**Princess Margaret Hematology Conference (PMHC)**
**March 26-28, 2026**
**Courtyard Marriott Downtown Hotel**
**Program – February 16, 2026**

# Thursday March 26, 2026

8:00-9:00
Registration and Breakfast
Location: Courtyard/Alexander/Spadina Foyers

9:00-9:15
Welcome and Introductions
Keith Stewart
Dennis Kim, John Kuruvilla
Location: Courtyard Ballroom A/B

9:15-10:15
Opening Keynote
Moderators: Dennis Kim, John Kuruvilla

Objectives: After active engagement in this session, participants will be able to:
- describe the foundational principles of TCR discovery and its application in developing targeted immunotherapies for hematologic malignancies;
- evaluate the interplay between cancer biology mechanisms (such as metabolism, genomic instability, and neuroimmunology) and TCR-based therapeutic strategies;
- identify potential challenges and opportunities in integrating multidisciplinary approaches to enhance immunotherapy efficacy in hematologic cancers.

Immunotherapy in Hematology
Tak Mak

10:15-10:45
Refreshment Break
Location: Courtyard/Alexander/Spadina Foyers

10:45-12:15
**Concurrent Sessions**

Breakout Session 1
Location: Courtyard Ballroom A

Chronic Myeloid Malignancies and Early Precursor Diseases
Moderator: Vikas Gupta

Objectives: After active engagement in this session, participants will be able to:
- understand the risk of progression of CHIP/CCUS to myeloid malignancies;
- discuss emerging data on role of interferon in ET/PV;
- describe investigational molecular targeted therapies in MPN.

Clonal Hematopoiesis, CCUS and Early MDS
Aniket Bankar

Emerging Role of Interferon in ET and PV
Dawn Maze

CALR Directed Therapies in MPN
Vikas Gupta

10:45-12:15
ILROG Steering
Moderators: Bouthaina Dabaja, Achy Yahalom
Location: Courtyard Ballroom B

12:15-1:45
Lunch
Location: Courtyard/Alexander/Spadina Foyers

1:45-3:15
**Concurrent Sessions**

Breakout Session 2
Myeloma
Moderator: Suzanne Trudel
Location: Courtyard Ballroom A

Objectives: After active engagement in this session, participants will be able to:
- discuss the evolving landscape of newly diagnosed multiple myeloma;
- describe how to investigate patients with Monoclonal Gammopathy of Renal Significance (MGRS);
- evaluate the clinical impact of evolving 1st line treatment on sequencing;
- evaluate the clinical impact and practical considerations related to administration of emerging anti-BCMA therapies in early relapse multiple myeloma;
- assess evidence and gaps related to sequencing of anti-BMCA agents with the RRMM treatment algorithm;
- identify treatment paradigms and controversies in the management of MGRS.

Evolving Frontline Strategies for Multiple Myeloma
Guido Lancman

Changing Landscape for 2nd Line Treatment for Relapsed Multiple Myeloma
Suzanne Trudel

Monoclonal Gammopathy of Renal Significance (MGRS) from the Perspective of a Hematologist
Vishal Kukreti

1:45-3:15
Breakout Session 3
Extranodal Lymphomas
Moderator: Badr Id-Said
Location: Courtyard Ballroom B

Objectives: After active engagement in this session, participants will be able to:
- understand the clinical behavior of indolent- and aggressive histology extranodal B-cell lymphomas and how these differ from their nodal counterparts;
- describe the clinical behavior of indolent and aggressive histology extranodal B-cell lymphomas and differentiate these from their nodal counterparts;
- describe the use of novel agents and combined modality therapy in the treatment of cutaneous lymphomas.

T-cell/NK Cases
Tomohiro Aoki

Case-based - Extranodal B-cell Lymphomas
Jillian Gunther

Illustrative Cases of Cutaneous Lymphomas
Richard Hoppe

3:15-3:45
Refreshment Break
Location: Courtyard/Alexander/Spadina Foyers

3:45-5:15
**Concurrent Sessions**

Breakout Session 4
Targeted Therapy in Acute Myeloid Leukemia: From Molecular Heterogeneity to Clinical Application
Moderator: Andre Schuh
Location: Courtyard Ballroom A

Objectives: After active engagement in this session, participants will be able to:
- describe the molecular heterogeneity of acute myeloid leukemia;
- review the clinical evidence supporting FLT3 inhibitors in AML;
- evaluate the role of IDH1 and IDH2 inhibitors in AML.

Chemo-immunotherapy in ALL
Maria Agustina Perusini

Targeted Therapy in AML
Andre Schuh

High Risk MDS
Karen Yee

3:45-5:15
Breakout Session 5
Image Guidance/Response Adaptation in Lymphoma
Moderator: Danielle Rodin
Location: Courtyard Ballroom B

Objectives: After active engagement in this session, participants will be able to:
- describe the role of functional imaging in the treatment of Hodgkin and Non-Hodgkin lymphoma in the context of the contemporary systemic therapy regimens;
- recognize sources of false-positive and false-negative PET scans in lymphoma;
- explain emerging concepts in treatment response for lymphoma.

Response Adaptation or Succinct Review of Current Indications for RT in DLBCL
George Mikhaeel

Imaging Dilemmas
Ur Metser

Pet Imaging
Vanessa Murad

Clinical Dilemmas
Abi Vijenthira

6:30
Faculty Dinner
TBD

# Friday March 27, 2025

7:30-8:30
Registration and Breakfast
Location: Courtyard/Alexander/Spadina Foyers

8:30-10:00
Concurrent Sessions

Breakout Session 6
Chronic Lymphocytic Leukemia and Low Grade Lymphoma
Moderator: Lena Specht
Location: Courtyard Ballroom A

Objectives: After active engagement in this session, participants will be able to:
- understand the role of fixed-duration combination regimens and novel BTK inhibitors in the management of chronic lymphocytic leukemia;
- identify which indolent lymphoma patients are suitable for very low-dose radiation therapy and describe the outcome of this treatment;
- understand how to incorporate novel immune therapies (e.g. bispecifics, CAR-T) into the management of follicular lymphoma.

Chronic Lymphocytic Leukemia
Abi Vijenthira

Advanced Stage FL
Robert Kridel

Low dose RT for Indolent NHL
Brandon Imber

8:30-10:00
Breakout Session 7
Delivering Durable Benefit: Allo-HCT for Older Adults, Maintenance, and Long-Term Complications
Moderator: Jonas Mattsson
Location: Courtyard Ballroom B

Objectives: After active engagement in this session, participants will be able to:
- discuss considerations for transplant of elderly and frail patients;
- explain perspective on new ways of reducing relapse post allo-BMT;
- list complications long-term after allo-BMT and best way to manage clinically.

Transplant of Older Patients
Rajat Kumar

Maintenance Therapy Post Allo-BMT
Dennis Kim

Long-term Complication After Allo-BMT
Corey Cutler

10:00-10:30
Refreshment Break
Location: Courtyard/Alexander/Spadina Foyers

10:30-12:15
CAR T Cell
Moderator: Christine Chen
Location: Courtyard Ballroom A/B

Objectives: After active engagement in this session, participants will be able to:
- share the status of CAR T-cell therapy in Canada;
- provide guidance on referring and managing patients preparing for CAR T;
- outline highlights and challenges of cell therapy modalities (BMT and CAR T).

The Landscape of CAR T in Canada
Sita Bhella

CAR T Patient Selection and Preparation
Caron Jacobson

Contrasting Cell Therapies: CAR T and AlloBMT
Christine Chen, Ivan Pasic

12:15-1:15
Hodgkin's Lymphoma Session
Moderator: Hans Eich
Location: Courtyard Ballroom A/B

Objectives: After active engagement in this session, participants will be able to:
- describe the role of combined modality therapy in Early Favourable Classical Hodgkin Lymphoma and identify patients for whom chemotherapy alone may be appropriate;
- identify patients with advanced cHL who are candidates for front-line therapy containing a PD-1 antibody or a chemotherapy regimen including brentuximab vedotin;
- understand the data supporting a second line approach in some patients with relapsed cHL where autologous stem cell transplantation could be omitted.

Illustrative Cases of Hodgkin's Lymphoma
Michael Crump

Illustrative Cases of Early-Stage Stage Hodgkin's Lymphoma
Sarah Milgrom

1:15-2:45
Lunch
Location: Courtyard/Alexander/Spadina Foyers

2:45:3:45
Abstract Oral Presentations
Moderator:
Location: Courtyard Ballroom A/B

Objectives: After active engagement in this session, participants will be able to:
- describe the latest research conducted in hematologic malignancies;
- discuss opportunities for future research collaborations and proposals.

2:45-2:55
1 - Evaluating optimal HCT bridging strategies in TP53-Mutated Myeloid Neoplasms
Akhil Rajendra Kurup[1], James Kennedy[2], Elliot Smith[1], Dawn Maze[1], Aniket Bankar[1], Steven Chan[1], Vikas Gupta[1], Mark D Minden[1], Maria Agustina Perusini[1], Guillaume Richard-Carpentier[1], Aaron Schimmer[1], Andre Schuh[1], Hassan Sibai[1], Karen Yee[1], Marta Davidson[1]
[1]Princess Margaret Cancer Centre, [2]Sunnybrook Health Sciences Centre

2:55-3:05
2 - Imaging Mass Cytometry to Define Spatial Immune Architecture and Neuro-Immune Signaling in Tumor Microenvironments
Xi Lei[1], Jennifer Gorman[2], Shirley Wang[1], Hartland Jackson[2], Ralph DaCosta[1]
[1]University Health Network, [2]Lunenfeld-Tanenbaum Research Institute

3:05-3:15
3 - Real-world Experience with First-Line Regimens in Transplant-Ineligible Patients with Multiple Myeloma
Danyal Ladha[1]
[1]Princess Margaret Cancer Centre

3:15-3:25
4 - Quadshot Radiotherapy as Bridging Therapy for Adult Lymphoma Patients: A Single-Institutional Experience
Johnathan Zeng[1], Andrea Ng[2], Andrew Smith[3], Jennifer Crombie[4], Chirayu Patel[5]
[1]Harvard Radiation Oncology Program, [2]Brigham & Women's Hospital, [3]Bennett Cancer Center, [4]Dana-Farber Cancer Institute, [5]Massachusetts General Hospital

3:25-3:35
5 - Capturing the Live Interactions Between T Cells and AML in the Bone Marrow Microenvironment Using Intravital Imaging
Sadaf Mazhab Jafari[1], Raheleh Niavarani[2], Ralph DaCosta[2], Xi Lei[2], Lyndsey DeGuzman[1]
[1]University of Toronto, [2]University Health Network

3:35-3:45
6 - Limited-Stage Mantle Cell Lymphoma: Real-World Outcomes According to Nodal vs. Extranodal Presentation
Sun-Hye Ko[1], Michael Crump[1], John Kuruvilla[1], David Hodgson[1], Danielle Rodin[1], Tomohiro Aoki[1], Sita Bhella[1], Robert Kridel[1], Richard Tsang[1], Vishal Kukreti[1], Abi Vijenthira[1], Woody Wells[1], Chloe Yang[1], Anca Prica[1]
[1]Princess Margaret Cancer Centre

3:45-5:15
MRD Symposium (Leukemia and LMT)
Moderator: Dennis Kim
Location: Courtyard Ballroom A/B

Objectives: After active engagement in this session, participants will be able to:
- analyze the impact of intratumoral heterogeneity and chemotherapy response patterns in acute myeloid leukemia (AML);
- evaluate the clinical utility and limitations of current MRD monitoring techniques (flow cytometry and molecular methods) in AML to determine appropriate timing and thresholds for treatment intensification or de-escalation in routine practice;
- select risk-adapted MRD-guided management strategies for patients with aggressive lymphomas during chemotherapy and surveillance settings, incorporating the latest consensus guidelines and prognostic implications.

