

Canadian Hematology Today 2026 Rising Stars Conference

Event Summary

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Acronyms

ABC	ACTIVATED B-CELL-LIKE
ABVD	DOXORUBICIN, BLEOMYCIN, VINBLASTINE AND DACARBAZINE
AE	ADVERSE EVENT
AI	ARTIFICIAL INTELLIGENCE
alloSCT	ALLOGENEIC STEM CELL TRANSPLANTATION
AML	ACUTE MYELOID LEUKEMIA
ASCT	AUTOLOGOUS STEM CELL TRANSPLANTATION
ASH	AMERICAN SOCIETY OF HEMATOLOGY
AV / A+V	ACALABRUTINIB AND VENETOCLAX
AVO	ACALABRUTINIB, VENETOCLAX AND OBINUTUZUMAB
axi-cel	AXICABTAGENE CILOLEUCEL
BEACOPP	BLEOMYCIN, ETOPOSIDE, DOXORUBICIN, CYCLOPHOSPHAMIDE, VINCRISTINE, PROCARBAZINE AND PREDNISONE
BPd	BELANTAMAB MAFODOTIN, POMALIDOMIDE AND DEXAMETHASONE
BrECADD	BRENTUXIMAB VEDOTIN, ETOPOSIDE, CYCLOPHOSPHAMIDE, DOXORUBICIN, DACARBAZINE AND DEXAMETHASONE
brexu-cel	BREXUCABTAGENE AUTOLEUCEL
BTKi	BRUTON TYROSINE KINASE INHIBITOR
BV	BRENTUXIMAB VEDOTIN
BV-AVD	BRENTUXIMAB VEDOTIN, DOXORUBICIN, VINBLASTINE AND DACARBAZINE
BVd	BELANTAMAB MAFODOTIN, BORTEZOMIB AND DEXAMETHASONE
CAR-T / CAR T-cell	CHIMERIC ANTIGEN RECEPTOR T-CELL
CCTG	CANADIAN CANCER TRIALS GROUP
CDA-AMC	CANADA'S DRUG AGENCY–AGENCE DES MÉDICAMENTS DU CANADA
cHL	CLASSICAL HODGKIN LYMPHOMA
cilta-cel	CILTACABTAGENE AUTOLEUCEL

Acronyms con't

CLL	CHRONIC LYMPHOCYTIC LEUKEMIA
CMPA	CANADIAN MEDICAL PROTECTIVE ASSOCIATION
CMRG	CANADIAN MYELOMA RESEARCH GROUP
CNS	CENTRAL NERVOUS SYSTEM
CNS-IPI	CENTRAL NERVOUS SYSTEM INTERNATIONAL PROGNOSTIC INDEX
CR	COMPLETE RESPONSE OR COMPLETE REMISSION, ACCORDING TO DISEASE CONTEXT
CRS	CYTOKINE RELEASE SYNDROME
ctDNA	CIRCULATING TUMOUR DNA
DA-EPOCH-R	DOSE-ADJUSTED ETOPOSIDE, PREDNISONE, VINCRISTINE, CYCLOPHOSPHAMIDE, DOXORUBICIN AND RITUXIMAB
DLBCL	DIFFUSE LARGE B-CELL LYMPHOMA
DR	DARATUMUMAB AND LENALIDOMIDE
DVd	DARATUMUMAB, BORTEZOMIB AND DEXAMETHASONE
DVRd	DARATUMUMAB, BORTEZOMIB, LENALIDOMIDE AND DEXAMETHASONE
EFS	EVENT-FREE SURVIVAL
EHA	EUROPEAN HEMATOLOGY ASSOCIATION
ELN	EUROPEAN LEUKEMIANET
ESMO	EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY
ET	ESSENTIAL THROMBOCYTHEMIA
FCR	FLUDARABINE, CYCLOPHOSPHAMIDE AND RITUXIMAB
FFPE	FORMALIN-FIXED, PARAFFIN-EMBEDDED
FL	FOLLICULAR LYMPHOMA
FLAG-IDA	FLUDARABINE, CYTARABINE, GRANULOCYTE COLONY-STIMULATING FACTOR AND IDARUBICIN
FLIPI24	FOLLICULAR LYMPHOMA INTERNATIONAL PROGNOSTIC INDEX 24

Acronyms con't

G-CSF	GRANULOCYTE COLONY-STIMULATING FACTOR
GCB	GERMINAL CENTRE B-CELL-LIKE
GemOx	GEMCITABINE AND OXALIPLATIN
GI	GASTROINTESTINAL
Glofit-GemOx	GLOFITAMAB, GEMCITABINE AND OXALIPLATIN
HMA	HYPOMETHYLATING AGENT
I+V	IBRUTINIB AND VENETOCLAX
ICANS	IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME
IHC	IMMUNOHISTOCHEMISTRY
IMS	INTERNATIONAL MYELOMA SOCIETY
IMWG	INTERNATIONAL MYELOMA WORKING GROUP
IPSET-thrombosis	INTERNATIONAL PROGNOSTIC SCORE FOR THROMBOSIS IN ESSENTIAL THROMBOCYTHEMIA
IPSS-del(5q)	INTERNATIONAL PROGNOSTIC SCORING SYSTEM FOR DEL(5q) MDS
IPSS-M	MOLECULAR INTERNATIONAL PROGNOSTIC SCORING SYSTEM
IPSS-R	REVISED INTERNATIONAL PROGNOSTIC SCORING SYSTEM
IsaKd	ISATUXIMAB, CARFILZOMIB AND DEXAMETHASONE
IV	INTRAVENOUS
iwCLL	INTERNATIONAL WORKSHOP ON CHRONIC LYMPHOCYTIC LEUKEMIA
IWG	INTERNATIONAL WORKING GROUP
JCO	JOURNAL OF CLINICAL ONCOLOGY
Kd	CARFILZOMIB AND DEXAMETHASONE
LBCL	LARGE B-CELL LYMPHOMA
LDAC	LOW-DOSE CYTARABINE
Liso-cel	LISOCABTAGENE MARALEUCEL
MCL	MANTLE CELL LYMPHOMA
MDS	MYELODYSPLASTIC SYNDROMES

Acronyms con't

MM	MULTIPLE MYELOMA
MPN	MYELOPROLIFERATIVE NEOPLASM
MRD	MEASURABLE RESIDUAL DISEASE
Nivo-AVD	NIVOLUMAB, DOXORUBICIN, VINBLASTINE AND DACARBAZINE
ORR	OVERALL RESPONSE RATE
OS	OVERALL SURVIVAL
PET	POSITRON EMISSION TOMOGRAPHY
PET-CT	POSITRON EMISSION TOMOGRAPHY–COMPUTED TOMOGRAPHY
PFS	PROGRESSION-FREE SURVIVAL
PFS2	PROGRESSION-FREE SURVIVAL THROUGH THE NEXT LINE OF TREATMENT
POD24	PROGRESSION OF DISEASE WITHIN 24 MONTHS
pola-R-CHP	POLATUZUMAB VEDOTIN, RITUXIMAB, CYCLOPHOSPHAMIDE, DOXORUBICIN AND PREDNISONE
PV	POLYCYTHEMIA VERA
PVd	POMALIDOMIDE, BORTEZOMIB AND DEXAMETHASONE
QTc	HEART RATE-CORRECTED QT INTERVAL
R-CEOP	RITUXIMAB, CYCLOPHOSPHAMIDE, ETOPOSIDE, VINCRISTINE AND PREDNISONE
R-CHOP	RITUXIMAB, CYCLOPHOSPHAMIDE, DOXORUBICIN, VINCRISTINE AND PREDNISONE
R-CODOX-M/R-IVAC	RITUXIMAB WITH CYCLOPHOSPHAMIDE, VINCRISTINE, DOXORUBICIN AND METHOTREXATE, ALTERNATING WITH RITUXIMAB, IFOSFAMIDE, ETOPOSIDE AND CYTARABINE
R-GemOx	RITUXIMAB, GEMCITABINE AND OXALIPLATIN
R2	LENALIDOMIDE AND RITUXIMAB
RBC	RED BLOOD CELL
RCT	RANDOMIZED CONTROLLED TRIAL

Acronyms con't

RS	RING SIDEROBLAST
sEPO	SERUM ERYTHROPOIETIN
SLL	SMALL LYMPHOCYTIC LYMPHOMA
TLS	TUMOUR LYSIS SYNDROME
VAF	VARIANT ALLELE FREQUENCY
VenO/Ven-O	VENETOCLAX AND OBINUTUZUMAB
VRd	BORTEZOMIB, LENALIDOMIDE AND DEXAMETHASONE
XVd	SELINEXOR, BORTEZOMIB AND DEXAMETHASONE


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FL: Relapsed Disease in 2026

DR. GWYNIVERE DAVIES

FL is the most common indolent B-cell lymphoma. Patient outcomes have improved substantially, with median OS now exceeding 20 years. However, early progression, treatment resistance, and histologic transformation remain important causes of lymphoma-related mortality.

Dr. Davies described the FLIPI24, a prognostic model combining age and four blood-based parameters (lactate dehydrogenase, hemoglobin, beta-2 microglobulin levels, and white blood cell count) to estimate the probability of an event within 24 months of starting treatment. The model distinguished risk groups, including a low-risk population with 5-year OS of approximately 96–97%, and a high-risk population with 5-year OS rates of 77% to 83% across external validation cohorts. Beyond assisting with counselling patients, Dr. Davies explained that better prognostication could be helpful for enrolling higher-risk populations that may benefit from intensified or novel treatment in trials.

Response duration generally shortens with successive relapses, although a prolonged first remission predicts a longer response to second-line treatment. Dr. Davies emphasized the need to investigate possible histologic transformation, pointing to a British Columbia cohort of 296 patients treated with bendamustine and rituximab followed by rituximab maintenance; approximately 13% of patients experienced POD24, and three-quarters of this population had transformed disease. The 2-year OS of patients with POD24 was demonstrated to be 38% in Freeman, 2019. PET-guided biopsy of the most active site can help identify these high-risk patients earlier and guide treatment.

Dr. Davies reviewed the inMIND study, which compared tafasitamab plus R2 with placebo plus R2 and demonstrated a median PFS of approximately 22 months in the investigational arm versus 14 months in the placebo arm. She highlighted differences in baseline risk of the study populations in the inMIND study compared to the AUGMENT trial,

Balancing patient characteristics and treatment efficacy/toxicity

Tafa-R²

- Lower CR rates than epcor-R² (cross trial comparison)
- Frequent 1.5 hour IV infusions
- Less monitoring, no step up dosing required
- Low additional toxicity compared to R²
- Low treatment discontinuation (9%)



Epcor-R²

- Longer PFS and higher CR rates including in POD24 population (cross trial comparison)
- Associated with increased toxicity including CRS (35%) and neurotoxicity
- Requires step up dosing, intensive monitoring and consideration of hospitalization
- Increased treatment discontinuation (19%)

which reported a median PFS of 39 months with R2. The benefits were demonstrated in POD24 (19 versus 11 months) and rituximab-refractory subgroups. Dr. Davies noted that the additional toxicity with tafasitamab was relatively limited, although the treatment is associated with an increased treatment burden due to frequent IV infusions.

Addressing subsequent therapy, Dr. Davies questioned whether prior CD19-targeted treatment should automatically exclude patients from CAR T-cell therapy. Limited post-tafasitamab treatment samples generally showed retained CD19 expression, and an abstract from EHA 2026 suggested that prior tafasitamab therapy did not compromise CAR T efficacy.

