Canadian Hematology Today

Canadian Hematology Today @ ASH 2025

Event Summary

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catalytic health
medical minds meet here

In This Report

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Acronyms

ALL	ACUTE LYMPHOBLASTIC LEUKEMIA
AML	ACUTE MYELOID LEUKEMIA
ASH	AMERICAN SOCIETY OF HEMATOLOGY
AVD	DOXORUBICIN, VINBLASTINE, DOXORUBICIN
BCMA	B-CELL MATURATION ANTIGEN
BEACOPP	BLEOMYCIN, ETOPOSIDE, ADRIAMYCIN, CYCLOPHOSPHAMIDE, VINCRISTINE, PROCARBAZINE, PREDNISONE
BMI	BODY MASS INDEX
BRECADD	BRENTUXIMAB VEDOTIN, ETOPOSIDE, CYCLOPHOSPHAMIDE, DOXORUBICIN, DACARBAZINE, AND DEXAMETHASONE
BR	BENDAMUSTINE-RITUXUMAB
BV-AVD	BRENTUXIMAB VEDOTIN PLUS AVD
BVd	BORTEZOMIB, DOXORUBICIN, AND DEXAMETHASONE
CAR	CHIMERIC ANTIGEN RECEPTOR
CCTG	CANADIAN CANCER TRIALS GROUP
CHLORO	CHLORAMBUCIL PLUS OBINUTUZUMAB
CLL	CHRONIC LYMPHOCYTIC LEUKEMIA
CML	CHRONIC MYELOID LEUKEMIA
CPX-351	CYTARABINE AND DAUNORUBICIN
CRS	CYTOKINE RELEASE SYNDROME
DLBCL	DIFFUSE LARGE B-CELL LYMPHOMA
DOAC	DIRECT ORAL ANTICOAGULANT
DPd	DARATUMUMAB, POMALIDOMIDE, DEXAMETHASONE
DRD	DARATUMUMAB, LENALIDOMIDE, DEXAMETHASONE
DVRd	DARATUMUMAB, BORTEZOMIB, LENALIDOMIDE, DEXAMETHASONE
DVd	DARATUMUMAB, BORTEZOMIB, DEXAMETHASONE
DVT	DEEP VEIN THROMBOSIS
EFS	EVENT-FREE SURVIVAL
EPOCH-R	ETOPOSIDE, PREDNISONE, VINCRISTINE, CYCLOPHOSPHAMIDE, DOXORUBICIN, RITUXIMAB
FCR	FLUDARABINE, CYCLOPHOSPHAMIDE, RITUXIMAB FL FOLLICULAR LYMPHOMA
FR	FLUDARABINE-RITUXUMAB
ICANS	IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME
IMS	INTERNATIONAL MYELOMA SOCIETY
ISAVRD	ISATUXIMAB, BORTEZOMIB, LENALIDOMIDE, DEXAMETHASONE

Acronyms con't

ISTH	INTERNATIONAL SOCIETY ON THROMBOSIS AND HAEMOSTASIS
MCL	MANTLE CELL LYMPHOMA
MDS	MYELODYSPLASTIC SYNDROMES
MRD	MINIMAL RESIDUAL DISEASE
NIVOAVD	NIVOLUMAB PLUS AVD
ORR	OVERALL RESPONSE RATE
OS	OVERALL SURVIVAL
PET	POSITRON EMISSION TOMOGRAPHY
POLABR	POLATUZUMAB VEDOTIN, BENDAMUSTINE, RITUXIMAB
POLA-R-CHP	POLATUZUMAB VEDOTIN, RITUXIMAB, CYCLOPHOSPHAMIDE, DOXORUBICIN, PREDNISONE
PFS	PROGRESSION-FREE SURVIVAL
R/R	RELAPSED/REFRACTORY
R-CHOP	RITUXIMAB, CYCLOPHOSPHAMIDE, HYDROXYDAUNORUBICIN, VINCRISTINE, PREDNISONE
RBC	RED BLOOD CELL
SLL	SMALL LYMPHOCYTIC LYMPHOMA
TKI	TYROSINE KINASE INHIBITOR
TEAE	TREATMENT-EMERGENT ADVERSE EVENTS
TRAE	TREATMENT-RELATED ADVERSE EVENT
VEN-HMA	VENETOCLAX IN COMBINATION WITH HYPOMETHYLATING AGENTS
VTE	VENOUS THROMBOEMBOLISM
VRD	BORTEZOMIB, LENALIDOMIDE, DEXAMETHASONE

Welcome & Opening Remarks


DIEGO VILLA, MD, MPH, FRCPC
ERIC TSENG, MD

Dr. Diego Villa and Dr. Eric Tseng welcomed everyone to the meeting and introduced the meeting's objectives:

- Provide current and high-quality information on the latest developments in the management of hematologic disease
- Create collegial learning opportunities that enable clinicians to directly apply new insights to their practice
- Respond to emerging professional needs for specific and in-depth information on the latest therapies and approaches to disease management in the Canadian market

Keynote: Building a Successful Career in Canada: Reflections and Thoughts

LAURIE SEHN, MD, MPH, FRCPC

Dr. Sehn began by sharing her career trajectory. She attended McGill University for both undergraduate studies and medical school. She then decided to pursue an internal medicine residency in New York City. She recommended stepping outside of one's "natural habitat," noting that practicing in a different clinical setting broadened her perspective and expanded her career opportunities.