AML Heterogeneity and Chemo Response
Andy Zeng

AML
Steve Chan

Lymphoma
Robert Kridel

5:15-6:30
Poster Viewing and Reception
Location: Courtyard Ballroom C and Foyer

# Saturday March 28, 2025

7:30-8:30
Breakfast
Location: Courtyard/Alexander/Spadina Foyers

8:30-10 :00
**Concurrent Sessions**

Breakout Session 8
Aggressive Lymphoma
Moderator: Umberto Ricardi
Location: Courtyard Ballroom A

Objectives: After active engagement in this session, participants will be able to:
- describe the clinical indications for antibody-drug conjugates, radiation therapy, and bispecifics in the management of aggressive histology lymphomas;
- appreciate the clinical circumstances in which regimens other than R-CHOP are appropriate;
- identify options to manage patients with significant comorbidities and how these impact prognosis.

Case-based Discussion
John Kuruvilla

Clinical Dilemmas
Inna Gong

Aggressive Histology Lymphomas
Christopher Kelsey

8:30-10:00
Breakout Session 9
Nursing – Developing Nursing Confidence in Clinical Practice: Fever Management and Shared Care
Moderator: Cindy Murray
Location: Courtyard Ballroom B

Approach to Fever in Malignant Hematology: Infection, CRS, and Beyond
Shea-Lyn Cutmore, Jessica Lois

Objectives: After active engagement in this session, participants will be able to:
- recognize fever early & understand its clinical significance;
- assess, differentiate & triage patients with fever;
- initiate prompt nursing interventions & ongoing monitoring.

Shared Care in the Management of Hematologic Malignancies
Kalique Dzidah, Rosemary Pivovarov

Objectives: After active engagement in this session, participants will be able to:
- describe shared-care models in hematologic malignancies;
- illustrate appropriate division of care using clinical scenarios;
- highlight effective communication & coordination strategies to optimize shared care delivery & continuity of care.

10:00-11:30
Shared Care Model of Non-intensive Treatment for AML Using VEN-AZA Regimen
Moderators: Peter Anglin, Anthony Naassan
Location: Courtyard Ballroom A

Objectives: After active engagement in this session, participants will be able to:
- evaluate the efficacy, safety profile, and patient selection criteria for the venetoclax-azacitidine (VEN-AZA) regimen in newly diagnosed AML patients in outpatient settings;
- implement a shared care model involving collaboration with community hematologists to optimize VEN-AZA administration, monitoring, and supportive care for AML patients in regional healthcare systems;
- compare the treatment outcomes from the Paradigm phase 2 study of VEN-AZA versus 7+3 induction chemotherapy in fit, newly diagnosed AML patients to inform treatment decision-making in clinical practice.

VEN-AZA for AML in the Community
Mitchell Sabloff

Bispecific Antibody Care and Post-CAR T-cell Care in the Community
Sita Bhella

Lymphoma Treatment in the Community
John Kuruvilla

10:00-11:00
ILROG Business Meeting
Moderators: Jullian Gunther, Brandon Imber
Location: Courtyard Ballroom B

11:30-12:00
Refreshment Break
Location: Courtyard/Alexander/Spadina Foyers

12:00-1:00
Leukemia & Lymphoma Society of Canada Research Symposium
The Future of Hematologic Malignancies - From the Lab to the Clinic
Moderator: Aaron Schimmer
Location: Courtyard Ballroom A

Objectives: After active engagement in this session, participants will be able to:
- describe three major recent discoveries in blood cancer pathogenesis and discuss their potential impact on clinical practice of blood cancer patients;
- compare emerging diagnostic technologies and targeted therapies in the Princess Margaret translational pipeline with current standard-of-care approaches;
- identify appropriate patient populations and clinical scenarios in which novel PM-developed diagnostics or therapies could be potentially applied.

Multidimensional Characterization of Tumor–Immune Architecture Reveals Clinically Relevant Classic Hodgkin Lymphoma Subtypes
Tomohiro Aoki

Microbiome Changes in Allogeneic Hematopoietic Cell Transplantation (Allo HCT)
Doris Ponce

12:00-1:00
Breakout 10
Pharmacy
Moderator: Melissa Lo
Location: Courtyard Ballroom A

Reactivation of Infections in Immunocompromised Patients
Speakers: Duke Boampong, Ivan Tyono

Objectives: After active engagement in this session, participants will be able to:
- interpret diagnostic strategies for latent infections and early reactivation;
- outline prevention and management strategies, including prophylaxis and treatment protocols.

Nursing Recognition and Management of CRS and ICANS in Patients Treated with Bispecific

Antibodies and CAR-T
Objectives: After active engagement in this session, participants will be able to:
- apply evidence-based nursing interventions for CRS and ICANS;
- demonstrate effective communication and documentation during escalation;
- educate patients and caregivers on warning signs and self-monitoring.

Shared Care in the Management of Hematologic Malignancies
Objectives: After active engagement in this session, participants will be able to:
- discuss communication strategies for multidisciplinary collaboration;
- evaluate best practices for patient transitions between centres;
- formulate recommendations for improving shared care coordination.

1:00-2:00
Closing Keynote
Moderators: Dennis Kim/John Kuruvilla
Location: Courtyard Ballroom A

Objectives: After active engagement in this session, participants will be able to:
- discuss the evolution of the Ontario CMH System over the past decade and shared care implementation;
- discuss future directions in Ontario CMH System for the next 10 years and opportunities for enhancement;
- identify obstacles and strategies to overcome them.

Advancing Complex Malignant Hematology in Ontario: From Evolution to Innovation in Shared Care
Chris Bredeson

2:00-2:10
Closing Remarks

# Abstracts

| Abstract Number | Presenting Author | Title |
|---|---|---|
| **7** | Ana Flavia Patino | Real-World Data Comparison of Asciminib 40 mg Twice Daily vs. 80 mg Once Daily in Chronic Myeloid Leukemia Patients |
| **8** | Yael Morgenstern | Emergence of New Somatic Mutations in CML Patients Optimally Responding to Tyrosine Kinase Inhibitor Therapy: Proposal of Long-Term Genomic Monitoring |
| **9** | Peter Meidahl Petersen | MR-Guided Adaptive Radiotherapy for Gastric Lymphoma, Preliminary Results from Ongoing Study. |
| **10** | Shane Neibart | Magnetic Resonance-Guided Adaptive Radiation Therapy for Intra-Abdominal Hematological Malignancies |
| **11** | Verna Cheung | Association of Clinical and Molecular Risk Factors with Severity of Anemia in Myelofibrosis |
| **12** | Yael Morgenstern | Extramedullary Disease in AML: A High-risk Feature Beyond ELN 2022 Classification |
| **13** | Zahra AlHaj Issa | Comparable Remission Rates in Therapy-related and Myelodysplasia-related Acute Myeloid Leukemia (AML) versus de novo AML Treated with Azacitidine and Venetoclax: A Contemporary Real-world Study. |
| **14** | Akhil Rajendra Kurup | FLT3 Inhibition with Midostaurin Offsets Poor Prognosis in NPM1/FLT3/DNMT3a Triple Mutated AML |
| **15** | Maryam Naimi | Utilizing Fluorescence Intravital Imaging to Investigate Bone Marrow Microenvironment Remodeling in Acute Myeloid Leukemia |
| **16** | Raheleh Niavarani | Deciphering the Mechanisms Underlying the Pathophysiology and Chemotherapy Resistance in Acute Myeloid Leukemia Using Intravital Imaging and Humanized NSGW41IL7 Mouse |
| **17** | Raheleh Niavarani | Redox-Driven Bone Marrow Vascular Remodeling Under Systemic Inflammation: Insights from Intravital Imaging and Sex-Specific Response |
| **18** | Xi Lei | Decoding Neurotransmitter Driven Immune Suppression in AML Through Intravital Imaging and Humanized Models |
| **19** | Christiano Freitas | Prognostic Impact of Molecular Genetic and Cytogenetic Alterations in Newly Diagnosed Acute Myeloid Leukemia Treated with Azacitidine and Venetoclax: A Real-world Cohort Study |
| **20** | Aarya Murali | Morphologic Leukemia-free State (MLFS) is Associated with Inferior Outcomes in Patients with Acute Myeloid Leukemia (AML) Treated with Front-line Azacitidine plus Venetoclax |
| **21** | Iman Moin | Neuroscience Informed Mind - Body Interventions to Reduce Symptom Burden in Patients with Hematologic Malignancies |

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| **22** | **Lais Marques Eiras** | Immune Checkpoint Inhibitor-induced Pure Red Cell Aplasia in a Patient with Advanced Cholangiocarcinoma: A Case Report |
| **23** | Christina Sit | The Hidden Burden: Financial, Physical, and Psychosocial Impacts of Travel to Treatment for Canadian Blood Cancer Patients |
| **24** | Sergio Rodriguez Rodriguez | Propensity Score Matching Analysis Comparing the Efficacy and Long-Term Outcomes of Belumosudil to the Best Available Treatment as a Historical Control, Used as Second-Line Therapy or Beyond for Chronic GVHD After Steroid Failure |
| **25** | Sergio Rodriguez Rodriguez | Clinically Meaningful Improvement of the Modified Lee Symptom Score in Patients Treated with Belumosudil for Steroid-Refractory Chronic GVHD: Evidence from Canadian Real-World Outcomes |

# Abstract Oral Presentations

1 - Evaluating Optimal HCT Bridging Strategies in TP53-Mutated Myeloid Neoplasms

Akhil Rajendra Kurup[1], James Kennedy[2], Elliot Smith[1], Dawn Maze[1], Aniket Bankar[1], Steven Chan[1], Vikas Gupta[1], Mark D Minden[1], Maria Agustina Perusini[1], Guillaume Richard-Carpentier[1], Aaron Schimmer[1], Andre Schuh[1], Hassan Sibai[1], Karen Yee[1], Marta Davidson[1]
[1]Princess Margaret Cancer Centre, [2]Sunnybrook Health Sciences Centre

Background: TP53-mutated myeloid neoplasms (MN) are associated with poor outcomes, and conventional therapies remain the mainstay of treatment. Allogeneic hematopoietic cell transplantation (HCT) offers potential long-term survival for a minority, but optimal pre-HCT disease control remains undefined. No standard bridging regimens exist. This study evaluated real-world bridging strategies and their impact on response, treatment-related mortality (TRM), overall survival (OS), and HCT rates in TP53-mutated MN.