In EPCORE FL-1, epcoritamab plus R2 also substantially improved PFS compared to R2 alone, with an estimated 16-month PFS of 85.5% versus 40% for R2. Benefits were evident in higher-risk subgroups. However, serious AEs approximately doubled (56% in the epcoritamab arm versus 29% in the R2 arm) with more CRS, infections, and hematologic toxicity with the combination. A schedule with three step-up doses was associated with lower CRS incidence than a schedule with two step-up doses (26% versus 45%). Dr. Davies explained that most CRS events resolved within one day and were managed with corticosteroids. Treatment selection therefore requires balancing efficacy, tolerability, and patient preferences.

For third-line treatment and beyond, Dr. Davies discussed CAR T-cell therapy versus bispecific antibodies. Long-term CAR T-cell studies showed durable remissions, but both acute and delayed toxicities warrant consideration, particularly in heavily pretreated patients. Mosunetuzumab and epcoritamab both produced CR rates of approximately 60%, with low neurotoxicity. An important difference was that epcoritamab was administered indefinitely while mosunetuzumab was offered as a fixed duration therapy. Odronextamab demonstrated a CR rate of 74%, but had higher rates of grade 3 or higher infections and is not available in Canada. Dr. Davies then reviewed final-analysis data on zanubrutinib and obinutuzumab from the ROSEWOOD study, which achieved a CR rate of 42% and resulted in a median PFS of 22 months. She concluded by recommending that physicians consider bispecific antibodies and CAR T-cell therapy in the third-line setting, depending on patient, disease and local capacity factors.



LBCL: Treatment and Management in 2026

DR. ISABELLE FLEURY

Dr. Fleury reviewed the evolving management of LBCL, emphasizing how tumour biology, patient fitness and treatment advances are reshaping care. LBCL accounts for approximately 30% to 40% of non-Hodgkin lymphoma, with a median age at diagnosis of 67 years. Nearly one-third of patients are ≥75 years of age, making fitness assessment central to treatment selection.

Gene-expression profiling distinguishes ABC and GCB subtypes, but practical limitations have encouraged reliance on IHC. The Hans algorithm has approximately 80% concordance with gene-expression profiling and should be reported as GCB versus non-GCB. Lymph2Cx, developed by the BC Cancer group, enables gene-expression classification using FFPE tissue, although access remains limited. Dr. Fleury emphasized that broader implementation could support biologically informed treatment.

Adverse prognostic features include clinical risk scores, CD5 expression, and *MYC* dysregulation, including double-expressor lymphoma, double-hit lymphoma and the dark zone signature, the latter of which identifies a particularly high-risk GCB subgroup that may include cryptic *MYC*/*BCL2* rearrangements. Dr. Fleury distinguished double-expressor lymphomas from lymphomas harbouring *MYC* and *BCL2* rearrangements. Dr. Fleury noted that emerging genetic classifications may eventually guide treatment but are not used in day-to-day practice.

Dr. Fleury then discussed ctDNA as a sensitive, non-invasive measure of disease burden offering prognostic value beyond PET-CT. She noted that ongoing prospective trials are investigating ctDNA-guided treatment adaptation.

For CNS relapse risk in DLBCL, Dr. Fleury described the CNS-IPI as useful for risk assessment but noted that a recent large, multicentre, retrospective study did not demonstrate a benefit from prophylactic high-dose methotrexate (Lewis et al., 2023). Primary testicular lymphoma warrants separate consideration, with CNS relapse risk potentially reaching 35%. Management includes upfront orchiectomy and end-of-treatment contralateral testicular radiation therapy. She cited IELSG10 and IELSG30 as supporting prophylactic approaches in this setting.

For limited-stage DLBCL, Dr. Fleury described a shift toward PET-adapted and radiation-sparing strategies. R-CHOP remains a longstanding advanced-stage standard, with reported median PFS of 4.8 years and median disease-specific survival not reached at 10 years. However, 15% of patients do not achieve a CR with R-CHOP and 25% relapse after an initial CR. Efforts to improve first-line therapy include the POLARIX trial, which demonstrated that pola-R-CHP resulted in a 65% PFS rate at 5 years, versus 59% with R-CHOP. OS was not significantly improved, but Dr. Fleury explained that exploratory analyses suggested greater benefit for patients with the ABC subtype and that pola-R-CHP reduced the need for subsequent therapy (Morschhauser et al., JCO 2025). Overall safety of pola-R-CHP is comparable to the R-CHOP combination.

Dr. Fleury also described the phase 3 frontMIND trial adding tafasitamab and lenalidomide to R-CHOP, which demonstrated a PFS benefit and showed benefit in both ABC and GCB subgroups. However, no statistically significant OS benefit was demonstrated, and there were increased rates of grade 3 or higher cytopenias and infections.

Patients with high-grade B-cell lymphoma remain underrepresented in trials. Intensified regimens include DA-EPOCH-R and R-CODOX-M/R-IVAC, although evidence in this population is limited. DA-EPOCH-R was not superior to R-CHOP in a phase 3 trial in an unselected DLBCL population. For patients who are ineligible for anthracyclines, Dr. Fleury shared data suggesting long-term disease control with R-CEOP in a matched retrospective comparison with R-CHOP. For older and frail patients, Dr. Fleury advocated for geriatric assessment, encouraging activity, integrating appropriate prophylaxis and cautious escalation of therapy, noting that early results of the R-polatuzumab-glofitamab combination demonstrated an 81% CR rate and 85% 1-year PFS in the older, frail population, with phase 3 evaluation ongoing.

Turning to second-line DLBCL therapy, Dr. Fleury emphasized relapse timing, prior tolerability and

eligibility for CAR-T or ASCT as key decision factors. Primary refractory disease and relapse within 12 months historically predicted poor salvage outcomes. However, the ZUMA-7 trial established an OS benefit with axi-cel (4-year OS of 55% versus 46%), while liso-cel demonstrated an EFS benefit. Dr. Fleury recommended early referral for CAR T-cell therapy and stressed that age alone should not exclude CAR T referral. She added that earlier intervention for CRS/ICANS reduces the severity and duration of events, and most cytopenias are reversible with time; however, long-term follow-up is needed to monitor for prolonged immunosuppression and late secondary malignancies.

For patients unable to receive CAR T-cell therapy, emerging alternatives include tafasitamab-lenalidomide and Glofit-GemOx. In the phase II L-MIND, second-line patients achieved a 53% CR rate with tafasitamab-lenalidomide, with the median duration of response not reached at 5 years in patients with one prior line of therapy, highlighting durable benefit in selected patients. The phase III STARGLO demonstrated an OS benefit with glofitamab-GemOx versus R-GemOx in transplant-ineligible patients, including primary refractory disease, reaching 59% CR rate with a 3-year OS of 47%. She noted the broad eligibility criteria, including creatinine clearance ≥30 mL/min. In the third line and beyond, CAR T-cell therapy offers curative potential, with reported 5-year OS rates of approximately 43% for axi-cel and 38% for liso-cel. Glofitamab and epcoritamab provide alternatives for patients ineligible for CAR T, each producing CR rates around 40%, with 3-year follow-up data supporting the durability of these reponses. Dr. Fleury concluded that molecular monitoring and biologically tailored treatment could improve outcomes while reducing toxicity. However, patients progressing after both CAR T and bispecifics remain a major unmet need.

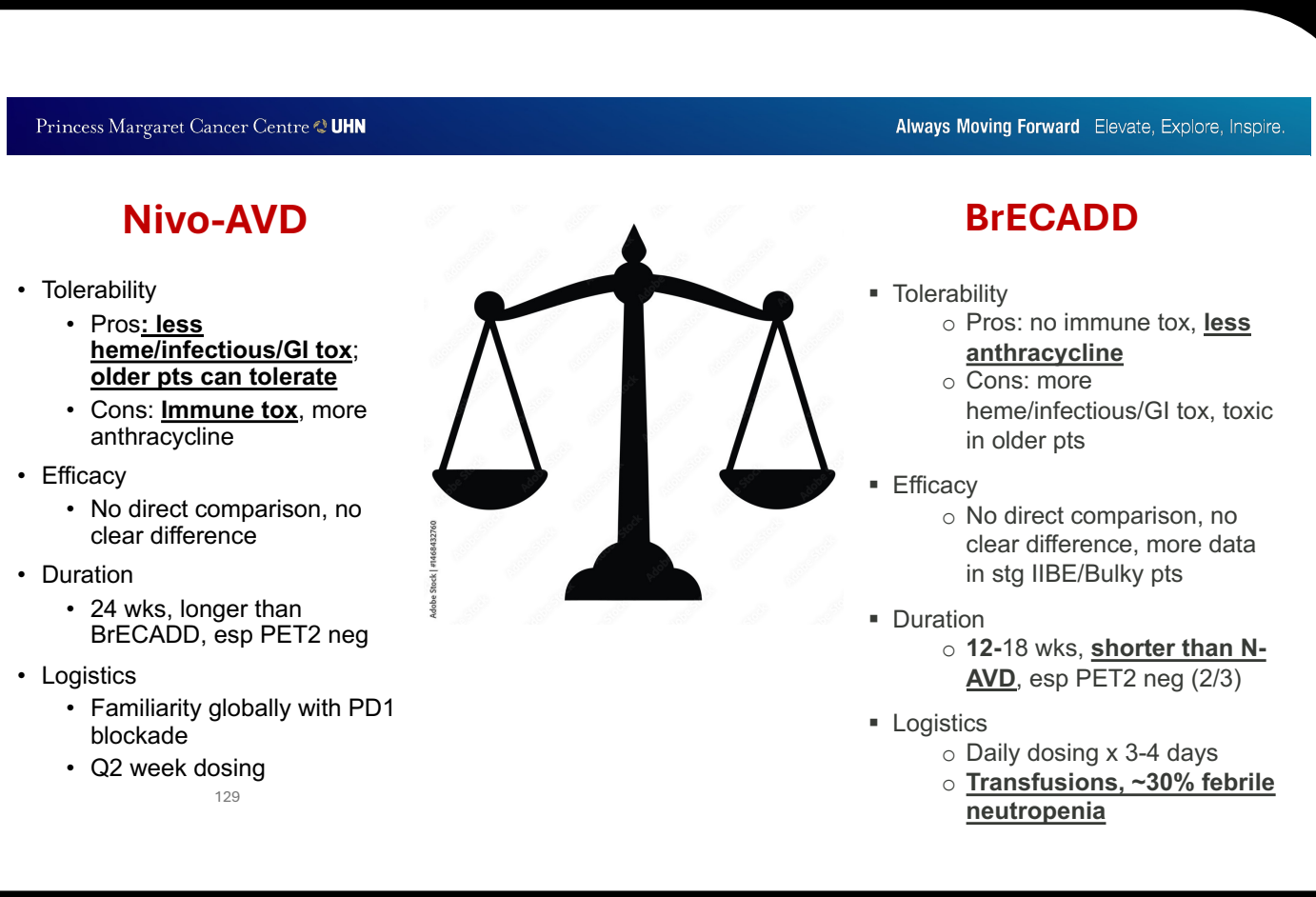


Approach to Hodgkin Lymphoma in 2026

DR. ANCA PRICA

Dr. Prica reviewed the treatment of limited-stage Hodgkin lymphoma, advanced Hodgkin lymphoma therapy, and upcoming options in the frontline treatment of cHL. She outlined Ontario access to BV-AVD and nivo-AVD in the frontline setting; pembrolizumab for transplant-ineligible patients with relapsed disease; BV after ASCT; and nivolumab and pembrolizumab for patients who progress after BV. She also noted efforts to secure funding for BrECADD. For limited-stage disease, treatment remains guided by favourable versus unfavourable features, disease distribution and PET response.

