



**Canadian
Hematology
Today**

Canadian Hematology Today 2026 Toronto Lymphoproliferative Conference

Event Summary

Toronto, ON • September 18, 2026

**catalytic
health**
medical minds meet here

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Scientific Steering Committee

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DR. MICHAEL JAIN

DR. MATTHEW KANG

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DR. ROBERT KRIDEL

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DR. SHONALI MIDHA

DR. MARK ROSCHEWSKI

DR. NIRAV SHAH

DR. LAURIE SEHN

DR. JULIE STAKIW

DR. JENNIFER WOYACH

Acronyms

A+V		Acalabrutinib plus venetoclax
ABC		Activated B-cell-like
ASCT		Autologous stem cell transplantation
Axicel		Axicabtagene ciloleucel
BCL2i		B-cell lymphoma 2 inhibitor
BCMA		B-cell maturation antigen
BelaPd		Belantamab mafodotin, pomalidomide, and dexamethasone
BR		Bendamustine and rituximab
Brexucel		Brexucabtagene autoleucel
BTK		Bruton's tyrosine kinase
BTKi		Bruton's tyrosine kinase inhibitor
CAR		Chimeric antigen receptor
Ciltacel		Ciltacabtagene autoleucel
CLL		Chronic lymphocytic leukemia
CRS		Cytokine release syndrome
CT		Computed tomography
ctDNA		Circulating tumour DNA
del(17p)		Deletion of the short arm of chromosome 17
DLBCL		Diffuse large B-cell lymphoma
DNA		Deoxyribonucleic acid
DPd		Daratumumab, pomalidomide, and dexamethasone
DVd		Daratumumab, bortezomib, and dexamethasone
EFS2		Event-free survival through second-line treatment
EHA		European Hematology Association
ERIC		Education and Research Initiative on CLL
FDG-PET		Fluorodeoxyglucose positron emission tomography

Acronyms con't

FISH		Fluorescence in situ hybridization
FLIPI		Follicular Lymphoma International Prognostic Index
GCB		Germinal centre B-cell-like
GemOx		Gemcitabine and oxaliplatin
I+V		Ibrutinib plus venetoclax
ICANS		Immune effector cell-associated neurotoxicity syndrome
ICML		International Conference on Malignant Lymphoma
ICU		Intensive care unit
IGHV		Immunoglobulin heavy-chain variable region
IsaKd		Isatuximab, carfilzomib and dexamethasone
ISS		International Staging System
Lisocel		Lisocabtagene maraleucel
MCD		Genetic subtype of DLBCL characterized by MYD88 L265P and CD79B mutations
MCL		Mantle cell lymphoma
MRD		Measurable residual disease
NCCN		National Comprehensive Cancer Network
NHL		Non-Hodgkin lymphoma
ORR		Overall response rate
OS		Overall survival
PCd		Pomalidomide, cyclophosphamide, and dexamethasone
PET		Positron emission tomography
PFS		Progression-free survival
PFS2		Progression-free survival through the next line of treatment
POD24		Progression of disease within 24 months of first-line treatment initiation
Pola-BR		Polatuzumab vedotin, bendamustine, and rituximab

Acronyms con't

Pola-R-CHP	Polatuzumab vedotin, rituximab, cyclophosphamide, doxorubicin, and prednisone
Pola-R-GemOx	Polatuzumab vedotin, rituximab, gemcitabine, and oxaliplatin
PVR	Pirtobrutinib, venetoclax, and rituximab
R-CHOP	Rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone
R-DHAP	Rituximab, dexamethasone, high-dose cytarabine, and cisplatin
R-GemOx	Rituximab, gemcitabine, and oxaliplatin
Tisacel	Tisagenlecleucel
VenO	Venetoclax and obinutuzumab
VR	Venetoclax and rituximab

Conference Objectives

The 2026 Canadian Hematology Today Toronto Lymphoproliferative Conference is an educational forum designed to inform and update Canadian hematologists on the latest advancements in treatment and management of lymphoproliferative disease.

- Provide current, high-quality insights on the latest developments in the management of lymphoproliferative disease.
- Create learning opportunities to share real-world experience and apply new knowledge to clinical practice.
- Foster meaningful discussions and knowledge exchange between clinician delegates and industry representatives.
- Address emerging professional needs with in-depth information on the latest therapies for lymphoproliferative disease in the Canadian market.



Sponsored Breakfast Symposium – Eli Lilly Canada: So Your BTKi Failed...Now What?

DR. MATTHEW KANG

Dr. Kang discussed treatment options for CLL after discontinuation of a covalent BTKi, emphasizing that the reason for stopping therapy should guide subsequent management. He presented Canadian real-world data involving 187 patients that demonstrated the median time to next treatment or death was 4.4 months among patients who discontinued a covalent BTKi because of progression, compared with 13.6 months among those who stopped because of intolerance. Outcomes were particularly poor after exposure to both a BTKi and a BCL2i. Of the 25 patients who had progressed on or become intolerant to both therapies, the median time to next treatment or death was only 1.2 months (Puckrin, 2025).

Rather than retreating patients who progress on a covalent BTKi with another covalent BTKi, Dr. Kang explained that venetoclax is a suitable alternative. In an ERIC analysis of more than 600 patients who received venetoclax after a covalent BTKi, the median time to next treatment or death was

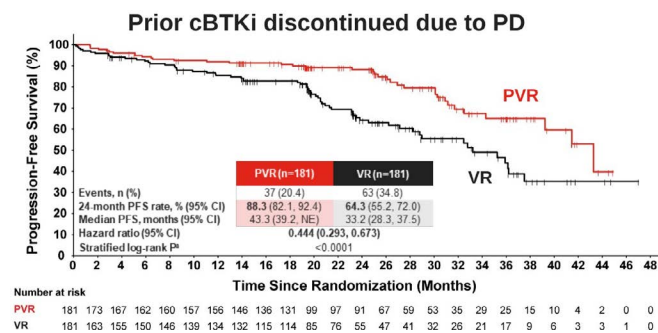
28 months among those who had discontinued BTKi therapy because of progression and 40 months among those who stopped due to intolerance. These findings illustrate that outcomes from MURANO, in which approximately 3% of patients had prior BTKi exposure, may not provide an appropriate benchmark for patients progressing after a BTKi. Dr. Kang explained the studies involved different populations and should not be compared directly.

