P=0.048), renal insufficiency and NRAS (P=0.031), paramedullary myeloma and TP53 (P=0.030), and extramedullary myeloma and NRAS (P=0.032). Multivariable regression hazard analysis indicated that NRAS (HR=3.66, 95% CI 1.20-11.22, P=0.023) and TET2 alterations (HR=4.70, 95% CI 1.37-16.11, P=0.014) significantly impacted the 2-year progression-free survival rate. Long-term responders lacked driver mutations, while relapsed/refractory MM cases showed increased RAS/RAF mutation variant allele frequencies. Additional mutations, along with an increased variant allele frequency, characterized relapsed/refractory MM.

Conclusion : Our ctDNA sequential analysis offers substantial insights into the biology of disease progression and MM prognosis, presenting a minimally invasive diagnostic approach. This work was supported by the National Research Foundation of Korea(NRF) grant funded by the Korea government(MSIT) (No. NRF-2021R1G1A1093870)

Keywords : Myeloma, Circulating tumor DNA, Cell-free dna, RAS, TP53



PP08-1

The *TERT rs2736100* polymorphism as genetic predisposition of myeloproliferative neoplasms in Asian population: A systematic review and meta-analysis

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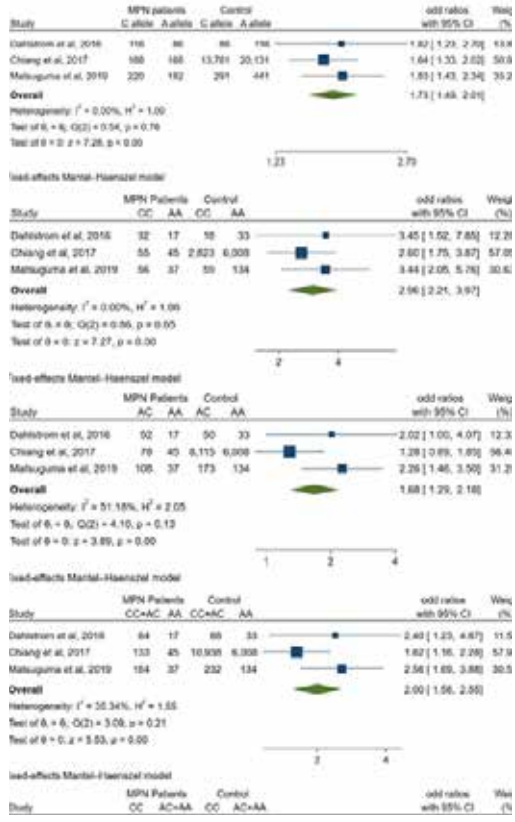
Background : Myeloproliferative neoplasms (MPN) are often characterized by specific genetic variation. Previous studies reported that a single nucleotide polymorphism (SNP) in the telomerase reverse transcriptase (TERT) gene, rs2736100, is highly associated with MPN risk among Caucasians. However, less is known whether this association is present in the Asian population. This study aimed to confirm the association between TERT rs2736100 polymorphism and MPNs among Asians.

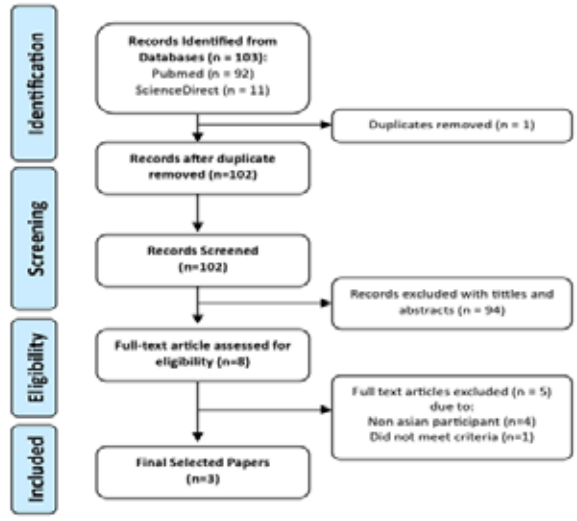
Method : We performed a comprehensive literature search from PubMed, ScienceDirect, and Cochrane Central databases using search terms ((TERT) OR (telomerase reverse transcriptase)) AND ((polymorphism) OR (genetic)) AND ((myeloproliferative disorder) OR (myeloproliferative neoplasm)) that were published from the year of 2000 up to October 2023. Case-control studies in the Asian population were collected using specific inclusion criteria and then assessed for study quality using the Newcastle-Ottawa Scale (NOS). Pooled odd ratios (ORs) with a 95% confidence interval (95% CI) were estimated using STATA 17 in different genetic models to evaluate the association between TERT rs2736100 polymorphism and MPNs.

Results : A total of 3 studies, including 480 MPN patients and 17.413 healthy controls were examined after an initial 102 titles and abstracts were screened and excluded. We found a significant association between TERT rs2736100 polymorphism and the risk of MPNs in allele model (C vs A) [OR 1.73; 95% CI 1.49–2.01]; homozygous model (CC vs AA) [OR 2.96; 95% CI 2.21–3.97]; heterozygous model (AC vs AA) [OR 1.68; 95% CI 1.29–2.18]; dominant model (CC+AC vs AA) [OR 2.00; 95% CI 1.56–2.55]; and recessive model (CC vs AC+AA) [OR 2.14; 95% CI 1.69–2.72].

Conclusion : This study confirmed that the TERT rs2736100 polymorphism is associated with the risk of MPNs in all genetic models, potentially increasing susceptibility among Asians. Further research involving a larger population is needed to explain the functional role of gene polymorphism in MPNs.

Keywords : Asian, Myeloproliferative neoplasms, Polymorphism, rs2736100, TERT





PP08-2

Molecular profile of myeloproliferative neoplasms

Jiyeon Kim[1], Yu Jeong Choi[1], Haerim Chung[2], Hye Won Kook[2], Ji Eun Jang[2], Doh Yu Hwang[2], Seung-Tae Lee[1], Jong Rak Choi[1], June-Won Cheong[2], Saeam Shin[1*]

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Background : In classic, BCR::ABL1-negative myeloproliferative neoplasm (MPN), *JAK2, CALR*, and/or *MPL* gene mutation is found in over 90% of patients. These genes are considered 'disease driver mutations', contributing to the expression of MPN phenotypes. Genes such as *TET2, ASXL1,* and *DNMT3A* are considered 'clonal driver mutations' and are thought to modify the phenotype only when present alongside *JAK2, CALR*, and *MPL*. In this study, we investigated the mutation profiles of MPN patients.

Method : We conducted a retrospective study on patients who underwent targeted NGS panel testing and were diagnosed with MPN from July 2017 to June 2023. The targeted NGS panel included 531 genes associated with hematological disorders. We examined the mutation profile of patients, specifically the prevalence of *JAK2, CALR, MPL,* and other accompanying genes. Additionally, the mutation profiles of cases that progressed to acute leukemia after MPN diagnosis were examined.

Results : Of 87 patients, among 37 essential thrombocythemia patients, 23 (62.2%) patients had sole *JAK2* or *CALR* mutations. *ASXL1* and *TET2* were the most commonly found genes among accompanying genes. In 31 polycythemia vera patients, 20 (64.5%) patients had sole *JAK2* mutations. *TET2* was the most frequent accompanying gene. Among 19 primary myelofibrosis patients, most patients (73.68%) had *JAK2* and other mutations, with *ASXL1* and *TET2* being the most reported. Eight patients had secondary leukemia, with seven diagnosed with acute myeloid leukemia and one with acute lymphoblastic leukemia. Six had *JAK2* mutations, with four having *TP53* mutations and two having *RUNX1* and *ASXL1*.

Conclusion : In this study, we investigated the mutation profile of MPN patients. There were differences in disease driver mutations and in accompanying clonal driver mutations dominantly found in each type of disease. Further research is needed to determine whether these differences in the mutation profile affect the prognosis of patients.

Keywords : Myeloproliferative neoplasms, Essential thrombocythemia, Polycythemia vera, Primary myelofibrosis, Mutation profile

PP08-3

Targeting *c-Abl* in myeloproliferative neoplasms: Benzylisoquinoline derivatives and their inclusion complexes form by molecular docking/ADMET profiles

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Background : Myeloproliferative Neoplasms (MPNs) encompass a group of hematologic disorders characterized by abnormal proliferation of myeloid cells. The aberrant activation of the c-Abl protein, often associated with the BCR-ABL1 fusion gene, plays a crucial role in the pathogenesis of Chronic Myeloid Leukemia (CML), a subtype of MPN. This abstract delves into the potential of benzylisoquinoline derivatives and their inclusion complexes with ß-cyclodextrin (CD) for Myeloproliferative Neoplasms treatment, utilizing molecular docking techniques and comprehensive assessments of Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET).

Method : In this investigation, 13 derivative compounds and 2 reference compounds were assessed as inhibitors for the c-Abl kinase domain (4XEY) against pivotal proteins implicated in Myeloproliferative Neoplasms, utilizing Autodock Vina 4. Furthermore, the SwissADME servers were employed to predict the ADMET profiles of these compounds. Subsequent exploration focused on forming CD inclusion complexes between selected benzylisoquinoline derivatives and carrier molecules, with the aim of bolstering stability and bioavailability, thereby optimizing targeted delivery.

Results : Compounds 13, 4, and 3 demonstrated the most substantial binding affinity (9.7, 9.1, and 8.9 kcal/mol, respectively), closely approaching the native ligand's affinity. The binding resemblance to the c-Abl active site fell within the 75-80% (Figure 1) range compared to dasatinib. Selected compound depicted superior ADMET properties. This dual assessment approach aimed to pinpoint promising candidates exhibiting robust c-Abl inhibitory effects, favorable pharmacokinetics, and heightened stability through CD inclusion complex strategies.

Conclusion : Our results showed that certain benzylisoquinoline derivatives, in CD inclusion complex form, exhibited stronger binding to the c-Abl protein and improved pharmacokinetic properties. This combined approach, integrating molecular docking and ADMET analyses, provided a thorough framework for choosing and developing these derivatives and their inclusion complexes as potential treatments for Myeloproliferative Neoplasms. Further experimental confirmation is essential to confirm the effectiveness and safety of

these promising candidates in both preclinical and clinical settings.

Keywords : Myeloproliferative neoplasms, c-Abl, Benzylisoquinoline, Inclusion complexes, Docking

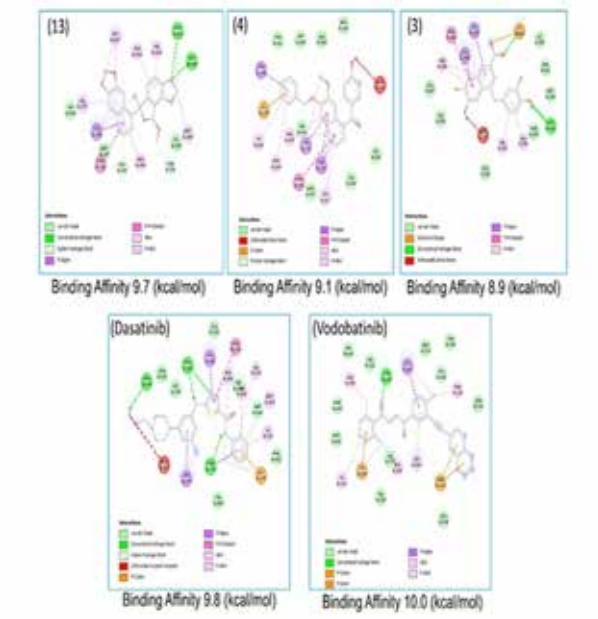

Figure 1. 2D-illustration of binding between c-abl protein and ligand (compound 13, 4, 3, native ligand dasatinib, and phase-2 c-abl inhibitor Vodobatinib)

PP08-4

Combination of hydroxyurea and anagrelide as first-line treatment for patients with essential thrombocythemia

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Background : To overcome either intolerance or resistance to hydroxyurea (HU) or anagrelide (AG) in essential thrombocythemia (ET), combination therapy has been explored in various studies. However, the majority of these studies focused on patients who exhibited resistance or intolerance to either HU or AG as second-line treatment. Hence, we evaluated the effectiveness and safety of upfront HU and AG combination therapy.

Method : We retrospectively analyzed data from 21 patients (9 male and 12 female) who received a combination of HU and AG as their initial treatment among the 241 patients diagnosed with intermediate- and high-risk ET based on IPSET-thrombosis score.

Results : At the time of diagnosis, the median age of patients was 62 years (range, 26-87), and the median platelet count was 912 x 10^9/L (range, 520-1720). There was a tendency for patients in the AG monotherapy group to be younger (p=0.068), and for patients in the combination group to have a higher proportion of high-risk patients compared to the other groups (p=0.081). In the combination group, the mean daily dose of HU and AG was 1142.5 mg/day (range, 500-2000) and 1.45 mg/day (range, 1.0-2.5), respectively. These doses were significantly lower than those administered in the monotherapy group (p=0.01 for HU and p<0.01 for AG). Treatment-related adverse events of any grade occurred in 52.3% of patients receiving HU plus AG combination therapy, 44.3% of those in HU monotherapy, and 43.4% of those in the AG monotherapy group. However, the HU plus AG combination therapy group demonstrated a significantly lower incidence of grade 3-4 AEs compared to the other two groups (p=0.008 for HU monotherapy vs combination therapy and p<0.01 for AG monotherapy vs combination therapy).

Conclusion : As a first-line treatment, the combination therapy of HU and AG demonstrated comparable clinical and laboratory responses with a low incidence of severe side effects compared to monotherapy.

Keywords : Hydroxyurea, Anagrelide, Combination therapy, Essential thrombocythemia, Frontline

PP08-5

Risk of thrombosis, hemorrhage and leukemic transformation in patients with myeloproliferative neoplasms: Anationwide longitudinal cohort study

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Background : Little is known about the risk of thrombosis, hemorrhage, leukemic transformation in patients with myeloproliferative neoplasms (MPNs), including essential thrombocythemia (ET), polycythemia vera (PV), and primary myelofibrosis (PMF).

Method : We performed a nationwide longitudinal cohort study using the Korean National Health Insurance System (NHIS) database. MPNs patients (n = 9,779) and their 1:4 age- and sex-matched controls (n = 39,116) were enrolled. The risk of thrombosis, hemorrhage, leukemic transformation was estimated using a Cox proportional hazards regression, and stratified analyses were performed for related factors.

Results : During a median of 7.9 years of follow-up, 17.6% of MPNs patients (1,723/9,779) and 10.8% of the matched controls (4,246/39,116) developed arterial thrombosis, 9.7% of MPNs patients (956/9,779) and 5.6% of the matched controls (2,200/39,116) developed venous thrombosis and 2.1% of MPNs patients (215/9,779) and 1.0% of the matched controls (424/39,116) developed hemorrhage. The overall risk of developing thrombosis, hemorrhage, leukemic transformation was higher in MPNs patients (adjusted hazard ratio [aHR] 1.907, 95% confidence interval [CI]: 1.801-2.018 for arterial thrombosis, aHR 2.069, 95% CI: 1.915-2.235 for venous thrombosis, aHR 2.273, 95% CI: 1.924-2.685 for hemorrhage, and aHR 77.523, 95% CI: 52.885-113.639 for leukemic transformation) than in the matched controls. Patients with MPNs had a 10-year cumulative incidence of leukemic transformation of 6.1%. In the stratified analyses, the increased risk of arterial thrombosis was more prominent in young age patients with MPNs (interaction p<.001), and urban residency (interaction p=0.011), whereas there was no substantial effect associated with sex, smoking.

Conclusion : The patients with MPNs have a higher risk of thrombosis, hemorrhage, and leukemic transformation than matched controls. Strategies are needed to reduce the burden of thrombosis, hemorrhage, leukemic transformation in MPNs patients.

Keywords : Thrombosis, Hemorrhage, Leukemia, Myeloproliferative neoplasm, Thrombocythemia

Table. Hazard Ratios and 95% Confidence Intervals for the Incidence of thrombosis, hemorrhage, leukemic transformation in MPNs patients Compared with the Matched Controls

	Events (n)	Follow-up duration (PY)	Incidence rate (/1,000PY)	Unadjusted Hazard ratio (95% CI)	Adjusted Hazard ratio* (95% CI)
Arterial thrombosis					
Matched controls	4,246	288,956	14.69	1 (reference)	1 (reference)
MPNs	1,723	58,798	29.30	1.904 (1.800-2.013)	1.907 (1.801-2.018)
Venous thrombosis					
Matched controls	2,200	300,764	7.38	1 (reference)	1 (reference)
MPNs	956	63,679	15.01	2.068 (1.916-2.231)	2.069 (1.915-2.235)
Hemorrhage					
Matched controls	424	306,230	1.38	1 (reference)	1 (reference)
MPNs	215	66,275	3.24	2.270 (1.926-2.675)	2.273 (1.924-2.685)
Leukemic transformation					
Matched controls	28	307,641	0.09	1 (reference)	1 (reference)
MPNs	482	65,736	7.33	76.573 (52.313-112.085)	77.523 (52.885-113.639)

* Adjusted for age, sex, smoking, residential area, hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation/flutter, and history of cancer.
Abbreviations: PY, person-years

PP08-6

Clinical features and outcomes of JAK2 unmutated erythrocytosis

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Background : Treatment strategies for JAK2 unmutated erythrocytosis vary due to the inconsistent risk of thrombosis. Furthermore, the clinical implications of erythrocytosis in Korean populations have rarely been described.

Method : We conducted a retrospective analysis of patients diagnosed with polycythemia vera (PV) or JAK2 unmutated erythrocytosis at Chungnam National University Hospital between January 2010 and December 2022.

Results : In total, 282 patients were enrolled, including 194 with erythrocytosis and 88 with PV. Compared with PV patients, pa-

tients with erythrocytosis were younger (66.5 [31–91] years vs. 52 [17–84] years; P = 0.026) and predominantly men (45.5% vs. 90.7%; P < 0.001. Hypertension (47.9% vs. 28.9%, P = 0.004), sodium-glucose cotransporter-2 inhibitor use (12.9% vs. 0%, P < 0.001), smoking (37.1% vs. 21.7%, P = 0.003), chronic obstructive pulmonary disease (COPD; 8.8% vs. 2.3%, P = 0.044), heart failure (6.7% vs. 0%, P = 0.013), and elevated body mass index (> 30 kg/m^2; 18.0% vs. 2.3%, P < 0.001) were more prevalent in erythrocytosis patients than in PV patients. The overall cumulative incidence of thrombosis was significantly higher in PV patients than in erythrocytosis patients (10-year incidence 51.2% vs. 14.7%; P < 0.001). Phlebotomy did not affect the cumulative incidence of thrombosis in erythrocytosis patients (0% vs. 6.8%, P = 0.280). Cox regression analysis identified diabetes mellitus (DM; HR 4.93, 95% CI 1.26-19.31, P = 0.022) and COPD (HR 11.88, 95% CI 2.59-54.55, P = 0.001) as independent risk factors for thrombosis in erythrocytosis patients. Overall survival was lower in PV patients than in erythrocytosis patients (10-year survival 65.8% vs. 95.4%, P = 0.064).

Conclusion : Although JAK2 unmutated erythrocytosis carries a significantly lower thrombotic risk than PV, individuals with erythrocytosis, particularly patients with DM and COPD, have a persistent risk of thrombotic vascular events.

Keywords : Erythrocytosis, JAK2, Piolycythemia Vera , Thrombosis

PP08-7

JAK2V617F, CALR and *MPL* mutation profiles in patients with myeloproliferative neoplasms, northeast Thailand

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Background : Mutations in the genes JAK2V617F, Calreticulin (*CALR*), and Myeloproliferative Leukemia virus oncogene (*MPL*) have been identified as drivers of Myeloproliferative Neoplasms (*MPNs*), including Polycythemia Vera (*PV*), Essential Thrombocytosis (*ET*), and Primary Myelofibrosis (*PMF*). *JAK2V617F, MPL,* and *CALR* mutations are included as major diagnostic criteria for MPN in the 2008 WHO diagnostic criteria. This study aims to determine the genetic profile of the JAK2V617F, MPL, and CALR mutations genes among patients with MPNs in Northeast Thailand.

Method : The retrospective evaluation focused on the *JAK2V617F, CALR,* and *MPL* mutation profiles in 201 patients with MPN in Northeast Thailand. Data were collected from January 2017 to January 2021. Peripheral blood and bone marrow samples were analyzed using Real-Time Quantitative Reverse Transcription PCR (*qRT-PCR*). The study population consisted of 82 cases of *PV*, 97 cases of *ET*, and 22 cases of *PMF*.

Results : The result showed that in 96.34% of PV, 84.49% of ET and 86.36% of PMF, we found mutations in *JAK2V617F, MPL* or *CALR*. Specifically, 72.14% carried JAK2V617F mutations, 14.92% had CALR mutations, 2.49% had MPL mutations, and 10.45% were triple negative. No *MPL W515L/K* mutation was detected, and *CALR* mutations were not found in PV cases. The predominant mutation type in both ET and PMF was the CALR Type 1 mutation.

Conclusion : The *JAK2V617F* mutation plays a pivotal role as a primary screening tool for diagnosing MPN. Based on our study findings, we recommend conducting *JAK2V617F* mutation testing as the initial diagnostic step when PV is suspected. Furthermore, the assessment of *JAK2V617F* and *CALR* mutations is crucial in the diagnostic process of MPN, especially ET. Therefore, we propose that every patient suspected of having a myeloproliferative neoplasm undergo screening for these mutations.

Keywords : Myeloproliferative neoplasms, JAK2V617F mutation, CALR mutation, MPL mutation, Northeast Thailand

JAK2 V617F allele burden in patients with Essential Thrombocythemia and Polycythemia Vera, Northeast Thailand

Characteristic	PV [n =82]	ET [n = 97]	PMF [n = 22]
JAK2V617F	79 (96.34%)	53 (54.6%)	13 (59.09%)
CALR exon 9+	0	26 (26.80%)	4 (18.18%)
MPL exon 10+	0	3 (3.09%)	2 (9.09%)
Triple negative	3	15	3

PP08-8

A pilot project to assess genotoxicity induced by hydroxyurea in patients with JAK2 positive polycythemia vera

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Background : Polycythemia vera (PV) is a myeloproliferative neoplasm. Hydroxyurea (HU) is used as first line therapy in patients with high-risk PV. Its also used in patients low-risk PV with higher thrombotic risk. Its genotoxic effects and possible mutagenicity have been a long-term concern. Cytokinesis blocked micronucleus (CBMN) assay is a method assessing biomarkers of DNA damage, namely micronuclei (MN) and is used to assess genotoxicity of HU in sickle cell anemia (SCA).

Method : Twenty adults with JAK 2 positive PV managed with HU (10) and venesection alone (10) were compared against age and sex matched controls (20). Frequency of MN in peripheral blood bi nucleated lymphocytes were counted by cytokinesis block micronucleus (CBMN) assay. Lymphocyte culturing and scoring of micronuclei were done according to standard protocol by International Atomic Energy Agency. Data analyzed with SPSS. Significance of difference in MN between the different groups were tested using paired t- test. The significance level adopted was $p<0.05$.

Results : A significant difference MN was seen between patients managed with HU(JPH) and the control population (p value =0.02). No significant difference in frequency of micronuclei was seen between patients managed with venesections (JPV) and control population (p value =0.05) A significant association between platelet count (t= .449 r=.047) and the number of micronuclei was observed, and strength of this correlation was increasing with increasing platelet count. There was no statistically significant association between number of MN with WBC count (t=.232 r=.324) constitutional symptoms (t=2.52) or increasing size of spleen (r=.021, t=.930).

Conclusion : Data demonstrated statically significant micronuclei in peripheral blood lymphocytes of JAK2 V617f positive PV patients treated with HU but not in patients managed with venesections alone. An indicator of increased susceptibility to DNA damage. Its a pilot study and a larger study is recommended.

Keywords : Polycythemia vera, Hydroxyurea, Cytokine block micronucleus assay

PP08-9

Progression of carotid plaque burden in patients with polycythemia vera and essential thrombocythemia

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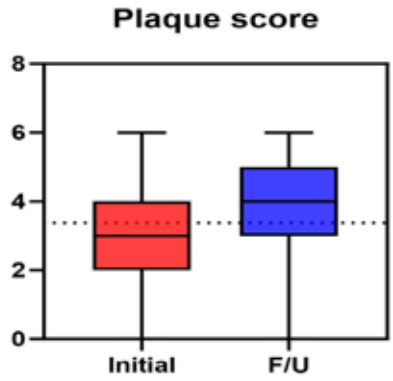
Background : Preventing vascular events is the main objective of treatment for patients with polycythemia vera (PV)/ essential thrombocythemia (ET). Carotid ultrasonography (USG) is a safe and noninvasive diagnostic tool that provides information about carotid artery characteristics and may be used for the early detection of coronary artery disease and stratification of cardiovascular and stroke risk. The carotid plaque burden was significantly higher in patients with PV/ET compared to the general population in our previous study. We aimed to monitor changes in carotid plaque burden throughout treatment in PV/ET patients.

Method : We conducted a retrospective evaluation of medical records and assessed carotid plaque burden in patients diagnosed with PV) or ET. Specifically, we focused on individuals who had undergone carotid ultrasonography (USG) at least twice at the Soonchunhyang University Seoul Hospital.

Results : Of the 56 patients, 30 were diagnosed with PV, while 26 were diagnosed with ET. The interval between the first carotid USG and the subsequent carotid USG was fifteen months. There were 18 newly diagnosed patients included in the study. The carotid plaque score exhibited an increase in the subsequent carotid USG in comparison to the initial carotid USG (3.38 ± 1.47 vs. 3.73 ± 1.46, $p = 0.0139$) (Figure). Plaque burden increased despite insignificant differences in leukocyte, platelet, and hemoglobin counts between the two groups. Hematologic improvement was observed even in patients who were newly diagnosed, however, there was a tendency for carotid plaque burden to worsen.

Conclusion : In conclusion, it was confirmed that the carotid plaque burden persisted in progression during follow-up with PV/ET patients. This requires a new treatment strategy to prevent plaque progression.

Keywords : Carotid plaque burden, Polycythemia vera , Essential thrombocythemia



PP09-1

Next generation sequencing is vital for accurate genotyping in inherited bone marrow failure syndromes

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Background : Inherited bone marrow failure syndromes (IBMFS) are a heterogenous group of disorders presenting with cytopenia(s) & a hypocellular bone marrow. Identification of the associated germline variant(s) by next generation sequencing (NGS) is vital for proper nomenclature and distinguishing from mimics like hypoplastic myelodysplastic syndrome & immune aplastic anemia (IAA). This guides appropriate clinical management.

Method : Retrospective analysis of 73 cases (IBMFS with atypical features & young IAA) presenting over 4.5 years was performed. Median age was 8.5 years (Range 2 months-44 years). M:F ratio was 3.8:1. Pancytopenia was the most common presentation. Physical abnormalities of IBFMS were seen in 5 patients. IAA was initially suspected in 15 (20.5%) patients. Chromosomal breakage study (CBS) was positive in 3 cases. NGS testing by a targeted gene panel was studied in most cases and by clinical-exome sequencing in 5-cases.

Results : Thirty-eight cases (52%) had presence of atleast one genetic variant.(Figure-1) A total of 47 genetic variants were identified. Variant zygosity included: heterozygous(21), homozygous(5), hemizygous(3) and compound-heterozygous(9). Variant types were exonic missense variants(38), splice site variants(4), indels in exons(2) and frameshift with chain termination(3). FA was the most common IBMFS; others were DKC, SCN, DBA, CAMT, radioulnar synostosis with amegakaryocytic thrombocytopenia and Shwachman-Diamond syndrome.(Table-1) Genotyping resulted in revision of clinical diagnosis in 18 cases. Seven cases which mimicked a BMF include: germline variants with predisposition to myeloid malignancy-2 (SAMD9, ANKRD26), immunodeficiency syndromes-3 (WAS, ADA2, STIM1) and others: 2 hemophagocytic lymphohistiocytosis & hereditary TTP (PRF1, ADAMTS13).

Conclusion : NGS identified gene variants in >50% IBMFS; this is particularly useful in atypical presentations like absent physical abnormalities and negative CBS; this avoids mislabeling an IBMFS as IAA. Accurate genotype identification guides appropriate clinical management, i.e., avoiding anti-thymocyte globulin, screening potential stem-cell donors in family for the variant. Antenatal counseling, screening for cancers, pulmonary & liver fibrosis can also be undertaken.

Keywords : Inherited bone marrow failure syndromes, Next generation sequencing, Fanconi anemia, Germline variants, Pancytopenia with hypocellular bone marrow

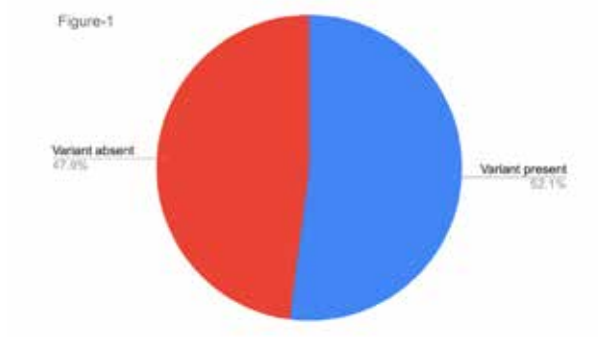

Table-1

	BMF and related disorders	Cases (N)
1	Fanconi anemia	10
2	Dyskeratosis congenita	6
3	Diamond Blackfan anemia	4
4	Shwachman-Diamond anemia	1
5	Severe congenital neutropenia	2
6	Congenital amegakaryocytic thrombocytopenia	2
7	Radioulnar synostosis with amegakaryocytic thrombocytopenia-2	2
8	Congenital dyserythropoietic anemia - II	1
9	Others (Stormorken syndrome, hTTP, Wiskott-Aldrich syndrome, SAMD9, ANKRD26 germline variant)	8

PP09-2

The frequency of clonal T cells and its correlation with clinical and laboratory parameters in adult-onset aplastic anemia

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Background : T-cell-mediated immune mechanisms play an important role in the pathogenesis of aplastic anemia/AA. The nature and patterns of T-cell expansion at presentation are likely to predict the response to therapy. We report the frequency of dominant T-cell clones(monoclonal/oligoclonal) in consecutive patients with AA and correlate with clinical and laboratory parameters.

Method : T-cell receptor gamma-gene rearrangement assay/ TCR-G-RA (Invivoscribe Inc, USA) by fragment length analysis (ABI3500) was performed in the bone-marrow samples of 92 consecutive adults (>12 years) with AA over 18 months. The presence of one or two peaks that have a height twice the height of two adjacent fragments and showed consistent patterns on duplicate testing was considered as dominant clone.

Results : The demographic profile of 92 patients is summarized in Table 1. The median age of the cohort was 34 years, and the male-to-female ratio was 1:1. Very severe aplastic anemia/VSAA constituted 20.7% of cases. A dominant clone was noticed in the TCR-G-RA in 26 (28.3%) of cases; which includes one/two dominant peaks in a polyclonal background in 21 cases, dominant/monoclonal peak without polyclonal cells in 2 cases and oligoclonal peaks in 3 cases. The remaining 66 cases did not show any dominant clone. The dominant clones were more frequent in non-severe (30%) or severe AA (28.5%) than VSAA (15.7%). In two cases, we used T-cell Receptor Constant β Chain-1 (TRBC1) flow-cytometry to confirm the presence of clonal T cells in terminally differentiated CD57+ CD8+ T cells.

Conclusion : Our study documented the presence of clonal T cells in 28.3% of AA, the most frequent being in non-severe and severe AA compared to very severe AA cases. We documented the clonal expansion of terminally differentiated CD57+CD8+T-cells by flow-cytometry in two cases with dominant clones. We plan to identify the T-cell subset involved in clonal expansion and to correlate with treatment response

Keywords : TCR rearrangement, Clonal T cells, Aplastic anemia, Bone marrow failure, Cytogenetics.

Table 1: Demographic profile and laboratory findings of patients (n=92)	
Age – median (range) years	34 (13-78)
Males: Females	1:1
Hemoglobin (g/L) median (IQR)	72 (59-82)
Total leukocyte count (x10^9/L) median (IQR)	2.4 (1.6-3.4)
Platelet counts (x10^9/L) median (IQR)	15 (7-25)
Absolute neutrophil count (per microlitres) median (IQR)	574 (241-1372)
Absolute lymphocyte count (per microlitres) median (IQR)	1609 (1046-2040)
Absolute reticulocyte count (per microlitres) median (IQR)	19618 (2950-53500)
Severity of aplastic anemia (n, %)	
Very severe	19 (20.7)
Severe	28 (30.4)
Non-severe	45 (48.9)
Pattern of TCR-gamma gene rearrangement (n, %)	
Dominant clone present	26 (28.3)
Polyclonal Pattern without dominant clone	66 (71.7)
Frequency of dominant clones between different groups (n, %)	
Very severe	3/19 (15.7)
Severe	8/28 (28.5)
Non-severe	15/45 (30)

PP09-3

Establishing reference range for relative telomere length in normal Indian individuals

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Background : Shorted telomeres (sTL) are associated with various hematological disorders. sTL (less than 1st or 2nd percentile matched for age) have diagnostic value in dyskeratosis congenita/DC and correlate with treatment response in acquired aplastic anemia. However, there is a lack of normal range for the population. We attempted to establish reference ranges for the Indian population in different age groups.

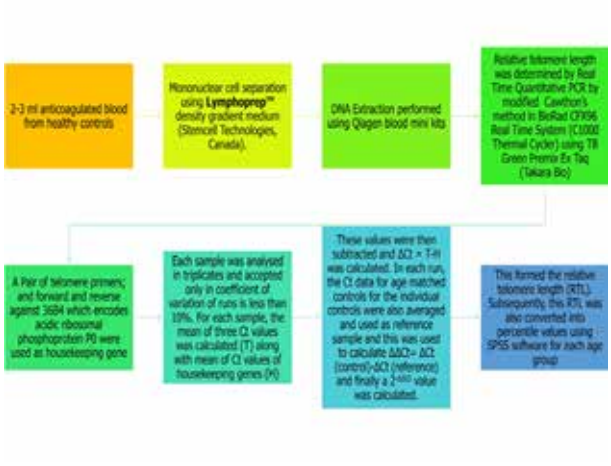
Method : The methodology is summarized in figure-1. For each sample, the mean of three Ct values was calculatedfor

telomeres(T) along with mean of Ct values of housekeeping genes(H) and, deltaCt = T-H was calculated. In each run, the Ct data for age-matched controls for the individual controls were also averaged and used as reference sample, and this was used to calculate deltadeltaCt= deltaCt(control)-deltaCt(reference) and finally a $2^{-deltadeltaCt}$ value was calculated. This formed the relative telomere length/RTL. Subsequently, this RTL was also converted into percentile values using SPSS software for each age group.

Results : During the study period, RTL was determined in a total of 379 samples from 137 normal controls. Their age ranged from 3-59 years (median-23 years). There were 86 males and 51 females. The RTL from same individuals were finally averaged. They were divided into four groups – <21 years (n=58), 21-30 years (n=46), 31-40 years (n=15) and >40 years (n=18). The median (range) of RTL in respective age groups were 1.03 (0.25-3.31), 0.89 (0.53-3.85), 1.03 (0.58-2.07), and 0.89 (0.48-2.76) respectively. The 1st percentile of RTL in the respective age groups were 0.25, 0.52, 0.58, and 0.48 respectively while, 2nd percentiles were 0.29, 0.53, 0.58, and 0.48 respectively.

Conclusion : We determined RTL in 137 normal individuals and determined normal reference ranges in various age groups. We plan to determine RTL in more number of controls (minimum 100 individuals in each age group) before using it for routine patient care

Keywords : Telomere length analysis, Inherited marrow failure, Aplastic anemia, Real-Time PCR, Reference range



PP09-4

Efficacy and safety of ATG + CsA + Romiplostim for untreated aplastic anemia: A phase 2/3 clinical trial

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Background : Romiplostim (ROMI) has been shown to promote tri-lineage hematopoiesis in patients with acquired aplastic anemia (AA) refractory to immunosuppressive therapy (IST) or eltrombopag; however, its effectiveness in the combination therapy with antithymocyte globulin (ATG) + cyclosporine (CsA) as a first-line treatment remains unknown.

Method : We conducted a phase 2/3 clinical trial to evaluate the efficacy and safety of rabbit ATG+CsA+ROMI in patients with AA requir-

ing transfusions who had not been exposed to IST. ROMI, 10 μg/kg was started on day 1 of ATG therapy and was given weekly for the first 4 weeks. The dose was adjusted from 5 to 20 μg/kg according to the prespecified dose adjustment procedure. If the patient had CR for 4 consecutive weeks after Week 14, the dosing frequency was changed to biweekly administration of the same dose. Treatment lasted until Week 26, but for those who agreed to continue treatment, ROMI administration was extended to Week 52. The primary endpoint was the hematological response rate (HRR) at Week 27.

Results : Seventeen patients (9 Japan, 7 Korea, and 1 Taiwan; 5 transfusion dependent NSAA, 6 SAA and 6 VSAA) were enrolled in the study. The median age was 44.0 years. Two patients discontinued ROMI before Week 27 (one patient died, and one was transferred to another hospital). The HRR (CR/PR) at Week 27 was 76.5%, of which 6 (35.3%) achieved CR. Four patients received ROMI biweekly after Week 14. No chromosomal abnormality or transformation into MDS and/or AML was observed.

Conclusion : ATG+CsA+ROMI should serve as a new first-line treatment option in patients with AA.

Keywords : Romiplostim, Cyclosporine A, Antithymocyte globulin, Acquired aplastic anemia, Bone marrow failure

PP09-5

Efficacy and safety of romiplostim combined with cyclosporine A as a first-line treatment in patients with aplastic anemia: A phase 2/3 clinical trial

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Background : Romiplostim (Rom), a thrombopoietin receptor agonist (TPO-RA), promotes tri-lineage hematopoiesis in patients with acquired aplastic anemia (AA) refractory to immunosuppressive therapy (IST) or eltrombopag. Its effectiveness in combination with cyclosporine (CsA) as first-line treatment remains unknown.

