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HKSH
The Hong Kong Society of Haematology

THE HONG KONG SOCIETY OF HAEMATOLOGY

ANNUAL SCIENTIFIC MEETING 2024

PROGRAMME BOOK

REWRITE THE NEXT CHAPTER

For patients with newly diagnosed AL Amyloidosis[1]

DARZALEX® SC + VCd

First FDA-approved treatment for AL Amyloidosis*

Notable MOD-PFS

42% reduction
in the risk of MOD-PFS[2]
vs VCd alone (HR:0.58; p=0.02)

Deepening Response

Rapid, deep and durable
>3x
the rate of hematologic CR[3]
DVCd 60% vs VCd 19%

Promising Organ Recovery

>2x
the rates of cardiac and renal response[3]
Cardiac: DVCd 53% vs VCd 24%
Renal: DVCd 58% vs VCd 26%

- AE profile consistent with regimen components, without additional safety signals identified[2,3]
- Low discontinuation rates due to TEAs(4.1%), which is comparable to regimen components(4.3%)[2]

DARZALEX® in combination with cyclophosphamide, bortezomib and dexamethasone is indicated for the treatment of adult patients with newly diagnosed systemic AL amyloidosis.[1] See **DARZALEX®** prescribing information for all indications, including its use in Multiple Myeloma.

*This claim is supported by the official announcement made by the Janssen Pharmaceutical Companies of Johnson & Johnson. Available at https://www.jnj.com/darzalex-faspiodaratumumab-and-hyaluronidase-fihj-becomes-the-first-fda-approved-treatment-for-patients-with-newly-diagnosed-light-chain-al-amyloidosis

AE= adverse event; AL= amyloid light chain; CR= complete response; DVCd= DARZALEX® (D) + Velcade (V) + Cyclophosphamide (C) + dexamethasone (d); FDA= Food and Drug Administration; MOD= major organ deterioration; PFS= progression-free survival; TEA= treatment emergent adverse event; VCd= Velcade (V), Cyclophosphamide (C) + dexamethasone (d).

References:
1. Darzalex® SC Hong Kong Prescribing Information P02. 2. Kastritis E, et al; ANDROMEDA Trial Investigators. N Engl J Med. 2021 Jul 1;385(1):46-58. 3. Comenzo R L, et al. Subcutaneous Daratumumab with Bortezomib, Cyclophosphamide, and Dexamethasone in Patients With Newly Diagnosed Light Chain (AL) Amyloidosis: 18-month Landmark Analysis of the Phase 3 ANDROMEDA Study. Presented at 63rd American Society of Hematology Annual Meeting & Exposition; December 11-14, 2021; Atlanta, GA/Virtual.

DARZALEX SOLUTION FOR SUBCUTANEOUS INJECTION 1800MG/15ML
ABBREVIATED PRESCRIBING INFORMATION
ACTIVE INGREDIENT(S): Daratumumab **INDICATION(S):** Multiple myeloma: 1) DARZALEX is indicated in combination with lenalidomide and dexamethasone or with bortezomib, melphalan and prednisone for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant; 2) in combination with bortezomib, thalidomide and dexamethasone for the treatment of adult patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant; 3) in combination with lenalidomide and dexamethasone, or bortezomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy; 4) in combination with pomalidomide and dexamethasone for the treatment of adult patients with multiple myeloma who have received one prior therapy containing a proteasome inhibitor and lenalidomide and were lenalidomide-refractory, or who have received at least two prior therapies that included lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or after the last therapy; 5) as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy. Light chain (AL) amyloidosis: DARZALEX is indicated in combination with cyclophosphamide, bortezomib and dexamethasone for the treatment of adult patients with newly diagnosed systemic AL amyloidosis. **DOSAGE & ADMINISTRATION:** 1800 mg administered subcutaneously over approximately 3-5 minute according to the dosing schedule in package insert. Refer to package insert for dose and schedule of other medicinal products in combination and recommended concomitant medicinal products. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients. **SPECIAL WARNINGS & PRECAUTIONS:** Infusion-related reactions: patients should be pre-medicated with antihistamines, antipyretics, and corticosteroids as well as monitored and counselled regarding IRRs; Neutropenia/thrombocytopenia: complete blood cell counts should be monitored periodically during treatment; Interference with indirect antiglobulin test (Indirect Coombs test); Interference with determination of complete response; Hepatitis B virus (HBV) reactivation: HBV screening should be performed in all patients before initiation of treatment. **SIDE EFFECTS:** Infusion-related reactions, fatigue, nausea, diarrhoea, constipation, pyrexia, cough, neutropenia, thrombocytopenia, anaemia, oedema peripheral, peripheral sensory neuropathy and upper respiratory tract infection. Refer to the full prescribing information for other side effects. **PREGNANCY & LACTATION:** DARZALEX is not recommended during pregnancy and in women of childbearing potential not using contraception. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from DARZALEX therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. **INTERACTIONS:** No interaction studies have been performed.
PLEASE REFER TO FULL PRESCRIBING INFORMATION BEFORE PRESCRIBING. API version to be quoted on promotional material: Darzalex SC aPI ver.1.0

CP-419207 Dec 2023

Janssen, a division of Johnson & Johnson (HK) Ltd
13/F Tower 1, Grand Century Place,
193 Prince Edward Road West, Mongkok, Hong Kong.
Tel: 2736 1711 Fax: 2736 1926
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Pharmaceutical Companies of Johnson & Johnson

DARZALEX®SC
daratumumab subcutaneous

Kyprolis® (carfilzomib) for injection

WHEN MULTIPLE MYELOMA RELPASES,

RESPOND WITH THE EFFICACY OF KYPROLIS®[1,2]

Around 4 in 10 patients with MM who start second-line therapy never start a third.[3]
Your treatment choice at first relapse matters for your patients with relapsed MM.[4]

	ASPIRE (KRd)	ENDEAVOR (Kd)
IMPROVED MEDIAN OS	**Median OS of 48.3 months** with KRd in relapsed MM patients compared to 40.4 months with Rd; (HR=0.794; 95% CI: 0.667-0.945; *p*-value (2-sided)=0.0091)[1,5] (OS was a secondary endpoint in ASPIRE)	**Median OS of 47.6 months** with Kd in relapsed or refractory MM patients compared to 40.0 months with Vd; (HR=0.791; 95% CI: 0.648-0.964; $p=0.010$)[1,6] (OS was a secondary endpoint in ENDEAVOR)
SUSTAINABLE EFFICACY	**Median PFS of 26.3 months** with KRd in relapsed patients compared to 17.6 months with Rd; (HR=0.69; 95% CI: 0.57-0.83; $p<0.0001$)[2]	**KYPROLIS® doubled the median PFS** compared to bortezomib; (**18.7 months** vs. 9.4 months; HR=0.533; 95% CI: 0.44-0.65; $p<0.0001$)[1,7]
DEEP RESPONSE	With KRd, **almost 1 out of 3 patients reached complete response** or better (31.8%)[2]	**KYPROLIS® doubled the rate of complete response** or better compared to bortezomib; (12.5% vs. 6.2%; $p=0.0005$)[1]

KYPROLIS® is now available in ONCE-WEEKLY and TWICE-WEEKLY dosing, so you can choose the treatment regimen that best suits your patients.[1]

Abbreviations: CI, confidence interval; **HR**, hazard ratio; **Kd**, carfilzomib and dexamethasone; **KRd**, carfilzomib, lenalidomide and dexamethasone; **MM**, multiple myeloma; **OS**, overall survival; **PFS**, progression-free survival; **Rd**, lenalidomide and dexamethasone; **Vd**, bortezomib and dexamethasone

References: 1. KYPROLIS® Hong Kong Prescribing Information. December 2020. 2. Stewart AK, *et al. N Engl J Med* 2015;372(2):142-152. 3. Yong K, *et al. Br J Haematol* 2016;175(2):252-264. 4. Durie BG. *Cancer Treat Rev* 2016;36 Suppl 2:S18-S23. 5. Siegel DS, *et al. J Clin Oncol* 2018;36(8):728-734. 6. Dimopoulos MA, *et al. Lancet Oncol* 2017;18(10):1327-1337. 7. Dimopoulos MA, *et al. Lancet Oncol* 2016;17(1):27-38.

Kyprolis® (Carfilzomib) Abbreviated Prescribing Information

Indications: Kyprolis is indicated in combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma who have received one to three lines of therapy. **Dosage & Administration:** Administration Precautions: Dose based on BSA to max 2.2 m², dose adjust for weight changes >20%. See full PI for dosing & administration information. Ensure adequate hydration before Cycle 1, Day 1 with oral fluids (30 mL per kg) and prior to each dose in Cycle 1 with IV fluids (250-500 mL). Administer after hemodialysis procedure for patients on hemodialysis. In combination with dexamethasone: Each 28 day period is considered one treatment cycle. Administer dexamethasone 30 mins to 4 hrs before Kyprolis. Treatment may be continued until disease progression or unacceptable toxicity occurs. Once weekly: Kyprolis is administered as a 30 min IV infusion once weekly for 3 weeks followed by a 13 day rest period. Administer Kyprolis at a starting dose of 20 mg/m² in Cycle 1 on Day 1. If tolerated, escalate the dose to 70 mg/m² on Day 8 of Cycle 1. Dexamethasone 40 mg is taken PO or IV on Days 1, 8, and 15 of all cycles and on Day 22 of Cycles 1 to 9. Twice weekly: Kyprolis is administered as a 30 minute IV infusion on two consecutive days, each week for 3 weeks followed by a 12 day rest period. Administer Kyprolis at a starting dose of 20 mg/m² in Cycle 1 on Days 1 and 2. If tolerated, escalate the dose to 56 mg/m² on Day 8 of Cycle 1. Dexamethasone 20 mg is taken PO or IV on Days 1, 2, 8, 9, 15, 16, 22, and 23 of each 28 day cycle. In combination with lenalidomide and dexamethasone: Administer Kyprolis as a 10 min IV infusion on two consecutive days, each week for 3 weeks followed by a 12 day rest period. Each 28 day period is considered one treatment cycle. The recommended starting dose of Kyprolis is 20 mg/m² in Cycle 1 on Days 1 and 2. If tolerated, escalate the dose to 27 mg/m² on Day 8 of Cycle 1. From Cycle 13, omit the Day 8 and 9 doses of Kyprolis. Lenalidomide 25 mg is taken PO on Days 1-21 and dexamethasone 40 mg PO or IV on Days 1, 8, 15, and 22 of the 28 day cycles. Continue treatment until disease progression or unacceptable toxicity occurs. Treatment for longer than 18 cycles should be based on individual benefit/risk assessment. **Contraindications:** None. **Warnings & Precautions:** Recommend: Control hypertension prior to starting Kyprolis, thromboprophylaxis (venous thrombosis). Consider: Uric acid-lowering drugs in patients at risk for tumor lysis syndrome, prophylaxis with antivirals for patients who are hepatitis B virus (HBV) carriers. Monitor: Clinical signs or symptoms of cardiac failure or cardiac ischemia (cardiac toxicities), blood loss (hemorrhage), thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS) (thrombotic microangiopathy); renal function with regular measurement of the serum creatinine and/or estimated clearance; platelet counts (thrombocytopenia), liver enzymes (hepatic toxicity and failure), serum potassium levels. Discontinue Kyprolis: In the event of drug-induced pulmonary toxicity. If Posterior Reversible Encephalopathy Syndrome (PRES) is suspected or if Progressive Multifocal Leukoencephalopathy (PML) diagnosis is confirmed. Others: Evaluate promptly if cardiac toxicity is suspected. Withhold Kyprolis for Grade 3/4 cardiac adverse reactions until recovery. Withhold for pulmonary hypertension until resolved or returned to baseline. Stop Kyprolis for Grade 3/4 dyspnea until resolved or returned to baseline. Infusion-related reactions up to 24 hrs after administration of Kyprolis. HBV reactivation. Kyprolis in combination with melphalan and prednisone is not indicated for transplant-ineligible patients with newly diagnosed multiple myeloma. **Pregnancy:** Kyprolis can cause fetal harm when administered to a pregnant woman. Use effective contraception during & after treatment (females: 6 mo; males 3 mo); consider alternate to oral or hormonal contraceptives. Do not administer to breastfeeding women. **Adverse Reactions:** Common: Anemia, neutropenia, thrombocytopenia, diarrhea, constipation, nausea, vomiting; fatigue, pyrexia, edema peripheral, asthenia, upper respiratory tract infection, bronchitis, viral upper respiratory tract infection, respiratory tract/infection, pneumonia, hypokalemia, hypocalcemia, hyperglycemia, muscle spasms, back pain, peripheral neuropathies, headache, insomnia; cough, dyspnea, rash, embolic and thrombotic events, hypertension. **Please read full prescribing information prior to administration (available upon request).** Kyprolis® is a registered trademark owned or licensed by Amgen Inc., its subsidiaries, or affiliates. Version: HKKYP01

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For medical inquiries or to report adverse events/product complaint, please contact 800 961 142 or email medinfo.JAPAC@amgen.com

AMGEN®
Amgen Hong Kong Limited
Suites 407-12, 4/F, One Island East, Taikoo Place, 18 Westlands Road, Quarry Bay, Hong Kong
Tel: (852) 2848 1178 Fax: (852) 2808 2820

HK-09219-KYP-2022-OCT

FOR FIRST-LINE TREATMENT OF DLBCL[1]

A clinical benefit full of life

reduced risk of disease progression, relapse, or death vs R-CHOP. That means more hope for the future, and more freedom from the threat of disease.[2]

Indication

POLIVY® in combination with rituximab, cyclophosphamide, doxorubicin, and prednisone (R-CHP) is indicated for the treatment of adult patients with previously untreated diffuse large B-cell lymphoma (DLBCL).

DLBCL=diffuse large B-cell lymphoma; R-CHOP=rituximab + cyclophosphamide + doxorubicin + vincristine + prednisone.

References: 1. **POLIVY®** Hong Kong Product Information. May 2022. 2. Tilly H, Morschhauser F, Sehn LH, et al. Polatuzumab vedotin in previously untreated diffuse large B-cell lymphoma. *N Engl J Med*. 2022;386(4):351-363.

Roche Hong Kong Limited
22/F FT Life Tower, 18 Sheung Yuet Road, Kowloon Bay
M-HK-00001510. Expiry date: 30/01/2026

Abbreviated Prescribing Information

POLIVY®
polatuzumab vedotin

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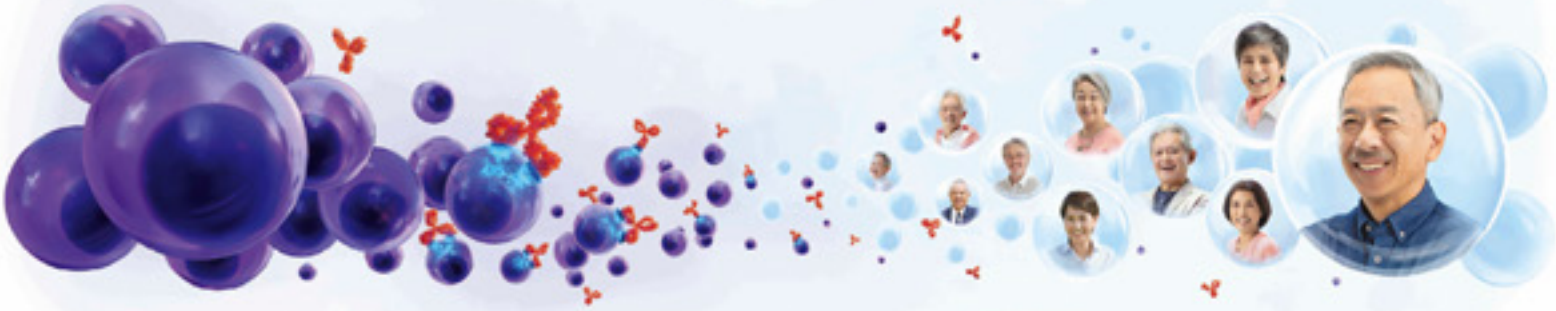
IN THE TREATMENT OF **RELAPSED REFRACTORY MULTIPLE MYELOMA**

SARCLISA (isatuximab)

ACHIEVE **GREATER OUTCOMES** FOR **YOUR PATIENTS**



IKEMA[2,4]: SARCLISA + Kd vs Kd (N=302)		**ICARIA**[3]: SARCLISA + Pd vs Pd (N=307)
mPFS 35.7 mo* vs 19.2 mo with Kd alone	**Superior PFS**[1]	**mPFS 11.53 mo** vs 6.47 mo with Pd alone
HR=0.58 (95.4% CI: 0.42-0.79)		**HR=0.596** (95% CI: 0.44-0.81; *P*=0.001)

IKEMA trial: SARCLISA + Kd[1,2]

IKEMA (EFC15246) was a multicentre, multinational, randomised, open-label, 2-arm, phase 3 study that evaluated the efficacy and safety of SARCLISA in 302 patients with relapsed and/or refractory multiple myeloma who had received 1 to 3 prior lines of therapy. Patients received either SARCLISA 10 mg/kg administered as an IV infusion in combination with Kd (n=179) or Kd alone (n=123), administered in 28-day cycles until disease progression or unacceptable toxicity. PFS was the primary endpoint; secondary endpoints included ORR, CR, ≥VGPR, MRD-, and OS. Median follow-up for the first interim analysis was 20.7 months.

ICARIA trial: SARCLISA + Pd[1,3]

ICARIA (EFC14335) was a multicentre, multinational, randomised, open-label, 2-arm, phase 3 study that evaluated the efficacy and safety of SARCLISA in 307 patients with relapsed and refractory multiple myeloma who had received at least 2 prior lines of therapy, including lenalidomide and a PI. Patients received either SARCLISA 10 mg/kg administered as an IV infusion in combination with Pd (n=164) or Pd alone (n=153), administered in 28-day cycles until disease progression or unacceptable toxicity. PFS was the primary endpoint; ORR was one of the secondary endpoints. Median follow-up for the first interim analysis was 11.6 months.

Most common adverse reactions[1,2,4]

- In ICARIA, the most frequent adverse reactions (≥20%) were neutropenia (47%), infusion reactions (38%), pneumonia (31%), upper respiratory tract infection (28%), diarrhoea (26%), and bronchitis (24%)
- In IKEMA, the most frequent adverse reactions (≥20%) were infusion reactions (46%), hypertension (37%), diarrhoea (36%), upper respiratory tract infection (36%), pneumonia (29%), fatigue (28%), dyspnoea (28%), insomnia (24%), bronchitis (23%), and back pain (22%).

SARCLISA is indicated:

- In combination with pomalidomide and dexamethasone, for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on the last therapy
- In combination with carfilzomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy

*Assessment by masked independent response committee (IRC)

References: 1. Sarclisa Hong Kong prescribing information based on EU SmPC 29 July 2021. 2. Moreau P, et al. Lancet 2021; 397: 2361–71. 3. Attal M, et al. Lancet. 2019;394(10214):2096–2107. 4. Moreau P, et al. Presented at ESMO Virtual Plenaries, 2022 and 6th COMy World Congress. 20th May, 2022.

Presentation: SARCLISA 20 mg/mL concentrate for solution for infusion. One ml of concentrate for solution for infusion contains 20 mg of isatuximab. Each vial contains 100 mg of isatuximab in 5 mL of concentrate (100 mg/5mL). Each vial contains 500 mg of isatuximab in 25 mL of concentrate (500 mg/25mL). Indications: I. In combination with pomalidomide and dexamethasone, for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on the last therapy. II. In combination with carfilzomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy. Dosage & Administration: Intravenous infusion. Each treatment cycle consists of a 28-day period. Treatment is repeated until disease progression or unacceptable toxicity.

Cycles	Dosing schedule
Cycle 1	Days 1, 8, 15, and 22 (weekly)
Cycle 2 and beyond	Days 1, 15 (every 2 weeks)

Premedication should be used prior to SARCLISA infusion with the following medicinal products: I. a. Dexamethasone 40 mg oral or intravenous (or 20 mg oral or intravenous for patients≥75 years of age), when administered in combination with isatuximab and pomalidomide. b. Dexamethasone 20 mg (intravenous on the days of isatuximab and/or Carfilzomib infusions, and oral on the other days) when administered in combination with isatuximab and carfilzomib. II. Acetaminophen 650 mg to 1000 mg oral (or equivalent). III. Diphenhydramine 25 mg to 50 mg intravenous or oral (or equivalent [e.g., cetirizine, promethazine, dexchlorpheniramine]). The intravenous route is preferred for at least the first 4 infusions. The above recommended dose of dexamethasone corresponds to the total dose to be administered only once before the infusion. The recommended premedication agents should be administered 15–60 minutes prior to starting a SARCLISA infusion. Contraindications: Hypersensitivity to the active substance or to any of its excipients. Precautions: Vital signs should be frequently monitored during the entire SARCLISA infusion. When required, interrupt SARCLISA infusion and provide appropriate medical and supportive measures. In case symptoms do not improve to grade≤3 after interruption of SARCLISA infusion, persist or worsen despite appropriate medicinal products, require hospitalisation or are life-threatening, permanently discontinue SARCLISA and institute appropriate management. Complete blood cell counts should be monitored periodically during treatment. Patients with neutropenia should be monitored for signs of infection. No dose reductions of SARCLISA are recommended. SARCLISA dose delays and the use of colony-stimulating factors (e.g. G-CSF) should be considered to mitigate the risk of neutropenia. Patients receiving SARCLISA should be closely monitored for signs of infection and appropriate standard therapy instituted. Antibiotics and antiviral prophylaxis can be considered during treatment. Physicians should carefully evaluate patients before and during treatment as per IMWG guidelines for assessment of SPM and initiate treatment as indicated. To avoid potential problems with RBC transfusions, patients being treated with SARCLISA should have blood type and screen tests performed prior to the first infusion. Phenotyping may be considered prior to starting SARCLISA treatment as per local practice. If treatment with SARCLISA has already started, the blood bank should be informed. Patients should be monitored for theoretical risk of haemolysis. If an emergency transfusion is required, non-cross-matched ABO/Rh-compatible RBCs can be given as per local blood bank practices. Drug Interactions: Isatuximab has no impact on the pharmacokinetics of pomalidomide or carfilzomib, or vice versa. Pregnancy and lactation: There are no available data on isatuximab use in pregnant women. Animal reproduction toxicity studies have not been conducted with isatuximab. Immunoglobulin G1 monoclonal antibodies are known to cross the placenta after the first trimester of pregnancy. The use of isatuximab in pregnant women is not recommended. It is unknown whether isatuximab is excreted in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, which is decreasing to low concentrations soon afterwards; however, a risk to the breast-fed child cannot be excluded during this short period just after birth. For this specific period, a decision must be made whether to discontinue breast-feeding or to discontinue/abstain from isatuximab therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. Afterwards, isatuximab could be used during breast-feeding if clinically needed. Undesirable effects: isatuximab in combination with pomalidomide and dexamethasone: Most common adverse reactions reported: pneumonia, upper respiratory tract infection, bronchitis, neutropenia. Febrile neutropenia, dyspnoea, diarrhoea, nausea, vomiting, infusion reaction. Isatuximab in combination with carfilzomib and dexamethasone: Most common adverse reaction reported: pneumonia, upper respiratory tract infection, bronchitis, hypertension, dyspnoea, cough, diarrhoea, vomiting, fatigue, infusion reaction. For other undesirable effects, please refer to the full prescribing information. Preparation: The preparation of the infusion solution must be done under aseptic conditions. Legal Classification: Part 1, First & Third Schedules Poison. Full prescribing information is available upon request.

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Sanofi Hong Kong Limited 1/F & Section 2/2 on 2/F,
JUU Southside, 38 Wong Chuk Hang Road, Hong Kong
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WELCOME MESSAGE

Dr. LAW Man Fai

Chairman
The Hong Kong Society of Haematology

Dear Members and colleagues,

It is my great pleasure to welcome all of you to the 51st Annual scientific meeting (ASM) of The Hong Kong Society of Haematology (HKSH). The treatment for various haematological diseases is rapidly evolving in the past 50 years. Over the years, the ASM of HKSH has become the largest haematology meeting in Hong Kong.

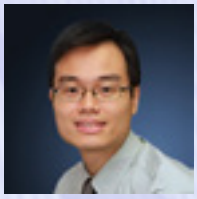
This year the Organising Committee has complied a programme consisting of a variety of haematological topics such as acute myeloid leukaemia, acute lymphoblastic leukaemia, lymphoma, multiple myeloma, amyloidosis, myelofibrosis and paroyxysmal nocturnal haemoglobiuria. We have also invited Prof. Lucy GODLEY, Clinical Director of Cancer Genetics of University of Chicago to speak to us on "Germline predisposition to haematological malignancies" in the Presidential Symposium of the ASM. We are honoured to have distinguished international speakers to share the updated information of the management of the diseases and their experiences with us.

Prof. Henry FUNG Chi Hang, the current Chairman of the Department of Bone Marrow Transplant and Cellular Therapies, Fox Chase Cancer Center at Temple University Hospital, Philadelphia will talk to us on the topic of "CAR-T cell therapy and bispecific antibodies in the treatment of haematological maliganacies" in our first Homecoming Symposium of ASM.

The new fellows will present the findings of their dissertations in the New Fellow presentation session of the meeting.

I would like to thank the Organising Committee, speakers, sponsors, and event organisers for their support and contribution to make the meeting a success. I look forward to seeing you in the meeting, and hope you will enjoy the inspiring presentations.