Dr. Kang then reviewed evidence for the non-covalent BTKi pirtobrutinib. In BRUIN CLL-321, patients previously treated with a covalent BTKi were randomized to pirtobrutinib or investigator's choice of idelalisib plus rituximab or bendamustine plus rituximab. Participants had received a median of three previous lines of therapy, and approximately half had also received a BCL2i. The median PFS was 14 months with pirtobrutinib versus 8.7 months in the control arm. Approximately 76% of those in the control arm crossed over to the pirtobrutinib arm. The relative benefit of pirtobrutinib appeared

This is the patient population I am most interested in

BRUIN CLL-322 · IRC-assessed PFS in patients whose prior covalent BTKi was stopped for progression

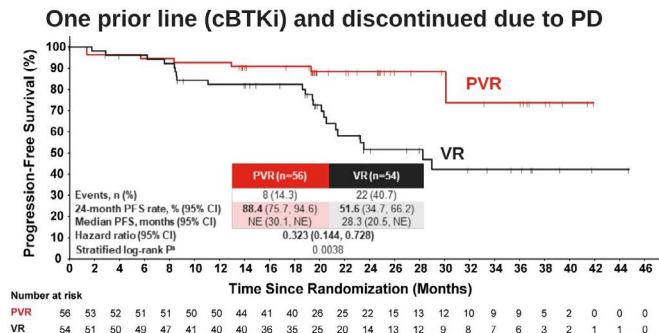
PRIOR cBTKi → PROGRESSION



n = 181 vs 181

24-month PFS 88.3% vs 64.3% · HR 0.444 (0.293–0.673)

ONE PRIOR LINE → cBTKi → PROGRESSION



n = 56 vs 54

24-month PFS 88.4% vs 51.6% · HR 0.323 (0.144–0.728)

It is the first time the data have pointed at this patient rather than around him. Prespecified subgroups, nominal p values, about 55 patients per arm on the right.

Daids MS, et al. EHA 2026. Across all patients with any prior cBTKi exposure (n = 256 vs 254): 24-month PFS 87.7% vs 70.0%, HR 0.509 (0.351–0.738) — curve in backup. Hazard ratios stratified by del(17p) presence and reported as nominal values.

VV-Canada Medical-US-DEL-0629

Health Canada has not established the safety and effectiveness of PVR, and market authorization has not been granted in Canada. Eli Lilly does not support the use of unauthorized regimens.



similar regardless of previous venetoclax exposure, although the median time to next treatment was shorter among patients who had already received venetoclax (20 months) compared to those who were venetoclax-naïve (29.5 months).

A newer study, BRUIN CLL-322, evaluated fixed-duration PVR against VR. At 2 years, PFS was 87% with PVR and 72% with VR. Among patients who had progressed on a covalent BTKi, the 2-year PFS was 88% with PVR versus 64% with VR, respectively. In the prespecified subgroup who had only one prior line of therapy (a covalent BTKi) and discontinued because of progression, the 2-year PFS was 88% with PVR and 52% with VR. PVR also produced deeper rates of MRD negativity. Dr. Kang highlighted that grade 3 or higher neutropenia occurred in approximately half of patients. However, the rate of discontinuation was similar in both the PVR and VR arms.

The PVR benefit was maintained in subgroups with high-risk features, including patients with *TP53* mutations and/or del(17p), complex karyotype, and unmutated IGHV disease. By contrast, the benefit of PVR was not demonstrated among patients who had stopped a previous BTKi because of intolerance, patients who had mutated IGHV disease, and patients who had not previously been exposed to a covalent BTKi. Dr. Kang cautioned that the subgroups were small and the subgroup findings are therefore not conclusive. While the preliminary data are compelling, PVR is not yet funded in Canada.

In practice, Dr. Kang recommended considering five questions when determining the subsequent therapy after a covalent BTKi: Why was the BTKi stopped? Which treatment classes has the patient already received? What is the disease biology? What are the patient preferences? What therapy is important to save for the next treatment? He underlined that for patients with high-risk biology, such as *TP53* mutations, del(17p), or complex karyotype, or those with demonstrated progression on a BTKi, treatment sequencing decisions are especially consequential.

Using case-based illustrations, Dr. Kang discussed his approach to patients with progressive, high-risk disease following a covalent BTKi. Where available, a relevant clinical trial may be considered; otherwise, funded venetoclax-based therapy represents a reasonable option for venetoclax-naïve patients. Patients who discontinued covalent BTKi because of toxicity may also be candidates for venetoclax or, depending on the toxicity, retreatment with another covalent BTKi. He recommended preserving pirtobrutinib for later sequencing in such patients, due to the lack of demonstrated benefit of PVR in patients who discontinued a BTKi for intolerance, rather than progression.

Multiple Myeloma: Primary Treatment and Relapse

DR. JULIE STAKIW

DR. SHONALI MIDHA

Dr. Stakiw examined treatment selection and sequencing for relapsed multiple myeloma from the Canadian perspective, where access is strongly determined by provincial funding. Dr. Stakiw emphasized that treatment decisions must consider patient-related factors including age, fitness, comorbidities, frailty, treatment preferences, social support, distance from a treatment centre, and insurance coverage; disease-related considerations including cytogenetic risk, disease burden, and response to previous therapy; and treatment factors including previous drug exposure, expected efficacy, toxicity, and reimbursement.

Presenting data showing remarkable progress in multiple myeloma therapy, Dr. Stakiw highlighted the importance of patient preference and balancing treatment control with quality of life. She advised that clinicians use the best available therapy as early as possible because some patients may not remain well enough to receive it later.

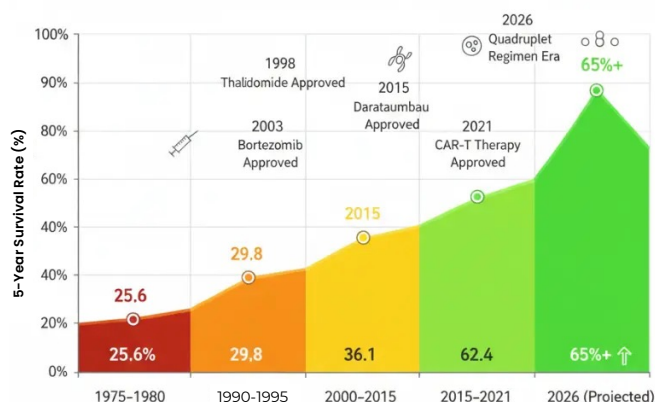
Discussing the case of a 71-year-old man with relapsed multiple myeloma after ASCT who

is relatively fit but has hypertension and type 2 diabetes, Dr. Stakiw discussed the option of a second ASCT. Canadian retrospective data suggest that ASCT may provide another 3 to 4 years of disease control, with benefit shown only when the first transplant produced a remission lasting at least 3 years. However, participants in these studies had a median age of approximately 54 years, limiting their applicability to patients in their 70s. Newer second-line regimens have also made repeat transplantation less compelling for many patients.