For early favourable disease, HD16 found that radiation therapy could not safely be omitted after two cycles of ABVD in PET-negative patients. The EORTC H10 study evaluated PET-adapted treatment after two cycles of ABVD in favourable and unfavourable disease and demonstrated that among PET-negative patients, two additional cycles of ABVD produced a substantial PFS disadvantage in favourable disease, compared with one additional cycle of ABVD and radiation therapy (5-year PFS rates of 87% versus 99%, respectively) while OS remained high (99.6% versus 100%, respectively). In unfavourable disease, the 5-year PFS was approximately 92% among patients who received radiation therapy plus ABVD, versus approximately 90% in patients who did not receive radiation therapy. In longer-term follow-up, the PFS disadvantage persisted in favourable disease: 10-year PFS was 85.4% without radiation therapy versus 98.8% with radiation therapy, without a significant OS difference. Dr. Prica therefore advocated individualized discussions about



radiation therapy.

When avoiding radiation therapy is important for a patient with a mediastinal mass, for instance, Dr. Prica highlighted HD17 as an approach. Patients received 2 cycles of escalated BEACOPP followed by 2 cycles of ABVD. Those achieving PET negativity could omit radiation therapy with excellent outcomes.

Novel agents are also moving into limited-stage treatment. Phase 2 studies incorporating PD-1 blockade (Nivo-AVD and pembrolizumab-AVD) have reported highly encouraging outcomes, including PFS estimates of 100% in some cohorts. BV-AVD studies have also shown durable disease control, including 5-year PFS above 90% in early-stage, non-bulky cHL (Abramson et al., 2022). BREACH reported PET-negative rates after two cycles of 82.3% with BV-AVD versus 75.4% with ABVD; both groups subsequently received radiation therapy.

Turning to advanced-stage disease, Dr. Prica highlighted the S1826 trial, which compared nivo-AVD with BV-AVD in stage III–IV disease and included adolescents. The updated 3-year PFS was 91% versus 82%, favouring nivo-AVD, with benefit across age groups (Herrera et al., ASH 2025). BV-AVD produced a greater burden of neuropathy and other toxicities, whereas nivo-AVD introduced immune-mediated AEs. Dr. Prica emphasized the importance of understanding long-term immune effects in young survivors. In patients 60 years old or older, nivo-AVD performed particularly well, with a 12-percentage-point difference in 1-year OS, compared to BV-AVD. BV-AVD was associated with 14% non-relapse mortality in this subgroup, reinforcing concerns about tolerability.

HD21 evaluated BrECADD against escalated BEACOPP, seeking to preserve efficacy while reducing toxicity. BrECADD demonstrated reduced toxicities, including anemia, thrombocytopenia, and transfusion requirements. However, febrile neutropenia occurred at rates of 28% with BrECADD (compared to 21% with BEACOPP). Findings also suggested less gonadal toxicity than with escalated BEACOPP. The 4-year PFS with BrECADD was approximately 94%, versus approximately 91% with escalated BEACOPP, meeting criteria for superiority.

Dr. Prica highlighted that cross-trial comparisons suggest that nivo-AVD offers less hematologic, infectious, and GI toxicity compared to BrECADD but entails immune risks and greater anthracycline exposure. PET-negative patients receiving BrECADD may finish after 4 cycles, approximately 3 months, versus 6 months with nivo-AVD. Dr. Prica emphasized that this difference can substantially affect education, employment and family life. Treatment decisions should therefore incorporate efficacy, immediate and long-term toxicity, fertility, treatment duration, and patient priorities.



Frontline CLL in 2026

DR. ROBERT PUCKRIN

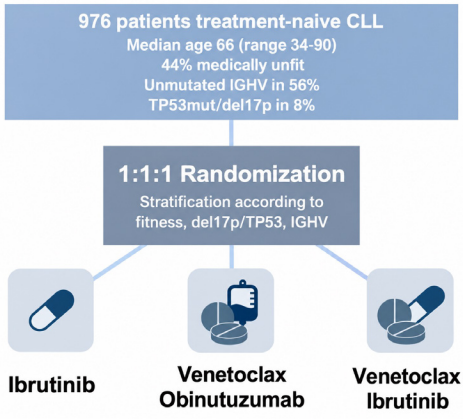
Dr. Puckrin noted that early intervention has not improved OS in asymptomatic disease, including with targeted therapy; active surveillance remains the standard until iwCLL criteria are met. He emphasized that CLL and SLL represent the same biological disease and should be treated similarly.

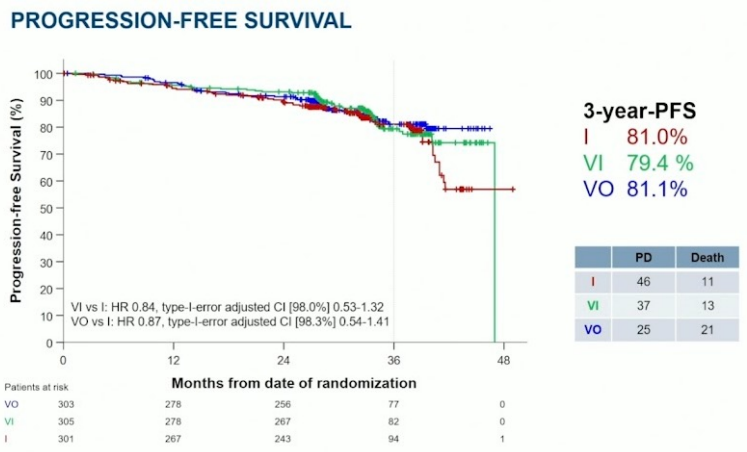
For first-line CLL/SLL, targeted therapies have replaced chemoimmunotherapy, showing improved effectiveness in both mutated and unmutated IGHV disease. Although FCR produced prolonged remissions and possible functional cures in approximately half of favourable-risk patients, it carried risks of cytopenias, infections and secondary malignancies, including MDS/AML in approximately 6% of patients. Targeted agents have improved efficacy and OS in several trials and patients who received first-line targeted therapy now have similar OS as age-matched controls.

Continuous BTK inhibition provides durable disease control, with RESONATE-2 demonstrating median PFS of approximately 9 years with ibrutinib. These agents are particularly effective in high genetic risk cases and may overcome the adverse prognostic impact of *del(17p)*/*TP53* mutations and unmutated IGHV. The second-generation BTKis acalabrutinib and zanubrutinib offer effective alternatives to ibrutinib with improved tolerability. Dr. Puckrin noted that zanubrutinib offers superior PFS compared to ibrutinib, whereas acalabrutinib has lower risks of hypertension and bleeding than ibrutinib. However, continuous BTKi therapy carries cumulative cardiovascular and bleeding risks and can lead to BTK resistance mutations. In addition, from a financial stewardship perspective, starting with continuous therapy and then switching to fixed-duration therapy can cost approximately twice as much as starting with fixed-duration therapy.

Dr. Puckrin then reviewed fixed-duration therapies, including VenO, I+V, and A+V. He noted that all options are highly effective, with mature trials reporting approximately 50% to 70% of patients remaining progression-free 5 years after treatment initiation. Fixed-duration treatment offers prolonged time off therapy but involves the logistical challenges of the venetoclax ramp-up. VenO carries higher rates of neutropenia and infections while ibrutinib-containing combination have higher rates of diarrhea, atrial fibrillation, and hypertension. Dr. Puckrin highlighted that he now uses fixed-duration treatment for most patients. However,

CLL17: fixed-duration versus continuous treatment for CLL





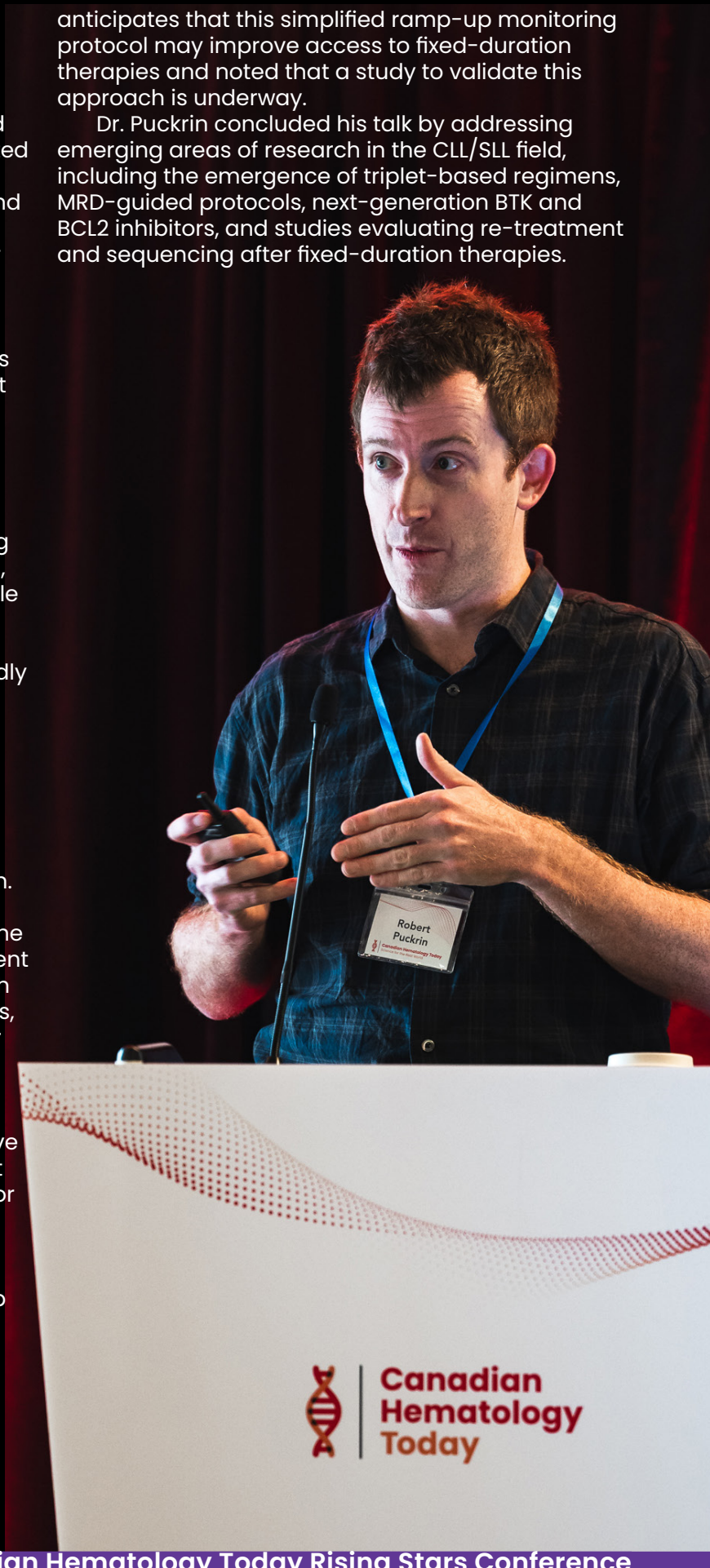
Fixed-duration Ven-O and I+V have non-inferior PFS and similar OS as continuous ibrutinib at 3 years

he noted safety concerns for some patients, as the long-term follow-up of CLL14 suggested an increased risk of secondary malignancies with VenO in older patients, and CLL17 and AMPLIFY demonstrated that obinutuzumab was associated with a numerically increased risk of infection-related mortality. The GLOW trial reported early cardiac or sudden deaths in four patients treated with I+V, and Dr. Puckrin recommended generally avoiding I+V in older unfit patients or those with cardiovascular comorbidities. He generally prefers A+V over I+V based on available efficacy and safety data. He considers VenO and A+V to both be excellent options for most patients with CLL/SLL and chooses treatment based on comorbidity profile, treatment logistics, and patient preferences.