After discovering an interest in oncology during her residency, Dr. Sehn pursued a combined hematology-oncology fellowship at the Dana-Farber Brigham Cancer Center. While in Boston, Dr. Sehn also pursued a Master's of Public Health. This made her comfortable discussing research methodology and statistics and designing clinical research trials. She recommended hematologists who are interested in clinical research pursue the "nuts and bolts training" of a public health or similar program.

Dr. Sehn encouraged trainees to actively seek mentors who model the career they aspire to build. She recommended formalizing the relationship, by directly asking the person if they would be willing to provide mentorship. Of course, mentorship is a two-way street, involving proactive steps on the trainee's part to identify the skills and knowledge they wish to gain.

Pursuing one's career ambitions while protecting personal time was a key message of Dr. Sehn's talk.

Dr. Sehn emphasized that creating work-life balance requires constant recalibration, and she encouraged the physicians in attendance to fit their work and research commitments into their family life, rather than vice versa. She recommended finding creative ways to build in travel, fitness, and family time. For example, she takes her family with her to the ASH meeting, so they can all go to Disney World together.

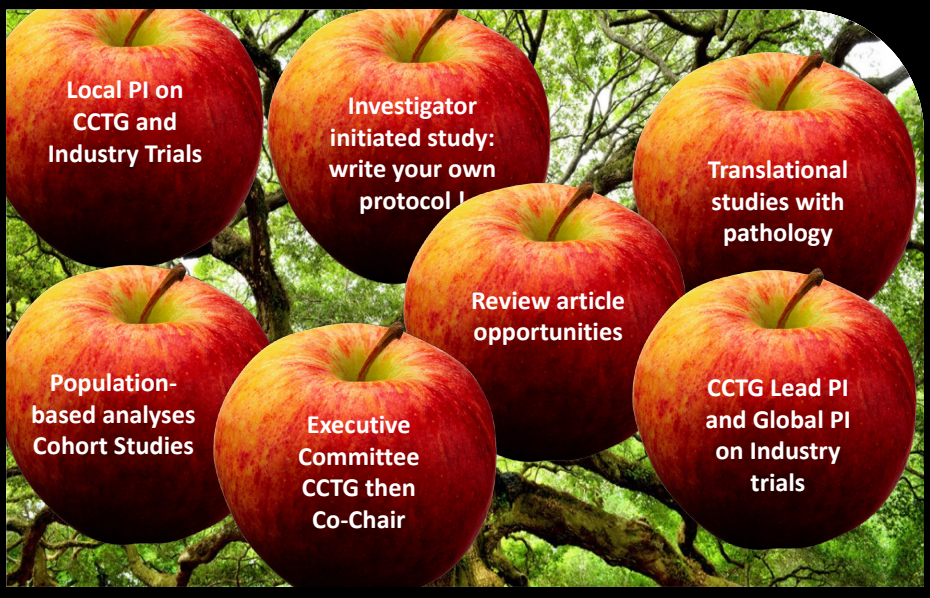
Dr. Sehn explained that Canadian hematologists are typically offered little protected research time. She recommended starting with small, manageable projects such as industry-sponsored studies, cohort studies, or population-based analyses of existing databases. Noting "there is no project that is too small," Dr. Sehn explained that all research offers the experience of submitting content to journals and writing an abstract and paper, and the opportunity to grow one's reputation in the field. In addition, Dr. Sehn recommended seeking speaking opportunities, including abstract presentations, as these allow physicians to meet other investigators and sponsors. She also encouraged physicians to write their own study protocol, as this represents a powerful learning opportunity.

Engaging with national organizations like the Canadian Cancer Trials Group and Canadian Research Institute are other ways to find networking, mentorship, and leadership opportunities. Again, Dr. Sehn recommended starting gradually, with a local chairmanship, for example, and leveraging these early opportunities to eventually lead trials and rise in leadership roles. Dr. Sehn also encouraged young researchers to become an expert in a niche topic, in addition to pursuing broader research topics. This way, young researchers can become "go-to" speakers or researchers on a niche topic.

Collaboration was another central theme of Dr. Sehn's talk. She advised working with colleagues who are doing similar work, such as translational scientists or pathologists. For example, an early career hematologist could approach a senior physician about coauthoring a review article for a journal such as *Blood*, to build up their name recognition. In addition to collaborating with people at one's institution, Dr. Sehn recommended finding collaborators outside of one's own institution as well, by asking mentors for recommendations and attending meetings.

Finally, Dr. Sehn stressed the importance of adaptability, persistence, and enjoying the journey. She emphasized that career development is incremental, and each new project helps clinical researchers better understand their own interests. She urged trainees to "throw darts" – to try new ideas, take calculated risks, and let small projects build into larger opportunities.