HKSH COUNCIL

	Dr. LAW Man Fai	Chairman
	Dr. Gloria HWANG Yu Yan	Hon. Secretary
	Dr. Rosalina IP Ka Ling	Hon. Treasurer
	Dr. Vivien MAK Wai Man	Scientific Officer
	Dr. William CHOI Wai Lap	
	Dr. HA Chung Yin	Council Members
	Dr. WU Saliangi	

MEETING INFORMATION

Venue	Meeting Rooms S221 – S230, 2/F, Hong Kong Convention and Exhibition Centre
Date & Time	6 April 2024 (Saturday) 14:00 – 20:10
Event Secretariat	Email: support@eventgenie.com.hk Tel: +852 5303 1320
Entitlement	All participants will be entitled: ▪ Access to all scientific sessions ▪ Programme book ▪ Certificate of attendance (subject to certain criteria requested by the respective Colleges)

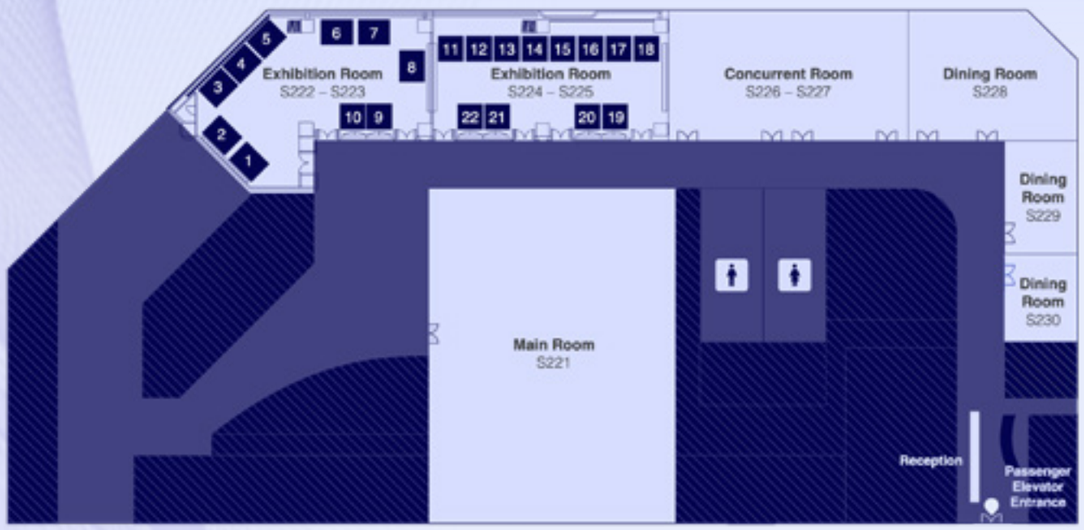
PROGRAMME

12:00 – 14:00	Lunch	
14:00 – 14:05	**Opening remarks** Dr. LAW Man Fai	
	Session 1: Myelofibrosis Chairpersons: Dr. LAW Man Fai, Dr. Gloria HWANG Yu Yan	
14:05 – 14:35	**Addressing the challenges of anaemia and thrombocytopenia in myelofibrosis** Prof. Dr. Haifa Kathrin AL-ALI (Germany)	
	Session 2: Amyloidosis Chairpersons: Dr. LAW Man Fai, Dr. Gloria HWANG Yu Yan	
14:40 – 15:10	**State of the art on the diagnosis and therapeutic in AL amyloidosis** Prof. Morie GERTZ (Untied States)	
	Presidential symposium Chairperson: Dr. LAW Man Fai	
15:15 – 15:55	**Germline predisposition to haematological malignancies** Prof. Lucy GODLEY (United States)	
15:55 – 16:00	**Outstanding new haematology fellow award presentation**	
16:00 – 16:05	Group photo	
16:05 – 16:35	Break time (Posters & Exhibits)	
	Session 4: Lymphoma Chairpersons: Dr. Gloria HWANG Yu Yan, Dr. Vivien MAK Wai Man, Dr. William CHOI Wai Lap	**Session 5: Acute leukemia** Chairpersons: Dr. LAW Man Fai, Dr. HA Chung Yin, Dr. Rosalina IP Ka Ling
16:35 – 17:05	**Unveiling breakthroughs in DLBCL therapies: Embracing the era of bispecific antibodies and ADCs** Prof. Georg LENZ (Germany)	**Future direction of ALL treatment in the new era of noval therapies** Prof. Robin FOÀ (Italy)
17:10 – 17:40	**Role of BTKi in the management of marginal zone lymphomas and follicular lymphoma** Prof. Chan Yoon CHEAH (Australia)	**A new era of acute myeloid leukemia management** Prof. Edgar JOST (Germany)
	Session 6: Paroxysmal nocturnal haemoglobinuria Chairpersons: Dr. Gloria HWANG Yu Yan, Dr. Vivien MAK Wai Man, Dr. William CHOI Wai Lap	**Session 7: Multiple myeloma** Chairpersons: Dr. LAW Man Fai, Dr. HA Chung Yin, Dr. Rosalina IP Ka Ling
17:45 – 18:15	**Rare but important to know – A novel mechanism for PNH management** Prof. Alexander RÖTH (Germany)	**Latest update on management of high-risk multiple myeloma** Prof. Thierry FACON (France)
18:15 – 18:30	Break time (Posters & Exhibits)	
	Homecoming symposium Chairperson: Dr. LAW Man Fai	
18:30 – 19:00	**T-cell re-direction therapies for treatment of lymphomas and myeloma** Prof. Henry FUNG Chi Hang (United States)	
	Young fellow & Best abstract presentation Chairpersons: Dr. LAW Man Fai, Dr. Rosalina IP Ka Ling	**Nursing symposium** Session co-hosted by Association of Hong Kong Nursing Staff Chairperson: Mr. Simon LEUNG | Moderator: Ms. Maryanne KWOK
19:05 – 19:15	**T-large granular lymphocytic leukaemia – Clinical and epidemiological perspectives from a single centre cohort** Dr. Ryan HO Chi Wai	**Nursing management on CRS** Ms. Jane ASTON (United Kingdom)
19:15 – 19:25	**A single-centre retrospective analysis of EBV-positive DLBCL with special focus on the plasma EBV DNA loads before, during and after treatment and the correlation with outcomes** Dr. Michael NGAI Cheong	
19:25 – 19:35	**Unsupervised machine learning for flow cytometric data analysis in T-lymphoblastic leukaemia (T-ALL) measurable residual disease (MRD) monitoring** Dr. Jamilla LI Wai Yan	
19:35 – 19:45	**Local experience of emicizumab in hemophilia A patients** Dr. Michael MAN Ho Yin	
19:45 – 19:55	**Bethesda assay for detecting anti-ADAMTS13 antibodies** Dr. Vivian YEUNG Ka Pik	
19:55 – 20:05	**Best abstract presentation** **Glofitamab real-world experience in a quaternary referral center** Dr. Thomas CHAN Sau Yan	
20:05 – 20:10	**Closing remarks** Dr. LAW Man Fai	
20:10 – 21:30	Dinner	

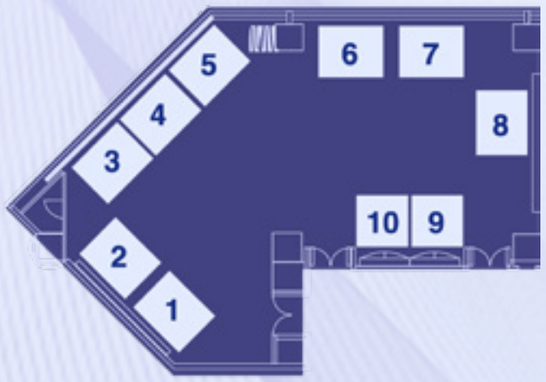
Session co-hosted by Hong Kong Haematology Nursing Association

HOUSE PLAN

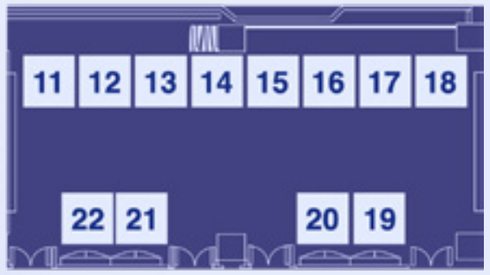
Meeting Rooms S221 – S230, 2/F, Hong Kong Convention and Exhibition Centre



Exhibition Rooms S222 – S223



Exhibition Rooms S224 – S225



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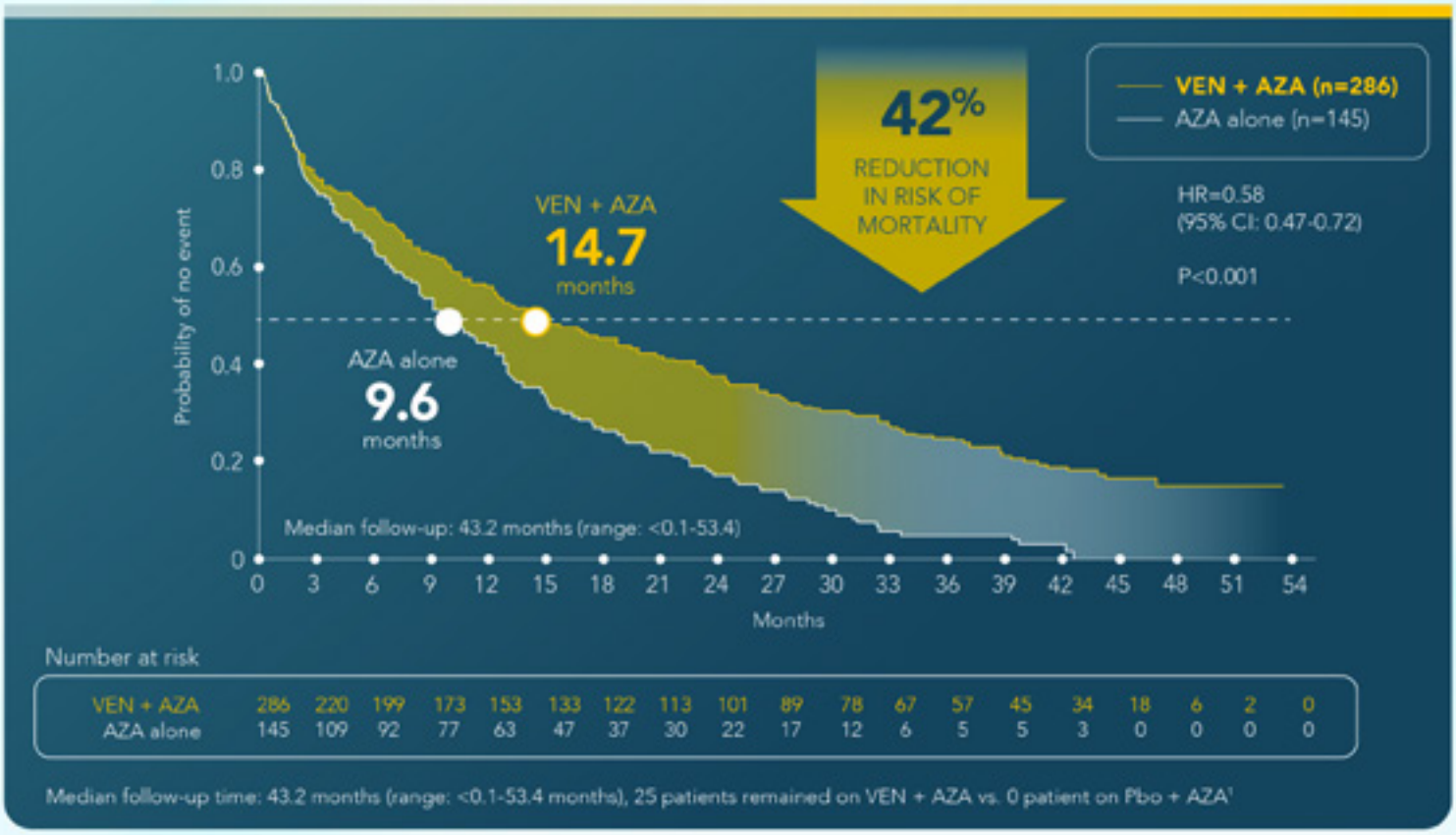
VEN + AZA sustains OS benefit

in IC-ineligible patients with 43.2 months of follow-up



Number at risk

VEN + AZA	286	220	199	173	153	133	122	113	101	89	78	67	57	45	34	18	6	2	0
AZA alone	145	109	92	77	63	47	37	30	22	17	12	6	5	5	3	0	0	0	0

Median follow-up time: 43.2 months (range: <0.1-53.4 months), 25 patients remained on VEN + AZA vs. 0 patient on Pbo + AZA[1]

100% OS analysis data cut-off: 1 Dec 2021.

The most frequently reported serious AEs (Grade ≥3) in patients receiving VENCLEXTA + AZA vs AZA alone, respectively, were febrile neutropenia (30% vs 10%), anaemia (5% vs 4%), neutropenia (5% vs 2%), atrial fibrillation (4% vs 1%), pneumonia (16% vs 22%), and sepsis (6% vs 8%).[2]

Abbreviations: AE=Adverse events; AML=Acute myeloid leukaemia; AZA=Azacitidine; CI=Confidence interval; HR=Hazard ratio; IC=Intensive chemotherapy; OS=Overall survival; Pbo=Placebo; VEN=VENCLEXTA.

References: 1. Pratz KW, et al. Oral Abstract #219. Long-term follow-up of the Phase 3 VIALE-A clinical trial of venetoclax plus azacitidine for patients with untreated acute myeloid leukemia ineligible for intensive chemotherapy. 64th ASH Annual Meeting 2022; December 10-13, 2022; New Orleans, LA, USA. **2.** DiNardo CD, et al. N Engl J Med. 2020;383(7):617-629. doi: 10.1056/NEJMoa2012971.

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Approval Code: HK-VENA-240001 22/FEB/2024

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CME ACCREDITATION

College	Credits	Group-Category
The Hong Kong College of Anaesthesiologists	5	PP-NA
Hong Kong College of Community Medicine	5	PP-PP
The College of Dental Surgeons of Hong Kong	Pending	Pending
Hong Kong College of Emergency Medicine	5	CME-PP
The Hong Kong College of Family Physicians	5	OEA-5.02
The Hong Kong College of Obstetricians and Gynaecologists	5	PP-PN
The College of Ophthalmologists of Hong Kong	Pending	Pending
The Hong Kong College of Orthopaedic Surgeons	5	PP-B
The Hong Kong College of Otorhinolaryngologists	2.5	PP-2.2
The Hong Kong College of Pathologists	5	CME-PP
Hong Kong College of Physicians	4.5	PP-PP
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Hong Kong College of Radiologists	5	B-PP
The College of Surgeons of Hong Kong	5	CME-PP
Medical Council of Hong Kong	5	CME-PASSIVECME

CNE ACCREDITATION

College	Credits
Association of Hong Kong Nursing Staff	4

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XOSPATA® is indicated as monotherapy for the treatment of adult patients who have relapsed or refractory acute myeloid leukaemia (AML) with a FLT3 mutation.[1]

TAKE A STAND
FOR LONGER SURVIVAL

Median Overall Survival [2]

9.3 Months with Xospata **VS** **5.6 Months** with salvage chemotherapy

HR=0.64 (95% CI: 0.49, 0.83); P < 0.001

Percentage of patients underwent transplantation [2]

25.5% with Xospata (n=63/247) **VS** **15.3%** with salvage chemotherapy (n=19/124)

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Scan for efficacy data of XOSPATA®

Abbreviations:
CI: confidence interval; FLT3: FMS-like tyrosine kinase 3; HR: hazard ratio; OS: overall survival

References:
1. Xospata® Prescribing Information Hong Kong 2. Perl AE, Martinelli G, Cortes JE, etal. Gilteritinib or chemotherapy for relapsed or refractory FLT3-mutated AML. N Engl J Med 2019;381(18):1728-40 3. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute myeloid leukemia (Version 2. 2021 -November) 4. Heuser M, et al. Annals of Oncology. 2020;31(6): 697-712. 5. NICE technology appraisal guidance. Available at: https://www.nice.org.uk/guidance/ta642/resources/gilteritinib-for-treating-relapsed-or-refractory-acute-myeloid-leukaemia-pdf-82609134829765, accessed on 22 Mar 2022.

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* Starting 2 weeks after the loading dose, maintenance doses are administered once every 4 or 8 weeks (depending on body weight).[1]

Reference: 1. Ultomiris Hong Kong Prescribing Information. March 2022.

Presentation: 300mg/3ml, and 1,100mg/11ml, concentrate for solution for infusion. **Indications:** Adult patients with paroxysmal nocturnal haemoglobinuria (PNH). Patients with a body weight of 10kg or above with atypical haemolytic uraemic syndrome (aHUS). **Dosage: (Adult PNH & aHUS, Pediatric aHUS with body weight ≥40kg) loading dose (IV infusion):** 2,400mg (≥40 to <60kg) / 2,700mg (≥60 to <100kg) / 3,000mg (≥ 100kg), followed by **maintenance dose (IV infusion):** 3,000mg (≥40 to <60kg) / 3,300mg (≥60 to < 100kg) / 3,600mg (≥ 100kg) starting 2 wks after loading dose administration and then every 8 wks. **(Paediatric aHUS with body weight <40kg) loading dose (IV infusion):** 600mg (≥ 10 to <20kg) / 900mg (≥ 20 to <30kg) / 1,200mg (≥ 30 to <40kg), followed by **maintenance dose (IV infusion):** 600mg (≥ 10 to <20kg) / 2, 900mg (≥ 20 to < 30kg) / 2,700mg (≥ 30 to <40kg) starting 2 wks after loading dose administration and then every 4 (≥ 10 to <20kg) / 8 (≥ 20 to <40kg) wks. **Switching from eculizumab to ravulizumab:** Loading dose of ravulizumab administered 2 wks after the last eculizumab infusion, and then maintenance doses administered per regimen above, starting 2 wks after loading dose administration. **Administration:** Diluted to a final concentration of 10 mg/ml, prior to administration by IV infusion using a syringe-type pump or an infusion pump over a minimal period of 25 to 75 minutes depending on body weight. **Contraindications:** hypersensitivity to ravulizumab or any excipients; unresolved Neisseria meningitidis infection; unvaccinated against Neisseria meningitidis, unless receiving prophylactic antibiotics until 2 wks after vaccination. **Precautions: Meningococcal Infection/Immunisation** - Vaccinate all patients at least 2 wks prior to initiating ravulizumab. If initiate <2 wks, administer prophylactic antibiotics until 2 wks after vaccination. Patients <18 yrs of age must be vaccinated against Haemophilus influenzae and pneumococcal infection. **Laboratory Monitoring: (PNH)** closely monitor patients for at least 16 wks to detect haemolysis and other reactions. **(aHUS)** closely monitor patients for severe TMA complications. **Use in Pregnancy/Lactation:** Women should use effective contraception during treatment with ravulizumab, and for up to 8 months after treatment; breastfeeding should be discontinued during treatment, and up to 8 months after treatment. Adverse Reactions: Very common (≥10%): upper respiratory tract infection, nasopharyngitis, headache, diarrhea, nausea, pyrexia, fatigue. Common (≥1% to <10%): dizziness, abdominal pain, vomiting, dyspepsia, rash, pruritus, arthralgia, back pain, myalgia, muscle spasms, influenza like illness, asthenia, infusion related reaction. **Full local prescribing information is available upon request. APLHK.ULT.0322**

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HK-8614 10/05/2023

OUR SPEAKERS

(Alphabetically ordered by last name)

Prof. Dr. Haifa Kathrin AL-ALI

Professor of Translational Oncology,
Head of the Krukenberg Cancer Center,
The University Hospital of Halle (Saale),
Germany

Ms. Jane ASTON

Bispecific Clinical Nurse Specialist,
The Newcastle Upon Tyne Hospitals NHS Foundation Trust,
United Kingdom

Prof. Chan Yoon CHEAH

Lymphoma lead and Fellowship Program Director,
Sir Charles Gairdner Hospital,
Australia

Prof. Thierry FACON

Professor of Haematology,
Department of Haematology,
Lille University Hospital,
France

Prof. Robin FOÀ

Professor of Hematology,
Head, Division of Hematology,
The Sapienza University of Rome,
Italy

Prof. Henry FUNG Chi Hang

Chair and Professor,
Department of Bone Marrow Transplant and Cellular Therapies,
Fox Chase Cancer Center,
United States

Prof. Morie GERTZ

Chair, Department of Medicine,
Professor of Hematology,
Mayo Clinic,
Rochester, United States

Prof. Lucy GODLEY

Inaugural Director, The Jeff and Marianne Silver Family Blood Cancer Institute,
Clinical Director of Cancer Genetics,
Robert H. Lurie Comprehensive Cancer Center,
Chicago, United States

Prof. Edgar JOST

Professor, Lead of Stem Cell Therapy,
Department for Hematology, Oncology,
Hemostaseology and Stem Cell Transplantation,
University Hospital RWTH Aachen,
Germany

Prof. Georg LENZ

Director, Department of Haematology, Oncology and Pneumology,
University Hospital Münster,
Germany

Prof. Alexander RÖTH

Senior Physician,
Head of Classical Hematology and Coagulation,
Department of Hematology and Stem Cell Transplantation,
West German Cancer Centre,
University Hospital Essen,
Germany

Addressing the challenges of anaemia and thrombocytopenia in myelofibrosis

Prof. Dr. Haifa Kathrin AL-ALI

Professor of Translational Oncology,
Head of the Krukenberg Cancer Center,
The University Hospital of Halle (Saale),
Germany

Abstract

Myelofibrosis (MF) is a myeloproliferative neoplasm (MPN), with dominated clinical phenotype of splenomegaly, constitutional symptoms, blood cell alterations, and the potential to develop vascular complications. Moreover, anaemia and thrombocytopenia are key characteristics in patients with MF. However, the underlying causes are incompletely understood. This symposium will be discussing the significant need and the burden of disease among patients with myelofibrosis who have anaemia and thrombocytopenia. The current treatment options for myelofibrosis and their limitations in the management of anaemia and thrombocytopenia. Besides, reviewing the clinical trial data from emerging treatments, with a focus on patients with myelofibrosis who have anaemia and thrombocytopenia.

State of the art on the diagnosis and therapeutic in AL amyloidosis

Prof. Morie GERTZ

Chair, Department of Medicine,
Professor of Hematology,
Mayo Clinic,
Rochester, United States

Abstract

Light-chain amyloidosis (AL) is a disease of protean manifestations due to a wide spectrum of organs that can be affected. It is characterized by the production of misfolded immunoglobulin light chain. These misfolded proteins aggregate into amyloid fibrils and deposit throughout the body, resulting in widespread organ dysfunction and ultimately death. Disease heterogeneity is driven by the degree of multi-systemic involvement; cardiac, renal, neurological, and gastrointestinal (GI) systems are affected to varying degrees in different patients. Timely diagnosis is crucial as there may only be a small window of opportunity where patients can benefit from treatment beyond which therapies may be less effective. Achieving rapid and maximal elimination of the plasma cell clone is crucial to long-term survival. This lecture would discuss the diagnosis of AL amyloidosis and latest advances in managing this disease that offer promising improvement in end organ function, survival, and quality of life.

Germline predisposition to haematological malignancies

Prof. Lucy GODLEY

Inaugural Director, The Jeff and Marianne Silver Family Blood Cancer Institute,
Clinical Director of Cancer Genetics,
Robert H. Lurie Comprehensive Cancer Center,
Chicago, United States

Abstract

Inherited hematologic malignancies were first described in 1999, with the recognition that deleterious germline RUNX1 variants lead to lifelong thrombocytopenia, platelet aggregation defects, and an increased risk of developing hematopoietic malignancies (HMs). Since then, deleterious germline variants in many genes have been identified that predispose to aplastic anemia (AA) and/or bone marrow failure (BMF), including those associated with Diamond Blackfan anemia, Fanconi anemia, dyskeratosis congenita/ telomere biology disorders (TBDs), GATA2, SAMD9/SAMD9L, DCLRE1B, severe congenital neutropenia, and Shwachman Diamond Syndrome, among others. Today, these germline syndromes are recognized increasingly, as evidenced by the inclusion of inherited predisposition disorders within the diagnostic criteria of numerous classification schema as outlined by the World Health Organization, European LeukemiaNet, National Comprehensive Cancer Network, and the International Consensus Classification.

Our group has sought to delineate the frequency with which deleterious germline variants cause BMF disorders, including myelodysplastic syndrome (MDS) and AA. We have shown that in those diagnosed at age 40 or younger, 19% of individuals with MDS/acute myeloid leukemia (AML) with prior history of MDS and 15% of those with AA have such alleles. In a more recent study, we collaborated with the Center for International Blood and Marrow Transplant Research to study paired peripheral blood samples from MDS patients across the entire age range of life and their related allogeneic hematopoietic cell transplant (HCT) donors. We used these samples to estimate that the frequency of deleterious germline predisposition alleles is at least 7%, and these positive cases were spread across the age spectrum. We know from work using a large cohort of children with MDS, LP/P germline variants in SAMD9/SAMD9L were identified 8% and in GATA2 in a mutually exclusive 7%. The age of presentation of MDS differed in these two genetic cohorts with SAMD9/SAMD9L prevalent in younger children and GATA2 more common in older children. Thus, the age at which MDS/AA is diagnosed is linked to the underlying biological pathway(s) driving hematopoietic cancers, with variants in genes encoding transcriptional regulators common in children, DNA repair and telomere biology genes dominating adulthood diseases, and DDX41 frequent in the elderly.

In allogeneic HCT, these germline LP/P variants can have significant consequences. HCT involves cytoreductive conditioning followed by hematopoietic stem cell infusion from a healthy donor. LP/P variants in the donor or host could impact the success of HCT. Host variants could suffer more severe toxicity from the cytoreductive conditioning, harming the stromal cells necessary for engraftment of the donor cells, increasing the risk of graft failure and life-threatening infections. Similarly, donor LP/P variants could lead to graft failure or donor derived leukemia from hyperproliferation of few stem cells without appropriate repair mechanisms. Our group has shown that transplant recipients with P/LP germline variants in DDX41 develop severe graft versus host diseaseeven when wild-type donors are used unless they receive post-transplant cyclophosphamide. However, whether other poor outcomes after allogeneic HCT are also due to deleterious germline variants is unknown. Moreover, donors are not routinely screened for the presence of germline LP/P variants in genes linked to BMF or leukemias. Further research is needed to address whether a deleterious germline variant in the patient or donor predisposes to adverse outcomes after HCT.

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More than **1,600 Truxima®** prescription cases have been reported[5,6]

Truxima® has received authorisation for use in below indications:

- Non-Hodgkin's Lymphoma[7,8,9]
- Diffuse Large B Cell Lymphoma[10]
- Chronic Lymphocytic Leukaemia[11]

* A phase III, randomised, and double-blind study in 140 patients with previously untreated advanced follicular lymphoma. Patients treated with Truxima® (n=70) showed comparable PFS, TTP and OS compared to originator rituximab (n=70). Truxima® was consistently well tolerated and showed comparable safety profiles, including immunogenicity, over the entire study period without any unexpected toxicities.