Method : A multi-national, open-label, phase 2/3 study was conducted in Japan and Korea (NCT04095936). Transfusion-dependent adult AA patients who were previously untreated with IST received Rom 10 μg/kg QW for the first 4 weeks. The dose was adjusted from 5 to 20 μg/kg from Week 5 and continued until Week 26. The primary endpoint was hematological response rate (HRR) at Week 27 based on response assessment criteria (Table 1). Secondary endpoints included HRR at Week 14; time to hematological response; and proportion of patients achieving transfusion independence or reduced requirement.

Results : Thirty-one patients were screened, of which 24 (7 platelet or red blood cell (RBC) transfusion dependent non-severe AA [NSAA], 13 severe AA [SAA], and 4 very severe AA [VSAA]) were enrolled. The median age was 52.0 years. HRR at Week 27 was 41.7% (10/24), of which 3 and 7 achieved CR and PR, respectively, 57.1 % in NSAA, 46.2% in SAA, and 0 % in VSAA subjects. HRR at Week 14 was 29.2%. Median time to first hematological response was 92.0 days (range, 31-133). Of 19 platelet-transfusion-dependent patients, 14 (73.7%) had decreased platelet transfusion requirements and 8 (42.1%) achieved platelet transfusion independence at Week 27. Of 22 RBC-transfusion-dependent patients, 15 (68.2%) had decreased RBC transfusion requirements and 9 (40.9%) achieved RBC transfusion independence at Week 27. The most frequently reported AE was nausea (n=7/29.2%).

Conclusion : Rom plus CsA produced high HRR at Week 27 (41.7%),

with manageable AEs, and could serve as a new first-line treatment option in patients with AA.

Keywords : Romiplostim, CyclosporineA, Thrombopoietin receptor agonist, Acquired aplastic anemia, Bone marrow failure

Table 1. Response Assessment Criteria

	Severity at Baseline	
	Patient with SAA/VSAA	Patients with Platelet or Erythrocyte Transfusion-dependent NSAA
CR (Complete response)	All of the following criteria were met: • Hemoglobin concentration ≥ 10g/dL • Neutrophil count ≥ 1000/μL • Platelet count ≥ 100,000/μL	
PR (Partial response)	Platelet and erythrocyte transfusion independence, and two or more of the following criteria were met: • Neutrophil count ≥ 500/μL • Platelet count ≥ 20,000/μL • Reticulocyte count ≥ 20,000/μL	Platelet and erythrocyte transfusion independence
NR (No response)	No longer meeting the above criteria	

PP09-6

Report of the first Delphi round of the ongoing asian aplastic anemia recommendation development: An evidence- and opinion-based consensus

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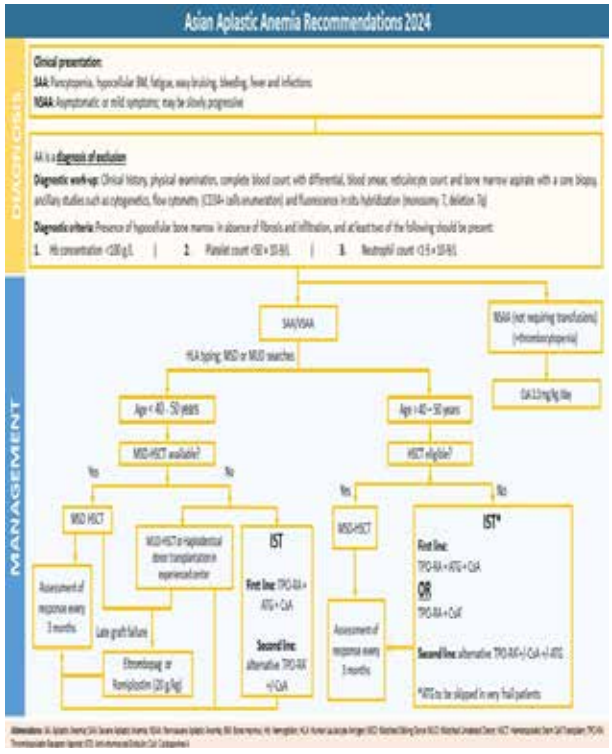
Background : The incidence and prevalence of Aplastic Anemia (AA) is 2–3 times higher in Asia, as compared with those in Europe and America. International guidelines are challenging to implement in the Asian setting. The limited availability of robust diagnostic tools and treatment modalities, together with variations in specific health care investments and policies, necessitate a more specific approach to the diagnosis and management of AA in Asia.

Method : Recognizing the need for guidance on the diagnosis and management of AA in Asia, a working group - the Asian Aplastic Anemia Working Group, was formed, comprising experts from South Korea, Japan, China, Hong Kong, Malaysia, Taiwan, and Thailand. The working group convened on 2 occasions virtually to yield 16 thematic statements on the diagnosis and management of AA. An e-Delphi process, employing an online platform, was used to solicit votes of the working group between June and October 2023, using a 5-point Likert scale (1: strongly disagree; 2: disagree; 3: partially agree; 4: agree; 5: strongly agree) with updated iterations of the statements after each round. Consensus was predefined as '≥80% level of agreement among the Delphi participants.'

Results : Sixteen thematic statements were developed, with 54 sub-statements covering the nuances of Asia-specific management considerations in AA. There were 3 statements on definition, clinical presentation, and aetiology, 4 statements on diagnosis and prognosis, and 9 statements on management covering specific problems including clonal evolution, supportive care and special populations. The first round of e-Delphi voting finished in October 2023, and 15 statements achieved consensus. However, statement 11 on 'management of SAA/VSAA' did not reach consensus in the first round and was therefore modified as according to inputs from Working Group members; currently undergoing the second round of voting.

Conclusion : This e-Delphi method yielded the first Asia-specific recommendations for the diagnosis and management of AA.

Keywords : Aplastic anemia, Recommendation statements, Asia, Expert consensus, Delphi



al., eJHaem 2022). A post-hoc subgroup analysis demonstrated comparable efficacy in Asian and Non-Asian PNH patients (Jun Ho Jang et. al., Poster No. 2727 © American Society of Hematology (2023). Reused with permission); safety was also analyzed.

Method : Fifty (50) adults with PNH, ≥ 1.5 upper limit of normal range (ULN) of LDH and complement inhibitor-naïve were randomized (1:1) to treatment sequence I (TS1: SB12 to ECU, n=25) or II (TS2: ECU to SB12, n=25), to receive 600 mg of SB12 or ECU intravenously every week for first 4 weeks and 900 mg for the fifth week, followed by 900 mg every 2 weeks thereafter. At Week 26, patients were switched to ECU or SB12, respectively, and treated until Week 50 (namely, Period 1 followed by Period 2 from Week 26). Safety endpoints included the incidence of adverse events (AEs), treatment-emergent AEs (TEAEs), serious AEs (SAEs), AEs of special interest (AESIs: infection-related AEs and infusion-related reactions). This safety subgroup analysis was conducted in pooled patients treated with SB12 or ECU in either Periods 1 or 2 by Asian and Non-Asian (race).

Results : Twenty-six (53%) Asian and 23 (47%) Non-Asian received at least one dose of either SB12 or ECU and were analyzed. The TEAEs occurred in 22 (84.6%) Asian and 20 (87.0%) Non-Asian, with similar incidence and safety profile between SB12 and ECU treatments. Majority of TEAEs were mild to moderate and transient.

Conclusion : SB12 showed comparable safety to ECU in both Asian and Non-Asian PNH patient subgroups, complementing results showing comparable efficacy by race.

PP09-7

Safety of SB12 (eculizumab biosimilar) in asian and non-Asian patients with paroxysmal nocturnal hemoglobinuria: Subgroup analysis of a global phase III randomized controlled trial

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PP10-1

Red cell enzymopathies in Indians: Molecular specturm and diagnostic approach in unexplained hemolytic anemias

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Background : Defective red-cell metabolic pathways lead to hereditary red-cell enzymopathies. Glucose-6-phosphate dehydrogenase (G6PD) and pyruvate kinase (PK) deficiencies are most prevalent. Deficiency of Glucose-phosphate-isomerase (GPI) and hexokinase (HK) also rarely occur. Patients present heterogeneous clinical phenotypes varying from mild to transfusion-dependent anemia, with/without pallor, unconjugated-hyperbilirubinemia, palpable spleen, etc. Molecular characterization of DNA by Sanger sequencing is tedious and costly. Therefore, next-generation-sequencing (NGS) has enhanced the diagnosis of rare unexplained-hemolytic disorders.

Method : Over the ten-years, based on routine laboratory investigations, patients with hemolytic anemia with or without pallor of unexplained etiology and suspected CDA were enrolled. Targeted-NGS was done by DNA library preparation followed by sequencing on MiSeq sequencing system and data analysis using BaseSpace Variant-Interpreter.

Results : Total of 31 cases of enzymopathies were encountered. Twenty-four cases were diagnosed with PK-deficiency, three GPI-deficiency, one HK-deficiency, and three G6PD-deficiency with nine different novel variants. Highly heterogeneous phenotypes were seen in 24 PK-deficiency patients. Among 24, 16 were transfusion-dependent and presented the phenotypes in early infancy. Four patients initially suspected to have CDA were confirmed as PK-deficiency after NGS. Three patients with GPI-deficiency [p.Phe304Leu (GPI-Chandigarh), p.Arg83Trp, p.Arg347His] with diverse phenotypes requiring occasional-to-transfusion dependent hemolysis were found. One severe case of HK-deficiency [p.Arg12Ter] had transfusion-dependent hemolysis with massive splenomegaly, and the child lost his life at one year of age. One novel variant (G6PD-Chandigarh [p.Tyr22]) and two G6PD-Guadalajara were identified in three patients of G6PD-deficiency who had neonatal jaundice with mild splenomegaly. After confirmed diagnosis, splenectomy was advised in all severe transfusion-dependent cases, and 11 cases become were transfusion-free, except for one case where transfusion requirement was reduced.

Conclusion : This study emphasizes the role of NGS (cost-effective, expeditious, and efficient) for molecular diagnosis of rare unexplained-hemolytic-disorders that remained undiagnosed by conventional tests. Targeted-resequencing provides accurate diagnosis. Data was applied for genetic counseling, family screening, and disease amelioration (splenectomy).

Keywords : Enzymopathies, Pyruvate kinase, Next-generation sequencing, Hemolytic disorders, Transfusion-dependent

PP10-2

Genotype analysis and clinical outcome in Indian patients with rare congenital anemias

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Background : A stepwise diagnostic algorithm and phenotype characterization are required to diagnose hemolytic anemias and suspected congenital dyserythropoietic anemia (CDA). In this study, we analyzed the genotype and evaluated the clinical outcome in such patients.

Method : After excluding the common causes of hemolysis, 107 Index cases [80 of unexplained hemolysis and 27 of suspected CDAs (CDA-II homozygous for SEC23B:p.Tyr462Cys were excluded] were enrolled. Next-generation sequencing (NGS) was done using Illumina's Custom Panels. Family screening/predictive testing was done (wherever available).

Results : In 80 patients with unexplained hemolysis, after genetic analysis, 18 had pyruvate kinase (PK) deficiency, three each had glucose-6-phosphate isomerase deficiency and G6PD deficiency (enzyme assays showed normal activity). Mediterranean stomatocytosis/macrothrombocytopenia was found in 15, and 2 had overhydrated stomatocytosis. Xerocytosis was found in 3 patients, while 8 had potentially pathogenic variants in membrane protein-coding genes. Surprisingly, unstable hemoglobin variants were found in 3 cases. The diagnosis was achieved in ~69% (55/80). Red blood cell morphology was not-contributory except for stomatocytosis. In 27 patients with CDA, only 6 had compound heterozygous variants in SEC23B. Surprisingly, six had PK deficiency, and three each had spectrin-related membranopathy and xerocytosis. One each had homocystinuria-megaloblastic anemia, cobalaminE type, X-linked thrombocytopenia/dyserythropoietic anemia, and CDA-type IV. After the genetic diagnosis, nine patients with PK deficiency, three with red cell membranopathies, two with G6PD deficiency, and one with unstable hemoglobin variant underwent splenectomy and are transfusion-free except for one where the requirement for transfusions was reduced. Splenectomy was deferred in cases of stomatocytosis. The change in therapy was instituted for patients with Mediterranean stomatocytosis/macrothrombocytopenia and homocystinuria-megaloblastic anemia.

Conclusion : In this study, a highly varied genetic spectrum was en-

countered for hemolytic anemias/CDAs. NGS-based genetic diagnosis is rapid, cost-effective, and has a high diagnostic yield (~70%). In our cases, accurate and timely diagnosis offered therapeutic benefits (performing/deferring splenectomy and change in therapy).

Keywords : Hemolytic anemia, Red cell disorders, Congenital dyserythropoietic anemia , Molecular diagnosis, Next-generation sequencing

PP10-3

Molecular genetic spectrum of non-transfusion-dependent beta thalassemia: A study of primary and secondary phenotype modifiers in 258 north Indian cases

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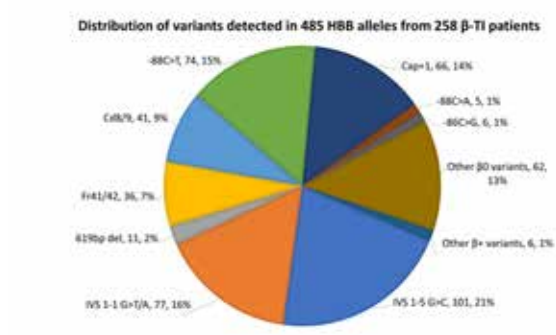
Background : Non-transfusion-dependent beta thalassemia (NTDβT) are enigmatic disorders displaying a wide spectrum of clinical symptoms, but are not transfusion-dependent to sustain life. Their heterogeneity is uniquely explained by underlying HBB gene variants (primary modifiers) along with co-inherited secondary modifiers like α-globin gene dosage and HbF modulators, mainly the Xmn1^{G}γ polymorphism. We report the molecular spectrum of a large north Indian β-TI patient cohort.

Method : Cases diagnosed clinically and on HPLC as NTDβT (n=258) over a period of 15 years (2008-2023) underwent testing for HBB gene variants using amplification-refractory mutation system-PCR and/or direct-DNA sequencing. Eight common α-globin gene deletions and supernumerary α-globin genes were tested for by multiplex gap-PCRs. Xmn1^{G}γ-polymorphism (-158^{G}γ C>T) was determined using restriction-fragment length polymorphism-PCR.

Results : Average age of diagnosis was 15 years (range 2 months to 63 years). Among HBB variants, IVS1-5 G>C (HBB:c.92+5G>C) was commonest [19.6% alleles]. The five commonest Indian β-thalassemia mutations: HBB:c.92+5G>C, HBB:c.92+1G>T/A, HBB:c.126_129delCTTT, HBB:c.27_28insG and NG_000007.3:g.71609_72227del619 comprised 51.6% alleles (vis-a-vis >90% in transfusion-dependent β-thalassemia historically). A β^{+} HBB promoter region variant -88C>T (HBB: c.-138C>T) was present on 14.3% alleles. Twenty-five patients (9.7%) were homozygous or compound heterozygous for β^{+} HBB variants. Overall, 71 cases showed co-inherited α-thalassemia, 11% had α-globin triplications. TI phenotype in 25 (9.7%) persons with β-thalassemia trait was explained by α-triplications. Xmn1Gγ was +/- in 27% and +/+ in 15%. Among 97 patients homozygous/compound heterozygous for severe HBB mutations, 37 (38%) had co-inherited α-thalassemia while 29 (30%) were Xmn1Gγ +/+. Only 10% patients with severe HBB mutations had neither α-thalassemia nor an Xmn1Gγ + allele, thus remaining unexplained.

Conclusion : Genetic analysis of NTDβT helped explain diverse clinical presentations in a majority of cases by revealing a high frequency of milder β^{+} HBB mutations, coinherited α-thalassemia or the Xmn1^{G}γ + allele (all reducing severity), or supernumerary α-globin genes (aggravating the disease in heterozygotes).

Keywords : Thalassemia intermedia, Non-transfusion dependent thalassemia, Xmn1Ggamma polymorphism, Beta globin gene, Alpha globin deletions



PP10-4

Blood count scattergrams are fingerprints of blood: Using AI to inform health status

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Background : The Complete Blood Cells analyzers generate more than 300 red cell, leukocyte and platelet parameters. However, in clinical practice, only 10-20 are utilized. These extended analytical parameters have potential to be used to generate real-time '3-Dimensional (3-D)' details of blood cells.

Method : The methodology of the present study was based on the waterfall model. The output data from a hematology analyzer (Sysmex XN-1000, Kobe Japan) in CSV format, having a total 433 columns, was pre-processed, scaled and labeled as per conclusions reported on their respective confirmatory tests. The extracted data was fed to the artificial intelligence Machine Learning models. The web application was developed on modern Python framework to automate and provide an option of 'drag and drop' the CSV file exported from analyzer, we connected pre-processing (data engineering), Machine Learning, and Prediction view by set of different tools.

Results : Analysis of 1.8 million data points (312 parameters x 5,800 samples) presented promising predictive potential, as, on principal component analysis (PCA) pilot the total variance was remained 41.6% showing that a linear combination of parameters can explain much variability. On a heat map the clustering and visualization advocated the predictive potential and signatory deviational trends (fingerprints) respectively of these 3-D blood cell features. Examples included separation of myeloid from lymphoid, chronic from acute, bacteria from viral, deficiency of iron from deficiency from vitamin B12 / Folic acid, and differentiation of haemoglobinopathies. The patterns of normal, immature and abnormal blood cells under the title of cell population data was well demonstrated from results of our machine learning models. Of note, we observed an accuracy of 85.6% along with 91.2% precision for Random Forest Classifier.

Conclusion : The cell population data derived from a complete blood count can provide a novel patient-specific haematological fingerprint that can assist in sequential health monitoring.

Keywords : CBC, Scattergram, Artificial intelligence, Fingerprint, Haematological dosorders

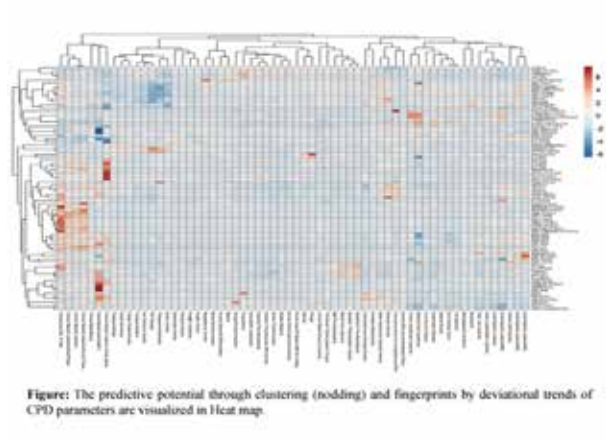

Figure: The predictive potential through clustering (nodding) and fingerprints by deviational trends of CPD parameters are visualized in Heat map.

PP10-5

Evaluation of diagnostic utility of CD43 and D200 in differentiating B-cell chronic lymphoproliferative disorders by flow cytometry

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Background : Diagnosis and subtyping of mature B cell Non-Hodgkin's lymphoma (NHL) in the bone-marrow (BM) and peripheral blood in a leukemic phase may be challenging due to overlapping cell morphology and immunophenotypic features. Flow cytometric immunophenotyping (FCI) has an important role in diagnosis of these chronic lymphoproliferative disorders (CLPD). In past, scoring systems and the addition of newer markers have improved the diagnosis. The present study aimed to evaluate the expression and diagnostic utility of CD200 and CD43 in cases of B-cell CLPDs by FCI.

Method : An observational study of staging and diagnostic BM aspirates or peripheral blood samples for immunophenotyping from all consecutive cases of suspected CLPDs referred to our center was done. We added CD43-APC750 and CD200-APC750 to our existing panel for FCI of CLPDs. Samples were processed with stain-

lyse-wash technique, were acquired on Beckman Coulter DxFLEX analyzer, and were analyzed using CytExpert. The diagnostic utility of CD200 and CD43 expression was determined by comparison with the gold standard diagnosis made by a combination of clinical features, morphology of tissue biopsies, FCI, immunohistochemistry, and cytogenetics using Fluorescent in situ Hybridisation (FISH).

Results : In the study duration, 36 cases of B-cell CLPDs were enrolled. Chronic lymphocytic leukemia(CLL) was the commonest subtype(27 cases), followed by mantle cell lymphoma(MCL, 4 cases), monoclonal B-cell lymphocytosis(MBL, 2 cases), splenic marginal zone lymphoma(SMZL, 2 cases) and hairy cell leukemia(HCL,one case). CD200 and CD43 were bright positive in all cases of CLL and MBL, whereas they were negative in all cases of MCL. In cases of SMZL and HCL, CD200 was positive, but CD43 was negative.

Conclusion : The addition of CD200 and CD43 plays an important role in the differential diagnosis of CLPDs. The absence of CD200 and CD43 strongly rules out a diagnosis of CLL and related neoplasms.

Keywords : Lymphoproliferative disorders, Flow cytometry , CD200, CD43

PP10-6

Hit me, baby, one more time: The experience of learning phlebotomy using a hybrid-based approach

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Background : In the field of medical laboratory science (MLS), phlebotomy is a fundamental skill that each MLS professional must possess. This process is taught to the student during their studies. However, the COVID-19 pandemic has caused schools to shift from traditional in-person teaching to online, blended, or hybrid instructional modalities, which has also forced skills-based classes to be delivered online.

Method : This phenomenological inquiry captures the collective experience of seven Filipino MLS interns who had experience with both online and onsite internships for the academic year. A series of in-depth, semi-structured, audio-recorded interviews were conducted and subjected to phenomenological reduction via thematic analysis.

Results : Six themes were identified through the analysis of the participants' responses. These are (1) confidence in phlebotomy skills; (2) preference for face-to-face setup; (3) imparting sufficient knowledge by tertiary institutions; (4) challenges experienced in phlebotomy; (5) improvement suggestions for hybrid-based learning; and (6) limitations of hybrid-based learning. The participants saw the gap produced by the hybrid setup due to the lack of practical opportunities to practice phlebotomy; however, the theoretical knowledge provided by the institution supported them in the practice of phlebotomy. Despite their development over time, MLS interns still preferred a face-to-face setup.

Conclusion : The emerged themes reflect the product of the individual and collective experiences of the respondents. The true-to-life essence captured in this study could be used as a platform to develop a meaningful and relevant learning environment and opportunities suitable in the context of MLS interns.

Keywords : Hybrid based learning, Phlebotomy, Online learning, Phenomenology

PP10-7

Low-cost LAMP-turbidimetric assay for detecting alpha(zero)-thalassemia (SEA deletion): Preventing and controlling Hb Bart's hydrops fetalis syndrome in Thailand

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Background : Homozygous α^0-thalassemia (SEA deletion) or Hb Bart's hydrops fetalis syndrome is a significant public health issue in Thailand and Southeast Asia. A prevention

and control program has been implemented in this region.

Method : This study focuses on retrospective laboratory data collected between January 2021 and April 2023 at a single center. Additionally, we developed a low-cost LAMP-turbidimetric assay to propose in the screening strategy.

Results : A total of 3,623 samples underwent screening tests (MCV, MCH, and DCIP), including 1,658 couple screenings (84.25%) and 310 single pregnant screenings (15.75%). Negative screenings, which did not require further investigation, were found in 75.51% for couple screenings and 46.58% for single pregnant screenings. At hemoglobin (Hb) analysis identified 129 couples which had fetuses at risk of severe thalassemia. Whereas molecular analysis during the retrospective period revealed 210 samples with different genotypes. These remaining samples were validated using the low-cost LAMP-turbidimetric assay to detect α^0-thalassemia (SEA deletion). The developed LAMP turbidimetric assay demonstrated a sensitivity and specificity of 100% (36/36 x 100) and 97.7% (170/174 x 100), respectively, when compared with gap-PCR. Furthermore, we propose a strategy involving the addition of the low-cost LAMP-turbidimetric assay before performing the gold standard. This strategy represents a cost-saving of USD 2,608 based on 210 samples that required DNA analysis.

Conclusion : Finally, the developed LAMP turbidimetric assays offer advantages such as reduced time, workload, cost savings, no need for highly developed instruments, and a straightforward interpreting process. Therefore, implementation of LAMP assays into routine settings would be improve the efficiency of prevention and control program for severe thalassemia disease in this region.

Keywords : Loop-mediated isothermal amplification, Turbidimetric, SEA deletion, Thalassemia, Anemia

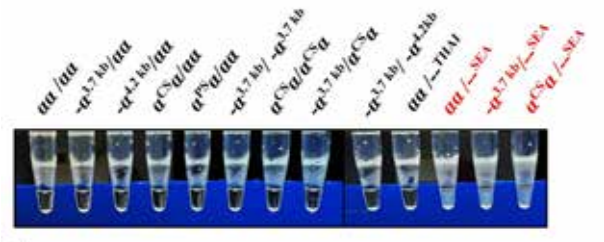

Figure
The developed LAMP turbidimetric assays for the detection of α^0-thalassemia (SEA deletion). The specificity of the developed assays was demonstrated in LAMP turbidimetric assays with different thalassemia genotypes which commonly found in Thailand.

Table LAMP turbidimetric assays for detecting α^0-thalassemia (SEA deletion) compared with conventional PCR analysis in positive screened parents (n=210). FP indicates false positive.

Screening (MCV,MCH,DCIP)	Hb Types	Hb A2/E	Hb F	α-globin gene	β-globin gene	LAMP turbidity	N (210)
+/-	A2A	2.5±0.3	0.1±0.2	αα/αα	β^A/β^A	N	23
				αα/αα	β^A/β^A	**FP**	2
				$-\alpha^{3.7}/\alpha\alpha$	β^A/β^A	N	45
				$-\alpha^{4.2}/\alpha\alpha$	β^A/β^A	N	1
				$\alpha^{CS}\alpha/\alpha\alpha$	β^A/β^A	N	1
				$\alpha^{QS}\alpha/\alpha\alpha$	β^A/β^A	N	2
				$-\alpha^{3.7}/-\alpha^{3.7}$	β^A/β^A	N	13
				$-\alpha^{3.7}/\alpha^{CS}\alpha$	β^A/β^A	N	1
				$--^{SEA}/\alpha\alpha$	β^A/β^A	**P**	21
+/-	A2A>3.5	5.5±0.8	1.7±3.1	αα/αα	B^A/β^A	N	16
				αα/αα	B^A/β^A	**FP**	1
				$-\alpha^{3.7}/\alpha\alpha$	B^A/β^A	N	2
				$-^{4.2}\alpha/\alpha\alpha$	B^A/β^A	N	2
+/-	CSA2A	2.2±0.3	0.1±0.1	$\alpha^{CS}\alpha/\alpha\alpha$	β^A/β^A	N	5
				$-\alpha^{3.7}/\alpha^{CS}\alpha$	β^A/β^A	N	1
+/-	A2FA	3.5	21.2	$-\alpha^{3.7}/\alpha\alpha$	β^A/β^A	N	1
+/-	A2ABartH	1.1±0.4	0.6±0.1	$--^{SEA}/-\alpha^{3.7}$	β^A/β^A	**P**	4
				$--^{THAI}/-\alpha^{3.7}$	β^A/β^A	N	1
+/+	EA	21.3±4.7	0.5±1.5	αα/αα	β^E/β^A	N	4
				$-\alpha^{3.7}/\alpha\alpha$	β^E/β^A	N	3
				$\alpha^{CS}\alpha/\alpha\alpha$	β^E/β^A	N	2
				$\alpha^{QS}\alpha/\alpha\alpha$	β^E/β^A	N	2
				$-\alpha^{3.7}/-\alpha^{3.7}$	β^E/β^A	N	1
				$-\alpha^{3.7}/-^{4.2}\alpha$	β^E/β^A	N	1
				$--^{SEA}/\alpha\alpha$	β^E/β^A	**P**	7
				$--^{CS}/\alpha\alpha$	β^E/β^A	**FP**	1
				$--^{SEA}/-\alpha^{3.7}$	β^E/β^A	**P**	1
				$--^{SEA}/\alpha^{CS}\alpha$	β^E/β^A	**P**	1
+/+	CSEA	21.2±2.5	0.7±0.7	$\alpha^{CS}\alpha/\alpha\alpha$	β^E/β^A	N	1
				$\alpha^{CS}\alpha/\alpha^{CS}\alpha$	β^E/β^A	N	1
				$-\alpha^{3.7}/\alpha^{CS}\alpha$	β^E/β^A	N	3
+/+	EE	95.7±4.4	2.8±3.0	αα/αα	β^E/β^E	N	21
				$-\alpha^{3.7}/\alpha\alpha$	β^E/β^E	N	12
				$-\alpha^{3.7}/-\alpha^{3.7}$	β^E/β^E	N	1
				$-\alpha^{3.7}/\alpha^{CS}\alpha$	β^E/β^E	N	1
				$--^{SEA}/\alpha\alpha$	β^E/β^E	**P**	1
				$--^{SEA}/-\alpha^{3.7}$	β^E/β^E	**P**	1
+/+	EFA	47.9±13.2	15.3±12.8	αα/αα	β^A/β^A	N	2
				$-\alpha^{3.7}/-\alpha^{3.7}$	β^A/β^A	N	1

PP10-8

Influencing of alpha-thalassemia-1 to HBE and HbA2 levels separated and quantified by capillary electrophoresis system in HbE heterozygotes: Simple and rapid screening using BbE levels alone

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Background : α-Thalassemia-1 screening in hemoglobin E (HbE) carriers was based primarily on HbE quantification. Generally, it is measured by high-pressure liquid chromatography (HPLC). The resulting HbE content was combined with HbA_2. Currently, the capillary electrophoresis (CE) can quantify HbE and HbA_2 separately. However, to be able to use the original cut-off value to screen for the α-thalassemia-1, it was still necessary to combine HbE with HbA_2.

Method : A total of 784 HbE heterozygotes were recruited. Quantification of the HbE and HbA_2 was analyzed via CE. α-Thalassemia-1 genes were identified using gap-polymerase chain reaction. Receiver operating characteristic (ROC) curves were constructed using the area under the curve (AUC). Cut-off values of HbE, HbA_2, and HbA_2+HbE levels for screening of α-thalassemia-1 were determined.

Results : The α-thalassemia-1 was identified in 111 (14.2%) samples, with mean 3.4±0.4%, 23.3±2.8%, and 26.8±2.9 for HbA_2, HbE, and HbA_2+HbE, respectively. α-Thalassemia-1 was not observed in 673 samples (85.8%), with mean 3.6±0.4%, 14.4±2.3%, and 18.0±2.5% for HbA_2, HbE, and HbA_2+HbE, respectively. The means of the three hemoglobin fractions were statistically different (P-value<0.05) between the groups with and without α-thalassemia-1. The ROC curves analysis of HbA_2, HbE, and HbA_2+HbE for α-thalassemia-1 screening revealed that HbE ≤ 18.5% had sensitivity, specificity, positive predictive value (PPV), negative predictive values (NPV), and AUC at 100.0%, 93.0%, 70.3%, 100.0%, and 0.977, respectively. While the HbA_2+HbE ≤ 21.7%, the values were 100.0%, 92.4%, 68.5%, 100.0%, and 0.973, respectively. Additionally, HbA_2 ≤ 4.5% showed sensitivity, specificity, PPV, and NPV, representing at 100%, 1.6%, 53.1%, and 100%, respectively.

Conclusion : α-Thalassemia-1 favorably influents the expression of HbE quantities. Co-inheritance of HbE heterozygote with α-thalassemia-1 resulted in a significantly decreased HbE content. The HbE content alone could be applied to screen for the α-thalassemia-1, without the need to be combined with the HbA_2 content.

Keywords : Heterozygous HbE, Alpha-thalassemia-1 gene, HbE level, Capillary electrophoresis, Cutoff value

PP10-9

Is digital morphology analyzer reliable for white blood cell differential in body fluids?: Performance assessment of Sysmex DI-60

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Background : Few studies have evaluated digital morphology (DM) analyzers in body fluid (BF). We evaluated the performance of DM analyzer, Sysmex DI-60 (Sysmex, Kobe, Japan) for white blood cell (WBC) differential in BF samples.

Method : We used five BF samples (two pleural and three ascitic fluids) that contained single dominant cell type (> 80%, neutrophils, lymphocytes, macrophages, abnormal lymphocytes, and malignant cells in each sample). We evaluated precision of DI-60 and compared WBC differential and turnaround time (TAT) between DI-60 and manual counting.

Results : Precision of DI-60 pre-classification and verification was excellent (%CV, 0.01–3.16%). After verification, DI-60 showed high sensitivity, specificity, and efficiency (range, 90.8 – 98.1%, 96.8 – 97.9%, and 92.5 – 98.0%, respectively) for dominant cell types in neutrophil- and lymphocyte-dominant samples. DI-60 and manual counting showed high correlations in major cell types (neutrophils, lymphocytes, macrophages, and others, r = 0.72 to 0.94) after verification in all samples; the absolute mean differences (%) between DI-60 and manual counting decreased after verification, except in macrophage-dominant sample. DI-60 showed significantly longer TAT (min:sec) than manual counting in all samples (median TAT/slide, 6:28 vs. 1:53, P < 0.0001), with remarkable differences in abnormal lymphocyte- and malignant cell-dominant samples (21:05 vs. 2:06; 12:34 vs. 2:25).

Conclusion : DI-60 may provide reliable data in neutrophil- and lymphocyte-dominant BF samples. However, it may require more time and higher workload for WBC differential especially in BF samples containing atypical cells. Further improvement is needed before applying DM analyzers for clinical practice in BF analysis.

Keywords : Digital morphology analyzer, DI-60, Body fluid, Performance, Turnaround time

PP10-10

Multiple primary cancers with hematologic malignancies and germline predisposition: A case series

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Background : Multiple primary (MP) cancers refer to the existence of more than one cancer in the same individual. The combination of MP cancers with hematological malignancies is relatively uncommon. In this study, we present five patients who diagnosed with MP cancers with hematological malignancies.

Method : We conducted a comprehensive analysis of their clinical characteristics, cytogenetic profiles, and both germline and somatic variants.

Results : Among these patients, two patients had the first cancers as solid cancer, not followed by cytotoxic therapy. The other three patients had the first cancers as hematologic cancer, followed by cytotoxic therapy, but the second cancers (hematologic malignancies) did not fit the definition of therapy-related myeloid neoplasm. Remarkably, two (40%) out of the five patients harbored pathogenic germline variants in cancer predisposition genes (CPG).

Conclusion : Germline variant testing should be considered when MP cancers with hematological malignancies require consideration for related donor stem cell transplantation.

Keywords : Multiple primary cancers, Hematologic malignancy, Germline predisposition, Next-generation sequencing

Table 1. Deleterious potential/presumed germline variants identified among five patients with multiple primary cancers hematologic malignancy.

	MP3*	MP4*
Gene (RefSeq)	*ATM* (NM_000051.3)	*TP53* (NM_000546.5)
Syndrome (inheritance)	Ataxia-telangiectasia (AR)	Li-Fraumeni syndrome (AD)
Coding DNA sequence	c.5288_5289insGA	c.730G>A
Amino acid change	p.Tyr1763fs (NMD)	p.Gly244Ser
VAF/total depth	0.46/392	0.31/290
ClinVar[a]/HGMD[b]	LP (★★)/DM (high)	P (★★)/ DM (high)
gnomAD exomes frequency (global/east asians)	0/0	0/0
ACMG classification	P (PVS1+PM2+PP5)	LP (PM1 + PM2 + PM5+ PP3 + PP5)

*Classified as both germline and somatic variants since these variants can be both.

†Presumed germline variants via non-malignant BM samples.

[a]ClinVar reports were described with clinical significance and review status. ★★ refers to the review status of ClinVar, criteria provided, multiple submitters, no conflicts.

[b]HGMD reports were described with variant class and confidence.

Abbreviations: RefSeq, reference sequence; AD, autosomal dominant; AR, autosomal recessive; NMD, nonsense mediated decay; VAF, variant allele frequency; HGMD, the Human Gene Variant Database; gnomAD, the Genome Aggregation Database; ACMG, American College of Medical Genetics and Genomics; P, pathogenic; LP, likely pathogenic; DM, disease causing variant; PVS, pathogenic very strong; PM, pathogenic moderate; PP, pathogenic supporting.

PP10-11

Development and clinical application of targeted NGS panels for hematological malignancies covering WHO/ICC 2022 guideline

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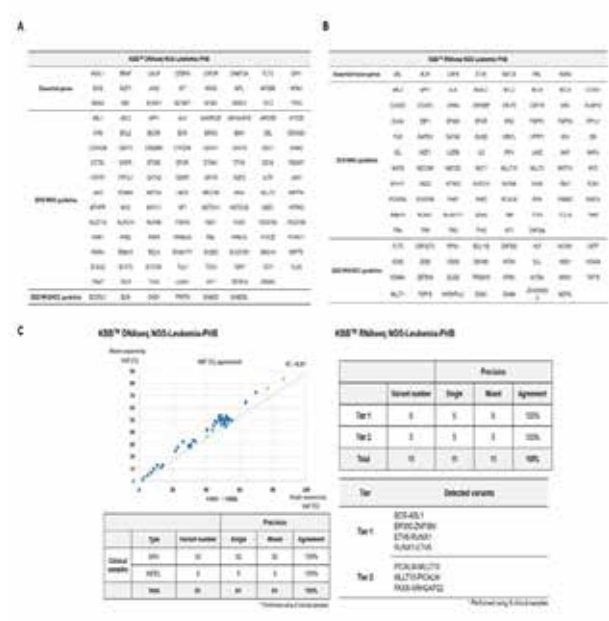
Background : Since 2020, we have successfully developed a targeted blood cancer NGS panel and have been using it efficiently in clinical settings. However, it needed to be upgraded due to recent new blood cancer diagnosis and classification guidelines by the World Health Organization and the International Collaboration for Cancer Classification (ICC) in 2022. Therefore, in this study, an updated targeted NGS panel that covers the updated guidelines was evaluated using clinical samples.