If a patient had not previously received a CD38 antibody and was refractory to lenalidomide, physicians in attendance voted in favour of IsaKd over other options. If the patient progressed again at age 73, treatment selection would require renewed consideration of frailty, Dr. Stakiw explained. She stressed that frailty is dynamic and should be reassessed during treatment rather than estimated only at baseline. PCd or BelAPd are reasonable options in this third-line setting, Dr. Stakiw said, adding that third-line therapy is often selected with the goal of bridging patients to BCMA-directed T-cell engaging therapy, which is not funded until the fourth line.

Dr. Stakiw highlighted that belantamab mafodotin can also be an effective third-line option when managed appropriately. Extending the dosing interval to every 60 or 90 days in response to ocular toxicity can preserve efficacy while allowing patients who have not progressed on treatment to remain eligible for a subsequent BCMA-directed bispecific antibody.

**Multiple Myeloma Survival Rate Evolution
(1975–2026)**



DR. JULIE STAKIW, DR. SHONALI MIDHA



Multiple Myeloma: Primary Treatment and Relapse

DR. JULIE STAKIW

DR. SHONALI MIDHA

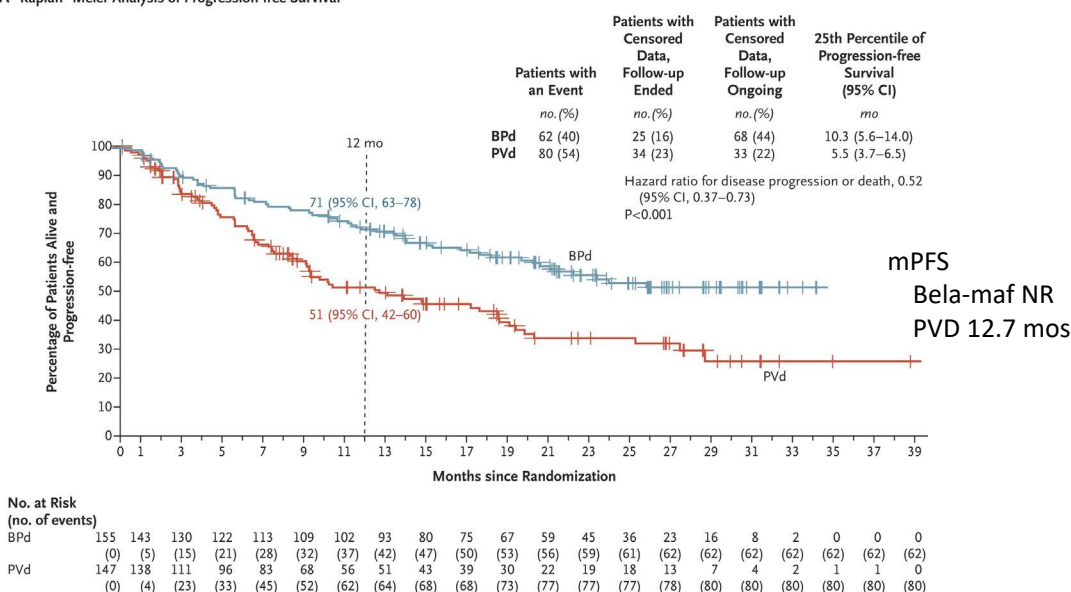
Dr. Shonali Midha reviewed the rapidly expanding multiple myeloma treatment landscape, focusing on therapeutic decision-making at early relapse and options for patients with high-risk disease. For newly diagnosed patients, treatment selection continues to be guided primarily by transplant eligibility and cytogenetic risk. Four-drug regimens incorporating a CD38 monoclonal antibody are increasingly preferred for both transplant-eligible and transplant-ineligible patients. Studies such as GMMG-HD7, PERSEUS, IMROZ, and CEPHEUS have demonstrated improved PFS with isatuximab- or daratumumab-containing quadruplets. Dr. Midha added that patients with standard-risk disease who achieve MRD negativity following induction may be able to forgo transplantation, thereby avoiding its acute and long-term toxicities. Transplantation generally remains advisable for patients with high-risk disease, although transplant may be avoided in patients with an MRD-negative response to

quadruplet therapy or due to patient comorbidities and preferences.

Early relapse presents a growing challenge because many patients are already exposed to immunomodulatory drugs, proteasome inhibitors and CD38 antibodies after one line of therapy. Among the available options, Dr. Midha favoured CAR T-cell therapy when it is accessible and the disease can be controlled during bridging therapy. In CARTITUDE-4, ciltacel substantially improved PFS rates at 30 months (59% versus 26%) and OS rates at 30 months (76% versus 64%) compared with standard-of-care therapy in lenalidomide-refractory patients. Important toxicities include CRS, cytopenias, infections, and neurotoxicity. Rare motor neuron and peripheral nerve toxicities occur, but are less common when CAR T-cell therapy is used in early relapse rather than in later relapse. Dr. Midha highlighted that PFS2 was not reached in the ciltacel arm, while PFS2 was 2 years in the standard-of-care

DREAMM-8: Belantamab Mafodotin-Pd vs. PVd

A Kaplan-Meier Analysis of Progression-free Survival



DR. JULIE STAKIW, DR. SHONALI MIDHA

arm, highlighting the benefit of an earlier use of CAR T-cell therapy.

Bispecific antibodies offer an off-the-shelf alternative to CAR T-cell therapy in early relapse.

In MajesTEC-3, teclistamab plus daratumumab markedly improved PFS among patients with one to three previous lines of therapy; 36-month PFS rates were 83% with the combination versus 30% with DPd or DVd. While only 5% of patients in the MajesTEC-3 study were exposed to a CD38-directed therapy, MajesTEC-9 similarly showed favourable outcomes with teclistamab monotherapy in a population previously exposed to CD38 treatment, with an 18-month PFS of 70% versus 20%. The benefit was identified across cytogenetic risk groups, age groups, class refractoriness, and ISS disease stage. However, while CRS and ICANS rates are lower with bispecific therapies compared to CAR T-cell therapy, infections remain a major concern: overall infection rates exceeded 80% in both studies, and approximately half were grade 3 or higher.