Clinical Research Career



Multiple Myeloma at ASH 2025

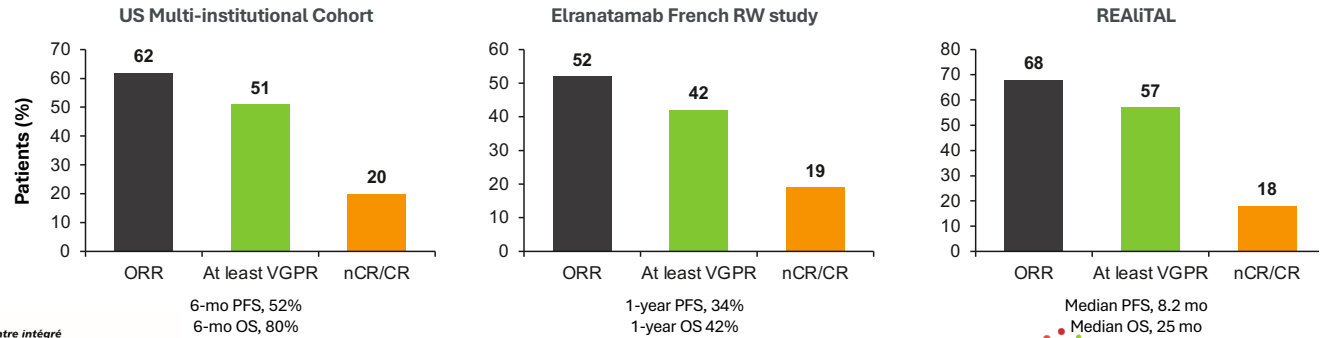
JEAN-SEBASTIEN CLAVEAU, MD

Dr. Claveau began by outlining current treatment standards in Canada for newly diagnosed multiple myeloma. For transplant-eligible patients, clinicians now routinely use DVRd. Evidence supporting this strategy comes from several trials including PERSEUS, which reported a 4-year PFS of 84% for patients receiving DVRd compared with approximately 68% for patients receiving VRd. The German HD7 study, which compared IsaVRD versus VRd, offers similar benefits (48-month PFS estimates are 76% for IsaVRd versus 69% for VRd). Updated findings presented at the IMS meeting, based on modelling analyses, suggest an estimated median PFS close to 17 years for patients who receive four cycles of DVRd induction, followed by autologous stem cell transplant, two cycles of consolidation with DVRd, and daratumumab maintenance. This represents a major shift from the era when expected survival in myeloma was approximately 5 to 6 years.

Most transplant-ineligible patients in Canada receive DRD, based on results of the MAIA trial, but quadruplet therapies (including DVRD and IsaVRD)

Real-world Outcomes with Bispecific Antibodies[1-3]

	Teclistamab	Elranatamab	Talquetamab
	US Multi-institutional Cohort N=110	French Cohort N=101	RealiTAL N=93
Prior lines of therapy, median (range)	6 (3–13)	5 (1–17)	5 (2–16)
Extramedullary disease	44%	36%	22%
High-risk cytogenetic profile	62%	36%	73%
Penta-drug refractory disease	76%	22%	40%
Prior BCMA-targeted therapy	35%	17%	25%



1. Mohan M, et al. *Blood Cancer J*. 2024;14(1):35. 2. Riedhammer C, et al. *Leukemia*. 2024;38:365-371. 3. Utlerval K. et al, EHA2025

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are being adopted in this setting in recent months. The MAIA trial demonstrated a median 6-year-period PFS of 52%. In contrast, the CEPHEUS trial, evaluating DVRd in non-transplant-eligible patients, has demonstrated an estimated a median PFS of almost 8 years.

Building on these recent advances, multiple myeloma researchers are turning to the integration of newer agents, such as CAR-T cells and bispecific antibodies, into first-line care. Abstract 654 examines linvoseltamab, a bispecific antibody, in both transplant-eligible and ineligible patients. Early results suggest favourable responses (ORR of 79%). All CRS events were grade 1 and only one ICANS event was reported. The second abstract (655), from a Chinese research group, reports on a BCMA- and CD19-targeted CAR T-cell therapy, following two cycles of VRd. Although the study involved a small cohort, all patients responded, and 100% had MRD negativity by flow cytometry. All CRS events were grade 1 and only one ICANS event was reported. The 30-month PFS was 88%. While it is unlikely that CAR T-cell therapy will be available in the near future for newly diagnosed patients in Canada, the study findings are nonetheless hopeful.

Dr. Claveau then described the treatment landscape in R/R myeloma in Canada. Patients now have access to teclistamab and elranatamab. Bispecific antibodies generally achieve ORRs of 50% to 70%, though responses are poorer in patients with high-risk cytogenetics, high tumour burden, and extramedullary disease. The REDIRECTT-1 trial (abstract 698) evaluated teclistamab and talquetamab in patients with high-risk, extramedullary disease, showing response rate of 78% and a 1-year PFS of 56%, which is notable given the very poor prognosis of these groups.

To decrease the incidence of CRS, prophylactic tocilizumab has been shown to reduce CRS rates, with the MAJESTEC study showing prophylactic tocilizumab resulted in a 65% relative reduction of CRS. Abstract 5794 showed rates of CRS were 10% and rates of ICANS were 5% among 40 R/R multiple myeloma patients receiving prophylactic tocilizumab in a Canadian setting.

Dr. Claveau then highlighted two late-breaking abstracts. The first study followed three patients who received in vivo CAR-T product. All reached MRD negativity at 1 month, with manageable cytopenias and no infections. The second late-breaking abstract reports impressive results from the MAJESTEC-3 of teclistamab with daratumumab versus standard daratumumab-based regimens (DPd or DVd) in R/R multiple myeloma patients. The 3-year PFS was 83%, compared to 30% in the control arms. Non head-to-head analyses show these results are comparable or even superior to results with cilta-cel and BVd, pointing to promising options in the future for R/R multiple myeloma patients in Canada.

Leukemia at ASH 2025

MOHAMED ELEMARY, MD, MSC, PHD, FRCP

Dr. Elemary reviewed selected leukemia-focused abstracts at ASH 2025, focusing on those with relevance to Canadian practice. Beginning with AML, Dr. Elemary discussed abstract 3418, which reports on outcomes of revumenib from the phase 2 AUGMENT-101 trial in R/R *NPM1* acute leukemia. The complete response rate was 26%, and the therapy was effective regardless of the type of previous therapy (responses were highest, however, in the five patients who had previously received a IDH1 or IDH2 inhibitor). Abstract 1001 describes revumenib in R/R AML patients with *KMT2Ar* mutations. In AML and ALL, complete response rates were 23%. Discussing safety results, Dr. Elemary noted that 27% of ALL patients and 58% of AML patients had a grade 3 or above TRAE.