† A study collecting real-world safety and effectiveness data on rapid infusion (RI) Truxima® from the medical records of 196 patients with non-Hodgkin's lymphoma or chronic lymphocytic leukaemia in 10 European centers, 6 months after the date of the first RI (index date); the infusion-related reaction rate was compared to previously published data. Ten percent of patients experienced an infusion-related reaction on day 1-2 just index, which was not significantly different to the rate for rituximab described previously (8.8%). Complete response and partial response to Truxima® was observed in 74% and 22% of patients, respectively. This real-world study demonstrates that the safety and effectiveness profile of RI Truxima® is similar to IRI of reference rituximab.

‡ A study collecting real-world data relating to the effectiveness and safety of Truxima® treatment from the medical records of 189 patients with diffuse large B cell lymphoma (24 centers, five European countries). For the primary outcome (clinical effectiveness), OS, PFS and best response (BR) were assessed. The one-year survival (95% confidence interval [95% CI]) of patients alive at 12-, 18-, and 30 months postindex (initiation of Truxima®) was 86% (82.4%–89.6%), 81% (76.9%–84.9%), and 76% (71.2%–80.7%), respectively. The PFS rate (percent; [95% CI]) at 12-, 18-, and 30 months postindex was 78% (74.2%–82.5%), 72% (67.9%–76.9%), and 67% (61.9%–71.7%), respectively. For 62% (n = 112) of patients, the BR to Truxima® was a complete response. Adverse events were consistent with known effects of chemotherapy.

§ Estimated total number of patients receiving Truxima® in real-world evidence studies listed in Chia D, et al. 2022.*

EMA=European Medicine Agency; FDA=Food and Drug Administration; OS=overall survival; PFS=progression free survival; RI=rapid infusion; TTP=time to progression.

Package leaflet: Information for the patient
Truxima® 100mg / 500 mg concentrate for solution for infusion
Read this leaflet carefully before you start taking this medicine because it contains important information for you. • Keep this leaflet. You may need to read it again. • If you have any further questions, ask your doctor, pharmacist or nurse. • If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4. **What is in this leaflet:** 1. What Truxima® is and what it is used for 2. What you need to know before you use Truxima® 3. How to use Truxima® 4. Possible side effects 5. How to store Truxima® 6. Contents of the pack and other information **1. What Truxima® is and what it is used for What Truxima® is** Truxima® contains the active substance "rituximab". This is a type of protein called a "monoclonal antibody". It is designed to stick to a type of white blood cell called "B-Lymphocyte". When sticking to the surface of this cell, rituximab causes the cell to die **What Truxima® is used for** Truxima® may be used for the treatment of several different conditions in adults. Your doctor may prescribe Truxima® for the treatment of **a) Non-Hodgkin's Lymphoma** This is a disease of the lymph tissue (part of the immune system) that affects a type of white blood cell called B-Lymphocytes. In adults, Truxima® can be given alone or with other medicines called "chemotherapy". In adult patients where the treatment is working, Truxima® may be used as a maintenance treatment for 2 years after completing the initial treatment. **b) Chronic lymphocytic leukaemia** Chronic lymphocytic leukaemia (CLL) is the most common form of adult leukaemia. CLL affects a particular lymphocyte, the B cell, which originates from the bone marrow and develop in the lymph nodes. Patients with CLL have too many abnormal lymphocytes, which accumulate mainly in the bone marrow and blood. The proliferation of these abnormal B-lymphocytes is the cause of symptoms you may have. Truxima® in combination with chemotherapy destroys these cells which are gradually removed from the body by biological processes. **2. What you need to know before you use Truxima® Do not take Truxima®** if • you are allergic to rituximab, other proteins which are like rituximab, or any of the other ingredients of this medicine (listed in section 6) • you have a severe active infection at the moment • you have a weak immune system • you have severe heart failure or severe uncontrolled heart disease and have rheumatoid arthritis, granulomatosis with polyangiitis or microscopic polyangiitis. Do not have Truxima® if any of the above apply to you. If you are not sure, talk to your doctor, pharmacist or nurse before you are given Truxima®. **Warnings and precautions** Talk to your doctor, pharmacist or nurse before you are given Truxima® • If you have ever had or might now have a hepatitis B infection. This is because in a few cases, Truxima® could cause hepatitis B to become active again, which can be fatal in very rare cases. Patients who have ever had hepatitis B infection will be carefully checked by their doctor for signs of this infection • you have ever had heart problems (such as angina, palpitations or heart failure) or breathing problems. If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before you are given Truxima®. Your doctor may need to take special care during your treatment with Truxima®. **Children and adolescents** Talk to your doctor, pharmacist or nurse before you are given this medicine if you, or your child, are under 18 years of age. This is because there is not much information about the use of Truxima® in children and young people. **Other medicines and Truxima®** Tell your doctor, pharmacist or nurse if you are taking / have recently taken or might take any other medicines. This includes medicines obtained without a prescription and herbal medicines. This is because Truxima® can affect the way some other medicines work. Also some other medicines can affect the way Truxima® works. **In particular, tell your doctor** • if you are taking medicines for high blood pressure. You may be asked not to take these other medicines 12 hours before you are given Truxima®. This is because some people have a fall in their blood pressure while they are being given Truxima®. • if you have ever taken medicines which affect your immune system – such as chemotherapy or immune suppressive medicines. If any of the above apply to you (or you are not sure), talk to your doctor, pharmacist or nurse before you are given Truxima®. **Pregnancy and breast-feeding** You must tell your doctor if you are pregnant, think that you might be pregnant or are planning to become pregnant. This is because Truxima® can transfer across the placenta and may affect your baby. If you can get pregnant, you and your partner must use an effective method of contraception while using Truxima®. You must also do this for 12 months after your last treatment with Truxima®. Do not breast-feed while you are being treated with Truxima®. Also do not breast-feed for 12 months after your last treatment with Truxima®. This is because Truxima® may pass into breast milk. **Driving and using machines** It is not known whether Truxima® has an effect on you being able to drive or use any tools or machines. **Truxima® contains sodium** This medicine contains 526 mg sodium in each 10 mL vial and 2632 mg in each 50 mL vial. This is equivalent to 26% (for 10ml vial) and 131% (for 50ml vial) of the recommended maximum daily dietary intake of sodium for an adult. **3. How to use Truxima® How it is given** Truxima® will be given to you by a doctor or nurse who is experienced in the use of this treatment. They will watch you closely while you are being given this medicine. This is in case you get any side effects. You will always be given Truxima® as a drip (intravenous infusion). **Medicines given before each Truxima® administration** Before you are given Truxima®, you will be given other medicines (pre-medication) to prevent or reduce possible side effects. **How much and how often you will receive your treatment a) If you are being treated for non-Hodgkin's Lymphoma** – If you are having Truxima® alone Truxima® will be given to you once a week for 4 weeks. Repeated treatment courses with Truxima® are possible. – If you are having Truxima® with chemotherapy Truxima® will be given to you on the same day as your chemotherapy. This is usually given every 3 weeks up to 8 times. • If you respond well to treatment, you may be given Truxima® as a maintenance treatment every 2 or 3 months for two years. Your doctor may change this, depending on how you respond to the medicine. **b) If you are being treated for chronic lymphocytic leukaemia** When you are treated with Truxima® in combination with chemotherapy, you will receive Truxima® infusions on day 0 cycle 1 then day 1 of each cycle for 5 cycles in total. Each cycle has a duration of 28 days. The chemotherapy should be given after the Truxima® infusion. Your doctor will decide if you should receive concomitant supportive therapy. If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse. **4. Possible side effects** Like all medicines, this medicine can cause side effects, although not everybody gets them. Most side effects are mild to moderate but some may be serious and require treatment. Rarely, some of these reactions have been fatal. **Infusion reactions** During or within the first 24 hours of the first infusion you may develop fever, chills and shivering. Less frequently, some patients may experience pain at the infusion site, blisters, itching, sickness (nausea), tiredness, headache, breathing difficulties, blood pressure raised, wheezing, throat discomfort, tongue or throat swelling, itchy or runny nose, vomiting, flushing or palpitations, heart attack or low number of platelets. If you have heart disease or angina, these infusion reactions might get worse. **Tell the person giving you the infusion immediately** if you develop any of these symptoms, as the infusion may need to be slowed down or stopped. You may require additional treatment such as an antihistamine or paracetamol. When these symptoms go away, or improve, the infusion can be continued. These reactions are less likely to happen after the second infusion. Your doctor may decide to stop your Truxima® treatment if these reactions are serious. **Infections Tell your doctor immediately if you get signs of an infection including:** • fever, cough, sore throat, burning pain when passing urine or feeling weak or generally unwell • memory loss, trouble thinking, difficulty walking or sight loss – these may be due to a very rare, serious brain infection, which has been fatal (progressive multifocal leukoencephalopathy or PML). You might get infections more easily during your treatment with Truxima®. These are often colds, but there have been cases of pneumonia or urinary infections. These are listed below under "Other side effects". **Skin reactions** very rarely, severe blistering skin conditions that can be life-threatening may occur. Redness, often associated with blisters, may appear on the skin or on mucous membranes, such as inside the mouth, the genital areas or the eyelids, and fever may be present. **Tell your doctor immediately if you have any of these symptoms. Other side effects include: a) If you are being treated for non-Hodgkin's Lymphoma or chronic lymphocytic leukaemia** very common side effects (may affect more than 1 in 10 people): • bacterial or viral infections, bronchitis • low number of white blood cells, with or without fever or blood cells called "platelets" • feeling sick (nausea) • bald spots on the scalp (alopecia), headache • lower immunity – because of lower levels of antibodies (called "immunoglobulins" (IgG) in the blood which help protect against infection) Common side effects (may affect up to 1 in 10 people): infections of the blood (sepsis), pneumonia, shingles, cold, bronchial tube infections, fungal infections, inflammation of sinuses, viral inflammation of the liver (hepatitis B) • low number of red blood cells (anaemia), low number of all blood cells, including neutrophils (which help fight infection) • high blood sugar level, weight loss, swelling in the face and hands, high levels of the enzyme "lactate dehydrogenase (LDH)" in the blood, low calcium levels in the blood • unusual feelings of the skin, such as numbness, tingling, pricking, burning, a creeping or skin feeling, reduced sense of touch, feeling restless, problems falling asleep, becoming very wet in the face and other areas of the skin as a consequence of dilation of the blood vessels • feeling dizzy or anxious • producing more tears, tear duct problems, inflamed eye • unpleasant sensations in the eyes, ear pain • heart problems – such as heart attack and uneven or fast heart rate • high or low blood pressure (low blood pressure especially when standing upright) • tightening of the muscles in the airways which causes wheezing (bronchospasm), inflammation in the lungs, throat or sinuses, being short of breath, runny nose • being sick (vomiting), diarrhoea, pain in the stomach, irritation or ulcers in the throat and mouth, problems swallowing, constipation, indigestion – eating disorders not eating enough, leading to weight loss • hives, increased sweating, night sweats • muscle problems – such as tight muscles, joint or muscle pain, back and neck pain • general discomfort or feeling uneasy or tired, shaking, signs of flu • multiple-organ failure. Uncommon side effects (may affect up to 1 in 100 people): • blood clotting problems, decrease of red blood cell production and increase of red blood cell destruction (aplastic, haemolytic anaemia), swollen or enlarged lymph nodes • low mood and loss of interest or enjoyment in doing things, feeling nervous • taste problems – such as changes in the way things taste • heart problems – such as reduced heart rate or chest pain (angina) – asthma, too little oxygen reaching the body organs • swelling of the stomach. Very rare side effects (may affect up to 1 in 10,000 people) • short term increase in the amount of some types of antibodies in the blood (called immunoglobulins – IgM) • chemical disturbances in the blood caused by breakdown of dying cancer cells • nerve damage in arms and legs, paralysis of face • heart failure • inflammation of blood vessels including those leading to skin symptoms • respiratory failure • damage to the intestinal wall (perforation) • severe skin problems causing blisters that can be life-threatening. Redness, often associated with blisters, may appear on the skin or on mucous membranes, such as inside the mouth, the genital areas or the eyelids, and fever may be present. • kidney failure • severe vision loss not known (it is not known how often these side effects happen) • a reduction in white blood cells which does not happen straight away • reduced platelets number just after the infusion – this can be severe, but can be fatal in rare cases • hearing loss. Loss of other senses Truxima® may also cause changes in laboratory tests carried out by your doctor. If you are having Truxima® with other medicines, some of the side effects you may get may be due to the other medicines. Reporting of side effects If you get any side effects talk to your doctor, pharmacist or nurse. This includes any side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine. **5. How to store Truxima®** Keep this medicine out of the sight and reach of children. Do not use this medicine after the expiry date which is stated on the carton and the vial after EXP. The expiry date refers to the last day of that month. Store in a refrigerator (2°C - 8°C). Keep the container in the outer carton in order to protect from light. Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines that you no longer use. These measures will help protect the environment. **6. Contents of the pack and other information What Truxima® contains** • The active ingredient in Truxima® is called rituximab. The 10mL vial contains 100mg of rituximab (10 mg/mL). The 50mL vial contains 500 mg of rituximab (10 mg/mL). • The other ingredients are sodium chloride, trisodium citrate dihydrate, polysorbate 80 and water for injections. **What Truxima® looks like and contents of the pack** Truxima® is a clear colourless solution supplied as a concentrate for solution for infusion. 10mL vial • Pack of 2 vials. 50mL vial • Pack of 1 vial. **Marketing Authorisation Holder** Celltrion Healthcare Hong Kong Limited, Suite 3305, 33rd Floor, Tower 5, The Gateway, Harbour City, 15 Canton Road, Tsim Sha Tsui, Kowloon. **Manufacturer** CELLTRION, Inc.20, Academy-ro 51 beon-gil, Yeonsu-gu, Incheon, 22014, Korea **This leaflet was last revised in July 2022.**

References. 1. Henry D, et al. Pharmacoeconomics of Cancer Therapies: Considerations With the Introduction of Biosimilars. Semin Oncol. 2014;41:513-520. **2.** European Medicines Agency. Truxima. Summary of Product Characteristics. Available at: https://www.ema.europa.eu/en/documents/product-information/truxima-epar-product-information_en.pdf. Accessed Feb 2023. **3.** U. S. Food and Drug Administration. Highlights of Prescribing Information. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761088s000lbl.pdf. Accessed Feb 2023. **4.** Choi D, Lee S, Kim S, Yoon S. A Developer's Perspective on Clinical Evidence and Benefits for Rituximab Biosimilar Uptake, with a Focus on CT-P10. Clin Drug Investig. 2022;42(4):285-308. **5.** Data on File, Celltrion Healthcare. **6.** Christian Buske, et al. Long-Term Efficacy and Safety Results of CT-P10 and Reference Rituximab in Patients with Newly Diagnosed Advanced Stage Follicular Lymphoma: Phase III Updated Study Results with Median Follow-up of 40 Months. Blood 2019; 134 (Supplement_1): 1528. **7.** Bishton M, et al. The safety and clinical effectiveness of rapid infusion with CT-P10 in patients with non-Hodgkin's lymphoma or chronic lymphocytic leukemia: A retrospective non-interventional post-authorization safety study in Europe. Hematol Oncol. 2022;40(3):370-380. **8.** Bishton, MJ, et al. Real-world clinical effectiveness and safety of CT-P10 in patients with diffuse large B-cell lymphoma: An observational study in Europe. eJHaem. 2022; 1– 10.

This material is for healthcare professionals only

HEALTHCARE CELLTRION

Celltrion Healthcare Hong Kong Limited
Suite 3305, 33rd Floor, Tower 5, The Gateway, Harbour City, 15 Canton Rd, Tsim Sha Tsui, Kowloon, Hong Kong

Megalotect CP® Biotest

HK Reg. No: HK-66874

Human cytomegalovirus immunoglobulin

Cytomegalovirus (CMV)-specific hyperimmune globulin preparation, with a standardised high antibody titre against CMV, for use in targeted prophylaxis post transplant[1]

Concomitant use of adequate virostatic agents should be considered for CMV-prophylaxis[1]

1. Megalotect CP® Biotest. Summary of Product of Characteristics

Hong Kong & Macau Distributor:

Biotest

Chong Lap (H.K.) Co. Ltd.
創立（香港）有限公司

Part I:
Unveiling breakthroughs in DLBCL therapies: Embracing the era of bispecific antibodies and ADCs

Prof. Georg LENZ

Director, Department of Haematology, Oncology and Pneumology,
University Hospital Münster,
Germany

Abstract

Diffuse large B-cell lymphoma (DLBCL) presents challenges in effective treatment due to its heterogeneity and aggressive nature. Recent progress in cancer research has resulted in the emergence of promising therapeutic strategies, notably CAR-T, bispecific antibodies and antibody-drug conjugates (ADCs). This talk will focus on the discussion of the latter ones. Challenges associated with the current and upcoming treatment paradigms and the role of these therapies will be discussed. Embracing these innovative approaches holds potential for transformative advancements in DLBCL treatment and improved patient outcomes.

Part II:
Role of BTKi in the management of marginal zone lymphomas and follicular lymphoma

Prof. Chan Yoon CHEAH

Lymphoma lead and Fellowship Program Director,
Sir Charles Gairdner Hospital,
Australia

Abstract

This talk delves into the evolving landscape of treating marginal zone lymphomas (MZL) and follicular lymphoma (FL) with a focus on the role of BTK inhibitors. Despite advancements in drug development and a deeper understanding of these diseases, some patients continue to grapple with recurrent episodes. The expanding array of therapeutic options for MZL and FL presents a paradox, prompting exploration into novel approaches. BTK inhibitors emerge as a promising avenue, offering patients a chemotherapy-free treatment option, thereby addressing the challenges associated with disease recurrence. This review underscores the potential of BTK inhibitors in reshaping treatment paradigms for individuals afflicted with MZL and FL.

Part I: Future direction of ALL treatment in the new era of noval therapies

Prof. Robin FOÀ

Professor of Hematology,
Head, Division of Hematology,
The Sapienza University of Rome,
Italy

Abstract

While the management of Philadelphia-positive Acute Lymphoblastic Leukaemia (Ph+ ALL) has evolved over the last decades, new and exciting treatments becomes increasingly available. Prof. Foa, who is the lead of the GIMEMA trial, will be sharing with us the exciting latest outcomes from GIMEMA trial, long-term follow up of chemo-free treatment for Ph+ALL, and the latest advances on MRD-guided treatment for both Ph- and Ph+ ALL.

Part II:
A new era of acute myeloid leukemia management

Prof. Edgar JOST

Professor, Lead of Stem Cell Therapy,
Department for Hematology, Oncology,
Hemostaseology and Stem Cell Transplantation,
University Hospital RWTH Aachen,
Germany

Abstract

Acute Myeloid Leukemia (AML) is an aggressive disease that brings formidable challenge for effective disease management. Intensive chemotherapy is the cornerstone of initial AML therapy for patients that are fit enough to receive it, and most patients achieve CR with induction. However, most patients eventually have a relapse. Clonal evolution, epigenetic reprogramming leading to aberrant DNA methylation, and persistence of leukemia-initiating cells despite chemotherapy are thought to be contributing factors of disease recurrence.

This presentation will discuss how rapidly evolving AML treatment options help addressing the unmet needs. As longer durations of first remission are associated with better survival outcomes, preventing early AML relapse is an important treatment goal in disease management. With continuous scientific advancement, the future direction of AML management will also be discussed.

Rare but important to know – A novel mechanism for PNH management

Prof. Alexander RÖTH

Senior Physician,
Head of Classical Hematology and Coagulation,
Department of Hematology and Stem Cell Transplantation,
West German Cancer Centre,
University Hospital Essen,
Germany

Abstract

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare and chronic disease originated from somatic mutation of phosphatidylinositol glycan-class A (PIG-A) gene in hematopoietic stem cells (HSCs). The subsequent loss of CD55 and CD59 in PIG-A-mutated red blood cells (RBCs)leads to ineffective complement inhibition and sensitization to intravascular hemolysis (IVH).

Additionally, hemoglobin released during hemolysis in PNH results in depleted nitric oxide (NO)levels at the tissue level, leading to an increased risk of thrombosis, amongst other symptoms. Patients' continual hemolysis, renal complications and increased risk of thrombosis pose significant impact on morbidity and mortality.

The availability of C5 inhibitors (C5i) ushered in a new era of complement treatment that demonstrated effective disease control and improvements in patients' quality of life. However, while inhibiting C5 abolishes IVH, the upstream C3 is left unchecked, leading to C3 deposition on RBCs and onset of EVH. As such, a substantial proportion of patients undergoing C5i treatment still experience fatigue, residual anemia and even require RBC transfusions.

To this end, multiple new agents are being developed to improve patient outcomes. These include C5 inhibitor crovalimab, C3 inhibitor pegcetacoplan, and factor B inhibitor iptacopan, amongst others. Approved recently by FDA, iptacopan is a novel, first-in-class, oral complement factor B inhibitor for the treatment of PNH. Factor B is upstream of C3 and C5 in the alternative complement pathway, and thus targeting factor B has the potential of inhibiting or preventing both IVH and EVH. Phase III clinical trial data of iptacopan in both treatment-naive and C5 inhibitor-exposed patient populations have shown highly promising data in terms of anemia control, transfusion avoidance, and quality of life improvements, with a balanced tolerabilityprofile.

This lecture will focus on the unmet medical needs surrounding PNH, highlight the impact and significance of novel agents in the treatment of PNH, and discuss relevant clinical cases.

Latest update on management of high-risk multiple myeloma

Prof. Thierry FACON

Professor of Haematology,
Department of Haematology,
Lille University Hospital,
France

Abstract

The presentation will begin with an overview of the clinical characteristics of high-risk multiple myeloma, highlighting the challenges associated with its treatment. It will discuss the key Phase 3 clinical trial data of anti-CD38 therapies, evaluating their efficacy and safety for the high-risk cytogenetic population. The lecture will also include the latest scientific updates on therapies in the upfront setting for newly diagnosed MM patients, based on emerging data from ongoing clinical trials.

T-cell re-direction therapies for treatment of lymphomas and myeloma

Prof. Henry FUNG Chi Hang

Chair and Professor,
Department of Bone Marrow Transplant and Cellular Therapies,
Fox Chase Cancer Center,
United States

Abstract

T-cell re-direction therapies specifically bi-specific antibodies and CART-cell based therapies have rapidly become the standard of care for selected patients with relapsed/refractory lymphomas and myeloma. The objective of this presentation is to review the state-of-the-art of this novel therapy in the treatment of lymphomas and myeloma. After this activity, the participants should be able to:

- Integrate into practice up-to-date efficacy and safety data on T-cell redirection therapies for the treatment of patients with lymphoma and myeloma.
- Based on the current best evidence, implement strategies for managing toxicities associated with T-cell redirection therapies.
- Discuss considerations associated with T-Cell redirection therapies including patient selection and referring patients to

Reach New Heights with BRUKINSA®

Guiding You Through WM[5], CLL[†], and R/R MZL[1] Terrain[1]

BRUKINSA® in WM:
NCCN-preferred category 1 regimen across 1L and previously treated WM[2]

ASPEN study:

BRUKINSA® showed efficacy across *MYD88*-mutant and wild-type WM[1,3,4]

***MYD88* mutant population**

A trend toward better response than ibrutinib[1,3]

CR or VGPR: **28%** Brukinsa vs **19%** Ibrutinib

***MYD88* wild-type population**

Response to BRUKINSA® remained outstanding[1,4]

27% CR or VGPR

50% MRR

BRUKINSA® in CLL:
NCCN-preferred regimen across 1L, 2L, and 3L regardless of del(17p)/*TP53* mutation[5]

SEQUOIA study:

1L CLL

Head-to-head superiority vs BR[1,6,‡]

2-year PFS: **86%** Brukinsa vs **70%** BR

HR 0.42 (95% CI 0.28–0.63), P<0.0001

ALPINE study:

R/R CLL

Head-to-head superiority vs ibrutinib[1,7]

2-year PFS: **78%** Brukinsa vs **66%** Ibrutinib

HR 0.65 (95% CI 0.49–0.86), P=0.002

BRUKINSA® in R/R MZL:
NCCN-preferred regimen for 2L and subsequent therapy*, even for older or infirm[8]

MAGNOLIA study:

BRUKINSA® showed high response (68% ORR) with durable disease control[1,9]

Brukinsa® zanubrutinib 80mg capsules

BeiGene

[†] BRUKINSA® as monotherapy is indicated for the treatment of adult patients with WM who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy.[1]
[†] BRUKINSA® as monotherapy is indicated for the treatment of adult patients with CLL.[1]
[‡] BRUKINSA® as monotherapy is indicated for the treatment of adult patients with MZL who have received at least one prior anti-CD20-based therapy.[1]
[‡] This head-to-head comparison included only patients without del(17p) mutation as BR was not considered a suitable option in those with del(17p).[6]
* Relapsed/refractory after at least one prior anti-CD20 monoclonal antibody-based regimen.*

Abbreviations: 1L, first-line; 2L, second-line; 3L, third-line; BR, bendamustine plus rituximab; CD, cluster of differentiation; CI, confidence interval; CLL, chronic lymphocytic leukemia; CR, complete response; DOR, duration of response; HR, hazard ratio; MRR, major response rate; MZL, marginal zone lymphoma; NCCN, National Comprehensive Cancer Network; ORR, overall response rate; PFS, progression-free survival; R/R, relapse/refractory; VGPR, very good partial response; vs, versus; WM, Waldenström's macroglobulinaemia.

References: 1. BRUKINSA® Hong Kong prescribing information (Jun 2023). 2. NCCN Guidelines for Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma (Version 2.2024). 3. Tam CS, et al. Blood. 2020;136(18):2038-2050. 4. Dimopoulos M, et al. Blood. 2020;4(23):6009-6018. 5. NCCN Guidelines for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (Version 1.2024). 6. Tam CS, et al. Lancet Oncol. 2022;23(8):1031-1043. 7. Brown JR, et al. N Engl J Med. 2023;388(4):319-332. 8. NCCN Guidelines for B-Cell Lymphomas (Version 1.2024). 9. Opat S, et al. Clin Cancer Res. 2021;27(23):6323-6332.