Personalizing first-line therapy involves considering *del(17p)* and/or *TP53* mutation and other high-risk features; disease burden; comorbidities and concomitant medications; and patient preferences. He presented data supporting continuous BTK inhibition for patients with *del(17p)*, although fixed-duration therapy can be reasonable for patients who are accepting of earlier relapse and need for subsequent treatment. Regarding unmutated *IGHV* status, CLL17 demonstrated broadly similar 3-year PFS across treatment groups within *IGHV* subgroups. Longer-term follow-up suggests that patients with unmutated *IGHV* have shorter remissions after fixed-duration therapy, although treatment-free intervals remain substantial. The CLL14 trial demonstrated median PFS around 5.5 years and median time to next treatment of approximately 7 years with VenO in this population. He also presented data showing that retreatment can extend disease control.Using case examples, he said he would recommend VenO for an older patient with cardiovascular disease, A+V for someone with hypogammaglobulinemia and recurrent infections, and all-oral treatment for patients facing travel or infusion-access barriers.

Addressing how to improve the venetoclax ramp-up, Dr. Puckrin emphasized that the 5-week venetoclax ramp-up and debulking strategies have significantly reduced or eliminated TLS risk in most patients. Following debulking with obinutuzumab or BTK inhibition before venetoclax therapy, the vast majority of patients no longer remain in the high tumour-burden TLS-risk category. TLS is now rare with Ven-O and usually occurs with obinutuzumab rather than with venetoclax. CAPTIVATE and GLOW reported no clinical TLS with I+V, while AMPLIFY reported rates of 0.3% and 0.4% with AV and AVO. He described a new simplified approach in Alberta using laboratory testing 24 hours after each dose increase, which can be performed at most community hospitals, and oral hydration. He anticipates that this simplified ramp-up monitoring protocol may improve access to fixed-duration therapies and noted that a study to validate this approach is underway.

Dr. Puckrin concluded his talk by addressing emerging areas of research in the CLL/SLL field, including the emergence of triplet-based regimens, MRD-guided protocols, next-generation BTK and BCL2 inhibitors, and studies evaluating re-treatment and sequencing after fixed-duration therapies.



GSK Sponsored Lunch Symposium: Sequencing With Intent: Making Every Line of Therapy Matter in the Real World

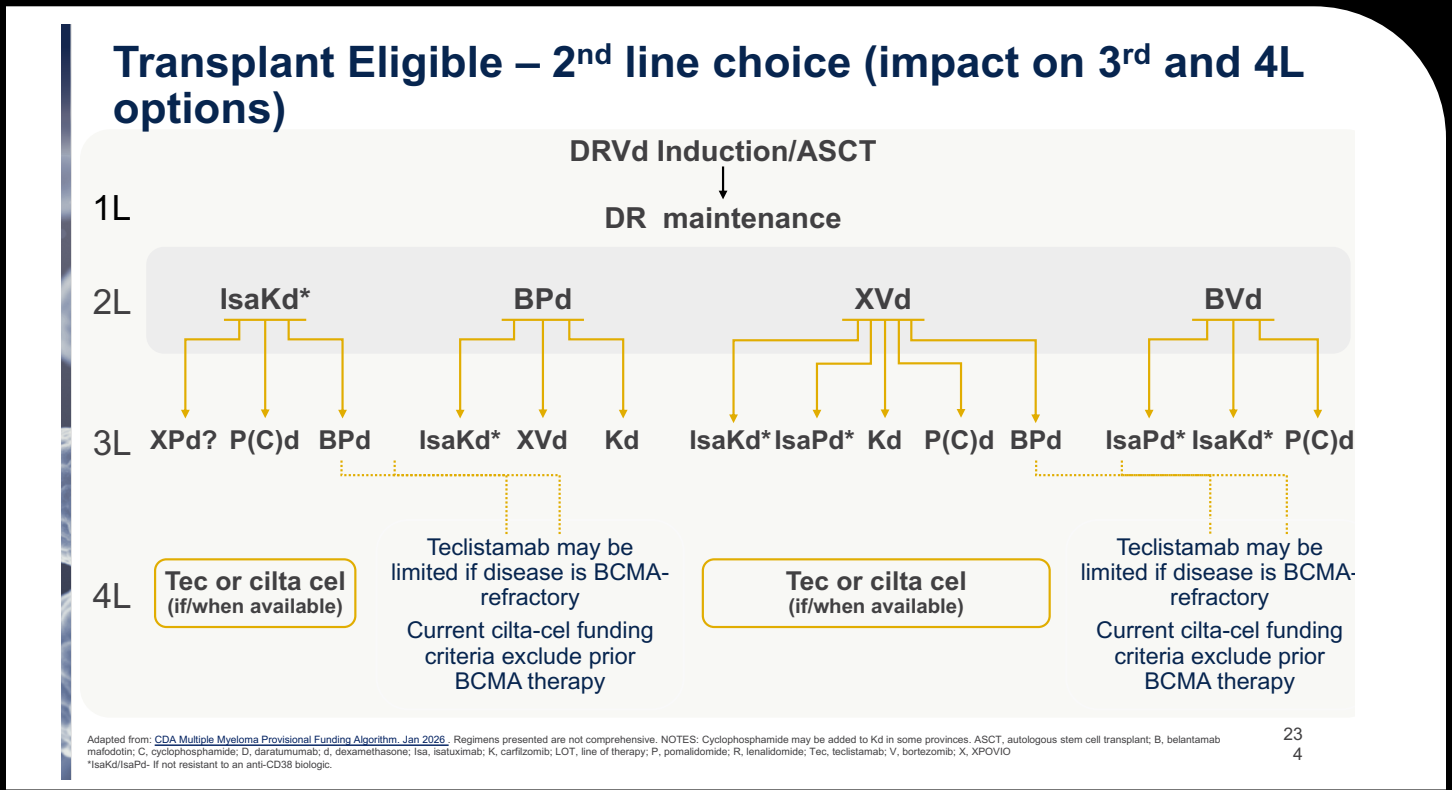
DR. PHILIP KURUVILLA

Dr. Kuruvilla emphasized the importance of optimizing each line of therapy, as patients may not reach subsequent lines. Canadian CMRG data showed attrition rates among patients who underwent ASCT of 7% after first-line therapy, 12% after second-line therapy and 23% after third-line therapy, with higher rates among patients who did not undergo ASCT (19%, 26% and 40%, respectively). He cautioned that these data are largely based on academic centres and may underestimate attrition in community practice.

The increasing use of frontline quadruplet therapy for both transplant-eligible and ineligible patients is changing the relapse landscape. For transplant-eligible patients, second-line options include IsaKd, BPd, XVd, and BVd. However, teclistamab may be limited if BPd in the second or third line results in BCMA-refractory disease. In addition, cilta-cel funding criteria for MM in Canada excludes prior BCMA therapy, meaning that BPd and BVd in the second line can limit future options. While in the past, the goal was to avoid lenalidomide refractoriness with MM treatment, the new goal, in Dr. Kuruvilla's view, is to avoid BCMA refractoriness.

He reviewed emerging BCMA-directed approaches, beginning with cilta-cel. CARTITUDE-4 enrolled lenalidomide-refractory patients, approximately one-third of whom received second-line treatment. He highlighted approximately 59% PFS and 76% OS at 30 months, while cautioning that longer follow-up is needed to determine whether apparent survival plateaus represent durable disease control.

Bispecific antibody outcomes have been similarly encouraging. In MajesTEC-3, teclistamab–daratumumab achieved approximately 83% PFS



at 36 months versus approximately 30% with daratumumab-based regimens. In MajesTEC-9, teclistamab achieved approximately 70% PFS at 18 months versus 27% with PVd or Kd.

Dr. Kuruvilla recommended against carfilzomib and pomalidomide regimens immediately after daratumumab-based therapy, citing CMRG data showing PFS under 6 months with these regimens immediately after daratumumab-based therapy. As an alternative, in the BOSTON study, XVd produced median PFS of approximately 14 months overall and approximately 10 months in lenalidomide-refractory patients. Laboratory findings suggest relationships between daratumumab resistance and selinexor sensitivity, as well as possible effects of selinexor on promoting T-cell fitness and reducing exhaustion. However, he stressed that these hypotheses require clinical validation.

Dr. Kuruvilla then reviewed the phase 3 DREAMM-7 and DREAMM-8 trials in patients with at least one prior line of therapy. DREAMM-7 compared BVd with DVd, while DREAMM-8 compared BPd with PVd. Both met their primary PFS endpoint. The median PFS was approximately 37 versus 14 months in DREAMM-7. Median PFS with BPd in DREAMM-8 was approximately 33 months, versus 12.5 months with PVd. Dr. Kuruvilla highlighted, however, that ocular toxicity is a major consideration with belantamab mafodotin. Approximately 80% to 90% of patients experienced ocular events, commonly blurred vision. Ocular toxicity could be severe: in DREAMM-8, grade 3 or 4 ocular events occurred in 43% of patients receiving BPd. Trial analyses showed maintained or improved quality of life, an important consideration when discussing the therapy with patients.

Addressing sequencing, Dr. Kuruvilla outlined three mechanisms of BCMA resistance: loss of BCMA target, T-cell exhaustion, and structural changes to the binding site. Small datasets suggest bispecific antibodies retain activity after prior BCMA-directed treatment. In 59 patients who received prior belantamab mafodotin, responses to teclistamab were similar to those in BCMA-naive patients (Razzo et al., 2025). DREAMM-7 PFS2 results also supported the feasibility of common classes after belantamab mafodotin, with median PFS2 not reached with BVd at approximately 52 months of follow-up, compared to a PFS2 of 33 months among patients who had received DVd. Among a small subgroup receiving subsequent fourth- to seventh-line bispecific therapy after belantamab mafodotin, median PFS was approximately 1 year.

Dr. Kuruvilla concluded that BCMA-directed therapies offer substantial efficacy. Until stronger evidence emerges, clinicians should prioritize the most effective accessible option for the patient's current disease.



MPN Treatment and Management in 2026

DR. DAWN MAZE

MPNs are associated with an increased risk of vascular events, constitutional symptoms including fatigue and pruritus, and an increased risk of transformation to AML. Dr. Maze focused her talk on the most common MPNs, PV, and ET. For PV, low-dose aspirin, therapeutic phlebotomy to maintain hematocrit below 45% and cardiovascular risk management remain foundational. Cytoreductive therapy is indicated for high-risk patients, defined by age ≥60 years or previous thrombosis, and selected low-risk patients (see ELN criteria). Dr. Maze highlighted the importance of optimal therapy, citing the prospective, observational REVEAL study, which enrolled 2,510 patients with PV. During the study, 9.7% of patients died; thrombotic complications were the most common cause, accounting for 33.1% of the 175 deaths with a known cause. Mean follow-up was approximately 110 weeks among patients who died.

Dr. Maze next discussed JAK2 VAF, which correlates with blood counts, thrombosis, splenomegaly and fibrotic progression in PV. PROUD-PV compared ropeginterferon alfa-2b with best available therapy/hydroxyurea in patients requiring cytoreduction who were untreated or had prior hydroxyurea exposure <3 years with no evidence of resistance or intolerance. The trial did not meet its 1-year noninferiority endpoint: complete hematologic response with normal spleen size occurred in 21% of patients treated with ropeginterferon alfa-2b versus 28% with hydroxyurea. However, longer follow-up in CONTINUATION-PV demonstrated that ropeginterferon alfa-2b led to a higher molecular response rate (69%) compared to the best available therapy arm (21%). At 5 years, complete hematologic responses occurred in 56% with ropeginterferon versus 44% in the standard-of-care arm, although the difference was not statistically significant. At 6 years, thrombotic events, myelofibrosis, acute leukemia, or death occurred at rates of 5.3% with ropeginterferon versus 16.2% with hydroxyurea/best available therapy.