Methods / Overview: This retrospective single-center study included adults (≥18 years) with TP53-mutated MN (MDS, AML and MPN in accelerated phase/blast phase) treated between January 2013 and October 2024. Intensive regimens included 3+7 and FLAG-based protocols; less-intensive regimens included hypomethylating agents (HMA) alone or with venetoclax (HMA-Ven). Responses were assessed using ELN 2022 (AML) and IWG 2023 (MDS) criteria. The primary endpoint was modified composite complete remission (mCRc) in AML/MPN-AP/BP and overall response rate (ORR) in MDS. Multivariable logistic regression identified predictors of response.

Results: Among 199 patients (AML 69.8%, MDS 18.1%, MPN-AP/BP 12.1%), 54.3% received intensive and 45.7% less-intensive therapy. Complex cytogenetics were present in 82.4%; 86.4% had multi-hit TP53.

In AML/MPN-AP/BP (n=163), mCRc rates were 32.4% with 3+7 and 70.0% with FLAG-based therapy ($p<0.001$). With less-intensive therapy, mCRc was 7.4% with HMA alone and 51.6% with HMA-Ven ($p<0.001$). In MDS (n=36), ORR was 100% with FLAG-based therapy, 64% with HMA alone, and 66.7% with HMA-Ven ($p=0.276$). Multi-hit TP53 status independently predicted inferior response (OR 0.305, $p=0.009$). TRM differed across regimens ($p=0.015$), highest with FLAG-based therapy.

Among HCT-eligible patients (n=74), 40 (54.1%) underwent HCT. In the intensive cohort (n=56), 50% proceeded to HCT compared with 64.7% (11/17) in the less-intensive cohort ($p=0.406$). Subgroup HCT rates were 63.6% with 3+7, 46.7% with FLAG-based therapy, 62.5% with single-agent HMA, and 66.7% with HMA-Ven ($p=0.535$).

Conclusion: Both intensive and less-intensive regimens can serve as bridging strategies to HCT in selected TP53-mutated MN. FLAG-based therapy achieved higher response rates but was associated with greater TRM, underscoring the need for individualized treatment selection.

# 2 - Imaging Mass Cytometry to Define Spatial Immune Architecture and Neuro-Immune Signaling in Tumor Microenvironments

Xi Lei[1], Jennifer Gorman[2], Shirley Wang[1], Hartland Jackson[2], Ralph DaCosta[1]
[1]University Health Network, [2]Lunenfeld-Tanenbaum Research Institute

Background / Objectives: In acute myeloid leukemia (AML), the bone marrow microenvironment (BME) becomes progressively remodeled into a hypoxic, immune-suppressive niche that protects leukemic blasts and impairs T-cell activity. Although nerves and immune cells are increasingly recognized as contributors to this dysfunctional environment, the spatial relationships among neural fibers, immune populations, stromal elements, and leukemic cells in living marrow remain poorly understood. In this project, imaging mass cytometry (IMC) served as a critical complement to intravital imaging by defining which immune and stromal cell states populate neurotransmitter-rich regions, how these niches evolve with AML progression, and how neuro-immune signaling may structure immune exclusion. The objective was to map the spatial architecture, phenotypes, and ligand-receptor neighborhoods associated with dynamic neurotransmitter activity in AML-infiltrated marrow.

Methods / Overview: IMC was performed on 5 μm FFPE bone marrow sections collected from early, intermediate, and late AML, including regions pre-identified by intravital imaging as neurotransmitter-high, hypoxic, or immune-excluded. Sections underwent lanthanide-metal-conjugated antibody staining using validated murine and human panels targeting leukemic blasts, T-cell subsets, γδ T cells, B-cell subsets, myeloid suppressor cells, macrophages, endothelial markers, stromal programs, and hypoxia-associated proteins. Laser ablation at 1 μm resolution generated multiplexed spatial proteomic maps. Data were normalized, denoised, and spillover-corrected prior to deep-learning-based segmentation (e.g., DeepCell). Single-cell intensities and coordinates were extracted for clustering (Phenograph/Leiden), cell-state annotation, and spatial analyses of neighborhood structure, nearest-neighbor interactions, and immune-excluded niche composition. IMC maps were co-registered to intravital fields using vascular, collagen, and marrow-architecture landmarks.

Results: IMC precisely resolved immune, stromal, vascular, and hypoxia-associated microenvironments that corresponded to regions of dynamic neurotransmitter signaling measured in vivo. This included identifying immunoregulatory B-cell states, patterns of T-cell exclusion and γδ T-cell localization, myeloid-driven suppressive programs, and stromal niches enriched for hypoxia. Integration with intravital imaging revealed how neurotransmitter “hotspots” aligned with immune shutdown, vascular remodeling, stromal activation, and leukemic-cell clustering across AML progression.

Conclusion: IMC provided a high-dimensional spatial framework linking functional neuro-immune signaling to the cellular architecture of AML-associated immune suppression. When integrated with real-time biosensor-based intravital imaging, this approach generated the first comprehensive atlas of how neurotransmitter-associated niches emerge in AML. These insights identify targetable immune and stromal programs within the leukemic marrow niche and offer a foundation for rational therapeutic strategies, including approaches aimed at disrupting neuro-immune signaling to restore effective anti-leukemia immunity.

3 - Real-world Experience with First-Line Regimens in Transplant-Ineligible Patients with Multiple Myeloma

Danyal Ladha[1]
[1]Princess Margaret Cancer Centre

Introduction: Regimens based on bortezomib and lenalidomide have been a mainstay of treatment for transplant-ineligible (TI) newly diagnosed multiple myeloma (NDMM) patients (pts). Recently, the phase 3 MAIA trial established DRd as the new standard of care (SoC), with a median progression-free survival (PFS) of 61.9 months compared to 34.4 months with Rd and a significant benefit in overall survival (OS). In Canada, DRd was funded via the public healthcare system for first-line NDMM TI patients in 2022. The aim of this retrospective study was to evaluate the initial real-world outcomes of this regimen in the context of treatments used prior to the introduction of anti-CD38 antibodies in frontline therapy.

Methods: We performed a retrospective observational study using the Canadian Myeloma Research Group Database (CMRG-DB), a prospectively maintained disease-specific database with >10,000 pts enrolled in 21 centres across Canada.

All NDMM TI pts >18 years treated with CyBorD, Rd, RVd, or DRd as first-line treatment between 01/01/2018 - 30/11/2024 were included. Pts were excluded if they were treated on a clinical trial, did not receive any treatment within 1 year of diagnosis, underwent stem cell transplant ≤1 year of diagnosis, or had amyloidosis, POEMS, or plasma cell leukemia.
The primary objective of the study was to determine the following outcomes observed with these first-line regimens: early mortality rate (at 6 months and 1 year), overall response rate (ORR), best response, PFS, and OS. Secondary objectives included assessing the pattern of usage of these different regimens between 01/2018 -11/2024, and identification of variables affecting 1-year early mortality, ORR, and PFS by regimen.

Descriptive analysis was used to report demographics, disease characteristics and treatment responses by regimen. Baseline characteristics were summarized by mean, standard deviation, median and ranges as appropriate. Time to event analyses were used to assess PFS and OS. Survival curves were constructed according to the Kaplan-Meier method and impact of covariates of interest were assessed using the log rank test.

Results: A total of 1,085 pts were eligible. Regimens included: CyBorD in 382 (35.2%), Rd in 292 (26.9%), RVd in 178 (16.4%) and DRd in 233 (21.5%). The median follow-up in months (95% CI) in these 4 cohorts was 41.0 (35.2, 44.7), 50.2 (45.4, 54.5), 29.7 (24.4, 34.4) and 9.3 (7.6, 11.3), respectively. The 6-month and 1-year mortality rates were 6.5% (95% CI 4.3-9.5) and 11.8% (95% CI 8.6-15.4) for CyBorD, 7.9% (95% CI 5.1-11.6) and 14.7% (95% CI 10.9-19.3) for Rd, 4.5% (95% CI 2.0-8.7) and 7.9% (95% CI 4.4-12.8) for RVd and 4.3% (95% CI 2.1-7.8) and 5.6% (95% CI 3.0-9.4) for DRd. The ORR/≥VGPR by regimen included: 95.9%/72.3% with RVd, 94.5%/71.9% with DRd, 89.2%/58.9% with CyBorD and 79.1%/45.3% with Rd. Median PFS was 41.4 months in RVd pts, 28.6 months in Rd pts and 20.2 months in CyBorD pts; an accurate median PFS was not yet available in DRd pts due to short follow-up. However, CyBorD pts had a statistically significant shorter median PFS, while there was no difference between the other regimens to date. Median OS was not yet reached for DRd, 62.2 months for RVd, 60 months for CyBorD, and 55.5 months for Rd (p=0.061). Of the 1,085 pts, 432 (39.8%) have received a 2nd line of therapy.

The use of DRd in Canada significantly increased from 1.1% in 2020 to 30.3% in 2022, and was the most common regimen in 2023 (77.5%) and 2024 (78.4%).

Conclusion: In this real-world retrospective study, we demonstrate that, after public funding, DRd rapidly became the most frequently utilized first-line treatment in Canadian patients with TI NDMM. Early mortality rates at 6 months and 1 year were very low with DRd. Response rates with DRd and RVd were the highest and each produced an ORR of approximately 95% and ≥VGPR of 72%. CyBorD patients had a significantly shorter PFS. However, an accurate evaluation of DRd's PFS efficacy is premature due to its recent introduction into the Canadian treatment algorithm and short follow-up period (9.3 months vs 29+ months in other cohorts). More mature results of DRd, in addition to analyses of potential variables correlated with outcomes, will be assessed in the future. Nevertheless, our findings suggest that both RVd and DRd are highly effective options for treatment of TI NDMM.

4 - Quadshot Radiotherapy as Bridging Therapy for Adult Lymphoma Patients: A Single-Institutional Experience

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Background: Adult lymphomas are a diverse group of hematologic malignancies that may relapse with bulky or symptomatic disease requiring urgent intervention. Radiation therapy remains highly effective in curative and palliative settings. In the era of targeted and cellular therapies, bridging therapy is often needed to maintain disease control during logistical delays; without it, patients may decline and lose eligibility. The “Quadshot” regimen, 14-14.8 Gy in 4 fractions delivered twice daily over 2 consecutive days, offers a rapid, well-tolerated option for cytoreduction and palliation. We report our institutional experience using Quadshot as bridging therapy in refractory aggressive lymphoma.

Methods: Patients with symptomatic or locally progressive refractory lymphoma who received ≥1 Quadshot course prior to next-line systemic therapy were included. Primary endpoints were local response, toxicity, and feasibility of proceeding with systemic therapy.

Results: 11 patients received 13 Quadshot courses (median age 74 years, range 47-90; 9 male). Histologies included diffuse large B-cell lymphoma (n=6), transformed lymphoma (n=3), peripheral T-cell lymphoma (n=1), and small lymphocytic lymphoma (n=1). Indications included pain, diplopia, and organ dysfunction from obstruction (gastric outlet, small bowel, lymphatic). Median maximum tumor diameter was 10.6 cm (range 3.5-18.4 cm); median time from simulation to treatment was 5 days (range 1-10). Symptom palliation was achieved in all symptomatic patients. Of 10 sites with PET assessment, 9 achieved complete response (Deauville 1-2). One patient received repeat Quadshot for recurrent obstruction with improvement. No grade ≥3 radiation toxicities were observed. All patients proceeded to planned systemic therapy without delay.