BRUKINSA® Prescribing Information
Name of the medicinal product: BRUKINSA® capsules 80 mg. **Qualitative & quantitative composition**: Each hard capsule contains 80 mg of zanubrutinib. **Pharmaceutical form**: White to off-white opaque hard capsule of 22 mm in length, marked with "ZANU 80" in black ink. **Therapeutic indications**: BRUKINSA® as monotherapy is indicated for the treatment of adult patients with Waldenström's macroglobulinaemia (WM) who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy. BRUKINSA® as monotherapy is indicated for the treatment of adult patients with marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based therapy. BRUKINSA® as monotherapy is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL). **Posology & method of administration**: The recommended total daily dose of zanubrutinib is 320 mg. The daily dose may be taken either once daily (four 80 mg capsules) or divided into two doses of 160 mg twice daily (two 80 mg capsules). Treatment with BRUKINSA® should be continued until disease progression or unacceptable toxicity. **Contraindications**: Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 (please refer to full prescribing information). **Special precautions for storage**: Do not store above 30°C. **Local registration certificate holder**: BeiGene (Hong Kong) Co., Limited. **Full prescribing information should be consulted prior to prescribing**. Hong Kong prescribing information (Jun 2023)

This material is intended for the reference of Healthcare Professionals only.

0224-BRU-PRC-155

privigen™
Immune Globulin Intravenous (Human), 10% Liquid
IVIg therapy made simple

Advancing Ig therapy. The first and only proline-stabilised 10% liquid human IVIg[1]

85+ Countries[2] | 1,000,000+ Patient-years exposure[3]

- Convenient, ready-to-use 10% liquid IgG[4]
- ≥98% Ig purity—only trace amounts of IgA (≤25 mcg/mL)[4]
- If well-tolerated, the rate of administration may gradually be increased to 4.8 mL/kg bw/hour[4]
- Multiple indications: PID, SID, CIDP, ITP, GBS, MMN, and Kawasaki disease[4]

Before prescribing, please review the approved Hong Kong Package Insert, November 2021

Privigen Human normal immunoglobulin solution for infusion (10%)

Indication: Replacement therapy in adults, and children and adolescents (0-18 years) in: • Primary immunodeficiency syndromes (PID) with impaired antibody production; • Secondary immunodeficiencies (SID) in patients who suffer from severe or recurrent infections, ineffective antimicrobial treatment and either proven specific antibody failure (PSAF)* or serum IgG level of <4 g/l. Immunomodulation in adults, and children and adolescents (0-18 years) in: • Primary immune thrombocytopenia (ITP), in patients at high risk of bleeding or prior to surgery to correct the platelet count; •Guillain-Barré syndrome; • Kawasaki disease(in conjunction with acetylsalicylic acid); • Chronic inflammatory demyelinating polyneuropathy (CIDP). Only limited experience is available of use of intravenous immunoglobulins in children with CIDP; • Multifocal motor neuropathy (MMN). ** PSAF = failure to mount at least a 2-fold rise in IgG antibody titre to pneumococcal polysaccharide and polypeptide antigen vaccines.* **Dosage:** In replacement therapy the dose may need to be individualised for each patient depending on the clinical response. *Replacement therapy in primary immunodeficiency (PID) syndromes* The recommended starting dose is 0.4 to 0.8 g/kg body weight (bw) given once, followed by at least 0.2 g/kg bw every 3 to 4 weeks. *Secondary immunodeficiencies* The recommended dose is 0.2 – 0.4g/kg bw every three to four weeks. *Primary immune thrombocytopenia (ITP)* • 0.8 to 1 g/kg bw given on day 1; this dose may be repeated once within 3 days, OR •0.4 g/kg bw given daily for 2 to 5 days. *Guillain-Barré syndrome* 0.4 g/kg bw/day over 5 days. Kawasaki disease 2.0 g/kg bw should be administered as a single dose. Patients should receive concomitant treatment with acetylsalicylic acid. *Chronic inflammatory demyelinating polyneuropathy (CIDP)* The recommended starting dose is 2 g/kg bw divided over 2 to 5 consecutive days followed by maintenance doses of 1 g/kg bw over 1 to 2 consecutive days every 3 weeks. *Multifocal Motor Neuropathy (MMN)* Starting dose: 2 g/kg given over 2-5 consecutive days. Maintenance dose: 1 g/kg every 2 to 4 weeks or 2 g/kg every 4 to 8 weeks. **Method of administration:** For intravenous use. Privigen should be infused intravenously at an initial infusion rate of 0.3 ml/kg bw/hr for approximately 30 min. If well tolerated, the rate of administration may gradually be increased to 4.8 ml/kg bw/hr. In PID patients who have tolerated the infusion rate of 4.8 ml/kg bw/hr well, the rate may be further gradually increased to a maximum of 7.2 ml/kg bw/hr. **Contraindications:** Hypersensitivity. Patients with selective IgA deficiency who developed antibodies to IgA. Patients with hyperprolinaemia type I or II. **Precautions:** Not indicated in patients with selective IgA deficiency where the IgA deficiency is the only abnormality of concern. Caution for hypersensitivity, haemolytic anaemia, aseptic meningitis syndrome, thromboembolism, acute renal failure, pulmonary adverse reactions, interference with serological testing, possibility of transmissible agents. In case of adverse reaction, IVIg products should be administered at the minimum rate of infusion and dose practicable. Privigen does not contain sucrose, maltose or glucose. Privigen contains less than 2.3 mg sodium per 100 ml. **Undesirable effects:** Headache, pain, pyrexia, influenza like illness, anaemia, haemolysis (), leukopenia, hypersensitivity, dizziness, hypertension, flushing, hypotension, dyspnoea, nausea, vomiting, diarrhoea, abdominal pain, hyperbilirubinaemia, skin disorder, myalgia, fatigue, asthenia, decreased haemoglobin, Coombs'(direct) test positive, increased alanine aminotransferase, increased aspartate aminotransferase, increased blood lactate dehydrogenase. **Date of last revision of PI:** Nov 2021

References

1. Morio T, et al. Immunological Medicine 2019; 42:4, 162-168 2. Data on file. Available from CSL Behring as DOF-PRI-10019. 3. Data on file. Available from CSL Behring as DOF-PRI-10020. 4. Hong Kong Privigen Package Insert, Nov 2021

Ig: immunoglobulin; IVIg: intravenous immunoglobulin; bw: body weight; PID: Primary immunodeficiency syndromes; SID: Secondary immunodeficiencies; CIDP: Chronic inflammatory demyelinating polyneuropathy; ITP: Primary immune thrombocytopenia; GBS: Guillain-Barré syndrome; MMN: Multifocal Motor Neuropathy

Biotherapies for Life™ **CSL Behring**

CSL Behring Asia Pacific Limited
4205 - 4208, AIA Tower, 183 Electric Road
North Point, Hong Kong

HKG-PVG-11220008
Date of preparation: Nov 2022

For sales distribution to HCPs

VELCADE® (bortezomib)

18 years of experiences in HK in MM treatment

Consistent clinical benefits Recommended by authorities[1-3]

VELCADE was recommended as:

ESMO guideline:

- A front-line agent in combination with other anti-myeloma agents for treating NDMM[1]

NCCN guideline:

- An agent in primary therapy of MM (NCCN 2023)[2]
- A front-line agent for treating MCL (NCCN 2023)[3]

Eligible for special patient populations[4]

No dose adjustments for VELCADE® are necessary for elderly patients (aged ≥65 years), patients with mild hepatic impairment and mild-to-moderate renal impairment.[4]

Indications approved in Hong Kong[4]

For the treatment of adult multiple myeloma (MM) patients who:

- Were previously untreated, and **ineligible for HSCT**[a]
- Were previously untreated, and **eligible for HSCT**[b]
- **Progressed on ≥1 prior therapy** and have already undergone or are otherwise ineligible for HSCT[c]

For the treatment of patients with previously untreated **mantle cell lymphoma** who are unsuitable for **HSCT**[d]

[a] As monotherapy or in combination with melphalan and prednisone
[b] In combination with dexamethasone, or with dexamethasone and thalidomide
[c] In combination with pegylated liposomal doxorubicin or dexamethasone
[d] In combination with rituximab, cyclophosphamide, doxorubicin and prednisone

References: 1. Dimopoulos MA, et al. Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2021;32(3):309-322. 2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma ver 3.2023. Available at: https://www.nccn.org/guidelines/nccn-guidelines/guidelines-detail?category=1&id=1445 (Access Date: 26 July 2023). 3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: B-Cell Lymphomas ver 5.2023. Available at: https://www.nccn.org/guidelines/nccn-guidelines/guidelines-detail?category=1&id=1480 (Access Date: 26 July 2023). 4. VELCADE® Hong Kong Prescribing Information P05

Abbreviations: ESMO: European Society for Medical Oncology; HSCT: haematopoietic stem cell transplantation; MCL: mantle cell lymphoma; MM: multiple myeloma; NCCN: National Comprehensive Cancer Network; NDMM: newly diagnosed multiple myeloma

VELCADE® for Injection 3.5 mg ABBREVIATED PRESCRIBING INFORMATION **ACTIVE INGREDIENT(S):** Bortezomib. **INDICATION(S):** As monotherapy or in combination with pegylated liposomal doxorubicin or dexamethasone is indicated for the treatment of adult patients with progressive multiple myeloma who have received at least 1 prior therapy and who have already undergone or are unsuitable for haematopoietic stem cell transplantation. In combination with melphalan and prednisone is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for high dose chemotherapy with haematopoietic stem cell transplantation. In combination with dexamethasone, or with dexamethasone and thalidomide, is indicated for the induction treatment of adult patients with previously untreated multiple myeloma who are eligible for high dose chemotherapy with haematopoietic stem cell transplantation. In combination with rituximab, cyclophosphamide, doxorubicin and prednisone is indicated for the treatment of adult patients with previously untreated mantle cell lymphoma who are unsuitable for haematopoietic stem cell transplantation. **DOSAGE & ADMINISTRATION:** Starting dose is 1.3 mg/m2 administered either as a 3-5 second bolus intravenous injection (IV) at a concentration of 1 mg/mL or via subcutaneous injection (SC) at a concentration of 2.5 mg/mL. Because each route of administration has a different reconstituted concentration, caution should be used when calculating the volume to be administered. Use a lower starting dose for patients with moderate or severe hepatic impairment. Dose must be individualized to prevent overdose. SC or IV use only. **CONTRAINDICATIONS:** Hypersensitivity to the active substance, boron, mannitol or nitrogen. 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SESSION 9: YOUNG FELLOW AND BEST ABSTRACT PRESENTATION

Part I: T-large granular lymphocytic leukaemia – Clinical and epidemiological perspectives from a single centre cohort

Dr. Ryan HO Chi Wai

Resident Specialist,
Division of Haematology,
Medical Oncology & Haematopoietic Stem Cell Transplantation,
Department of Medicine,
Queen Mary Hospital

Abstract

T-large granular lymphocytic leukaemia (T-LGLL) is a rare chronic mature lymphoproliferative disorder of T/natural killer (NK) lineage, which has a distinctive association with autoimmunity, including autoimmune connective tissue disorders and immune-mediated cytopenia. Prevailing treatment recommendations in the literature have been driven by Western patients, in whom the disease biology might be different. In the present study, 121 patients diagnosed as having T-LGLL in Queen Mary Hospital between 2009 and 2023 were identified using molecular study record. As the largest Asian T-LGLL cohort to date, patients in this study showed remarkable differences in disease phenotype and treatment response, as compared with Western patients. Asian patients were more likely to have pure red cell aplasia and less likely to have neutropenia, splenomegaly or rheumatoid arthritis. Asian patients also responded favourably to cyclosporine and were less likely to respond to methotrexate and cyclophosphamide. Salvage therapy is challenging, with alemtuzumab being a better option when immunosuppressants had failed. Recognizing the difference between Asian and Western patients is pivotal in providing optimal care for T-LGLL.

Part II: A single-centre retrospective analysis of EBV-positive DLBCL with special focus on the plasma EBV DNA loads before, during and after treatment and the correlation with outcomes

Dr. Michael NGAI Cheong

Resident,
Department of Medicine,
Queen Mary Hospital

Abstract

In this study, the clinicopathological features, treatment responses and plasma EBV DNA before, during and after treatment with its correlation with outcomes of EBV-positive diffuse large B-cell lymphoma (DLBCL) were evaluated. Of 42 patients included, the median age was 74 years (18-98). There was a male predominance, with 40.5% of cases having B symptoms and 59.5% of cases having good ECOG performance (≤1). Most patients had < 2 sites of extranodal involvement, no bone marrow infiltration, elevated LDH, advanced Ann Arbor (stage III/IV) and high IPI score (3-5). Histology was mostly of non-GCB subtype with CD30 positivity. Twenty-one patients had plasma EBV DNA data at diagnosis, with a median of 40,848 copies/ml. At interim (after 2-4 cycles of treatment), 25% (5/20) had persistent EBV DNA positivity, which correlated with an inferior outcome. At end-of-treatment, 14 patients had plasma EBV DNA data, which were all undetectable. For first-line therapy, 61.9% achieved CR. At a median follow up of 19 months, the 5-year overall survival (OS) was 47.5% and the 5-year disease-free survival (DFS) was 40.7%. With log-rank test, age > 70 years, presence of B symptoms, bone marrow involvement, Ann Arbor stage III to IV, IPI score 3-5, persistence of plasma EBV DNA at interim assessment and not achieving CR after first line treatment were associated with shorter OS. Presentation plasma EBV DNA levels > 1 x 105 copies/ml was associated with shorter DFS. On multivariate analysis using cox proportional hazard regression model, achieving CR as best response after first line treatment was the only factor significantly associated with better OS.

Part III: Unsupervised machine learning for flow cytometric data analysis in T-lymphoblastic leukaemia (T-ALL) measurable residual disease (MRD) monitoring

Dr. Jamilla LI Wai Yan

Resident Specialist,
Department of Pathology,
Queen Mary Hospital

Abstract

Background and Objective

Measurable residual disease (MRD) status is strongly associated with clinical outcomes in haematological malignancies and can be monitored by multi-colour flow cytometry. Conventional MRD analysis by manual gating is time-consuming, operator-dependent and requires significant expertise. Challenges unique to MRD analysis include small size of the target population, and unpredictable target population immunophenotype due to disease heterogeneity and immunophenotypic shifts during treatment. FlowSOM is a clustering tool that employs unsupervised machine learning for analysis of flow cytometric data. This study aimed to explore the performance of FlowSOM in analysis of T-lymphoblastic leukaemia (T-ALL) MRD flow cytometric data.

Methods

Flow cytometric data files from samples sent to Queen Mary Hospital for T-ALL MRD testing from January 2021 to March 2022 were retrieved. FlowSOM was applied retrospectively for automatic clustering of events and the antigen expression profile for each cluster was reviewed by qualified pathologist/flow cytometrist to identify cluster(s) representing residual disease. Results were compared with those obtained using manual gating.

Results

A total of 142 tubes from 36 samples were analysed. These included different leukaemia-associated immunophenotypes (LAIPs), including early T-cell precursor (ETP-ALL) or near-ETP phenotypes, and samples with antigenic shifts during monitoring. Sampled timepoints included post-induction chemotherapy, post-consolidation, maintenance, pre-haemopoietic stem cell transplant (HSCT) and post-HSCT.

Residual disease was positive in 14 and negative in 22 samples by conventional analysis. Analysis by FlowSOM achieved a 100% concordance rate in terms of positivity / negativity call for each sample.

Amongst 142 tubes analysed, residual disease was quantifiable in 62 tubes by conventional analysis. MRD level ranged from 0.038% to 35.146%. Residual disease was quantifiable by FlowSOM in 60 tubes. Residual disease identified on conventional analysis was not identifiable by FlowSOM in 3 tubes. On the other hand, residual disease was quantifiable by FlowSOM in 2 tubes where conventional analysis failed to isolate the leukaemic population, and in total, there were 23 tubes where FlowSOM analysis outperformed human analysis in terms of quantification accuracy.

MRD levels derived from conventional analysis and FlowSOM analysis showed clinically acceptable agreement and high degree of correlation ($R^2 = 0.997$).

Conclusion

This study serves as proof of concept for the use of machine in clinical flow cytometric data analysis. FlowSOM facilitates quick, accurate and reproducible analysis of flow cytometric data in T-ALL MRD monitoring and can serve as an alternative or supplementary method to conventional analysis in the clinical laboratory.

Part IV: Local experience of emicizumab in hemophilia A patients

Dr. Michael MAN Ho Yin

Resident,
Department of Medicine,
Queen Elizabeth Hospital

Abstract

Hemophilia A can cause multiple complications including hemarthrosis, soft tissue bleeding and even life-threatening mucosal bleeding in severe cases. Although exogenous replacement of factor VIII has been safely used for this group of patients in decades, development of alloantibodies against factor replacement remains to be a significant challenge and exposing these patients into high risk of morbidity and mortality. Despite appearance of bypassing agents such as activated factor eight inhibitor bypass activity (i.e. FEIBA) and Novoseven, the treatment and prophylaxis in some cases is still discouraging and can bring devastating outcome in these patients' life. Emicizumab, a newer therapy not basing on factor replacement, has been approved by the Food and Drug Administration since 2018. Multiple international studies (HAVEN) were performed with satisfactory results and they brought new hopes to these patients. In this retrospective review, we would like to examine the local data and outcomes of patients with hemophilia A, with and without inhibitors, who were treated with emicizumab. Our aim was to assess how these local findings compare to the results reported in the HAVEN trials. By focusing on this specific patient population, we hoped to determine the consistency and generalizability of the outcomes observed in the HAVEN trials within our own local context in terms of effectiveness, cost and safety aspects of emicizumab.

Part V: Bethesda assay for detecting anti-ADAMTS13 antibodies

Dr. Vivian YEUNG Ka Pik

Associate consultant,
Department of Pathology,
Princess Margaret Hospital

Abstract

Introduction

Thrombotic thrombocytopenic purpura (TTP) is an uncommon but critical life-threatening haematological disorder. It is characterized by microangiopathic haemolytic anaemia, severe thrombocytopenia and organ ischaemia linked to disseminated microvascular platelet rich-thrombi. Severely deficient ADAMTS13 activity together with the presence of anti-ADAMTS13 antibody is indicative of immune-mediated TTP (iTTP). Methodologies used for antibody detection include enzyme-linked immunosorbent assays (ELISA) and functional inhibitor assays based on Bethesda-like mixing studies. Most anti-ADAMTS13 antibodies are inhibitory in nature and can be detected by both methods, while non-inhibitory antibodies can only be detected by the former. This study sought to explore the utility of Bethesda assay in detecting anti-ADAMTS13 antibodies and to determine if it has an advantage over ELISA.

Methods

Samples with clinical suspicion of TTP or for monitoring of TTP sent to Princess Margaret Hospital from March 2023 to January 2024 were included. ADAMTS13 activity was measured by chemiluminescence assay (CLiA). Samples with ADAMTS13 activity <30% proceeded to anti-ADAMTS13 antibody detection by ELISA assay and Bethesda assay using CLiA.

Results

A total of 153 samples were included. Forty six samples from 33 patients underwent testing for anti-ADAMTS13 antibody. Their clinical diagnosis included iTTP, congenital TTP, autoimmune disease, disseminated intravascular coagulopathy, malignancy and haemolytic uraemic syndrome. The concordance rate of Bethesda assay and ELISA was 84.8% (k = 0.73). Five of the 46 samples were tested positive by ELISA but negative by Bethesda assay. Four of them had clinical diagnosis of autoimmune disease and 1 diagnosed as early iTTP relapse. One sample was tested negative by ELISA but positive by Bethesda assay, and 1 sample showed borderline results by ELISA but tested positive by Bethesda assay. Both were eventually diagnosed as iTTP. The sensitivity and specificity of Bethesda assay for detecting anti-ADAMTS13 antibody at first presentation and at relapse of iTTP were 90% and 100% respectively.

Conclusion

Bethesda assay showed good agreement with ELISA assay in detecting anti-ADAMTS13 antibody and was more discriminatory in the setting of autoimmune disease. Bethesda assay by CLIA also has faster turnaround time with better automation and limited operator involvement. Its utility as an alternative method in routine laboratory diagnosis of iTTP could be considered.

Part VI: Best abstract presentation
Glofitamab real-world experience in a quaternary referral center

Dr. Thomas CHAN Sau Yan

Consultant,
Department of Medicine,
Queen Mary Hospital

Abstract

Background
Glofitamab is a bispecific monoclonal antibody that targets CD20 and CD3, with a unique 2:1 (bivalency for CD20; monovalency for CD3) configuration. In the pivotal trial leading to regulatory approval1, glofitamab demonstrated remarkable efficacy in patients with relapsed or refractory diffuse large B cell lymphoma (DLBCL). Objective responses were observed in 80% of patients, with 39% achieving complete response. Additionally, complete response was maintained in 78% of patients at 12 months, suggesting that the response might be durable. Most grade 3 or 4 adverse events were hematologic in nature and generally manageable.
Despite its efficacy in clinical trials, the real-world safety and efficacy of glofitamab have not been extensively studied, particularly in patient groups such as those with prior exposure to hepatitis B virus (i.e. occult HBV infection, as evidenced by positive anti-HBV core antigen antibody). Here, we report a single-institution experience of glofitamab in Chinese patients with relapsed or refractory DLBCL, with one-third of them having occult HBV infection.

Methods
This is a retrospective study to evaluate the safety and efficacy of glofitamab in Chinese patients with relapsed or refractory DLBCL. Patients were enrolled through a compassionate program and were required to have failed at least three prior lines of therapy. Patients with active central nervous system lymphoma or active HBV infection (defined as detectable serum hepatitis B surface antigen) were ineligible for treatment. Glofitamab was administered according to the published protocol. Patients with occult HBV infection were given antiviral prophylaxis with entecavir. Response assessment was made according to published criteria2. Survival was analyzed using Kaplan-Meier method. Statistical calculations were performed with SPSS Statistics version 28.

Results
Nine men and six women at a median age of 60 (range: 41-83 years) were treated. Underlying diseases were DLBCL (N=12;80%); transformed follicular lymphoma (N=1, 7%); transformed marginal zone lymphoma (N=1, 7%); and high-grade B-cell lymphoma (N=1, 7%). Other relevant features included staging (I, N=1, 7%; II, N=1, 7%; IV, N=13, 87%); cell of origin (germinal centre B-cell: N=7, 47%; non-germinal centre B-cell: N=7, 47%; not available: N=1, 7%); double-expressor status (positive: N=9, 60%; negative: N=1, 7%; unknown: N=5, 33%); double-hit status(positive: N=3, 20%; negative: N=3, 20%;, unknown: N=9, 60%), prior lines of therapy (median: 6, range: 3-8); prior chimeric receptor T-cell therapy (N=7, 47%); prior autologous transplant (N=4, 27%); elevated serum lactate dehydrogenase (N=9, 60%), and occult HBV infection (N=5, 33%). Eleven patients had a response assessment, showing complete response N=6, 55%), partial response (N=1, 9%) and no response/progressive disease (N=4, 36%). At a median follow-up of 7 months (range 1-22 months) (Figure 1), the median progression-free survival (PFS) was 12 months and the median overall survival (OS) was 15 months(Figure 2). Adverse events included >= grade 3 haematological (anaemia: N=7, 47%; neutropenia: N=8, 53%; thrombocytopenia: N=5, 33%); CRS (grade 1: N=4, 27%; grade 2: N=3, 20%); and cytomegalovirus retinitis (N=1; 6%).

Conclusion
Glofitamab showed similar efficacy in real-world patients compared with published results. It was safe in patients with occult HBV infection given antiviral prophylaxis.

Nursing management on CRS

Ms. Jane ASTON

Bispecific Clinical Nurse Specialist,
The Newcastle Upon Tyne Hospitals NHS Foundation Trust,
United Kingdom

Abstract

The presentation will cover the nature of Cytokine release Syndrome (CRS) which is the most common side effect of bispecific antibodies. Explain the mode of action of Bispecific antibodies and how this can result in CRS. Discussing ASTCT Consensus grading to evaluate patients and how CRS is treated in relation to this grading.

With the administration of Bispecifics antibodies there are methods to mitigate CRS and I will discuss these which include step up dosing amongst others and the use of steroids prior to infusion.

Examples will be used to demonstrate how CRS is graded in practice and highlight the management required. Data and a case study will also be discussed from my experience of Bispecific antibodies delivery.

XPOVIO®
(selinexor)

XPOVIO® (selinexor) + Dexamethasone (Xd) for the treatment of penta-refractory multiple myeloma

References:
1. XPOVIO® (selinexor) [prescribing information], Antengene (Hong Kong) Ltd, July 2023.
2. Benkova K, Mihalyova J, Hajek R, Jelinek T. Selinexor, selective inhibitor of nuclear export: unselective bullet for blood cancers. Blood Rev. 2021;46:100758.
3. Azmi AS, Uddin MH, Mohammad RM. The nuclear export protein XPO1 - from biology to targeted therapy. Nat Rev Clin Oncol. 2021;18(3):152-169.
4. Chari A, et al., Oral Selinexor–Dexamethasone for Triple Class Refractory Multiple Myeloma. N Engl J Med 2019;381:727-38.

Hong Kong Approved Indication:

• XPOVIO® in combination with dexamethasone is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.

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Abstract I: Subcutaneous panniculitis-like T-cell lymphoma with homozygous germline HAVCR2 mutation: A case report

Lam Wing Kit[1], Lee Wai Kwan Victor[1], Kong Shun Yin[2], Wong Tsz Fung Winson[1], Yip Sze Fai[1]

[1] Department of Clinical Pathology, Tuen Mun Hospital
[2] Department of Medicine and Geriatrics, Tuen Mun Hospital

Abstract

A 30-year-old man was admitted for on-and-off fever for 2 weeks. He also complained of painful nodules over trunk and limbs for 4 months. He had a previous history of painful nodules occurred for months and subsided spontaneously in his teenage but he didn't attend medical attention. On physical examination, there were multiple tender erythematous nodular swellings over chest wall and bilateral thighs with no lymphadenopathy. Ultrasound abdomen showed hepatosplenomegaly. Complete blood count showed mild anaemia (hemoglobin 11.0 g/dL). He had mildly elevated ALT of 120 U/L, markedly elevated lactate dehydrogenase of 1194 U/L and ferritin of 26625 pmol/L. He had worsening anaemia and neutropenia and bone marrow examination showed some haemophagocytosis with no obvious marrow infiltration. A skin biopsy was performed and showed subcutaneous panniculitis-like T-cell lymphoma (SPTCL). Further Sanger sequencing targeting HAVCR2 gene exon 2 was performed on the bone marrow aspirate specimen. Homozygous p.Y82C mutations, (NM_032782.5:c.245A>G), was detected. Confirmatory germline testing on hair follicles was not performed since there was no lymphomatous involvement in bone marrow. The patient was given cyclosporin A 100 mg BD PO and prednisolone 30 mg BD PO. The skin lesions gradually improve and steroid was tailed down gradually. After 3 months of treatment, the skin lesions were completely resolved. His ferritin returned to normal (588 pmol/L) and LDH is slightly elevated at 239 U/L.