Another emerging approach targets iron availability. Rusfertide, a hepcidin mimetic, blocks ferroportin to reduce iron availability for erythropoiesis and improve hematocrit control without frequent phlebotomy. In the phase 3 VERIFY trial, patients requiring frequent phlebotomies received rusfertide or placebo, with or without

ELN Guidelines for Cytoreduction in PV

High Risk	Low Risk		
CYTOREDUCTION INDICATED	**CYTOREDUCTION RECOMMENDED**	**CYTOREDUCTION SHOULD BE CONSIDERED**	**CYTOREDUCTION CAN BE CONSIDERED**
Age ≥60y, and/or Prior thrombosis	Poor phlebotomy tolerance Symptomatic progressive splenomegaly Persistent leukocytosis >20 × 10^9/L for at least 3 months	Progressive[1] and persistent leukocytosis >15 x 10^9/L for at least 3 months Extreme thrombocytosis >1500 × 10^9/L or bleeding Inadequate Hct control with phlebotomies[2]	High symptom burden not relieved by phlebotomy, antiplatelet therapy or antihistamines In select patients with relevant cardiovascular risk after primary prevention strategies

[1]At least 100% increase if baseline <10 × 10^9/L or at least 50% increase if baseline >10 × 10^9/L
[2]At least 6 phlebotomies/year for at least 2 years

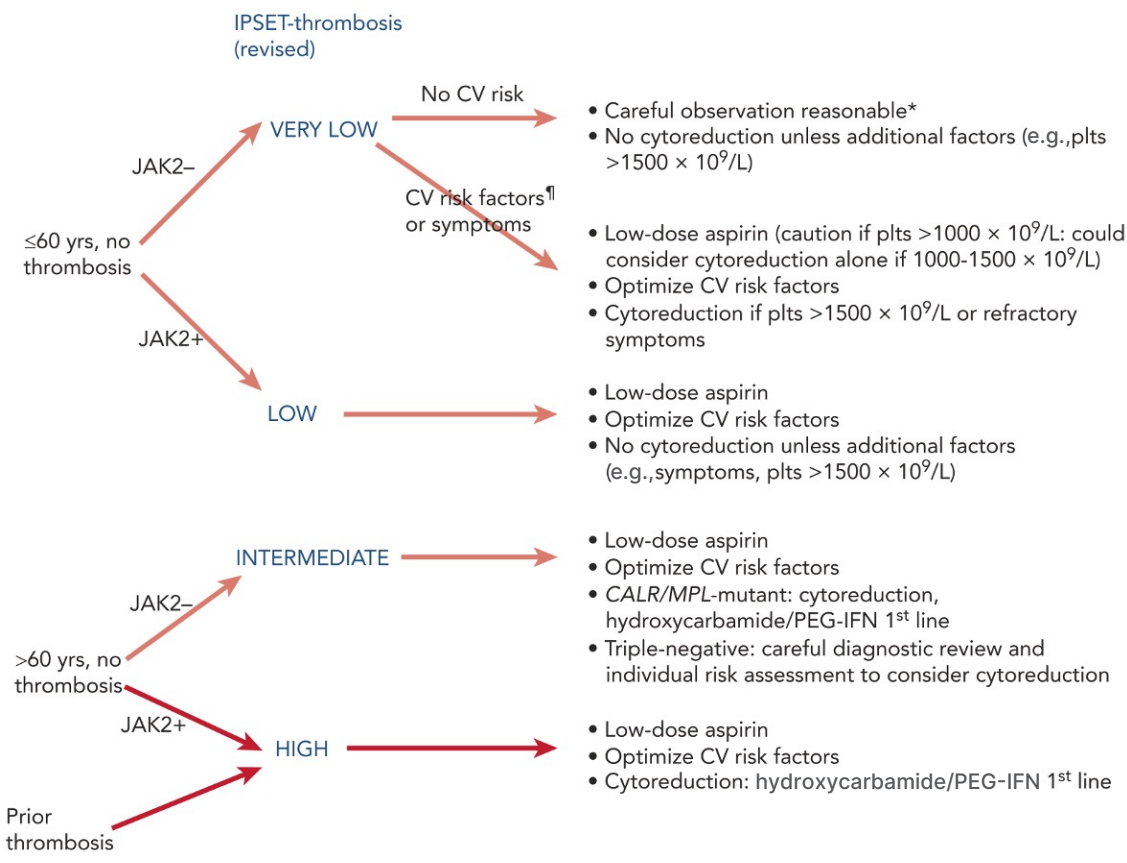
concurrent cytoreduction. The primary endpoint was absence of phlebotomy eligibility and no phlebotomy during weeks 20–32. This was achieved by 77% of patients in the rusfertide arm versus 33% in the placebo arm. Hematocrit control was sustained, and injection-site reactions were the most common AEs.

Turning to ET, Dr. Maze reviewed IPSET-thrombosis-based risk stratification, noting that selected patients without JAK2 mutations or cardiovascular risk factors may be managed with observation alone.

The mutant CALR-directed therapy INCA033989 has shown encouraging phase 1 activity in patients with high-risk ET who were resistant or intolerant to prior cytoreduction. In an analysis reported at ASH in 2025, 93% remained on treatment, no dose-limiting toxicities occurred and the maximum tolerated dose had not been reached. Grade ≥3 anemia and/or neutropenia occurred in five patients (all had received hydroxyurea before or during the event); lipase increases were also observed but resolved in all 9 patients. Platelet responses were rapid and durable, particularly at higher doses, with correlated reductions in VAF. A randomized phase 3 comparison with best available therapy is planned.

Finally, the SURPASS-ET study, published in 2025, compared ropeginterferon with anagrelide after hydroxyurea resistance or intolerance. Durable modified ELN responses at months 9 and 12 occurred in 43% versus 6%, respectively.

She concluded that preventing thrombotic events remains central to PV and ET management. However, emerging therapies increasingly aim to modify disease by addressing molecular disease drivers.



Treatment and Management of MDS in 2026

DR. RENA BUCKSTEIN

Dr. Buckstein began by reviewing SintraREV, which demonstrated that lenalidomide 5 mg daily for 2 years delayed transfusion dependence in patients with non-transfusion-dependent, lower-risk del(5q) MDS. Transfusion dependence developed in 25% of treated patients versus 65% receiving placebo. Median time to dependence was not reached in the treatment arm, compared with 11.6 months in the placebo arm. Hemoglobin increased by 27 g/L, without differences in OS, AML progression or TP53 expansion. However, neutropenia occurred in 63% of patients in the treatment arm versus 19% in the placebo arm.

Noting the importance of additional mutations, Dr. Buckstein then described the IPSS-del(5q), a disease-specific prognostic model developed from 682 patients across 19 centres. Adverse variables included hemoglobin below 10 g/dL, platelets ≤100 × 10^9/L, at least two gene mutations, male sex, SF3B1 mutation, and biallelic *TP53* or *TP53* VAF above 20%. The model identified higher-risk patients whose risk could be underestimated by IPSS-R and IPSS-M. Median leukemia-free survival was 69 months in patients classified as standard risk under the IPSS-del(5q) model versus 32 months in those identified as high risk.

Dr. Buckstein emphasized that even a low transfusion burden (less than one unit per month) is associated with worse survival, and that transfusion dependence is associated with iron overload, poorer quality of life and substantial demands on patients and caregivers.

Turning to treatments targeting ineffective erythropoiesis, Dr. Buckstein reviewed luspatercept and elritercept. In MEDALIST, luspatercept produced at least 8 weeks of transfusion independence in 38% of patients versus 13% with placebo. The median duration of the longest continuous response was 31 weeks. Dr. Buckstein noted that lower baseline transfusion burden predicted better responses. Early fatigue, diarrhea, and asthenia occurred, but generally diminished within 2 to 3 months.

Summary

What the evidence on HMA therapy in MDS tells us

AZA ≈ DEC-C for survival

Equivalent OS in higher-risk MDS and likely CMML

DEC-C: faster time to response, more myelosuppression

Lower risk: transfusion independence

HMAs achieve TI rates of 35–45% in lower-risk disease

Venetoclax + HMA deepens response

Higher response rates with excess blasts (ASXL1? TP53?)

More patients reach transplant and survive after it

Patients prefer oral therapy

Oral therapy is preferred by MDS patients who value QoL highly

Depth of response matters

Patients achieving cCR on HMA outlive those with lesser responses

Added benefit of cCR before allo-HCT is unproven

More combinations coming

Further combination studies on an HMA backbone are underway

COMMANDS compared luspatercept with epoetin alfa in erythropoiesis-stimulating agent-naive, transfusion-dependent patients with lower-risk MDS. Among patients with baseline sEPO above 200 and below 500 U/L, response rates were approximately 37% for luspatercept versus 11% for epoetin alfa; for those with baseline sEPO of 200 U/L or lower, the response rates were 66% and 41%, respectively. Responses in RS-negative disease were similar between treatments, but response durability favoured luspatercept. A recent analysis suggested a possible, but not statistically significant, OS benefit with luspatercept (Garcia-Manero, EHA 2026).

Turning to elritercept, Dr. Buckstein shared encouraging phase 2 activity in both RS-positive and RS-negative disease, supporting the ongoing phase 3 RENEW and ELRiSE MDS studies. Roxadustat, on the other hand, failed to reach the primary endpoint in MATTERHORN, with transfusion independence rates of approximately 48% in the roxadustat arm versus 33% in the placebo arm. However, the subgroup receiving at least 2 RBC units every 4 weeks showed transfusion independence rates of 36% versus 11.5%, prompting further investigation.

Discussing HMA therapies, Dr. Buckstein explained that HMAs can achieve transfusion independence in approximately 40–45% of patients with lower-risk MDS, although disease-modifying effects remain uncertain. In the ASCERTAIN phase 3 trial, oral decitabine and cedazuridine demonstrated pharmacokinetic equivalence to IV decitabine. Reported outcomes included an ORR of 62%, a CR rate of 22%, median OS of 32 months and transfusion independence in 52% of patients who were RBC transfusion dependent at baseline. Most cytopenias were severe with the oral therapy, highlighting the importance of careful dose adjustment and delays where appropriate.

For younger, higher-risk patients proceeding to alloSCT, Dr. Buckstein reviewed the IWG 2023 response criteria. In a validation analysis, composite CR was associated with survival of 21 months versus 10 months without composite CR. However, achieving composite CR or reducing marrow blasts below 5% before alloSCT did not clearly improve post-transplant outcomes. She highlighted emerging data for oral azacitidine-cedazuridine and shared a Canadian matched-pair analysis that found no statistically significant survival differences between azacitidine and decitabine.

Finally, Dr. Buckstein reviewed HMA combinations. VERONA increased responses and transfusion independence with venetoclax plus azacitidine but did not improve OS. She would selectively consider the combination to obtain a rapid response before transplant in younger patients with excess blasts and wild type TP53, while acknowledging access limitations and the unapproved indication. She concluded with emerging approaches, including bexmarilimab, eltanexor, enasidenib, lisaftoclax, and mesutoclax.