When both approaches are available, current evidence favours administering CAR T-cell therapy before a BCMA-directed bispecific antibody. Prior bispecific exposure has been associated with poorer CAR T-cell outcomes. However, fixed-duration treatment with bispecific agents may limit T-cell exhaustion and change the recommended treatment sequencing approach.

If BCMA-directed treatment is required prior to CAR T-cell therapy, Dr. Midha said she would favour belantamab mafodotin, although its ocular toxicity requires close monitoring and shared care with ophthalmologists.

Major unmet needs remain for patients whose disease progresses after CAR T-cell therapy or bispecific agents. Emerging approaches include cereblon E3 ligase modulators, and novel, dual-targeting combinations such as teclistamab and talquetamab, and etentamig, pomalidomide, and dexamethasone. Ixertin combinations can also be considered as a bridge to T-cell engaging therapies to optimize the immune microenvironment. Dr. Midha concluded that optimal sequencing remains unresolved and must account for disease aggressiveness, previous class exposure, treatment availability, comorbidities, and patient goals.



Follicular Lymphoma: What's New in 2026

DR. LAURIE SEHN
DR. REID MERRYMAN

Dr. Sehn reviewed the rapidly evolving treatment landscape for relapsed or refractory follicular lymphoma, emphasizing the shift from retreatment with chemoimmunotherapy toward immune-based therapies.

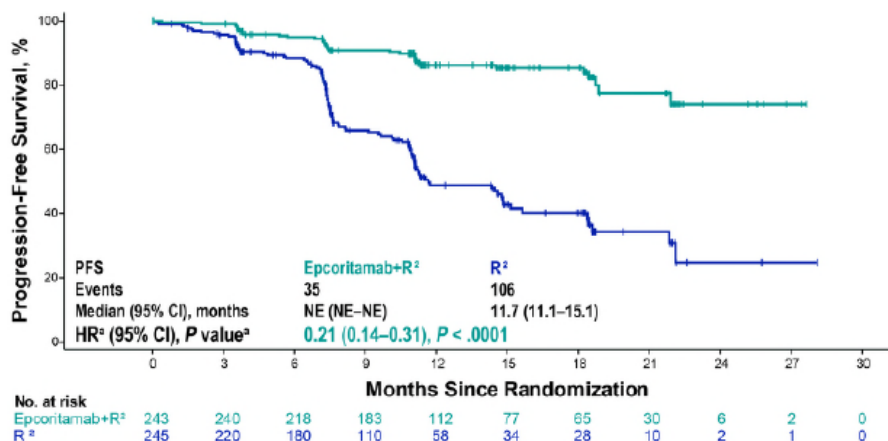
Approximately 15% to 20% of patients with follicular lymphoma are categorized as POD24, which is associated with poorer survival. Because many early relapses involve histologic transformation, Dr. Sehn stressed the importance of investigating patients with POD24 for transformed disease. Novel agents are strongly preferred for these patients.

Dr. Sehn explained that retreatment with BR is not recommended in the second-line setting, due to its limited efficacy, and its association with myelosuppression and bone marrow toxicity. When chemoimmunotherapy is the most appropriate course of action, Dr. Sehn generally favours cyclophosphamide, vincristine, and prednisone, adding obinutuzumab for rituximab-refractory disease. She was cautious about ASCT as retrospective studies have not demonstrated an

overall 5-year survival benefit and the toxicity of ASCT is increasingly difficult to justify as effective immunotherapies become available.

Lenalidomide plus rituximab is now an established second-line option based on the AUGMENT trial, which demonstrated a median PFS of 28 months in a relapsed or refractory indolent NHL population, compared with 14 months in the placebo and rituximab arm (Leonard et al, 2022). For the higher-risk, rituximab-refractory patients encountered in practice, two phase 3 trials indicate that adding another immunotherapy to the rituximab-lenalidomide backbone can substantially improve outcomes. In the inMIND trial, adding tafasitamab to lenalidomide-rituximab improved ORR and PFS. Median PFS was 22 months with the triplet versus 14 months with lenalidomide-rituximab alone. Benefits extended across clinically important subgroups, including patients with POD24 or rituximab-refractory disease. Toxicity was broadly comparable, although infections were somewhat more frequent in the tafasitamab arm. A study presented by Sehn et al at ICML in 2025 showed

Epcoritamab+R² Resulted in Superior PFS per Independent Review Committee (IRC) With 79% Risk Reduction



- Concordance rate was 94% for PFS between IRC and investigator assessment
- The estimated 16-month PFS was 85.5% (95% CI: 79.7, 89.7) for epcoritamab+R² and 40.2% (95% CI: 31.8, 48.4) for R²

Falchi L et al, The Lancet, 2025

DR. LAURIE SEHN, DR. REID MERRYMAN

that 23 of 24 post-treatment biopsy samples in which lymphoma was detected remained CD19-positive, including seven of eight samples from patients who received tafasitamab. The patient who was CD19-negative had 80% CD19-negative tumour cells at first-line screening. While evidence is limited, the risk of CD19 loss following tafasitamab therapy appears to be very low.

Similarly, EPCORE FL-1 showed that adding the bispecific antibody epcoritamab to lenalidomide-rituximab markedly improved ORR and PFS. Cytokine release syndrome events were generally low grade, making outpatient treatment reasonable. However, grade 3 or higher neutropenia and serious infections were substantially higher in the epcoritamab arm. Dr. Sehni highlighted that infection risk is an important consideration for frailer patients. She noted, however, that infections were effectively treated in the trial and the rates of fatal adverse events did not differ between the experimental and control arms.

She concluded by explaining that the choice between tafasitamab-lenalidomide-rituximab versus epcoritamab-lenalidomide-rituximab will likely be based on indirect efficacy and toxicity comparisons, logistical considerations (with tafasitamab requiring more frequent clinic visits), and patient choice.



Follicular Lymphoma: What's New in 2026

DR. LAURIE SEHN
DR. REID MERRYMAN

Dr. Merryman reviewed third-line treatment options for follicular lymphoma, beginning with bispecific antibodies. Phase 2 studies of epcoritamab, mosunetuzumab, and odronextamab included heavily pretreated populations, approximately half of whom had POD24 and half of whom had high-risk FLIPI scores. The ORRs were approximately 80%, with complete response rates ranging from 60% to 74%, and 3-year PFS rates of approximately 40% across the trials.