Conclusions: Quadshot radiotherapy is a safe, well-tolerated, and pragmatic bridging strategy for adult patients with bulky or symptomatic lymphoma. Its 2-day schedule allows rapid transition to systemic therapy and stabilization of acutely ill patients. This approach represents a viable bridging modality in the era of targeted therapies and merits prospective validation.

5 - Capturing the Live Interactions Between T Cells and AML in the Bone Marrow Microenvironment Using Intravital Imaging

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Acute myeloid leukemia (AML) is an aggressive hematologic malignancy with poor survival, driven in part by its ability to remodel the bone marrow microenvironment (BME) into a leukemia-supportive and immunosuppressive niche. As AML progresses, the BME increasingly limits effective T-cell responses; however, the real-time behavior of $CD8^+$ and $CD4^+$ T cells within the AML bone marrow remains poorly understood. Conventional ex vivo approaches fail to capture dynamic immune interactions in vivo, highlighting the need for intravital imaging platforms capable of resolving spatiotemporal immune behavior.

In this study, a femur window chamber (FWC) was used to enable longitudinal intravital fluorescence imaging of the bone marrow in immune-competent C57BL/6J mice inoculated with the genetically heterogeneous C1498 murine AML cell line expressing mCherry. This approach allows repeated visualization of the same bone marrow regions over time, providing direct insight into immune-tumor interactions during AML progression. Fluorescent dextran was administered to visualize functional vasculature, while fluorescently conjugated antibodies against CD3, CD4, and CD8 were used to label endogenous T-cell populations in vivo. Time-lapse imaging and Z-stack acquisition were performed to monitor leukemic burden, vascular structure, and T-cell distribution and movement throughout disease development. Quantitative analyses were applied to assess changes in T-cell abundance, dispersion, and spatiotemporal dynamics within the BME.

Using this platform, dynamic remodeling of the bone marrow microenvironment was observed during AML progression, accompanied by shifts in $CD3^+$, $CD4^+$, and $CD8^+$ T-cell distribution and behavior in regions of leukemic infiltration. These data support the concept that AML progression is associated with time-dependent alterations in immune organization within the bone marrow.

Overall, this work establishes femur window chamber-based intravital imaging as a powerful tool to capture live immune-tumor interactions in AML. Defining the spatiotemporal behavior of T cells within the leukemic bone marrow provides a foundation for future studies examining immunotherapeutic interventions and strategies aimed at restoring effective anti-leukemia immunity.

6 - Limited-Stage Mantle Cell Lymphoma: Real-World Outcomes According to Nodal vs. Extranodal Presentation

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Background / Objectives: Treatment of mantle cell lymphoma (MCL) has evolved substantially with the adoption of targeted and chemo-free strategies. However, optimal management of limited-stage disease (Ann Arbor stage I-II) remains poorly defined due to its rarity and limited contemporary data. We previously reported outcomes of early-stage MCL largely from the pre-rituximab era. This study evaluates clinical characteristics, treatment patterns, and outcomes of limited-stage MCL in the modern therapeutic era.

Methods / Overview: We performed a retrospective review of adults (≥18 years) diagnosed with stage I-II MCL between January 2003 and October 2024, identified through an institutional cancer registry. Disease presentation was classified as nodal or primary extranodal (with or without regional nodal involvement). Treatment approaches were grouped as radiotherapy (RT) alone or chemotherapy-based regimens, which could include RT and/or autologous stem cell transplantation (ASCT). Primary endpoints were progression-free survival (PFS) and overall survival (OS), analyzed using Kaplan-Meier methods and Cox proportional hazards models.

Results: Among 421 newly diagnosed MCL patients, 36 (8.6%) had limited-stage disease (15 stage I, 21 stage II). Median age was 64 years, and 64% were ≥60. Treatment included RT alone (28%), chemotherapy plus RT (44%), chemotherapy followed by ASCT (17%), and chemotherapy alone (11%); median RT dose was 30 Gy. Seventeen patients had nodal disease, while 19 had primary extranodal involvement, all within the head and neck region. With a median follow-up of 72.5 months, 13 patients progressed -10 with nodal disease and 3 with extranodal disease. Progression was more frequent in nodal versus extranodal presentations (77% vs. 30%, P=0.007) and in patients treated with RT alone versus chemotherapy-containing regimens (54% vs. 13%, P=0.018). OS did not differ significantly between groups. PFS was significantly prolonged in extranodal compared with nodal disease (not reached vs. 72 months; P=0.023). In nodal disease, RT alone was associated with increased risk of progression compared with chemotherapy-based therapy (hazard ratio 8.6, P=0.009).

Conclusion: Limited-stage MCL demonstrates favorable long-term survival. Extranodal head and neck disease is common and associated with significantly prolonged PFS. Chemotherapy-containing regimens provide superior disease control over RT alone in nodal presentations, while treatment modality did not significantly influence outcomes in extranodal disease.

Abstract Poster Presentations

7 - Real-World Data Comparison of Asciminib 40 mg twice daily vs. 80 mg once daily in Chronic Myeloid Leukemia Patients

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Introduction: Asciminib (ASC) is a first-in-class STAMP inhibitor approved for patients with Philadelphia chromosome-positive chronic-phase chronic myeloid leukemia (CML-CP) previously treated with ≥2 tyrosine kinase inhibitors.

Objective: To compare efficacy and safety of ASC 80 mg once daily (QD) versus 40 mg twice daily (BID) in real-world CML-CP patients.

Methods: We conducted a retrospective, single-center study of CML-CP patients treated with ASC as third-line therapy or beyond. Dosing was selected by physician discretion and/or patient preference. Endpoints included dose modifications, failure-free survival (FFS), event-free survival (EFS), and molecular responses.

Results: Fifty-one patients were included (median age 61 years; range 31-83; 45% female). One patient (2%) received ASC as second-line therapy; most received it as third line (69%), while 30% received it as fourth line or beyond. ASC was initiated due to intolerance (61%) or resistance (39%) to prior TKIs. At baseline, 31% had BCR::ABL1 >10% IS; all were in chronic phase. Twenty-seven patients (53%) received ASC 40 mg BID and 24 (47%) received 80 mg QD, with comparable baseline characteristics. Dose modifications occurred more frequently in the BID cohort (70% vs. 25%; p=0.001), with similar rates of dose reduction due to adverse events (30% BID, 25% QD). Among those requiring dose reduction, most were reduced to 40 mg once daily; additional strategies included reductions to 20 mg QD or intermittent dosing (7 BID, 6 QD). Grade ≥3 adverse events included thrombocytopenia (n=3), musculoskeletal pain (n=3), cardiac events (n=2) (QTc prolongation, premature ventricular contractions), and symptomatic pancreatitis (n=1). Among patients undergoing dose escalation for suboptimal response (n=6, 22%), all initially on 40 mg BID, three patients (5.9%) discontinued ASC due to lack of molecular response (two QD, one BID), and one progressed to accelerated phase. Five BID patients achieving MMR were later switched to QD dosing; no escalations occurred in the QD group. With a median follow-up of 729 days (range 112-1016), 2-year FFS was 96% (95% CI [74-99%]) for BID and 91% [69-98%] for QD (HR 2.46; p=0.463), while 2-year EFS was 84% [62-94%] and 82% [58-93%], respectively (HR 1.27; p=0.73). At 24 weeks, MR2 rates were 84% [60-97%] for BID vs. 83% [52-98%] for QD (HR 0.77; p=0.44); MMR rates were 75% [48-89%] vs. 75% [43-95%] (HR 1.03; p=0.08); and MR4 rates were 83% [59-96%] vs. 46% [17-77%] (HR 0.53; p=0.147).

Conclusions: In this real-world analysis, ASC 40 mg BID and 80 mg QD demonstrated similar response rates and favorable safety profiles in CML-CP patients previously treated with ≥2 TKIs. Overall efficacy was well maintained. The QD regimen was associated with fewer dose escalations and treatment discontinuations, supporting its convenience and potential advantage in routine clinical practice.

8 - Emergence of New Somatic Mutations in CML Patients Optimally Responding to Tyrosine Kinase Inhibitor Therapy: Proposal of Long-term Genomic Monitoring

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Introduction: Next-generation sequencing (NGS) has revealed a broader range of somatic mutations in chronic myeloid leukemia (CML) patients, associated with long-term outcomes. Current ELN guidelines recommend NGS profiling for patients progressing to blast phase, but not as routine at diagnosis or during follow-up. With effective suppression of the Philadelphia chromosome-positive clone (Ph+), some patients develop clonal evolution in Philadelphia-negative cells (Ph-), such as monosomy 7 or trisomy 8, typically detected via metaphase cytogenetics. It is plausible to expect these clones carry somatic mutations that could be identified earlier by NGS. However, the dynamics of somatic mutations in optimally responding patients remain underexplored, particularly for the emergence of new mutations. We hypothesized that such mutations may arise in Ph- cells and sought to characterize their genetic profiles, growth kinetics, and clinical relevance.

Methods: We analyzed paired peripheral blood samples from 51 CML patients. DNA was extracted from mononuclear cells and sequenced using a single-molecule-tagging, molecular inversion probe (smMIP)-based approach. A custom CML-specific smMIP panel targeting 37 genes was used (limit of 0.1%). Mutation DT was calculated using two time points with the formula: $DT=(T2-T1)\times\log(2)/[\log(VAF2)-\log(VAF1)]$.

Results: Median age was 61 years (range: 17-80). Disease risk was stratified at diagnosis with 8 (16%), 27 (53%) and 14 patients (26%) as low, intermediate and high Sokal risk group. First-line therapy included Imatinib in 36 patients (71%) and second-generation TKIs in 15 patients (29%). Sequencing was performed prior to TKI therapy and at a median of 398 days post-TKI therapy. At the time of 2nd sample collection, 42 pts (82%) had achieved an optimal response. Among them, somatic mutations were detected in 21 pts (50%). Eight patients (16%) had mutations at diagnosis with similar allele frequencies, while 13 (26%) acquired new mutations during TKI therapy. Frequently mutated genes among optimal responders with emerging mutations included DNMT3A, TET2, ASXL1, and EZH2. Median time to mutation emergence was 227 days (range: 105-7578), with a median DT of 59 days (range: 22-1909). All patients achieving optimal responses with emerging mutations eventually achieved MR4 with a median follow-up of 2.7 years (range: 294-7601 days).

Conclusions: We observed a distinct somatic mutation dynamics during TKI therapy. Emergence of somatic mutations was observed in CML patients achieving optimal response. Thus, their presence is not necessarily a marker of disease progression. Our findings support baseline mutation profiling in all CML patients at diagnosis. Many detected mutations are consistent with clonal hematopoiesis, potentially contributing to clonal evolution in Ph- after optimal TKI response. We recommend regular monitoring of these mutations during TKI therapy. Given the median DT of ~60 days, annual NGS surveillance may be a practical strategy for early detection of clonal changes.