Method : To adhere to the recent guidelines, the currently used targeted NGS panel (KBB DNA/RNAseq NGS Leukemia PHB; KBlueBio Inc., Hwasun, Korea) was reviewed. Its analytical performance was validated using standard NA12878 and clinical samples. The clinical samples consisted of 19 genomic DNA and 20 total RNA samples extracted from the bone marrow or peripheral blood of patients with hematologic malignancies, including acute myeloid leukemia, acute lymphocytic leukemia, myelodysplastic syndrome/myeloproliferative neoplasm, multiple myeloma, and lymphoma.

Results : The updated DNA panel comprises 125 genes including 6 new genes. The updated RNA panel has 116 genes including 31 new genes. The accuracy, repeatability, reproducibility, sensitivity, and detection limit of the updated NGS panels were evaluated using standard materials, and the results met the predefined criteria. A comparison of the updated DNA panel with the old panel using 19 clinical samples revealed an overall concordance rate of 100% between the two panels for all mutations (95% confidence interval (CI): 99.72–100.00%). Similarly, the updated RNA panel also met the predefined criteria. The overall concordance rate between the updated RNA panel and the old panel was 99.72% in 20 clinical samples (95% CI: 99.00–99.72%).

Conclusion : The old targeted DNA/RNA NGS panel was successfully updated according to the 2022 WHO and ICC guidelines, and can be used to accurately and efficiently detect the genetic variants of blood cancers.

Keywords : Targeted NGS panel, 2022 WHO/ICC guideline, Hematological malignancies



PP10-12

Parasite-derived particles: A new approach to diagnose malaria

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Background : Quantitation of malaria parasites is essential for the treatment. However, the currently used flow cytometry can assess only the percentage of infected erythrocytes. To optimize the flow cytometry approach for enumeration of parasite-derived particles of the malaria specimen.

Method : The infected erythrocytes were incubated with acridine orange (AO) and an RBC lysing solution. The numbers of parasite-derived particles were quantitated using the FACSCalibur analyzer and calibrated with size-standard bead and

counting beads. The fluorescence of the AO-stained parasite-derived particles was examined using a fluorescent microscope.

Results : The number of parasite-derived particles was correlated with the percentage of infected RBCs obtained from manual counting ($r2 = 0.93$, $p < 0.0001$). A dilution assay demonstrated that the counting method was linear in the range between 20 to 45,900 particles/μL; however, stored specimens exhibited an increase in the number of malaria particles. The fluorescence of AO-stained malaria parasites was confirmed. An electron microscopic study demonstrated that different stages of malaria parasites existed in lysed RBC specimens in the form of membrane-bounded spherical cells.

Conclusion : Altogether, the potential use of flow cytometry for enumeration of parasite-derived particles was demonstrated. The developed approach is reliable and straightforward for malaria parasite enumeration in the routine laboratory.

Keywords : Parasite-derived particles, Malaria , Flow cytometry, Diagnosis

PP10-14

Automated blood cell counter-derived unghosted cells (UGC): Exploring a novel red cell research parameter for clinical insights and diagnostic significance in diverse clinico-pathological contexts

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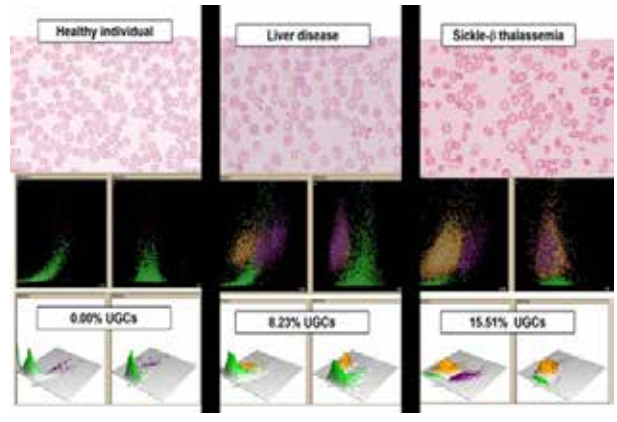
Background : Unghosted cells (UGC) represent a novel red cell research parameter obtained on the UniCel DxH 800 Cellular Analysis System (Beckman Coulter Inc.). In this study, we assessed the reference ranges and clinical utility of UGC across a diverse range of physiological and pathological states and correlated their frequencies with peripheral smear morphological findings.

Method : This prospective observational study enrolled 400 participants, encompassing 63 healthy individuals, 130 beta thalassemia traits, 73 persons with variant hemoglobins, 75 iron deficient individuals, 26 cases of liver disease, 14 persons with spherocytosis, and 19 cord blood samples. EDTA samples (approximately 3 ml) were collected and analyzed on UniCel DxH 800 instruments in the CDR mode. UGC percentage and absolute counts were recorded along with all other analyser output data, and correlated with peripheral smear findings.

Results : The median UGC% in healthy individuals was 0.00% (range (0.00-0.01%). Among beta thalassemia trait, median UGC% was 0.09% (0.0-13.11), in iron deficiency anemia the median was 0.01% (0-2.76), other hemoglobinopathies 0.01% (0-15.51), liver disease 0.395% (0-8.23), spherocytosis 0% (0-0.01), and cord blood samples 0.08% (0-0.34). A highly significant correlation was observed between the morphological target cell count and the UGC% ($r=0.7208$, $p<0.0001$). The differences in UGC% between the β-thalassemia trait and iron-deficient subgroups ($p<0.0001$), β-thalassemia trait and healthy individuals (<0.0001) and liver disease and healthy individuals ($p=0.0002$) were also highly statistically significant. Figure 1 depicts three representative cases.

Conclusion : Our comprehensive dataset represents the largest-scale investigation to date of UGC in pathological blood samples within the global scientific literature. This innovative automated parameter holds significant promise for clinical diagnostics, particularly in the assessment of patients with hemoglobin disorders and related conditions marked by elevated fetal hemoglobin levels. Furthermore, its application may provide valuable insights into the pathogenetic mechanisms of anemia in both liver disease and nutritional anemias.

Keywords : UGC, Unghosted red cells, Counter, Blood cell counter, Reticulocyte



PP10-15

Plasma soluble CSF1R is a promising prognostic indicator for pediatric Langerhans cell histiocytosis

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Background : Langerhans cell histiocytosis (LCH) is a rare hematologic neoplasm characterized by a clonal proliferation of Langerhans-like cells. Colony-stimulating factor 1 receptor (CSF1R) is a membrane-bound receptor and highly expressed in LCH cells and tumor-associate macrophages.

Method : In this study, a soluble form of CSF1R protein (sCSF1R) was identified by plasma proteome profiling, and its role in evaluation of LCH prognosis was explored. We prospectively measured plasma sCSF1R levels using ELISA in 104 LCH patients and 10 healthy children. Plasma sCSF1R levels were higher in LCH cases than in healthy controls ($P < 0.001$) and significantly differed among the three disease extents, with the highest level in MS RO+ LCH ($P < 0.001$). Accordingly, immunofluorescence showed the highest level of membrane-bound CSF1R in MS RO+ patients. Furthermore, plasma sCSF1R levels at diagnosis could efficiently predict the prognosis of LCH patients treated with the standard first-line treatment (AUC =0.782, $P < 0.001$).

Results : Notably, dynamic monitoring of sCSF1R levels could early predict relapse in patients undertaking BRAF inhibitor treatment. Drug sensitivity in vitro data showed that sCSF1R increased the resistance to Ara-C in THP-1 cells expressing ectopic BRAF-V600E.

Conclusion : Collectively, plasma sCSF1R at diagnosis and during follow-up is of great clinical importance in pediatric LCH.

Keywords : CSF1R, Langerhans cell histiocytosis, Prognosis, Relapse, Proteomics analysis

PP10-16

Predictive value of the complete blood count in determining the length of hospital stay among Filipino patients with COVID-19: A single center study

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Background : The present study aimed to evaluate the potential role of the complete blood count (CBC with neutrophil-lymphocyte count (NLR) and platelet-lymphocyte count (PLR)) in predicting the severity and length of hospital stay of Filipino patients with COVID-19.

Method : A single-center retrospective data collection was performed in a tertiary healthcare facility in Pampanga, Philippines. Electronic clinical data from January to December 2021 were retrieved using a data abstraction form and statistically analyzed.

Results : A total of 260 data sets were obtained from and were classified as ICU (n=22) and non-ICU (n=238) patients. A comparison of the CBC-related parameters between the two groups showed significant differences in terms of RBC count, lymphocyte count, hemoglobin levels, and NLR. Linear regression analysis between the selected CBC parameters and length of hospital stay adjusted for age, sex, and comorbidities was also done. It showed significant outcomes for monocyte, eosinophil, basophil, and RBC count, as well as for hemoglobin and hematocrit. Of all the CBC parameters that showed significant outcomes, lymphocyte count showed the highest predictive potential in identifying length of hospital stay with a sensitivity of 95.5% and specificity of 40.3%.

Conclusion : Overall, our results show that some routine markers may indicate the length of stay of COVID-19 Filipino patients. Given the limitations of this retrospective research, further studies may be done to investigate the utility of the said markers as predictors of COVID-19 disease severity in the target population.

Keywords : Complete blood count, COVID-19, Filipino

PP10-17

Unveiling the distinctive gene expression profile of Ph-like acute lymphoblastic leukemia

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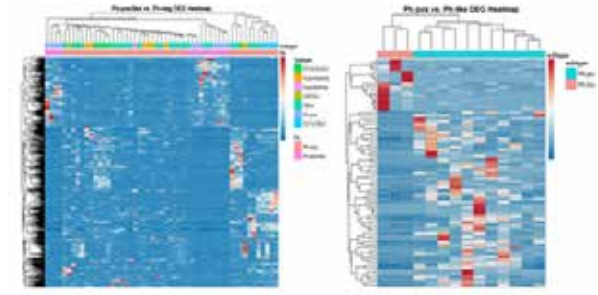
Keywords : Acute lymphoblastic leukemia, BCR::ABL1 like ALL, Ph-like ALL, RNA sequencing, Genomic profiling



Background : Philadelphia chromosome-like acute lymphoblastic leukemia(Ph-like ALL) is a subgroup of B-cell precursor ALL(B-ALL) which by gene expression analysis clusters with Philadelphia-positive ALL although lacking the BCR::ABL1 fusion. Ph-like with ALL is associated with poor treatment response and poor prognosis. Therefore, diagnosis of Ph-like ALL is crucial for proper risk stratification and patient management. We aim to identify gene expression profiles uniquely observed in Ph-like ALL.

Method : 53 patients diagnosed with B-ALL at our institution were included in this study. Total RNA was extracted from diagnostic bone marrow aspirates. RNA sequencing(RNA-seq) was performed using the TruSeq Stranded mRNA kit and NextSeq 550Dx Instrument from Illumina. Gene count data was obtained from RNA-seq data. First, Ph-like ALL and Ph-positive ALL were treated as one group, and the common differentially expressed genes of Ph-like and positive were selected through differentially expressed gene(DEG) analysis with other B-ALLs. After that, genes that differentially expressed between Ph-like and Ph-positive within the corresponding DEG were reselected.

Results : This study included eleven cases of Ph-positive ALL, three cases of Ph-like ALL, and 39 cases of B-ALL belonging to other subtypes. We identified 18 upregulated genes and 61 downregulated genes(log2FoldChange > 2, FDR < 0.05). The distinction between Ph-like ALL and Ph-positive ALL became evident through principal component analysis conducted on 79 selected DEGs. The upregulated genes exhibited variations among Ph-like ALL samples, whereas the downregulated genes showed consistent patterns across all samples. Following gene set enrichment analysis(GSEA), it was observed that 12.7% of the downregulated genes were associated with the enzyme-linked receptor protein signaling pathway(p-value = 0.0001585). Other notable findings also showed elevated rates and low p-values for various processes.

Conclusion : In this study, we identified a specific gene expression profile unique to Ph-like ALL, suggesting potential of RNA-seq based diagnosis. This enhances understanding of poor prognosis mechanisms without BCR::ABL1 translocation.

PP10-18

Genetic differences in myelodysplastic syndrome and clonal cytopenia of undetermined significance

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Background : Clonal hematopoiesis of undetermined significance (CCUS) is defined as persistent cytopenia not explained by other causes accompanied by clonal hematopoiesis (CH). We aimed to investigate the differences in mutation profiles associated with clinical features between CCUS and myelodysplastic syndrome (MDS) in patients with cytopenia.

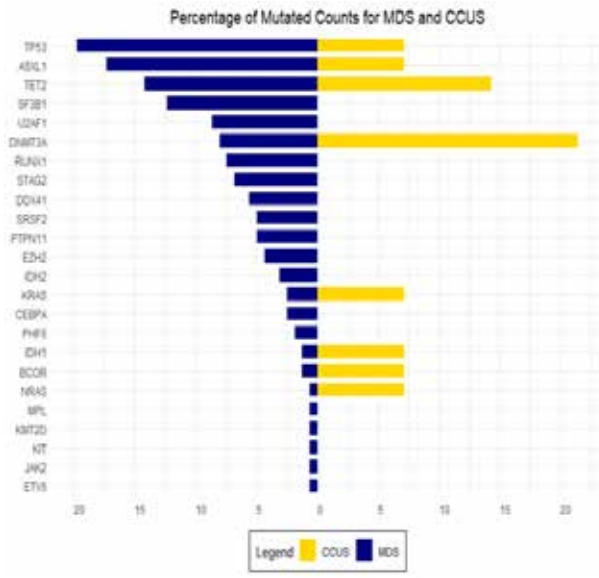
Method : We included patients with persistent one or more cytopenia who underwent next-generation sequencing (NGS) at our institution. Hybrid capture-based NGS was performed using custom probes targeting 30- or 531- hematologic cancer-related genes (Dxome, Seongnam, Korea) and NextSeq 550Dx Instrument (Illumina, CA, USA). Somatic variants were categorized as tiers 1, 2, or 3 based on oncogenicity and clinical significance according to AMP/ASCO/CAP guidelines.

Results : A total of 245 patients were included in this study. 162 MDS and 14 CCUS patients were included. More than half of patients with MDS had at least one tier 1/2 somatic variant (119 out of 162 patients; 73.5%). The average number of mutations was 2.4 (range, 1.0-9.0), and the average variant allele frequency (VAF) was 26.98% (0.035-88.00%). Top five mutated genes in MDS were TP53 (n = 32, 15.17%), ASXL1 (n = 28, 13.27%), TET2 (n = 23, 10.90%), SF3B1 (n = 20, 9.48%), and U2AF1 (n = 14, 6.64%). CCUS patients had an average number of 1.38 (1.0-6.0) somatic variants and the

average VAF was 20.14% (4.0-45.4%). Only two mutated genes were significant in CCUS, which were DNMT3A (n = 3, 27.27%) and TET2 (n = 2, 18.18%). These mutation proportions were higher than that of MDS, which were 6.19% and 10.90% for each DNMT3A and TET2.

Conclusion : We investigated the differences in genetic profile between MDS and CCUS. Regarding the differences, our findings could be applied to detect and manage CCUS in the clinic. Additional research about the specific genetic features of CCUS is needed to diagnose and manage cytopenia patients appropriately.

Keywords : Myelodysplastic syndrome, Clonal cytopenia of undetermined significance, NGS



PP10-19

Clinical and molecular spectrum of *DDX41* variants in Korean patients with hematologic malignancies

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Background : Hereditary hematologic malignancy is characterized by an increased risk for hematologic malignancies due to germline variants in cancer predisposition genes. Among them, germline *DDX41* variants are the most frequent especially in adults and found in 1.5% of myeloid neoplasms. In this study, we investigated the frequency and significance of *DDX41* variants in Korean patients.

Method : We retrospectively reviewed 713 patients who were suspected as hematologic malignancies and underwent targeted sequencing of 50 genes in our institution from August 2020 to July 2023. Among them, we analyzed the clinical characteristics of patients with *DDX41* variants.

Results : Of 713 patients, 29 patients had germline and/or somatic *DDX41* variants and a total of 22 variants were identified. Fifteen variants were presumable germline variants, and 11 patients (1.5%) were diagnosed as hematologic neoplasms with germline DDX41 variant presenting as 6 MDS (6/90, 6.7%), 4 AML (4/165, 2.4%), and 1 MPN (1/148, 0.7%). The median age of hematologic neoplasms with germline DDX41 variant was 69 with male predominance (8:3). DDX41 Y259C variant was the most common germline variant (63.6%) and the R525H variant was the most common somatic variant (24.1%).

Conclusion : Our study demonstrated the clinicopathological characteristics of *DDX41* variants in Korean patients with hematologic malignancies. Our findings highlight the importance of assessment of DDX41 variants in hematologic malignancies.

Keywords : DDX41, Somatic, Germline, Variant, Hereditary hematologic neoplasm

PP10-20

Clinical application of TRBC1 expression for diagnosis of T-cell lymphoma

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Background : Flow cytometric evaluation of aberrant T-cell marker expressions for malignancy is challenging due to a lack of definite clonal evidence and loss of antigens in reactive conditions. Recently, T-cell Receptor Constant Beta Chain 1 (TRBC1) expression has been reported to be monotypic in T-cell malignancy, serving as a potential clonal marker. In this study, we assessed the reference value of TRBC1 expression in healthy individuals and also evaluated the diagnostic utility of TRBC1 in suspected lymphoma patients.

Method : We established the reference range of TRBC1 using peripheral blood samples from 20 healthy individuals. We also reviewed 158 flow cytometry cases performed for lymphoma diagnosis between March 2023 and November 2023 covering bone marrow (n=98), peripheral blood (n=16) and body fluids (n=44), including cerebrospinal, pleural, ascitic and pericardial fluids. Nine monoclonal antibodies were used for the analysis: CD45, CD3, CD4, CD8, CD56, CD2, CD5, CD7 and TRBC1 (Ancell Corporation). Data were acquired using a BD FACSLyric Flow Cytometer (Becton Dickinson) and analyzed with Kaluza software (Becton Dickinson).

Results : TRBC1 expression of 20 healthy individuals was polytypical. The median proportion of TRBC1 expression of CD4+ T-cells and CD8+ T-cells were 38.6% (range, 33.9–46.1%) and 26.3% (10.9–44.2%), respectively (P<0.001). Total of 15 among 158 cases, bone marrow (n=6), body fluids (n=2), and peripheral blood (n=7), were diagnosed with mature T-cell lymphoma histologically and showed monotypical TRBC1 expression patterns; CD3+CD4+CD8−TRBC1+ (n=4), CD3+CD4+CD8−TRBC1− (n=5), CD3+CD4−CD8+TRBC1+ (n=1), CD3+CD4−CD8+TRBC1− (n=4), and CD3+CD4+CD8−TRBC1dim+ (n=1). In 143 non-malignant cases, there were significant differences in TRBC1 expression levels between CD4+ T-cells and CD8+ T-cells (median, 41.8% vs. 31.1%, P<0.001) without statistical differences between sample types (All P>0.05).

Conclusion : Flow cytometric evaluation of TRBC1 expression is useful for detecting clonal T-cell population in bone marrow, body fluids and peripheral blood, and is applicable as a clonal marker for T-cell lymphoma diagnosis.

Keywords : Clonality, Flow cytometry, T-cell lymphoma, TRBC1

PP10-21

Hematological laboratory findings and its association with clinical spectrum of COVID-19 in pregnant women in Yogyakarta, Indonesia

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Background : It has been almost four years since the World Health Organization (WHO) declared COVID-19 a global pandemic on March 11, 2020. Until the end of 2023, this disease continue to be a global threat. Hematological parameters were significant in predicting the severity of the disease in the general population. However, studies on hematological profiles of pregnant women with COVID-19 in developing countries and its association with clinical severity are scarce.

Method : This was a retrospective, single-center cohort study involving all pregnant women who tested positive for COVID-19 in Wonosari Regional General Hospital, Yogyakarta, Indonesia, from January 2020 to August 2021. Data regarding the clinical spectrum of COVID-19 grouped based on the National Institute of Health (NIH) classification, and laboratory findings were extracted from medical records. One way ANOVA was used was to analyze the association between laboratory findings and the severity of COVID-19.

Results : This study involved 33 pregnant women aged 20-43 who tested positive for COVID-19, the mean (SD) of gestational age was 38.33 (2.231) weeks. Out of them, 4 (11.8%) were asymptomatic, 19 (55.8%) had mild symptoms, and 10 (29.4%) had moderate symptoms. The mean (SD) of red blood cells (RBC) was 4.09 (0.47) 10^6/µL, hemoglobin (Hb) was 11.53 (1.34) g/dL, hematocrit (HCT) was 35.35 (4.08) %, platelet was 217.03 (73.26) 10^6/µL, total white blood cells (WBC) was 10055.76 (3985.29) /µ, and NLR was 6.30 (4.11). Statistical analysis revealed that there was a significant correlation between the severity of COVID-19 in pregnant women and RBC (p-value = 0.048), Hb (p value=0.044), HCT (p value=0.020), platelets (p value= 0.015) and total WBC (0.038).

Conclusion : Some hematological parameters are significantly associated with the clinical spectrum of COVID-19 in pregnant women. Initial laboratory examination can be beneficial in predicting the severity of the disease in pregnant women, leading to better monitoring and treatments.

Keywords : COVID-19, Hematology, Pregnancy, Severity, Clinical spectrum

PP12-1

Effect of omega 3 unsaturated fatty acid supplements on perioperative bleeding after spinal surgery

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Background : Omega 3 fatty acids (n-3FA) have been widely used

and sold over-the-counter as anti-coagulants. The ban on the use of omega 3 fatty acids prior to surgery is due to concerns of bleeding associated with altered platelet function. Bleeding complications in spinal surgery can occur in several ways, including large amounts of blood loss during spinal surgery leading to hemodynamic instability or small amounts of bleeding leading to epidural hematomas that compress spinal cord elements. If a patient has recently taken n-3FA supplements and is about to have a spinal surgical procedure, the procedure is often canceled or postponed.

Method : Patients with one- or two-level spinal decompression and instrumental arthrodesis between L3 and S1, or iliac crest bone graft harvesting. Patients who had used n-3FA within 14 days prior to surgery were analyzed and compared with the control group with respect to demographics, use of other anticoagulants prior to surgery. Patients with abnormal coagulation parameters, known bleeding disorders or other medications that could affect surgical blood loss were excluded

Results : Patients were taking n-3FA supplements, and stopped on average 2-3 days before surgery. There were no significant differences between groups in demographic parameters, use of other anticoagulants, and timing of surgery. Estimated blood loss was higher in the control group but the difference was not significant.

Conclusion : There was no increase in intraoperative blood loss or postoperative bleeding complications associated with preoperative n-3FA supplement use up to a mean of 2.3 days before surgery. There was no significant pre- and postoperative effect of n-F3A with an increase in bleeding time and a quantitative decrease in platelet aggregation.

Keywords : Spinal surgery, Omega-3, Polyunsaturated fatty acids, Bleeding spinal cord, n-3fa

PP12-2

Insulin resistance and increased risk of pulmonary embolism in leukemia, lymphomas and related disorders

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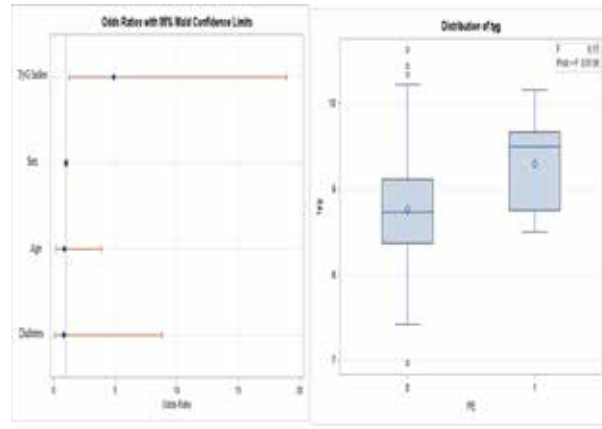
Background : Pulmonary embolism (PE) is a life-threatening condition characterized by the blockage of arteries in the lungs, often resulting from blood clots originating in other parts of the body. While PE is commonly associated with cardiovascular diseases, its occurrence and risk factors in specific patient populations, such as those with hematologic cancers, remain less explored. In this study, we investigated the relationship between hematologic cancer and the development of PE, along with the potential influence of insulin resistance.

Method : A retrospective analysis was conducted on 119,229 patients with histology-confirmed cancer. Clinical and demographic data were collected from UKbiobank. Statistical analysis included descriptive statistics, ANOVA, and logistic regression. Adjustments were made for age, sex, and diabetes mellitus status.

Results : Among 119,229 patients with histology-confirmed cancer, 442 (0.37%) were diagnosed with hematologic cancer, which includes leukemia, lymphomas, and related disorders. Within this group, 7 patients (1.57%) developed pulmonary embolism (PE). The mean TyG index in patients without PE was 8.75±0.56, while in patients with PE, it was 9.28±0.57. Analysis of variance (ANOVA) revealed a significant difference (F=6.15, p=0.0136) between the two groups. In logistic regression, controlling for age, sex, and diabetes mellitus status, the results indicated that insulin resistance increased the risk of PE in hematologic cancer patients by 386.5% (odds ratio [OR]=4.865, 95% confidence interval [CI]=1.253-18.891), independent of age, sex, and diabetes mellitus status.

Conclusion : Hematologic cancer patients with insulin resistance exhibited a significantly increased risk of developing pulmonary embolism, independent of age, sex, and diabetes mellitus status.

Keywords : Lymphoma, Leukemia, Diabetes



PP12-3

Non-cirrhotic portal hypertension in a patient with essential thrombocythemia: A case report and literature review

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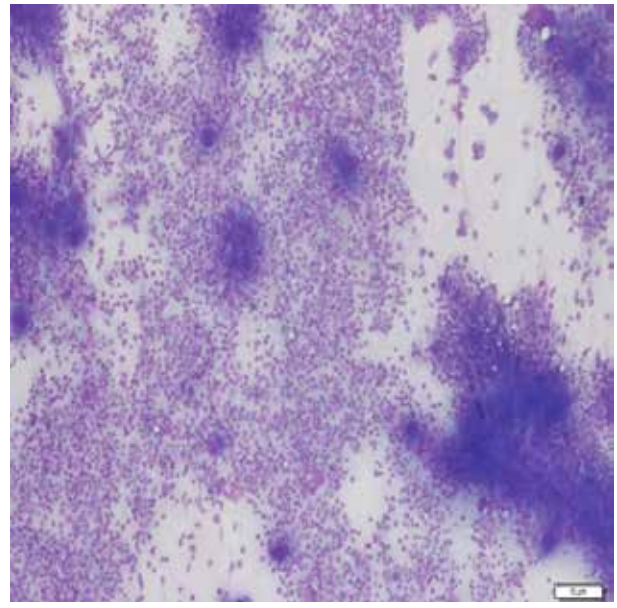
Background : Essential thrombocytosis (ET) is a myeloproliferative disorder characterized by a clinically significant increase in platelet count in the absence of an identifiable cause. The development of portal hypertension-induced gastroesophageal varices is most commonly associated with cirrhosis, while non-cirrhotic portal hypertension can result from splenic vein obstruction compression or intrahepatic thrombus formation. However, non-cirrhotic portal hypertension induced by ET has been reported rarely.

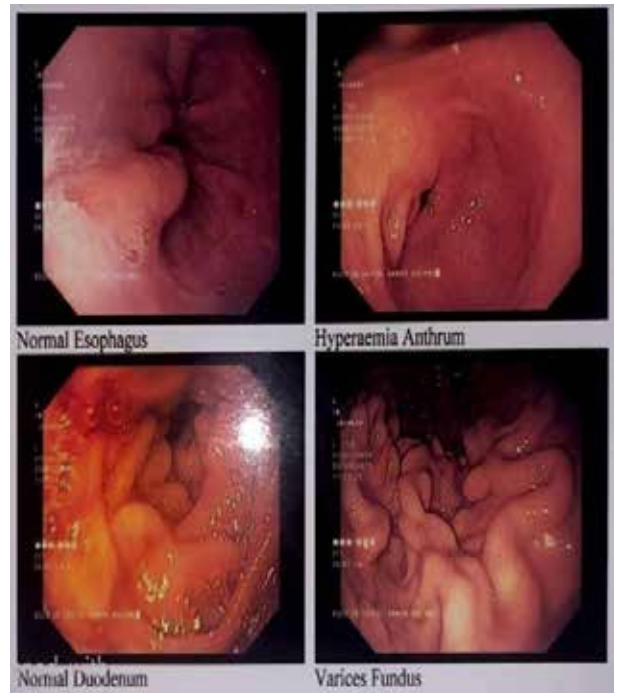
Method : In this study, we present a rare case of non-cirrhotic portal hypertension induced by Essential thrombocytosis (ET).

Results : A 62-year-old man, without a history of liver disease, was admitted to ER complaining of recurrent hematemesis for the last 6 months. Physical examination revealed icteric sclera, splenomegaly, and hepatomegaly, but no sign of liver cirrhosis. Laboratory examination revealed a platelet count of 774 × 10^9/L suggesting a significantly increased platelet count. Prothrombin time, liver function tests, bilirubin, hepatitis panel, and albumin levels showed no abnormalities. Endoscopic showed gastric varices mosaic-like mucosal pattern and hyperaemic antrum. Abdominal CT revealed splenomegaly, portal vein thrombosis, and portal hypertension. A bone marrow biopsy was done and showed the result of ET. The patient was given hydroxyurea for daily medication. ET is often accompanied by marked splenomegaly, which might increase the portal vein blood flow and provoke portal hypertension. This patient repeatedly suffered from a rupture of gastroesophageal varices caused by portal hypertension, accompanied by marked splenomegaly. Integrated examinations in this patient also supported non-cirrhotic portal hypertension induced by ET

Conclusion : This case report should raise awareness of the importance of preventing non-cirrhotic portal hypertension complications in patients with ET by conducting a comprehensive examination for optimal decisions and management.

Keywords : Essential thrombocythemia, Endoscopic, Gastroesophageal varices, Non-cirrhotic portal hypertension





PP12-4

Bernard Soulier syndrome caused by two novel heterozygous mutations in GP1BA gene: A case report and literature review

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Background : Bernard Soulier syndrome (BSS) is a rare inherited macrothrombocytopenia, usually autosomal recessive, which is charactered by prolonged bleeding, thrombocytopenia and abnormally large platelets. The gene mutations reported to participate in the cause of BSS include GP1BA, GP1BB and GP9, which defected GPIb-IX-V complex and thereby impaired the structure and function of platelets. The present study aimed to report three novel gene mutation sites in GP1BA.

Method : The clinical feature, laboratory tests, and mutation detection of a pediatric BSS patient diagnosed at the Children's Hospital of Soochow University, Suzhou, China was analyzed respectively.

Results : Whole exome sequencing found that there were two likely pathogenic heterozygous mutations (c.95_101del and c.1012del) in GP1BA gene. Flow cytometry analysis of platelet membrane glycoproteins indicated that the expression of GP1b was 0.28%, which was much lower than normal (100%). Platelet aggregation tests indicated that platelet aggregation was inhibited by ristocetin-induced (1.7%), ADP- (14.5%) and arachidonic-acid-induced platelet aggregation (5.6%). The literature review indicated that there were 53 mutations included 253 patients were reported in GP1BA gene, 29 mutations included 90 patients in GP1BB gene, and 32 mutations included 114 patients in GP9 gene.

Conclusion : The two novel gene mutation sites in the present case have not been reported previously, which enrich the GP1BA mutation spectrum.

Keywords : Bernard Soulier syndrome, Inherited thrombocytopenia, Pediatric, GPIb-IX-V complex, GP1BA

PP12-5

Paediatric thrombosis: A five-year experience from a tertiary care center of Pakistan

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Background : Advances in imaging techniques and longer survival of chronic medical conditions contribute to the increase in paediatric thrombosis. We aim to determine the incidence, underlying risk factors, management and clinical outcome of paediatric thrombosis at a multidisciplinary facility of Pakistan.

Method : A retrospectively analysis of the medical records of patients in the paediatric age group admitted at the Aga Khan University hospital from January 2018 to September 2023 was performed. Site of thrombosis, associated risks factors, management options and outcome of thrombotic event were evaluated.

Results : Of the 22,320 paediatric hospitalization, 35 paediatric patients were diagnosed with thrombosis (15 cases per 10,000 admissions). The median age of the study group was 15 years and twenty patients (57%) were male. The commonest site of thrombosis was in lower limb venous 11 (31%), followed by upper limb venous thrombosis 6 (17%), abdominal vein thrombosis 7 (20%), cerebral venous thrombosis 5 (14%), pulmonary embolism and arterial thrombosis 3(9% each). Eighty three percent had underlying clinical condition including central venous catheter [CVC] (26%), malignancy and infection (14% each), antiphospholipid antibody syndrome (9%), inherited thrombophilia (9%), congenital heart disease (6%), while thrombotic thrombocytopenic purpura and autoimmune disorder (3% each). Twelve (34%) patients were treated with heparin only, 8 (23%) received heparin followed by warfarin while warfarin as a single agent was given in 2 (5.7%) patients. One patient died of pulmonary embolism while 9 (25%) had persistence or recurrence of thrombosis.

Conclusion : Incidence of paediatric thrombosis was 0.15%. CVC placement was the most common associated risk factor. Warfarin and heparin both were found to be safe anticoagulation option. Recurrence rate was found to be high.

Keywords : Thrombosis, Children, Risk factors

PP12-6

Cannabinoid receptor 2 signaling: Role in megakaryocyte development and neuro-immune regulation

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Background : Megakaryocytes (MKs), a rare population of bone marrow cells, are responsible for the production of platelets, which are necessary for normal blood clotting. Thrombocytopenia (low platelet count, $<150 \times 10^9$/L), may be due to many factors including cancer and autoimmune diseases. This is a common problem among leukemia patients that can lead to hemorrhagic complications. Here, we investigated the role of virodhamine (an endocannabinoid) in megakaryocyte differentiation and subsequent thrombopoiesis.

Method : Human megakaryoblastic leukemia Dami cells were cultured in RPMI1640 medium and were treated with cannabinoid receptor 2 agonist virodhamine and expression of megakaryocyte differentiation specific markers (CD41 and CD61) was assessed by qRT-PCR. Morphological assessment was performed by microscopy. Cell cycle analysis, determination of mitochondrial membrane potential, and Annexin V assay were performed by flow cytometry. Intracellular ROS was determined using DCFDA.

Results : We evaluated role of thrombopoietic potential of virodhamine. Virodhamine treatment increased the number of cells that show platelet-like protrusion, polyploid nucleus and MK-specific maturation markers (CD41 and CD61) that are key features of megakaryocyte differentiation. Cell cycle analysis showed that virodhamine treatment increased the portion of cells in G0/G1 phase, while decreasing the percentage of cells in S phase, suggesting virodhamine induces differentiation of cells. Platelet production is a result of megakaryocytic apoptosis, which is probably caused by elevated levels of mitochondrial reactive oxygen species (ROS) and enhanced calcium concentration in cell. Intracellular calcium level and early apoptotic cells were found to be increased with virodhamine treatment. Virodhamine treatment showed cleavage of Poly ADP-ribose polymerase (PARP) which is substrate of caspase-3, suggesting induction of apoptosis. We have also observed down-regulation of phospho-PI3K activity and up-regulation of phospho-MAPK activity in virodhamine treated cells.

Conclusion : Dami cells treated with virodhamine underwent differentiation, characterized by extended cytoplasmic protrusions, and expression of MK specific markers of differentiation.

Keywords : Megakaryocyte, Cannabinoid receptor, Platelets

PP12-7

Plasma levels of three different types of direct oral anticoagulants measured with anti-factor Xa assay in patients with non-valvular atrial fibrillation: Comparison with heparin assays

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Background : Direct oral anticoagulants (DOAC) inhibit the active site of thrombin or factor (F) Xa.Although drug monitoring is not routinely requested, the measurement of DOAC levels in plasma is useful in some cases. In this study, we investigated the trough and peak levels of three different DOAC in patients with non-valvular atrial fibrillation (NVAF) and compared results between anti-Xa and heparin assays.

Method : A total of 566 NVAF patients were included for the study. Among them, 321 patients were treated with 5 mg apixaban orally twice daily, 208 with 60 mg edoxaban daily, and 37 with 20 mg rivaroxaban daily. Blood samples were collected using 3.2% sodium citrate tubes after three weeks of DOAC treatment and both trough and peak levels were measured using Biophen DiXal (anti-Xa) and Heparin LRT chromogenic assays (Hyphen BioMed, Neuville Sur Oise, France) with a Sysmex CS-5100 analyzer (Sysmex Corp., Kobe, Japan). Prothrombin time (PT) and activated partial thromboplastin time (aPTT) tests were also performed.

Results : The median age was 69, 69.5, and 72 years in apixaban, edoxaban and rivaroxaban treatment, respectively. The trough and peak levels for apixaban, edoxaban, and rivaroxaban were 109.58±68.22, 203.0±108.76, 52.85±38.51, 225.89±116.07, 75.57±79.38, and 292.24±135.81 ng/mL, respectively with anti-Xa assay. Heparin LRT assays for the trough and peak levels with apixaban, edoxaban and rivaroxaban were 116.78±68.88, 215.3±109.63, 50.94±27.37, 217.67±109.16, 65.77±76.51, and 283.22±144.42 ng/mL, respectively. The peak levels were statistically higher with all three DOAC than those of trough ($p<0.0001$). Both the anti-Xa and heparin assays showed excellent correlations ($r\geq0.97$, $p<0.0001$) regardless of the trough or peak levels and DOAC types.

Conclusion : The results suggested that chromogenic method for the assay of direct factor Xa inhibitors showed reliable trough and

peak levels for three types of DOAC in NVAF patients. We could obtain comparable results between the anti-Xa and heparin assays.

Keywords : Anti-Xa assay, Chromogenic assay, Direct oral anticoagulants, Heparin assay, Non-valvular atrial fibrillation

PP12-8

Evaluation of neutrophil extracellular traps as a novel circulating marker in acute ischemic stroke patients and the correlation with cytokines

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Background : Neutrophil extracellular traps (NETs) are extracellular web-like structures composed of cytosolic and granule proteins assembled on a scaffold of decondensed chromatin. Recent studies have revealed that inappropriate NETs production may be associated with an uncontrolled inflammatory response. In particular, due to the importance of neutrophils in thrombogenesis, studies on NETs are being actively conducted. The aim of this study was to evaluate circulating nucleosome levels as a biomarker of NETosis in patients diagnosed with acute ischemic stroke (AIS), to determine the suitability of circulating nucleosomes as a novel marker and to reveal the correlation between cytokines involved in inflammation.