CRS was initially a major concern with bispecific antibodies. However, step-up dosing and prophylactic corticosteroids have reduced its severity, allowing these drugs to be administered safely in the outpatient setting. ICANS was uncommon and generally low-grade in the trials.

CAR T-cell therapies produced even higher response rates in third-line follicular lymphoma. Trials of axicel, lisocel, and tisacel reported ORRs of 86% to 97% and complete response rates of 68% to 94%. Estimated 3-year PFS ranged from approximately 53% to 68%. The 5-year PFS rate of approximately 50% with axicel is particularly encouraging. Axicel was associated with more CRS and ICANS than the other CAR T-cell products (the rate of grade 3 or higher ICANS was 15% with axicel,

versus 1% for tisacel and 2% for lisocel) while serious infections remained a concern across the class.

Dr. Merryman also reviewed the phase 2 ROSEWOOD trial, in which zanubrutinib and obinutuzumab improved response rates and PFS compared with obinutuzumab alone. Data presented at ASH 2025 demonstrated that the median PFS was approximately 22 months, compared with 10 months in the control arm (Zinzani et al, 2025). Cytopenias and infections were the most common serious toxicities; Dr. Merryman highlighted the 9% risk of grade 3 or higher COVID-19 infection in the trial and the 15% risk of grade 3 or higher pneumonia.

In the absence of head-to-head trials, treatment selection requires balancing efficacy, toxicity, convenience, and patient preference. Zanubrutinib-obinutuzumab and lenalidomide-rituximab are relatively accessible and likely less toxic, but appear less effective. Bispecific antibodies offer strong efficacy and allow for outpatient administration, whereas CAR T-cell therapy may provide the most durable disease control but requires specialized centres and carries greater logistical burdens. Dr. Merryman recommended CAR T-cell therapy when occult transformation is suspected because it is



Phase II trials - Efficacy

	N	Median prior lines	POD24	High-risk FLIPI	ORR	CMR	PFS	Citations
Mosunetuzumab	90	3	52%	42%	80%	60%	Median PFS - 24.0 m 3-year PFS – 43%	Sehn, Blood 2024
Epcoritamab	128	3	53%	60%	82%	63%	Median PFS – 15.4 m 3-year PFS – 38%	Linton, ICML 2025
Odronextamab	157	3	49%	58%	81%	74%	Median PFS 23.0m 3-year PFS - 38%	Jagadeesh, ASCO 2025

also highly effective against DLBCL. Many patients prefer time-limited therapy, which is why Dr. Merryman often chooses mosunetuzumab or rituximab and lenalidomide with epcoritamab rather than indefinite therapy.

Dr. Merryman concluded by reiterating the emerging concern about serious infection, including occasional fatal infections, as repeated B-cell-depleting therapy can prevent immune recovery. Future research should focus on identifying risk factors for infection and developing improved mitigation strategies.



Evolving Clinical Applications of Genomics in DLBCL

DR. MARK ROSCHEWSKI

DR. ROBERT KRIDEL

Dr. Roschewski reviewed the potential of ctDNA to guide treatment decisions in DLBCL. He described ctDNA as a precision-medicine tool that can be used before the start of therapy to choose risk-adapted treatment paradigms, during therapy to guide response-adjusted paradigms, and at the end of therapy to guide salvage therapy.

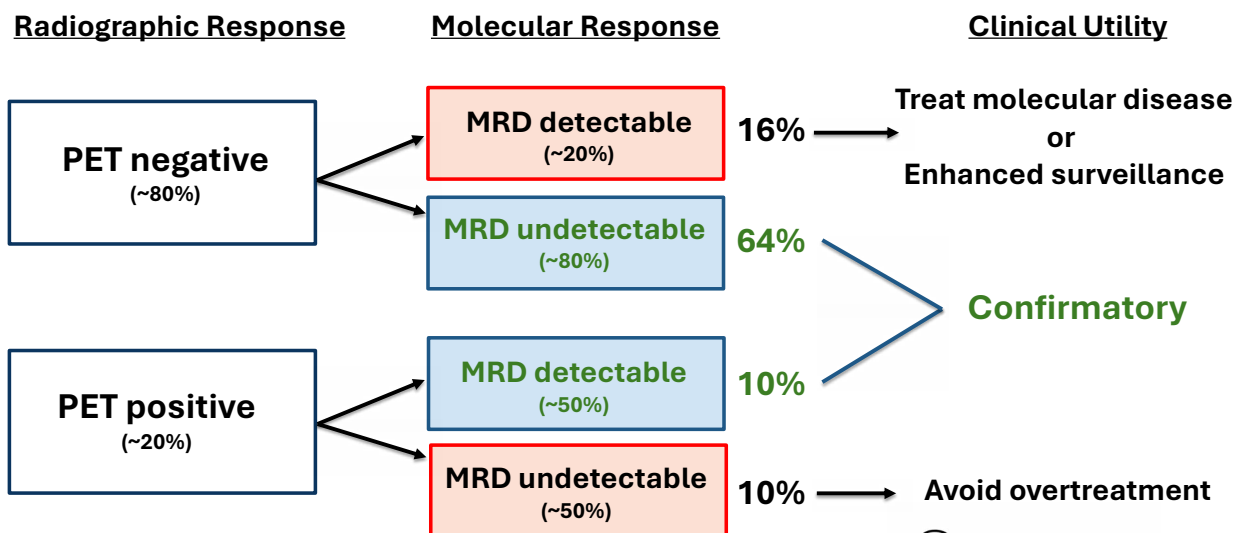
He noted that FDG-PET is unable to detect MRD, is not specific for lymphoma, and involves radiation exposure. Tissue biopsy, meanwhile, is limited by procedural risks, interobserver variability, sampling error due to heterogeneity (which is exacerbated by the move towards smaller biopsies), and inaccessible anatomic sites. ctDNA testing, by comparison, is noninvasive, highly sensitive and specific, and provides quantitative results that correlate with tumour burden in real-time. However, assays must reliably distinguish tumour-derived DNA from normal cell-free DNA, particularly when there is minimal disease burden. Lack of standardization in sample collection, processing, and shipping is another challenge.