9 - MR-guided Adaptive Radiotherapy for Gastric Lymphoma, Preliminary Results from Ongoing Study

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Background: MR-guided adaptive radiotherapy (MR-ART) may benefit patients with gastric lymphoma by providing superior soft-tissue contrast for daily guidance, enabling tracking of internal anatomy and gating, and thus accommodating large anatomical changes. This allows the stomach to be kept at prescribed dose while reducing dose to the heart and the left kidney.

Objectives: The purpose of this study is to report a preliminary analysis from an ongoing protocol for MR-ART for patients with gastric lymphoma and investigate if daily adaption with MR-ART improves target coverage relative to no adaption.

Materials/Methods: At present 11 patients with gastric lymphoma have been recruited. All patients were planned in (comfortably deep) inspiration breath-hold on the MR-linac (MRIdian, ViewRay) using intensity modulated radiotherapy (IMRT). The prescription dose was 24 Gy in 12 fractions for 7 patients and 36 Gy for two patients and 30 Gy for one. The patients were treated adaptively and with internal gating on the superior region of the stomach near the heart.

Results: Data from 11 included pt's is analyzed. The treatment with daily adaption with MR-ART showed large improvements in target coverage relative to the predicted plan (Figure 1). The results for the volume (cubic centimeters) of the heart and kidneys risk receiving 5 Gy or 10 Gy (V5Gy or V10Gy) were kept at the same level when comparing the predicted plan to the reoptimized adapted plan.

Conclusion: Preliminary results from this protocol on MR-ART for patients with gastric lymphoma show large improvements in target coverage with similar doses to organs at risk for patients treated with reoptimized plan relative to the predicted plan. Treatment planning, daily recontouring, reoptimization of the plan, and treatment delivery with gating on the MR-linac is feasible. Further analyses will be done including all included patients.

10 - Magnetic Resonance-Guided Adaptive Radiation Therapy for Intra-Abdominal Hematological Malignancies

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Background/Objectives: Radiation therapy (RT) for intra-abdominal hematologic malignancies poses unique challenges due to the mobility of the target, necessitating large margins. Treatment delivery advancements have enabled precise targeting of tumors and sparing of normal tissue. We investigated if magnetic resonance (MR)-guided RT (MRgRT) improves the therapeutic index of RT for abdominal tumors due to superior tumor visualization, real-time tracking, and plan adaptation.

Methods/Overview: We retrospectively reviewed all patients with hematologic malignancies treated with MRgRT at our institution. Tumor motion was calculated from real-time MR-tracking cine. Planning target volume (PTV) coverage of tumors pre-adaptation and post-adaptation were compared using the Wilcoxon signed rank test. PTV margins for MRgRT-based planning were compared to simulated conventional PTV margins for conservative (larger), base, and aggressive (smaller) scenarios using the Wilcoxon rank-sum test.

Results: Nine patients were treated with MRgRT between 2021-2025. Most patients had indolent lymphomas (6, 67%), and the remaining patients (3, 33%) had diffuse large B-cell lymphoma, solitary plasmacytoma, and nodular lymphocyte-predominant Hodgkin lymphoma. Three (33%) patients had cecal, ileal, and pancreatic tumors, while the remaining six patients had duodenal (3, 33%) and mesenteric (3, 33%) tumors. Delivered dose was 4 Gy/2 fractions (1, 11%), 20 Gy/5 fractions (4, 44%), 25 Gy/5 fractions(3, 33%), and 30 Gy/5 fractions(1, 11%). The 95$^{th}$ percentile of target motion for all patients and fractions was 1.6 cm, which was largely driven by superior-inferior displacement. PTV coverage was superior after adaptation (median coverage 97% [range: 94.6-99.6] vs. 91% [range: 8.7-96.2], $p<0.001$). PTV volumes were significantly reduced using MRgRT, with median relative volume reductions of 88%, 85%, and 80% for conservative, base, and aggressive cases, corresponding to 1027cc, 772cc, and 554cc of tissue spared ($p<0.001$).

Conclusion: MRgRT offers significant normal-tissue sparing advantages over conventional RT. Future work will optimize patient selection for MRgRT based on predicted tumor motion.

11 - Association of Clinical and Molecular Risk Factors with Severity of Anemia in Myelofibrosis

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Background: Anemia with hemoglobin under 100g/L is recognized as a poor prognostic factor in patients with myelofibrosis (MF). Close to 50% of patients have transfusion requiring anemia within 1-year of diagnosis. MF-related anemia can be challenging to manage as it is often multifactorial including: related to underlying disease or associated complications, inflammation, abnormal iron metabolism, treatment, and comorbidities. As part of standard of care a detailed anemia work-up (DAW) is completed according to the consensus guidelines for MF patients with anemia (Koshminder et al, Leukemia 2024).

Method: To better understand anemia in myelofibrosis, we conducted a retrospective chart review of 116 myelofibrosis patients presenting with anemia, at Princess Margaret. The data set contains patient characteristics such as sex, fibrosis grade, EPO level, DIPSS, MIPSS70 2.0 at index date (date of anemia work-up), prior bleeding history, molecular mutations (JAK2, CALR, MPL, ASXL1, SF3B1, SRSF2, U2AF1, ZRSR2, IDH1, IDH2, EZH2, and TP53), and clinical parameters such as complete blood counts, iron studies, and CRP. Univariate analysis was conducted using Chi-square and Kruskal Wallis test, appropriate. Anemia was defined by both the sex-specific range proposed in 2024 by the International-Working Group-European LeukemiaNet (Tefferi et al, Blood, 2024), and the recent consensus guidelines (Koshminder et al, Leukemia, 2024).

Results: A total of 116 patients were included in the analysis; 36 (31%) female, and 80 (69%) male. The median age was 72 (range 31-87) years. Through our DAW other cause of anemia were found, i.e. bleeding (11%), hemoglobinopathy (3.5%), concurrent malignancies (5%). More male vs female patients had moderate (N=47 [61.8%] vs N=29 [38.2%], p<0.0001) and severe anemia (N=8 [53.3%] vs N=7[46.7%], p<0.0001). MPN driver mutations (JAK2, CALR and MPL) did not have an impact to severity of anemia (p=0.32). Interestingly 33% of patients had a spliceosome mutation. Amongst the spliceosome mutations SRSF2 and U2AF1 were associated with severity of anemia (p=0.04 and 0.01, respectively). Clinical parameters such as platelet level (p=0.001), albumin (p=0.019), reticulocyte count (p=0.007), ferritin (p=0.0002), and EPO level (p=0.001) were shown to have an impact on severity of anemia, even when adjusted for sex-specific anemia. Additionally, when adjusted for sex-specific severity of anemia, the presence of SF3B1 had an impact in severe anemia (N=7 [20.6%] p=0.023), as well as U2AF1 (N=10 [28.6%] p=0.006) for both sexes.

Conclusion: We found that 20% of MF patients have main cause of anemia other than underlying disease or drugs. We also show that male patients with MF have higher frequency as well as severity of anemia compared to female patients. Spliceosome mutations such as SRSF2 and U2AF1 have significant associations with severity of anemia. Further work is in progress to understand the impact of therapy responses to various interventions for MF patients with anemia.

12 - Extramedullary Disease in AML: A High-risk Feature Beyond ELN 2022 Classification

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Background: Extramedullary disease (EMD) in acute myeloid leukemia (AML) involves leukemic infiltration outside the bone marrow and is observed in up to 25% of patients. Despite its frequency, EMD is not currently incorporated into the ELN 2022 risk stratification system. Recent studies have demonstrated molecular discordance between leukemic cells in the bone marrow and those found at EMD sites, raising concerns that molecular profiling based solely on bone marrow samples may not adequately guide clinical management of patients with EMD. Objective: To characterize the clinical features and treatment outcomes of EMD in a large, retrospective cohort of AML patients treated over two decades at Princess Margaret Cancer Centre.

Methods: We conducted a retrospective analysis of 617 adult AML patients, categorizing them into non-EMD (n=371) and EMD groups (n=246). We compared complete remission (CR) rates, relapse rates, rates of allogeneic hematopoietic stem cell transplantation (allo-HSCT), overall survival (OS), and event-free survival (EFS). Propensity score matching (PSM) was used to adjust for differences in age, ELN risk category, induction regimen, and allo-HSCT. Multivariate analyses (MVA) were performed to identify independent prognostic factors.

Results: Among the 246 patients with EMD, 53 (21.5%) had isolated EMD, while 193 (78.5%) presented with concurrent bone marrow involvement. CR rates following induction therapy were similarly high in both groups (96% in isolated EMD vs. 89% in combined involvement; p=0.18). Relapse rates (32% vs. 34%; p=0.77) and rates of allogeneic HSCT (40% vs. 32%; p=0.32) were also comparable, indicating similar outcomes between isolated EMD and concurrent marrow involvement with EMD. After PSM (168 matched pairs), EMD was associated with inferior OS (median 14.2 vs. 64.1 months; and EFS :9.5 vs. 55.9 months; both p<0.0001). MVA confirmed EMD as an independent adverse prognostic factor for OS (HR 1.87, 95% CI 1.2-2.91, p=0.005) and EFS (HR 1.93, 95% CI 1.36-2.75, p=0.0002). Among EMD patients, allo-HSCT was associated with improved EFS (HR 0.49, 95% CI 0.24-0.99, p=0.048), although OS benefit did not reach significance (HR 0.60, p=0.20). The most common EM involvement sites were the skin (39%) and central nervous system (15%). Neither specific EMD site involvement, nor mutations frequently identified in EMD patients (NPM1, TET2, ASXL1, DNMT3A) were significantly associated with differences in OS or EFS.

Conclusions: This large, retrospective study emphasizes the negative prognostic impact of EMD in AML, independent of ELN risk stratification, even among patients classified as favorable-risk. Although allo-HSCT may offer some improvement in disease control, it does not fully overcome the poor prognosis linked to EMD. Additionally, these results underscore the importance of site-specific molecular profiling in guiding therapeutic decisions. EMD warrants inclusion in future AML risk stratification models and prospective therapeutic trials.

13 - Comparable Remission Rates in Therapy-related and Myelodysplasia-related Acute Myeloid Leukemia (AML) versus de novo AML Treated with Azacitidine and Venetoclax: A Contemporary Real-world Study.

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Background: Patients with secondary acute myeloid leukemia (sAML), including therapy-related AML (t-AML) and myelodysplasia-related AML (AML-MR), historically have inferior outcomes compared with de novo AML (dn-AML) when treated with intensive chemotherapy. Azacitidine plus venetoclax (Aza-Ven) is increasingly used in this population due to improved efficacy and tolerability. However, outcomes and prognostic factors among biologically distinct sAML subgroups treated with Aza-Ven remain incompletely defined. We evaluated our center's clinical outcomes of frontline Aza-Ven in patients with t-AML and AML-MR compared with dn-AML.