Moving to FLT3 inhibitor therapy, Dr. Elemary shared long-term data from MD Anderson evaluating the triplet regimen of venetoclax, azacitidine, and gilteritinib in newly diagnosed *FLT3*-mutated AML, 23% of whom had RAS-pathway mutations (abstract 45). In 30 patients, the triplet achieved a complete response rate of 96% and MRD negativity of 93%. Patients who proceeded to transplant had better outcomes, supporting continued use of stem cell transplant. The 3-year

Mutation Subgroups

Mutation	CPX-351 CR/CRi (%)	Ven-HMA CR/CRi (%)
NPM1-mut	*100*	*89*
TP53-mut	*32*	*45*
IDH1-mut	*60*	*76*
IDH2-mut	*63*	*77*
SF3B1-mut	*71*	*45*
STAG2-mut	*44*	*86*
CEBPA-mut	50	88

Conclusions

- **Ven-HMA is at least as effective as CPX-351** in ND-AML, including AML-MR—**despite CPX-351 being used in younger/fitter patients**.
- **Ven-HMA appears less toxic**, with fewer infectious complications.
- Subgroup differences (especially **post-MDS AML** favoring Ven-HMA and ***SF3B1-mut* AML** favoring CPX-351) warrant further study.
- Findings may help develop **mutation-specific predictive models** for treatment selection.

relapse-free survival was reported at 43% and OS at 46%, which is significant for a non-intensive treatment approach.

Another important study (abstract 1602) evaluated CPX-351 versus venetoclax-azacitidine in 600 patients, showing that venetoclax-azacitidine remains an ideal treatment approach when compared with a more intensive therapy. The complete response rates were 55% among patients who received CPX-351 compared to 60% among patients who received venetoclax-azacitidine, while the median OS was 10 months for CPX-351, versus 13 months for venetoclax-azacitidine. For patients with post-MDS AML, the median OS was 15 months with venetoclax-azacitidine compared to 8 months with CPX-351. Patients with *SF3B1* mutations appeared to respond particularly well to CPX-351, while responses were superior with venetoclax-azacitidine among patients with *STAG2* and *CEBPA* mutations, potentially opening the door to individualized approaches in the future according to mutational status.

In MDS, Dr. Elemary emphasized a subgroup analysis from the COMMANDS trial (abstract 792), a phase 3 study comparing luspatercept with epotin alfa. The trial showed that luspatercept was superior across all subgroups, including patients with low baseline endogenous erythropoietin levels (<100 U/L), a group previously thought most likely to benefit from erythropoietin replacement.

In ALL, research in 2025 centred around blinatumomab. Abstract 439 reported on the final results of the phase 3 GIMEMA ALL2820 trial comparing ponatinib plus blinatumomab to imatinib and age-adjusted chemotherapy for newly diagnosed adult Ph+ ALL patients. Complete hematologic response and MRD negativity rates were significantly better in the experimental arm. The 18-month EFS rate was 89.9% in the blinatumomab arm, versus 76.8% in the control arm. Dr. Elemary also reviewed abstract 643, confirming the benefit of blinatumomab consolidation in high-risk Ph-negative ALL, particularly for MRD-positive disease and for patients with *IKZF1* deletions. While patients in the blinatumomab group saw improved disease-free survival, OS, MRD negativity, and stem cell transplant outcomes, no benefit was seen in patients with KMT2A mutations.

In CML, Dr. Elemary focused on asciminib. The ASC4FIRST trial compared frontline asciminib with either imatinib or a second-generation TKI in newly diagnosed CML. The new ASH data focused on tolerability, showing fewer dose reductions, more symptom-free days, and improved patient-reported outcomes with asciminib. Fatigue and cognitive and social functioning scores all favoured asciminib compared to imatinib and second-generation TKI therapy.

An exploratory analysis of the ASC4FIRST trial (abstract 73) suggested that while asciminib benefits all patients regardless of ASXL1 status, results of asciminib are superior in patients without ASXL1 mutations. Persistence of ASXL1+ mutations were associated with higher risks of treatment failure and *BCR::ABL1* mutation development.

Lymphoma at ASH 2025

ROBERT KRIDEL, MD

Dr. Kridel began with frontline DLBCL management in Canada, noting that R-CHOP remains the standard therapy for most patients. Double-hit lymphoma patients are typically treated with dose-adjusted EPOCH-R. Multiple trials attempting to improve on R-CHOP have been negative. The key exception is the POLARIX trial. Recent 5-year data presented in July demonstrated a 6% PFS benefit with Pola-R-CHP compared to R-CHOP. In the relapse setting, the treatment landscape has shifted toward use of CAR T-cell therapy in the second line, supported by the ZUMA-7 and TRANSFORM trials. Auto-transplant remains an option for selected patients. PolaBR and third-line bispecific antibodies also play important roles.

Dr. Kridel highlighted abstract 475, assessing tucidinostat plus R-CHOP in untreated MYC/BCL2 double-expressor DLBCL patients in a randomized phase 3 study. The 3-year EFS was 56.8% in the tucidinostat plus R-CHOP arm versus 47.7% in the R-CHOP arm.