Dr. Roschewski argued that ctDNA could address important limitations of PET imaging. Approximately 20% of patients with a negative scan still relapse within 5 years (Kostakoglu, 2021). Conversely, the positive predictive value of a positive PET scan is approximately 50%, which means that patients should undergo a biopsy before receiving salvage therapy. Dr. Roschewski remarked that a tissue biopsy may not occur in all cases following a positive PET scan.

New PhasED-Seq assays that identify phased variants improve analytical sensitivity. Phased variants are multiple genetic abnormalities occurring on the same cell-free DNA molecule. Because the probability that these changes would occur together by chance is extremely low, PhasED-Seq assays can more confidently identify tumour-derived DNA.

Studies using this approach have shown that ctDNA levels decline rapidly during treatment. A study by Roschewski et al published in 2025 showed that 25% of patients had undetectable ctDNA after

Incorporation of MRD with PET response at EOT



one treatment cycle, and close to half of patients had undetectable ctDNA after two cycles, raising the possibility of substantially reducing treatment based on ctDNA response. At the end of therapy, an undetectable ctDNA result was associated with a survival probability exceeding 95%, making it more prognostic than a PET scan. Detectable ctDNA was associated with substantially poorer outcomes, although approximately 30% of patients with detectable disease did not progress within 5 years.

Combining PET and ctDNA results may reduce uncertainty. Among patients with a negative PET scan, ctDNA distinguished those at very low risk of relapse from those with residual molecular disease. It also helped interpret positive PET findings. Approximately half of PET-positive patients had undetectable ctDNA and might therefore avoid immediate salvage therapy. However, PET scan results do not risk-stratify ctDNA results (Roschewski et al, 2025). Current NCCN guidance allows clinicians to consider ctDNA when an end-of-treatment PET scan is positive, rather than obtaining a tissue biopsy, to determine whether subsequent therapy is necessary.

Dr. Roschewski then presented an algorithm for incorporating ctDNA testing results into clinical decisions at the end of therapy. He noted that the clinical significance of a negative PET scan accompanied by detectable ctDNA remains uncertain. The randomized phase 2 ALPHA3 study is assessing consolidation therapy versus monitoring for these patients. A phase 3 randomized study is also assessing the use of ctDNA testing after two cycles to determine the escalation, continuation, or de-escalation of therapy.



Evolving Clinical Applications of Genomics in DLBCL

DR. MARK ROSCHEWSKI

DR. ROBERT KRIDEL

Dr. Kridel reviewed how genomic classification may help personalize frontline treatment for DLBCL. Although DLBCL is generally treated as a single disease, it encompasses biologically distinct subtypes with different oncogenic mechanisms and clinical outcomes.

Targeting ABC biology has generated promising subgroup signals, such as in the REMoDL-B and PHOENIX trials, but no definitive frontline success, suggesting that cell-of-origin alone may be insufficient for treatment selection.

Gene-expression profiling is the gold standard, but many centres rely on immunohistochemical surrogates. The Hans algorithm, which classifies patients as GCB or non-GCB, is considered the most widely accepted surrogate. Dr. Kridel presented Princess Margaret Cancer Centre data showing substantial discordance between the Hans algorithm and gene-expression profiling.

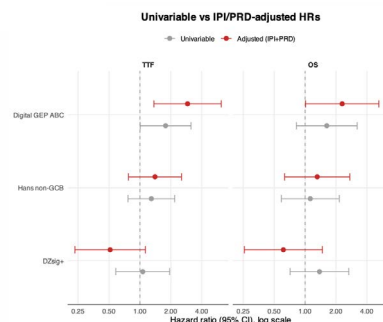
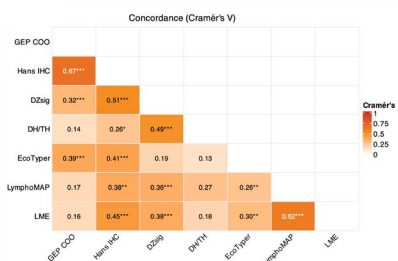
Approximately 8% of cases classified as GCB by Hans immunohistochemistry were ABC by gene expression, while 15% classified as non-GCB were actually GCB. Importantly, only gene-expression-based classification predicted inferior time-to-treatment failure. Hans immunohistochemistry was not prognostic.

This distinction has become clinically important following the POLARIX trial of pola-R-CHP.

At 5 years, the regimen resulted in an approximately 6% improvement in PFS overall, but its benefit was concentrated largely among patients with ABC DLBCL. Access policies may therefore depend on cell-of-origin classification even though reliable gene-expression assays are not routinely available across Canada. In contrast, the frontMIND study found that the benefit of adding tafasitamab and lenalidomide to R-CHOP was demonstrated across cell-of-origin groups.

COO Assessment in R/R DLBCL – PMH experience

- 116 patients with relapsed/refractory LBCL profiled on relapse biopsy specimens at Princess Margaret Cancer Centre.
- COO assigned by Hans immunohistochemistry and digital gene expression profiling (NanoString LExA120/Lymph2Cx-based approach).
- Hans IHC and digital GEP showed **substantial but imperfect concordance** (Cramér's V = 0.67, $p < 0.001$)
- **Misclassification occurred in both directions:** 8% of Hans-GCB cases were classified as ABC by GEP, while 15% of Hans non-GCB cases were classified as GCB by GEP. In addition, GEP identified an unclassified group not captured by IHC.
- **Only GEP-derived COO retained prognostic significance.** ABC by digital GEP independently predicted inferior time-to-treatment failure (HR 2.86-2.98), whereas Hans COO was not prognostic in multivariable analysis.



abbvie

Gong et al, unpublished

Dr. Kridel also discussed double-hit lymphoma, which accounts for approximately 8% of DLBCL and is highly concentrated within the GCB subtype (about 13% of patients with GCB disease have double-hit lymphoma, compared with 1% of those with ABC DLBCL). Gene-expression signatures can identify patients with double hit lymphoma. Approximately half of signature-positive cases have double-hit lymphoma by FISH (Hilton et al, 2019; Sha et al, 2018). Additionally, some FISH-negative cases harbour MYC rearrangements that are detectable through whole-genome sequencing (Hilton et al, 2019).

Large sequencing studies have further divided DLBCL into genetic subtypes defined by recurring combinations of mutations and structural abnormalities. Exploratory analyses suggest

that these subtypes may predict response to targeted therapies. MCD disease, for example, may particularly benefit from ibrutinib or polatuzumab, although patient numbers remain small (Wilson et al, 2021).