Method : A total of 72 subjects were enrolled, of which 62 were patients diagnosed with AIS and 10 were controls who visited for health checkup. Circulating levels of NETs were assessed by measuring the plasma concentrations of nucleosomes. Additionally, cytokines were measured using luminex multiplex cytokine assay and compared in the patient and control groups.

Results : The concentration of nucleosomes was significantly higher in patients with AIS compared to the control group (P<0.001). Univariable analyses demonstrated that significant risk factors in the AIS group were age, diabetes mellitus, hypertension, and nucleosome concentration (p=0.002, 0.013, 0.011, <0.001, respectively). Receiver operating characteristic curve analysis revealed area under the curve values of 0.944 for nucleosomes concentration in the AIS group. Additionally, the Spearman correlation coefficient 0.27 was confirmed between Netosis and the P-selectin/CD62P.

Conclusion : This study confirmed an increased circulating level of NETs in patients with AIS during the initial presentation. Also, correlation between Netosis and P-selectin/CD62P was also confirmed. The findings suggest that NETs could serve as a novel circulating marker for the initial diagnosis of AIS. It also suggests the need for further research on Netosis, neutrophils, and thrombogenesis caused by P-selectin/CD62P in AIS patients.

Keywords : Neutrophil extracellular traps, Netosis, Thrombogenesis, Acute ischemic stroke, Cytokine

Variables	AIS (N=62)	Control (N=10)	P AIS vs. control
Demographic characteristics			
Age(y), mean ± SD	71.08 ± 11.20	65.30 ± 4.35	.002
Male, no.(%)	36 (58.1)	5 (50.0)	.633
Underlying disease			
Diabetes mellitus, no.(%)	25 (40.3)	0 (0.0)	.013
Hypertension, no. (%)	39 (62.9)	2 (20.0)	.011
Dyslipidemia, no. (%)	10 (16.1)	3 (30.0)	.290
Social history			
Alcohol intake, no (%)	18 (29.0)	3 (30.0)	.950
Current smoking, no (%)	16 (25.8)	0 (0.0)	.069
Laboratory data			
NET (nucleosome), mean ± SD	254.73 ± 179.77	70.60 ± 28.39	<.001

Abbreviation: AIS; acute ischemic stroke, NET; neutrophil extracellular traps.

PP12-9

Thrombopoietin-independent generation of platelet-like particles from megakaryoblastic cells

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Background : The use of megakaryoblastic leukemia MEG-01 cells can help reveal the mechanisms of thrombopoiesis. However, conventional in vitro activation of platelet release from MEG-01 cells requires thrombopoietin, which is costly. Here, we aim to develop a more straightforward and affordable method.

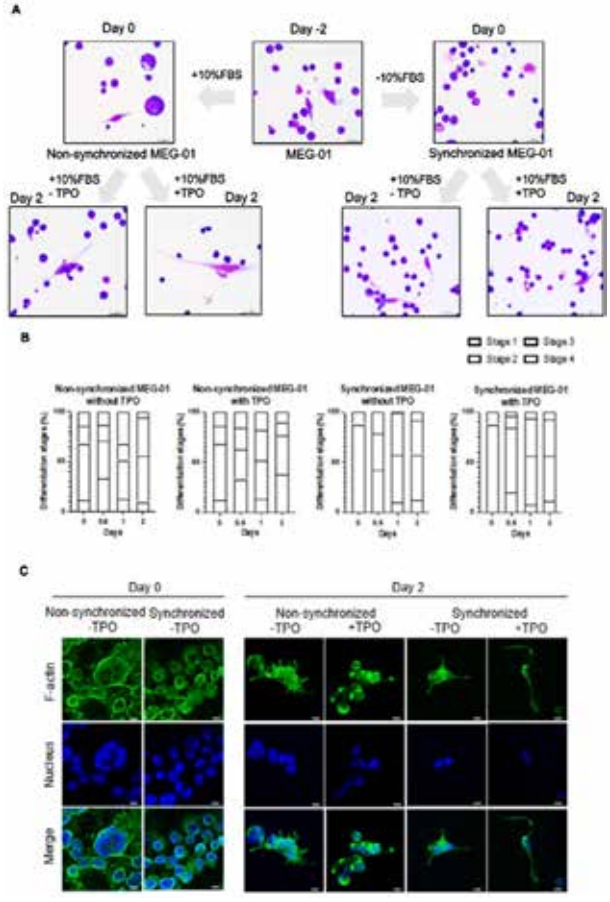
Method : Synchronization of the MEG-01 cells was initially performed using serum-free culture, followed by sponta-

neous cell differentiation in the presence of serum. Different stages of megakaryoblast differentiation were classified based on cell morphology, DNA content, and cell cycle.

Results : The MEG-01 cells released platelet-like particles at a level comparable to that of the thrombopoietin-activated MEG-01 cells. The platelet-like particles were distinguishable from PLP-derived extracellular vesicles and could express P-selectin following ADP activation. Importantly, the platelet-like particles induced fibrin clotting in vitro using platelet-poor plasma.

Conclusion : Altogether, this thrombopoietin-independent cell synchronization method is an effective and straightforward method for studying megakaryopoiesis and thrombopoiesis.

Keywords : Platelet-like particles, Thrombopoietin, Thrombopoiesis, Microvesiculation , Megakaryocyte



Characterization	Stage 1	Stage 2	Stage 3	Stage 4
Morphology	Myeloblast-like cells	Promegakaryocyte-like cells	Megakaryocyte-like cells	Proplatelet-like cells
Cell size; μm Median (min-max)	18 (10-29)	25 (19-60)	42 (13-135)	81 (7-205)
N:C ratio	0.6-1:1	0.5-0.9:1	0.3-0.9:1	0.1-0.5:1
Nuclear shape	Round, oval	Round, oval, kidney shape	Round, oval, lobulated (2 or more lobes)	Round, oval, lobulated (2 or more lobes)
Nuclear position	Central or eccentric	Central or eccentric	Central	Central
Nuclear color	Red-purple fine	Red-purple, increase chromatin	Red-purple	Red-purple
Nucleoli	1-3	1-4	1-2	1-3
Nucleoli color	Purple	Purple	Purple	Purple
Membrane shape	Round	Round, occasional vacuole	Abundant pseudopodia, extensive membrane blebbing	Elongated pseudopod, cytoplasmic protrusions, proplatelet-like structures, and distinctive platelet-sized particles
Cytoplasmic color	Basophilic	Less basophilic	Pale blue with a pink cast	Pale blue with a pink cast
Number of lobes	0	1-2	1-8	1-12
Cytoplasmic granule	-	-	Fine azurophilic granules	Fine azurophilic granules

PP12-10

Evaluation of FVIII PK profile in Korean hemophilia a patients assessed with myPKFiT: A retrospective chart review

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Background : Substantial interpatient variation in pharmacokinetics (PK) causes a significant difference in the amount of factor VIII (FVIII), which is required to sustain the desired factor level. However, there is limited information on FVIII PK among Korean hemophilia patients.

Method : Severe to moderate hemophilia A patient's PK result assessed using myPKFiT from January 2018 to November 2021 was collected from 5 Korean hemophilia treat-

ment centers. PK differences by age, blood type, inhibitor history, vWF:Ag, and body mass index were evaluated. And the correlation between the PK profile and the prophylaxis regimen was analyzed for each product in severe patients.

Results : PK data from 48 patients (age range: 5-52 years) treated with octocog alfa and 81 patients (age range: 14-64 years) treated with rurioctocog alfa pegol were obtained. The median half-lives of octocog alfa and rurioctocog alfa pegol were 9.9 (range: 6.3–15.2) hours and 15.3 (range: 10.4–23.9) hours, respectively. The half-life, time to 1%, and clearance for each product did not differ by age group, but the half-life and time to 1% of blood type-O patients were shorter than those of non blood type-O patients. In the regression analysis, the PK of octocog alfa showed a statistically significant difference by age, whereas the PK of rurioctocog alfa pegol showed correlations with vWF:Ag. When the impact of time to 1% on the FVIII dose and frequency were analyzed, only frequency in patients using rurioctocog alfa pegol showed a statistically significant difference, but the coefficient of determination was 0.1016.

Conclusion : Through this study, we could confirm a significant interpatient variation in the PK of FVIII in Korean patients with hemophilia A. For optimized prophylaxis, the FVIII prophylaxis regimen should be personalized according to the PK profile of the individual.

Keywords : Hemophilia A, FVIII, Pharmacokinetics, Prophylaxis, Korean

PP12-11

Heparin-calibrated anti-factor Xa assay for the measurement of direct anticoagulant such as apixaban, rivaroxaban and edoxaban

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Background : The purpose of this study was to determine whether measuring the level of DOAC was possible with heparin-calibrated chromogenic anti-factor Xa activity (AXA). The second aim was to evaluate the suitability of heparin-calibrated AXA concentrations corresponding to 30 and 50 ng/mL of DOAC, for antidote treatment decisions in surgery or bleeding.

Method : Platelet poor plasma was aliquoted and stored - 70℃ until analyzed. AXA were measured using two reagents and dedicated analyzers (Sysmex CS-5100 analyzer and STA R Max3). Four types of calibrator were used. (1) Stago DOAC (rivaroxaban, edoxaban, apixaban) specific calibrator, (2) Stago LMWH calibrator, (3) Sysmex UHF calibrator (4) Sysmex LMWH calibrator. Regression analysis was used to characterize the relationship between assays. Receiver operating characteristic (ROC) curves were analyzed to analyze the diagnostic power of heparin calibrated AXA corresponding to 30 ng/mL and 50 ng/mL DOAC levels for antidote management, and the concordance rate were calculated.

Results : The correlation coefficient were ranged 0.75-0.91 in rivaroxaban, 0.81-0.94 in apixaban. The correlation coefficient between edoxaban calibrated AXA and Sysmex LMWH/ Sysmex UHF calibrator calibrated AXA was not good (r=0.47). The correlation between DOAC calibrated AXA and Sysmex UFH or LMWH was linear at low to medium levels in rivaroxaban and apixaban. The correlation graph was not good between between DOAC calibrated AXA and Sysmex UFH or LMWH in edoxaban The concordant rate (90-100%) is good for determining antidote management level by heparin calibrated AXA compared with those of DOAC calibrated AXA.

Conclusion : When using heparin calibrated AXA for measuring DOAC, there are limitations in calculating accurate concentrations. There were scant data for evaluating heparin calibrated AXA for the decision making of antidote. The present study suggest that heparin calibrated AXA is clearly helpful in confirming the presence of DOACs to make antidote management in emergency situations.

Keywords : DOAC, Rivaroxaban, Apixaban, Edoxaban, Anti-factor Xa

PP12-12

Beneficial role of Moringa oleifera leaves extract in a rat model of deep vein thrombosis

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Background : Moringa oleifera is a medicinal plant with great therapeutic potential. The leaves of Moringa oleifera are used by Indians in herbal medicines to treat metabolic disease. It is used for medicinal purposes due to its choleretic, diuretic,

antitumor, antioxidant, antiinflammatory, and hepatoprotective properties. Aim of current study was to investigated the antithrombotic effects of ethanolic extract of Moringa oleifera leaves (MOL) in a rat model of deep vein thrombosis (DVT).

Method : DVT was induced in rat model by inferior vena cava (IVC) ligation. Sixty mice were treated with dose of (MOL 100 and 200 mg/kg) dissolved in saline was orally administered to the experimental rats. The thrombi were harvested and weighed. The IVC was analyzed histologically and by transmission electron microscopy. The cytokines interleukin (IL)-6, IL-8, and tumor necrosis factor-α (TNF-α) were detected by enzyme-linked immunosorbent assay. Expression of cellular adhesion molecules (CAMs) in thrombi was examined by Western blot.

Results : MOL significantly reduced thrombus length and weight ($P < .001$) and protected the integrity of the endothelium. MOL inhibited thrombogenesis-promoting factors P-selectin and CAMs, and promoted thrombogenesis-demoting factors CD34, vascular endothelial growth factor receptor-2. Compared with the control, MOL significantly lowered the cytokines IL-6 , IL-8 and TNF-α.

Conclusion : Present data showed that MOL significantly inhibited the propagation of thrombus. Taken together, our data suggest that, antithrombotic properties of MOL are likely to be directly associated with endothelial protection and regeneration, platelet aggregation, and inhibition of inflammatory cell and thrombus adhesion.

Keywords : Beneficial role of moringa oleifera leaves extract in a rat model of deep vein thrombosis, Rat model , Moringa oleifera leaves , Inferior vena cava

PP12-13

Acquired hemophilia A in an adult female without familial predisposition: A one-in-a-million rarity case report with review of the literature

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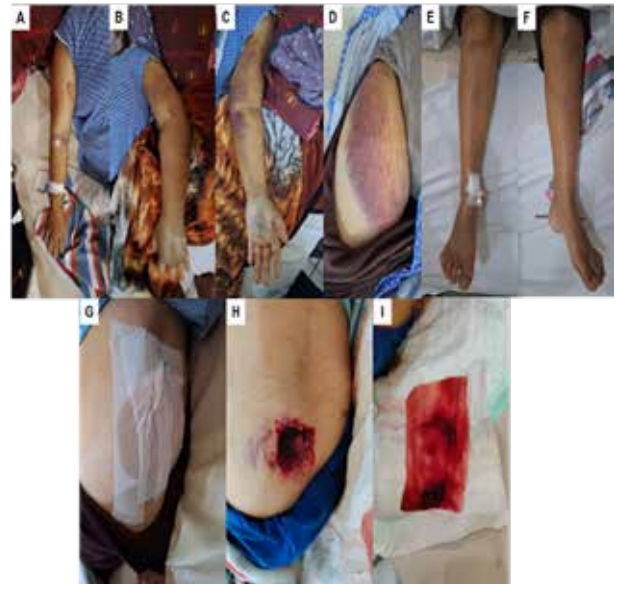
Background : Hemophilia A is typically an inherited bleeding disorder caused by a deficiency or absence of clotting factor VIII (FVIII). However, acquired hemophilia A (AHA), with a scarce incidence of about 1.5 cases per million people/year, is different because it is caused by the spontaneous development of inhibitory autoantibodies against the FVIII. We report a rare case of AHA in a female adult without a familial predisposition to the disorder. A 48-year-old Asian female was admitted to a tertiary hospital with swelling on left forearm accompanied by ecchymosis and bleeding from the bone marrow aspiration (BMA) puncture site. Ecchymosis since 4 months ago without prior history of any trauma. History of malignancy, autoimmune disease, or family history of bleeding disorders was denied. Physical examination found swelling on her left arm with multiple ecchymosis on left forearm, as well as right inguinal and femoral area (Bleeding Grade: II-III). Hematological panels showed marked prolonged hemostasis, predominantly aPTT, anemia, and thrombocytosis. BMA result was megaloblastic anemia with Fe deficiency and reactive thrombocytosis. The patient was initially given intravenous lyophilized prothrombin complex concentrate 500 IU, FFP and cryoprecipitate transfusion; however, ecchymosis and bleeding had not resolved and the aPTT was not correctable with mixing study. Coagulation factor examination was performed and showed profound deficiency of FVIII (value: 1%); however, autoimmune panel, e.g. Lupus Anticoagulant & anti-cardiolipin were negative. The patient was then given intravenous FVIII 20 IU/kg/day (~ 400 IU) for 2-3 days and complaints of bruising improved and bleeding stopped. The patient was successfully discharged and now routinely followed-up in outpatient clinics. AHA is a rare type of hemophilia. Our case highlighted the need for early diagnosis and prompt treatment with clotting factor FVIII replacement could greatly improve patient outcome.

Keywords : Acquired hemophilia a, Factor viii, Prolonged hemostasis, Lupus anticoagulant



PP12-14

Treatment of bleeding episodes with Efanesoctocog alfa in patients with severe haemophilia A in the phase 3 XTEND-1 study

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Background : The Phase 3 XTEND-1 (NCT04161495) study showed that once-weekly efanesoctocog alfa was well tolerated in adults and adolescents with severe hemophilia A and provided superior bleed prevention to prior FVIII prophylaxis. Here, we report the use of efanesoctocog alfa for treatment of bleeding episodes (BEs) during XTEND-1.

Method : Patients on prior prophylaxis were enrolled into Arm A (52 weeks, once-weekly efanesoctocog alfa prophylaxis [50 IU/kg], n=133). Patients receiving prior on-demand therapy entered Arm B (26 weeks, on-demand efanesoctocog alfa [50 IU/kg], then 26 weeks, once-weekly prophylaxis, n=26). BEs were treated with single-dose efanesoctocog alfa (50 IU/kg) and additional doses (30 or 50 IU/kg) as needed every 2–3 days. The number, location of treated BEs, dose and number of injections to resolve BEs, were evaluated. Patient response to bleed treatment was evaluated on 4-point ISTH scale.

Results : Median (range) annualized bleed rate was 0.0 (0.0–11.0) in Arm A, and 21.1 (8.3–33.4) and 0.0 (0.0–4.1) for 6-month on-demand and prophylaxis periods of Arm B, respectively. Of 362 BEs treated, 86 occurred in Arm A and, 268 and 8 in on-demand treatment and prophylaxis periods, respectively, of Arm B. In Arm A, 33 (38%) BEs were spontaneous, 45 (52%) traumatic, and 8 (9%) of unknown etiology. Corresponding values in Arm B were 197 (74%), 62 (23%), and 9 (3%) for on-demand period, and 5 (63%), 2 (25%), and 1 (13%) for prophylaxis period. Most BEs occurred in joints (79%) and muscles (14%). A single injection was sufficient to resolve 96.7% of BEs. Median (range) total efanesoctocog alfa dose for BE resolution was 50.9 (50.0–51.8) IU/kg. Most (94.9%) patient assessments of BE treatment response were excellent or good.

Conclusion : A single 50 IU/kg dose of efanesoctocog alfa effectively treated 96.7% of BEs regardless of bleed type and location.

Keywords : Hemophilia A, Bleeding, Efanesoctocog alfa, XTEND-1

PP12-15

Change in hemophilia joint health score (HJHS) during the phase 3 XTEND-1 study of efanesoctocog alfa in patients with severe hemophilia A

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Background : Hemophilic arthropathy and chronic joint pain occurs even with current standard of care (SoC) for hemophilia A. In Phase 3 XTEND-1 study (NCT04161495),once-weekly efanesoctocog alfa was well tolerated in adults and adolescents with severe haemophilia A and provided superior bleed prevention to prior FVIII prophylaxis. Here, joint health changes from baseline to Week 52 using Hemophilia Joint Health Score (HJHS) v2.1 in patients from XTEND-1 study are reported.

Method : Patients on prior FVIII prophylaxis were enrolled into Arm A (52 weeks of once-weekly efanesoctocog alfa prophylaxis [50 IU/kg]) and patients receiving prior on-demand therapy entered Arm B (26 weeks of on-demand efanesoctocog alfa [50 IU/

kg], then 26 weeks of once-weekly prophylaxis). Six joints (left and right ankle, elbow, and knee) were scored according to 9 HJHS domains. Gait was scored based on walking and climbing stairs. Total score was the sum from all 6 joints plus gait score.

Results : Baseline mean (standard deviation [SD]) HJHS was 18.1 (18.4) in Arm A (n=116) and 26.3 (13.2) in Arm B (n=25). Significant improvements in total HJHS from baseline to Week 52 were observed; least squares (LS) mean (95% confidence interval [CI]) change was –1.54 (–2.70, –0.37; P=0.0101; n=107) in Arm A and –4.1 (–7.94, –0.25; P=0.0382; n=22) in Arm B. In Arm A, HJHS domains with greatest mean (SD) change from baseline to Week 52 were swelling –0.3 (1.2), muscle atrophy –0.3 (1.2), crepitus on motion –0.3 (1.2), and flexion loss –0.3 (1.6) andin Arm B, were swelling –0.6 (1.1), swelling duration –0.4 (0.7), crepitus on motion –0.6 (1.8), flexion loss –0.7 (3.1), joint pain –0.4 (1.5), and strength –1.2 (2.4).

Conclusion : These data suggest that once-weekly efanesoctocog alfa prophylaxis may improve joint health in adults and adolescents with severe hemophilia A, and offer benefits above current SoC FVIII prophylaxis.

Keywords : Hemophilia A, Hemophilia joint health score, XTEND-1, Efanesoctocog alfa

PP12-16

Inflammation and hypercoagulability in type 2 diabetes mellitus with chronic kidney disease

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Background : Diabetes mellitus (DM) is the major cause of end stage renal disease. Patients with chronic kidney disease (CKD) have a higher risk of mortality, mostly from cardiovascular complications. Previous studies have shown that inflammatory cytokines are involved in the pathogenesis of microvascular diabetic complications, including CKD. We aimed to findrelationships among hypercoagulability and inflammation and their biomarkers in the development of complications in type 2 diabetes (DT2).

Method : 77 patients with DT2 aged 56.41±10.03 years were studied. Control group included 50 healthy subjects the same age. All patients underwent standard clinical and laboratory examination, with an assessment of the levels of tumour necrosis factor alpha (TNF-alpha), interleukin-6 (IL-6), coagulation and fibrinolysis parameters (von Willebrand factor (VWF)activity, plasminogen activator inhibitor-1 (PAI-1)). Patients were excluded if they had a past history of a thrombocytosis; a history of venous thromboembolism; cancer; pregnancy; recent surgery; hyperthyroidism.

Results : The levels of TNF-alpha, IL-6, PAI-1, VWF in patients with DM were higher than in the control group: TNF-alpha (12.42 [7.8;20.0] vs. 9.8 [3.89;11.20] pg/mL), IL-6 (3.14 [1.7;9.1] vs. 1.5 [1.5;1.7] mg/mL), PAI-1 (29.12±6.18 vs. 12.81±1.71 IU/ml), VWF (121.37±27.12 vs. 99.07±16.12 %), $p<0.05$. The levels of TNF-α, Il-6, PAI-1, VWF were significantly higher in diabetic patients with CKD 5 in comparison with stages 1-4. A significant correlation was found between serum creatinine and IL-6 ($r=0.70$, $p<0.001$), VWF ($r=0.46$, $p<0.001$), PAI-1 ($r=0.49$, $p<0.001$) as well as between IL-6 and VWF ($r=0.52$, $p=0.003$). Multivariable linear regression analysis revealed significant associations between decreased eGFR and higher VWF and IL-6 in DT2 patients and CKD.

Conclusion : Endothelial dysfunction, hypercoagulability, inflammation are intrinsically interconnected, playing a very important role in the development of vascular complications. Several biomarkers associated to these processes and their complex networks are altered in diabetic patients who have microvascular complications, such as nephropathy.

Keywords : Hypercoagulability, von Willebrand factor , CKD, Diabetes

PP12-17

Diagnostic challenges and its clinical implications in women with inherited bleeding disorders

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Background : Inherited bleeding disorders in women can lead to severe bleeding episodes and life-threatening complications. It is estimated that approximately fifteen percent of patients with bleeding disorders are misdiagnosed. This study was carried out to assess the frequency and characteristics of women with inherited bleeding disorders who were initially misdiagnosed and received inappropriate management.

Method : This study was conducted at the Haematology Department of Fauji Foundation Hospital, Rawalpindi, Pakistan, from August 2017 -August 2022. We retrospectively reviewed the records of all the women, aged 16 to 60 years, who presented at the inpatient or outpatient of our hospital for evaluation of bleeding diathesis but were initially misdiagnosed and received inappropriate management.

Results : A total of 93 women were diagnosed with a bleeding disorder, 44% (n=41) were diagnosed with an inherited bleeding disorder, 56% (n=52) with an acquired bleeding disorder, 19% (n = 8) women with inherited bleeding disorders were initially misdiagnosed. Five women with Bernard-Soulier Syndrome had been initially misdiagnosed as 'immune thrombocytopenic purpura' out of which 3 underwent unnecessary splenectomy while 2 women received immunosuppressants and immunoglobulins. One woman with factor V deficiency was misdiagnosed as having a left iliac fossa abscess and underwent surgical excision which led to life-threatening bleed during surgery. One woman with von Willebrand disease had been misdiagnosed as having hemophilia A and received inappropriate factor concentrates. One patient with Glanzmann thromboasthenia was misdiagnosed as von Willebrand disease which led to excessive bleeding and inappropriate use of factor concentrate.

Conclusion : Misdiagnosis of inherited bleeding disorders in women can lead to life-threatening consequences. There are chances of misdiagnosis and improper management in women if thorough clinical evaluation and comprehensive laboratory evaluation are not carried out.

Keywords : Bleeding disorder, Bernard soulier syndrome, ITP, Von-Willebrand, Glanzmann thromboasthenia

PP13-1

The relationship between allogeneic hematopoietic stem cell transplantation recipients and COVID-19 vaccination: A literature review

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Background : COVID-19 caused by SARS-CoV-2 infection has become a global pandemic with significant impacts on various aspects of health. Several reports reveal that some hosts with weakened immune systems, such as hematopoietic stem cell transplantation (HSCT) recipients, have difficulty obtaining immunogenicity. COVID-19 vaccination has proven effective in overcoming this pandemic problem. This literature will discuss the impact of COVID-19 vaccination on allogeneic HSCT recipients.

Method : Literatures were identified through database searches on PubMed, Haematologica, and Elsevier by taking data for the last two years. Several studies were identified and the terms used are allogeneic hematopoietic stem cell transplantation and COVID-19 Vaccination.

Results : Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a risk factor for severe COVID-19. There are three vaccination doses that can increase immunogenicity in both normal people and HSCT recipients. The efficiency of two doses of an mRNA-based COVID-19 vaccine was reported to be lower in allotransplant patients than in healthy controls. There is also the possibility of seroconversion failure during the third dose of vaccination, but there is still a high possibility of increased immunity. A study states that this could be caused by patients who receive HSCT lacking T cells or even not producing SARS-CoV-specific T cells. However, antibody and T cell responses continued to increase after vaccination.The safety and efficacy of COVID-19 vaccination has been proven and there has been no confirmation of complications due to COVID-19 vaccination in allogeneic HSCT recipients, but this is still being researched to date.

Conclusion : Recipients of allogeneic hematopoietic stem cell transplantation (allo-HSCT) experience immunosuppression so they are susceptible to COVID-19 infection, but this can be overcome with three-stage COVID-19 vaccination. COVID-19 vaccination has been proven to increase immunity making it safe and effective without any confirmed complications in allogeneic HSCT recipients.

Keywords : HSCT, Allogeneic, COVID-19, Stem cell, Vaccination

PP13-2

Risk factors for positive posttransplantation measurable residual disease in patients with acute lymphoblastic leukemia

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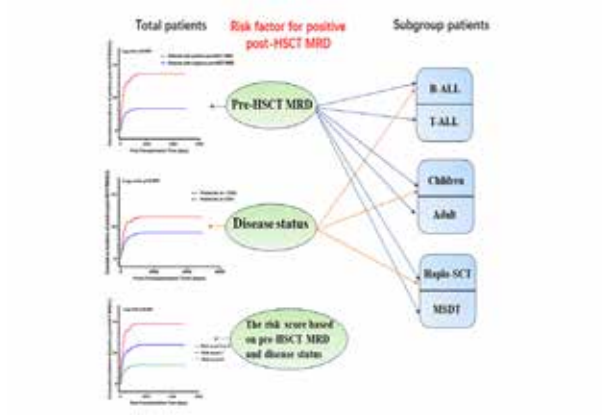
Background : The level of MRD before and after transplantation is related to inferior transplant outcomes, and post-hematopoietic stem cell transplantation measurable residual disease (post-HSCT MRD) has higher prognostic value in determining risk than pre-HSCT MRD. However, no work has been devoted to the risk factors for positive post-HSCT MRD in patients with ALL. This study evaluated the risk factors for post-HSCT MRD positivity in patients with acute lymphoblastic leukemia (ALL) who underwent allogeneic HSCT (allo-HSCT).

Method : A total of 1683 ALL patients were enrolled. Cox proportional hazard regression models were built for time-to-event outcomes. Multivariate analysis was performed to determine independent influencing factors from the univariate analysis.

Results : Both in total patients and in T-ALL or B-ALL, pediatric or adult, HLA-matched sibling donor transplantation or haploidentical HSCT subgroups, positive pre-HSCT MRD was a risk factor for post-HSCT MRD positivity ($p < 0.001$ for all). Disease status [complete remission 1 (CR1) vs. ≥CR2] was also a risk factor for post-HSCT MRD positivity in all patients and in the B-ALL, pediatric, or haploidentical SCT subgroups ($p = 0.003$; $p = 0.035$; $p = 0.003$, respectively). A risk score for post-HSCT MRD positivity was developed using the variables pre-HSCT MRD and disease status. The cumulative incidence of post-HSCT MRD positivity was 12.3%, 25.1%, and 38.8% for subjects with scores of 0, 1, and 2-3, respectively ($p<0.001$). Multivariate analysis confirmed the association of the risk score with the cumulative incidence of post-HSCT MRD positivity and relapse as well as LFS and OS.

Conclusion : Our results indicated that positive pre-MRD and disease status were two independent risk factors for post-HSCT MRD positivity in patients with ALL who underwent allogeneic HSCT. These risk factors and the risk score for post-HSCT MRD positivity could be used to identify a specific population who could be considered for prophylaxis or early preemptive therapy.

Keywords : Measurable residual disease, Posttransplantation, Acute lymphoblastic leukemia, Risk factors



PP13-3

Effects of donor-specific anti-HLA antibodies(DSA) for primary graft failure of haploidentical hematopoietic stem cell transplantation in thalassemia major

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Background : Donor-specific anti-HLA antibodies (DSA) have been recently recognized as an important barrier against successful engraftment of donor cells, which can affect transplant survival.

Method : HLA antibodies were examined using the Luminex-based single Ag assay for 270 patients with thalassemia major who underwent HSCT from January 2018 to September 2023 in our center, and the correlations of GR and DSA were also analyzed. Of the total 270 patients, seventy-six (28.14%) patients were tested for antibodies corresponding to donor HLA Ags (DSA positive). All the 76 patients were going plasmapheresis, platelet transfusion, buffy coat depletion and antibody neutralization, and were administered with rituximab, bortezomib, fodarabine and dexamethasone, grouped by different levels of the median fluorescence intensity (MFI) : A. 7 patients in High DSA group (MFI > 10000); B. 19 patients in Median DSA group (MFI 5000-10000); C. 50 patients in low DSA group. The correlation between MFI,

nucleated cells and CD34 count with engraftment was analyzed.

Results : The 194 patients with a test of negative DSA had no primary GR. Among 76 DSA positive patients, 3 patients (Group A) had primary GR. GR occurred in 3 of 26 patients with high and median DSA (MFI>5000), and there was no GR in 50 patients with low DSA (MFI 500-4999). The difference between the two groups was statistically significant [P =0.037]. The average number of nucleated cells (10^8/kg) in group A and B was 19 and 18, and the average CD34 count (10^6/kg) was 14.04 and 21.69.

Conclusion : Post-transplant testing and treatment for patients with DSA are crucial for successful engraftment. GR occurs more likely in the condition of median or higher DSA(MFI > 5000), under which the CD34 counts (10^6/kg) of the transfusion dosage of donor cells reach above 20 is recommended.

Keywords : Donor-specific anti-HLA antibodies(DSA), HSCT, Thalassemia major, Graft failure

Table 1

Group	No GR	GR	P
MFI >5000	23	3	0.037
MFI 500-4999	50	0	

PP13-4

Post-transplant complications revealed by mycophenolate mofetil related transporters and metabolic enzymes gene polymorphisms in pediatric patients with hematological disorders

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Background : Haploidentical hematopoietic stem cell transplantation (Haplo-HSCT) serves as an important option for patients without an HLA matched donor in treating hematological disorders, while patients may experience various complications after transplantation. Mycophenolate mofetil (MMF), a cornerstone drug for graft-versus-host disease (GvHD) prophylaxis, effectively reduces the incidence of acute GvHD, and the efficacy of MMF varies among individuals associated with MMF-related transporters and metabolic enzymes single gene polymorphisms (SNPs). However, limited studies have systematically reported the correlations between the MMF-related SNPs and post-transplant complications.

Method : Here, we conducted a retrospective study involving 90 pediatric patients with hematological disorders who underwent haplo-HSCT at a single center. All patients were subjected to MMF-related SNP testing, combined with common clinical characteristics, to be correlated with post-transplant complications.

Results : We observed that all 15 MMF-related SNPs were in Hardy-Weinberg equilibrium. Based on multivariate Cox regression analysis of post-transplant complications, we discovered that SLCO1B1 (521T>C) variant genotype was an independent protective factor for chronic GvHD (HR = 0.25, 95% CI, confidence interval (CI) (0.08-0.84). For viral infection, CYP2C8 (1291+106T>C) variant genotype was an independent risk factor for cytomegalovirus infection (HR = 2.98, 95% CI (1.18-7.53)). As to hemorrhagic cystitis, SLCO1B1 (1865+4846T>C) variant genotype was an independent protective factor, while older age was considered as an independent risk factor (HR = 0.41, 95% CI (0.19-0.85); HR = 2.52, 95% CI (1.14-5.54), respectively). No statistical significance was discovered between common clinical characteristics and MMF-related SNPs with other complications, including grade II-IV/III-IV acute GvHD, Epstein-Barr virus infection, peri-engraftment syndrome, and capillary leak syndrome.

Conclusion : Our findings highlight the significance of MMF-related transporters and metabolic enzymes SNPs in the development of post-transplant complications, contributing to facilitating personalized risk assessment and improving the clinical management in haplo-HSCT patients.

Keywords : Post-transplant complications revealed by mycophenolate mofetil related transporters and metabolic enzymes gene polymorphisms in pediatric patients with hematological disorders, Haploidentical hematopoietic stem cell transplantation, Haploidentical hematopoietic stem cell transplantation, Single gene polymorphism, Single gene polymorphism

Figure 1. MMF-related transporters and metabolic enzymes SNPs detected in 90 pediatric patients

Figure 2. Impact of MMF-related transporters and metabolic enzymes SNPs on post-transplant complications

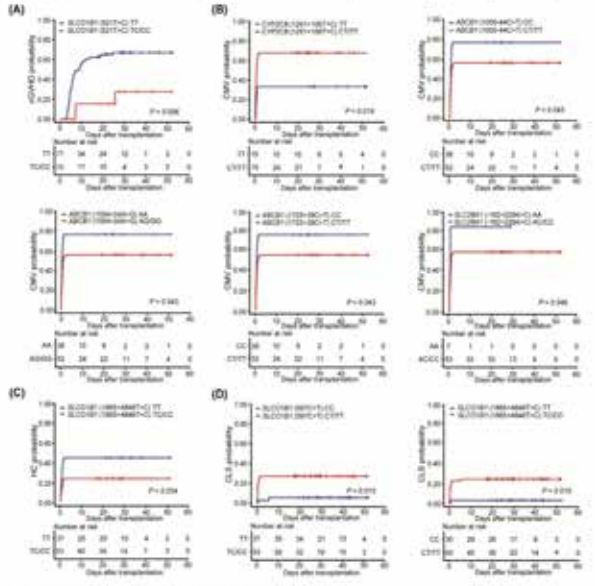
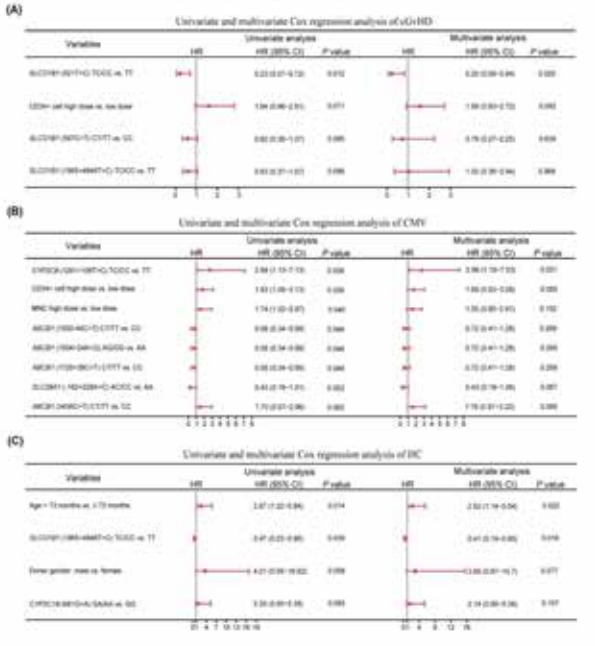


Figure 3. Forest plot analysis of post-transplant complications



PP13-5

Mesenchymal stem cells assisted successful treatment of pediatric patient with toxoplasma encephalitis after hematopoietic stem cell transplantation: A case report and literature review

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Background : Toxoplasma encephalitis (TE) is a rare but often life-threatening infection that can occur after hematopoietic stem cell transplantation (HSCT). Due to limited access to first-line drugs for acute TE, trimethoprim-sulfamethoxazole (TMP-SMX) is used as an alternative. However, the treatment effect of cerebral toxoplasmosis was highly unsatisfactory. Therefore, Novel treatment methods are urgently needed to optimize patient management.

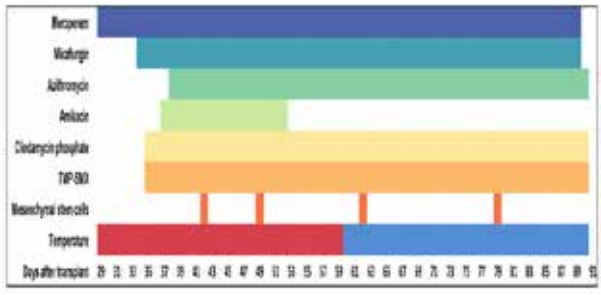
Method : Here, we report the first case of treatment of toxoplasma encephalitis in a pediatric patient following allogeneic hematopoietic stem cell transplantation, employing mesenchymal stem cells (MSCs) as an adjunct to anti-toxoplasmosis therapy.