Another novel combination, R-Pola-Glo, also showed high and durable response rates (ORR 96% 1-year PFS rates of 85%, and 1-year OS rates of 90%) in elderly and frail patients (abstract 61). Toxicities included a CRS rate of 31%, most of which were low-grade, and a 4% rate of ICANS; 22% of patients experienced grade 3 to 5 infections, of

Ongoing frontline, randomized trials in FL
Theme: chemo-free

Trial	Experimental arm	Comparator	Phase
EPCORE FL-2	Epcoritamab + R2	R2	III
GOLSEEK-2	R-golcadomide	Immunochemotherapy	II
MorningLyte	Mosunetuzumab + lenalidomide	Immunochemotherapy	III
OLYMPIA-1	Odronextamab	Investigator's choice	III
OLYMPIA-2	Odronextamab + chemo	Rituximab-chemo	III
SOUNDTRACK-F1	AZD0486 (surovatamig) + rituximab	Immunochemotherapy	III
SWOG 2308	Mosunetuzumab	Rituximab	III

which three were fatal. Dr. Kridel noted these results are encouraging, warranting further study of the combination.

In relapsed DLBCL, Dr. Kridel highlighted a large real-world cohort of 312 patients treated with either epcoritamab or glofitamab (abstract 402). Dr. Kridel explained that 42% of those who progressed after bispecific therapy received no further therapy and among those treated, outcomes were extremely poor, with median OS of only 4 months. In a hopeful development, abstract 480 reports on a BCL6 degrader achieved promising response rates in a heavily pretreated population, with an ORR of 73% and complete response rate of 21% (36% in FL versus 11% in DLCBL).

Turning to FL, Dr. Kridel noted that in advanced, high tumour-burden FL, bendamustine-rituximab remains the most common frontline therapy in Canada. Relapsed FL treatment is variable, with options including retreatment with chemotherapy or lenalidomide-rituximab.

Abstracts 1807 and 228 centre on mosunetuzumab therapy in low- and high-tumour burden FL in the frontline setting. The ORR was 98% and the 12-month PFS was 98% in the low tumour-burden patients, compared to 87% and 86%, respectively, in the high-tumour burden patients. Abstract 3600 similarly reports strong efficacy of odronextamab combined with chemotherapy in a phase 2 study. Ongoing trials are studying chemotherapy-free regimens for FL patients.

In the R/R FL setting, Dr. Kridel highlighted abstract 466, reporting on the phase 3 EPCORE FL-1 trial of epcoritamab plus rituximab-lenalidomide. The novel combination produced an ORR of 96%, a complete response rate of 75%, and a hazard ratio for PFS of 0.21. Toxicities included high rates of grade 3 and 4 neutropenia and infections. Dr. Kridel noted the regimen could establish a new benchmark for chemo-free therapy in R/R FL.

In MCL, Dr. Kridel described the early results of a trial comparing acalabrutinib, venetoclax, and rituximab in treatment-naïve MCL patients. In 108 patients, the ORR was 95% (88% in those with *TP53* mutations) and complete response rates were 54%. Among the few patients who have completed induction, 100% were MRD-negative. Noting that MCL patients who are referred for CAR T-cell therapy often have rapidly progressing disease, Dr. Kridel highlighted GLPG510, a novel CAR T-cell product that has a remarkable 7-day time from apheresis to infusion. In 20 patients, the complete response rate was 100% with an MRD negativity of 89% and a 12-month PFS of 83% (abstract 662).

In Hodgkin lymphoma, Dr. Kridel reviewed updated results from the S1826 trial (abstract 151), confirming sustained PFS benefit of NivoAVD over BV-AVD, especially in patients older than 60 (3-year PFS was 82% for NivoAVD versus 58% for BV-AVD in this subgroup). He also reviewed the positive results from a large German trial evaluating PET-guided BrECADD versus eBEACOPP in advanced-stage classical Hodgkin lymphoma (abstract 152). The 5-year PFS was 93.6% in the BrECADD arm, compared to 90.6% in the control arm, and the trial demonstrated notably less toxicity and a shorter treatment duration with PET-guided BrECADD.

Chronic Lymphocytic Leukemia at ASH 2025

ALINA GERRIE, MD

Dr. Gerrie organized her overview around four major themes: the optimization of time-limited frontline therapies, novel targeted agents, immune-based strategies, and new data in Richter transformation.

She began with the plenary session on the CLL17 study. This study has potential practice-changing implications as it compared fixed-duration venetoclax-obinutuzumab, venetoclax-ibrutinib, and continuous ibrutinib monotherapy in frontline CLL over nearly 3 years of follow-up. There was no PFS difference across all 3 arms, despite that patients in the time-limited arms had been off therapy for almost 2 years at the 3-year assessment. However, the PFS results of venetoclax-obinutuzumab were slightly lower among TP53-mutated patients (62% compared to 69% and 79% for venetoclax-ibrutinib and continuous ibrutinib monotherapy respectively). Overall survival was similar across treatment groups.

The UK FLAIR platform trial compared MRD-guided ibrutinib plus venetoclax against two control arms: ibrutinib with or without rituximab, and FCR.