Dr. Kridel concluded by highlighting the phase 2 GUIDANCE-01 trial, which assigned patients to molecularly defined treatment groups and added subtype-specific targeted agents to an R-CHOP backbone. This strategy improved response rates, PFS, and OS and is now being evaluated in a phase 3 trial. Dr. Kridel explained that genomic classification may ultimately allow clinicians to select more effective frontline regimens while the addition of on-treatment molecular monitoring with ctDNA/MRD may enable truly personalized frontline therapy.



CLL: Optimal Sequencing in 2026

DR. JENNIFER WOYACH
DR. CHRIS HILLIS

Dr. Woyach emphasized that choosing the best CLL treatment requires more than selecting the most effective or durable therapy. As many patients will receive only one or two lines of therapy, quality of life and patient preference are central considerations.

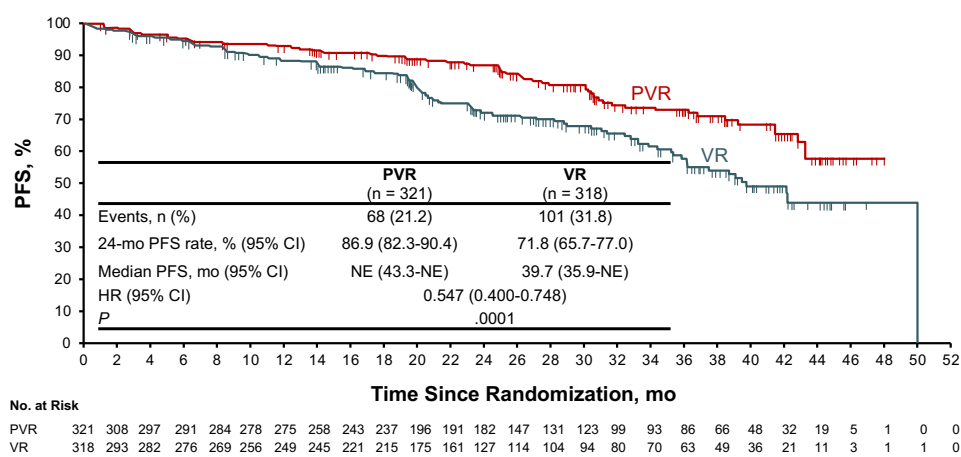
Before each new line of therapy, Dr. Woyach recommended repeating FISH, cytogenetic, and *TP53* mutation testing. Clinicians should also reassess comorbidities and potential drug interactions. She emphasized that relapse alone does not necessarily call for immediate treatment. Patients with lymph nodes detected by CT scan or an increase in white blood cells after time-limited therapy can be monitored. Similarly, patients with lymph nodes detected on exam or an increase in white blood cells during continuous treatment do not need immediate treatment, but are likely to require it in the near future. Conversely, patients who experience a return of autoimmune conditions or have symptomatic enlargement of lymph nodes, splenomegaly, or fatigue or other constitutional symptoms warrant treatment.

Dr. Woyach highlighted that the first line of therapy shapes the next choice. For patients relapsing after chemoimmunotherapy, both covalent BTK inhibitors and venetoclax-based

treatment produce extended PFS. After fixed-duration venetoclax-obinutuzumab, a BTKi is an effective option; Dr. Woyach cited a retrospective study reporting an 84% ORR and median PFS of 32 months in patients with CLL who had been exposed to venetoclax (Mato, 2020). Venetoclax retreatment is also promising, although evidence remains limited. In the MURANO trial, the ORR was 72.2% in 18 patients who received venetoclax retreatment, with a complete response rate of 6%. A retrospective multicentre study of 46 patients, 91% of whom received venetoclax retreatment in the relapsed/refractory setting, reported an ORR of 79.5% and a median PFS of 25 months (Thompson, 2022). In the ongoing ReVenG study, an update presented at EHA in 2025 reported that all 15 patients evaluated at the end of treatment had responded, and 11 of 13 assessed for MRD had undetectable disease.

Evidence is also limited after fixed-duration BTKi-venetoclax combinations. Limited prospective data presented at EHA 2025 by Dr. Wierda et al. and retrospective data (Jain et al, 2024; Tam et al, 2022) suggest that either drug, or both together, remain effective. Dr. Woyach noted that resistance mutations have generally not been detected at

BRUIN CLL-322: PVR Prolonged PFS Compared With VR in R/R CLL



16 events of Richter transformation occurred in the VR arm vs 8 events in the PVR arm

DR. JENNIFER WOYACH, DR. CHRIS HILLIS



relapse, although longer-term data are needed.

For patients previously exposed to a covalent BTKi, venetoclax monotherapy is an effective second-line option (Woyach et al, 2023). Pirtobrutinib is also effective in the post-BTKi and double-exposed settings. In the BRUIN CLL-321 trial, median PFS with pirtobrutinib was 14 months, but median time to next treatment was 24 months. Dr. Woyach noted that progression was detected on CT scans, performed every 3 months, to contextualize the difference between the median PFS and time to next treatment outcomes. She also pointed out that median PFS was 22 months in patients who were BCL2i naïve, compared with 17 months in patients exposed to both therapies.

Newer options improve the effectiveness of fixed-duration strategies in the relapsed setting. Presenting the BRUIN CLL-322 trial of PVR versus VR in relapsed or refractory CLL, Dr. Woyach noted that longer-term follow-up is required to determine which patients derive the most benefit from PVR. Lisocel is also available in the United States for some patients with double-exposed CLL. However, complete remissions were limited to approximately 20% of patients.

CLL: Optimal Sequencing in 2026

DR. JENNIFER WOYACH
DR. CHRIS HILLIS

Dr. Hillis reviewed frontline treatment selection in CLL, emphasizing how decisions made at the start of therapy may affect subsequent treatment options. Although sequencing remains important, he argued that clinicians should generally choose the best available frontline therapy rather than prioritizing preserving options for later lines. He noted that the overall CLL population now has an approximately 90% 5-year survival relative to age- and sex-matched controls. Some patients may require only one line of therapy during their lifetime, making it especially important to use the most appropriate regimen first.