Methods: We performed a retrospective cohort study of adults with AML treated with frontline Aza-Ven between 2017 and 2024 in our center. Patients were classified into three mutually exclusive groups: t-AML, AML-MR, and dn-AML. Therapy-related AML was defined by prior exposure to cytotoxic chemotherapy or radiotherapy. AML-MR included patients with prior myelodysplastic syndrome or myelodysplastic/myeloproliferative neoplasm, or those with myelodysplasia-related gene mutations or cytogenetic abnormalities. Remaining patients were categorized as dn-AML. Composite complete remission (CRc) included complete remission and remission with incomplete or partial hematologic recovery. Overall response rate (ORR) included CRc and morphologic leukemia-free state. Overall survival (OS) was analyzed using Kaplan-Meier with log-rank testing, with exploratory Cox regression analyses.

Results: A total of 132 patients were included: 29 with t-AML, 73 with AML-MR, and 30 with dn-AML. Patients with t-AML had similar age, ECOG 0-1 status, and frequency of non-favorable ELN 2024 risk compared with dn-AML, but higher rates of TP53 mutations, complex karyotype, and non-favorable ELN 2022 risk.

CRc rates at any time were 71% in t-AML versus 69% in dn-AML (p=0.25), including 58% versus 59% after cycle 1 (p=0.25). ORR at any time was 75% versus 86% (p=0.15), including 67% versus 79% after cycle 1 (p=0.11). Sixty-day mortality was 17% versus 7% (p=0.25). Median OS was 13.1 versus 16.0 months (p=0.30), with 24-month OS rates of 29% and 48%. Within t-AML, TP53 mutations (HR 2.67, p=0.05) and adverse ELN 2022 risk (HR 8.07, p=0.05) were marginally associated with inferior OS.

CRc at any time was 65% in AML-MR versus 69% in dn-AML (p=0.82), including 45% versus 59% after cycle 1 (p=0.11). ORR at any time was 87% versus 86% (p=0.92), including 69% vs 79% after cycle 1 (p=0.15). Sixty-day mortality was 7% in both groups. Median OS was 12.4 versus 16.0 months (p=0.30), with 24-month OS rates of 33% and 48%. Within AML-MR, signaling pathway mutations (FLT3-ITD, NRAS/KRAS; HR 3.32, p<0.01) and adverse ELN 2024 risk (HR 1.99, p=0.04) were associated with inferior OS.

Conclusion: Frontline Aza-Ven achieved remission rates in sAML comparable to dn-AML, with no significant difference in OS. Prognostic factors differed between t-AML and AML-MR, underscoring biological heterogeneity and suggesting variable utility of current risk stratification systems in the venetoclax era.

14 - FLT3 Inhibition with Midostaurin Offsets Poor Prognosis in NPM1/FLT3/DNMT3a Triple Mutated AML

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Background / Objectives: FLT3-mutated (FLT3m) acute myeloid leukemia (AML) with co-occurring DNMT3A and NPM1 mutations (triple-mutated; TM+) has historically been associated with inferior outcomes, based largely on studies predating routine incorporation of FLT3 inhibitors into induction therapy. TM+ patients appear particularly sensitive to FLT3 inhibitors in the relapsed/refractory setting. We evaluated whether the addition of midostaurin to intensive chemotherapy mitigates the adverse prognostic impact of TM+ status in a real-world cohort of FLT3m AML.

Methods / Overview: This retrospective single-center study included adults (≥18 years) with FLT3m AML treated with intensive chemotherapy between January 2015 and January 2023, with available next-generation sequencing data. Patients were grouped by midostaurin exposure (M+ vs M−) and TM status (TM+ vs TM−). Relapse-free survival (RFS) and overall survival (OS) were estimated using Kaplan-Meier methods. Inverse probability of treatment weighting (IPTW)-adjusted analyses were performed using propensity scores derived from clinically relevant covariates.

Results: Among 242 patients, 92 (38%) were M− and 150 (62%) were M+. TM+ prevalence was similar (30.4% M−; 29.3% M+). In the M− cohort, 3-year OS was lower in TM+ versus TM− patients (39% vs 58%; p=0.146) and significantly inferior after censoring for transplant (13% vs 58%; p=0.048). In contrast, within the M+ cohort, 3-year OS was comparable between TM+ and TM− patients (67% vs 55%; p=0.328), including after censoring for transplant (38% vs 35%; p=0.662).

IPTW-adjusted analysis demonstrated superior 3-year OS among TM+ patients treated with midostaurin compared with M− patients (65% vs 36%; HR 0.44, p=0.019), whereas no survival difference was observed among TM− patients (HR 0.89, p=0.65).

Conclusion: In FLT3m AML, incorporation of midostaurin during intensive induction appears to attenuate the adverse prognostic impact of triple-mutated disease. Survival disadvantage in TM+ patients was evident in the absence of midostaurin but not when midostaurin was used, suggesting that the benefit of FLT3 inhibition may be influenced by co-mutation profile.

15 - Utilizing Fluorescence Intravital Imaging to Investigate Bone Marrow Microenvironment Remodeling in Acute Myeloid Leukemia

Maryam Naimi[1], Samridhi Bhardwaj[1], Lyndsey DeGuzman[2], Sadaf Jafari[2], Raheleh Niavarani[3], Xi Lei[2], Emily Chen[2], Michael Edson[4], Ralph DaCosta[2]
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Background: Acute myeloid leukemia (AML) progression is strongly influenced by dynamic remodeling of the bone marrow microenvironment (BME), including increasing hypoxia and impaired immune surveillance, yet these processes cannot be visualized longitudinally at single-cell resolution. The femur window chamber (FWC), developed by the DaCosta Lab, enables real-time intravital fluorescence imaging of immune and leukemic cells within intact murine bone marrow.

Objectives: To investigate (i) how leukemic expansion remodels the BME over time, (ii) how T-cell populations and motility change during AML progression, and (iii) whether human immune-tumor interactions can be visualized in humanized NSGW41-hIL7 mice bearing human AML.

Methods: FWC devices were surgically implanted to allow longitudinal intravital imaging. In murine studies, C57BL/6J mice were inoculated with C1498-mCherry AML and vasculature was labeled with fluorescent dextran; CD3, CD4, and CD8 T cells were tracked using antibody-conjugated fluorophores. Humanized NSGW41-hIL7 mice were inoculated with OCI-AML2 cells expressing mCherry, HRE-dUnaG (hypoxia), and H2B-iRFP670 (chromatin damage). γδ T cells were labeled with anti-human γδTCR. Imaging spanned 0-24 days; image analysis (Imaris) quantified fluorescence intensities, colocalization, and T-cell motility, with flow cytometry and IHC for validation.

Results: Intravital imaging revealed progressive leukemic engraftment accompanied by increasing hypoxia (HRE-dUnaG) and chromatin damage (H2B-iRFP670), with significant increases in fluorescence intensities between days 9-20, confirmed by anti-mCherry IHC. T-cell abundance declined with disease progression: $CD3^+$, $CD4^+$, and $CD8^+$ cells were increasingly depleted, with $CD8^+$ cells dropping sharply after day 10. $CD4^+$:$CD8^+$ ratios rose, indicating enhanced immunosuppression, and T-cell motility decreased. In humanized NSGW41-hIL7 mice, time-lapse imaging captured γδ T-cell migration toward AML cells, supported by increased circulating $CD3^+$/γδ$TCR^+$/$IFN\gamma^+$ activation and higher Annexin V-positive AML cell death compared to non-humanized controls.

Conclusion: FWC intravital imaging enables quantitative tracking of leukemic progression, hypoxia, and immune dysfunction in vivo. These findings illustrate how the AML microenvironment becomes increasingly hypoxic and immunosuppressive and establish a platform for evaluating immunotherapies aimed at restoring effective anti-leukemic immunity.

16 - Deciphering the Mechanisms Underlying the Pathophysiology and Chemotherapy Resistance in Acute Myeloid Leukemia Using Intravital Imaging and Humanized NSGW41IL7 Mouse

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Background: Acute myeloid leukemia (AML) is aggressive and heterogeneous; resistance to therapy and relapse are driven in part by AML-induced remodeling of the bone marrow (BM) microenvironment and immune suppression. The temporal dynamics of human T-cell (particularly γδ T-cell) interactions with AML in vivo remain poorly defined, limiting opportunities to optimize treatment timing and overcome resistance. We developed an intravital fluorescence platform to longitudinally visualize AML-immune interactions within intact BM.

Objectives: (i) Establish a live, single-cell-resolution framework to track leukemic burden and BM remodeling; (ii) quantify the timing and dynamics of human γδ T-cell infiltration and cytotoxic engagement with AML; and (iii) generate hypotheses for aligning chemotherapy schedules with T-cell activity to improve AML killing.

Methods: We combined a femur window chamber (FWC) with humanized NSGW41-IL7 mice engrafted with human AML (e.g., OCI-AML2). Leukemia cells expressed mCherry, HRE-dUnaG (hypoxia), and H2B-iRFP670 (DNA damage). Vasculature was labeled with fluorescent dextran; human γδ T cells were visualized using anti-human γδTCR. Time-lapse intravital imaging captured cell trafficking over minutes to weeks, with image analysis for fluorescence intensities, distances, and motility; flow cytometry and IHC provided orthogonal validation. Parallel murine C57BL/6J studies with C1498-mCherry AML quantified $CD3^+$/$CD4^+$/$CD8^+$ dynamics and T-cell speeds.

Results: The platform enabled stable, repeat imaging of BM vasculature, AML cells, hypoxia, and DNA damage. In humanized mice, γδ T cells were consistently detected from ~days 4-16 post-AML inoculation, with maximal cytotoxic activity between days 6-10, coinciding with increased AML DNA damage (H2B-iRFP670) and reduced leukemic burden (mCherry). Time-lapse sequences showed γδ T cells migrating toward AML cells with quantifiable approach speeds. Flow cytometry demonstrated activation of $CD3^+$/$γδTCR^+$/$IFNγ^+$ populations, and Annexin V analyses indicated higher AML cell death in humanized versus non-humanized controls. In the murine model, progressive AML correlated with depletion of $CD3^+$, $CD4^+$, and $CD8^+$ T cells, rising $CD4^+$:$CD8^+$ ratios, and reduced T-cell motility, consistent with increasing immunosuppression.

Conclusion: Intravital BM imaging in humanized NSGW41-IL7 mice reveals a defined window of γδ T-cell infiltration and cytotoxicity against AML and quantifies concurrent hypoxia and DNA-damage dynamics. These data establish a translational platform to time conventional chemotherapy (e.g., post-exhaustion recovery) with endogenous T-cell activity and to evaluate immunotherapies aimed at restoring effective anti-leukemic immunity.

17 - Redox-Driven Bone Marrow Vascular Remodeling Under Systemic Inflammation: Insights from Intravital Imaging and Sex-Specific Response

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Background: The bone marrow (BM) vasculature regulates oxygen, nutrient, and drug delivery while supporting hematopoietic and mesenchymal stem cell niches. Disturbances in vascular integrity contribute to skeletal aging, osteopathologies, and hematologic disorders.