MCL Treatment and Management in 2026

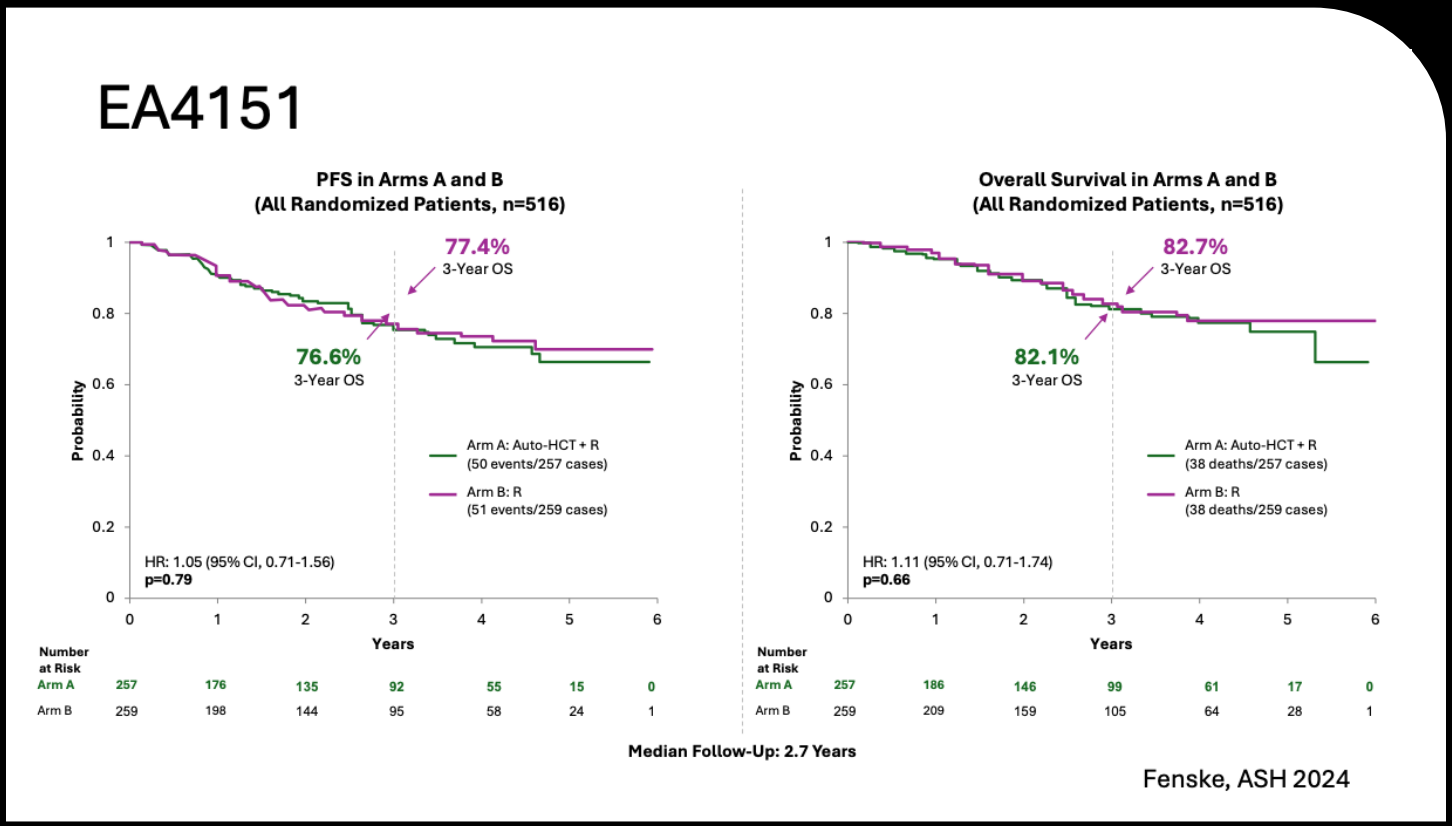
DR. DIEGO VILLA

Dr. Villa discussed how frontline BTKi-based regimens are changing the roles of ASCT, CAR-T and alloSCT in MCL. He emphasized that treatment decisions must account for efficacy, toxicity and how Canadian access restrictions affect subsequent therapy.

Beginning with ASCT, he reviewed updated TRIANGLE results with approximately 4.5 years of follow-up. Outcomes were similar between the ibrutinib-containing arms with and without ASCT, calling into question the value of transplantation in this setting. Exploratory analyses suggested possible benefit in patients with blastoid disease, elevated Ki-67, high p53 expression, or other high-risk features. However, he stressed that these analyses involved small numbers and wide confidence intervals.

He emphasized that the potential benefit of transplant in particular subgroups must be balanced against toxicity. In the TRIANGLE study, the transplant-containing arm had more grade ≥3 AEs during maintenance and follow-up, particularly infections and blood and lymphatic system disorders. Dr. Villa described similar concerns in the Canadian RECTANGLE clinical trial, where severe infections forced some patients to discontinue maintenance therapy post-transplant. For high-risk patients likely to need CAR T-cell therapy in the near future, he questioned exposing them to additional intensive chemotherapy.

He then described the shift toward chemotherapy-free frontline combinations involving a BTKi, an anti-CD20 antibody and other targeted agents (often a BCL2 inhibitor). He stressed that newer studies including BOVen, TRAVERSE, OASIS II and WINDOW-3 omit ASCT. BOVen, combining zanubrutinib, obinutuzumab and venetoclax in *TP53*-mutated MCL, produced an ORR of 96%, a CR rate of 88% and a 2-year PFS of 72%. Patients achieving CR and undetectable MRD could stop after 24 cycles. Although encouraging, the study included only 25 highly selected patients and documented toxicities including diarrhea and neutropenia. He cautioned against assuming these findings would translate



into Canadian access to that specific regimen.

ASCT remains relevant when frontline chemoimmunotherapy does not include a BTKi, although EA4151 challenges its necessity in patients achieving deep responses. In this study, 74% received intensive induction and only 8% received a BTKi. Patients in MRD-negative CR were randomized to ASCT followed by rituximab maintenance or maintenance alone, with no significant difference in PFS or OS. Dr. Villa highlighted the potential Canadian applicability but cautioned that the study used clonoSEQ; alternative MRD assays cannot automatically be considered equivalent.

Turning to CAR T-cell therapy, Dr. Villa reviewed the ZUMA-2 trial, in which 68 patients treated with brexu-cel had an ORR of 91%, with approximately two-thirds achieving CR. A U.S. real-world consortium reported comparable outcomes despite roughly three-quarters of patients being ineligible for ZUMA-2. TRANSCEND also demonstrated encouraging responses with liso-cel in 83 evaluable patients, with a potentially more favourable toxicity profile, although this product is currently unavailable in Canada for MCL.

Dr. Villa explained that the Canadian brexu-cel funding algorithm requires at least two prior systemic therapies, including a BTKi. Patients progressing during or shortly after frontline BTKi-containing therapy may therefore need another treatment before accessing CAR T. Dr. Villa argued that this requirement reflects an outdated treatment sequence, and he urged clinicians to contribute to CDA-AMC's consultation on second-line reimbursement for patients with refractory disease or relapse within 1 year of frontline BTKi treatment.

He also recognized the need to improve disease control while patients await CAR T-cell therapy and reduce treatment-related toxicity. The Canadian CCTG IND.245 clinical trial is evaluating sonrotoclax plus zanubrutinib before CAR T-cell therapy, aiming to control disease and potentially mitigate CRS. In the trial, zanubrutinib therapy continues for 3 months after the CAR T-cell infusion.

Finally, Dr. Villa discussed the diminishing role of alloSCT. Although potentially curative, available evidence shows substantial non-relapse mortality and ongoing relapse risk. ESMO guidelines recommend it only for younger, fit patients when CAR T-cell therapy is unavailable or has failed (Eyre, 2025). As potentially safer therapies, including bispecifics, emerge, alloSCT is moving later in treatment, potentially compromising feasibility and outcomes.



First-line MM Treatment and Management in 2026

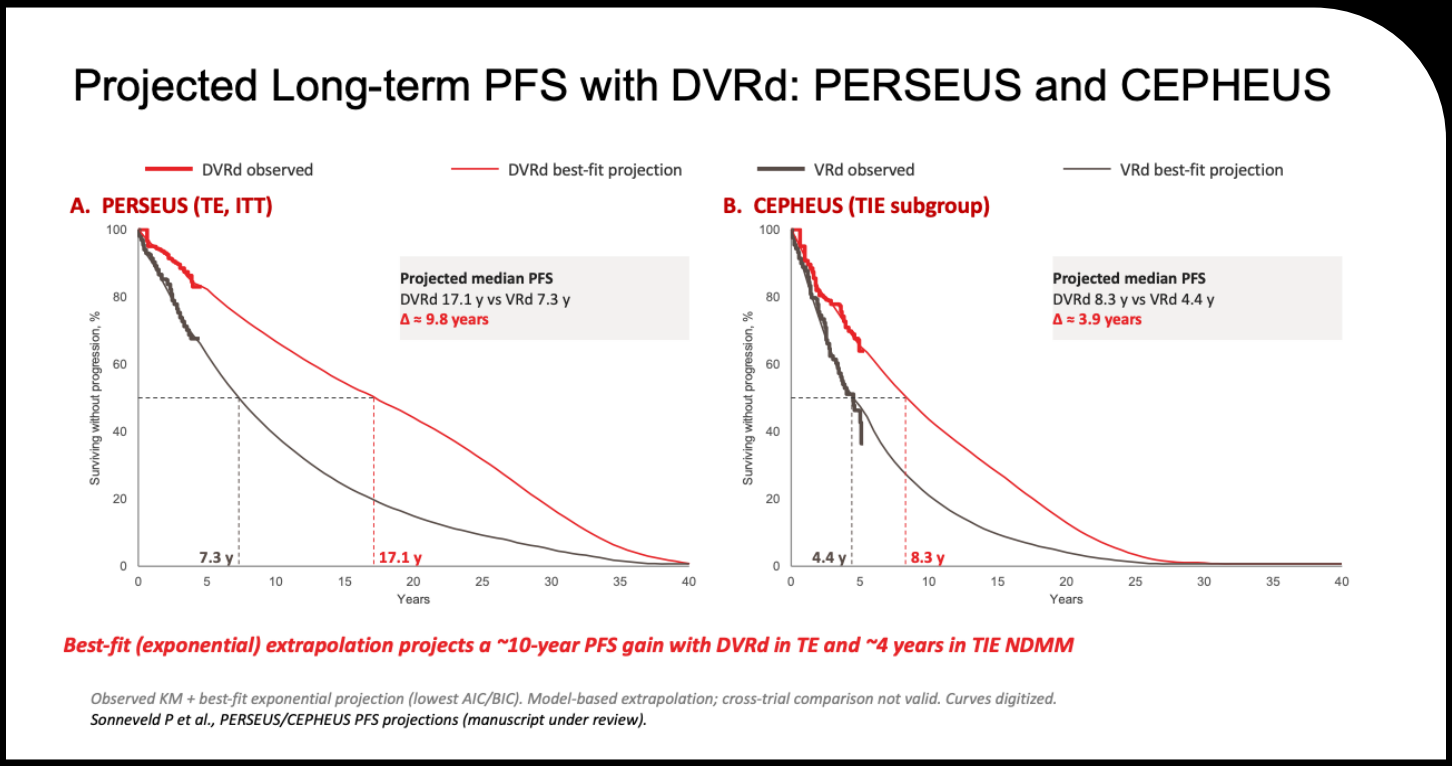
DR. PAOLA NERI

Dr. Neri opened by noting that while median survival in MM is approximately 8 years, transformations in treatment have made functional cures a realistic possibility for some patients. She outlined the IMS proposed definition of a cure, including a sustained CR, MRD negativity at 10^{-6} sensitivity, cessation of therapy for 5 years, and negative functional imaging at the beginning and end of that period.