Canada's Drug Agency Funding Algorithm for CLL/SLL (Jan. 2025)

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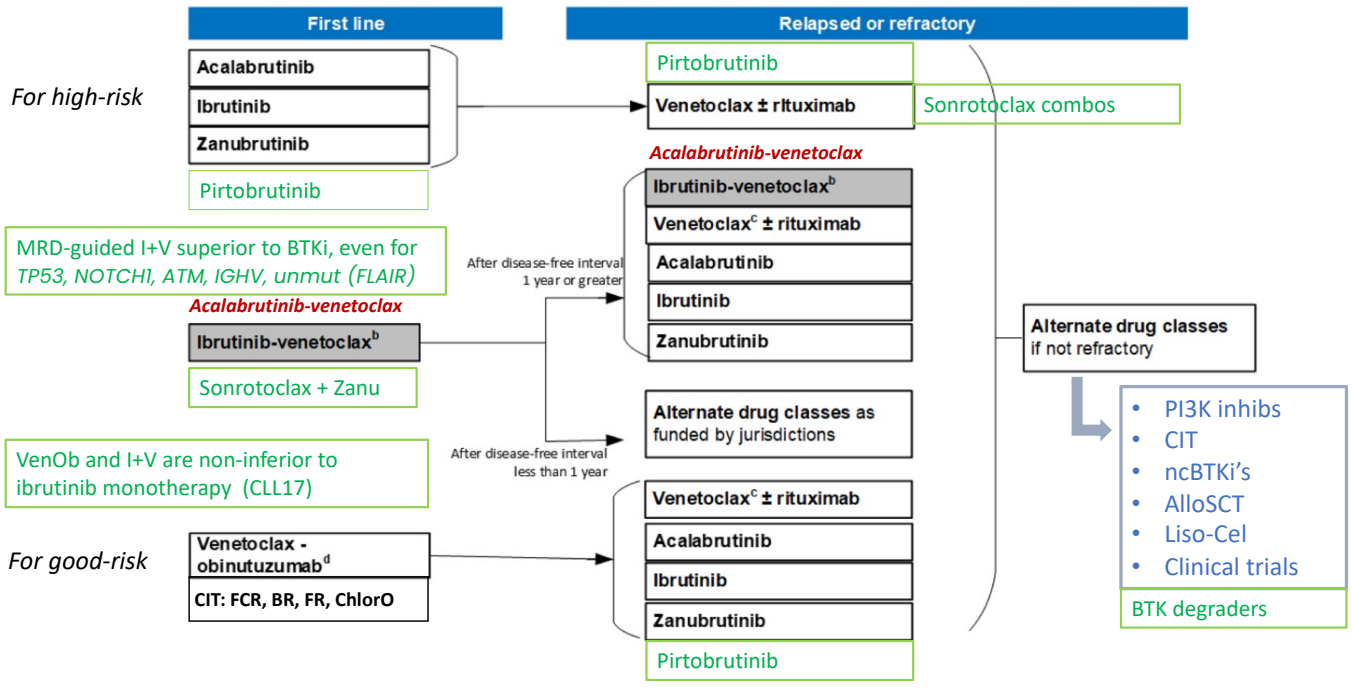


Five-year PFS results presented at ASH 2025 showed that 100% of patients who had TP53-mutations and received ibrutinib and venetoclax arms are in remission, versus 82% in the ibrutinib +/- rituximab and 44% in the FCR group. Abstract 796 describes resistance development in the three groups in the UK FLAIR trial. Among small numbers of patients with progression who had mutational testing, 21% developed BTK mutations. None of the patients in the time-limited ibrutinib and venetoclax cohort developed a BTK mutation.

Dr. Gerrie also highlighted early data for sonrotoclax combined with obinutuzumab, noting high response rates and the absence of tumour lysis syndrome outside of the initial obinutuzumab infusion (abstract 793). A large phase 3 trial is underway comparing sonrotoclax-obinutuzumab versus sonrotoclax-rituximab and venetoclax-rituximab in the R/R setting.

The late-breaking abstract (3) on pirtobrutinib versus bendamustine plus rituximab in patients with CLL/SLL is also significant, as it is the first study to evaluate pirtobrutinib in the frontline setting. Pirtobrutinib demonstrated superior 2-year PFS (93%) compared with bendamustine-rituximab (70%), with benefit observed across all subgroups, including patients with IGHV-mutated disease. Overall survival was also superior in the pirtobrutinib arm, despite a crossover rate of 50%. Toxicity was favorable, with only 4% of patients discontinuing for adverse events, and very low rates of atrial fibrillation. A separate head-to-head study (abstract 683) showed pirtobrutinib was non-inferior to ibrutinib in both treatment-naïve and R/R patients, again with lower rates of atrial fibrillation and hypertension.

Dr. Gerrie then reviewed emerging data on BTK degraders, starting with updated efficacy and safety results of the BTK degrader BGB-16673 in patients with R/R CLL/SLL (abstract 82). At 12 months of follow-up, the ORR was 86%, complete response rates were 4.6% and 12-month PFS was 79% in heavily pretreated patients. Bexobrutideg, another novel BTK degrader, demonstrated similar efficacy and safety results in a phase 1a/b trial in R/R CLL (abstract 86). The ORR was 79% and responses deepened over time.

Moving on to immune-based therapies, Dr. Gerrie described a real-world, retrospective series of 30 patients treated with lisocabtagene maraleucel after a median of 6 prior lines of therapy. Interestingly, 90% of patients had prior non-covalent BTK inhibition. Despite this, the ORR was 83% and the complete response rate was 60%, which was higher than trial outcomes. Dr. Gerrie highlighted that 60% of patients had recently received pirtobrutinib, and these patients saw complete response rates of 72%, suggesting pirtobrutinib may be an important bridging therapy.