Methods and Results: We investigated BM vascular remodeling under systemic inflammatory stressors, including ionizing radiation, aging, high-fat diet-induced obesity, and acute myeloid leukemia (AML), in immunocompetent (C57BL/6) and immunodeficient (NSGW41) mice. Intravital imaging enabled real-time visualization of distinct vessel subtypes, revealing impaired perfusion, increased permeability, and structural disorganization across conditions. Ex vivo profiling demonstrated elevated NOX4 expression and TBARS accumulation, coupled with reduced NOS3 expression, indicating a redox imbalance driving endothelial dysfunction. Comparative analyses showed that immunodeficient mice exhibited more severe vascular disruption than immunocompetent counterparts, and sex-specific differences emerged, with female mice displaying greater oxidative stress and vascular remodeling.

Conclusions: Systemic inflammatory stressors converge on a redox-mediated mechanism of BM vascular remodeling, with severity influenced by immune status and sex. Intravital imaging provided spatial and temporal resolution of these changes, positioning the BM vasculature as both a sensor and target of inflammatory damage. These findings highlight NOX4/NOS3 imbalance as a potential therapeutic axis for preserving vascular integrity and hematopoietic resilience under chronic inflammatory stress.

18 - Decoding Neurotransmitter Driven Immune Suppression in AML Through Intravital Imaging and Humanized Models

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Background / Objectives: Acute myeloid leukemia (AML) remodels the bone marrow microenvironment (BME) into hypoxic, immunosuppressive niches that blunt effective T-cell responses and promote relapse. However, the upstream cues coordinating crosstalk among nerve fibers, immune cells, and leukemic blasts in living marrow remain undefined, in part because real-time neurotransmitter activity cannot typically be mapped in vivo. We aim to visualize and quantify neurotransmitter (e.g., cholinergic) signaling within AML-infiltrated BME, determine its timing, magnitude, and cellular sources (nerve- vs. immune-derived), and test whether perturbing this axis reprograms immunosuppressive niches and restores anti-leukemia immunity.

Methods / Overview: We combined longitudinal intravital imaging through the femur window chamber (FWC) with genetically encoded neurotransmitter biosensors to map neurotransmitter dynamics at single-cell resolution in murine and humanized NSGW41-IL7 AML models. Time-lapse microscopy tracked leukemic burden, vascular structure, neural fibers, and endogenous T-cell trafficking (CD3/CD4/CD8; γδ T cells) across early, intermediate, and late disease. Imaging mass cytometry (IMC) delineated spatial immune states and ligand-receptor neighborhoods in neurotransmitter-rich microdomains. Interventions evaluated whether disrupting immune-associated cholinergic programs could dismantle suppressive niches and augment T-cell function within the BME.

Results: Pilot intravital datasets in AML demonstrated stable, repeat imaging of marrow vasculature and leukemic cells over weeks, with quantifiable T-cell abundance, motility, and γδ T-cell engagement of AML cells; activation of $CD3^+/\gamma\delta TCR^+/IFN\gamma^+$ populations and increased leukemic cell death in humanized mice supported functional immune-tumor interactions. These results established feasibility to layer live neurotransmitter readouts onto our AML platform and to resolve temporal shifts in nerve- versus immune-derived signaling that structured immunosuppressive niches.

Conclusion: This study delivered the first in vivo, single-cell-resolved map of neuro-immune-leukemia signaling in intact marrow, defined when and from whom neurotransmitters arose during AML progression, and tested whether targeting this axis restored T-cell function. By uncovering a druggable neuro-immune pathway, the work created a translational foundation for rational combination or timing strategies (e.g., aligning chemotherapy with endogenous T-cell activity) and, ultimately, for exploring the repurposing of approved neuronal or neuro-immune-modulating agents in AML.

19 - Prognostic Impact of Molecular Genetic and Cytogenetic Alterations in Newly Diagnosed Acute Myeloid Leukemia Treated with Azacitidine and Venetoclax: A Real-world Cohort Study

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Background: Azacitidine plus venetoclax (Aza-Ven) is the standard of care for older or unfit patients with newly diagnosed acute myeloid leukemia (AML). However, clinical outcomes remain heterogeneous, and the prognostic impact of genetic abnormalities in this setting is not fully defined. The European LeukemiaNet (ELN) 2024 risk classification was developed for Aza-Ven-treated patients, but external validation remains limited.

Methods: We retrospectively analyzed patients treated with Aza-Ven at Princess Margaret Cancer Centre between 2017 and 2024. Clinical, cytogenetic, and molecular data were collected, and patients were risk-stratified using ELN 2024. Overall survival (OS) and response rates were assessed. Composite complete remission (CRc) included CR, CRi, and CRh. Overall response rate (ORR) included CRc, MLFS, and PR. Survival analyses used Kaplan-Meier estimates and Cox regression models.

Results: A total of 132 patients were included (median age 73 years; 62% male). Prior MDS or MDS/MPN was present in 20%, and 23% had complex karyotype (CK). The most frequent mutations were ASXL1 (26%), SRSF2 (25%), TET2 (21%), DNMT3A (18%), and NPM1 (18%); 17% had TP53 and 16% had NRAS/KRAS mutations.

The CRc rate was 61% and ORR was 76%. With a median follow-up of 21.4 months, median OS was 13.2 months; 1- and 2-year OS rates were 56% and 35%, respectively. Patients with IDH1 or IDH2 mutations had superior OS (HR 0.37, $p<0.01$), while NRAS/KRAS mutations were associated with inferior OS (HR 2.16, $p=0.02$). TET2 mutations (HR 1.85, $p=0.02$), CK (HR 1.77, $p=0.03$), and high mutation burden (≥4 mutations; $p=0.05$) were associated with worse OS. TP53 mutation showed a trend toward inferior survival (HR 1.61, $p=0.10$).

By ELN 2024, adverse-risk patients had significantly worse OS compared with favorable risk (HR 1.93, $p=0.04$).

Conclusions: In this real-world cohort, we validate the favorable prognosis of IDH1/2 and DDX41-mutated AML and the adverse impact of NRAS/KRAS mutations, CK, TET2 mutations, and high mutation burden in patients treated with Aza-Ven. Larger multicenter studies are needed to refine risk stratification in this population.

# 20 - Morphologic Leukemia-free State (MLFS) is Associated with Inferior Outcomes in Patients with Acute Myeloid Leukemia (AML) Treated with Front-line Azacitidine plus Venetoclax

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Background: Azacitidine plus venetoclax (Aza-Ven) is now standard of care for newly diagnosed acute myeloid leukemia (AML) in patients (pts) ineligible for intensive chemotherapy. In this study, we sought to investigate the impact of incomplete hematological recovery after Aza-Ven on long-term survival.

Methods: We conducted a retrospective study of pts diagnosed with AML, who received front-line treatment with Aza-Ven between 2017 and 2024. Reponses were categorised based on the 2022 European Leukemia Network (ELN) recommendations for AML. The primary outcome was overall survival (OS).

Results: Our cohort consisted of 132 cases, with 82 (62%) male pts. The median age was 74 years (range, 34 - 90). Bone marrow assessments (BMA) were performed in 117 (89%) pts after cycle 1. The median OS in our whole cohort was 13 months (95% CI: 11 - 16 months).
Pts who achieved MLFS after cycle 1 were more likely to have had previous exposure to hypomethylating agents (HMA) (13% vs 0%, p<0.01) as well as mutations in *ASXL1* (42.9% vs 19%, p=0.03), *STAG2* (23.8% vs 3.4%, p<0.01) and *TET2* (38.1% vs 15.5%, p=0.03). Pts achieving CR/CRi after cycle 1 also more commonly had favourable risk disease as per ELN 2024 (49.2% vs 26.1%, p=0.03), compared to those who achieved MLFS.

There was no significant difference in measurable residual disease (MRD) positivity assessed by flow cytometry between pts who achieved CR/CRi versus MLFS (38% vs 53%, p=0.26) and MRD status was not associated with OS (HR 0.89, 95% CI 0.42-1.89, p=0.77) among pts achieving mCR.

Pts achieving CR/CRi (n=59) after cycle 1 had significantly longer median OS at 22.5 months, compared to those who achieved MLFS (n=23) at 6.6 months (HR 0.45, 95% CI: 0.24 - 0.85, p=0.01).

Conclusion: Patients who achieve MLFS after Aza-Ven have significantly worse OS compared with those who achieve CR/CRi.

# 21 - Neuroscience Informed Mind - Body Interventions to Reduce Symptom Burden in Patients with Hematologic Malignancies

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Patients with hematologic malignancies experience significant physical and psychological symptom burden throughout diagnosis, treatment, and survivorship. Anxiety, fatigue, sleep disturbance, and emotional distress are common and can negatively impact quality of life and treatment tolerance. Emerging evidence from neuroscience highlights the role of autonomic nervous system dysregulation in stress response, symptom perception, and emotional processing. Mind - body interventions that promote nervous system regulation may offer a supportive, low-risk approach to addressing these challenges.

This poster presents a neuroscience-informed, mind - body supportive care approach incorporating breath regulation, gentle movement, guided mindfulness, and principles of psychological safety and connection for individuals undergoing treatment for hematologic malignancies. Patient-reported outcomes related to anxiety, emotional distress, fatigue, sleep quality, and overall well-being were assessed before and after participation using standardized symptom assessment measures.

Participants reported improvements in emotional distress, anxiety, and sleep quality following engagement in the intervention, along with enhanced coping and perceived emotional support during treatment. The approach was feasible, well tolerated, and positively received by patients across different stages of care.

These findings suggest that neuroscience-informed mind - body interventions may serve as a valuable adjunct to palliative and supportive care in hematologic oncology. By targeting stress physiology and emotional regulation, such interventions may help reduce symptom burden and improve quality of life. Further prospective studies are warranted to explore integration within multidisciplinary cancer care models.

22 - Immune Checkpoint Inhibitor-induced Pure Red Cell Aplasia in a Patient with Advanced Cholangiocarcinoma: A Case Report

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Background: The use of immune checkpoint inhibitors (ICI) and immunotherapy for the treatment of both solid organ and hematologic malignancies has been steadily increasing in the last 10 years. ICIs can induce a variety of immune-related adverse events (irAEs), including life-threatening hematological irAEs (heme irAEs), which require timely recognition for effective disease management and optimal outcomes.

Case Report: A 76-year-old man was diagnosed with Stage IV intrahepatic cholangiocarcinoma with satellite liver lesions. After responding to eight cycles of palliative intent chemotherapy with cisplatin plus gemcitabine and durvalumab, he underwent a partial liver resection and cholecystectomy and received postoperative radiotherapy. Following disease progression, treatment with cisplatin plus gemcitabine and durvalumab was restarted. After two more cycles of chemotherapy, the patient presented with fatigue, persistent rash, and a normocytic anemia associated with a very low reticulocyte count requiring blood transfusions. Further workup and bone marrow investigations led to a diagnosis of ICI-induced pure red cell aplasia (PRCA). The PRCA successfully responded to cyclosporine, without disease recurrence following tapering, and a brief course of prednisone was given for the rash. The patient remains transfusion independent and ICI therapy was not restarted. After 28 months from his initial cancer diagnosis and 12 months following chemotherapy discontinuation, his cholangiocarcinoma continues to be in sustained remission with no new lesions. Notably, he has considerably exceeded the median progression free survival reported in clinical trials (7.2 months) in patients with advanced cholangiocarcinoma on this treatment.