Increasingly, the objective of treatment is to sustain MRD negativity at a sensitivity of 10^{-6} to achieve cure. Dr. Neri cited a meta-analysis of more than 44 studies linking MRD negativity with improved PFS in both transplant-eligible and transplant-ineligible patients. She emphasized the need of integrating MRD assessment into practice.

Treatment selection also requires consideration of patient, disease, and treatment factors. She highlighted that age alone should not determine frailty; formal assessment is necessary. Fit patients should receive full-dose therapy, while frail patients may benefit from dose reductions or less intensive combinations. Discussing disease risk, Dr. Neri reviewed the IMS-IMWG high-risk criteria incorporating *del(17p)*, *TP53* mutations, del(1p), β2M, and other cytogenetic abnormalities. She emphasized that transplant eligibility should be informed by fitness, organ function, age, and patient preference.

For transplant-ineligible patients, treatment has progressed in the last 10 years from doublets to triplets to anti-CD38-containing quadruplets. She reviewed CEPHEUS, which evaluated DVRd versus VRd in patients who were transplant-ineligible or had deferred transplantation. After eight cycles, treatment continued without bortezomib. She highlighted improved 72-month PFS in the transplant-ineligible subgroup with the quadruplet versus VRd (59% versus 38%), with a numerical trend toward improved OS. Benefits were evident across standard-risk and high-risk subgroups. IMROZ similarly supported adding isatuximab to VRd, producing deeper responses and improved PFS. She noted, however, that IV



isatuximab requires more frequent clinic visits than subcutaneous daratumumab.

For frail patients, Dr. Neri highlighted the IFM 2017-03 study, which investigated a dexamethasone-sparing approach in a population with a median age exceeding 80 years. The findings supported a treatment approach utilizing daratumumab and lenalidomide without dexamethasone, with median PFS of 53 months and OS of 68% at 4 years. She noted that improved tolerability can help patients remain on treatment, an important consideration when dexamethasone-related adverse effects limit treatment compliance.

Turning to transplant-eligible patients, Dr. Neri reviewed the PERSEUS trial, which evaluated DVRd induction, ASCT, DVRd consolidation and daratumumab and lenalidomide maintenance, versus VRd induction, ASCT, VRd consolidation and lenalidomide maintenance. After at least 2 years of maintenance, patients meeting sustained MRD-negativity criteria could discontinue daratumumab while continuing lenalidomide, with daratumumab restarted if MRD returned. She highlighted data presented at the last IMS 2026 showing that rates of sustained MRD negativity at 10^{-6} with CR or better were more than twice as high with DVRd followed by DR maintenance when compared with VRd followed by R maintenance, including responses sustained for at least 24 months. In addition, DVRd substantially improved PFS in both standard- and high-risk groups when compared with VRd.

In addition, Dr. Neri highlighted modelling that projected PFS approaching 17 years for transplant-eligible patients in PERSEUS and approximately 8 years for transplant-ineligible patients in CEPHEUS.

GMMG-HD7 provided evidence supporting an isatuximab-containing quadruplet in transplant-eligible patients, although the trial reported lower rates of MRD negativity than the PERSEUS trial.

ASCT remains the standard of care for eligible patients, although its future role may change in the near feature. Early studies of frontline CAR T and T-cell engagers have reported exceptionally high response rates and MRD-negativity rates when used as first line of therapy in NDMM. These studies are likely to raise the question of whether there will be a role for ASCT in the near future.



AML Treatment and Management in 2026

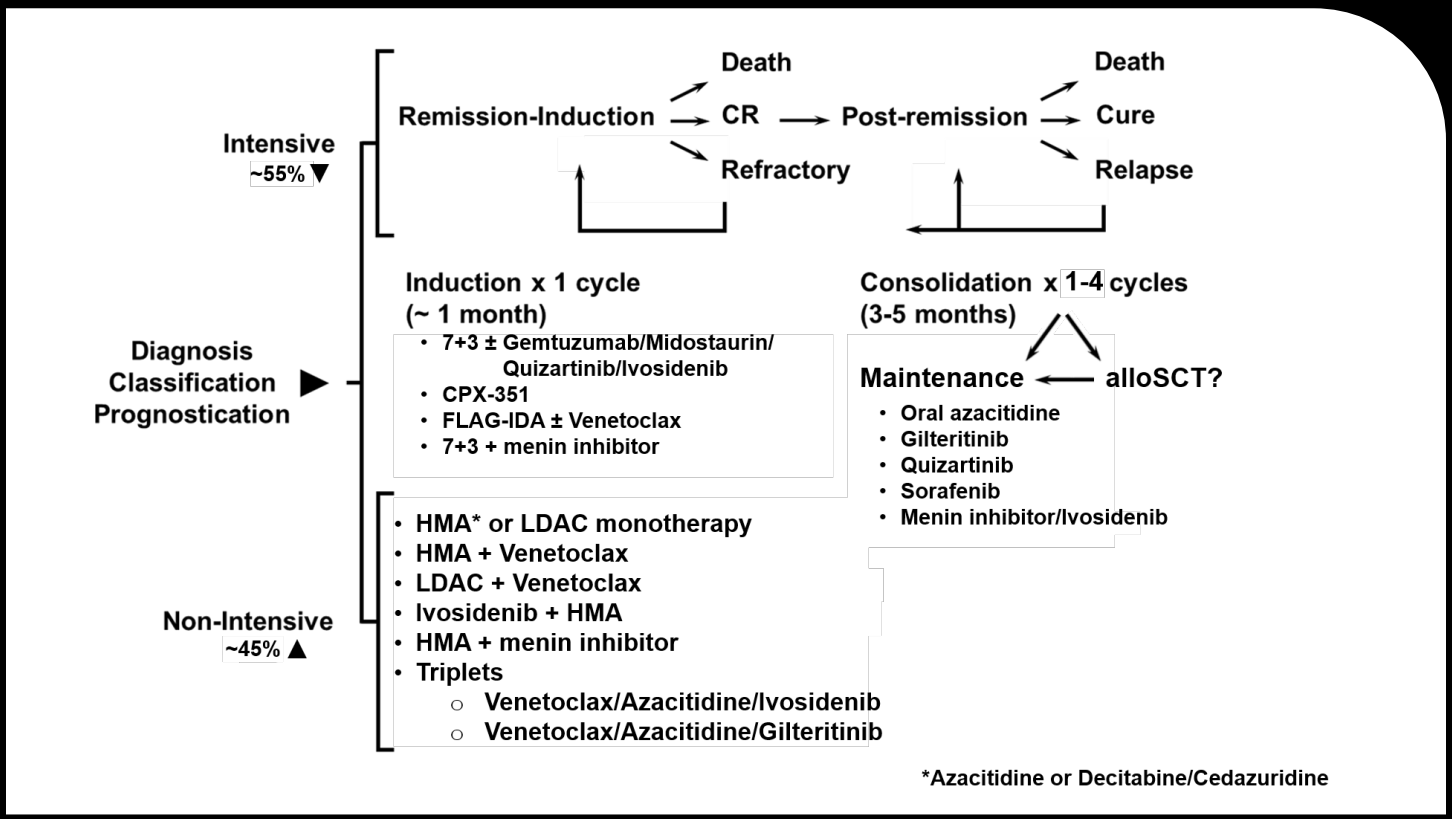
DR. ANDRE SCHUH

Dr. Schuh reviewed changes in AML treatment, including additions to intensive induction, maintenance therapy, and non-intensive combinations. Beginning with intensive treatment, he noted that the protocol of 7 days of cytarabine and 3 days of daunorubicin remains a backbone of AML treatment, despite its introduction in 1973. Adding gemtuzumab ozogamicin to this backbone remains controversial. ALFA-0701 supported its approval based on improved EFS, but a meta-analysis found no survival benefit in patients with adverse cytogenetic risk. Favourable-risk patients had an OS benefit at 6 years (76% versus 55%), while intermediate-risk patients had a smaller benefit. Considering the risk of veno-occlusive disease, many clinicians therefore restrict gemtuzumab ozogamicin to favourable-risk patients and avoid the combination or use fewer induction doses for intermediate-risk patients.

Dr. Schuh then compared midostaurin and quizartinib as additions to the 7+3 regimen. RATIFY established midostaurin with induction and consolidation, but maintenance was not approved in North America. Quizartinib is more selective and potent, although it requires monitoring for QTc prolongation. QuANTUM-First demonstrated improved median OS (32 versus 15 months) with the addition of quizartinib, with benefit also observed among patients who did not undergo transplant. Maintenance therapy continued for up to 36 cycles, compared with 12 months in RATIFY. Dr. Schuh recommended quizartinib for FLT3-ITD AML in patients without significant QTc concerns.

Briefly discussing other intensive approaches, Dr. Schuh expressed a preference for FLAG-IDA over CPX-351 in higher-risk patients, with venetoclax added in very high-risk disease. Upfront menin inhibitor combinations are available through clinical trials.

Turning to maintenance, Dr. Schuh highlighted oral azacitidine for eligible patients not proceeding to alloSCT. QUAZAR AML-001 enrolled patients aged 55 years and older who had achieved CR or CR with incomplete blood count recovery after frontline treatment, with or without consolidation. Results demonstrated a median OS of 25 months versus



15 months with placebo. Maintenance did not appear to compromise subsequent salvage therapy. Dr. Schuh explained that nausea generally improves after the initial cycles and recommended a treatment duration of 4 to 5 years, but noted that the optimal duration remains uncertain.

For non-intensive treatment, VIALE-A established venetoclax and azacitidine therapy, demonstrating a median OS of 14.7 months. Dr. Schuh contrasted this with VIALE-C, which evaluated venetoclax–LDAC and included a higher-risk population and permitted patients with prior azacitidine exposure. Although VIALE-C missed its primary OS endpoint, additional follow-up showed a statistically significant benefit. He considered the uneven provincial access to this combination an unmet need.

In IDH1-mutated AML, the AGILE trial of ivosidenib–azacitidine demonstrated a median OS of approximately 29 months and transfusion independence in 54% versus 17% with placebo and azacitidine. Differentiation syndrome and QTc prolongation require monitoring, but infections and febrile neutropenia were not higher in the ivosidenib arm. He cautioned against direct comparisons with VIALE-A because patient populations and control-arm outcomes differed. He also shared promising early triplet data combining venetoclax, azacitidine, and ivosidenib, with reported composite CR rates exceeding 90%.

Finally, Dr. Schuh addressed intensive versus non-intensive treatment. He emphasized that non-intensive induction does not preclude subsequent alloSCT. Selection should incorporate fitness, comorbidities, geography, social circumstances and patient preferences, alongside the burden of potentially prolonged therapy.

Addressing the debate between venetoclax–azacitidine and intensive chemotherapy, Dr. Schuh presented the PARADIGM trial, which randomized 172 patients, 72% of whom had adverse-risk disease, to venetoclax–azacitidine or intensive chemotherapy. The venetoclax–azacitidine regimen improved EFS (median EFS was 14.5 months versus 6 months with intensive chemotherapy), but no significant OS difference was demonstrated. Dr. Schuh questioned how much the EFS advantage reflected treatment changes in the first two months, which would be expected to be higher in the intensive chemotherapy arm. He concluded that venetoclax and azacitidine may help selected higher-risk, younger patients reach alloSCT, but its role in favourable-risk patients remains uncertain, with Canadian reimbursement presenting an additional barrier.



Panel Discussion

MODERATED BY DR. ALISSA VISRAM AND DR. MARY-MARGARET KEATING

What role does AI play in your daily practice, and does it improve efficiency?