The Hepatitis A Virus-Cellular Receptor 2 (HAVCR2) gene encodes the T-cell immunoglobulin and mucin domain-containing protein 3 (TIM-3), a critical negative regulator acting as a negative checkpoint in innate immune and inflammatory responses. Recent studies have identified germline homozygous or compound heterozygous mutations on HAVCR2 gene in 59-85% of SPTCL patients including familial and sporadic cases, and are associated with a younger age of onset of disease. About 20% of the cases also show haemophagocytic lymphohistiocytosis (HLH). The currently reported germline HAVCR2 mutations associated with SPTCL were p.Y82C, p.I97M, and p.T101I mutations, with p.Y82C being the most frequently reported mutation as seen in this patient. The reported minor allele frequency of p.Y82C in South Asians was 2.1 x 10-2. Remarkable enrichment of the p.Y82C homozygote was also reported in SPTCL (odds ratio 1.2 x 105), suggesting a strong association between HAVCR2 (TIM-3) germline mutations and familial or sporadic SPTCL and/or HLH.

The presence of HLH in SPTCL is associated with adverse prognosis (5-year survival of <50% in cases with HLH compared with 90% in cases without HLH). There is no standard treatment approach for SPTCL. Common treatment options would include immunosuppressive therapy (steroid plus cyclosporin A) and chemotherapy (CHOP +/- E followed by haematopoietic stem cell transplantation). Ruxolitinib has also recently been reported to be efficacious in paediatric cases of SPTCL-HLH with germline homozygous mutation of HAVCR2 (p.Y82C).

Reference:
1. Gayden T, et al. Germline HAVCR2 mutations altering TIM-3 characterize subcutaneous panniculitis-like T cell lymphomas with hemophagocytic lymphohistiocytic syndrome. Nat Genet. 2018 Dec;50(12):1650-1657.
2. Polprasert C, et al. Frequent germline mutations of HAVCR2 in sporadic subcutaneous panniculitis-like T-cell lymphoma. Blood Adv. 2019 Feb 26;3(4):588-595.
3. Zhang Q, et al. Efficacy of ruxolitinib for HAVCR2 mutation-associated hemophagocytic lymphohistiocytosis and panniculitis manifestations in children. Br J Haematol. 2023 Jul;202(1):135-146.

Abstract II: Distinct cytomorphological features in DUX4-rearranged B-ALL

Lam Wing Kit, Wong Ching Ching Alice

Department of Clinical Pathology, Tuen Mun Hospital

Abstract

A 35-year-old man presented with dizziness, exertional dyspnoea and palpitations for 1 month without fever. Complete blood count showed anaemia (haemoglobin, 4.0 g/dL), leucopenia (3.70 × 109/L) and neutropenia (1.60 × 109/L) with occasional circulating blasts on the peripheral blood smear.

Bone marrow examination was performed. The bone marrow aspirate showed 91% medium-sized blasts with around half of them showing "cup-like" nuclei and around a third of them showing cytoplasmic and/or nuclear blebs. Some of the blasts showed both features. Some leukaemic cytoplasmic fragments were also noted in the background. Flow cytometry showed B-lymphoblasts which were positive for CD34, CD19, CD79a (cytoplasmic), CD10 (weak), CD13 (weak) and HLA-DR. The B-lymphoblasts showed co-expression of CD2 and CD371. Karyotype was normal (46,XY). Targeted next-generation sequencing showed IKZF1 partial deletion (exons 4 to 7), PTPN11 pathogenic variant (p.G503V) and multiple NRAS pathogenic variants (p.G12A, p.G12D, p.G12S, p.G13D). Targeted RNA sequencing showed presence of IGH::DUX4 fusion, confirming the diagnosis of B-lymphoblastic leukaemia/lymphoma (B-ALL) with DUX4 rearrangement. The patient was given paediatric-inspired intensive chemotherapy and achieved complete remission. He was planned to have allogeneic hematopoietic stem cell transplantation.

B-ALL with DUX4 rearrangement is a new provisional entity in the 5th edition of the World Health Organization Classification of Haematolymphoid Tumours which is more common in children, adolescents and young adults and is associated with good prognosis. DUX4 rearrangements in B-ALL are usually cytogenetically cryptic. Co-expression of CD2 and CD371 in B-ALL is strongly associated with DUX4 rearrangement. Yet, morphological description of this entity is scarce. "Cup-like" nuclei in blasts are known to be associated with acute myeloid leukaemia with NPM1 and/or FLT3-ITD mutations but are less recognized in B-ALL. Moreover, cytoplasmic and nuclear blebs are hitherto not described as a distinctive feature in any specific subtype of B-ALL. The distinct cytomorphological features of the disease may hint a diligent search for the underlying DUX4 rearrangements as they are often cytogenetically cryptic. Further study on the link between the morphological and molecular features of B-ALL with DUX4 rearrangement cases would be of value.

References:

1. Li Z, Lee SHR, Chin WHN, et al. Distinct clinical characteristics of DUX4- and PAX5-altered childhood B-lymphoblastic leukemia. Blood Adv. 2021 Dec 14;5(23):5226-5238.
2. Lejman M, Chałupnik A, Chilimoniuk Z, Dobosz M. Genetic Biomarkers and Their Clinical Implications in B-Cell Acute Lymphoblastic Leukemia in Children. Int J Mol Sci. 2022 Mar 2;23(5):2755.
3. Li W, Cooley LD, August KJ, et al. Cuplike nuclear morphology is highly associated with IKZF1 deletion in pediatric precursor B-cell ALL. Blood. 2019 Jul 18;134(3):324-329.

Abstract III: An elderly man with traumatic subdural hematoma and newly diagnosed inherited factor VII deficiency

Chan Cheuk Yin Derek, Chan Wai See Joyce, Lam Sze Man Cindy, Luk Yan Yan Samantha, Lau Chi Kuen

Department of Medicine, Tseung Kwan O Hospital

Abstract

Inherited deficiency in factors VII, XIII, XI, X, V, II are collectively known as rare inherited coagulation disorders (RICDs). Among them, the prevalence of factor VII deficiency ranked 4th with an incidence of 1 in 500,0001. However, local data and management guideline on RICDs were lacking. Our team would like to present a case with newly diagnosed inherited factor VII deficiency who suffered from internal haemorrhage.

A 86-year-old man was admitted in January 2024 for accidental fall with head injury. Computed tomography of brain (CTB) showed acute subdural hematoma over right temporoparietal region (0.4cm) and right frontal region (trace amount). There was also incidental finding of old lacunar infarcts at bilateral external capsules. He had known history of essential hypertension, hypercholesterolemia, lower urinary tract symptoms and chronic kidney disease. He was not on any antiplatelet or anticoagulant. He also denied use of over-the-counter medications or medications from family members. He did not have any history of bleeding. His Glasgow Coma Scale (GCS) remained 15/15 and limb power remained full during the in-patient stay.

The international normalised ratio (INR) on admission was prolonged to 2.3. Whereas the activated thromboplastin time (APTT) was normal. He received intravenous vitamin K1 injection and repeated plasma transfusions. However, the INR remained prolonged ranging from 1.8-2.3.

CTB was repeated 2 days later which revealed a new left subdural effusion of 0.4cm. 1:1 mixing study was arranged. The prolonged INR was corrected with the 1:1 mixing study, suggestive of factor deficiency. Subsequent factor level assessment revealed isolated factor VII deficiency of 12% (reference interval 50-150%).

Upon further enquiry, patient denied any parental consanguinity. He had 6 siblings all without major bleeding but all suffered from ischemic stroke. He received two doses of intravenous Factor VIIa injection at the dosage of 35microgram/kg, given 12 hours apart. No major side effect was encountered. Follow-up CTB showed resolution of the subdural effusion and hematoma. Patient was discharged uneventfully.

The human factor VII gene is located on chromosome 13 and the inheritance is autosomal recessive2. The correlation between factor VII level and bleeding tendency is poor3, 4. Common presentations of factor VII deficiency include excessive haemorrhage after invasive procedures, menorrhagia, mucosal or intramuscular bleeding5. Experts recommend a target of greater than 20% if a patient with known inherited factor VII deficiency with bleeding or before undergoing invasive intervention1. Recombinant factor VIIa, plasma transfusion and prothrombin complex concentrate (PCC) are all suitable choices.

Although the factor VII levels of the siblings of the patient could not be assessed, it was interesting to observe a high frequency of thrombosis among the family. Paradoxical arterial or venous thromboses in inherited factor VII deficiency patients have been reported (3-4%)6. Therefore, in addition to bleeding, physicians should also pay attention to any signs and symptoms suggestive of thromboembolism.

Our team would like to use this case to illustrate the diagnosis and management of factor VII deficiency. It is hoped that with the collaboration and sharing between local haematologists, we could manage RICDs better in the future.

Reference:

1. Mannucci PM, Duga S, Peyvandi F. Recessively inherited coagulation disorders. Blood. 2004 Sep 1;104(5):1243-52. doi: 10.1182/blood-2004-02-0595. Epub 2004 May 11. PMID: 15138162.
2. Wulff K, Herrmann FH. Twenty two novel mutations of the factor VII gene in factor VII deficiency. Hum Mutat. 2000;15(6):489-96. doi: 10.1002/1098-1004(200006)15:6<489::AID-HUMU1>3.0.CO;2-J. PMID: 10862079.
3. Peyvandi F, Mannucci PM, Asti D, Abdoullahi M, DI Rocco N, Sharifian R. Clinical manifestations in 28 Italian and Iranian patients with severe factor VII deficiency. Haemophilia. 1997 Oct;3(4):242-6. doi: 10.1046/j.1365-2516.1997.00137.x. PMID: 27214858.
4. Giansily-Blaizot M, Verdier R, Biron-Adréani C, Schved JF, Bertrand MA, Borg JY, Le Cam-Duchez V, Briquel ME, Chambost H, Pouymayou K, Dutrillaux F, Favier R, Martin-Toutain I, Verdy E, Gay V, Goudemand J, Navarro R, Durin A, d'Oiron R, Lambert T, Pernod G, Barrot C, Peynet J, Bastenaire B, Sie P, Stieltjes N, Torchet MF, de Moerloose P; Study group of FVII deficiency. Analysis of biological phenotypes from 42 patients with inherited factor VII deficiency: can biological tests predict the bleeding risk? Haematologica. 2004 Jun;89(6):704-9. Erratum in: Haematologica. 2007 Nov;92(11):1584. LeCam-Duchez, V [corrected to Le Cam-Duchez, V]. PMID: 15194538.
5. Herrmann FH, Wulff K, Auerswald G, Schulman S, Astermark J, Batorova A, Kreuz W, Pollmann H, Ruiz-Saez A, De Bosch N, Salazar-Sanchez L; Greifswald Factor FVII Deficiency Study Group. Factor VII deficiency: clinical manifestation of 717 subjects from Europe and Latin America with mutations in the factor 7 gene. Haemophilia. 2009 Jan;15(1):267-80. doi: 10.1111/j.1365-2516.2008.01910.x. Epub 2008 Oct 30. PMID: 18976247.
6. Ruiz-Saez A. Occurrence of thrombosis in rare bleeding disorders. Semin Thromb Hemost. 2013 Sep;39(6):684-92. doi: 10.1055/s-0033-1353391. Epub 2013 Aug 8. PMID: 23929306.

Abstract IV: Incidence and treatment outcome of acquired thrombotic thrombocytopenic purpura in a single institution in Hong Kong

HWANG Yu Yan[1], LEUNG Yuk Yan Rock[2]

[1] Department of Medicine, Queen Mary Hospital, Hong Kong SAR
[2] Department of Pathology, Queen Mary Hospital, Hong Kong SAR

Abstract

Introduction
Acquired thrombotic thrombocytopenic purpura (aTTP) is a rare potentially fatal microangiopathic anemia. Hemolytic anemia and organ ischemia in aTTP are caused by acquired severe deficiency of ADAMTS13 (a disintegrin and metalloprotease with thrombospondin type 1 repeats, member 13) due to the presence of autoantibody. In the past, diagnosis of aTTP was made by the presence of clinical pentad. The availability of measurement of ADAMTS13 antigen and activity level and detection of anti-ADAMTS13 antibody significantly improves our accuracy in making the diagnosis of aTTP in recent years. Reported incidence ranges from 1.5 to 6 cases per million adults per year in European and American populations. [1-4] Similar data in Asians is scarce. We therefore conduct a retrospective review on local incidence and treatment outcome of aTTP in one teaching Hospital in Hong Kong over a period of ten years.

Method
Patients' data are collected from our haematology laboratory, apheresis centre and outpatient clinic during the period from January 2014 to January 2024. Patient fulfilling clinical criteria of aTTP (fever, microangiopathic haemolytic anemia, thrombocytopenia, neurological manifestation and/or renal impairment) supported by laboratory investigation results including ADAMTS 13 assay will be included.

Results
There were seven patients diagnosed aTTP over a period of ten years. As we are serving a population of one million, the calculated incidence would be 0.7 case per million per year, which is lower than that reported in Caucasians and other Western populations. Male to female ratio was 5:2 and median age at presentation was 46 (range 35 to 59). Four patients had no precipitating factor identified, while the remaining three had underlying conditions (Sjogren's syndrome, HHV6 viral myocarditis and ischemic heart disease on ticagrelor). Six of the patients had ADAMTS13 assay and all of them had ADAMTS13 activity level below 10 IU/dL (normal range 60.6 -130.6 IU/dL) at presentation. Five of the six patients with ADAMTS13 antibody measured upon diagnosis were positive. Median platelet and haemoglobin at presentation were 15x109 /dL and 8.5g/dL respectively. Two patients had fever, three had neurological manifestations but only one of them had renal impairment. All of them were treated with corticosteroids, plasma exchange and anti-CD20 monoclonal antibody. Median number of sessions of plasma exchange was 10 (range 1-30). Among two of them, splenectomy was performed because of suboptimal response to corticosteroid and anti-CD20 monoclonal antibody. One patient died from fulminant cardiac failure within one day of commencing treatment. The median progression free survival and overall survival of this cohort of patients are 53 months and 57 months respectively.

Limitations
This is retrospective analysis of a single centre. Recall and misclassification bias may affect accuracy of our data analysis.

Reference:
1. Mariotte E., Azoulay E., Galicier L., Rondeau E., Zouiti F., Boisseau P., Poullin P., de Maistre E., Provôt F., Delmas Y., et al. Epidemiology and pathophysiology of adulthood-onset thrombotic microangiopathy with severe ADAMTS13 deficiency (thrombotic thrombocytopenic purpura): A cross-sectional analysis of the French national registry for thrombotic microangiopathy. Lancet Haematol. 2016;3:e237–e245.
2. Scully M., Yarranton H., Liesner R., Cavenagh J., Hunt B., Benjamin S., Bevan D., Mackie I., Machin S. Regional UK TTP registry: Correlation with laboratory ADAMTS 13 analysis and clinical features. Br. J. Haematol. 2008;142:819–826.
3. Reese J.A., Muthurajah D.S., Kremer Hovinga J.A., Vesely S.K., Terrell D.R., George J.N. Children and adults with thrombotic thrombocytopenic purpura associated with severe, acquired Adamts13 deficiency: Comparison of incidence, demographic and clinical features. Pediatr. Blood Cancer. 2013;60:1676–1682.
4. Miesbach W., Menne J., Bommer M., Schönermarck U., Feldkamp T., Nitschke M., Westhoff T.H., Seibert F.S., Woitas R., Sousa R., et al. Incidence of acquired thrombotic thrombocytopenic purpura in Germany: A hospital level study. Orphanet. J. Rare Dis. 2019;14:260.

Abstract V: Multidisciplinary approach to transform patient blood management into culture and practice: Experience of a cluster-wide endeavour

Kong SY[1], Lau KN[2], Li KSJ[3], Wong CCA[2],Yip SF[2]

[1] Department of Medicine and Geriatrics, Pok Oi Hospital
[2] Department of Clinical Pathology, Tuen Mun Hospital
[3] Department of Medicine and Geriatrics, Tuen Mun Hospital

Abstract

Introduction

Patient blood management (PBM) is a patient-centred, evidence-based multidisciplinary approach and has been shown to improve patient outcome. Single unit transfusion (SUT) and restrictive transfusion strategy (RTS) are important PBM measures. The SUT rate in 2014 and RTS rate in 2019 were only 30% and 47.1-51% in New Territories West Cluster (NTWC) respectively.

The potential under-recognition of iron deficiency (ID) in NTWC was highlighted by the fact that 53.8% of ID patients showed apparently-normal iron (Fe) profile (TSAT ≤ 20% and ferritin within gender-specific reference range). Alternate-day regimen of oral Fe replacement has been shown to be more effective. However, only 2% of ID patients were given oral Fe of alternate days in NTWC.

Objective

Through PBM implementation in NTWC, we aim at

- Provision of easy access to blood product usage key performance indicators for PBM stakeholders
- Reduction of number of blood transfusion
- Improvement of SUT and RTS rate and Fe replacement rate in ID patients

Methodology

A PBM subcommittee was established in September 2022 to promote the PBM implementation in NTWC and to review PBM parameters periodically for strategic navigation:

- The RTS rate from the Management Information Portal
- The SUT rate from the Clinical Data Analysis and Reporting System
- The blood product utilization rate from the Blood Bank System
- The ID patient identification via the Laboratory Information System

At departmental level, PBM projects were carried out to tackle ID through Fe replacement:

- Patients with menorrhagia in Departments of Accident and Emergency and Obstetrics and Gynaecology
- Oncological patients in Department of Clinical Oncology
- Patients undergoing colectomy in Department of Anesthesia and Operating Theatre Services
- Systemic modification in Fe profile request, oral Fe prescription interface and ID diagnostic information supplementation in ferritin report by Department of Medicine and Geriatrics

Result & Outcome

At cluster level, the transfusion rate of NTWC (3.3-4.2%) was consistently lower than that of Hospital Authority (3.8-4.6%) from 3Q21 to 2Q23. The SUT rate of NTWC has improved from 30% in 2014 to 50% in 2021. The RTS rate of NTWC improved from 47.1% in 1Q19 to 72.6% in 2Q23.

At departmental level, PBM projects made a difference across various patient groups with ID. The mean reduction of packed cell required per head reduced from 2.02 to 1.19 ($p < 0.05$) for patients with menorrhagia. Blood transfusion was fewer in overall oncological patients (1.1 ± 2.0 vs. 0.5 ± 1.0, $p < 0.05$) and hospice patients (1.3 ± 2.1 vs. 0.6 ± 1.0, $p < 0.05$) with PBM implementation. The number of patients with colectomy requiring transfusion reduced by 69% ($p < 0.05$) with Fe replacement.

A rising trend of Fe replacement in ID patients with apparently-normal Fe profile was shown with PBM measures (61.8% vs. 74.8%, $p = 0.108$). There was a significant increase in oral Fe prescription in alternate-day regimen (2% vs. 57%, $p < 0.05$).

Conclusion

The success of PBM implementation lies in data-driven strategic planning and close collaboration among PBM stakeholders. By reinforcing the importance of SUT and RTS and precise recognition and treatment of ID, we hope to move beyond traditional transfusion to successful PBM implementation.

Abstract VI: Prospective study on pembrolizumab in relapsed/refractory NK/T cell malignancies

Chan TSY, Tse EWC

Queen Mary Hospital, Hong Kong

Abstract

Background

Pembrolizumab, a monoclonal antibody against programmed death 1 receptor (PD-1) has been shown highly effective in relapsed/refractory (R/R) extranodal NK/T cell lymphoma (ENKTL) failing L-asparaginase, with an overall response rate (ORR) of 57-100%1, 2. In R/R mature T cell lymphoma, the use of pembrolizumab also results in an overall response rate of 33%3. In this prospective phase II study, we aim to evaluate the efficacy of pembrolizumab in a consecutive cohort of patients with R/R ENKTL or peripheral T-cell lymphoma (PTCL).

Methods

This was a phase II prospective study. The primary endpoints were the efficacy and safety of pembrolizumab in patients with R/R ENKTL and PTCL. Consecutive patients of age >18 with ENKTL and PTCL with measurable lesions on positron emission tomography/computerized tomography (PET/CT), who failed at least one line of prior therapies were recruited. Pembrolizumab was administered at 200mg intravenously every three weeks for up to two years (35 cycles) unless there was intolerable toxicity or disease progression. Survival was analyzed using Kaplan-Meier method. Statistical calculations were performed with SPSS Statistics version 28.

Results

ENKTL cohort:

Ten women and six men at a median age of 57 (range: 41-83 years) were included. Fourteen patients had been treated with L-asparaginase-containing regimens. Ten patients (62.5%) had relapsed disease while six patients (37.5%) had refractory disease. Response assessments were performed in all patients, and their best responses were as below: complete response (CR), N=7, 44%; partial response (PR), N=1, 6%; indeterminate response (IR), N=2, 13%; stable or progressive disease (SD/PD), N=6, 38%. At a median follow-up of 24 months (range 1-51 months), the median progression-free survival (PFS) was 10 months and the median overall survival (OS) was 25 months.

PTCL cohort:

Four men and four women at a median age of 60 (range: 22-80 years) were included. Underlying diseases were peripheral T cell lymphoma, not otherwise specified (PTCL-NOS) (N=4, 50%), angioimmunoblastic T-cell lymphoma/PTCL with T-follicular helper phenotype (AITL/PTCL-TFH) (N=2, 25%), hepatosplenic T-cell lymphoma (HSTCL) (N=1, 12.5%) and systemic Epstein-Barr Virus (EBV)-positive T cell lymphoma of childhood (N=1, 12.5%). All patients had advanced-stage diseases (stage 3, N=1, 12.5%; stage 4, N=7, 87.5%). The median line of the prior regimens was 2 (range: 1-3). At a median follow-up period of nine months, the progression-free survival was 5 months and overall survival was 7 months (Figure 2). Toxicity included IRAE in two patients (endocrine, N=1, grade 1; pulmonary, N=1, grade 4) and haematological toxicity in three patients (37.5%) (anaemia, N=1, grade 2; neutropenia, N=1, grade 1; thrombocytopenia, N=1, grade 1).

Conclusion

Pembrolizumab is a safe and effective rescue therapy for R/R ENKTL with potentially durable remission. A subgroup of patients with PTCL (e.g. systemic EBV-positive T-cell lymphoma of childhood) may also benefit from pembrolizumab therapy.

Abstract VII: VEXAS-associated myelodysplastic syndromes

Carmen KM Cheung, Carmen Michelle Yuen, Lydia HP Tam

Prince of Wales Hospital

Abstract

VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome was first described by David Beck and colleagues in December 2020.1 It was shown to be associated with hematological disorders, in particularly myelodysplastic syndrome (MDS).

Herein, we are going to report a patient suffered from VEXAS syndrome and MDS.

A 73 years old gentleman presented with fever, generalized pruritic erythematous papules, polyarthritis and relapsing polychondritis in early 2017. A skin biopsy was performed which the histology showed interstitial neutrophilic and granulomatous dermatitis. Patient was treated with high dose prednisolone in April 2017. The skin lesions showed initial improvement but worsen again whenever prednisolone dose was being tapered, and therefore, cyclosporin was added. He was admitted for pyrexia of unknown origin (PUO), relapse of polychondritis and pancytopenia (haemoglobin 7.9g/dL, white blood cell 2.8 x 109/L, platelet 77 x 109/L) in November 2017. A bone marrow exam was performed which showed hypercellular marrow with dysmegakaryopoiesis, mild dyserythropoiesis and subtle dysgranulopoiesis, compatible with myelodysplastic syndrome with multilineage dysplasia (MDS-MLD). Patient received extensive work up for PUO including Gallium scan, skin biopsy and bronchoscopy which were all not revealing. Subsequently a PET/CT was performed and showed multiple miliary lung nodules in bilateral lung fields. Patient was given empirical anti-tuberculosis treatment. He then received regular azacitidine infusion since April 2018. His disease was under stable control since then and all the immunosuppressants can be tapered off. In view of his typical presentation of severe adult-onset autoinflammatory disease and MDS in elderly male, his bone marrow slide was reviewed which demonstrated vacuoles in the erythroid and granulocytic precursor cells.

VEXAS syndrome is caused by a somatic missense mutation in codon 41 of ubiquitin-like modifier activating enzyme 1 (UBA1), an X-linked gene which encodes the enzyme that initiates ubiquitination. Reduction in ubiquitylation leads to the accumulation of unfolded proteins and activation of autoimmune pathways, leading to an uncontrollable inflammatory response.

VEXAS syndrome is a disease with multisystem involvement with hematological manifestations including macrocytic anemia, bone marrow vacuoles, thrombotic events, MDS and multiple myeloma.2 The characteristic vacuolation is commonly found in myeloid and erythroid precursors on bone marrow specimens although absent of vacuoles does not exclude the diagnosis.

To date, treatment for VEXAS is not standardized with majority of the patients requiring use of immunosuppressant like high-dose steroid. The use of azacitidine was shown to be able to improve autoinflammatory symptoms allowing a reduction or discontinuation of steroid.3 The treatment responses observed in our patient is in line with the literature. Hypomethylating agents were believed to have immunomodulatory effects by reducing the proliferative capacity of regulatory T cells. A concomitant reduction of pro-inflammatory T-helper cells, Th1 and Th17 after azacitidine treatment was also observed.4 Further study to elucidate the pathophysiological mechanism between these two syndrome and evaluation on therapeutic options is warranted.

Reference:

1. Beck DB, Ferrada MA, Sikora KA, et al. Somatic Mutations in UBA1 and Severe Adult-Onset Autoinflammatory Disease. N Engl J Med. 2020 Dec 31;383(27):2628-2638.
2. Patel N, Dulau-Florea A, Calvo KR. Characteristic bone marrow findings in patients with UBA1 somatic mutations and VEXAS syndrome. Semin Hematol. 2021 Oct;58(4):204-211.
3. Comont T, Heiblig M, Rivière E, et al. Azacitidine for patients with Vacuoles, E1 Enzyme, X-linked, Autoinflammatory, Somatic syndrome (VEXAS) and myelodysplastic syndrome: data from the French VEXAS registry. Br J Haematol. 2022 Feb;196(4):969-974.
4. Costantini B, Kordasti SY, Kulasekararaj AG, et al. The effects of 5-azacytidine on the function and number of regulatory T cells and T-effectors in myelodysplastic syndrome. Haematologica. 2013 Aug;98(8):1196-205.