Conclusion: This case underscores the importance of early recognition and management of heme irAEs, including rare conditions such as PRCA, in patients receiving immunotherapy treatment. Further, our report contributes to a growing body of evidence exploring the potential link between serious irAEs, such as heme irAEs, and achieving deep responses to ICIs.

# 23 - The Hidden Burden: Financial, Physical, and Psychosocial Impacts of Travel to Treatment for Canadian Blood Cancer Patients

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Accessing care often requires patients with blood cancers in Canada to travel long distances, posing additional challenges beyond the disease itself. This study aimed to examine the financial, physical, and psychosocial impact of travel to treatment among Canadian blood cancer patients and their caregivers.

Survey data were collected from 457 respondents between November 2024 and January 2025. Results revealed that 59.7% of participants traveled over 100 km to receive care, with 67.6% having to do so for more than a year. The travel demands were associated with substantial financial strain—48.2% of respondents reported a ≥10% reduction in household income. The physical toll was also significant, with 64.5% reporting fatigue worsened by travel. Psychosocial impacts included extended separation from family (52.8% lived away from their immediate family for more than three months) and emotional distress, as 46.1% expressed feelings of guilt about being a burden.

These findings underscore the need for targeted policy and support interventions to mitigate the adverse effects of travel for cancer care in Canada.

24 - Propensity Score Matching Analysis Comparing the Efficacy and Llong-term Outcomes of Belumosudil to the Best Available Treatment as a Historical Control, Used as Second-line t-Therapy or Beyond for Chronic GVHD After Steroid Failure

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Background: ROCKstar study demonstrated that Belumosudil (BEL), a selective Rho-associated coiled-coil kinase 2 (ROCK2) inhibitor, has clinical efficacy in managing chronic graft-versus-host disease (cGvHD) in patients who failed 2nd line therapy or beyond. Multiple studies based on real-world experiences reported similar results of improved overall response rate and failure-free survival (FFS). A prospective randomized controlled trial (RCT) comparing BEL with best available therapy (BAT) as a control is still lacking. Propensity-score matching (PSM) analysis is a statistical methodology balancing out a bias coming from imbalanced distribution of patient characteristics at baseline between the variable of interest (e.g., treatment option). Thus, it could mimic RCT by comparing treatment outcomes indirectly after balancing biased covariates.

Objectives: The present study compared treatment outcomes between BEL-treated patients and cGvHD patients treated with BAT as a historical cohort. PSM was applied to control for biased confounding variables between the two groups. FFS, OS, and steroid dose reduction were evaluated as statistical endpoints.

Methods: We retrospectively analyzed treatment outcomes in a total of 523 patients treated at second line or beyond, including 216 pts treated with BEL collected from 3 countries (Canada, Spain, and Germany) and 307 treated with BAT. For the BAT group as a historical control, we retrieved the clinical data of patients who developed chronic GvHD and were treated at Princess Margaret Cancer Centre between 2006 and 2014 before novel agents were available: 163 treatments (53.1%), 77 (25.1%), 36 (11.1%), and 33 (10.7%) were given as 2nd, 3rd, 4th, and ≥5th line, respectively. Treatment included prednisone in 284 (92.5%), mycophenolate in 145 (47.2%), azathioprine (AZA) in 144 (46.9%), a calcineurin inhibitor in 54 (17.6%), hydroxychloroquine in 51 (16.6%), extracorporeal photopheresis in 20 (6.5%), and rituximab in 10 (3.3%). A propensity score was calculated from the following unbalanced clinical factors: age (≥60 vs. <60), GvHD severity (severe vs. mild/moderate), HCT-CI score (≥3 vs. <3), and treatment line (≥4th vs. <4th). We extracted 84 patients (42 in each group) for comparison between BEL and BAT groups after balancing clinical factors.

Results: With a median follow-up in survivors of 16.3 months (0-102), the BEL group were older (34.3% vs. 17.9% ≥60 years, p<0.001), more frequent with severe cGvHD (80.1% vs. 19.2%, p<0.001), and at 4th line of treatment or beyond (75.9% vs. 21.8%, p<0.001) compared to the BAT group; patients in the BAT group had a higher HCT-CI score (35.7% vs. 16.8% ≥3, p<0.001). In terms of 12 months' FFS rate, BEL group showed a 66.8% [58.9-73.5] vs 39.7% [33.7-45.7] in BAT group (p<0.001), whereas 12 months' OS rates were 92.6% [86.6-95.9] and 84.9% [79.4-89.0] (p=0.006), respectively. No differences were found for FFS (p=0.400) or OS

(p=0.126) when comparing patients who received AZA vs. those who did not in BAT group. At months 0, 3, and 6, 45.5% (46.2% vs. 0.7%, p<0.001), 45.3% (45.3% vs. 0%, p<0.001), and 35.1% (37.1% vs. 0%, p<0.001) more patients in BEL group could discontinue prednisone compared to BAT group, respectively. After the PSM subgroup, no differences were found between the BEL vs. BAT group for age (42.9% vs. 45.2%, p=1), severe cGvHD (38.1% in both, p=1), HCT-CI ≥3 (16.7% vs. 14.3%, p=1), or 4th line of treatment and beyond (33.3% vs. 31.0%, p=1). The BEL group showed 72.0% [55.0-83.4] 12 months' FFS rate vs 25.3% [10.6-43.1] for BAT (p<0.001), whereas 12 months' OS rates were 92.1% [77.3-97.4] and 88.4% [60.8-97.0] (p=0.317), respectively. Both univariate (UVA) and multivariate analysis (MVA) (BEL vs. BAT, HCT-CI ≥3, severe cGvHD, age ≥ 60, and previous acute GvHD) for FFS confirmed BEL superiority over BAT (hazard ratio (HR) 0.288 [0.155-0.535], p<0.001; no differences for the other factors). For OS, UVA showed that BEL had a trend for a higher OS (HR 0.282, p=0.067), while severe cGvHD (HR 3.719, p=0.058) for lower OS; no differences were found in MVA. In the PSM subgroup, 33.3% (33% vs. 0%, p<0.001) and 47.1% (50% vs. 2.9%, p<0.001) more patients in the BEL group could discontinue prednisone at months 3 and 6, respectively, compared to the BAT group.

Conclusion: The current study confirmed that BEL was superior to BAT as second-line therapy or beyond in cGvHD patients after therapy failure concerning FFS and steroid tapering.

25 - Clinically Meaningful Improvement of the Modified Lee Symptom Score in Patients Treated With Belumosudil for Steroid-Refractory Chronic GVHD: Evidence from Canadian Real-World Outcomes

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Background: Belumosudil (BEL), a selective Rho-associated coiled-coil kinase 2 (ROCK2) inhibitor, has shown clinical efficacy in the management of chronic graft-versus-host disease (cGvHD), particularly in reversing fibrosis. Patient-reported outcomes (PROs) are increasingly recognized as valuable tools for assessing treatment response in cGvHD, such as the modified Lee Symptom Score (mLSS) serving as a practical tool for evaluating symptom burden.

Objectives: The current study aims to assess the clinical activity of BEL based on the symptom burden longitudinally measured by the mLSS in cGvHD patients treated with BEL after multiple prior therapy failures.

Methods: This retrospective, multicentre study evaluated clinical outcomes and longitudinal improvement in mLSS following BEL therapy in patients with cGVHD who had failed multiple lines of therapy. We included 87 patientswho started BEL therapy between March 2023 and June 2024 and had the mLSS assessed as a standard of care. The 7-domain mLSS (skin, eye/mouth, breathing, eating/digestion, muscle/joints, energy, mental/emotional health) was assessed at baseline, 3, 6, and 12 months after the initiation of BEL. The sum of these domains was calculated to derive the total mLSS. A fibrotic sum score (FSS) was invented, calculated by summing the scores for limited joint movement, difficulty swallowing solids and liquids, and thickened skin, representing cGvHD manifestation of fibrosis. Clinically meaningful improvement (CMI) was defined as a reduction of ≥7 points in mLSS, ≥2 points in the FSS, and ≥ 1 point in each domain. Longitudinal changes in overall mLSS, FSS, and the sum of mLSS in each domain were analyzed using repeated measures with a general linear model (GLM), as well as the proportion of patients showing clinically meaningful improvement (CMI).

Results: A total of 87 patients with cGVHD were treated with BEL and had mLSS data available. At the time of starting BEL, 68% (n=59) patients had severe grade cGvHD, with a median of 3 (1-7) affected organs, and had received a median of 4 (2-10) prior lines of therapy. Most patients (82%, n=69/84) started BEL at 200 mg daily. With a median follow-up duration of 15.8 months among survivors (range 1-27) after BEL, the 6- and 12-month FFS rates were 82.3% (95% CI [71.9-89.2]) and 72.2% [60.0-81.3], respectively. The mLSS scores showed gradual decline pattern over time: 25.9 ± 1.6 (mean±SE; n=87), 19.0±1.8 (n=59), 16.7±2.3 (n=34), and 16.9±2.7 (n=20) at baseline, 3, 6, and 12 months ($p<0.001$ by repeated measures using GLM). Compared to the baseline, the mLSS was reduced by 4.4 ± 0.9, 6.1 ± 1.5, and 8.3 ± 2.2 at 3, 6, and 12 months, respectively. The proportion of patients who achieved a CMI-mLSS at 3, 6, and 12 months was 46% (n=27/59), 53% (n=18/34), and 65% (n=13/20); when analyzed for the best improvement, 62% (n=37/60) of the patients showed a CMI-mLSS. When comparing both the continuous mLSS and the proportion of CMI-mLSS to overall response rate and clinical benefit, the only difference was found in patients with a CMI-mLSS at 6 months (76%, n=13/17), who had a higher clinical benefit rate compared to those without a CMI-mLSS (33%, n=5/15; $p=0.031$). Similarly, the mean FSS scores were 4.2±0.4 (n=48), 2.4±0.5 (n=25), 2.4±0.7 (n=14), and 2.3±0.9 (n=8) at baseline, 3, 6, and 12 months, suggesting a significant reduction of fibrotic component of cGvHD over time with BEL therapy ($p<0.001$ by GLM). The proportion of patients who achieved a CMI-FSS at 3, 6, and 12 months was 20% (n=5/25), 43% (n=6/14), and 62%

(n=5/8). When analyzed for the best improvement within 12 months of BEL treatment, 31% (n=8/26) showed a CMI-FSS. Except for the eating/digestion domain (15%), a minimum of 30% of patients demonstrated a CMI in each domain; the highest CMI was reported in muscle/joints (58%), followed by eye/mouth (54%), skin (50%), breathing (42%), energy (38%), and mental/emotional health (31%).

Conclusion: Our study reports a significant improvement in symptom burden with BEL therapy, as measured by the mLSS, over time. While it is challenging to observe objective response in fibrotic component of cGvHD only by NIH consensus criteria, the mLSS is a feasible and practical tool for capturing early clinical improvement, esp. fibrotic component, following BEL treatment, This highlights the importance of longitudinal monitoring of the mLSS and the urgent need for a reliable tool to assess symptom burden improvement with novel cGVHD therapies.