Results : The patient experienced fever on the 28th day post-transplantation, and subsequently exhibited poor mental status, decreased muscle strength, diminished responses, and slowed breathing. TE was diagnosed based on the patient's clinical symptoms, cranial MRI, and Next-Generation Sequencing (NGS) results of blood and cerebrospinal fluid samples. Despite receiving a combination of TMP-SMX, clindamycin phosphate, and later adding azithromycin for anti-infection treatment, the patient continued to experience recurrent fever. On the 42th day post-transplantation, the patient received the first intravenous and intrathecal infusion of MSCs. Remarkably, following this treatment, the patient's fever gradually decreased. Subsequently, additional intravenous and intrathecal infusions of MSCs were administered on the 49th, 56th, 62th, 79th, and 103th days post-transplantation. During the treatment period, the NGS read count decreased in both blood and cerebrospinal fluid samples. Also the cranial MRI results showed progressive improvement. On the 91th day post-transplantation, the patient was discharged from the hospital with a stable mental status, clear consciousness, and normal body temperature The patient is currently receiving maintenance treatment with oral azithromycin, sulfamethoxazole-trimethoprim, and clindamycin prescribed by our institution.

Conclusion : Intravenous and intrathecal administration of mesenchymal stem cells (MSCs) in combination may potentially serve as an effective therapeutic approach for the treatment of post-trans-

plant toxoplasma encephalitis.

Keywords : Mesenchymal stem cells, Toxoplasma encephalitis, Hematopoietic stem cell transplantation, Pediatric



PP13-6

Avapritinib is effective and safe for preemptive treatment in pediatric acute myeloid leukemia with t(8;21) and KIT mutation after allogeneic hematopoietic stem cell transplantation

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Background : Acute myeloid leukemia (AML) with t(8;21) (q22;q22), which forms RUNX1::RUNX1T1 fusion gene, is classified as a favorable-risk group. However, the presence of mutations in KIT exon 17 results in an adverse prognosis in this group. Avapritinib, a novel tyrosine kinase inhibitor targeting KIT mutation, has been approved for treating gastrointestinal stromal tumors and systemic mastocytosis. It effectively treats minimal residual disease (MRD) in AML cases harboring RUNX1::RUNX1T1 and KIT mutations after allogeneic hematopoietic stem cell transplantation (allo-HSCT). However, clinical application in pediatric AML is lacking.

Method : We report a retrospective study of four pediatric patients with AML with t(8:21) and KIT exon 17 mutation who were treated with avapritinib. They were treated using the CALSIII-AML18 protocol, registered as ChiCTRI800015883. Four patients were treated with avapritinib for RUNX1::RUNX1T1-positive AML after allo-HSCT, three of them failed to demethylate drugs and donor lymphocyte infusion targeting RUNX1::RUNX1T1-positivity allo-HSCT. The starting dose of avapritinib was 50 mg/day and the administration would be adjusted if the patients experienced ≥ grade 3 adverse events. We followed up and observed adverse events during avapritinib treatment.

Results : Three patients with RUNX1::RUNX1T1 positivity had turned negative after 1, 2, and 7 months of avapritinib treatment and remained so during follow-up, while one patient retained the lowest relative value for months. During treatment with avapritinib, the most common adverse event was neutropenia, of which three of the four patients had grade 3–4. One patient developed grade 2 thrombocytopenia. Besides, two patients had grade 1 puffiness. All adverse events were tolerated and improved after clinical observation and medication adjustments.

Conclusion : This case series indicates that avapritinib may be effective and safe for preemptive treatment of children with AML with t(8;21) and KIT mutation after allo-HSCT, providing a treatment option for preventing relapse after allo-HSCT.

Keywords : Acute myeloid leukemia, Allogeneic hematopoietic stem cell transplantation, Avapritinib, KIT mutation, Preemptive treatment

PP13-7

Post-transplant serum ferritin level predicts severe acute graft-versus-host disease in umbilical cord blood transplantation for acute leukemia

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Background : Allogeneic hematopoietic stem cell transplantation (allo-HSCT) using umbilical cord blood is a valuable therapy option for patients with acute leukemia (AL). Acute graft-versus-host disease (aGVHD) remains the most frequently encountered complication. Little is known about risk factors for aGVHD after umbilical cord blood transplantation (UCBT) in children, and it is unclear whether they are similar to those in adults.To investigate risk factors for aGVHD and to assess whether serum ferritin (SF) is a potential biomarker for aGVHD in pediatric patients with AL undergoing UCBT.

Method : We conducted a retrospective cohort study of 71 patients

with AL who underwent UCBT at the Children's Hospital of Soochow University between 2017 and 2022. We evaluated several factors related to aGVHD, including age, sex, disease, HLA matching, ABO matching, disease status at transplant, conditioning intensity, anti-thymocyte globulin, conditioning drug dose, neutrophil engraftment time, platelet engraftment time, mononuclear cells, $CD34^+$, and SF levels within 2 weeks pre- and 2 weeks post-transplant. Univariate and multivariate analyses were performed using the proportional subdistribution hazard regression model of Fine and Gray. Analyses of overall survival (OS) were performed using the Kaplan–Meier method, and differences were compared using log-rank tests.

Results : Of the 71 patients, 23 (32.4%) experienced grade II–IV aGVHD, of whom 18 (25.4%) developed grade III–IV aGVHD. Patients with grade II–IV and III–IV aGVHD have worse 5-year OS (69.4% ± 10%, p=0.01; and 60.6% ± 11.6, p=0.007, respectively). Conditioning intensity was a risk factor for grade II–IV aGVHD (hazard ratio [HR]: 0.36, 95% confidence interval [CI]: 0.15–0.87, p=0.024) and grade III–IV aGVHD (HR: 0.34, 95% CI: 0.13–0.89, p=0.027). An SF level >1650 ng/mL within 2 weeks post-transplant was independently associated with an increased risk of severe aGVHD (HR: 3.61, 95% CI: 1.09–11.97, p=0.036).

Conclusion : Post-transplant SF was an independent risk factor for developing severe aGVHD.

Keywords : Acute graft-versus-host disease, Acute leukemia, Umbilical cord blood transplantation, Ferritin, Children

PP13-8

A prospective pilot study of graft-versus-host disease prophylaxis with postbiotics in allogeneic hematopoietic stem cell transplantation

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Background : Conditioning chemotherapy, antibiotics, and diet changes reduce intestinal microbiome diversity during allogeneic hematopoietic stem cell transplantation (allo-HSCT). Numerous studies show that acute graft-versus-host disease (aGVHD) incidence and mortality increase as microbiome diversity decreases during the engraftment period. We suggested that rapid microbiome diversity restoration may prevent aGVHD. Postbiotics are metabolites generated by probiotic microorganisms that exhibit biological activity within the host.

Method : A prospective study was conducted to evaluate the clinical effects and microbial changes in postbiotics intake in allo-HSCT recipients at Soonchunhyang university seoul hospital. The patients ingested butyrate (sodium butyrate 600mg x 2capsules/day, BODYBIO®) from the engraftment period (D+14~D+21) until day 90~100 after the transplantation. Fecal samples were obtained from both the historical control group and the postbiotics group at three time points: before transplantation, at engraftment, and 100 days after transplantation. (NCT#05808985)

Results : Fifty-one samples of stool(postbiotics, n=25;control, n=26) were obtained from sixteen patients(postbiotics, n=8;control group, n=8). The cumulative incidence of all grades of aGVHD was similar in the postbiotics group(n=5) compared to the historical control group(n=5). The incidence of grade(Gr) 3 to 4 aGVHD was lower in the postbiotics group(n=1) compared to the historical control group(n=3). In particular, the historical control group exhibits three cases of lower gastrointestinal GVHD(Gr2, n=2;Gr4, n=1), whereas the postbiotics group reported lesser severe two cases(Gr1, n=1;Gr2, n=2). Patients self-reported that the median intake of postbiotics was 84%. The only discernible occurrence during administration was the unpleasant smells emitted by butyrate. Furthermore, there were no anticipated adverse effects associated with butyrate administration. Analysis of the microbiome is in progress; details may be revealed at the ICKSH 2024 meeting.

Conclusion : In conclusion, the administration of postbiotics lacking of specific adverse effects is anticipated to prevent aGVHD. Long-term follow-up of a larger cohort of patients is needed to define the role of butyrate in allo-HSCT.

Keywords : Graft-versus-host disease, Prophylaxis, Postbiotics, Allogeneic hematopoietic stem cell transplantation

PP13-9

Efficiency of peripheral blood stem cell collection by Optia Spectra machine at hematologic department in Cho Ray hospital

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Background : Optia Spectra machine serves to collect peripheral blood stem cells very effectively and is widely used around the world. At Cho Ray Hospital's Hematology Department, we also apply stem cell collection in peripheral blood using the Optia Spectra machine in donor or patients with multiple myeloma and non-Hodgkin's lymphoma who are indicated for stem cell transplantation which has shown to be high effective in stem cell collection. That's why we conducted this study to evaluate the efficacy of peripheral blood stem cell collection with Optia Spectra.

Method : The multiple myeloma or lymphoma patient who are indicated for stem cell transplantation or donor achieved CD34+ > 20 cells/µl after mobilization using the cross - Descriptive method from 5/2017 to 4/2023

Results : There were 148 cases of peripheral blood stem cell collection with Optia Spectra. The mean age of the study group was 48.16 ± 14.34. Male / female ratio 1.05/1. Diagnosis includes: Multiple myeloma was 41.22%, Non-Hodgkin lymphoma was 40.54%, Primary intracerebral lymphoma was 4.73%, Hodgkin lymphoma was 8.78% and stem cell donor was 4.73%. Chemotherapy regimen before apheresis: 1 line was 64.19%, 2 line was 31.08%. Mobilization regimen included: Endoxan – G-CSF 75.68%, G-CSF 14.86%, Chemotherapy-G-CSF 3.38%, Endoxan – G-CSF – Plexirafor 2.70% and G-CSF – Plexirafor 3.35%. The mean stem cell volume was 142.88 ± 26.29 ml, and the CD34 cell count was 1753.46 ± 1637.46 cells/µl with a survival rate of 98.18 ± 2.17%. The efficacy of CD34+ cells collection achievement ratio was 81.08%. Side effects of collection procedure was chill 3.38%, numbness of the hands - limbs 2.03%. Other side effects were not recorded.

Conclusion : Peripheral blood stem cell collection with Optia Spectra was performed at Hematologic Department in Cho Ray Hospital. The efficacy of peripheral blood stem cell collection with Optia Spectra was 81.08% with almost no side effects.

Keywords : Hematopoietic stem cell, Stem cell collection, Peripheral blood stem cell, Multiple myeloma, Non-Hodgkin lymphoma

PP13-10

Level of knowledge of Filipino nurses on care of patients undergoing hematopoietic stem cell transplant

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Background : Hematopoietic stem cell transplantation (HSCT) is a potentially curative treatment for some patients with blood disorders such as severe aplastic anemia, leukemia, and thalassemia.

Method : This study described the nurse's level of knowledge on HSCT and their accessibility to trainings regarding HSCT. A self-administered questionnaire was given to 320 nurses and 297 nurses agreed to participate in the study. Inclusion criteria included those who are registered nurses, had at least 1 year of clinical experience, and is currently working in the Philippines at the time of the study. Data collection was done in April to May 2023 in both government and private hospitals and academe.

Results : Results showed that 27.3% of the participants had low level of knowledge about HSCT, while 67% had average, and 6% had high level of knowledge. Most participants had advanced nursing degrees, with 39.4% having a master's degree and 36.4% having a doctoral degree. 6 out of 10 participants were currently employed in the academe, while 21% were from government hospitals and 18% were from private hospitals. It was found out that years of experience, place of employment and highest level of education were positively correlated with level of knowledge (chi2 = 22.67, p value<0.0001). It was also found out that 93.94% of the participants did not have any training about stem cell transplantation; while 73% agreed to their need of the training. The top reasons for not getting any training on HSCT were "no training provided" (66.57%), "no time" (36.36%) and "no money" (21.21%). Most participants (81.8%) believed that they do not have enough knowledge and skill to care for HSCT patients.

Conclusion : Based on the results of the study, there is an urgent need for HSCT training among Filipino nurses to equip them in caring for patients undergoing stem cell transplant.

Keywords : Stem cell transplant, Filipino nurses

PP13-11

The impact of cytomegalovirus reactivation on relapse in acute leukemia patients undergoing allogeneic stem cell transplantation

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Background : Cytomegalovirus (CMV) reactivation after allogeneic hematopoietic stem cell transplantation (HCT) is a major infectious complication; however, its impact on the risk of relapse remains still controversial. This study aims to assess the influence of CMV reactivation on relapse and mortality following HCT in patients with acute leukemia.

Method : We retrospectively analyzed 1009 patients with acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) who underwent HCT between 2000 and 2017 at Asan Medical Center. We collected clinical data from the HCT registry of Asan Medical Center. CMV reactivation was defined as ≥1 pp65-positive cell per 2×10^5 polymorphonuclear neutrophils.

Results : We included 703 patients with AML and 306 patients with ALL. The 2-year cumulative incidence of relapse (CIR) rate and non-relapse mortality (NRM) rate for all patients were 38.4% and 12.8%, respectively. The 5-year overall survival (OS) rate was 45.6%. Of all patients, 559 experienced CMV reactivation within one year post-HCT. The median CMV reactivation period after HCT was 28 days (range, 0–358 days). In AML, CMV reactivation reduced the CIR at 2-year (32.8% vs. 38.8%, respectively, P=0.054) compared to those without CMV reactivation. In multivariate analysis, standard-risk disease (hazard ratio [HR]=0.385, P<0.001), occurrence of chronic graft-versus-host disease (HR 0.625, P=0.001), and CMV reactivation (HR 0.676, P=0.007) were significantly associated with lower CIR. However, CMV reactivation significantly increased NRM rate (15.6% vs. 9.4%, respectively, P=0.022; HR=1.690, P=0.011). In ALL, CMV reactivation was not associated with a lower CIR (HR=0.728, P=0.085) or increased NRM (2-year NRM: 14.6% vs. 7.6%, P=0.198). Furthermore, CMV reactivation did not correlate with inferior OS in either AML or ALL.

Conclusion : Our findings suggest that CMV reactivation may offer a benefit in preventing relapse in AML patients.

Keywords : Cytomegalovirus, Acute leukemia, Relapse, Non-relapse mortality, Allogeneic hematopoietic stem cell transplantation

PP13-12

The efficacy of haploid hematopoietic stem cell transplantation in the treatment of children with Diamond-Blackfan anemia

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Background : Diamond-Blackfan anaemia (DBA) is a rare inherited marrow failure disorder, characterized by hypoplastic anaemia, congenital anomalies and a predisposition to cancer as a result of ribosomal dysfunction. Currently, stem cell transplantation is the only curative option for the haematological DBA phenotype.Sibling matched donor is recommended for higher success of HSCT. However, most children lack sibling matched donor because of the policy of one child in one family in China before. In this study we reported the efficacy of haploid hematopoietic stem cell transplantation (haplo-HSCT) for children with diamond blackfan anemia(DBA).

Method : Five cases of children with DBA were received haplo-HSCT in the Children's Hospital of Soochow University between June 2018 and June 2023. The median age was 6.1 years; HLA matching at 5 ~ 8/10 locus. The grafts were bone marrow combined with peripheral blood The conditioning regimens included fludarabine, busulfan, as well as antithymocyte globulin (Flu +Bu+ATG). Ciclosporin/ tacrolimus, togethor with mycophenolate morphenate and methotrexate, were used to prevent graft versus host disease (GVHD) .

Results : All the patients were successfully transplanted and achieved hematopoietic and immune reconstitution. The median follow-up time was 44.8 (4.8-59.2) months. The median time of neutrophil and platelet engraftment were 11 days and 9 days after transplantation respectively. The time of erythropoiesis reconstitution was 25 days after transplantation. One patient developed grade IV acute GvHD (aGVHD), 2 patients developed grade I aGVHD, and 1 patient developed chronic GvHD (cGVHD) who were controlled later. Cytomegalovirus infection occurred in 3 patients and Epstein-Barr virus infection occurred in 1 patient after transplantation, and cured by ganciclovir treatment. No other complications occurred during and after transplantation. All patients survived without disease and achieved erythroid reconstitution, and the overall survival rate was 100%.

Conclusion : Haplo-HSCT is an effective treament for pediatric patients with DBA and the conditioning regimen of Flu +Bu+ATG was recommended.

Keywords : Diamond-Blackfan anemia, Haploid hematopoietic stem cell transplantation, Children

PP13-13

Aerosolized pentamidine for pneumocystis jirovecii pneumonia prophylaxis in adult patients undergoing allogeneic hematopoietic cell transplantation

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Background : Pneumocystis jiroveci pneumonia (PJP) is a serious opportunistic infection after allogeneic hematopoietic cell transplantation (HCT). The preferred regimen for PJP prophylaxis is trimethoprim-sulfamethoxazole (TMP-SMX), but TMP-SMX can delay engraftment and has some toxicities such as myelosuppression. Aerosolized pentamidine is one of the prophylactic agents of PJP and we analyzed the efficacy and tolerability of aerosolized pentamidine after allogeneic HCT.

Method : 116 patients who received aerosolized pentamidine prophylaxis after allogeneic HCT between 2018 July and 2022 February were analyzed. Pentamidine isethionate 300mg was nebulized every 4 weeks from the neutrophil recovery until the time of immunosuppressant discontinuation or occurrence of unacceptable toxicity. Pulmonary function tests (PFT) were performed before and after HCT, and forced expiratory volume (FEV1), forced vital capacity (FVC), diffusing capacity of the lung for carbon monoxide (DLCO) were analyzed.

Results : Among the 116 patients, 8 patients (6.9%) had underlying pulmonary disease before transplantation; chronic obstructive pulmonary disease (5 patients), Asthma (1 patient), interstitial lung disease (1 patient), pneumoconiosis (1 patient). After median follow-up of 45.9 months, the median duration of aerosolized pentamidine administration was 4.1 months (range 1.0-32.9 months), and PJP occurred in 2 patients (1.7%). Pneumonia other than PJP occurred in 24 patients (20.7%), and chronic pulmonary graft-versus-host-disease incidence was 13.8%. Aerosolized pentamidine was well tolerated and the incidence of adverse events was 7%. All of the adverse events were grade 1-2; loss of appetite (3 patients), nausea and vomit (1 patient), skin rash (1 patient), blood tinged sputum (1 patient), headache (1 patient) and dyspepsia (1 patient). PFT analysis before and after HCT are described in Table 1.

Conclusion : Aerosolized pentamidine is well tolerated without severe adverse events and effective in preventing PJP after allogeneic HCT. There was no deterioration of lung function after use of aerosolized pentamidine.

Keywords : Pentamidine, Prophylaxis, Allogeneic hematopoietic cell transplantation

Table 1. Pulmonary function test (PFT) results of the 23 patients who performed post-transplant PFT during aerosolized pentamidine prophylaxis.

PFT parameter	Pre-transplant	Post-transplant	*p*-value
FEV1/FVC, median (range)	0.81 (0.63-0.92)	0.81 (0.53-0.93)	0.941
FEV1/FVC <0.70, n (%)	2 (8.7%)	2 (8.7%)	1.000
FEV1, median (range)	88.3 (64.7-106.7)	84.6 (34.4-109.2)	0.300
FEV1 <80%, n (%)	6 (26.1%)	7 (30.4%)	1.000
DLCO, median (range)	67.2 (27.5-92.4)	78.8 (60.4-104.5)	0.002
DLCO <75%, n (%)	16 (69.6%)	10 (45.5%)	0.227-

PP14-1

Inflammation stimulates the stem system in a model of hematopoietic ectopic foci

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Background : Mesenchymal cells are components of various mammalian tissues and organs. The stem system and mesenchymal stem cells (MSCs) in particular are responsible for maintaining the pool of various tissue cells, and are activated when repair is requested. One of the models for studying the stem system and mesenchymal cells in vivo is the model of hematopoietic ectopic foci (HEF) formed under the capsule of the mouse kidney during transplantation of a bone marrow fragment. It was noted earlier that the size of HEF is increased in irradiated recipients, which is similar to the effect of IL1b administration. We decided to test the hypothesis that systemic inflammation can stimulate the growth of hematopoietic territory in vivo in HEF.

Method : We transplanted donor BM under the recipient kidney capsule as previously described (10.3389/fcell.2022.993056). Nes-GFP transgenic and non-transgenic parental line C57Bl/6 mice

were used as donors. C57Bl/6 mice were taken as recipients. A part of the recipients were pre-immunized in two steps with Freund's complete adjuvant and either GFP or BSA. Forty-two days after implantation, the cellularity of HEF was counted in a hemocytometer.

Results : We analyzed data on HEF s in a series of experiments with immunization (n=13) and without immunization (n=14). Immunization against GFP did not reduce the cellularity of transgenic HEFs. The data were pooled regardless of the BM donor mouse strain. In HEFs from immunized recipients we observed a 2.3-fold increase in mean size (p=0.006).

Conclusion : We hypothesize that the previously observed increases in foci size under irradiation and found after immunization may have a common mechanism associated with systemic inflammation. Such stimulation of hematopoietic territory growth has not previously been demonstrated. The results obtained demonstrate stimulation of the stem system function under the action of inflammatory process on the example of HEF.

Keywords : Stem system, Inflammation, Regeneration, Hematopoietic ectopic foci, HEF

PP14-2

Administration of human tumor necrosis factor alpha to mice restores formation of ectopic foci of hematopoiesis lost by serial blood loss and results in the formation of foci of

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Background : TNFα can increase expression of interleukin-1β (IL-1β) in human stromal cells of different origin. Recent studies demonstrate that IL-1β is a growth factor for bone marrow (BM) mesenchymal progenitor cells in a model of ectopic foci of hematopoiesis (EFH) in mice. We hypothesized that TNFα may also affect the size of ectopic foci of hematopoiesis. The aim of this study was to investigate the role of TNFα in the formation of EFH in mice.

Method : Female CBF1 (F1 hybrid mice (CBAxC57Bl/6)) mice were used. Phosphate buffered saline ("PBS" group, n=4), bovine serum albumin ("BSA" group, n=4) or human recombinant TNFα ("TNF" group, n=4) was injected intraperitoneally once, 48 hours before implanting BM under the renal capsule. BSA and TNFα dose was 5 μg/mouse. BM of one femur was obtained from syngeneic donor and implanted under each kidney of a recipient. Blood was sampled from the tail of each recipient mouse one day before, 2 hours, and 48 hours after factor administration. The volume of blood sampled varied between 50-300 μL.

Results : The incidence of foci formation was abnormally low in PBS and BSA groups (25% and 16.7%, respectively) and was significantly lower than the incidence in TNF (62.5%) group (Figure). Administration of hTNFα to mice resulted in a tendency to the formation of EFH with increased cellularity compared to the control group (p=0.076) of recipient mice that were administered PBS (Figure).

Conclusion : We conclude that TNFα is another inflammatory factor activating signaling affecting the function of BM stromal progenitor cells, including MSCs. Its preliminary administration to mice restores the ability to form such foci in the organism of recipient mice, which is lost or strongly reduced without TNFα administration due to serial sampling of peripheral blood. The research was supported by Russian Science Foundation (project No. 22-25-00459, https://rscf.ru/project/22-25-00459/).

Keywords : Tumor necrosis factor alfa, TNF, MSC, Ectopic focus of hematopoiesis, Blood loss

A

Group	Foci implanted/obtained	Focus cellularity, 10^6 cells
Control (PBS)	2/8	1,3
		1,7
BSA	1/6	N/A
TNF	5/8	3,5
		2,2
		2,1
		3,7
		6,5

B

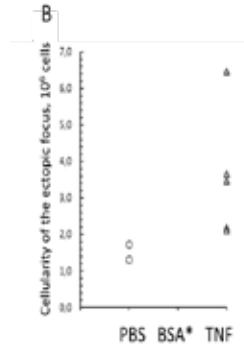

Figure. A. Results of the analysis of foci of ectopic hematopoiesis. B. The sizes of individual foci of hematopoiesis in the experimental groups. * In the group receiving BSA, only one foci was formed out of six successfully implanted bone marrow fragments, the size of which was so small that it was impossible to estimate it reliably.

PP14-3

Nes-GFP+ MSCs preserve functionality after bone marrow transplantation in a wild-type mice immunized vs-GFP.

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Background : Immune privilege (IP) is the ability of cells and tissues in the body to evade immune surveillance. In contrast with IP of non-pathological stem cells, IPs in cancer and cancer stem cells represent a major challenge for therapy. This study investigate the strength of immune privileges of mesenchymal stem cells (MSCs) and other Nestin-GFP$^+$ progenitors in bone marrow (BM).

Method : We used our previously developed model based on foci of ectopic hematopoiesis (10.3389/fcell.2022.993056). We transplanted BM fragments (n=16) from a Nes-GFP transgenic mice under the kidney capsule of a GFP-immunized non-transgenic recipients (n=8) with a fully immune system. After 6 weeks, the foci formed and were examined for the presence of GFP$^+$ cells by flow cytometry. Five primary foci were retransplanted to non-immunized non-transgenic recipients (n=3). MSCs and some progenitors in Nes-GFP are marked by GFP in opposite to their progeny.

Results : The efficiency of immunization of GFP recipient mice was confirmed by ELISA. The formation of primary and secondary foci of ectopic hematopoiesis was shown. The presence of GFP$^+$ cells in the obtained foci was confirmed. The proportion of GFP$^+$CD45$^-$ cells in primary and secondary foci was 0.8×÷1.8×10e(-5) and 0.8×÷1.9×10e(-5), respectively. The proportion of GFP$^+$CD45$^+$ cells in primary and secondary foci was 24.1×÷3.8×10e(-5) and 4.6×÷3.8×10e(-5), respectively. Interestingly, IPs in this model were also detected for cells with a phenotype different from MSCs.

Conclusion : The stem system's IPs offer protection to MSCs and other Nestin-GFP+ progenitor cells of transgenic BM against non-transgenic recipient immunized vs GFP for over six weeks. The results argue in favor of preservation of MSC functionality, demonstrating the ability to form and maintain primary and secondary haematopoietic territory after transplantation. We speculate that nestin may be a marker for a larger set of resting stem cells with strong IPs, including cancer stem cells.

Keywords : MSC, Nestin, Immune privileges, Stem system, Hematopoietic ectopic foci

PP14-4

Thioredoxin-interacting protein regulates megakaryopoiesis and platelet counts

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Background : Thioredoxin-interacting protein (TXNIP) is ubiquitously expressed in blood cells, including hematopoietic stem cells (HSCs), monocytes, and platelets. TXNIP binds to and inhibits antioxidant thioredoxin to regulate the reactive oxygen species (ROS) production and promotes glucose transporter 1 and 4 (GLUT1, 4) endocytosis, suppressing glycolysis and promoting mitochondrial respiration. Mitochondria play a role in cellular metabolism, including differentiation, division, and apoptosis, all driven by energy production through mitochondrial respiration and oxidative phosphorylation (OXPHOS). Moreover, mitochondria undergo dynamic conformational changes such as fission and fusion, and increased levels of mitochondrial reactive oxygen species (mtROS) are particularly associated with fission. Recently it has been studied that not only the levels of total ROS but also mtROS are crucial for the megakaryocyte (MK) maturation and proplatelet formation. Also, mitochondrial dysfunction is linked to altered platelet count. In the present study, we aimed to investigate the role of TXNIP in megakaryopoiesis and platelet biogenesis.

Method : Wild-type (WT) and Txnip$^{-/-}$ mice were studied. BM-derived MKs were analyzed to investigate the role of TXNIP in megakaryopoiesis. We stained BM MKs with both mitochondrial superoxide indicator MitoSOX and anti-CD41 antibody and assessed mtROS levels in each cell model. The CD34$^+$ HSCs isolated from human cord blood (CB) were differentiated into MKs.

Results : Txnip$^{-/-}$ mice develop thrombocytopenia at 4–5 months that worsened with age. During ex vivo megakaryopoiesis, Txnip$^{-/-}$ MkPs remained small, with decreased levels of MK-specific markers. Critically, Txnip$^{-/-}$ MkPs exhibited reduced mtROS, of which was related to AKT activity. The effects of TXNIP on MKs were recapitulated during the differentiation of human CB-derived CD34$^+$ HSCs.

Conclusion : We provide evidence that the megakaryopoiesis pathway becomes exhausted with age in Txnip$^{-/-}$ mice. Overall, this study demonstrates that TXNIP may play a critical role in initiating megakaryocyte differentiation from HSCs or MEPs, regulating metabolism and mitochondrial function.

Keywords : Aging, Megakaryopoiesis, Mitochondria, Thrombocytopenia, TXNIP

PP14-5

Understanding the role of hippo signaling pathway in hematopoiesis using hematopoietic-specific MST1/2 deficiency mice model

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Background : Hematopoiesis is the process by which the body produces blood cells. All blood cells differentiate from a single hematopoietic stem cell. Various signaling pathways regulate hematopoiesis. Hippo signaling pathway is known as a regulator of organ size and tissue homeostasis in various organisms coordinated by regulating cell proliferation and survival. Recent studies revealed that hippo signaling pathway is important in hematopoiesis. The serine/threonine kinases Mammalian STE20-like (MST) 1/2 protein are components of hippo signaling pathway. Mst1/2 whole-body double knockout mice exhibit embryonic lethality, characterized by severe growth retardation. Several studies using a genetically engineered mouse model have provided physiological results in regulation of hematopoiesis via conditional knockout of hippo signaling molecules. We used hematopoietic-specific Mst1/2 double knockout mice to understand hippo signaling pathway in hematopoiesis.

Method : Production of hematopoietic-specific Mst1/2 deleted mice (referred to as DKO) by intercrossing Mst1/2-floxed transgenic mice with vav1-iCre transgenic mice. Body weight and Organ(Spleen/Thymus) weight were measured to check weight difference between DKO mice and WT mice. Peripheral blood was collected to conduct complete blood count (CBC). Bone marrow (BM) cells, splenocytes, thymocytes were collected to analyze flow cytometry (FC). RT-qPCR and single cell RNA-sequencing were conducted to compare Mst1/2 DKO and WT mice.

Results : DKO mice exhibit body weight loss, but their spleen and thymus weight are heavier than WT mice, also show splenomegaly. In CBC, DKO mice exhibit myeloid skewing. In FC, T cell population was decreased spleen and blood of DKO mice. In BM, DKO mice show long-term hematopoietic stem cell (LT-HSC) accumulation. In thymus, DKO mice show decreased thymocytes in early T cell differentiation.

Conclusion : Consistent with previous studies, we observed myeloid skewing and decrease T cell population. Additionally, we find accumulation of LT-HSC. Further investigation will be conducted to determine the role of the Hippo signaling pathway in hematopoiesis.

Keywords : Hippo signaling pathway, MST1/2, Hematopoiesis, Hematopoietic stem cell, HSC

PP15-1

Early intrathecal dexamethasone effectively alleviate immune effector cell-associated neurotoxicity syndrome

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Background : CAR-T therapy as a frontline treatment is limited due to cytokine-release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Although intravenous corticosteroids are recognized as effective treatment options for CRS and CANS, it is associated with inferior prognosis. Therefore, exploring new treatment approaches may be beneficial in improving outcomes for these patients.

Method : This study involved 18 patients with R/R B-ALL treated with CAR-T developed ≥CRS grade 2 and ICANS. If the CRS progressed to garde 3 after the failure of tocilizumab therapy, intravenous glucocorticoids was used as the recommended protocol. In our center, once the patient occurred with ICANS intrathecal (IT) dexamethasone was accepted as soon as possible. For patients with CRS grade >2 and ICANS, a combination of intravenous and IT therapies was employed.

Results : Among the 18 patients, 7 underwent IT dexamethasone alone, while 11 patients received a combination of intravenous and IT dexamethasone therapy. 88.9% patients achieved remission of CRS and ICANS symptoms. The median time from intrathecal therapy to grade 1 ICANS was 1 day (ranging of 1 to 7 days). And the median time from the onset of fever to the normal temperature was 5 days (ranging from 4 to 8 days). The median length of ICU stay was 6 days (ranging from 2 to 11 days). IT dex did reduce the levels of clinical inflammatory markers such as C reactive protein, which was decreased in 14 out of 18 patients, and Procalcitonin, which was reduced in 12 out of 18 patients. As to cytokine, we observed

a significant decrease in IL-2 and IFNγ levels in the blood following the IT Dex, with a similar trend observed in the cerebrospinal fluid.

Conclusion : Intrathecal dexamethasone has been shown to effectively treat ICANS and reduce the need for high-dose systemic corticosteroids.

Keywords : Chimeric antigen receptor T cells, Immune Effector Cell-associated neurotoxicity syndrome, Intrathecal, Dexamethasone

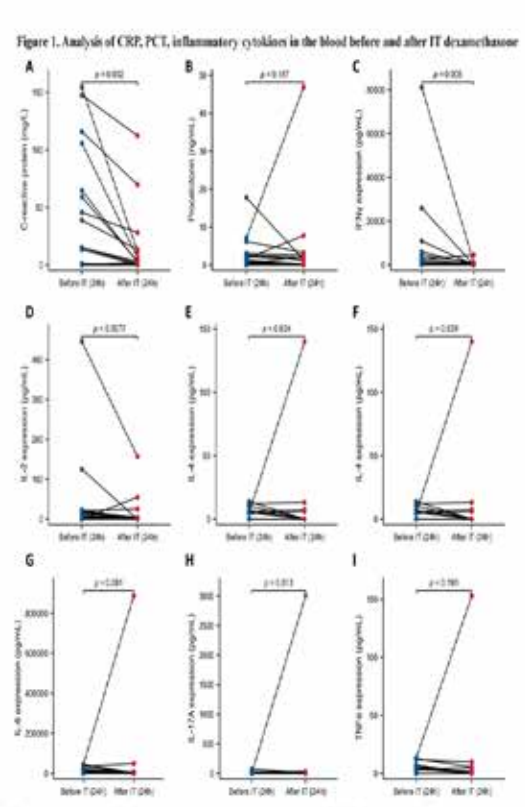

Figure 1. Analysis of CRP, PCT, inflammatory cytokines in the blood before and after IT dexamethasone

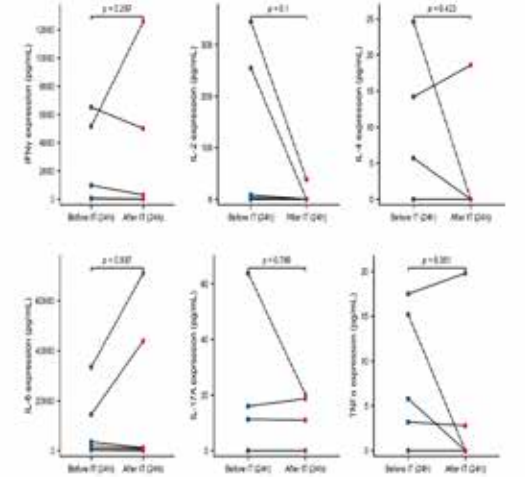

Figure 2. Analysis of inflammatory cytokines in the cerebrospinal fluid before and after IT dexamethasone

Table 2 Efficacy of IT Dexamethasone In the Treatment of CRS Combined with ICANS

Patient	Group	IT times	Cumulative dose of IT Dex	Cumulative dose of intravenous Dex (mg)	The first time of IT post CAR-T(Days)	Time to IT Dex post CAR-T(Days)	CRS Remission	CRS During Time (Days)	ICANS Remission	Time to ICANS Grade(Days)	Time to Normal Temperature (Days)	The Duration of ICU Admission (Days)	Using Tocilizumab	Using Anakinra
pt1	CT+DT	4	15	105.00	2	D2,D6	Yes	10	Yes	2	5	6	Yes	No
pt2	CT+DT	2	20	168.56	6	D6,D8	No	Die	No		8	4	Yes	No
pt3	CT+DT	8	27	64.50	6	D6,D7,D8, D9,D10	Yes	8	Yes	2	7	7	Yes	No
pt4	CT+DT	9	42.5	15.90	6	D6,D7,D8, D9	Yes	8	Yes	4	9	10	Yes	No
pt5	DT	2	10		6	D6,D7	Yes	4	Yes	1	4	2	Yes	No
pt6	CT+DT	4	25	457.25	2	D2,D3,D4	No	Die	No		5	3	Yes	No
pt7	CT+DT	3	15	7.50	4	D4,D5,D6	Yes	11	Yes	7	5	11	Yes	No
pt8	DT	2	10		7	D7	Yes	5	Yes	1	5	7	Yes	No
pt9	DT	3	7.5		10	D10,D11,D12	Yes	9	Yes	1	8		Yes	No
pt10	DT	1	5		5	D5	Yes	4	Yes	1	4		Yes	No
pt11	DT	4	22.5		5	D5,D6,D7	Yes	4	Yes	1	5		Yes	No
pt12	CT+DT	3	12.5	17.50	7	D7	Yes	8	Yes	1	5		Yes	yes
pt13	CT+DT	9	45	8.50	4	D4,D5,D6,D7, D8,D9	Yes	8	Yes	3	7	7	Yes	No
pt14	DT	2	10		4	D4	Yes	5	Yes	1	5		Yes	No
pt15	CT+DT	1	5	13.15	7	D7	Yes	9	Yes	3	8	5	Yes	yes
pt16	CT+DT	1	5	9.50	7	D7	Yes	12	Yes	1	7	7	Yes	yes
pt17	CT+DT	1	5	182.81	5	D5	Yes	7	Yes	1	4	2	Yes	yes
pt18	DT	2	10		4	D4,D5	Yes	6	Yes	1	6	4	Yes	No

PP15-2

Non-viral engineering of off-the-shelf universal CAR T cells using CRISPR and transposons

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Background : Chimeric antigen receptor (CAR) T cell adoptive immunotherapy is a promising therapeutic modality for lymphoid malignancies. Nevertheless, lymphopenic conditions in pediatric and heavily treated patients who previously received chemotherapies and/or stem cell transplantation may lead to inadequate T cell numbers, suboptimal CAR T cell functions, and unsuccessful CAR T cell production. Allogeneic CAR T cells could overcome some of these limitations provided that the risk of graft-versus-host disease (GvHD) can be successfully mitigated. In this study, we validated a non-viral T cell engineering platform based on SB transposons and CRISPR-Cas9 as a potential universal off-the-shelf allogeneic CAR T cell therapy.