Finally, Dr. Gerrie summarized new epcoritamab data in Richter transformation. In heavily pretreated patients, epcoritamab monotherapy achieved a moderate ORR of 48% in chemotherapy-ineligible patients, while epcoritamab plus lenalidomide resulted in an ORR of 82% in chemotherapy-ineligible patients and epcoritamab with R-CHOP resulted in an ORR of 73% in treatment-naïve patients with Richter transformation. Median PFS remained poor, at 10 months in those treated with epcoritamab with R-CHOP and 6 months among those treated with epcoritamab plus lenalidomide.

Dr. Gerrie closed by highlighting how the new data may shape therapies for CLL in Canada (see image).

Thrombosis at ASH 2025

YAN XU, MD, FRCPC, MSC

Canadian guidelines for managing a first unprovoked VTE have long recommended that patients continue long-term anticoagulation therapy. Previous trials, including AMPLIFY-Extension and EINSTEIN-Choice, demonstrated that long-term DOACs result in clear reductions in VTE recurrence without a significant increase in bleeding. However, the studies did not compare full-dose versus low-dose therapy.

The RENOVE trial, published in Lancet this year, followed more than 2,000 patients who were randomized to receive full-dose or low-dose DOAC therapy after completing 6 to 24 months of full-dose anticoagulation. Both groups had low VTE recurrence rates over 5 years (2.2% in the low-dose DOAC arm versus 1.8% with full-dose therapy). Due to the low overall rate of events, the trial did not meet the non-inferiority endpoint. However, low-dose DOAC therapy was associated with a 60% reduction in bleeding events, compared to full-dose therapy.

In another recent development, the COBRRA trial compared apixaban with rivaroxaban in the acute treatment phase. The trial, presented this year at ISTH, found apixaban was associated with a 60% relative risk reduction in clinically relevant bleeding and a nearly 90% relative risk reduction in major

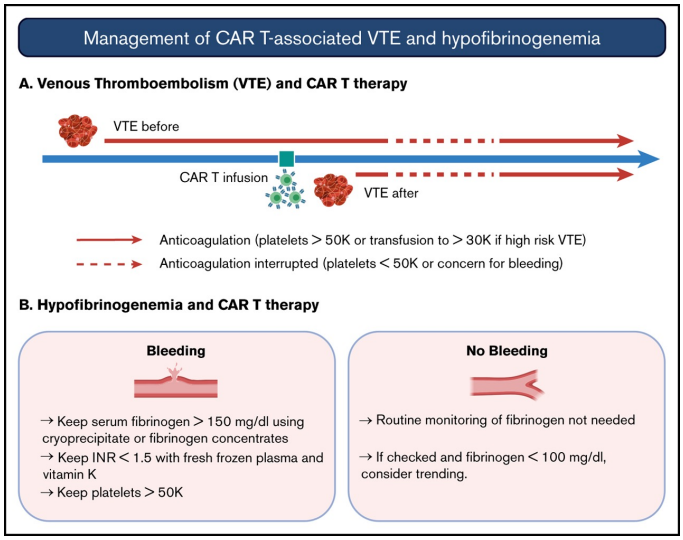
CAR-T and VTE – Summary

VTE in CAR-T patients is common in absence of prophylaxis (7–9%)

- Typically front-loaded (within first 30–60 days of infusion)

CAR-T associated coagulopathy especially hypofibrinogenemia) and bleeding risk is a challenge

- However, existing cohorts suggest safety of prophylactic A/C
- Generally used fibrinogen top-up (threshold not clear in setting of A/C but at least 1 g/L)



bleeding. This data raises the question of whether apixaban leads to better overall patient outcomes in the secondary prevention phase. To answer this, Dr. Francis Couturaud and colleagues conducted a post-hoc analysis of over 2,700 patients enrolled in the RENOVE study. Noting that treatment choice was not randomized, Dr. Xu explained the analysis found no significant difference in bleeding between the two agents when used as secondary prevention. VTE recurrence rates were similar across groups.

Shifting to cancer-associated thrombosis, Dr. Xu underscored that the VTE recurrence risk is higher in this setting, compared to unprovoked VTE. In 2002, Dr. Prandoni and colleagues demonstrated one in five patients with active cancer had a symptomatic recurrent event after stopping anticoagulant therapy. A 2023 study from Japan showed that even for distal cancer-associated DVTs, VTE recurrence rates were 8.5% in those who had 3 months of anticoagulation therapy versus 1.2% in patients who continued the therapy for 1 year. The data thus supports extended anticoagulation in this population.

The API-CAT trial suggests low-dose therapy is appropriate in the setting of cancer-associated VTE. The trial followed more than 800 patients with active cancer and symptomatic DVT or pulmonary embolism at high risk of recurrence. Dr. Xu noted that pancreatic and gastrointestinal cancers (the most prothrombotic cancer types) were underrepresented in the trial. After a median of 8 months of initial therapy, patients were randomized to continue either full-dose or low-dose apixaban. Low-dose therapy was non-inferior for preventing VTE recurrence and reduced major and clinically relevant bleeding by approximately 25%.

Dr. Xu then summarized data from the Dutch "Follow that CAR" registry, which included 240 patients treated mainly with axicabtagene ciloleucel (Abstract 315). Thrombosis occurred in 15 patients, with a 1-year cumulative incidence rate of 6.6%. In addition, 25 patients experienced bleeding, 11 of which were major bleeding events and one of which was fatal. The 1-year cumulative incidence of bleeding was 11%. The median time to thrombosis was 28 days. A subgroup analysis showed that prophylactic-dose anticoagulation was not significantly associated with a higher risk of bleeding compared with no anticoagulation. However, therapeutic-dose anticoagulation was associated with markedly higher bleeding risk, compared to those who did not receive anticoagulation therapy (21% versus 7%). Summarizing the trial, Dr. Xu explained that VTE in patients who receive CAR T-cell therapy is common in the absence of prophylaxis (7% to 9%). While the risk of VTE must be balanced with respect to the risk of CAR T-cell therapy-associated hypofibrinogenemia, the cohort study suggests prophylactic anticoagulation is safe in this setting. While opinions vary, many clinicians use a fibrinogen replacement threshold of at least 1 g/L when providing prophylactic anticoagulation in this setting.