Dr. Puckrin: I used the paid subscription version of ChatGPT to generate graphics for my slides. I provide the content and ask it to create a graphic, which it can do beautifully. It saves time arranging boxes in PowerPoint. You have to be careful and make sure that AI does not introduce false or biased statements.

Dr. Neri: We use AI for coding and analyzing single-cell data in the research setting. You still need a bioinformatician to oversee and check the data generated, but AI provides considerable support to expedite genomic analysis. In the future, I'm optimistic that it will help integrate clinical and genomic information to guide more precise treatment decisions for myeloma patients.

Dr. Davies: I find OpenEvidence helpful because it links directly to articles, allowing me to verify the original sources. I find it helpful to bring up recent efficacy and safety data before presenting new options to patients. OpenEvidence is free for Canadian physicians with a Medical Identification Number.

Dr. Keating: I also use AI to prepare patient handouts about a disease or treatment. Patients can focus on the conversation rather than taking notes, and it saves me time.

Dr. Prica: I've found Claude helpful for drafting reference letters based on a student's or mentee's CV, which I then edit. It also generated useful questions for a workshop that I recently took part in.

Dr. Davies: There is an Epic module for AI-generated notes, and Hamilton Health Sciences has been piloting it. Friends in family medicine use various tools, but hallucinations are a major concern. CMPA and the Canadian Medical Journal have released articles cautioning about symptoms, diagnoses, and treatment that were never discussed during a patient's visit and the importance of verifying documentation.

How do you keep up with new evidence, particularly when you're new to a field?

Dr. Fleury: I receive regular alerts from journals including *Blood, The Lancet* and the *New England Journal of Medicine*. I scan the table of contents to identify papers worth reading. Meetings also help



me identify the research I want to explore in more detail.

Dr. Villa: It gets easier as you build a foundation. Once you understand an area, you can add new evidence in layers. For me, staying current involves continuous engagement with colleagues, advisory boards, research, clinical trials and meetings such as ASH. Writing papers and serving as a trial PI require you to learn the evidence. Repeated exposure to the same data from trials also helps me to retain information.

Dr. Neri: In myeloma, post-IMS and post-ASH meetings are particularly useful. They summarize major findings and provide a Canadian perspective, which matters because international data may not immediately apply to our practice.

Dr. Prica: I've also heard about AI tools that turn papers into an interview-style podcast. I haven't tried this myself, but it could be useful for learning during a commute.

Dr. Visram: I follow several myeloma experts on social media. When important study results are published, their commentary can highlight nuances in interpretation that may not be obvious when reading the publication.

Let's talk about clinical trials. How do you discuss trials with patients and help them participate?

Dr. Neri: In Calgary, approximately 60% of our myeloma patients are on clinical trials, which provide access to therapies we could not otherwise be offered. In my discussion with patients I explain the treatment options available as standard treatments alongside the trial options. It helps to mention that a treatment is already approved in the U.S. but accessible here only through a clinical trial.

Dr. Villa: Successful recruitment starts with opening trials that make sense for your patients. We cannot open every study offered to us. I favour RCTs where both arms offer appealing options, or single-arm studies that provide guaranteed access to a novel therapy that would otherwise not be available. Protocol complexity also matters, as excessive demands can be a deal breaker for patients and institutions.

Dr. Fleury: I think patients often assume that clinical trials include an arm receiving placebo without active treatment, so it's important to present the trials in detail. You need to be convinced that the trial is a good option for the patient.

Dr. Prica: I present the standard of care first, then the trial, and explain the advantages and disadvantages of a clinical trial. Potential benefits include access to a better treatment and a dedicated research team.

How do you balance academic trials focused on optimizing treatment with industry trials offering access to newer therapies?

Dr. Villa: A clinical trials unit needs a balanced "portfolio" of larger industry studies that help support trials of organizations like the CCTG and investigator-initiated trials. That balance allows you to pursue academic questions while also providing access to treatments and being fiscally responsible.

Dr. Neri: We also need to consider resource requirements and try to have trials for NDMM, early and late relapsed MM. Many CAR T-cell and bispecific studies require hospital admission, so we cannot open



Panel Discussion con't

MODERATED BY DR. ALISSA VISRAM AND DR. MARY-MARGARET KEATING

too many of these trials simultaneously and we try to open the ones where we see a clinical gap to ensure enrollment.

Dr. Davies: Early in your career, you may assume you must accept a protocol as presented, but investigators can provide feedback and may sometimes influence the eligibility criteria. For example, feedback about the importance of rituximab maintenance helped make a frontline FL study more relevant to Canadian practice and supported strong recruitment.

Hospital capacity also shapes our choices. We have deliberately deprioritized some bispecific studies with mandated admissions to preserve beds for phase 1 studies or CAR T-cell therapies where hospitalization is essential.

What practical steps can early-career physicians at smaller centres take to bring trials to their site?

Dr. Fleury: I recommend building connections with industry representatives and other investigators. Review ClinicalTrials.gov, and try to find a niche that matches the unmet need of your patient population.

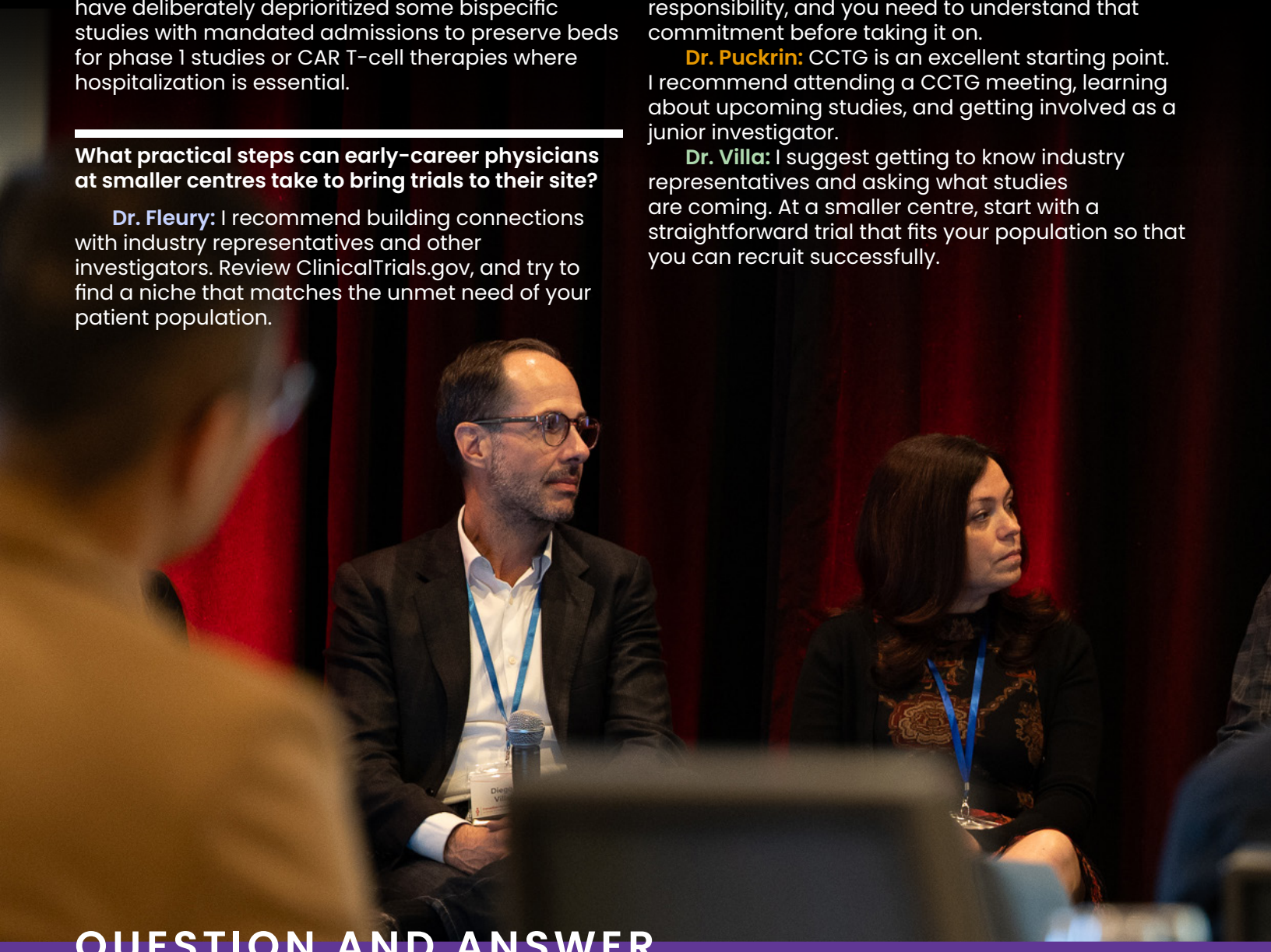
You need to demonstrate that your centre can open a study efficiently and recruit suitable patients very quickly. Existing infrastructure and a track record of successful enrolment are valuable.

Dr. Prica: I recommend asking colleagues at a nearby academic centre to put your name forward when sponsors seek additional sites. You can build your network of industry representatives by expressing interest in advisory boards and meetings that help establish those connections.

Dr. Neri: It's important to keep in mind that being a principal investigator carries substantial responsibility, and you need to understand that commitment before taking it on.

Dr. Puckrin: CCTG is an excellent starting point. I recommend attending a CCTG meeting, learning about upcoming studies, and getting involved as a junior investigator.

Dr. Villa: I suggest getting to know industry representatives and asking what studies are coming. At a smaller centre, start with a straightforward trial that fits your population so that you can recruit successfully.



As new faculty, how do you decide which opportunities to accept and which to decline?

Dr. Neri: Number one, you don't want to say yes to too many things. Prioritize based on your preferred ratio of clinical work and research. It also helps to be present at key meetings, actively engage with senior faculty members at these meetings, and build your involvement gradually.

Dr. Villa: In a public health care system, even protected research time can be difficult. My practical test is whether an opportunity matters enough that I would be willing to work on it during evenings, weekends or long-haul flights, because that is realistically when I do much of my research.

Dr. Davies: When you are starting out, you may not realize that you have some flexibility in building your schedule. After learning how I work best, I have structured my week to have Mondays as protected time where I do not plan for meetings or clinics and minimize distractions. I suggest figuring out how you work best and communicating that clearly with administrative staff and in structuring your clinical time, as you can.

I have also found an academic coach valuable. A coach serves a different role from a mentor. They can help you address very specific day-to-day challenges and help you identify career goals and how to practically work towards them, for example.

Dr. Prica: Mentors or sponsors can act as sounding boards, particularly when you feel pressured to accept something or you're unsure about an opportunity. An objective person outside your immediate group can be especially helpful.

What should early-career physicians look for in a mentor, and how can they find one?

Dr. Villa: There is a difference between mentors and role models. An external mentor can offer perspective on opportunities and challenges that you may not recognize yourself. Fellowships, advisory board meetings, real-world collaborations, and conferences all provide opportunities to build relationships with mentors.

Dr. Neri: A good mentor helps you see the bigger picture rather than simply solve the immediate problem. Finding a mentor can be as simple as reaching out to someone you respect and asking whether they would be willing to offer advice.

Dr. Visram: I suggest assessing how a potential mentor supports other mentees. Do they promote their mentees? Do they share opportunities with them? Those are important indicators of someone you want to work with.

Dr. Puckrin: Starting locally to find a mentor often makes the most sense. I also recommend staying in touch with mentors after they retire as they remain incredible sources of wisdom and guidance.

Dr. Prica: Don't be afraid to be explicit with your mentor about what you hope to do, whether that is speaking at conferences or pursuing a particular research area. It is also reasonable to directly ask senior physicians to keep you in mind when relevant opportunities arise.





About the Organizer

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