Method : CD19-CAR genes were stably expressed in electro-

porated human T cells using hyperactive Sleeping Beauty (SB) transposons. To minimize GvHD risk, endogenous T cell receptor (TCR) expression was inactivated using TCR gene-specific CRISPR-Cas9 ribonucleoproteins (RNPs). Efficacy and safety was assessed by adoptive transfer of CD19-CAR/TCR-negative T cells in NALM6 leukemic tumor-bearing immunodeficient mice. Signaling pathways were examined by assessing phosphorylation states of essential protein kinases and by transcriptomic analyses.

Results : With optimized transfection and enrichment schemes, relatively robust CD19-CAR expression (90%) and CRISPR-mediated TCR inactivation (99% TCR-negative cells) levels were obtained, without clonal dominance nor transposon integration bias. Expanded CAR/TCR-negative cells exhibited a predominant memory phenotype and remained fully functional, consistent with increased IFN-γ, GM-CSF, and TNF-α production and absence or low expression of PD1 and CTLA4 exhaustion markers. Transplantation of CD19-specific CAR/TCR-negative T cells into a xenograft tumor model resulted in complete tumor remission and absence of GvHD. CRISPR-mediated TCR inactivation inhibited T cell signaling/protein phosphorylation and gene expression linked to the PI3K signaling pathway consistent with reduced GvHD risk.

Conclusion : This is the first non-viral SB transposon-CRISPR combination strategy that serves as a safe and effective alternative for generating next-generation CD19-specific CAR T while reducing GvHD risk and easing potential manufacturing constraints.

Keywords : Chimeric antigen receptor, Transposon, Crispr, Immunotherapy, Leukemia

PP16-1

Buffy coat pooled platelets: A cost-effective alternative to single donor apheresis platelets in hemato-oncology patients in Indian scenario - a randomized crossover trial

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Background : In its latest amendment of 2020, the Drugs and Cosmetics Act of the Indian parliament licensed Buffy Coat Pooled Platelets (BCPP) for clinical use for the first time in India. Prior to this amendment, only two types of platelets were being used – the whole blood derived platelets and plateletpheresis derived Single Donor Apheresis Platelets (SDAP). In other parts of the world, BCPP has been in regular use since 1970s, hence this trial was conducted prior to implementation of BCPP in routine clinical practice on patients at our centre. The objectives of this study were to determine the feasibility of BCPP preparation and to evaluate its efficacy and safety in non-refractory, hemato-oncological patients in comparison to SDAP and also, to conduct an in-depth cost analysis of preparation of both these products in Indian context.

Method : Five 'O' positive buffy coats extracted from whole blood were pooled and suspended in Platelet Additive Solution. In a randomized cross-over study design, 93 hemato-oncological patients were enrolled and randomly assigned either BCPP or SDAP as their first transfusion product. Upon subsequent requisition for the same patient, the alternate platelet type was issued as second transfusion product. To assess the efficacy, corrected count increment (CCI) and percentage platelet recovery (PPR) were calculated from blood samples collected one hour after transfusion. Inter-transfusion interval was noted and each patient was examined for signs of adverse transfusion reactions. For cost analysis, all resources consumed at each step of BCPP and SDAP preparation were identified and measured.

Results : As per Tables attached.

Conclusion : In non-refractory, hemato-oncological patients, BCPP is non-inferior to SDAP in terms of one-hour post-transfusion CCI and PPR, and superior in terms of post-transfusion platelet increment and inter-transfusion interval. BCPP costs significantly lesser than SDAP and it can act as a good alternative to SDAP in resource-constrained settings like India.

Keywords : Platelets, Apheresis, Cost analysis, Hemato-oncology, Buffy coat pooled platelets

Results:

The Quality Control characteristics, Post-transfusion response indicators and cost distribution have been depicted in the following table:

		SDAP	ECPP
Quality Control parameters	Volume (mean)	220 ml	240 ml
	Platelet Count per bag (mean)	3.1 x 10^{11}	3.9 x 10^{11}
	Anti A and Anti B titre (median)	Not done*	1:8 and 1:16
Post Transfusion response parameters	Platelet increment (mean)	30,839	37,043
	CCI (mean)	15,554	15,003
	PPR (mean)	36.42%	38.04%
	Transfusion Interval (median)	72 hours	96 hours
Cost parameters (per bag)	Human Resources	₹ 212.38	₹ 164
	Capital Infrastructure	₹ 329.36	₹ 0.48
	Furniture	₹ 21.15	₹ 0.65
	Equipment	₹ 681	₹ 120.41
	Drugs	₹ 21.43	₹ 0
	Consumables	₹ 8957.89	₹ 3777.6
	Overheads	₹ 264.35	₹ 141.8
	Total Unit Cost	**₹ 10,497.4**	**₹ 4063.9**

*Titres not done for SDAP as they were transfused to ABO matched patients.

Table 2: Estimated difference in the outcomes, and 95% CI between the study arms

End Point	Non-inferiority margin: 10% of average SDAP	Estimated Difference (95% CI) ECPP v/s SDAP p-value		Decision	Explanation
		Univariable	Multivariable*		
Platelet increment	3,084	6,264 (4,772 – 7,637) p < 0.001	6,202 (4,742 – 7,661) p < 0.001	Superior	Since 95% CI doesn't cross 0
Corrected Count increment	1,555	-550.5 (-1120 – 19.7) p = 0.06	-549.3 (-1129 – 30.8) p = 0.06	Non-Inferior	Since 95% CI doesn't cross the non-inferiority margin
Percent Platelet Recovery	3.6	-1.61 (-3.0, - 0.23) p = 0.02	-1.62 (-3.02, - 0.21) p = 0.02	Non-Inferior	Since 95% CI doesn't cross the non-inferiority margin
Transfusion interval**	7.2	35.05 (10.48 – 59.63) p = 0.01	35.3 (10.5– 59.5) p = 0.01	Superior	Since 95% CI doesn't cross 0

PP16-2

Strategies in blood supply management during the COVID-19 pandemic: Experiences of local blood bank managers

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Background : The lockdowns implemented during the height of the COVID-19 pandemic have caused blood banks to not receive any voluntary blood donors in their facilities. This leads to the depletion of blood supplies resulting in shortage. Hence, in this research, we explored the strategies implemented by blood bank managers in Central Luzon, Philippines to mitigate the blood product shortage.

Method : Blood bank staff, medical doctors, and administration representatives from blood service facilities in Central Luzon, Philippines were recruited for a recorded interview. Recordings were then transcribed and translated before undergoing thematic analysis following the method of Braun and Clarke in 2013.

Results : To address the challenges of the decreasing blood supply during the height of the community quarantine, blood supply managers in the region implemented various strategies such as cancellation of non-emergency surgeries, rational blood use, enhanced auditing of blood stocks, and, most importantly, further empowerment of the local blood network towards 100% voluntary and non-remunerated donation. Anecdotally, this pandemic may have been contingent on unearthing some areas for improvement in the current blood supply management system in the locale. More importantly, it allowed blood supply managers to reflect and appreciate the importance and benefits of an efficient and well-communicated network between blood service facilities.

Conclusion : Overall, despite the hardships experienced by blood banks during the height of the pandemic, blood supply managers were able to mitigate this by implementing creative solutions that can be further worked into meaningful policies.

Keywords : Blood supply management, COVID-19, Philippines

PP16-3

Blood supply in Central Luzon, Philippines in the context of the COVID-19 pandemic: A retrospective analysis

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Background : Disasters like the COVID-19 pandemic may pose significant threats to the service delivery of blood service facilities. Due to the implementation of lockdowns, blood banks are unable to cater to blood donors which may result in a depleted blood supply. In this research, we performed a retrospective analysis of the blood supply between the years 2019 and 2020 in Central Luzon, Philippines.

Method : We sought the permission of the Department of Health – Central Luzon Center for Health Development (DOH-CLCHD) to gather secondary data on blood collection, utilization, and wastage. Specifically, the data obtained for this study were documentation of blood donations and blood inventory control reports of dispensed and unused blood units for the years 2019 and 2020. The data collected were then summarized in a customized spreadsheet and statistically analyzed.

Results : From the six provinces in Central Luzon, there was a decrease in voluntary blood donations from 2019 and 2020 by 31.87%. A high drop in the number of donors was observed during the 2nd quarter of the year 2020, during the height of the community lockdowns. However, during this time it can be noted that there is an increase in the number of replacement blood donors by 28.82%. There was an increase of 10.91% in unused or wasted blood products. It can also be noted that a decrease of 21.53% in whole blood donation was noted, which is the highest among the different blood components.

Conclusion : The findings of this study reflect the general picture of blood supply management in Central Luzon, Philippines from 2019 going into 2020, the first year of the COVID-19 health crisis. It was found that there was a decrease in blood supply and voluntary donations, especially during the second quarter of 2020 when community quarantines and enhanced health protocols were implemented.

Keywords : Blood supply management, Philippines, COVID-19

PP16-4

Motivators and barriers towards voluntary blood donation among Generation Z university students: Experience from a local higher education institution

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Background : Many healthcare organizations worldwide are concerned about a lack of safe blood. According to references, tertiary-level students are prospective lifelong blood donors and blood drive activists, as well as the healthiest demographic; therefore, addressing their worries and issues concerning blood donation is critical if the goal is to improve the supply of safe blood. Thus, this research identified the factors that influence Filipino Generation Z (GenZ) university students to donate blood.

Method : With ethical approval, a cross-sectional study using a self-administered questionnaire was done among 327 tertiary-level GenZ students from a higher education institution (HEI) in Angeles City, Philippines. Responses were then coded in a customized spreadsheet. Reports were presented in frequency and percentage, and the association between the respondents' sociodemographic characteristics and their motivators and barriers to donating blood was examined using a Chi-square test.

Results : Overall, only 6.7% of Gen Z students had ever donated blood, these are mostly male students (68.2%) and non-allied health students (77.3%). However, despite the low history of blood donation, most respondents stated that they would be willing to give blood and that their motivations in giving blood include: (1) good for their health (2) assisting others in need and (3) expanding the blood supply. The lack of a call to action to donate blood is the primary obstacle to blood donation cited by the respondents.

Conclusion : The HEI observed low rates of blood donors among its students. Despite these low rates, the students are very much willing to donate blood. Hence, recruitment campaigns should emphasize both the altruism and personal benefits of donors.

Keywords : Blood donation, Generation Z, Willingness, Motivators, Barriers

PP16-5

Suggestion for optimization of CD3+ t cell apheresis for CAR-T therapy: A retrospective analysis of parameters and predictive models

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Background : Chimeric antigen receptor T (CAR-T) cell therapy has demonstrated favorable outcomes in refractory or relapsed B-cell lymphoma and B cell acute lymphocytic leukemia. In South Korea, Kymriah (tisagenlecleucel), a CD19-directed CAR-T, is the only approved commercial CAR-T therapy available. However, consensus for the apheresis process to collect enough $CD3^+$ T cells for CAR-T therapy are currently lacking. We aimed to identify new parameters highly correlated with the estimated minimal processing volume.

Method : In this retrospective study, we included all adult patients who underwent autologous cell collection for Kymriah manufacture at Cellular Therapy Center of Asan Medical Center, Seoul, Korea. CBC and viable $CD3^+$ cell count of pre-apheresis peripheral blood and collection bag, and the collection process data were collected. We calculated collection efficiency 2 (CE2) and estimated minimal processing volume targeting $CD3^+$ cell count of 1.5×10^9.

Results : From August 2022 to November 2023, 40 patients were involved, and two of them underwent collection twice. The median age was 62.5 years, with 22 males, and 37 diagnosed with DLBCL. The average processed volume was 13.1L, ranged from 8.2L to 18.6L. Calculated CE2 was variable, with median 74.1%, ranged from 36.3% to 143.6%. The most relevant single parameter to the estimated minimal processing volume with a target of 1.5×10^9 for $CD3^+$ cells in the collection bag was the peripheral blood $CD3^+$ count, with an R^2value of 0.8976. The product of the pre-collection $CD3^+$ count and the body weight had a highly significant correlation (R^2 0.9175) with the estimated processing volume.

Conclusion : Predicting processing volume for cell collection accurately with a single indicator is challenging. However, utilizing new parameters based on patient body weight and pre-collection peripheral blood test results can offer a simple and quick method to estimate blood processing volume effectively.

Keywords : CAR-T, Cell collection, Colleciton efficiency, Apheresis

PP16-7

Serodetection of cytomegalovirus IgG antibody among blood donors: Preliminary findings from a teaching hospital in the Philippines

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Background : Blood transfusion recipients and blood bank staff are equally concerned about infections brought on by the cytomegalovirus (CMV). There may be negative effects if immunocompromised people, newborns, or pregnant women get transfusions from CMV-positive units. The National Health Bureau in the Philippines has not yet made CMV testing of blood units mandatory; as a result, it is essential to determine the seroprevalence of such an infection to reduce its potential impacts.

Method : The study determined the seroepidemiology of CMV immunoglobulin G (IgG) antibodies among blood donors from a tertiary hospital in the Philippines. The study used the samples of 126 blood donors who passed the routine blood donation screening and assessment at the institution. Enzyme-linked immunoassay was then used to qualitatively determine the presence of CMV IgG among the accepted blood donors.

Results : Among the 126 blood donors included in the study, 104, or 82.5%, were seropositive for the CMV IgG antibody. The majority of those who tested positive were males (81.7%), those belonging to the age group of 20-29 years old (48.1%), those who were single (60.6%), and those who were employed (68.3%). Consequently, none of these factors showed a significant association with CMV IgG antibody positivity ($p = 0.22$-0.99).

Conclusion : Overall, a high seropositivity rate for CMV IgG was noted among the blood donors from the selected hospital. Since CMV detection is not yet included in the panel of tests for blood units in the Philippines, it is strongly recommended that blood banks utilize strategies such as leukoreduction to mitigate the potentially life-threatening complication of CMV transfusion among immunocompromised individuals and neonates.

Keywords : Cytomegalovirus, IgG antibody, Blood donors, Philippines

PP16-8

Educational outcomes and perceptional change of medical students after visiting blood donation centers

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Background : Blood donation is the most popular and crucial procedure in supplying blood. Educating primary care physicians about blood donation and transfusion is critical since they are vital components of health care. The Division of Hematology and Oncology at Soonchunhyang University Seoul Hospital in Korea introduced a novel initiative called the Blood Donation Center Visiting Program in the clerkship education for final-year medical students.

Method : The Blood Donation Centre Visiting Program was implemented for hematology and oncology clerkship from 2021 to 2023. As part of the program, students visited a blood donation center, one group at a time, each week. They gained practical knowledge about the blood donation process, with some students actively participating in blood donation. An online survey on the program was conducted with 287 eligible students after the program over the past 3 years.

Results : Of the 287 students, 203 participated in the survey. Among the 203 students, 126 (62.1%) donated blood during their visit to the blood donation center as part of the program. The main reasons for not donating blood during the visit were as follows: current medication, and COVID-19-related issues. As a result of participating in this program, 88.7% of the students reported an increase (from 71.4% to 90.1%) in their knowledge and willingness to donate blood. Moreover, of the 64 students who were repeat donors after the program, 14 had never donated blood prior to the program.

Conclusion : The blood donation education program has brought about positive changes in students' perceptions and enhanced their knowledge of blood donation. Educational field trips for medical students at blood centers should be encouraged.

Keywords : Blood donation, Educational outcomes, Perceptional change, Medical students, Blood donation centers

Figure 3

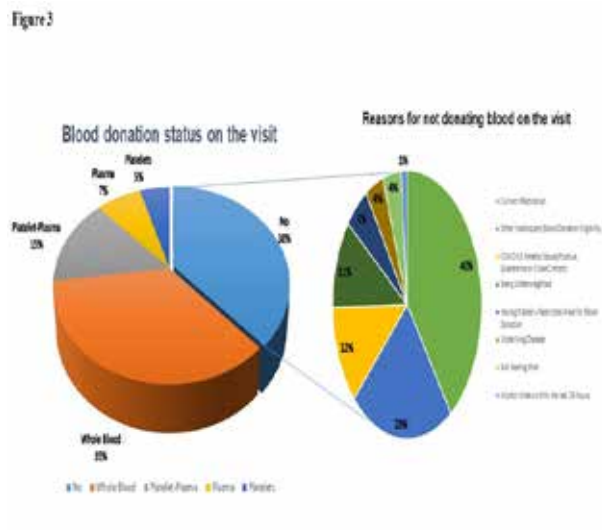

Table 5. Participants' subjective perception change about blood donation before and after The Blood Donation Center Visiting Program and actual repeated blood donations after the program (n=203)

	Number (%)
Knowledge improvement on blood donation after the	
Yes	180 (88.7)
No	23 (11.3)
Perception of the importance of blood donation after	
Yes	171 (84.2)
No	32 (15.8)
Willingness to donate blood	
Yes (before the program)	145 (71.4)
Yes (after the program)	183 (90.1)
Actual repeated blood donations after the program	
Yes	64 (31.5)
No	139 (68.5)

PP16-9

Assessing centrifugal and membrane approaches in plasma exchange for kidney disease management: A comparative study

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Background : Therapeutic plasma exchange (TPE) can be performed by two distinct technologies: centrifugal TPE (cTPE), based on specific gravity, or membrane TPE (mTPE), based on molecular size. This study conducts a head-to-head comparison between these technologies, aiming to which technology has more effective Plasma removal efficiency (PRE), and more cost-effective modality in a developing world with resource-constrained setting like ours.

Method : A prospective, open-labeled, randomized trial was conducted at a tertiary care facility in Northern India from June 2022 to April 2023. A total of 122 TPE procedures were performed on 18 patients, and data were meticulously recorded. The Spectra Optia (Terumo, Lakewood, Colorado, USA) and Octonova device (Diamed, Cologne, Germany) with P2 dry filter (Fresinus Medical Care Deutschland; Germany) were used for cTPE and mTPE procedures, respectively.

Results : While both procedures showed comparable plasma removal, the mean total time for mTPE (124.3 ± 8.9) was significantly less than cTPE (147.7 ± 34.1; $p < 0.001$). Significant differences were also observed in PRE between cTPE (67.2%) and mTPE (29.6%; $p < 0.001$). Cost analysis revealed an overall 55.5% higher cost in cTPE (INR 13,489) compared to mTPE.

Conclusion : Our findings suggest that plasma removal efficiency was significantly better in cTPE compared to mTPE procedures with lesser blood volumes processed. Although mTPE showed lower PRE, requiring multiple procedures for equivalent efficiency, the overall cost was comparable. Thus, cTPE may be considered the preferred choice over mTPE. However, Larger clinical trials with expanded sample sizes are necessary to validate these findings.

Keywords : Therapeutic plasma exchange, Centrifuagal therapeutic plasma exchange, Membrane therapeutic plasma exchange, Plasma removal efficiency

PP16-10

Inconvinence and loss due to red cell transfusion dependence in patients with blood diseases and cancers: A patient-reported experience and outcomes study

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Background : Transfusion dependence refers to the condition of receiving periodic red blood cell (RBC) transfusion at intervals of 8 weeks or less. While the immunologic side effects of RBC transfusion and complications arising from prolonged transfusion dependence, such as iron overload, are well known, the socioeconomic and psychological impacts of the RBC transfusion dependence are not well understood.

Method : We surveyed 82 transfusion-dependent patients with malignant or benign hematological disorders at Seoul National University Hospital. The questionnaire, including a transfusion-specific domain and the Hospital Anxiety and Depression Scale (HADS), aimed to capture patient responses on discomfort and losses during the transfusion process. Clinical data were extracted from records, and the results were summarized using statistical measures. Chi-square tests or Fisher's exact tests were applied cross-analysis of transfusion details and key survey parameters.

Results : Inconvenience from transfusions was not associated with transfusion duration but was higher with frequent transfusions and concurrent platelet transfusions. Concerns about subsequent transfusion side effects were highest within the first six months, decreasing with prolonged transfusion duration. Residents in rural area reported more income reduction due to transfusion schedules than urban residents. Factors like transfusion duration, frequency, platelet transfusions, and serum ferritin, did not affect economic burden. Thirty respondents (36.6%) reported reduced household income due to repeated transfusions.

Conclusion : Early-stage, low-volume transfusion patients often express heightened concerns about side effects. Clear explanations and a conducive environment are crucial for adapting to transfusion therapy. To alleviate economic burdens in patients living in rural areas, establishing nearby healthcare facilities with specialized

expertise in secure transfusion services is warranted.

Keywords : Red cell transfusion, Transfusion dependence, Patient-reported outcomes measure, Iron overload, Transfusion

PP16-11

Temporal dynamics of platelet glycoprotein VI and reactive oxygen species: Insights from fresh and stored platelet concentrates

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Background : Platelet function is crucial for hemostasis and wound healing, and alterations in platelet characteristics during storage in transfusion bags may impact their efficacy. This study aimed to evaluate the levels of the platelet collagen receptor, glycoprotein (GP) VI, and intracellular GPVI-dependent reactive oxygen species (ROS) generation. Understanding the temporal dynamics of these parameters is essential for assessing the quality and functionality of platelets over time.

Method : Fresh platelets and platelet concentrates stored for varying durations (6, 8, 11, and 14 days) post-collection were analyzed using flow cytometry. Surface levels of GPVI and ROS activity were measured, and the GPVI-specific agonist, collagen-related peptide (CRP), was employed to induce intraplatelet ROS generation. The Syk inhibitor, BAY 61-3606, was used to assess the role of Syk activation in ROS generation. Basal ROS levels were compared between healthy individuals and pooled platelet concentrates.

Results : Both fresh platelets and pooled platelet concentrates exhibited a similar pattern of GPVI-induced intraplatelet ROS generation when stimulated with CRP. However, levels of GPVI and ROS generation showed a time-dependent attenuation during storage. Approximately one third of total ROS generated occurred within 2 minutes, and further ROS generation was dependent on Syk activation. Interestingly, the basal ROS level in pooled platelet concentrate was higher than in healthy individuals. Surprisingly, despite using a GPVI-specific agonist, no correlation was found between GPVI receptor levels and ROS generation in both fresh platelets and pooled platelet concentrate.

Conclusion : The findings indicate that levels of both receptor and ROS generation decrease in a time-dependent manner, suggesting a regression in the quality of platelets over time. This study contributes valuable insights into the dynamics of platelet function and oxidative stress during storage, emphasizing the importance of time-sensitive considerations in platelet transfusion practices.

Keywords : Platelet concentrates, Platelet glycoprotien VI , ROS, Platelet quality

PP17-1

How far we should care about education, wealth, and macroeconomic variables to prevent anemia prevalence among pregnant women?

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Background : Anemia is a hematologic disorder that is the most common maternal problem during pregnancy. The rates of anemia morbidity and mortality among pregnant women are high and increase every year. Pregnant women in Southeast Asia were anemic by 52% in 2020 and 20-40% of the 500 postpartum maternal deaths cases were caused by anemia. The prevalence of anemia among pregnant women in ASEAN-5 countries falls in 100 countries with the highest cases.

Method : Using World Bank and UNDP panel data years 2000-2020, this research analyzes socio-economic determinants such as health expenditure (percentage of GDP), education, GDP per capita, the illiterate rate of adult women, human development index (HDI), the female share of employment in senior and middle management, labor force participation rate in ASEAN-5 (Indonesia, Malaysia, Thailand, Philippines, and Vietnam).

Results : Data were analyzed by robust random effect estimation with STATA MP.14. As the results are shown in the graph on average the level of anemia increases in almost all countries, except the Philippines. The Philippines has a decrease in the prevalence of anemia among pregnant women each year. The prevalence of anemia among pregnant women in-

creased with an increase in adult female illiterate rate, labor force participation, and female share of employment. Meanwhile, increasing health expenditure, GDP per capita, and HDI will decrease the prevalence of anemia among pregnant women.

Conclusion : The high prevalence of anemia among pregnant women indicates anemia to be a major public health problem in ASEAN countries. The variables of education, wealth, and macroeconomics do matter in reducing anemia cases in pregnant women by increasing health expenditure, GDP per capita, and HDI. Providing support access for working mothers and strategies to reduce the number of illiteracies among women will give positive changes regarding pregnant women's health issues in ASEAN-5.

Keywords : Pregnant women , Anemia, Socioeconomic status, Education attainment, Wealth on health

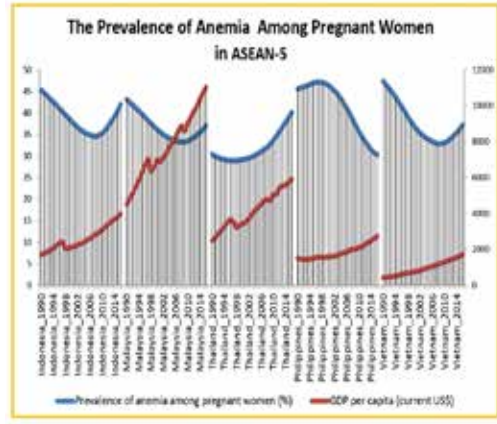
Table I. The Effects of Socio-Economic Determinants on The Prevalence of Anemia Among Pregnant Women in ASEAN-5 Countries

Regression with STATA MP 14.

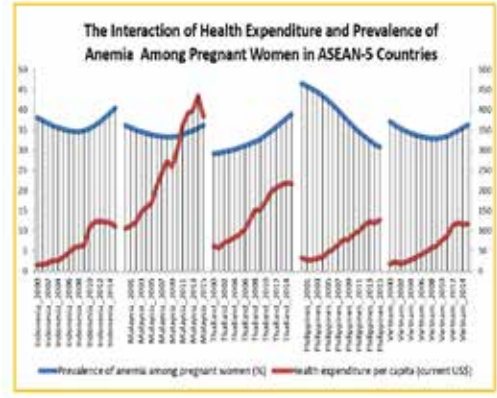
Variable	(1) OLS	(2) Robust Fixed Effects	(3) Robust Random Effects
healthexp	-1.821*	-2.093*	-1.821*
	(0. 983)	(0.790)	(0.575)
femaleilliter	0.275***	0.243**	0.275***
	(0. 061)	(0.0784)	(0.0861)
GDP	-0.380**	-0.712**	-0.381
	(0 .181)	(0.244)	(0.195)
laborpart	0 .036	0.0412	0.0365
	(0 .082)	(0.0669)	(0.0479)
diarrecyfunde	0 .334***	0.300	0.334*
	(0 .096)	(0.144)	(0.155)
hdi	-21.834***	-33.91***	-21.80*
	(7.726)	(6.150)	(10.17)
educ	(0 .115)**	0.108**	0.115**
	(0 .052)	(0.0317)	(0.0425)
_cons	22.384	35.83**	22.38
	(9.951)**	(11.82)	(15.54)
N (sample)	85	85	85

Standard errors in parentheses
* $p<0.05$, ** $p<0.01$, *** $p<0.001$

Regression with Ordinary Least Square (OLS) estimation will be overestimated. Robust random effect estimation will fixed the serial correlation problem



Source: Worldbank data (author's calculation)



PP17-2

V736A (rs855791) polymorphism in the *TMPRSS6* gene is associated with iron deficiency anemia development in females: A meta-analysis

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Background : Several studies suggested that mutations in the TMPRSS6 gene affect hepcidin production, which may lead to the development of iron deficiency anemia (IDA). Hence, this meta-analysis determines the association of the V736A or the rs855791 polymorphism in the TMPRSS6 gene with IDA development.

Method : Related studies were searched in PubMed as of November 9, 2023. The resulting studies were screened by two of the authors and data were extracted and collated in a customized spreadsheet. Review Manager 5.4.1 was used for the computation of the odds ratios (ORs) and 95% confidence intervals (CIs).

Results : A total of 187 studies were screened. From this, only six studies satisfied the inclusion criteria and were included in the meta-analysis. Analysis of the allelic model showed a high degree of inter-study heterogeneity which prompted us to determine the cause through sub-group analysis. Sub-groups were conceptualized based on the participant characteristics (females of reproductive age/with menstruation, females aged 50-70 years old, males and females combined). Based on this, significant and homogenous findings were observed for the allelic, co-dominant, and dominant models of the association between the polymorphism and the development of IDA among females of reproductive age/with menstruation. Non-significant and highly heterogeneous outcomes were noted for the other sub-groups.

Conclusion : Overall, based on the pooled findings, females of reproductive age/with menstruation who possess the polymorphism are more likely to develop IDA than health controls. However, further studies are needed to verify these claims.

Keywords : Iron deficiency anemia, V736A, rs855791, Meta-analysis

PP17-3

A meta-analysis on the association of gestational diabetes mellitus with tissue plasminogen activator

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Background : Gestational diabetes mellitus (GDM), characterized by elevated blood glucose levels during pregnancy, is associated with long-term health implications, often linked to factors like obesity and family history. In parallel, tissue plasminogen activator (TPA), a crucial enzyme in clot dissolution, is implicated in hematologic changes linked to GDM. This meta-analysis explores the global burden of GDM, specifically focusing on TPA levels. The aim is to establish TPA as a potential biomarker, elucidating its role in GDM-related hemostatic alterations, providing groundwork for subsequent clinical investigations and interventions.

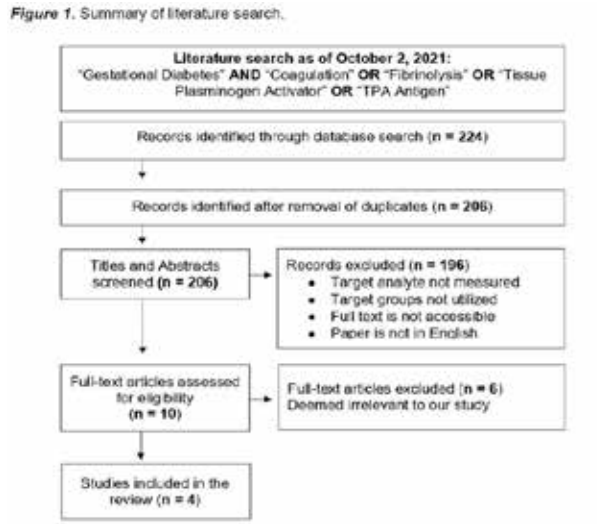
Method : The search approach entails a comprehensive review of the literature using search phrases like "tissue plasminogen activator" and "gestational diabetes." Case-control studies that included TPA plasma level data are used as inclusion criteria to separate respondents into two groups: those with a history of GDM and those with uncomplicated pregnancies. Using Review Manager version 5.4, four eligible studies are included, comprising a total sample size of 2113 individuals.

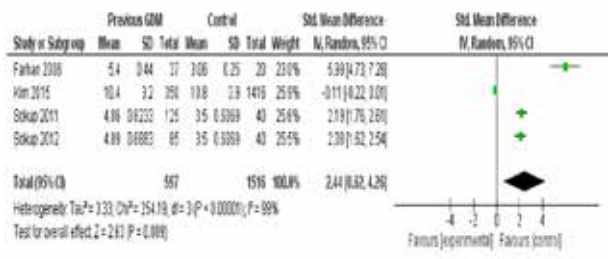
Results : Despite the recognized differences in participant characteristics across studies, the results demonstrate a significant rise in TPA levels in women who had previous GDM compared to those who did not experience any pregnancy-related issues. This observed increase in TPA levels highlights potential therapeutic relevance, shedding light on the biomarker's role in predicting outcomes within the context of GDM.

Conclusion : The standardized mean difference and 95% confidence interval underscore the complex association between TPA and GDM, indicating a need for further studies. Despite limitations in source reliability, the study emphasizes TPA's significance as a potential marker in women with a history of GDM. This research provides a foundation for future investigations into the broader applicability of TPA as an indicator in GDM-related clinical assessments and treatments.

Keywords : Tissue plasminogen activator, Diabetes, TPA, DM

Figure 1. Summary of literature search.





CI: confidence interval; df: degrees of freedom; GDM: gestational diabetes mellitus; SD: standard deviation; SMD: Standardized mean difference.

PP17-4

Association of temperature, rainfall, and humidity with the incidence of pregnancy-related anemia in Central Luzon, Philippines

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Background : Evidence of the impact of weather conditions on the incidence of anemia has been increasing throughout the years. However, studies in tropical countries such as the Philippines, where weather conditions are in the extremes remain limited. Hence, we performed this research to provide initial information on the association between select climatological variables and the incidence of maternal anemia in Central Luzon, Philippines.

Method : This study used a retrospective research design wherein data on climatological variables (average temperature, amount of rainfall, and relative humidity) on the incidence of maternal anemia, and the proportion of women who received iron with folic acid supplementation were extracted from online databases. All data were collated in a customized spreadsheet and statistically analyzed using SPSS.

Results : The incidence of anemia in the region was low at 2.36% of the estimated eligible population. On the other hand, the proportion of women receiving iron and folic acid supplementation is 44.87%. The association of the selected climatological variables with the incidence of anemia, rate of testing, and rate of receiving the supplements was determined using Spearman's rank correlation. Based on the analysis done, no significant relationship was found between temperature, rainfall, and humidity with the incidence of maternal anemia. However, it is interesting to note that the number of pregnant women getting tested for anemia and the rate of those receiving supplements are associated with the amount of rainfall and temperature.

Conclusion : Overall, the study shows no direct relationship between the incidence of maternal anemia with the selected climatic variables. Significant associations were noted between the rate of testing and the rate of receiving supplements with the selected climatic variables. Further observational studies are needed to verify the findings of this retrospective analysis.

Keywords : Anemia, Temperature, Rainfall, Humidity

PP17-5

Diagnostic reliability of Mentzer index for beta-thalassemia trait: A systematic review and meta-analysis

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Background : The Mentzer Index is a tool which relies on values of RBC and MCV that are readily available in a complete blood count test result, making it cost-efficient and useful in diagnosing β-thalassemia trait. This will allow healthcare practitioners to diagnose patients more easily, resulting in timely interventions and appropriate therapy for those affected by this genetic condition. A systematic review for the Mentzer Index is essential to comprehensively assess its clinical and prognostic value in diagnosing β-thalassemia trait.

Method : PRISMA guidelines was utilized to assess relevant journals from Pubmed, Science Direct, Web of Science, and Google scholar databases, available until June 26, 2023. These studies underwent a stringent screening for methodological quality us-

ing the QUADAS-2 checklist to assess the bias and validate their acceptability in the analysis. Data were collated and analyzed to determine the diagnostic accuracy (PPV, NPV, and sensitivity and specificity) of Mentzer index test using a bivariate model.

Results : After precise validation, a total of 33 studies were deemed eligible and were included in the analysis. Based on QUADAS-2 assessment, no study showed a high risk or high applicability concern and thus, the present study is classified as a high-quality report. Based on the pooled results, the Mentzer Index has an accuracy of 0.84 (95% CI:0.80-0.88) in diagnosing β-thalassemia trait. Its sensitivity and specificity were more than 80 and are considered to be high at 0.81 (95% CI: 0.66-1.47) and 0.84 (95% CI: 0.71-1.55), respectively.

Conclusion : Overall, Mentzer Index shows a high degree of diagnostic accuracy which is promising in terms of its potential for β-thalassemia trait. As depicted by its high levels of sensitivity and specificity. Since the result of the method's application in diagnosing β-thalassemia trait is substantial, the same study should be conducted to assess its application to other forms of anemia such as iron deficiency.

Keywords : Beta-thalassemia trait, Mentzer index, Meta-analysis

PP17-6

Hydroxyurea for improving leucocytosis with a splenectomized thalassemia patient in a resource limited setting.

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Background : Thalassemia is the most common genetic blood disease in the world. It is because of the genetic defect for synthesis of alpha or beta globin chain for hemoglobin. In Cambodia, the prevalence of thalassemia is repported as around 40 %. Hydroxyurea is DNA synthesis inhibitor. Its use in sickle cell disease is approved but its use in thalassemia is not not approved yet.

Method : A 25 years old female patient came to the Hebron Medical Center, Cambodia for dyspnea and weakness. She was already diagnosed of thalassemia and got splectomy for severe splenomegaly in the previous hospital more than 7 years ago. Her initial CBC showed severe leucocytosis, thromcocytosis and severe anemia. But her general condition looks stable with stable vital signs though she looked icteric. After some weeks of follow up, we concluded that she had no severe infection and the cause of severe leukocytosis is from splectomy.

Results : After using Hydroxyurea 500mg/day, the symptoms of dyspnea, chest discomfor were reduced. The WBC count, platelet count was decreased and the RBC count is silightly increased. The patient can work without the blood transfusion though her hemoglobin is around 6.9 mg/dL.

Conclusion : Hydroxyurea could be considered for the thalassemia patients with severe leucocytosis and thrombocytosis after splectomy. It can improve qulaity of life by reducing the leucocytosis related symptoms and reduce the blood transfusion. But its use should be carefully monitored and needs further evidence of benefit in the long term use for thalassemia patients.

Keywords : Hydroxyurea, Thlassemia, Splenectomy, Leucocytosis

PP17-7

Classification and prognostic stratification based on genomic features in myeloidysplastic neoplasms, myeloproliferative neoplasms and their overlapping conditions

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Background : Genomic classification has emerged as the predominant paradigm in hematologic malignancies; however, the current classification system continues to prioritize clinical attributes in the diagnosis of Myeloproliferative Neoplasms (MPN), Myelodysplastic Neoplasms (MDS), and their overlapping diseases. Here, we aimed to describe the genomic landscape and clusters of MPN and/or MDS, in order to identify potential diagnostic and prognostic information, thereby contributing to the development of a more refined classification system.