Abstract VIII: Insights into optimal ferritin level for erythropoiesis: The first study in Asians using hospital big data approach

Lam Wing Kit, Wong Tsz Fung Winson, Yip Sze Fai

Department of Clinical Pathology, Tuen Mun Hospital

Abstract

Introduction

Treating iron deficiency is important in optimising erythropoiesis as well as cognitive development in children. Serum ferritin is commonly used to diagnose iron deficiency, but the optimal cutoff for diagnosis remains controversial. The World Health Organization (WHO) defines iron deficiency using cutoff levels <15 μg/L for adults and <12 μg/L for children. The Royal College of Pathologists Australasia (RCPA) recommends a cut-off of <20 μg/L (<45 pmol/L) for diagnosing paediatric iron deficiency and <30 μg/L (<68 pmol/L) for diagnosing adult iron deficiency. Functional relationship between ferritin and red cell parameters has been studied previously in Caucasians but not in Asians. This is the first study aiming to determine the erythropoiesis-based ferritin cutoffs for iron deficiency in Asian population using a hospital big data approach.

Methods

The complete blood count (CBC) and ferritin results of patients aged <65 years in the New Territories West Cluster between July 2019 and December 2023 were retrieved using the Laboratory Information System. The analysers used were Beckman Coulter DxH 800 haematology analyser for CBC and Abbott Alinity analyser for ferritin test. Same patient results after the first episode were excluded. CBC and ferritin test results on the same date from the same patient were merged for analysis. Data were analysed separately for young children (<5 years), older children (5-12 years), adolescents (13-17 years), and adults (18-64 years) (further separated into male and female groups). Red cell parameters were analysed using a quadratic plateau model in R software to derive threshold ferritin values.

Results

195,887 CBC and 87,786 ferritin results for the adult group and 35,918 CBC and 2,816 ferritin results for the paediatric and adolescent group were retrieved, with 4,481 and 446 merged results in the adult group and the paediatric and adolescent group respectively with ferritin 60 μg/L after data cleaning and filtering. In all groups, the Hb, MCV, MCH and MCHC values showed a positive correlation (negative correlation for RDW) with ferritin until a threshold value (summarized in the Table). The derived threshold ferritin values are in general higher than the WHO cutoff with some of them also higher than the RCPA cutoff.

Table

CBC Parameters	Threshold ferritin value (μg/L)				
	Age <5 years	Age 5 to <13 years	Age 13 to <18 years	Adult male	Adult female
Hb	10.2	19.1*	14.9	20.7*	18.9*
Hct	9.5	16.4*	13.8	19.9*	18.6*
MCV	11.8	10.1	17.1*	27.4*	19.7*
MCH	12.0*	14.0	18.5*	25.1*	19.7*
MCHC	10.7	26.6**	17.6*	21.1*	17.9*
RDW	21.2**	26.4**	19.2*	35.7**	22.8*
Established ferritin cutoff value (μg/L)					
WHO	<12	<15	<15	<15	<15
RCPA	<20	<20	<20	<30	<30

*: threshold ferritin value > WHO cutoff
**: threshold ferritin value > both WHO and RCPA cutoffs

Conclusion

This is the first study in Asians showing that iron-restricted erythropoiesis potentially occurs earlier than the established ferritin cutoffs for iron deficiency. Further exploration is needed to assess the clinical significance of diagnosing and managing patients using erythropoiesis-based ferritin cutoffs.

Reference:

1. Gingoyon A, et al. Chronic Iron Deficiency and Cognitive Function in Early Childhood. Pediatrics. 2022 Dec 1;150(6):e2021055926.
2. Markus C, Saxon B, Metz M. Ferritin as a functional biomarker of iron status in children and young adults. Br J Haematol. 2019 Feb;184(4):640-642.
3. Sezgin G, et al. Clinical thresholds for diagnosing iron deficiency: comparison of functional assessment of serum ferritin to population based centiles. Sci Rep. 2020 Oct 26;10(1):18233.

Abstract IX: Clinical application of the second revision of the international staging system (R2-ISS) and weighted cytogenetic scoring system (wCSS) in multiple myeloma patients receiving bortezomib based treatment

Hoi Ki Karen Tang[1], Chi Yeung Fung[1], Lisa Siu[2], Ho Wan Alvin Ip[3], Sze Fai Yip[4], Ka Ngai Harry Lau[5], Harold Lee[6], Grace Lau[6], Chi Kuen Lau[7], Kwan Hung Leung[8], Bonnie Kho[9], Yu Yan Hwang[1], Cheong Ngai[1], Joycelyn Sim[1], Eric Tse[1], Yok Lam Kwong[1], Chor Sang Chim[10]

[1] Department of Medicine, Queen Mary Hospital, University of Hong Kong, Pok Fu Lam Road, Hong Kong.
[2] Department of Pathology, Queen Elizabeth Hospital, Kowloon, Hong Kong.
[3] Department of Pathology, Queen Mary Hospital, University of Hong Kong, Pok Fu Lam Road, Hong Kong.
[4] Department of Medicine, Tuen Mun Hospital, Tuen Mun, Hong Kong.
[5] Department of Pathology, Tuen Mun Hospital, Tuen Mun, Hong Kong.
[6] Department of Medicine, Princess Margaret Hospital, Kowloon, Hong Kong.
[7] Department of Medicine, Tseung Kwan O Hospital, Kowloon, Hong Kong.
[8] Department of Medicine, United Christian Hospital, Kowloon, Hong Kong.
[9] Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Chai Wan, Hong Kong.
[10] Department of Medicine, Queen Mary Hospital, University of Hong Kong, Queen Mary Hospital, Pok Fu Lam Road, Hong Kong Department of Medicine, Hong Kong Sanatorium & Hospital, Happy Valley, Hong Kong.

Abstract

Introduction

Although Revised International Staging System (R-ISS) is widely used for the prognostication of myeloma patients, considerable limitations exist including large proportion of R-ISS II patients with variable outcomes, 1q gain/1p deletion and concurrent high risk cytogenetic abnormalities not considered. New prognostication systems have been reported, including the weighted cytogenetic scoring system (wCSS)(1) and the second revision of the ISS (R2-ISS)(2). Herein, we would like to compare the outcomes of patients receiving bortezomib based induction using R-ISS, R2-ISS and wCSS.

Methods

Symptomatic newly diagnosed myeloma patients treated in seven haematology centres* from January 2006 to January 2020 in Hong Kong were included in this retrospective study. The fluorescence in-situ hybridization (FISH) comprising of IGH/FGFR3, IGH/MAF, TP53/CEP17, CDKN2C/CKS1B probes were used. At least 200 nuclei were analysed. The cut-off for positivity was above 10% for fusion or break apart probes and 20% for numerical abnormalities in accordance with international consensus. As trisomies 5 and 21 were not part of the FISH panel, they were not included in wCSS calculation.

Results

The entire NDMM cohort comprised of 475 patients and complete staging data (ISS, lactate dehydrogenase and FISH) was evaluable in 221 patients (46.5%). The median event free survival (EFS) and overall survival (OS) were 34 months and 101 months respectively in the evaluable group. Within this evaluable group, 22 had del 17p (10%), 44 had t(4,14) (19.9%), 137 had chromosome gain 1q (1q+) (62%) and 19 had del 1p (8.6%).

R-ISS could stratify NDMM patients for both EFS and OS (Fig. 1). For R2-ISS, there was significant difference in EFS between R2-ISS stages I versus IV but not for stages I versus II or I versus III. There were significant differences in OS between R2-ISS stages I versus III and I versus IV but not for stages I versus II (Fig. 2). Using wCSS, there was significant difference in EFS between low risk versus high-risk groups but not for low risk versus intermediate risk groups. There were significant differences in OS between the low risk versus intermediate risk groups and low risk versus high-risk groups (Fig. 3). We looked at the discriminatory ability of the three scoring systems to predict death from those who survived using the C index. The C indexes of ISS, R-ISS, R2-ISS and wCSS were 0.597, 0.614, 0.641, 0.631 respectively, meaning that there is no added benefit of using R2-ISS and wCSS over R-ISS.

Conclusion

Our study did not show superiority of using R2-ISS and wCSS compared with R-ISS in stratifying patients on bortezomib based treatment. A clear distinction was not achieved between R2-ISS group I versus II and III versus IV in our cohort, as reported by others(3-6). Key difference in our study population was the higher percentage of 1q+, thus contributing to the higher number of R2-ISS stage 4 patients. Moving forward, it is important for new scoring systems to identify high-risk/ ultra-high-risk patients for risk adapted therapies to be implemented to improve long term outcomes.

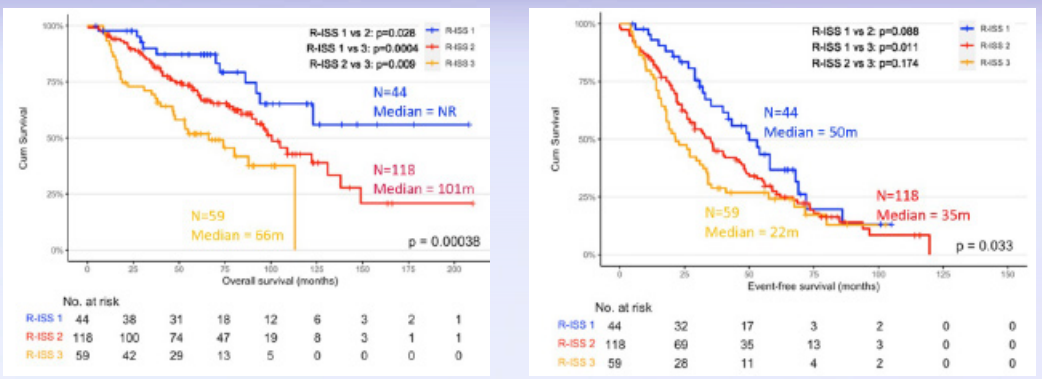

Figure 1. OS and EFS according to R-ISS for the evaluable cohort

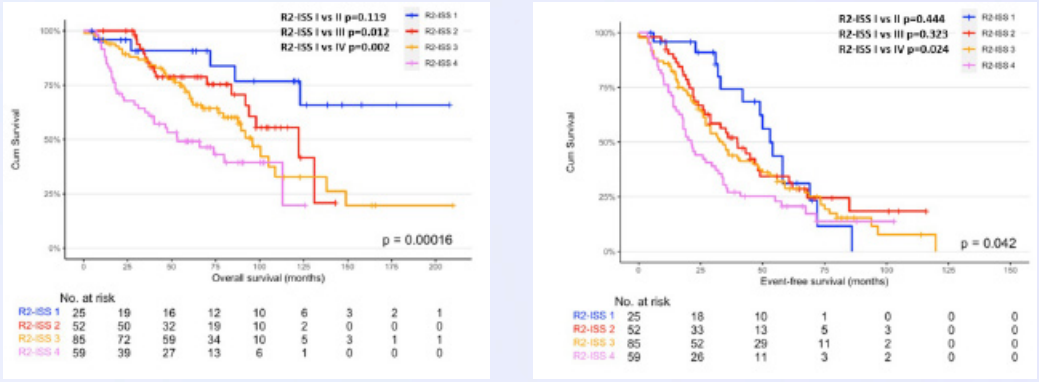

Figure 2. OS and EFS according to R2-ISS for evaluable cohort

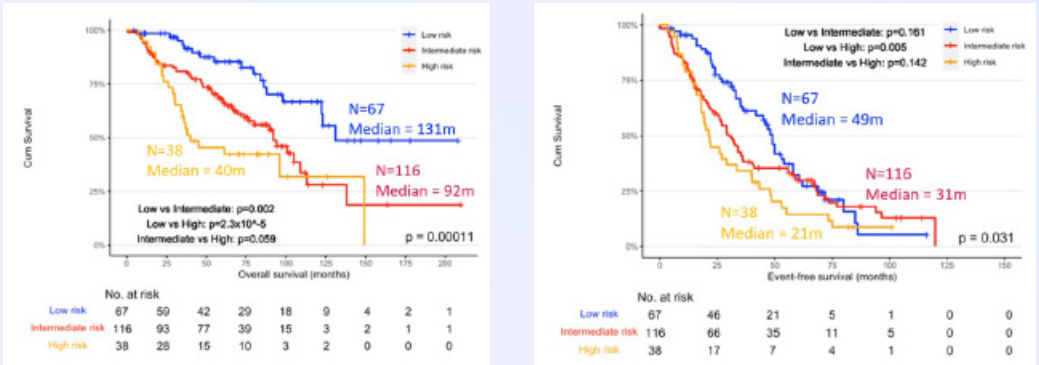

Figure 3. OS and EFS according to wCSS for the evaluable cohort

* Queen Mary Hospital, Princess Margaret Hospital, Tuen Mun Hospital, Pamela Youde Nethersole Eastern Hospital, United Christian Hospital, Tseung Kwan O Hospital and Queen Elizabeth Hospital

References

1. Perrot A, Lauwers-Cances V, Tournay E, Hulin C, Chretien ML, Royer B, et al. Development and Validation of a Cytogenetic Prognostic Index Predicting Survival in Multiple Myeloma. J Clin Oncol. 2019;37(19):1657-65.
2. D'Agostino M, Cairns DA, Lahuerta JJ, Wester R, Bertsch U, Waage A, et al. Second Revision of the International Staging System (R2-ISS) for Overall Survival in Multiple Myeloma: A European Myeloma Network (EMN) Report Within the HARMONY Project. J Clin Oncol. 2022;40(29):3406-18.
3. Guo W, Zhan A, Mery DE, Munshi MN, Makhoul O, Baily C, et al. Application of R2-ISS risk stratification to patients with multiple myeloma treated with autologous stem cell transplants at UAMS. Blood Adv. 2023;7(21):6676-84.
4. Kamal Alzahrani OP, Zhongya Wang, Denái R. Milton, Mark R. Tanner, Qaiser Bashir, Samer A. Srour, Neeraj Y. Saini, Paul Lin, Jeremy Ramdial, Yago Nieto, Hans Lee, Krina K. Patel, Elisabet E. Manasanch, Partow Kebriaei, Sheeba K. Thomas, , Donna M. Weber, Robert Z. Orlowski, Elizabeth J. Shpall, Richard E. Champlin, and Muzaffar H. Qazilbash. Impact of Revised International Staging System 2 (R2-ISS) Risk Stratification on Outcomes of Patients with Multiple Myeloma Receiving Autologous Hematopoietic Stem Cell Transplantation. Blood. 2023;142.
5. Tan JLC, Wellard C, Moore EM, Mollee P, Rajagopal R, Quach H, et al. The second revision of the International Staging System (R2-ISS) stratifies progression-free and overall survival in multiple myeloma: Real world data results in an Australian and New Zealand Population. British Journal of Haematology. 2023;200(2):e17-e21.
6. Yang P, Zhou F, Dong Y, Gao G, Xue H, Liang X, et al. The R2-ISS in a Multicenter Cohort of Chinese Patients With Newly Diagnosed Multiple Myeloma. HemaSphere. 2023;7(4):e857.

Abstract X: A lean six sigma approach to improvement of paediatric iron deficiency care

Lam Wing Kit[1], Wong Tsz Fung Winson[1], Lee Yuen Han Tracy[2], Li Chak Ho[2], Yip Sze Fai[1]

[1] Department of Clinical Pathology, Tuen Mun Hospital
[2] Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital

Abstract

Introduction
Iron deficiency is common in children and adolescents with significant implications for their growth and development in addition to iron deficiency anaemia. The Royal College of Pathologists Australasia recommends a cut-off of <20 ng/ml (<45 pmol/L) for diagnosing paediatric iron deficiency. We aimed to evaluate the impact of a Lean Six Sigma intervention on the diagnosis and treatment of paediatric iron deficiency.

Methods
A retrospective review was conducted on children and adolescents below 18 years who were tested to have a ferritin level <45 pmol/L in the New Territories West Cluster between July 2022 and December 2023. Patients with known iron deficiency, on iron replacement or recent transfusion within 1 year were excluded. A Lean Six Sigma approach was used to identify and address key factors contributing to the under-diagnosis and under-treatment of paediatric iron deficiency. A pre-intervention survey was performed to review the diagnosis and treatment of paediatric iron deficiency in the period July to December 2022. Root causes and potential interventions were identified. Multidisciplinary meeting involving haematopathology, biochemistry and the paediatric haematology and oncology teams was arranged to engage the stakeholders for interventions. After intervention, a repeat survey was performed to review the diagnosis and treatment of paediatric iron deficiency in the period November to December 2023.

Results
Of 164 pre-intervention and 61 post-intervention ferritin results below 45 pmol/L in patients under 18 years old, 64 and 20 new cases were identified, respectively. Pre-intervention, 54.7% (35/64; 1.6σ) were diagnosed with iron deficiency and 50% (32/64) were given iron replacement. The rate of WHO-defined anaemia was 71.9% (46/64). In a follow-up period of 180 days, patients receiving iron replacement had a median best haemoglobin improvement of 2.3 g/dL compared with 0.1 g/dL in patients without ($p<0.00001$).
The major problems identified in the process included: 1) only reference interval was available in the ferritin laboratory report but not the decision cut-off for diagnosing paediatric iron deficiency (lower limit of reference interval ranges from 12 (1-4 years) to 31 (5-13 years) pmol/L in the paediatric and adolescent groups); and 2) lack of clear guidance for diagnosis and management of iron deficiency. Specific interventions included an addition of the decision cut-off of <45 pmol/L for diagnosis of paediatric iron deficiency in the ferritin laboratory reports and a teaching session organized by the paediatric haematology and oncology team on the diagnosis and management of iron deficiency.
Post-intervention, the diagnosis rate improved significantly from 54.7% (35/64; 1.6σ) to 90.0% (18/20; 2.8σ) ($p=0.0032$). Of note, the paediatric team has identified 100% (12/12) of cases post-intervention compared with 59.6% (31/52) pre-intervention ($p=0.0047$). The iron replacement prescription rate improved from 50% (32/64) to 75.0% (15/20) ($p=0.0421$).

Conclusion
The Lean Six Sigma intervention was successful in identifying the problems in the process of diagnosis and treatment of paediatric iron deficiency, and offers insights to the potential solutions. This study highlights the potential of Lean Six Sigma as a tool for improving the quality of paediatric iron deficiency management.

Abstract XI: Mixed phenotype acute leukaemia with KMT2A amplification: A case series study and review of literature

Ka Ngai LAU[1], Ting Hon Stanford LI[2], Ka Yan NG[2], Wai Shan WONG[2], Coty CHEUNG[3], Natalie Pui Ha CHAN[3], Joyce Sin CHEUNG[3], Wing Kit LAM[1], Alice Ching Ching WONG[1], Sze Fai YIP[1]

[1] Department of Clinical Pathology, Tuen Mun Hospital
[2] Department of Pathology, Queen Elizabeth Hospital
[3] Department of Anatomical and Cellular Pathology, Princes of Wales Hospital

Abstract

Introduction: Gene amplification is rare in Acute Myeloid Leukaemia (AML) and is usually manifested as double minutes (dmin) or heterogeneously staining region (hsr) cytogenetically. Commonly amplified genes include MYC and KMT2A in AML. Previous studies established that AML with KMT2A amplification is a rare distinct disease subtype different from AML with KMT2A rearrangement. It is characterized by morphological dysplasia, highly complex karyotype and is associated with frequent TP53 deletions/mutations and dismal clinical outcomes. Rare case reports of B-lymphoblastic leukaemia with KMT2A amplifications were reported. However, Mixed Phenotype Acute Leukaemia (MPAL) with KMT2A amplifications at diagnosis have not been reported in the literature.

Method: We reviewed and reported the clinicopathological findings of 3 MPAL cases with KMT2A amplification. They all had cytogenetic studies, fluorescence in situ Hybridization (FISH) for KMT2A and myeloid panel next generation sequencing (NGS) performed at diagnosis. FISH for MYC was performed in 2 cases.

Results: We identified 2 male patients and 1 female patients with a median age of 60. None of the patients had history of malignancy nor received chemotherapy or radiotherapy. 2 patients were diagnosed with MPAL, B/Myeloid and 1 patient had MPAL, T/Myeloid. 2 patients had mild prolongation of prothrombin time (PT) at presentation. One of them developed significant coagulopathy with both prolongation of PT and activated partial thromboplastin time during salvage chemotherapy. She developed massive intracranial haemorrhage requiring ICU admission. All cases showed blasts containing cytoplasmic vacuoles and morphologic dysplasia with the presence of hypogranular and hypolobated neutrophils. Complex karyotypes were demonstrated by cytogenetic studies in all cases. 2 cases showed deletion of 5q. FISH for KMT2A demonstrated KMT2A amplification (>5 copies) in all cases. 1 case showed concomitant MYC amplification (>5 copies), and another showed gain of MYC (3 copies). All cases harboured TP53 mutations. The 3 patients all underwent HyperCVAD induction chemotherapy. They all had primary refractory disease and subsequently received either FLAG-IDA, inotuzumab or FLAG as salvage chemotherapy. None of them achieved remission and succumbed with a mean overall survival of 82 days.

Discussion: Our cases of MPAL with KMT2A amplification demonstrate similar clinicopathological features as AML with KMT2A amplification. A novel finding of concomitant gain or amplification of MYC is seen in 2 of the MPAL cases and this warrants further study. Novel therapy is needed for this distinctively rare subtype of leukaemia.

References

1. Cuthbert, G., Thompson, K., McCullough, S. et al. MLL amplification in acute leukaemia: a United Kingdom Cancer Cytogenetics Group (UKCCG) study. Leukemia 14, 1885–1891 (2000).
2. Tang G, DiNardo C, Zhang L, et al. MLL gene amplification in acute myeloid leukemia and myelodysplastic syndromes is associated with characteristic clinicopathological findings and TP53 gene mutation. Hum Pathol. 2015;46(1):65-73.

Abstract XII: Monitoring iron deficiency anaemia management is a useful indicator in patient blood management implementation

Lau Ka Ngai[1], Kong Shun Yin, Jacky[2], Li Ka Shu Justin[3], Wong Alice Ching Ching[1], Yip Sze Fai[1]

[1] Department of Clinical Pathology, Tuen Mun Hospital
[2] Department of Medicine and Geriatrics, Pok Oi Hospital
[3] Department of Medicine and Geriatrics, Tuen Mun Hospital

Abstract

Introduction: We performed an audit of management of patients with iron deficiency anaemia (IDA) in 2023 and found that 25% (19/75) of the IDA patients in the study period (2021 cohort: 15th-19th June 2021) were not given iron replacement. Among those who were given oral iron replacement, only 6% (3/53) were prescribed with 100mg elemental iron alternate day dosing, which is the latest evidence-based recommended dosing [1]. We enhanced laboratory result screening by addition of clinical decision cut-off of ferritin <67pmol/L in the footnotes of ferritin result reporting. Additionally, alternate day oral iron sulphate was included in the prescription set. A re-audit of patients with iron deficiency anaemia in NTWC was conducted to evaluate the effectiveness of these measures and to identify areas for further improvement.

Method: Adult patients with ferritin test performed in NTWC in the week 10th-16th December 2023 were retrieved from the Laboratory Information System. Patients with known iron deficiency were excluded. Iron deficiency was defined as ferritin <67pmol/L. Anaemia was defined by haemoglobin <12g/dL for females and <13g/dL for males, according to the WHO definition. Clinical information was reviewed from the EPR, including selected laboratory investigations (CBC and iron profile interpretation), iron replacement therapy, blood product utilization and readmission due to symptomatic anaemia.

Results: We compared the re-audit results from the 2023 cohort with that of the 2021 cohort (Table 1). Overall transfusion rates were similar (13% vs 15%). All cases adopted single unit transfusion. There were fewer cases given transfusion but missing iron replacement in the 2023 cohort (9% (1/11) vs 25%(4/10) in 2021). Readmission due to symptomatic anaemia was fewer in the 2023 cohort (1 vs 4 in 2021). There is a significant increase in prescription with the 100mg elemental iron alternate day dosing from 6% (3/53) in 2021 cohort to 65% (33/51). However, the overall iron replacement rates were similar for both cohorts (75% in 2021 vs 73% in 2023). We explored the possible factors associated with the persistence of missing iron replacement. Subgroup analysis (Table 2) identified that the iron replacement rates were comparatively lower for IDA patients among obstetrics, surgery and accident & emergency specialties (42% (8/19)) than medical & geriatrics, family medicine and gynaecology units (85% (44/52)). None of the 3 IDA patients presented to the EMW were given iron replacement. We observed that the mean haemoglobin level was lower among those given iron replacement compared with those without (9.2g/dL vs 10.4g/dL p=0.0265).

Discussion: The re-audit results showed improvement in IDA management with fewer readmission due to symptomatic anaemia and fewer cases being given transfusion but missing iron replacement. More patients were prescribed with 100mg elemental iron alternate daily dosing. However, the overall iron replacement rates were similar between the two cohorts. We postulated that IDA might be overlooked when patients presented with conditions without obvious anaemic symptoms. Additionally, iron replacement is less likely to be given if patient has a higher haemoglobin level. Further and continuous effort in education on recognition and management of IDA among different specialities is warranted. Our study illustrated that monitoring iron replacement rate among IDA patients could be a useful indicator in PBM implementation.

Table 1: Comparison of the 2023 cohort with the 2021 cohort

	2021 cohort	2023 cohort
Number of IDA patients	75	73
Gender		
Male:Female	15:60	19:54
Location		
Inpatient (%)	17/24 (71%)	17/23 (74%)
Outpatient (%)	35/47(74%)	33/43 (77%)
AED (%)	4/4(100%)	3/4(75%)
EMW (%)	0/0	0/3 (0%)
Transfusion		
Yes	10(13%)	11(15%)
No	65(87%)	62(85%)
Transfusion but missing iron replacement	4/10 (25%)	1/11(9%)
Readmission due to symptomatic anaemia	4	1
Iron replacement		
Yes (%)	56 (75%)	53 (73%)
No (%)	19 (25%)	20 (28%)
Iron replacement regime		
Oral	Total:53	Total:51
100mg elemental iron alternate day (%)	3(6%)	33(65%)
100mg elemental iron daily/BD/TDS (%)	50(55%)	17(33%)
50mg elemental iron daily (%)	0(0%)	1(2%)
Intravenous	7	6

Table 2: Subgroup analysis on the iron replacement by specialties

Specialty	2023 cohort
M&G (%)	24/28 (86%)
A&E (%)	3/7 (43%)
GYN (%)	10/12(83%)
FM (%)	10/12(83%)
OBS (%)	2/5(40%)
SURG (%)	3/7(43%)
RT (%)	1/1(100%)
ORTH (%)	0/1(0%)

References
1.Stoffel NU, Zeder C, Brittenham GM, Moretti D, Zimmermann MB. Iron absorption from supplements is greater with alternate day than with consecutive day dosing in iron-deficient anemic women. Haematologica. 2020;105(5):1232-1239.
2.Cook JD. Diagnosis and management of iron-deficiency anaemia. Best Pract Res Clin Haematol 2005;18:319-332.