Benign Hematology at ASH 2025

SIRAJ MITHOOWANI, MD

Dr. Mithoowani reviewed six oral abstracts in classical hematology, which he found to be interesting and clinically relevant. He began with abstract 307, on the long-term safety and effectiveness of systemic bevacizumab for chronic severe bleeding in idiopathic gastrointestinal angiodysplasia, esophageal varices, and angiodysplasia of von Willebrand Disease and acquired von Willebrand syndrome. Patients with this condition often require frequent red blood cell transfusions and intravenous iron. In a cohort of 23 older, comorbid patients treated with bevacizumab, the need for hematologic support dropped from a mean of 14.2 red blood cell units before therapy to 0.6 units in the 7 to 12 months after treatment. TEAEs included proteinuria (30%), hypertension (26%) and fatigue (13%), with three treatment-related discontinuations. There were no VTE or arterial thromboembolism events. Although non-randomized, the trial points to a promising option for a population with high transfusion burden and frequent emergency department visits.

The second abstract (8) examined clonal hematopoiesis in sickle cell disease. Using archived blood samples from more than 7,000 individuals, investigators assessed the prevalence of clonal

Changes in complete blood count (CBC) and white blood cell (WBC) differential associated with overweight and obesity: A patient-level meta-analysis of randomized trials

Results

- 2,904 overweight and obese individuals (BMI range 26.5–51.4 kg/m^2), 22.4% male, mean age 46 yrs, 95% White

CBC parameter	Pooled meta-analysis regression coefficient (per 1kg/m^2 BMI)
WBC	**+0.06 x 10^9**
Platelet count	+0.84 x 10^9
ALC	**+0.01 x 10^9**
ANC	**+0.04 x 10^9**
RBC	+0.01 x 10^{12}
Hemoglobin	-0.04 x 10^9
MCV	-0.05 fL

Session: 905. Outcomes Research: Non-Malignant Conditions Excluding Hemoglobinopathies (4:45pm)

hematopoiesis across predefined gene categories, including epigenetic regulators *(DNMT3A/TET2)* and DNA damage response genes *(TP53, PPM1D, CHEK2, ATM)*. The study found 6,661 clonal hematopoiesis variants in 2,673 individuals. Clonal hematopoiesis occurred earlier and was more prevalent in sickle cell disease compared to non-sickle-cell disease controls, and was largely driven by an increased prevalence of DNA-damage response genes. There was no increased prevalence of *TP53* mutations in patients with sickle cell disease. Dr. Mithoowani noted the findings suggest a biological basis for the elevated risk of myeloid leukemia observed in sickle cell disease.

Dr. Mithoowani then highlighted the multi-centre, double-blinded, randomized PROLONG trial (abstract 736). In the first phase, patients with immune thrombocytopenia who were refractory to corticosteroids were randomized to either rituximab and dexamethasone or rituximab alone. In the second phase, the study randomized the responders to receive maintenance rituximab or no maintenance therapy. The study showed that even among patients who didn't respond to corticosteroids, rituximab plus dexamethasone produced higher response rates than rituximab alone, and delayed the time to first bleeding event. Dr. Mithoowani encouraged his colleagues to attend the presentation for the results of the second phase of the trial.

Noting that classical hematologists receive many referrals for benign complete blood count changes, Dr. Mithoowani turned to a patient-level meta-analysis (abstract 1094) that explored how obesity affects complete blood count parameters. Using data from five randomized trials involving approximately 2,900 overweight and obese individuals, investigators found that a high BMI was associated with small increases in leukocyte, neutrophil, lymphocyte, platelet, and red cell counts, and small decreases in hemoglobin and mean corpuscular volume. Dr. Mithoowani noted that while obesity can modestly influence laboratory results, clinicians should avoid attributing marked abnormalities to BMI.

The TRACTION trial, described in a late-breaking abstract, is a large Canadian-led study, that investigated whether routine tranexamic acid reduces transfusion requirements in major non-cardiac surgery. More than 8,200 high-risk surgical patients were included in a randomized, crossover design involving 10 hospitals. The study found that 9.8% of patients in the placebo arm required red blood cell transfusion, compared to 7.4% in the tranexamic acid group. There were no differences between the two groups in other safety outcomes, including stroke or myocardial infarction. The results support tranexamic acid as a potentially broadly applicable blood-conservation strategy.

The last study Dr. Mithoowani reviewed was late-breaking abstract on the VAYHIT2 trial, a randomized trial of ionalamab plus eltrombopag versus placebo plus eltrombopag in 152 patients with primary immune thrombocytopenia who failed first-line corticosteroid treatment. The study found ionalamab combined with either 9 mg/kg or 3 mg/kg eltrombopag prolonged the time to treatment failure and increased the proportion of patients achieving long-term remission at 6 or more months. Safety profiles were similar between groups, with no treatment-related discontinuations. Dr. Mithoowani noted that the rapid development of novel agents continues to reshape immune thrombocytopenia management.

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