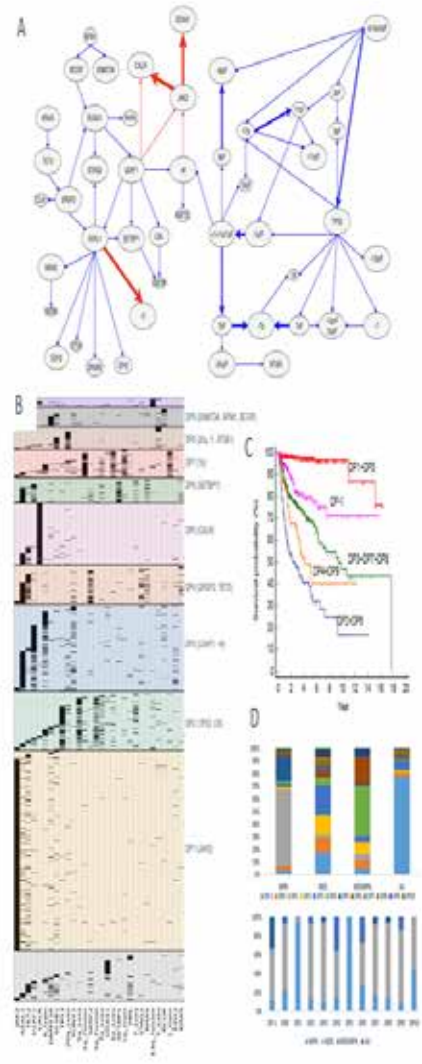
Method : Genomic data encompassing 84 genes and cytogenetics, along with clinic-laboratory information from 1,585 patients diagnosed with MPN (n=715), MDS (n=698), MDS/MPN (n=78), and Aplastic Anemia (n=94) according to the WHO 2022 classification, were compiled from the Clinical Data

Warehouse of the Catholic Medical Center. Bayesian network analysis and the Dirichlet process were performed to identify genomic associations and subgroups. Survival analyses were conducted using the Kaplan-Meier method and the log-rank test.

Results : A normal karyotype was reported in 1,066 patients, and 1,271 patients presented with at least one mutation (median: 2, 1-8). Thirty-two types of chromosomal abnormalities and 29 mutated genes were recurrently found (>1%). In the Bayesian network analysis using recurrent genomic events, JAK2, CALR, and DDX41 occurred mutually exclusive. BCOR mutation co-occurred with NPM1 and DNMT3A. TP53 mutation showed significant associations only with chromosomal events (Fig.1A). The Dirichlet process (DP) identified 9 distinct genomic clusters (Fig.1B). MPN-like clusters included DP1 (JAK2) and DP5 (CALR) and demonstrated excellent survival outcomes. MDS/MPN-like clusters were DP4 (SRSF2, TET2) and DP6 (SETBP1, ASXL1). MDS-like clusters were DP3 (U2AF1, +8), DP2 (TP53, complex karyotype), DP7, and DP8 (1q, 20q, -Y). In survival analysis, DP2 and DP6 had the worst outcomes, whereas DP4 and DP9 were intermediate, and DP3, DP7, and DP8 had better outcomes (Fig.1C-D).

Conclusion : Using a computational approach, we defined genomic clusters that are deeply characterized by specific phenotypes and prognoses

Keywords : Genomic classification, Myeloproliferative neoplasms , Myelodysplastic neoplasms, Bayesian network, Dirichlet process



PP17-8

Epidemiology and clinical aspects of hematology malignancies in Cote d'ivoire

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Background : The cancer number is increasing in the word. The hematology malignancies include many disease divided to lymphoproliferatifs syndrome, myeloproferative syndrome and myelodysplasique syndrome incidence also are going higher. If the stastitics are well knowned in develop countries the situation is quite different in developing countries particular in Côte d'Ivoire. The authors show the epidemiology and clinical aspects of hematology malignancies in Abidjan for better follow up.

Method : This retrospective study concern patients with diagnostic of hematology malignancies follow from 2017 January 1st to 2021 December 31 at Cocody teaching hospital and the center national radiotherapy and medical oncology. The technic of diagnostic were bone marrow smear cytometry immunochemistry karyotype.

Results : We found 168 cases of hematology malignancies (8,81%) meaning 33,6 cases per year. Concerning lymphoproliferative Syndrome and Myeloproliferative syndrome we noted a sex ratio of 1,7 and 21. The average age of LPS was 49,42 years; the patients between 50-60 years where the most common with 32,1% The average age of MPS 48,4 years with the limit of 19-70 years the average age for the acute leukemia was 47 years. The agricultures workers was the most Common with 17,9%. Concerning the incidence of hematology malignancies lymphoproliferative syndrome (LPS) was found with 79,8% follow by Myeloproliferative syndrome (MPS). Among LPS non Hodgkin lymphoma non Burkitt was the most representative with prevalence of 51,8% but CML was the most important of MPS. The period from first symptom and 1st medical check-up was between one to three months. Poly adénopathy and fever were the frequent symptom founded at 56%. The laboratory specific exam for the diagnostic of LPS was immunochemistry, karyotype and molecular biology for MPS.

Conclusion : The hematology malignancies in Côte d'Ivoire even though underestimate the incidence is increasing.

Keywords : Epidemiology, Hematology malignancies, Cote d'ivoire

PP17-9

AI-powered precision: Elevating cell enumeration with innovative applications

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Background : Cell counting is an important test in the field of hematology laboratory. The standard method for cell counting is using a manual hemocytometer. However, due to the skill and expertise limitations of the analysts, there is a possibility of the result errors occurring. Presently, automated cell counting machines have been introduced as an alternative but it has some limitations. This leads to the objective of this study, which is the development of a cell counting application using Artificial Intelligence (AI) and the assessment of its quality.

Method : The application was developed for evaluate the number of red blood cells, nucleated cells, and abnormal cells from pictures using Roboflow and YOLOv5 programs, and its performance was tested using Google colab.

Results : The results showed this application's overall precision, recall, and mean average precision was 93.0%, 93.5%, and 95.5%, respectively. Moreover, application was evaluated a cell count and compared to experts, there was no statistic significant differences (p=0.20). When the application was tested for cell count with ascitic fluid from patients, it was found an accuracy of cell counting approximately 91.35%.

Conclusion : This study demonstrates that the innovative application for cell counting using Artificial Intelligence can be further developed for widespread use in laboratory settings.

Keywords : Cell counting, Artificial intelligence, Hematology laboratory

PP17-10

Establishment of hereditary hemolytic anemia registry in Korea

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Background : Hereditary hemolytic anemias (HHA) are rare in Korea, but a rising prevalence attributed to diagnostic advancements and immigration is noted. The RBC Disorder Working Party (WP) of the Korean Society of Hematology (KSH) played a crucial role in establishing diagnostic procedures, and pediatric HHA studies from 1997 to 2016 revealed an increase in hemoglobinopathies and enzymopathies, highlighting the prevalence of membranopathies. Recognizing complications of HHA, the necessity of a patient registry underscores the importance of proactive measures for tailored care.

Method : The RBC Disorder WP the KSH and the Benign Hematology Committee of the Korean Pediatric Hematology-Oncology Group (KPHOG) collaborated to establish a secure eCRF system for the HHA Registry. Criteria and methods for item selection were discussed and documented with input from the KPHOG Clinical Research Support Center. The myTrial System, certified for quality, ensures stability and security, utilizing the KT Cloud Server for server hardware and security.

Results : Demographic details and clinical characteristics of HHA patients were expert-selected fields in the eCRF. Both retrospective and prospective patient registration is allowed across multiple Korean institutions. To ensure precision, a device confirms entries beyond normal ranges. The system also permits text input for bone marrow and blood smear results. Auto Queries streamline data entry, supplemented by periodic SAS Program queries for unverifiable aspects. Post-study, data will be stored for three years at KPHOG. The estimated annual registry entries include 30-40 HHA patients from over 30 hospitals.

Conclusion : Collaborative efforts between RBC Disorder WP of the KSH and Benign Hematology Committee of the KPHOG established the HHA Registry eCRF system in Korea, a milestone in understanding HHA. Active engagement of researchers presents a future challenge, envisioning HHA patient participation from various hospitals, poised to contribute significantly to global epidemiological research, advancing HHA understanding, diagnosis, and treatment.

Keywords : Hereditary hemolytic anemia, Registry, Korea

PP17-11

Pro-adrenomedullin and procalcitonin as biomarkers for predicting infections and response to antimicrobial therapy in febrile neutropenic children

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Background : Febrile neutropenia (FN) is an oncological emergency. The major limitation of using cultures is the longer time required to identify the pathogen and the risk of false-positive cultures. Therefore, this study aimed to evaluate the effectiveness of biomarkers [Proadrenomedullin (pro-ADM) and procalcitonin (PCT)] in children with FN.

Method : Children of ≤18 years of age with cancer having FN were enrolled. Blood samples were collected for pro-ADM and PCT during FN on D1, D3-4, and D7-10 days of antibiotics. The primary objective was to compare the diagnostic performance of proADM and PCT in diagnosing clinically documented infections (CDI)/

microbiologically documented infections (MDI)/fever of no focus (NF). The secondary objective was to compare the prognostic utility of proADM and PCT in identifying those with adverse outcomes.

Results : A total of 326 patients were recruited in this study. The median age of this cohort was 5 years (IQR:3; 8 years). The commonest malignancy was acute leukemia. Median PCT (IQR) (ng/ml) on D-1, D3-4 and D 7-10 were 0.30 (0.1-1.67), 0.17 (0.06;0.68) and 0.11 (0.04; 0.51) and median ProADM (pmol/L) were 28.1 (12.4; 62.9) 27.2 (11.4; 61.4) and 29 (13.3; 64.9) respectively. Patients with MDI had higher PCT and ProADM values on D1 of FN, but these did not differentiate between MDI, CDI, and NF. On D7-10 of FN, the PCT was significantly higher in MDI patients (P=0.003). The ProADM on D1, D3-4, and D7 did not differentiate between MDI, CDI, and NF. The level of PCT on D1 (P=0.0006), D3-4 (P=0.002), D7-10 (P=0.002), and ProADM on D1 (P=0.02) predicted the adverse outcome of patients on D-30 of enrollment.

Conclusion : In children with cancer, on D7-10 of FN, the PCT was significantly higher in MDI patients. The PCT on D1, D7-10, and ProADM on D1 of FN predicted the adverse outcome on D-30 of follow-up.

Keywords : Febrile neutropenia, Leukemia, Children, Pro-adrenomedullin, Procalcitonin

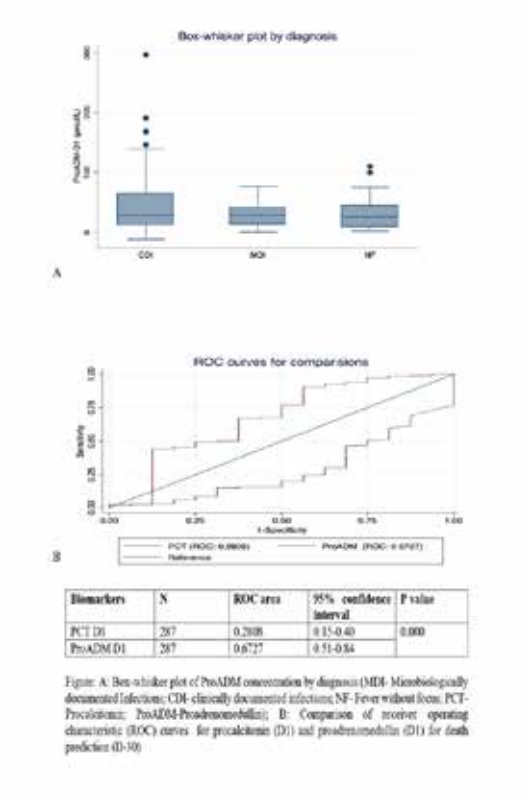
A

Biomarkers	CDI	MDI	NF	P-value
D-1 of FN	n=251	n=22	n=31	
Median PCT (IQR) (ng/ml)	0.3 (0.1; 1.69)	0.55 (0.22; 1.43)	0.14 (0.06; 1.24)	0.07
Median ProADM (IQR) (pmol/L)	28.4 (12.5; 64.9)	28.6 (13.5; 80.9)	26.4 (9; 43.7)	0.34
D3-4 of FN	n=225	n=22	n=31	
PCT (ng/ml)	0.16 (0.06;0.6)	0.41 (0.09; 2.56)	0.1 (0.05; 0.23)	0.06
ProADM (pmol/L)	27.2 (11.3; 68.8)	19.2 (12.6; 33)	29.7 (11; 49)	0.36
D7-10 of FN	n=167	n=20	n=23	
PCT (ng/ml)	0.1 (0.05; 0.48)	0.56 (0.11; 1.8)	0.08 (0.02; 0.22)	**0.003**
ProADM (pmol/L)	28.9 (13.7; 65.9)	36.5 (17.9; 67.3)	21.3 (10.7; 55)	0.55

B

Biomarkers	Day-30 outcome (n=306)		p-value
D-1 of FN	Alive (n=286)	Mortality (n=18)	
Median PCT (IQR)	0.25 (0.09; 1.24)	4.7 (0.31;18)	**0.0006**
Median ProADM (IQR)	28.4 (13; 63.5)	14.6 (2.2; 31)	**0.02**
D3 of FN	Alive (n=265)	Mortality (n=13)	
Median PCT (IQR)	0.16 (0.06; 0.54)	1.28 (0.43; 24)	**0.002**
Median ProADM (IQR)	27.2 (11.6; 61.7)	13.6 (0.74; 42)	0.21
D7 of FN	Alive (n=200)	Mortality (n=10)	
Median PCT (IQR)	0.10 (0.04; 0.38)	2.8 (0.7;10.5)	**0.002**
Median ProADM (IQR)	29 (13.7;67)	25.6 (12.3; 46)	0.62

Table: A: Comparison of procalcitonin and proadrenomedullin levels in patients with clinically documented infections (CDI), microbiologically documented infections (MDI), and those with fever with no focus (NF); B: Correlation of biomarkers on D-1 of febrile neutropenia and final outcome (D-30); FN- Febrile neutropenia; MDI- Microbiologically documented Infections; CDI- clinically documented infections; NF- Fever without focus; PCT-Procalcitonin; ProADM-Proadrenomedullin



Biomarkers	N	ROC area	95% confidence interval	P value
PCT D1	287	0.2808	0.15-0.40	0.000
ProADM D1	287	0.6727	0.51-0.84	

Figure: A: Box-whisker plot of ProADM concentration by diagnosis (MDI- Microbiologically documented Infections; CDI- clinically documented infections; NF- Fever without focus; PCT-Procalcitonin; ProADM-Proadrenomedullin); B: Comparison of receiver operating characteristic (ROC) curves for procalcitonin (D1) and proadrenomedullin (D1) for death prediction (D-30)

PP17-12

Elevated IL-6 as a biomarker of immune reconstitution inflammatory syndrome in pediatric leukemia patients with invasive disseminated candidiasis

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Background : Immune reconstitution inflammatory syndrome (IRIS) is known to occur during the course of invasive fungal diseases, defined as a clinical worsening or a new presentation of the infection after the reversal of immune deficiency. The purpose of this study was to observe changes in cytokine levels during IRIS in children diagnosed with proven disseminated candidiasis acquired during treatment of underlying hematologic malignancy.

Method : Specimen of children <18 years old with underlying hematologic malignancies, diagnosed with proven disseminated

candidiasis was collected prospectively. Retrospective analyses of pro-inflammatory cytokines (IL-2, IL-6, IFN-γ, TNF-α, and IL-17) and anti-inflammatory cytokines (IL-10, IL-12) were done from body fluids during episodes of clinical worsening or new-onset fever.

Results : A total of 5 cases were included in the analyses: four with underlying acute lymphoid leukemia (ALL) and one with juvenile myelomonocytic leukemia (JMML). Candidiasis involvement was observed in the following organs: lungs (n=4, 80%), liver (n=3, 60%), kidney (n=2, 40%), blood (n=2, 40%), spleen (n=1, 20%), and eyes (n=1, 20%). Compared to disease controlled states, patients with suspected IRIS had significantly elevated IL-6 (14.95 pg/mL vs 411.65pg/mL, P=0.008). IL-10 levels were elevated in disease progression state. The IL-6/IL-10 ratios in patients with IRIS were significantly higher than in patients with disease controlled states (median ratio 15.1 vs 0.6, P=0.006).

Conclusion : IL-6 elevation and IL-6/IL-10 ratio elevation may be a biomarker for IRIS in children with invasive disseminated candidiasis.

Keywords : Leukemia, Fungal infection, Immune reconstitution inflammatory syndrome, Cytokine

PP17-13

Unleashing the potential of exosomal *MALAT1* lncRNA in liquid biopsy: A promising approach for Wilms' tumor

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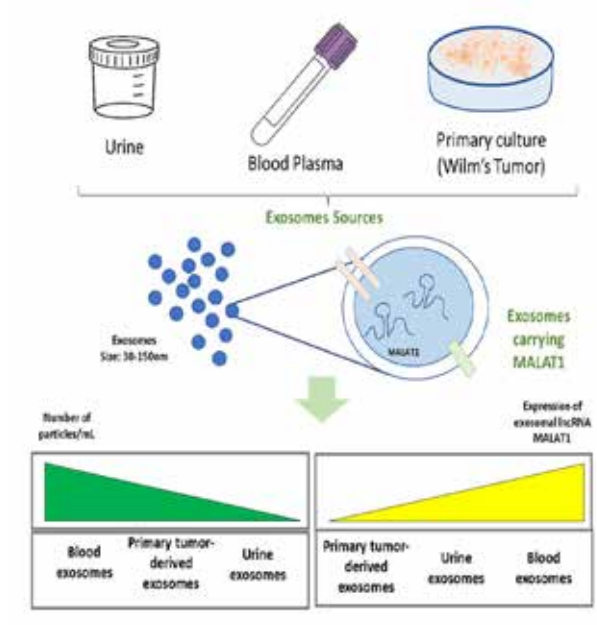
Background : Wilms' tumor (WT) is an infrequent pediatric kidney cancer originating from embryonal cells. Exosomes, cell-produced extracellular vesicles, facilitate cellular communication through biomolecule transport. Long non-coding RNAs (lncRNAs), promising cancer biomarkers, are explored for WT diagnosis, prognosis, and monitoring. This study posits that dysregulation of the metastasis-associated lung adenocarcinoma transcript-1 (MALAT1) lncRNA in WT may impact cellular transformation and the microenvironment.

Method : We assessed MALAT1 expression in 30 Wilms' tumor (WT) samples and corresponding normal tissues via quantitative PCR (qPCR). Exosomes were isolated from primary tumor cells, urine, and plasma using a precipitation and affinity-binding kit. Characterization of isolated exosomes employed transmission electron microscopy (TEM), nanoparticle tracking analysis (NTA), and dynamic light scattering (DLS). MALAT1 expression in these exosomes was quantified by qPCR.

Results : In primary culture, exosome count was 9.01×10^8/mL, urine showed 1.64×10^8/mL, and plasma recorded 4.65×10^8/400 µL. Total RNA yield: 1.28 µg (primary-cultured supernatant: 1mL), 1.47 µg (urine: 1mL), and 1.65 µg (plasma: 400µL). Significantly, MALAT1 lncRNA expression was downregulated in WT samples (p=0.008). Interestingly, exosomes from primary culture and urine exhibited similar MALAT1 expression (p=0.9267). Notably, plasma exosomes demonstrated higher MALAT1 levels compared to primary culture (p=0.0102) and urine (p=0.0022).

Conclusion : This study constitutes the initial demonstration of MALAT1 lncRNA presence in diverse samples, both invasive and non-invasive, from Wilms' tumor (WT) patients. The observed downregulation of MALAT1 in WT samples indicates a potential involvement in the pathogenesis and progression of the disease. The discovery of exosomal MALAT1 underscores the diagnostic and prognostic potential of exosomes and lncRNAs in WT. Subsequent research is imperative to delineate the functional significance of MALAT1 in WT and evaluate its viability as a therapeutic target.

Keywords : Wilms' tumor, LncRNA, MALAT1, Exosome, Liquid biopsy



PP17-14

Clinical characteristics and management outcomes of patients with tumors of the hematopoietic and lymphoid tissues at Mittaphab hospital, Vientiane capital, LAO PDR

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Background : Tumors of the hematopoietic and lymphoid tissues (THL) is a major cause of morbidity and mortality in the world. However, the clinical features, types and treatment outcomes vary from one to another country. Nothing is known in Lao PDR, a resource-limited regarding.

Method : A retrospective study was conducted on a sample of 183 THL adult patients who were admitted at the internal medicine ward and Lao cancer center of Mittaphab hospital between January 2020 and 31 July 2022. Their socio-demographic and clinical characteristics, management and initial outcome were analyzed.

Results : 183 THL patients were diagnosed during the study period with mean age of 46.61 years old (18-92 years old) and 59.02% of male. Leukemia (58.46%) was the most common, followed by lymphoma (26.22%) and multiple myeloma (5.46%). The mean duration of illness was 11.8 weeks (range: 1-99 weeks). For staging, all of MM and CLL presented with late stage and 54% for lymphoma. The most common initial signs and symptoms were weight loss (75.96%), followed by fatigue (74.86%), hepatomegaly (33.88%), splenomegaly (37.16%), lymph node enlargement (31.69%), bleeding (31.15%) and fever (25.14%). Most of cases were diagnosed based on morphology exam. Of this, 50.27% had severe anemia (HB<8g/dl) and 42.62% had low MCV. 49.8% had Leukocytosis and 49.73% for thrombocytopenia. 91.26% received the supportive treatment; and 54.64% received the standard treatment. Of this, 70.49% were better/stable status. 8.20% were death, and 21.31% were discharged without recovery. The factors associated with good outcome were receiving standard treatment, older age (>49 years) and having no chest pain and no hepatomegaly.

Conclusion : Tumors of the hematopoietic and lymphoid tissues were diagnosed at late stage. This study highlights the importance of early diagnosis and appropriate treatment in order to improve the management outcome of THL patients.

Keywords : Tumors of the hematopoietic and lymphoid tissues (THL), Clinical characteristics, Management outcome, Lao PDR

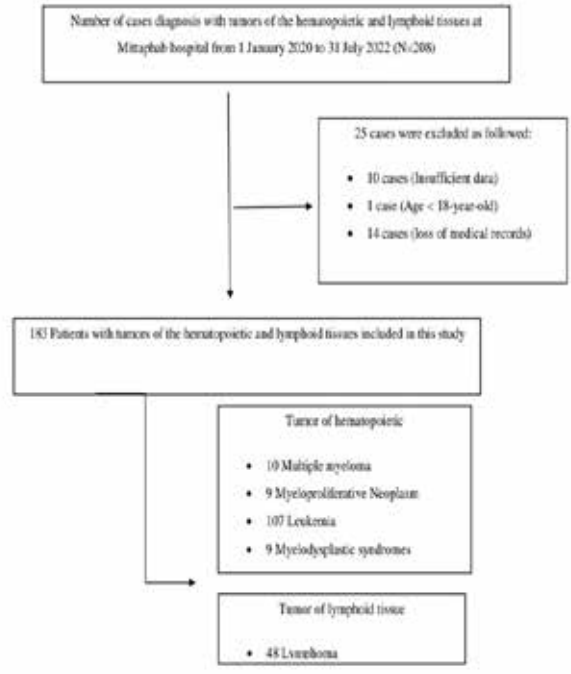

Figure 27: flow chart of THL patients included in this study

Table 30: Initial Clinical and management outcome of patients with tumors of the hematopoietic and lymphoid tissues

Variables	Classification of THL								
Initial management outcome	Total (183)	MM (10)	MPN (9)	Lymphoma (48)	AML (36)	CML (44)	ALL (14)	CLL (13)	MDS (9)
Better/Stable	70.49	70.00	88.89	75.00	52.78	77.27	50.00	76.92	88.89
Death	8.20	0	0	6.25	16.67	9.09	7.14	7.69	0
Go home	21.31	30.0	11.11	18.75	30.56	13.64	42.86	15.38	11.11

PP18-1

Do gender equality on mother bargaining power really matter on the prevalence of anemia among children?

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Background : Anemia in children is often overlooked. In Indonesia, anemia incidence among pregnant women reaches 55% and aged 0-17 increased by 48% compared to the past two decades due to poor socioeconomic status and lack of proper nutrition knowledge. Parents, especially mothers, play a role in preventing anemia from an early life stage through "The First 1000 Days" program (MoH, 2020). Study shows that the more bargaining power a mother has, the higher the nutritional status of children (Lepine & Strobl, 2013; Dewi, 2020).

Method : Using the longitudinal data of the Indonesia Family Life Survey (IFLS) wave 5, this study aims to examine the status of mothers' bargaining power on the prevalence of anemia among children and adolescents aged 0-17.

Results : This study uses women's share income in the household and maternal knowledge as a proxy variable for women's bargaining power. There was a positive and significant relationship between the mother's shared income with total household expenditures household for health care and food intake. Mother bargaining power in household decision-making has a positive impact on the children's nutritional status compared to mothers who were not involved at all (0.175 standard deviations). Social capital has a positive relationship with the mother's knowledge and education level (0.012 standard-deviation). However, parent working status in the formal sector has a negative effect on the anemia prevalence among children (1.90 times). This is due to the trade-off between the role of work and the domestic role of children, which causes an increase in the probability of undernutrition in children (-0.03 standard-deviation). Working fatigue during pregnancy increases anemia prevalence among pregnant women in the second trimester (0.038 standard-deviations).

Conclusion : Gender inequality reduction seems promising to affect higher nutritional status among children. It is required to provide sufficient facilities and proper dietary intake for working mothers to tackle the trade-off problem.

Keywords : Children anemia, Mother bargaining power, Household decision making, Maternal knowledge, Nutritional status

PP18-2

Ginseng as an antidepressant to improve the quality of life in hematologic malignancies: A systematic review

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Background : As we know, cancer is a non-communicable disease followed by a condition where there is an abnormality of cell growth that grows rapidly and uncontrollably. Based on data obtained from the World Health Organization noted that based on prevalence data for the last 5 years, the incidence of malignancies in Asia occupies 33.3% of the world's population. Patients with malignancies are usually closely related to the incidence of anxiety disorders due to the shadow of low life expectancy. Therefore, we tried to find out more about natural, easily available drugs to prevent cancer proliferation and can minimize the incidence of depression in patients.

Method : This literature research was conducted using PubMed, ElSevier, and ScienceDirect by retrieving data from the last ten years of any literature used. The terms used were mental health, hematologic malignancies, ginseng, and antitumor. We found that the terms were interrelated.

Results : From the results of the literature study, it was found that ginseng can decrease the risk of lymphatic and hematopoietic tissue malignancy. Ginseng contains ingredients to suppressed hematologic malignancies and depression. One of them is ginsenosides as an antitumor. Ginseng harvested at the age of 5-6 years is considered to have the best quality because it has higher levels of ginsenosides. Ginseng also contains polysaccharides and pectin which has been shown to inhibit the action of galectin-3 which is a β-galactoside binding protein associated with biomarkers of tumor formation. For antidepressant, ginseng also have dammarane sapogenins which are more easily absorbed by the body compared to ginsenosides which can increasing serotonin levels.

Conclusion : From the results of the study, it can be concluded that the content of ginseng in the form of ginsenosides, polysaccharides, pectins, and dammarane sapogenins can work to improve the quality of life of patients with hematologic malignancies by working as antitumor and antidepressant.

Keywords : Mental health, Hematologic malignancies, Ginseng, Antitumor

PP18-3

Long-term outcomes of coronavirus disease 2019 and risk factors forprolonged SARS-CoV-2 infection in lymphoma patients: Multicenter, retrospective cohort study

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Background : Patients with hematologic malignancies exhibit persistent severe acute respiratory syndrome coronavirus 2 positivity over long periods after coronavirus disease 2019 (COVID-19) diagnosis. However, the frequency of, risk factors for, and prognosis of prolonged COVID-19 in immunocompromised patients remain unclear. Therefore, we investigated the long-term outcomes of COVID-19 in lymphoma patients and identified the associated factors and impact of prolonged COVID-19 on mortality.

Method : A multicenter retrospective cohort study of 583 lymphoma patients was conducted in 3 tertiary hospitals in South Korea.

Results : Patients receiving lymphoma treatment who were quarantined after obtaining a diagnosis of COVID-19 by PCR or antigen test from August 2021 to September 2022 were examined. Results Overall, 115 patients (19.7%) were diagnosed with COVID-19. Among 77 patients with clinical data, 24 had prolonged COVID-19. Patients in the prolonged COVID-19 group showed higher rates of receiving rituximab maintenance therapy following bendamustine and rituximab (BR) treatment for follicular lymphoma. This group did not show significant differences in clinical presentation within 30 days of COVID-19 diagnosis; however, it showed higher rates of re-admission due to COVID-19 pneumonia compared with the non-prolonged COVID-19 group. BR treatment followed by rituximab maintenance therapy is one of the risk factors for persistent PCR positivity, delayed or persistent pneumonia, and COVID-19 related admission after quarantine period. Prolonged COVID-19 was an independent risk factor for 1-year mortality.

Conclusion : Prolonged COVID-19 was more frequent in lymphoma patients who received BR treatment followed by rituximab maintenance therapy and associated with unfavorable long-term outcomes and higher 1-year mortality.

Keywords : Lymphoma, COVID19, Bendamustine

Table 1. Risk Factors for Each Long-term Outcomes

PCR positive (more than 30 days after diagnosis)	(+) n=17	(-) n=60	p-value	Odds Ratio	CI	p-value
Age>=65	5 (29.4)	18 (30.0)	0.963			
BR Chemotherapy	9 (52.9)	15 (25.0)	0.028	3.375	1.104-10.317	0.033
Total COVID-19 Pneumonia	**(+) n=36**	**(-) n=41**	**p-value**			
Age>=65	15 (41.7)	8 (19.5)	0.064	3.326	1.097-10.081	0.034
BR followed by Rituximab maintenance	11 (30.6)	4 (9.8)	0.021	4.011	1.046-15.382	0.043
COVID-19 Pneumonia within 30 days	**(+) n=18**	**(-) n=59**	**p-value**			
Age>=65	11 (61.1)	12 (20.3)	0.001	6.155	1.968-19.247	0.002
BR followed by Rituximab maintenance	3 (16.7)	12 (20.3)	1.000			
Delayed/persistent COVID-19 Pneumonia after 30 days	**(+) n=18**	**(-) n=59**	**p-value**			
Age>=65	5 (27.8)	18 (30.5)	0.825			
BR followed by Rituximab maintenance	9 (50.0)	5 (10.2)	<0.001	8.833	2.527-30.879	0.001
Admition due to COVID-19 after quarantine period	**(+) n=15**	**(-) n=62**	**p-value**			
Age>=65	4 (26.7)	19 (30.6)	1.000			
BR followed by Rituximab maintenance	9 (50.0)	5 (10.2)	<0.001	11.1	2.758-44.678	0.001

CI: Confidential Interval, PCR: Polymerase Chain Reaction, COVID-19: Coronavirus disease 2019, BR: bendamustine+rituximab

PP18-4

Role of wearable technology and geo-fencing device in management of physiological data and quality of life relation to myelodysplastic syndrome patients

Vikas Sharma[1,2*], Madhu Gautam[1], Sagar Lavania[2]

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[2] Neurology, S N Medical College And Hospital, Agra, India

Background : Management of myelodysplastic syndromes (MDS) is most often intended to slow the disease, ease symptoms and prevent complications. Common measures include blood transfusions and medications to boost blood cell production. To study role of wearable devices (fire-boltt quantum watch) and geo-fencing technology to monitor daily life routine activities on health and quality of life data in MDS patients in Gurugram city, India .

Method : Total of 68 MDS patients were taken as subject with an equal ratio of male and female. Wearable monitoring devices like fire-boltt quantum watch and geo-fencing device were put on the wrist of MDS patients for 30 days and a questionnaire was filled out by each patient. In all subjects, blood pressure, blood glucose was measured on daily basis with day to day data of their monitoring of step count, calorie burnt, motion time, sleep monitoring, calorie consumption, monitoring heart rate

to know daily routines and recording them for health purpose. Wearable bands, automatically provides a cueing sound with sensing alert when patients move out of the geo-fenced area and which stays until the subject resumes walking in virtual boundary.

Results : Wearable device reading showed that there was a significant normal heart rate ($p<0.05$), increase calorie burnt with a significant decrease of blood glucose and blood pressure levels ($p<0.01$), and increased significantly ($p<0.05$) sleep duration in active physically workout, include walking in MDS patients compared to less physically workout MDS patients, identified by professional physiotherapists. There is significantly normalize in memory loss and wandering events after one month with changing lifestyle routine among MDS patients.

Conclusion : With this study we show that , by using, wearable device ensured online assistive feedback for MDS patients, it is possible with their health awareness, exercising and motivate further studies.

Keywords : Myelodysplastic syndrome patients, Wearable technology, Quality of life, Management

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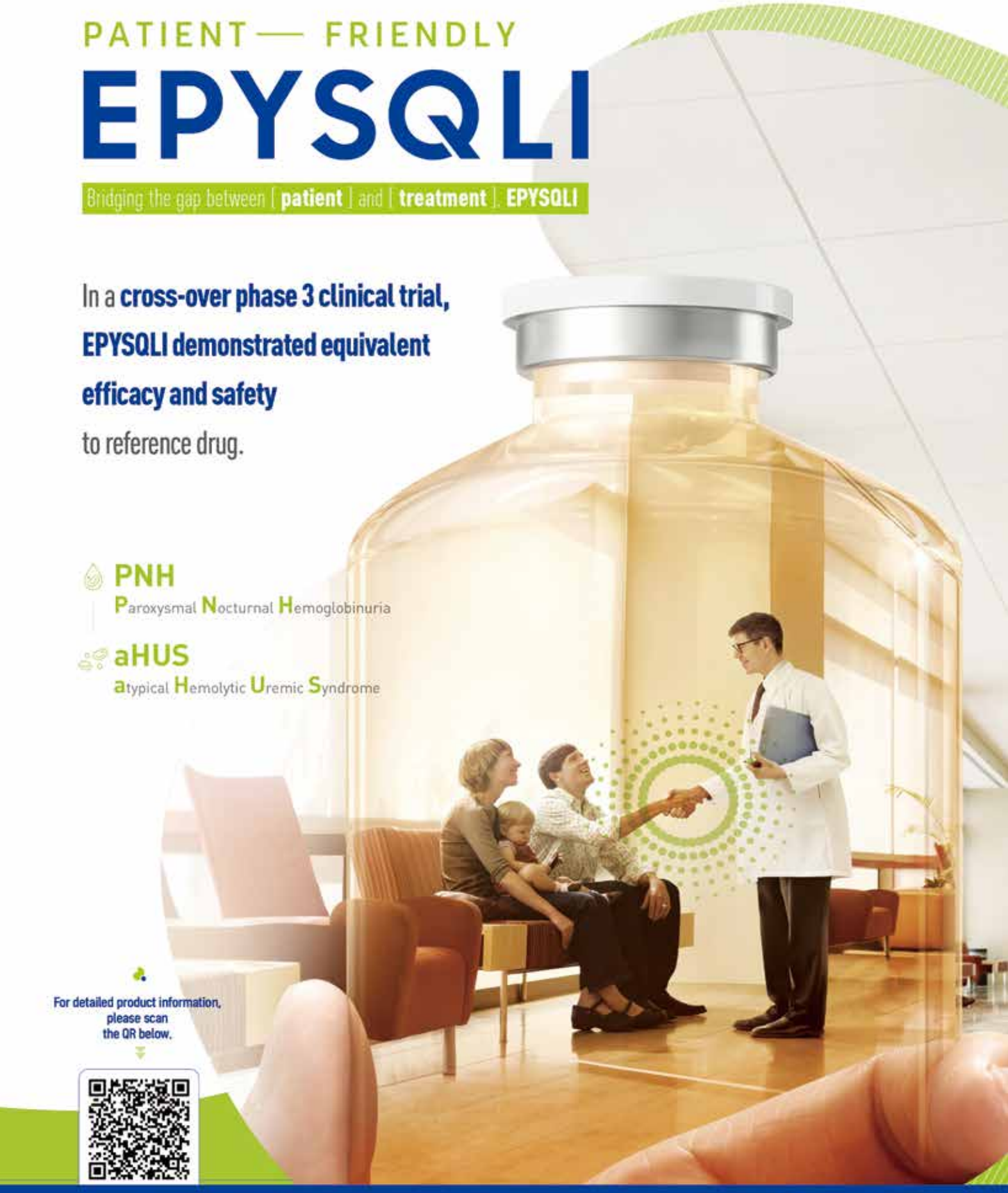

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Indication[1]

In **combination with azacitidine or decitabine** for the treatment of newly diagnosed acute myeloid leukemia (AML) in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.

Viale-A trial[2]**:** A phase III, multicenter, randomized, double-blind, placebo-controlled trial was conducted to evaluate the efficacy and safety of azacitidine plus venetoclax, as compared with azacitidine plus placebo (the control regimen) in older patients with AML.

MEDIAN OVERALL SURVIVAL[2]

Overall survival (OS)

VEN+AZA **14.7 mo** Vs. AZA+pla **9.6 mo**

VEN+AZA significantly increased mOS by 5.1mo vs AZA; OS benefit across subgroups

34.0%

Risk Reduction of mortality

HR=0.66 (95% CI: 0.52–0.85)
P<0.001

Doubled remission (CR+CRi)[2]

VEN+AZA **66%** (95% CI, 60.6 – 71.9) vs. AZA alone **28%** (95% CI, 21.1 – 36.3)

Median time to first remission (CR or CRi)[2]

VEN+AZA **1.3 mo** (range: 0.6 – 9.9) vs. AZA alone **2.8 mo** (range: 0.8 – 13.2)

Longer remission, Median duration (CR+CRi)[2]

VEN+AZA **17.5 mo** (95% CI, 13.6 – not reached) vs. AZA alone **13.4 mo** (95% CI, 9.8 – 15.5)

• The appropriate dose-modification is required for the management of adverse events.[1]

AML, acute myeloid leukemia; CI, confidence interval; CR, complete response; CRi, complete response with incomplete hematologic recovery; HR, hazard ratio; mo, month; pla, placebo; VEN+AZA, venetoclax with azacitidine. [Reference] 1. 벤클렉스타® 정 제품설명서. 개정년월일 2021년 1월 8일 2. DiNardo CD, et al. Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia. N Engl J Med. 2020;383:617-629.