Abstract XIII: Hepatitis-associated severe aplastic anemia: A case report

Chi-hang Kevin, Kwok[1]; Wai-man Vivien, Mak[2]; Sze-ki Sandy, Ho[2]; Wing-bing Lydia, Ho[2]; Wai-nga Grace, Lau[2]; Ka-lok Luke, Chan[2]; Kwok-kuen Harold, Lee[2]

1 Department of Medicine, Yan Chai Hospital
2 Department of Medicine and Geriatrics, Princess Margaret Hospital

Abstract

Background
Hepatitis-associated aplastic anemia (HAAA) is a rare variant of aplastic anemia (AA). The onset of aplastic anemia is preceded by an episode of hepatitis. The bone marrow failure can be severe and it will be fatal if untreated. We presented a case of HAAA who were treated in our centre.

Case presentation
A 19-year-old man was first admitted due to acute hepatitis in February 2020. He presented as vomiting and diarrhea for one day. Alanine transaminase (ALT) was 823U/L and bilirubin was 99umol/L with normal alkaline phosphatase (ALP). Diagnostic tests, including hepatitis workup, autoimmune markers, were unable to determine the cause of hepatitis. He quickly recovered and his blood test results returned to normal.

In September 2020, he was admitted for two-week history of gum bleeding. He was found to have pancytopenia (white blood cells [WBC] 0.9 × 109/L; absolute neutrophil [ANC] 0.6 x109/L; haemoglobin [Hb] 7.4 g/dL; platelets 14 × 109/L). Bone marrow examination showed markedly hypocellular marrow and cytogenetic analysis did not reveal any abnormalities. Paroxysmal nocturnal hemoglobinuria (PNH) screening was unremarkable. A diagnosis of severe aplastic anemia (SAA) was reached, with hepatitis being the suspected cause.

In October 2020, the patient commenced treatment with horse anti-thymocyte globulin (ATG) plus cyclosporine, and oral eltrombopag at a daily dose of 75 mg. Our patient has shown good treatment response and his blood count has has been normalized since October 2021. In his latest follow-up visit in February 2024, he showed no signs of bleeding and findings of his blood test were normal (WBC 6.0 × 109/L; ANC 3.8x 109/L; Hb 13.8g/dL; platelets 238 × 109/L). There was no treatment-related adverse events observed during the entire course of treatment.

Discussion
Hepatitis-associated aplastic anemia (HAAA) is a rare but severe illness that usually occurs in 2-5% of newly diagnosed cases of acquired aplastic anemia.1 It is predominantly seen in younger males, like in our patient. Severe aplastic anemia usually develops 2–3 months after acute hepatitis attack in patients with HAAA1. However, our patient developed HAAA seven months after the hepatitis episode. Most cases of HAAA are seronegative for known hepatitis viruses, including hepatitis A, B, C and G, like in our patient.2 Treatment of HAAA is similar to SAA. The haematopoietic stem cell transplantation (HSCT) being the front-line treatment for young and adult SAA patients.3-4 However, in situations where HLA-matched sibling donors are lacking, as in our patient, immunosuppressive therapy using a combination of horse ATG and cyclosporine is recommended.4 Existing data have shown that around 60% of SAA patients respond to this standard immunosuppressive therapy.2 Clinical outcomes of SAA has been improved after addition of eltrombopag SAA patients.5 Our patient responded well to ATG/cyclosporine A/eltrombopag treatment.

Conclusion
HAAA is well known immune-mediated variant of AA. We have to be vigilant to hepatitis patients that develop symptoms and signs of pancytopenia and perform further investigations for early diagnosis of potential AA.

References:
1. Gonzalez-Casas R, Garcia-Buey L, Jones E, Gisbert J, Moreno-Otero R. Systematic review: hepatitis-associated aplastic anaemia—a syndrome associated with abnormal immunological function. Aliment Pharmacol Ther. 2009;30(5):436–43
2. Brown KE, Tisdale J, Barrett AJ, et al. Hepatitis-associated aplastic anemia. N Engl J Med 1997;336:1059–64
3. Alshaibani A, Dufour C, Risitano A, de Latour R, Aljurf M. Hepatitis-associated aplastic anemia. Hematol Oncol Stem Cell Ther. Published online November 2020. doi:10.1016/j.hemonc.2020.10.001
4. Killick SB, Bown N, Cavenagh J, et al. Guidelines for the diagnosis and management of adult aplastic anaemia. Br J Haematol. 2016;172(2):187-207. doi:10.1111/bjh.13853
5. Peffault de Latour R, Kulasekararaj A, Iacobelli S, et al. Eltrombopag Added to Immunosuppression in Severe Aplastic Anemia. N Engl J Med. 2022;386(1):11-23. doi:10.1056/NEJMoa2109965

Abstract XIV: Carfilzomib-induced thrombotic microangiopathy successfully salvaged with eculizumab

Lau WN, Mak WM, Lee KK, Ho SK, Kwok CH, Ho WB, Chan KL, Chan HY, Wu LY, Wong SW

Princess Margaret Hospital

Abstract

Introduction

Carfilzomib, a second-generation irreversible proteasome inhibitor, is commonly used in the management of multiple myeloma. Thrombotic microangiopathy is a rare but potentially life-threatening complication associated with carfilzomib. Prompt recognition and treatment are crucial to prevent further organ damage and improve patient outcomes. Eculizumab, a terminal complement inhibitor, has shown promising results in the management of carfilzomib-induced TMA.

We report a patient with IgA-kappa plasma cell myeloma who developed thrombotic microangiopathy (TMA) following treatment with carfilzomib and was successfully salvaged with eculizumab.

Case Presentation

A 62-year-old man with IgA-kappa plasma cell myeloma relapsed 3 years after autologous hematopoietic stem cell transplantation following induction with bortezomib, thalidomide and dexamethasone (VTD). He presented with profound pancytopenia and IgA-kappa paraproteinemia of 40g/L in 2023. Bone marrow examination showed diffuse sheets of clonal plasma cells with markedly suppressed trilineage haematopoiesis. Carfilzomib and dexamethasone (KD) were initiated as salvage therapy. Leukopenia and thrombocytopenia resolved after the first cycle of treatment and his IgA-kappa paraproteinemia dropped to 12g/L. However, after the 8th dose, he developed microangiopathic haemolytic anaemia, thrombocytopenia, and acute kidney injury with creatinine peaking at 842 umol/L. ADAMTS13 activity was only slightly reduced at 47.1%. A diagnosis of carfilzomib induced TMA was made and carfilzomib was discontinued.

He was given two sessions of haemodialysis and was treated with eculizumab shortly after the diagnosis of carfilzomib-induced TMA. After the 4th dose of eculizumab, his platelet was normalized and his renal function had significantly improved with creatinine down to 113 umol/L. He was given five doses of eculizumab in total.

Discussion

The mechanism of carfilzomib-induced thrombotic microangiopathy (TMA) is not fully understood. However, it is believed that complement activation of the alternative pathway plays a crucial role. Carfilzomib, as an irreversible proteasome inhibitor, may disrupt the normal turnover of complement regulators, leading to excessive complement activation and subsequent endothelial injury, formation of microvascular thrombi, and end-organ damage. Additionally, carfilzomib inhibits NFκB, reducing vascular endothelial growth factor (VEGF) levels and potentially causing glomerular endothelial injury and renal TMA [1].

Recognition of carfilzomib-induced TMA is essential, and discontinuation of the drug is the initial step in management. Eculizumab has shown promising results in rapidly improving haematological parameters and reversing renal dysfunction in some patients [2].

Conclusion

This case highlights carfilzomib-induced TMA as a potential complication of carfilzomib therapy in patients with multiple myeloma. Prompt recognition and early initiation of eculizumab can successfully salvage patients with this life-threatening condition. Further research is needed to better understand the underlying mechanisms and risk factors associated with carfilzomib-induced TMA and optimize its management.

References:

1. Eigbire-Molen O, Hermelin D, Blackall D. Carfilzomib-Induced Thrombotic Microangiopathy: Focus on Pathogenesis. J Med Cases. 2022;13(6):274-280.
2. Rassner M, Baur R, Wasch R, Schiffer M, Schneider J, Mackensen A, Engelhardt M. Two cases of carfilzomib induced thrombotic microangiopathy successfully treated with Eculizumab in multiple myeloma. BMC Nephrol. 2021;22(1):32

Abstract XV: HIV-associated lymphoma: Single center experience and literature review

Wong Ka Wai Keith, Tsoi Yee Lei Laura, Wu Wing Fong

Tuen Mun Hospital

Abstract

Background:
HIV-associated lymphoma (HAL) is a leading cause of death in individuals living with HIV/AIDS, with diffuse large B-cell lymphoma (DLBCL) and Burkitt lymphoma (BL) being the commonest subtypes.

Method:
A retrospective analysis of patients diagnosed with HAL between 2001 and 2024 at Tuen Mun Hospital was conducted, reviewing demographics, disease properties, management, and clinical outcomes.

Result:
A total of 9 cases were identified. The male-to-female ratio was 8:1, with a median age at diagnosis of 44-years-old. There were 5 cases of DLBCL and 4 cases of Burkitt lymphoma.

Clinically, all cases were diagnosed at stage 4. Central nervous system (CNS) involvement was observed exclusively in Burkitt lymphoma cases.

Interestingly, 3 DLBCL patients developed lymphoma while receiving highly active antiretroviral therapy (HAART), with mean CD4 count as high as 656 x 10^6/L at time of diagnosis. In contrast, the HIV status was revealed only after lymphoma diagnosis in all Burkitt lymphoma cases. The mean CD4 count at diagnosis of lymphoma for those not receiving HAART was 147 x 10^6/L and 157 x 10^6/L for DLBCL and Burkitt lymphoma cases, respectively.

All of our patients received HAART. Excluding 1 case opted for palliative care, CHOP and DA-EPOCH were used for DLBCL, while intensive chemotherapy (CODOX-M/IVAC, hyper-CVAD) was used for Burkitt lymphoma cases. Those receiving active treatments all had addition of Rituximab except for 1 case due to financial concern.

All 6 patients who completed treatment achieved complete remission with 100% 1-year survival rate. Excluding 1 patient who died of pneumocystis jirovecii pneumonia related to noncompliance to HAART, the other 5 cases remained in remission without relapse.

Discussion:
Since the introduction of HAART, there has been a significant reduction (79%) in the incidence of systemic non-Hodgkin lymphoma (NHL).[1] It is postulated that the immunosuppressed state plays a role in developing NHL, and HAART is associated with improved CD4 levels.[2] However, in our study, 3 DLBCL patients developed lymphoma while receiving HAART with a high CD4 count. This signifies that CD4 count is not the sole determining factor in the development of HAL, especially for DLBCL.

CHOP is historically the standard treatment for DLBCL, but DA-EPOCH is an emerging alternative in recent years. In contrast, most patients with Burkitt lymphoma who are fit are preferred to receive intensive chemotherapy especially when there is CNS or marrow involvement, as alternatives like DA-EPOCH are associated with greater risk of treatment failure in advanced disease.[3] Addition of rituximab also showed higher complete response rates.[4] Concerns of excessive toxicity associated with very low CD4 counts (<50 x 10^6) can be overcome by adequate infection prophylaxis and screening.[5]

Conclusion:
In conclusion, all cases presented as advanced disease and Burkitt lymphoma has a higher likelihood of CNS involvement. Incorporating HAART along with tailored chemotherapy and targeted agents like Rituximab can improve treatment responses, and patients who adhere to treatment generally have a favorable prognosis. Further studies are warranted to validate these findings and explore optimal treatment strategies for different subtypes of HAL.

References:
Polesel J, Franceschi S, Suligoi B, et al. Cancer incidence in people with AIDS in Italy. Int J Cancer. 2010;127(6):1437-1445.
Mbulaiteye SM, Biggar RJ, Goedert JJ, Engels EA. Immune deficiency and risk for malignancy among persons with AIDS. J Acquir Immune Defic Syndr. 2003;32(5):527-533.
Dunleavy K, Roschewski M, Abramson JS, et al. Risk-adapted therapy in adults with Burkitt lymphoma: updated results of a multicenter prospective phase II study of DA-EPOCH-R. Hematol Oncol. 2017;35(suppl 2):133-134
Barta SK, Xue X, Wang D, et al.. Treatment factors affecting outcomes in HIV-associated non-Hodgkin lymphomas: a pooled analysis of 1546 patients. Blood. 2013 Nov 7;122(19):3251-62.
Noy A. Optimizing treatment of HIV-associated lymphoma. Blood. 2019 Oct 24;134(17):1385-1394.

Abstract XVI: Acute myeloid leukaemia genotyping by nanopore targeted sequencing

Tsz Fung Wong, Ka Ngai Lau, Tze Wing Fan, Sze Fai Yip

Division of Haematology, Clinical Pathology, Tuen Mun Hospital

Abstract

Background and Objective

Accurate and rapid genotyping of acute myeloid leukaemia (AML) is important for diagnostic, prognostic and therapeutic purposes. According to the 2022 edition of the European LeukaemiaNet (ELN) recommendations for diagnosis and management of AML, FMS-like tyrosine kinase-3 internal tandem duplication (FLT3-ITD), FLT3 tyrosine kinase domain (FLT3-TKD), IDH1, IDH2, NPM1 gene mutations should be identified within 3-5 days. Results of TP53 and other myelodysplasia-related gene mutations should be available within the first treatment cycle. Current methodologies for detecting these recurrent gene mutations in AML include polymerase chain reaction (PCR) followed by fragment size analysis with capillary electrophoresis, PCR-restriction fragment length polymorphism (RFLP) assay, Sanger sequencing and next-generation sequencing (NGS), which are tedious, time-consuming and not cost-effective. Oxford Nanopore Technologies (ONT) Nanopore sequencing is a rapidly growing technology that offers numerous advantages over traditional approaches. This study aimed to develop a Nanopore targeted sequencing assay for detecting FLT3-ITD, FLT3-TKD, IDH1, IDH2, NPM1 and TP53 gene mutations in AML cases.

Methods

A total of 67 AML blood samples from 2021 - 2023 were retrieved in the Haematology Laboratory at Tuen Mun Hospital. PCR covering FLT3 exon 14-15, FLT3 exon 20, IDH1 exon 4, IDH2 exon 4, NPM1 exon 11 and TP53 exons 2-11 was performed after DNA extraction. The library was prepared using ONT library preparation kit according to manufacturer's instructions. Sequencing was performed in the R10.4.1 flow cell on the ONT MinION device. An in-house developed bioinformatics pipeline was used for variant identification. Findings of FLT3-ITD and other gene mutations were compared with reference methodologies, fragment size analysis followed by Sanger sequencing and NGS respectively, previously performed in referral laboratories. Reported allelic ratio of FLT-ITD from referral laboratories was converted to variant allele frequency (VAF) for statistical comparison.

Results

The result concordance rate between Nanopore sequencing and reference methodologies was 100%, with a coefficient of correlation ≥ 0.7 and a bias of -8.4%. It was noted that the negative bias was mainly due to the underestimation of VAF in FLT3-ITD. After excluding the FLT3-ITD data, high correlation (R ≥ 0.9) and minimal bias (-0.11%) were observed. Nanopore sequencing achieved a 100% concordance rate of repeatability and reproducibility analysed by running known positive and negative samples in triplicate within a single run and in three different days respectively in terms of positivity / negativity calls for each sample. A commercial DNA reference standard with known VAFs of different variants was used to validate the limit of detection of the assay. All defined variants were detected by Nanopore sequencing between 4% to 6% of VAFs, which were consistent with the stated VAFs of the reference standard (approximately 5% by NGS).

Conclusion

This study serves as a proof that the use of Nanopore sequencing is an alternative approach to the traditional methods for AML genotyping. However, fragment size analysis remains an indispensable tool for FLT3-ITD detection with accurate determination of VAF. On the whole, Nanopore sequencing is capable of generating accurate and reproducible results with acceptable sensitivity in a rapid and all-in-one fashion and hence helps to provide molecular information with diagnostic, prognostic and therapeutic values in AML patients.

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P-CORP-23N03 09/23

ACKNOWLEDGEMENT

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Patients achieved early platelet Boost with Romiplate®1*

Fast onset of action

- Median time to platelet response was 2.1 weeks[1]
- 88% of patients achieved a platelet response[2#]

Sustained Response

- 61% of patients sustained platelet counts ≥ 50 x 10^9/L for ≥ 11 months during the treatment period[1]

Abbreviated Package Insert of ROMIPLATE Power for Solution for Injection 250mcg

Composition: Romiplostim. **Indications:** Treatment of primary immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments (e.g. corticosteroids & immunoglobulins); **Dosage and Administration:** SC inj Initially 1 mcg/kg (ABW) q1w, may be increased by increments of 1 mcg/kg until achieving a PLC ≥ 50 x 10^9 /L. Max: 10 mcg/kg q1w. **Contraindications:** Hypersensitivity to romiplostim or any of the excipients or E. coli-derived proteins. **Precautions:** Recurrence of thrombocytopenia & bleeding after discontinuation. Increased bone marrow reticulin. Thrombotic/thromboembolic complications. Progression of existing myelodysplastic syndrome (MDS). Immunogenicity. Alterations in RBC & WBC. Renal & hepatic impairment. May impair ability to drive or operate machinery. Pregnancy & lactation. Child <18 yr. **Common adverse reactions:** Upper respiratory tract infection, hypersensitivity, headache. **Serious adverse reactions:** reoccurrence of thrombocytopenia and bleeding after cessation of treatment, increased bone marrow reticulin, thrombotic/thromboembolic complications, progression of existing MDS to AML. **P/P:** Powd for soln for inj (vial) 250 mcg x 1's. Approved version of package insert: Jan 2023

Please refer to the full prescribing information before prescribing. Further information is available upon request.
* Platelet response was defined as a platelet count ≥ 50 x 10^9/L # Based on Overall Platelet Response in non-splenectomized patient

Reference: 1. Newland A, Godeau VP, Priego V, et al. Remission and platelet responses with romiplostim in primary immune thrombocytopenia: final results from a phase 2 study. *Br J Haematol. 2016;172(2):262-273.* **2.** Vishnu P, Aboulafia DM. Long-term safety and efficacy of romiplostim for treatment of immune thrombocytopenia. *J Blood Med. 2016;7:99-106.* **3.** Hong Kong Prescribing Information, Sep 2019.

THIS MATERIAL IS MEANT FOR HEALTHCARE PROFESSIONALS ONLY

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HK-RPT-23-00001 AUG 2023

Spot. Confirm. Stop.

Acquired Haemophilia – Stop it – NovoSeven®

Treatment with NovoSeven® is efficacious and well tolerated[1-7]

Spot: Acquired Haemophilia

- Rare, but severe bleeding disorder caused by autoantibodies against coagulation factors, most commonly FVIII[8]
- Approximately 1 in 1.5 million persons affected annually[9]
- Occurs in patients with no previous history of bleeding[10,11]
- 21% overall mortality rate[12]
- Fatal bleeds may occur at any time until the inhibitor has been eliminated[10,11]

Confirm: Diagnosis

- Acute onset of severe and life-threatening bleeding or wide-spread subcutaneous bleeds[11]
- Isolated prolonged activated partial thromboplastin time (aPTT) with normal prothrombin time (PT)[10,11]

Stop: NovoSeven® offers

- 95% effective or partially effective as first-line therapy[1]
- Well tolerated with low incidence of adverse events[2-4,13] and no risk of human to human pathogen transfer [5-7]
- Rapid and flexible dosing for convenient administration and optimal, predictable response[13]
- Precise mode of action – controls bleeding at site of vascular injury[14]

NovoSeven®: Prescribing Information (Please consult the full prescribing information before prescribing) NovoSeven® 1 mg (50 KIU) powder and solvent (vial or pre-filled syringe) for solution for injection. **Composition:** eptacog alfa (activated); eptacog alfa (activated) is recombinant coagulation factor VIIa (rFVIIa) produced in baby hamster kidney cells (BHK Cells) by recombinant DNA technology, 1 mg/vial (corresponds to 50 KIU/vial). 1 mg/ml eptacog alfa (activated) after reconstitution. **List of excipients:** Powder: Sodium chloride, Calcium chloride dihydrate, Glycylglycine, Polysorbate 80, Mannitol, Sucrose, Methionine, Hydrochloric acid, Sodium hydroxide. Solvent: Histidine, Hydrochloric acid, Sodium hydroxide, Water for injections. **Indications:** Treatment of bleeding episodes and prevention of bleeding in those undergoing surgery or invasive procedures in the following patient groups: • patients with congenital haemophilia with inhibitors to coagulation factors VII or IX (> 5 BU), • patients with congenital haemophilia who are expected to have a high anamnestic response to factor VII or factor IX administration; • patients with acquired haemophilia; • patients with congenital FVII deficiency; • patients with Glanzmann's thrombasthenia with antibodies to GP IIb-IIa and/or HLA, and with past or present refractoriness to platelet transfusions. **Posology:** Haemophilia A or B with inhibitors or expected to have a high anamnestic response: **Mild to moderate bleeding episodes (including home therapy):** Early intervention has been shown to be efficacious in the treatment of mild to moderate joint, muscle and mucocutaneous bleeds. Two dosing regimens can be recommended: 1) Two to three injections of 90 µg per kg body weight, administered at three-hour intervals. If further treatment is required, one additional dose of 90 µg per kg body weight can be administered. 2) One single injection of 270 µg per kg body weight. The duration of the home therapy should not exceed 24 hours. There is no clinical experience with administration of a single dose of 270 µg per kg body weight in elderly patients. **Serious bleeding episodes:** An initial dose of 90 µg per kg body weight is recommended and could be administered on the way to the hospital where the patient is usually treated. The following dose wakes according to the type and severity of the haemorrhage. Dosing frequency should initially be every second hour until clinical improvement is observed. If continued therapy is indicated, the dose interval can then be increased to 3 hours for 1 – 2 days. Thereafter, the dose interval can be increased successively to every 4, 6, 8 or 12 hours for as long as treatment is judged as being indicated. A major bleeding episode may be treated for 2 - 3 weeks but can be extended beyond this if clinically warranted. **Invasive procedure/surgery:** An initial dose of 90 µg per kg body weight should be given immediately before the intervention. The dose should be repeated after 2 hours and then at 2 – 3 hour intervals for the first 24 – 48 hours depending on the intervention performed and the clinical status of the patient. In major surgery, the dose should be continued at 2 – 4 hour intervals for 6-7 days. The dose interval may then be increased to 6–8 hours for another 2 weeks of treatment. Patients undergoing major surgery may be treated for up to 2–3 weeks until healing has occurred. *Acquired Haemophilia:* NovoSeven should be given as early as possible after the start of a bleeding episode. The recommended initial dose, administered by intravenous bolus injection, is 90 µg per kg body weight. Following the initial dose of NovoSeven further injections may be given if required. The duration of treatment and the interval between injections will vary with the severity of the haemorrhage, the invasive procedures or the surgery being performed. The initial dose interval should be 2 – 3 hours. Once haemostasis has been achieved, the dose interval can be increased successively to every 4, 6, 8 or 12 hours for as long as treatment is judged to be indicated. *Factor VII deficiency:* The recommended dose range is 15 – 30 µg per kg body weight every 4– 6 hours until haemostasis is achieved. Dose and frequency of injections should be adapted to each individual. Limited clinical experience in long term prophylaxis in paediatric population has been gathered in the paediatric population below 12 years of age, with a severe clinical phenotype. Dose and frequency of injections for prophylaxis should be based on clinical response and adapted to each individual. *Glanzmann's thrombasthenia:* The recommended dose is 90 µg (range 80–120 µg) per kg body weight at intervals of two hours (1.5–2.5 hours). At least three doses should be administered to secure effective haemostasis. The recommended route of administration is bolus injection as lack of efficacy may appear in connection with continuous infusion. For those patients who are not refractory, platelets are the first line treatment for Glanzmann's thrombasthenia. **Contraindications:** Hypersensitivity to the active substance, or to any of the excipients, or to mouse, hamster or bovine protein. **Interaction with other medicinal products and other forms of interaction:** The risk of a potential interaction between NovoSeven and coagulation factor concentrates is unknown. Simultaneous use of prothrombin complex concentrates, activated or not, should be avoided. Anti-fibrinolytics have been reported to reduce blood loss in association with surgery in haemophilia patients, especially in orthopaedic surgery and surgery in regions rich in fibrinolytic activity, such as the oral cavity. Experience with concomitant administration of anti-fibrinolytics and rFVIIa treatment is however limited. Based on a non-clinical study it is not recommended to combine rFVIIa and rFXIII. There are no clinical data available on interaction between rFVIIa and rFXIII. **Fertility, pregnancy and lactation** *Pregnancy:* As a precautionary measure, it is preferable to avoid the use of NovoSeven® during pregnancy. Data on a limited number of exposed pregnancies within approved indications indicate no adverse effects of rFVIIa on pregnancy or on the health of the foetus/newborn child. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. *Breastfeeding:* It is unknown whether rFVIIa is excreted in human breast milk. The excretion of rFVIIa in milk has not been studied in animals. A decision on whether to continue/discontinue breastfeeding or to continue/discontinue therapy with NovoSeven® should be made taking into account the benefit of breastfeeding to the child and the benefit of NovoSeven® therapy to the woman. *Fertility:* Data from non-clinical studies as well as post-marketing data show no indication that rFVIIa has a harmful effect on male or female fertility. **Undesirable effects:** Rare (> 1/10,000, < 1/1,000): Disseminated intravascular coagulation and related laboratory findings including elevated levels of D-dimer and decreased level of AT, coagulopathy, hypersensitivity, headache, arterial thromboembolic events (myocardial infarction, cerebral infarction, cerebral ischaemia, cerebral artery occlusion, cerebrovascular accident, renal artery thrombosis, peripheral ischaemia, peripheral arterial thrombosis and intestinal ischaemia), angina pectoris, nausea, injection site reaction including injection site pain, increased fibrin degradation products, increase in alanine aminotransferase, alkaline phosphatase, lactate dehydrogenase and prothrombin. Uncommon (> 1/1,000, < 1/100): Venous thromboembolic events (deep vein thrombosis, thrombosis at i.v. site, pulmonary embolism, thromboembolic events of the liver including portal vein thrombosis, renal vein thrombosis, thrombophlebitis, superficial thrombophlebitis and intestinal ischaemia), rash (including allergic dermatitis and rash erythematous), pruritus and urticaria, therapeutic response decreased, pyrexia. Inhibitory antibody formation: In post-marketing experience, there have been no reports of inhibitory antibodies against NovoSeven® or FVII in patients with congenital haemophilia A or B. Development of inhibitory antibodies to NovoSeven has been reported in a post-marketing observational registry of patients with congenital FVII deficiency. Not known: Intracardiac thrombus, anaphylactic reaction, flushing, angioedema. **Overdose:** Four cases of overdose have been reported in patients with haemophilia in 16 years. The only complication reported in connection with an overdose was a slight transient increase in blood pressure in a 16 year-old patient receiving 24 mg rFVIIa instead of 5.5 mg. No cases of overdose have been reported in patients with acquired haemophilia or Glanzmann's thrombasthenia. In patients with factor VII deficiency, where the recommended dose is 15–30 µg/kg rFVIIa, one episode of overdose has been associated with a thrombotic event (occipital stroke) in an elderly (> 60 year) male patient treated with 10–20 times the recommended dose. In addition, the development of antibodies against NovoSeven and FVII has been associated with overdose in one patient with factor VII deficiency. The dose schedule should not be intentionally increased above the recommended doses due to the absence of information on the additional risk that may be incurred. **Administration:** NovoSeven® (eptacog alfa activated) is administered intravenously over 2–5 minutes. **Caution:** Some needleless connectors with an internal spike used with central venous access devices (CVADs) may be incompatible with the pre-filled glass syringe and prevent administration. Therefore, use of an alternative sterile 10 ml luer-lock plastic syringe may be required for withdrawal and injection of the reconstituted solution. Follow the instructions for use for the CVAD and needleless connector. **Storage:** 3 years shelf life when product is stored below 25°C. Store powder and solvent below 25°C and protect from light. Do not freeze solvent vial/pre-filled syringe. After reconstitution, chemical and physical stability has been demonstrated for 6 hours at 25°C and 24 hours at 5°C. It is recommended the product be used immediately after reconstitution if not used immediately, storage time and storage conditions prior to use are the responsibility of the user, and should not be longer than 24 hours at 2°C – 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions. The reconstituted solution should be stored in the vial. Date of review: 2022 Feb. NovoSeven® is a registered trademark owned by Novo Nordisk Health Care AG and the Aps bull logo is a registered trademark of Novo Nordisk A/S. © 2017 Novo Nordisk Healthcare AG, Zurich, Switzerland.