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[효능·효과] · 이 약에 감수성이 있는 다음의 전신성 진균감염: 크립토콕쿠스증, 북아메리카 분아균증, 산재성 콘디다증, 피시디오이데스진균증, 아스페르길루스증, 모균증 및 일부 아메리카 점막피부 리슈마니아증 · 호중구 감소 환자의 불명열(FEVER OF UNKNOWN ORIGIN: 항생물질을 투여한 지 96시간 후에도 호전되지 않는 원인불명의 지속성 열병) · 면역기능이 있는 상인 및 소아의 내장 리슈마니아증의 1차 치료 · 면역결핍환자(HIV양성환자 등)에서 내장 리슈마니아증의 1차 치료 **[용법용량]** 30~60분에 걸쳐 점적 정맥주사. 투여용량이 5 MG/KG/DAY를 초과하는 경우에는 2시간 이상의 점적 정맥주사가 권장됨. 권장 투약농도는 암포테리신B로서 0.2~2.0MG/(역가)/ML로 환자에 따라 투여용량 조정 · 전신성 진균 감염: 체중 KG당 1일 1.0MG(역가). 필요 시 체중 KG당 5.0MG(역가)까지 증량 · 호중구 감소 환자의 불명열: 초기용량으로 1일 체중 KG당 1MG(역가), 증상에 따라 1일 체중 KG당 3MG(역가)까지 증량 · 내장리슈마니아증: 21일간 1일 체중 KG당 1.0~1.5MG(역가) 또는 10일간 1일 체중 KG당 3.0MG(역가) · 재발 위험성으로 필요에 따라 유지요법 또는 감염치료 실시 **[경고]** 일반적이고 임상적으로 명확하지 않은 전균감염증에 투여하지 않음. 진균에 대한 피부 또는 혈청 검사에 양성을 보이는 것만으로는 충분하지 않음. 세균감염, 바이러스질환 또는 일반적인 바이러스, 기생충 또는 미코박테륨 감염에 따른 불명열인 경우에는 사용하지 않도록 함. **[금기]** · 이 약 및 이 약이 성분에 과민반응 환자 **[일반적주의]** · 내성균 발현 방지 위해 감수성 확인 및 최소기간 투여 · 중증의 아나필락시 및 아나필락시양 반응 시 즉시 중지 · 혈청 크레아티닌 상승, 저칼륨혈증, 저마그네슘혈증의 발생률이 고용량 투여군에서 더 높게 나타남 · 간장, 신장 및 혈액학적 평가 정기 실시 · 신독성에 대한 고려 필요 · 당뇨 환자의 경우 백당 함유 제품임에 유의 · 신부전 과정 중 투여하지 않도록 함. **[이상반응]** · 임상시험 시 나타난 이상반응 (10% 이상: 발열, 냉감/오한, 저칼륨혈증, 구역, 구토 / 1% 이상~10% 미만: 크레아티닌 상승, BUN 상승, 저마그네슘혈증, 저칼슘혈증, 고혈당증, 저나트륨혈증, ALP 증가, 빌리루빈혈증, 간기능검사 이상, 설사, 복통, 호흡곤란, 홍조, 혈관확장, 저혈압, 두통, 요통, 흉통, 빈맥(변맥), 발진 / 0.1% 이상~1% 미만: 경련, 기관지 연축, 혈소판 감소, 아나필락시양 반응, 정맥염 / 빈도 불명확: 빈혈, 아나필락시 반응, 과민증, 심정지, 부정맥, 심부전, 신기능 저하, 혈관신경부종, 혈관근육테타(지질혈증과 관련), 근골격계 통증(관절통 또는 뼈의 통증으로 표현됨) · 시간 후 이상반응 (드물게 아나필락시양 반응, 매우 드물게 폐관부종 보고, 가끔 및 심각한 알레르기 반응) · 혈액상의 변화, 일시적인 청각장애, 이명, 시력장애, 복시, 혈압상승, 혈압저하, 부정맥, 심박동정지, 가벼적인 간효소증가(트랜스아미나제), 백혈구 감소, 무과립구증, 백혈구 증가, 호산구 증가, 드물게 가벼적인 신기능장애 · 암포테리신B 투여와 관련하여 저칼륨혈증을 동반하는 횡문근융해증이 나타날 수 있으므로 관련 증상이 나타나는 경우 투여 중지 · 연속검사 간섭: 이 약을 투여 중인 환자의 샘플을 PHOSM 분석으로 검사 시 혈청 인산염이 상승한 것처럼 보일 수 있음 **[임부, 수유부 및 소아에 대한 투여]** 임부 및 수유부, 생후 1개월 미만의 환자에 대한 안전성 및 유효성은 확립되지 않았음 **[수입자]** 길리어드 사이언스 코리아㈜, 서울특별시 중구 을지로5길 26 센터원빌딩 서관 15층 (대표전화: 02-6030-3300, 제품관련문의: 0079-814-800-9172(수신자부담)) **[문안작성년월일]** 2021. 08. 18 (AMB-2108-01)

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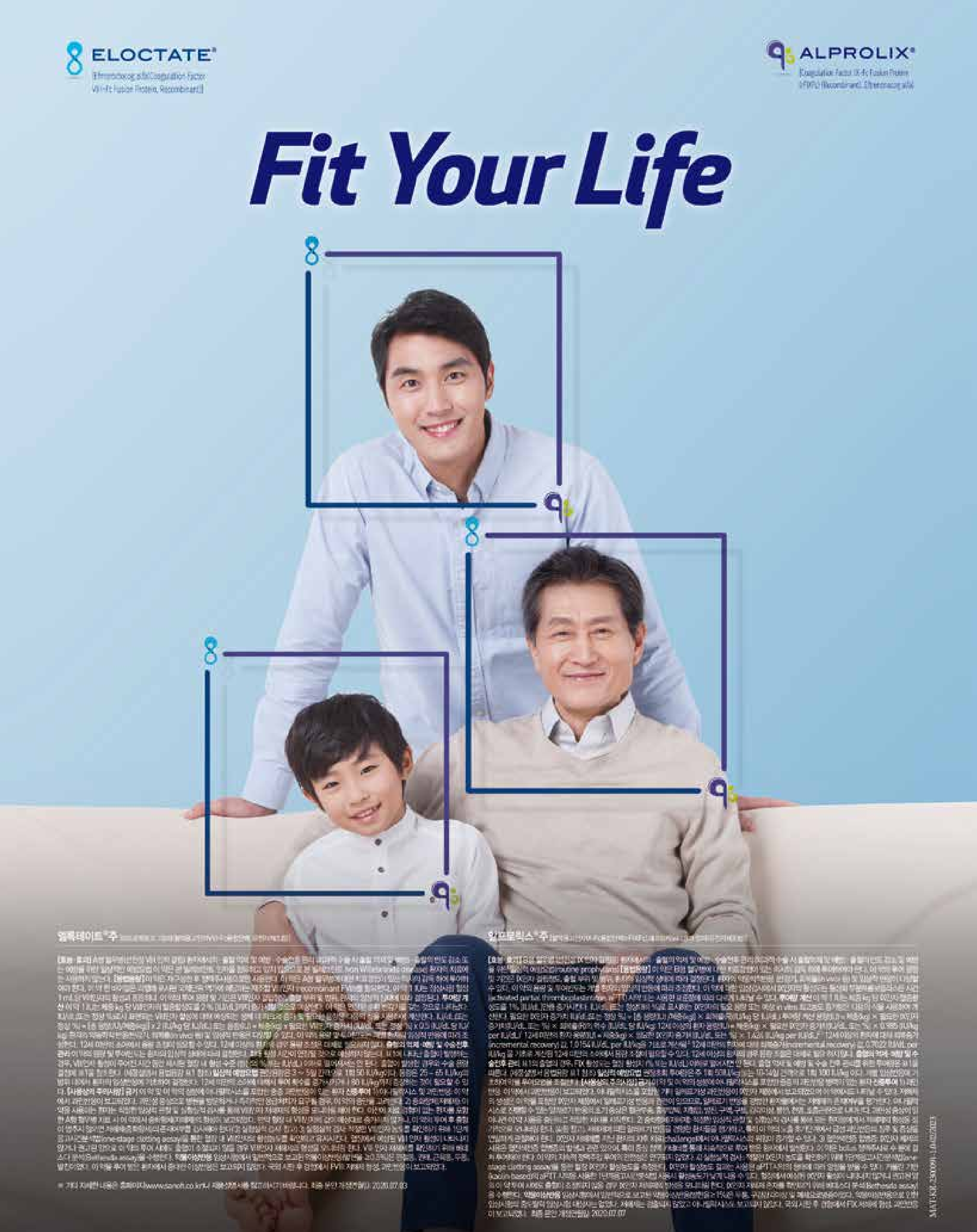

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In CMV prophylaxis

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Indication

- PREVYMIS™ is an antiviral drug indicated for prophylaxis of cytomegalovirus (CMV) infection and disease in adult CMV-seropositive recipients [R+] of an allogeneic hematopoietic stem cell transplant (HSCT).[1,2]

†[NCCN guideline] Consider letermovir as primary prophylaxis for CMV+ allogeneic HCT recipients.
CMV : cytomegalovirus; **HSCT,** hematopoietic stem cell transplantation; **R+,** recipient positive.

References 1. PREVYMIS™. Tab. Prescribing Information. MSD Korea.(Revision date 23 November 2021) **2.** PREVYMIS™ .IV. Prescribing Information. MSD Korea. (Revision date 23 November 2021) **3.** Ljungman P, *et al.* Guidelines for the management of cytomegalovirus infection in patients with haematological malignancies and after stem cell transplantation from the 2017 European Conference on Infections in Leukaemia (ECIL 7). *Lancet Infect Dis.* 2019 Aug;19(8):e260-e272. **4.** National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Prevention and treatment of cancer-related infections. Version 3. 2022.

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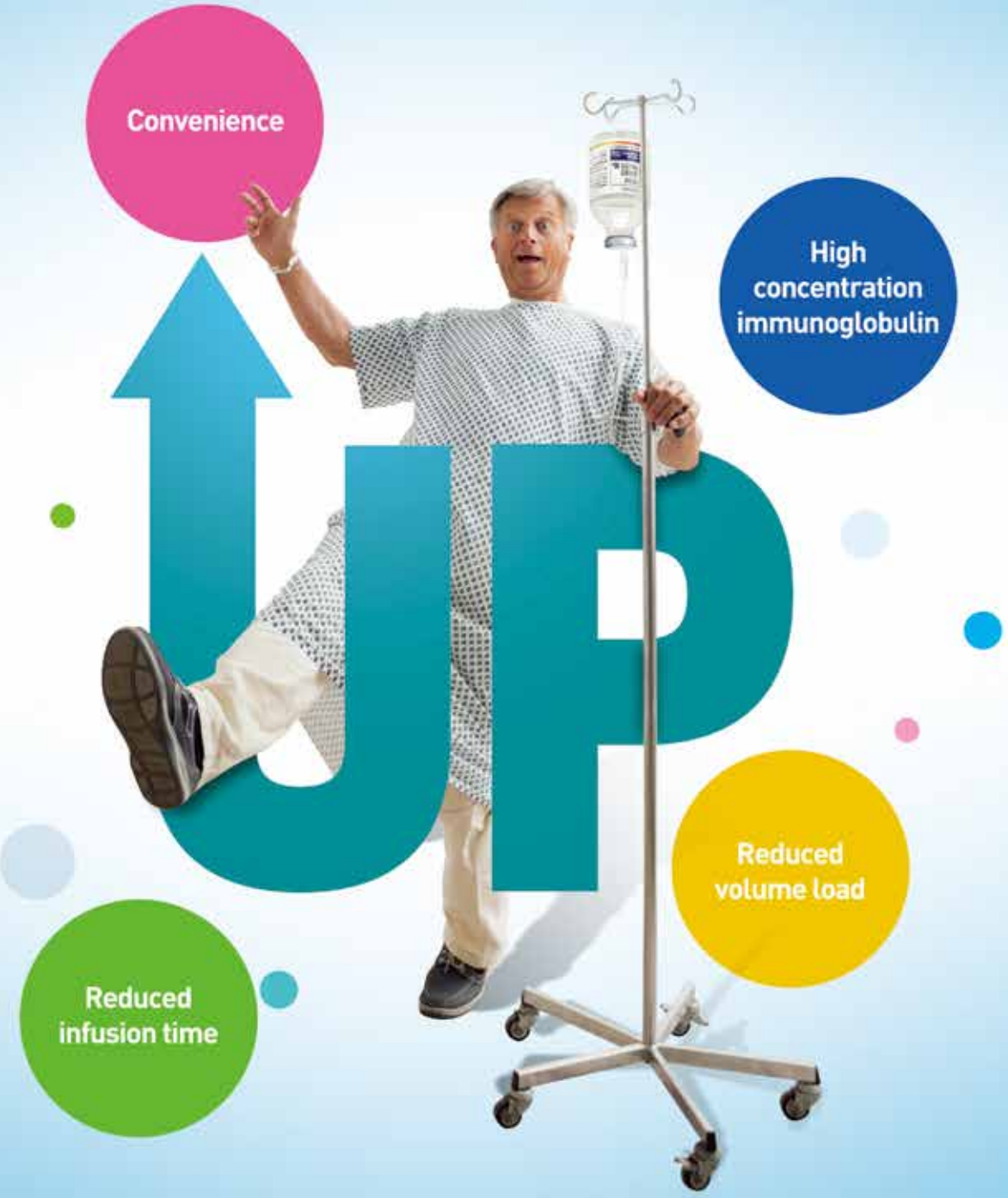

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The cornerstone of a long journey for caring for Multiple Myeloma patient's lives[1]

Reference 1. NCCN Clinical Practice Guidelines in Oncology, Multiple Myeloma, Version 2, 2024

Neulasta®
(pegfilgrastim)

FN Prophylaxis through every cycle

Neulasta® used **first and every cycle**
helps reduce the incidence of
febrile neutropenia

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ULTOMIRIS® is the Standard of care for patients with PNH[1]

울토미리스® 주
(라불리주맙)
Product
Information

※ 보다 자세한 사항은 울토미리스®주 (라불리주맙)
제품설명서 전문을 참고하시기 바랍니다.

울토미리스 주 (라불리주맙)

울토미리스 주 (라불리주맙)
100mg/mL

PNH; Paroxysmal Nocturnal Hemoglobinuria

1. Jong Wook Lee et al, The role of the alternative pathway in paroxysmal nocturnal hemoglobinuria and emerging treatments, Expert Review of Clinical Pharmacology 2022, Vol. 15, No.7, 851-861

한국아스트라제네카 서울 강남구 영동대로 517 아셈타워 21층 전화: (02)2188-0800 팩스:(02)2188-0852 https://www.astrazeneca.co.kr/

AstraZeneca

The First STAMP inhibitor[1], SCEMBLIX®

SCEMBLIX® demonstrated superior response rate and favorable tolerability by Specifically Targeting the ABL1 Myristoyl Pocket (STAMP) in BCR-ABL1[1,3]

For Adult with Ph+ CML-CP after 2 or more TKIs

- **SUPERIOR EFFICACY** (vs. bosutinib)
  - Nearly doubled MMR rate (25.5% vs. 13.2%) and higher CCyR[a] (39.8% vs. 16.1%) at Week 24[1]
  - Maintained higher MMR rate (37.6% vs. 15.8%) and CCyR[a] (39.8% vs. 16.1%) at Week 96[4]
- **FAVORABLE TOLERABILITY** (vs. bosutinib)
  - Tolerability profile consisted based on a longer median duration of exposure (23.7 months vs. 7.0 months) at Week 96[b,4]
  - Nearly 4 times lower discontinuation rate due to AEs (7.7% vs. 26.3%)[4]

[a] The median follow up was 14.9 months (Data cutoff of May 25, 2021).
[b] The median follow up was 2.3 years (Data cutoff of October 6, 2021).
[c] In patients without CCyR at baseline (SCEMBLIX®, n=103; bosutinib, n=44).
[d] The median duration of exposure in days by the data cutoff was 23.7 (range, 0.0–46.2) months for SCEMBLIX® and 7.0 (range, 0.0–44.8) months for bosutinib.

Study design[1]: [illegible] was multicenter, open-label, [illegible] with CML-CP previously treated with ≥ 2 TKIs who were resistant to or intolerant of dasatinib, nilotinib, and bosutinib and had no T315I mutation were randomized 2:1 to receive either SCEMBLIX® 40 mg twice daily (n=157) or bosutinib 500 mg once daily (n=76). The primary endpoint was the rate of MMR at week 24. Median follow-up was 14.9 months.

Study design[4]: Adults with CML-CP (also ≥2 prior TKIs with a resistance or [illegible] were randomized 2:1 to SCEMBLIX® 40 mg twice daily (n=157) or bosutinib 500 mg once daily (n=76), stratified by baseline MCyR status. After a median follow-up of 2.3 years (96.9 months), additional follow-up since the primary analysis, updated efficacy and safety results were reported as of October 6, 2021. The key secondary objective was to compare MMR rate at week 96 for SCEMBLIX® versus bosutinib.

CML, chronic myeloid leukemia; TKI, tyrosine kinase inhibitor; STAMP, [illegible] by targeting the [illegible] Myristoyl Pocket; Ph+ CML-CP, Philadelphia chromosome positive chronic myeloid leukemia in chronic phase; MMR, major molecular response; CCyR, complete cytogenetic response; CML-CP, chronic myeloid leukemia in chronic phase; MCyR, major cytogenetic response

References 1. Réa D, et al. Blood. A phase 3, open-label, randomized study of asciminib, a STAMP inhibitor, vs bosutinib in CML after 2 or more prior TKIs. 2021 Nov 25;138(21):2031-2041. **2.** (생물의약품안전처 의약품통합정보MA)(e허가)(e.mfds.go.kr) **3.** Manley PW, et al. Leuk Res. 2020 Nov;98:106456. **4.** Hochhaus A, et al. Asciminib vs bosutinib in chronic-phase chronic myeloid leukemia previously treated with at least two tyrosine kinase inhibitors: longer-term follow-up of ASCEMBL. Leukemia. 2023 Jan 30. Online Published. <doi: 10.1038/s41375-023-01829-9.>

PRODUCT INFORMATION

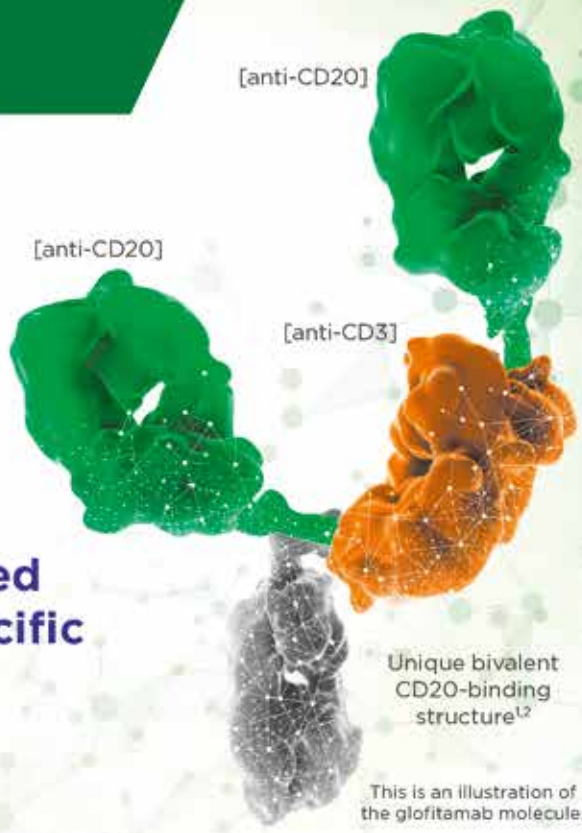
NOVARTIS

SCEMBLIX® (asciminib) 20mg, 40mg tablets

ASC20230004

COLUMVI® Now approved in 3L+ diffuse large B-cell lymphoma[1]

COLUMVI® glofitamab



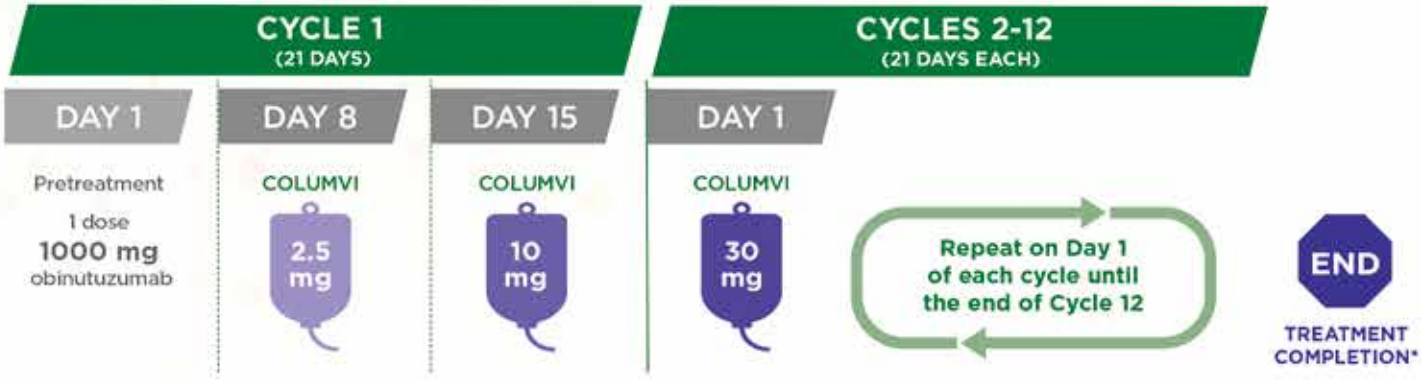
This is an illustration of the glofitamab molecule.

Durable complete remissions achieved with a unique T-cell engaging bispecific antibody[2,3]

Indication

COLUMVI as monotherapy is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma (DLBCL), after two or more lines of systemic therapy.

Dosing



COLUMVI duration of infusion
Cycles 1-2: Administer over **4 hours**† | **Cycles 3-12:** Administer over **2 hours**†

*Treatment with COLUMVI is recommended for a maximum of 12 cycles or until disease progression or unmanageable toxicity. Each cycle is 21 days.
†For patients who experience CRS with their previous dose of COLUMVI, the time of infusion may be extended up to 8 hours.
‡At the discretion of the treating physician. If the patient experienced CRS with a previous dose, the duration of infusion should be maintained at 4 hours.
-Administer COLUMVI to well-hydrated patients. Counsel all patients on the risks, signs, and symptoms of Cytokine release syndrome(CRS) and advise to seek medical attention immediately should they experience signs and symptoms of Cytokine release syndrome(CRS).

References: **1**. Columvi_Korean PI 2023-12-07-1.0 **2**. Dickinson MJ, Carlo-Stella C, Morschhauser F, et al. Glofitamab for relapsed or refractory diffuse large B-cell lymphoma.N Engl J Med. 2022;387(24):2220-2231. doi:10.1056/NEJMoa2206913. **3**. Falchi L, Presented at the American Society of Clinical Oncology Annual Congress 2023, Chicago, IL, June 3-6, 2023.

•For more detailed product inquiries and to report adverse events, please contact Roche Korea (02) 3451-3600.
•The most up-to-date product information can be found on the Roche Korea website (www.roche.co.kr).

Roche Korea Company Ltd. 17th Floor GT Tower (East) 411 Seocho-Daero Seocho-Gu Seoul South Korea (06615) / Tel +82 2 3451 3600 / https://www.roche.co.kr

Product Information
Columvi (Glofitmab)

M-KR-00002464

MINJUVI®

The second-line treatment secures long-lasting remission for adult patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL) who are not eligible for autologous stem cell transplant (ASCT).[1,2]

MINJUVI® (tafasitamab): the first anti-CD19 mAb approved in combination with lenalidomide in DLBCL, from second-line and beyond.[3]

MINJUVI®
tafasitamab | 200mg
Powder for solution for infusion

5-year follow-up analysis[2]

- Best ORR: 57.5% (n=46, 95% CI 45.9-68.5), CR: 41.3%, PR: 16.3%
- **Median DoR: Not Reached** (Median Follow-up: 44.0 months, 95% CI 29.9-57.0) (secondary outcome)

5 year Data

Patients with one pLoT had higher ORR compared with patients with ≥2 pLoT.[2]

Modified from ref.2

Study design[2]: L-MIND trial was open label, multicentre, single arm, Phase II trial evaluating the efficacy and safety of MINJUVI® in combination with lenalidomide, followed by MINJUVI® monotherapy in adult with R/R DLBCL after 1-3 prior systemic DLBCL therapies, with at least one anti-CD20-containing therapy. To assess long-term outcomes, updated analysis reported with ≥35 months' follow-up. Primary endpoint was ORR, defined as the proportion of complete and partial responders, assessed according to the 2007 International Working Group response criteria for malignant lymphoma.

ASCT, autologous stem cell transplantation; **CI**, confidence interval; **CR**, complete response; **DLBCL**, diffuse large B-Cell lymphoma; **DoR**, duration of response; **NTE**, non-transplant eligible; **ORR**, overall response rate; **pLoT**, prior line of therapy; **PR**, partial response; **R/R**, relapsed and refractory.

References 1. 민쥬비™주 국내 허가사항 (최종개정일 : 2023-06-09) 2. Duell J, et al. Haematologica. 2024;109(2):553-566. 3. MINJUVI® (tafasitamab) SmPC. October 2023.

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XOSPATA®
gilteritinib

TAKE A STAND FOR LONGER SURVIVAL

Median Overall Survival[1]

9.3 Months with Xospata VS **5.6** Months with salvage chemotherapy

Composite complete remission (CRc)* rate[1]

54.3% with Xospata VS **21.8%** with salvage chemotherapy

Percentage of patients underwent transplantation[1]

25.5% with Xospata VS **15.3%** with salvage chemotherapy

> "Reimbursment criteria is expanded for all *FLT3*+ R/R AML patient from March 1st."[2]

FLT3: Fms-like tyrosine kinase 3, **R/R**: Refractory or relapsed, **AML**: Acute myeloid leukemia

* Composite complete remission was defined as the composition of complete remission, complete remission with incomplete hematologic recovery, and complete remission with incomplete platelet recovery.

References 1. Perl AE, et al. Lancet Oncol. 2019;20(7):984-997. 2. Xospata tablet 40mg [Gilteritinib fumarate] [package insert]. Seoul: Astellas Pharma Korea, Inc.; 2022.

Precaution in use

1. Warnings 1) **Differentiation Syndrome**: Of 319 patients treated with this drug, 6 experienced differentiation syndrome. Differentiation syndrome is associated with rapid proliferation and differentiation of myeloid cells and may be life-threatening or fatal if not treated. Symptoms of differentiation syndrome in patients treated with this drug included fever, dyspnea, pleural effusion, pericardial effusion, pulmonary edema, hypotension, rapid weight gain, peripheral edema, renal, and renal dysfunction. Some cases had concomitant acute kidney injury/renal dysfunction. Differentiation syndrome occurred as early as 1 day and up to 82 days after this drug initiation and has been observed with or without concomitant myelodysplasia. If differentiation syndrome is suspected, initiate corticosteroids and hemodynamic monitoring until improvement. Taper corticosteroids after resolution of symptoms and withdraw corticosteroids for a minimum of 3 days. Symptoms of differentiation syndrome may recur with premature discontinuation of corticosteroid treatment. If severe signs and/or symptoms persist for more than 48 hours after initiation of corticosteroids, interrupt this drug until signs and symptoms are no longer severe (see Posology and method of administration and 4. Adverse reactions, section). **2) Posterior Reversible Encephalopathy Syndrome (PRES)**: There have been reports of PRES with symptoms including seizure and altered mental status in patients (3%) treated with this drug. Symptoms have resolved after discontinuation of treatment. A diagnosis of PRES requires confirmation by brain imaging, preferably magnetic resonance imaging (MRI). Discontinue this drug in patients who develop PRES (see Posology and method of administration and 4. Adverse reactions, section). **3) Prolonged QT interval**: Among the patients with this drug, 7% were found to have a QTcF greater than 500 msec and 3% had an increase from baseline QTcF greater than 60 msec. This drug has been associated with prolonged cardiac ventricular repolarization (QT interval) (see 4. Adverse reactions, section). Perform electrocardiogram (ECG) prior to initiation and during treatment with this drug, on day 8 and 15 of cycle 1, and prior to the start of the next and subsequent cycles. Interrupt this drug or reduce the dose of this drug for treatment correction in patients who have a QTcF >500 msec. Hypokalemia or hypomagnesemia may increase the QT prolongation risk. Correct hypokalemia or hypomagnesemia prior to and during this drug administration (see Posology and method of administration and 4. Adverse reactions, section). **2. Contraindications**: Hypersensitivity to the active substance or to any of the excipients of the product. Anaphylactic reactions have been reported. **3. Precautions**: There have been reports of pneumocytosis in patients (4%) treated with this drug. Evaluate and monitor patients who develop signs and symptoms suggestive of pancreatitis, until symptoms resolve, interrupt and reduce the dose of this drug for treatment correction in patients who develop pancreatitis. **4. Adverse reactions**: The safety of this drug was evaluated in 319 patients with relapsed or refractory AML who received at least one dose of 120 mg of this drug. The clinical trials included one multinational active-controlled, phase 3 trial (ADMIRAL trial) and two supporting single-arm trials (phase 1/2 trial, 1,30 mg dose arms of 201812-0009 and 2019-0142-0002). At the time of final analysis, the median duration of exposure to this drug was 111 days (range 4 to 1522 days). The most frequent adverse drug reactions (ADRs) with this drug were alanine aminotransferase (ALT) increased (82.7%), aspartate aminotransferase (AST) increased (80.9%), blood alkaline phosphatase increased (69.7%), fatigue (60.4%), nausea (29.8%), constipation (28.2%), cough (28.2%), peripheral edema (24.1%), dyspnea (24.1%), dizziness (20.4%), hypotension (17.2%), pain in extremity (14.7%), epistaxis (13.8%), arthralgia (12.5%) and myalgia (12.5%). The most frequent serious adverse reactions (≥2 %) reported in patients were acute kidney injury, diarrhea, ALT increased, dyspnea, AST increased, hypotension and differentiation syndrome. Adverse reactions observed during clinical studies are listed below by frequency category. Frequency categories are defined as follows: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

[Table 2] Adverse reactions observed during clinical studies

Adverse drug reaction	This drug 120 mg daily (N=319)		
	All Grades %	Grades ≥3 %	Frequency category
Cardiac disorders			
Pericardial effusion	3.1	0.9	Common
Pericarditis	1.6	0	Common
Cardiac failure	1.3	1.3	Common
Electrocardiogram QT prolonged	8.8	3.5	Common
Gastrointestinal disorders			
Diarrhea	20.1	3.1	Very common
Nausea	29.8	1.9	Very common
Constipation	28.2	0.6	Very common
General disorders and administration site conditions			
Fatigue	60.4	3.1	Very common
Peripheral edema	24.1	0.3	Very common
Pyrexia	13.8	2.5	Very common
Malaise	4.4	0	Common
Immune system disorders			
Anaphylactic reaction	1.3	1.3	Common
Investigations			
Alanine aminotransferase increased*	82.1	12.9	Very common
Aspartate aminotransferase increased*	80.9	9.3	Very common
Blood alkaline phosphatase increased*	68.7	1.9	Very common
Blood creatine phosphokinase increased*	13.8	6.3	Very common
Musculoskeletal and connective tissue disorders			
Back pain/pain in extremity	14.7	0.6	Very common
Arthralgia	12.5	1.3	Very common
Myalgia	12.5	0.3	Very common
Musculoskeletal pain	4.7	0.3	Common
Nervous system disorders			
Dizziness	20.4	0.3	Very common
Posterior reversible encephalopathy syndrome	0.9	0.6	Uncommon
Renal and urinary disorders			
Acute kidney injury	9.4	2.2	Common
Respiratory, thoracic and mediastinal disorders			
Cough*	28.2	1.3	Very common
Dyspnea	24.1	4.4	Very common
Differentiation syndrome	3.4	2.2	Common
Vascular disorders			
Hypotension	17.2	7.2	Very common

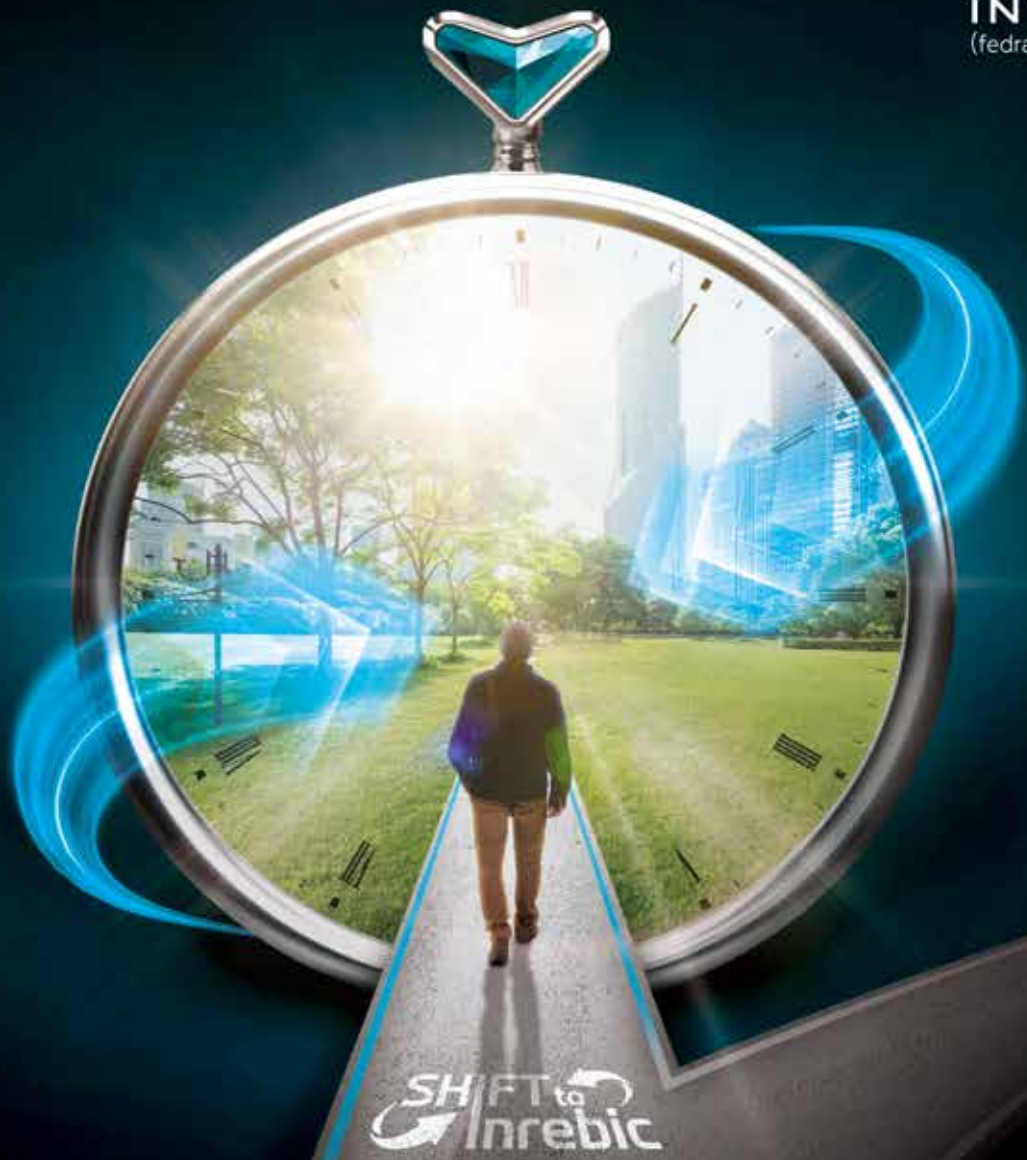
Preferred term in MedDRA (v 19.1). * Frequency is based on central laboratory values.

Description of selected adverse reactions 1) **Differentiation syndrome**: Of 319 patients treated with this drug in the clinical studies, 11 (3%) experienced differentiation syndrome. Of the 11 patients who experienced differentiation syndrome, 3 (0.9%) recovered after treatment or after dose interruption of this drug. For recommendations in case of suspected differentiation syndrome (see Posology and method of administration and 1. Warning section). **2) Posterior Reversible Encephalopathy Syndrome (PRES)**: Of the 319 patients treated with this drug in the clinical studies, 2 (0.6) experienced PRES in a dark, reversible, neurological disorder, which can present with rapidly evolving symptoms including seizure, headache, confusion, visual and neurological disturbances, with or without associated hypertension. Symptoms have resolved after discontinuation of treatment (see Posology and method of administration and 1. Warning section). **3) QT prolongation**: Of the 317 patients treated with this drug at 120 mg with a post-baseline QTcF value in clinical studies, 6 patients (2%) experienced a QTcF >500 msec. Additionally across all doses, 12 patients (2.3%) with relapsed/refractory AML had a maximum post-baseline QTcF interval >500 msec (see Posology and method of administration and 1. Warning and 11) Pharmacodynamic properties section of 14. Information for experts section).

14 revision date: 2022.11.03

astellas Astellas Pharma Korea, Inc.

INREBIC
(fedratinib) capsules
100mg



It's time to consider INREBIC!

2nd line treatment option for Myelofibrosis in 10 years!

Fedratinib has been linked to several adverse reactions in patients. In pivotal study, 1.2% of patients treated with Inrebic reported serious encephalopathy, including Wernicke's, with most events resolving with residual neurological symptoms. Gastrointestinal toxicity was a common adverse reaction, with nausea, vomiting, and diarrhea occurring in 68% of patients. Anemia was also reported in 52% of patients treated with 400 mg of Inrebic. Thrombocytopenia was reported in 14% and 9% of patients, with the median time to first onset of any grade occurring around 70 days. Neutropenia was reported in 3.5% of patients. Hepatic toxicity was reported in 52% and 59% of patients treated with 400 mg of Inrebic. Elevated amylase/lipase and creatinine were reported in 24% and 40% of patients treated with Inrebic. The median time to onset of any grade was approximately 1 month.

*Fedratinib was approved in S.Korea in 2022 after the approval of Ruxolitinib in 2013.

References

1. Ruxolitinib 처방정보. 식품의약품안전처. 2. 인리버빅. 처방정보. 식품의약품안전처. 3. National Comprehensive Cancer Network (NCCN). Myeloproliferative Neoplasms Guidelines Version 3. 2023. Available at (https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf) Accessed on 12 Dec 2023.

INREBIC capsule (fedratinib)

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2610-KR-240000N / Mar 2024 / Mar 2024

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ICKSH 2025

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See you at ICKSH 2025 again!

The Korean Society of Hematology
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