References: 1. Sumner MJ, *et al.* Haemophilia 2007;13:451-61. **2.** Hay CR, *et al.* Thromb Haemost 1997;78:1463-7. **3.** Abshire T, Kenet G. Haemophilia 2008;14:898-902. **4.** Baudo F, *et al.* Haematologica 2004;89:759-61. **5.** Hedner U, Erhardtsen E. Transfusion 2002;42:114-24. **6.** Croom KF, McCormack PL. BioDrugs 2008;22:121-36. **7.** Ma AD, Carrizosa D. Hematology Am Soc Hematol Educ Program 2006:432-7. **8.** Delgado J, *et al.* Br J Haematol 2003;121:21-35. **9.** Collins PW, *et al.* Blood 2007;109:1870-7. **10.** Huth-Kuhne A, *et al.* Haematologica 2009;94:566-75. **11.** Collins P, *et al.* BMC Res Notes 2010;3:161. **12.** Bitting RL, *et al.* Blood Coagul Fibrinolysis 2009;20:517-23. **13.** NovoSeven® Summary of Product Characteristics. **14.** Hoffman M, Monroe DM. 3rd. Dis Mon 2003;49:14-21.

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Further information is available from
Novo Nordisk Hong Kong Ltd
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02-2024-HK-COM-ADV-909-V1

Hope of life beyond CD30+ lymphoma[1*]

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Abbreviated Prescribing Information (EU-DEC20-HK-MAR21)

ADCETRIS 50 mg powder for concentrate for solution for infusion.

Active Ingredient: Brentuximab vedotin Indication: Treatment for adult patients with previously untreated CD30+ Stage IV Hodgkin lymphoma (HL) in combination with doxorubicin, vinblastine and dacarbazine (AVD); Treatment of adult patients with CD30+ HL at increased risk of relapse or progression following ASCT; Treatment for relapsed or refractory CD30+ Hodgkin lymphoma (HL) following autologous stem cell transplant (ASCT) or at least 2 prior therapies when ASCT or multi-agent chemotherapy is not a treatment option; In combination with cyclophosphamide, doxorubicin and prednisone (CHP) for the treatment of adult patients with previously untreated systemic anaplastic large cell lymphoma (sALCL); relapsed or refractory sALCL; Treatment of adult patients with CD30+ cutaneous T-cell lymphoma (CTCL) after at least 1 prior systemic therapy. Dose & Administration: Previously untreated HL: In combination with chemotherapy (doxorubicin [A], vinblastine [V] and dacarbazine [D]) (AVD)), 1.2mg/kg IV infusion over 30 min on days 1 and 15 of each 28-day cycle for 6 cycles. HL at increased risk of relapse or progression following ASCT & CTCL after at least 1 prior systemic therapy: 1.8 mg/kg IV infusion over 30 min every 3 wk up to max of 16 cycles. Previously untreated sALCL: In combination with chemotherapy (cyclophosphamide [C], doxorubicin [H] and prednisone [P] [CHP]), 1.8 mg/kg IV infusion over 30 minutes every 3 weeks for 6 to 8 cycles. Relapsed or refractory HL & relapsed or refractory sALCL: 1.8 mg/kg IV infusion over 30 min every 3 wk, patients who achieve stable disease or better should receive a minimum of 8 cycles and up to a max of 16 cycles. Contraindications: Hypersensitivity to brentuximab. Combined use of brentuximab & bleomycin. Pregnancy & lactation. Special Population: Closely monitor for new or worsening neurological, cognitive or behavioural signs or symptoms suggestive of progressive multifocal leukoencephalopathy (PML); new or worsening abdominal pain suggestive of acute pancreatitis; new or worsening pulmonary symptoms; emergence of serious & opportunistic infections; immediate & delayed infusion-related reactions. Discontinue use if anaphylaxis & Stevens-Johnson syndrome occurs. Patient w/rapidly proliferating tumour & high tumour burden at risk of tumour lysis syndrome. Monitor for symptoms of neuropathy. Patient experiencing new or worsening peripheral neuropathy may require delay & dose reduction or discontinuation of treatment. Monitor CBC prior to therapy; serum glucose. Patient w/ an elevated BMI w/ or w/o history of DM; renal & hepatic impairment; on controlled Na-diet. Women of childbearing potential should use 2 methods of contraception during & until 30 days after therapy. Men should not father a child during therapy & for up to 6 mth after last dose. May affect ability to drive or operate machinery. Childn & elderly. Adverse Reactions: Infection, sepsis/septic shock, upper resp tract infection, herpes zoster, pneumonia, neutropenia, anaemia, thrombocytopenia, hyperglycaemia, peripheral sensory neuropathy, peripheral motor neuropathy, dizziness, demyelinating polyneuropathy, cough, dyspnoea, diarrhoea, nausea, vomiting, constipation, elevation of ALT/AST, alopecia, pruritus, rash, myalgia, arthralgia, back pain, fatigue, pyrexia, infusion-related reactions & chills.

For detailed information, please consult full prescribing information.
For reporting suspected side effects for Takeda products at AE.HongKong@takeda.com
For asking medical information and other inquiries for Takeda products at medinfohk@takeda.com

Reference: 1* Adcetris Package Insert, EU-DEC20-HK-MAR21

C-APROM/HK/ADCE/0041(02/2024)

TREANDA®
(bendamustine HCl)
for Injection

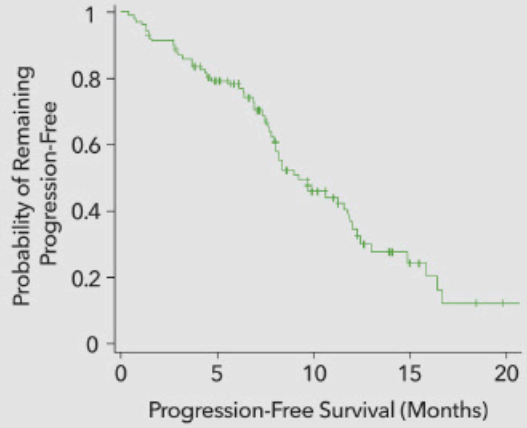
Non-Hodgkin Lymphoma (NHL)

2nd Line Meaningful & Enduring 2nd-Line Responses[1]

88% ORR
in patients sensitive to their last chemotherapy regimen

64% ORR
in patients who are refractory to their last chemotherapy regimen

9.3 months
median PFS
(95% CI, 8.1-11.9 months)



9.2 months
median DOR
(95% CI, 7.1-10.8 months)

Chemosensitive Patients	10.0 months (95% CI, 8.4-11.7 months)
Chemorefractory Patients	6.3 months (95% CI, 4.9 months-NA)

Study design: Eligible patients (N = 100, ages 31-84 years) received bendamustine at a dose of 120 mg/m² by intravenous infusion on Days 1 and 2 every 21 days for 6 to 8 cycles. Histologies included follicular (62%), small lymphocytic (21%), and marginal zone (16%) lymphomas. Patients had received a median of 2 previous regimens (range, 0-6 previous regimens), and 36% were refractory to their most recent chemotherapy regimen. Primary endpoints included overall response rate (ORR) and duration of response (DOR). Secondary endpoints were safety and progression-free survival (PFS).[1]

* Bendamustine with obinutuzumab or rituximab.[2]
† Bendamustine combine with rituximab as one of the options for follicular lymphoma with high tumour burden.[3]

CI = confidence interval; DOR = duration of response; ESMO = European Society for Medical Oncology; NA = not available; NCCN = National Comprehensive Cancer Network; ORR = overall response rate; PBS = Pharmaceutical Benefits Scheme; PFS = progression-free survival.

References: 1. Kahl BS, et al. Bendamustine is effective therapy in patients with rituximab-refractory, indolent B-cell non-Hodgkin lymphoma: results from a Multicenter Study. Cancer. 2010;116:106-14. 2. National Comprehensive Cancer Network. B-Cell Lymphomas (Version 2.2023) [Internet]. 3. Dreyling M, Ghielmini M, Rule S, et al. Newly diagnosed and relapsed follicular lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2016;27:v83-v90.

Preferred Treatment Agent[2-3]
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TRE-HK-0018 March 2025

JAKAVI® ruxolitinib

Broad clinical benefits of JAKAVI® in MF BEYOND ANEMIA STATUS

IMPROVEMENTS IN DUAL KEY TREATMENT GOALS[1]
REGARDLESS OF ANEMIA STATUS

Clinical benefits maintained regardless of baseline anemia[1]				Benefits not diminished with development or worsening anemia at Week 12[1]			
Nonanemic patients at baseline		Anemic patients at baseline*		No new or worsening anemia		New or worsening anemia	
42.3% (60/142)	vs.	**34.3%** (35/102)	**≥35%** spleen reduction by week 48	**36.1%** (39/108)	vs.	**41.2%** (56/136)	
47.5% (38/80)	vs.	**47.6%** (30/63)	**≥50%** TSS reduction by week 24	**46.9%** (30/64)	vs.	**48.1%** (38/79)	

- **Consistent OS benefits** were demonstrated **regardless of baseline anemia or the development of anemia** during JAKAVI® treatments in post-hoc analysis of COMFORT studies[2]
- **Significantly longer OS** was observed with early JAKAVI® intervention over BAT and placebo (**5.3 years vs. 2.3 years**) in the 5-year pooled analysis of COMFORT studies after adjusting for crossover in the RPSFT model (HR=0.35; 95%CI: 0.23-0.59)[3]
- **Only 1% of discontinuation rate due to anemia and thrombocytopenia** despite >40% and ≥8% of grade 3 or 4 anemia and thrombocytopenia respectively in COMFORT studies[4,5]

CARRY ON JAKAVI® WITH DOSE OPTIMIZATION[6]
to achieve consistent benefits among MF patients regardless of anemia status

*Includes transfusion-dependent and non–transfusion-dependent patients.

Study design[4,5]: Data was pooledfrom the COMFORT I and COMFORT II studies. COMFORT I was a double-blind trial where patients with intermediate-2 or high-risk MF were randomized to receive JAKAVI® BID (n=155) or placebo (n=154). The primary end point was the proportion of patients with a reduction in spleen volume of 35% or more at 24 weeks. Secondary end points included the durability of response, changes in symptom burden (assessed by the total symptom score), and overall survival. In COMFORT II, 219 patients with intermediate-2 or high-risk primary MF, post–polycythemia vera MF, or post–essential thrombocythemia MF to receive oral JAKAVI® or the best available therapy. The primary end point and key secondary end point of the study were the percentage of patients with at least a 35% reduction in spleen volume at week 48 and at week 24, respectively.

Abbreviation: : BAT: Best available therapy; MF: Myelofibrosis; OS: Overall survival; RPSFT: Rank-preserving structural failure time; TSS: Total Symptom Score

References: 1. Al-Ali HK, et al. Effect of new or worsening anemia on clinical outcomes in patients with myelofibrosis (MF) treated with ruxolitinib (RUX): a post hoc analysis of the COMFORT-I and -II trials. Presented at: European Hematology Association 2023 Hybrid Congress; June 8-11, 2023; Frankfurt, Germany. 2. Gupta V, et al. The impact of anemia on overall survival in patients with myelofibrosis treated with ruxolitinib in the COMFORT studies. *Haematologica.* 2016;101(12):e482-e484. 3. Verstovsek S, et al. Long-term survival in patients treated with ruxolitinib for myelofibrosis: COMFORT-I and -II pooled analyses. *J Hematol Oncol.* 2017;10(1):156. 4. Verstovsek S, et al. A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis. *N Engl J Med.* 2012;366(9):799-807. 5. Harrison C, et al. JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis. *N Engl J Med.* 2012;366(9):787-98. 6. Verstovsek S, et al. Ten years of treatment with ruxolitinib for myelofibrosis: a review of safety. *J Hematol Oncol.* 2023;16(1):82. 7. JAKAVI (ruxolitinib) Hong Kong prescribing information (Apr 2022).

JAKAVI® is indicated for:[7]
- the treatment of adult patients with polycythaemia vera who are resistant to or intolerant of hydroxyurea.
- the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis.
- the treatment of patients aged 12 years and older with acute graft versus host disease or chronic graft versus host disease who have inadequate response to corticosteroids or other systemic therapies.

HK2402260366

NOVARTIS

Novartis Pharmaceuticals (HK) Ltd
7/F, Citi Tower, One Bay East, 83 Hoi Bun Road, Kwun Tong, Kowloon, H.K.
Tel: 2882 5222 Fax: 2577 0274

ONUREG® (azacitidine)

FRONTLINE ORAL AML MAINTENANCE THERAPY PROVEN TO EXTEND OVERALL SURVIVAL[1]

SEE AML TREATMENT IN A DIFFERENT LIGHT

ONUREG® provided ~10 months longer OS
compared with placebo in patients with AML in first remission following induction therapy with or without consolidation[1]

24.7 MONTHS with ONUREG® (95% CI: 18.7, 30.5)	VS	14.8 MONTHS with PLACEBO (95% CI: 11.7, 17.6)

HR 0.69 (95% CI: 0.55, 0.86; *P*=0.0009)[2]

AML=acute myeloid leukemia; CI=confidence interval; HR=hazard ratio; OS=overall survival.

See below for study design of the QUAZAR AML-001 trial, which evaluated the efficacy and safety of ONUREG® vs placebo as maintenance therapy in patients with AML in first remission following induction therapy* with or without consolidation.

* Intensive induction Chemotherapy

ONUREG TABLETS 200MG
ONUREG TABLETS 300MG
ABBREVIATED PRESCRIBING INFORMATION

ACTIVE INGREDIENT: ONUREG (azacitidine) is supplied as film-coated tablets containing 200 mg or 300 mg of azacitidine for oral use.

INDICATIONS: ONUREG is indicated for continued treatment of adult patients with acute myeloid leukemia who achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy.

DOSAGE AND ADMINISTRATION: The recommended dosage of ONUREG is 300 mg orally once daily with or without food on Days 1 through 14 of each 28-day cycle. Continue ONUREG until disease progression or unacceptable toxicity. Administer an antiemetic 30 minutes prior to each dose of ONUREG for the first 2 cycles. Antiemetic prophylaxis may be omitted after 2 cycles if there has been no nausea and vomiting. If the absolute neutrophil count (ANC) is less than 0.5 Gi/L on Day 1 of a cycle, do not administer ONUREG. Delay the start of the cycle until the ANC is 0.5 Gi/L or more. ONUREG is a hazardous drug. Follow applicable special handling and disposal procedures. Monitor complete blood count every other week for the first 2 cycles and prior to the start of each cycle thereafter. Increase monitoring to every other week for the 2 cycles after any dose reduction for myelosuppression.

CONTRAINDICATIONS: ONUREG is contraindicated in patients with known severe hypersensitivity to azacitidine or its components.

WARNINGS AND PRECAUTIONS: Risks of Substitution with Other Azacitidine Products: Due to substantial differences in the pharmacokinetic parameters, the recommended dose and schedule for ONUREG are different from those for the intravenous or subcutaneous azacitidine products. Do not substitute ONUREG for intravenous or subcutaneous azacitidine. Myelosuppression: Monitor complete blood counts and modify the dosage as recommended. Provide standard supportive care, including hematopoietic growth factors, if myelosuppression occurs. Increased Early Mortality in Patients with Myelodysplastic Syndromes: The safety and effectiveness of ONUREG for treatment of myelodysplastic syndromes have not been established. Treatment of patients with myelodysplastic syndromes with ONUREG is not recommended outside of controlled trials. Embryo-Fetal Toxicity: Based on the mechanism of action and findings in animals, ONUREG can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with ONUREG and for at least 6 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with ONUREG and for at least 3 months after the last dose.

ADVERSE REACTIONS: Serious adverse reactions occurred in 15% of patients who received ONUREG. Serious adverse reactions in ≥ 2% of patients who received ONUREG were pneumonia (8%) and febrile neutropenia (7%). One fatal adverse reaction (sepsis) occurred in a patient who received ONUREG. Permanent discontinuation of ONUREG due to an adverse reaction occurred in 8% of patients. Adverse reactions which resulted in permanent discontinuation of ONUREG in > 1% of patients included nausea (2.1%), diarrhea (1.7%), and vomiting (1.3%). Interruptions of ONUREG due to an adverse reaction occurred in 35% of patients. Adverse reactions which required an interruption of ONUREG in > 5% of patients included neutropenia (20%), thrombocytopenia (8%), and nausea (6%). Dose reductions of ONUREG due to an adverse reaction occurred in 14% of patients. Adverse reactions which required a dose reduction in > 1% of patients included neutropenia (6%), diarrhea (3.4%), thrombocytopenia (1.7%), and nausea (1.7%). The most common (≥ 10%) adverse reactions were nausea, vomiting, diarrhea, fatigue/asthenia, constipation, pneumonia, abdominal pain, arthralgia, decreased appetite, febrile neutropenia, dizziness, and pain in extremity. The following adverse reactions have been identified during postapproval use of intravenous or subcutaneous azacitidine: Hypersensitivity reaction, Interstitial lung disease, Tumor lysis syndrome, Sweet's syndrome (acute febrile neutrophilic dermatosis), Necrotizing fasciitis (including fatal cases), Differentiation syndrome.

USE IN SPECIFIC POPULATIONS: Pregnancy: Based on its mechanism of action and findings in animals, ONUREG can cause fetal harm when administered to a pregnant woman. There are no available data on ONUREG use in pregnant women to evaluate for a drug-associated risk. Advise pregnant women of the potential risk to the fetus. Lactation: There are no data regarding the presence of azacitidine in human milk or the effects on the breastfed child or milk production. Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with ONUREG and for 1 week after the last dose. Females and Males of Reproductive Potential: ONUREG can cause embryo-fetal harm when administered to pregnant women Pregnancy testing is recommended for females of reproductive potential before starting ONUREG. Advise females of reproductive potential to use effective contraception during treatment with ONUREG and for at least 6 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with ONUREG and for at least 3 months after the last dose. Based on animal data, ONUREG may impair male or female fertility. Pediatric Use: The safety and effectiveness of ONUREG in pediatric patients have not been established. Geriatric Use: No overall differences in safety or effectiveness of ONUREG were observed between these patients and younger patients. Renal Impairment: Monitor patients with severe renal impairment more frequently for adverse reactions and modify the ONUREG dosage for adverse reactions. No dose adjustment of ONUREG is recommended for patients with mild to severe renal impairment. Hepatic Impairment: ONUREG has not been studied in patients with pre-existing severe hepatic impairment. A recommended dosage of ONUREG has not been established for patients with moderate hepatic impairment. No dose adjustment of ONUREG is recommended for patients with mild hepatic impairment.

DRUG INTERACTION STUDIES: Coadministration of omeprazole (a proton pump inhibitor) with ONUREG increased azacitidine AUC0-INF by 19% and had no effect on Cmax. Azacitidine does not inhibit CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP3A4, or CYP2E1 at clinically relevant concentrations. Azacitidine is not an inducer of CYP1A2, CYP2C19, or CYP3A. Azacitidine is not a substrate of P-glycoprotein (P-gp). Azacitidine does not inhibit P-gp, breast cancer resistance protein (BCRP), organic anion transporters (OAT) OAT1 and OAT3, organic anion transporting polypeptides (OATP) OATP1B1 and OATP1B3, or organic cation transporter (OCT) OCT2 at clinically relevant concentrations.

Please refer to the full prescribing information before prescribing. Prescribing information is available on request.
Date of revision of the text: July 2023

Study design and survival outcomes: The efficacy of ONUREG® was evaluated in QUAZAR AML-001, a multicenter, randomized, double-blind, placebo-controlled, phase III study. Eligible patients were aged 55 years or older, had AML, and were within 4 months of achieving first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) with intensive induction chemotherapy with or without consolidation therapy. A total of 472 patients who were ineligible for hematopoietic stem cell transplant (HSCT) were randomized 1:1 to receive ONUREG® 300 mg (n=238) or placebo (n=234) orally on Days 1 to 14 of each 28-day treatment cycle. Efficacy was established on the basis of OS and relapse-free survival (RFS). The trial demonstrated a statistically significant improvement in OS for patients randomized to ONUREG® compared with placebo (24.7 months with ONUREG® vs 14.8 months with placebo; HR: 0.69 [95% CI: 0.55, 0.86] *P*=0.0009). RFS was also significantly improved with ONUREG® vs placebo (10.2 months vs 4.8 months, respectively; P<0.001).[1,2]

Reference: 1. Wei AH, Döhner H, Pocock C, et al. Oral Azacitidine Maintenance Therapy for Acute Myeloid Leukemia in First Remission. N Engl J Med. 2020;383(26):2526-2537. 2. ONUREG® Hong Kong Prescribing Information July 2023

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Bristol Myers Squibb™
Bristol-Myers Squibb Pharma (HK) Ltd.
Room 3001-3002, 30/F, Windsor House, 311 Gloucester Road, Causeway Bay, Hong Kong
Tel: (852) 2510 6188 Fax: (852) 2510 6199

2011-HK-2300001 10-Nov-2023

SHINGRIX
(ZOSTER VACCINE RECOMBINANT, ADJUVANTED)

GSK

A NEW GENERATION OF HERPES ZOSTER VACCINE

PREVENT SHINGLES
DON'T GIVE IT A CHANCE[1]

ELIGIBLE GROUPS[1]

18+ YEARS OLD AT INCREASED HZ RISK

50+ YEARS OLD

THE ONLY HZV* WITH OVER 90% VACCINE EFFICACY[1-2]

HZ = Herpes zoster
HZV = Herpes zoster vaccine
^Efficacy adults aged 50 years or above
* In adults aged 50 years or older

References: 1. GlaxoSmithKline. Shingrix Hong Kong Prescribing Information. GDS04. 2. MSD. Live attenuated Zoster Vaccine Prescribing Information.

For Shingrix Full Prescribing Information, please scan the below QR code

Shingrix Succinct Safety Statement Contraindications: Hypersensitivity to the active substances or to any of the excipients. **Special warnings and precautions for use:** As with all injectable vaccines,appropriate medical treatment and supervision should always be readily available in case of an anaphylactic event following the administration of the vaccine. Aswith other vaccines, vaccination with Shingrix should be postponed in subjects suffering from an acute severe febrile illness. However, the presence of a minor infection, such as a cold, should not result in the deferral of vaccination. Do not administer the vaccine intravascularly or intradermally. Subcutaneous administration is not recommended. Maladministration via the subcutaneous route may lead to an increase in transient local reactions. Shingrix should be given with caution to individuals with thrombocytopenia or any coagulation disorder since bleeding may occur following intramuscular administration to these subjects. Syncope (fainting) can occur following, or even before, any vaccination as a psychogenic response to the needle injection. This can be accompanied by several neurological signs such as transient visual disturbance, paraesthesia and tonic-clonic limb movements during recovery. It is important that procedures are in place to avoid injury from faints. There are no safety, immunogenicity or efficacy data to support replacing a dose of Shingrix with a dose of another HZ vaccine. There are limited data to support the use of Shingrix in individuals with a history of HZ and in frail individuals including those with multiple comorbidities. Healthcare professionals therefore need to weigh the benefits and risks of HZ vaccination on an individual basis.

For adverse event reporting, please call GlaxoSmithKline Limited at (852) 2189 8989 (Hong Kong) [or (853) 2871 5569 (Macau)], or send an email to us at HKAdverseEvent@gsk.com. Please read the full prescribing information prior to administration. Full Prescribing Information is available upon request at GSK, 23/F, Tower 6, The Gateway, 9 Canton Road, Tsim Sha Tsui, HK.

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