Contemporary frontline regimens include continuous second-generation BTKi therapy, dual-target fixed-duration therapy of A+V or I+V, and fixed VenO therapy. As the efficacy is high across these options, selection should be guided by disease biology, patient preferences, anticipated life expectancy, and the trade-off between continuous and fixed-duration therapy. Dr. Hillis explained that frailty has relatively little influence on his approach

because modern CLL therapies are generally well tolerated. Indeed, studies of acalabrutinib and VenO suggest that successfully treating CLL may improve frailty rather than worsen it.

Sequencing becomes particularly relevant when patients are expected to live for more than 7 to 10 years after starting treatment. In Ontario, funded second-line options remain partly determined by the regimen used in the frontline setting.

Disease biology should inform discussions about treatment goals. In general, fixed-duration therapy is recommended for IGHV-mutated disease, due to superior efficacy, and is often the preferred frontline option for IGHV-unmutated disease as well. Dr. Hillis said that he also prefers fixed-duration therapy in the frontline setting, as the repeated clinic visits for ramp-up dosing will be more difficult in later line settings.

For patients with TP53 aberrations or del(17p), continuous covalent BTKi therapy remains the preferred approach. Nevertheless, fixed-duration VenO can provide reasonable time to next treatment

FRONTLINE CLL • 2026

Evidence at a glance

EVIDENCE CUT
05 SEP 2026

THE EVIDENCE FRAME RCT = randomized NR = nonrandomized uMRD4 = <10 ⁻⁴	ACALA acalabrutinib CONTINUOUS • 2G cBTKi ELEVATE-TN + Ph3 RCT • n=179 age 70 • FU 74.5 mo	ZANU zanubrutinib CONTINUOUS • 2G cBTKi SEQUOIA + Ph3 • n=241 RCT* +111 del17p NR • FU 78.7 mo	VenO ven + obinutuzumab FIXED 12c • IV + ORAL CLL14 + Ph3 RCT • n=216 age 72 / CIRS 9 • FU 110.1 mo	A+V acala + ven FIXED 14c • ALL ORAL AMPLIFY + Ph3 RCT • n=291 age 61 • FU 40.8 mo • TP53x	I+V ibrutinib + ven FIXED 15c† • ALL ORAL CLL17 Ph3 n=305 • FU 34.2 mo CAPTIVATE n=202 • FU 68.9 mo
DURABILITY reported efficacy landmark	72-mo PFS 61.5% OS 75.5% • med PFS NR HR 0.24 vs ClbO	78-mo PFS 70.9% PFS2 81.3% • HR 0.28 vs BR 72-mo OS 84%	Median PFS 76.6 mo 9-y PFS 25.6% • OS 59.3% median TTNT 91.9 mo	36-mo PFS 76.5% OS 94.1% • med PFS NR HR 0.65 vs FCR/BR	3-y PFS 79.4% OS 96.0% • CLL17 CAPTIVATE 5.5-y PFS 66% (OS 97%)
TP53 / IGHV biologic risk signal	TP53: 72-mo PFS 56% uIGHV: 72-mo PFS 60% small, descriptive subsets	del17p: 72-mo PFS 64% 72-mo OS 83% • n=111 NR IGHV m/u: 65% / 64%	TP53: med PFS 49.0 mo vs 79.2 WT uIGHV 64.7 vs mIGHV 104.9 mo	TP53 aberration excluded uIGHV: 36-mo PFS 68.9% no randomized TP53 evidence	TP53: 5.5-y PFS 36% vs 70% no TP53 uIGHV 55% vs mIGHV 79% (CAPTIVATE)
DEPTH / OFF TX MRD timing + treatment-free	CR/CRi 19% uMRD not a treatment target 47% on drug at 6 y	CR/CRi 24% MRD not a stopping endpoint 59% on drug at 6 y	uMRD4: PB 75.5% • BM 56.9% EOT+3 mo 39.6% no next tx at 9 y	PB uMRD4 45% EOT: 38% at +3 mo all off after cycle 14	uMRD4: PB 47.2% • BM 40% CLL17 EOT • CAPTIVATE 69/69% FLAIR BM 66.2% ≤2 y†
SAFETY / BURDEN time-at-risk matters‡	AF 8.9% • HTN 11.2% major hemorrhage 5.6% 6-y cumulative • AE stop 17.9%	AF 7.1% • HTN 22.9% bleeding 52.1% (g≥3 7.5%) g≥3 infection 30% • ~5-y cumulative	g3/4 neutropenia 52.8% g3/4 infection 17.5% • lab TLS 1.4% (0 clinical) 5-wk ramp + 6 IV O infusions	g≥3 neutropenia 32.3% infection 12.4% • AF 0.7% • TLS 0.3% all oral; 5-wk ven ramp	Cardiac 23.8% • AF 12.5% serious AE 46.9% • early stop 22.1% all oral; 5-wk ven ramp (CLL17)
DECISION SIGNAL best fit + watch-out	Broad genomic coverage Best when continuous TP53 evidence / simple start outweigh finite therapy. WATCH: BID indefinite exposure; preserves BCL2.	Mature continuous + PFS2 Strong continuous option; prospective del17p cohort. WATCH: high-risk arm NR; cumulative HTN/bleeding; preserves BCL2.	Longest off-therapy proof Deep, validated MRD; finite 1 y. WATCH: TLS/IV logistics; TP53/uIGHV relapse earlier; preserves BTKi.	Finite all-oral 2G doublet Low observed AF/TLS. WATCH: 41-mo data, fit/TP53-WT, CIT comparator; uses both classes.	Direct RCT + duration depth Fixed and MRD-guided evidence. WATCH: ibrutinib CV, TP53 durability, 15c ≠ FLAIR; uses both classes.

† FLAIR was MRD-guided (up to 6 y), not 15-cycle fixed duration. ‡ Unless grade is specified, AE rates are any-grade; safety is trial-specific and exposure-dependent. MRD specimen/timing/denominator differ. COVID-era deaths affected AMPLIFY/CLL17.

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Clinical synthesis, not a guideline • Regulatory availability varies by jurisdiction • PFS/OS percentages must not be compared without the trial context shown

DR. JENNIFER WOYACH, DR. CHRIS HILLIS

and warrants discussion. In selected younger patients, using obinutuzumab-based therapy upfront may preserve continuous BTK inhibition for a later line while taking advantage of the limited opportunity to use obinutuzumab. While noting that patients with high-risk disease who receive fixed-duration therapy may experience shorter remissions than those with lower-risk disease, Dr. Hillis noted that treatment-free intervals can be meaningful to patients' quality of life. Dr. Hillis explained that PFS requires careful interpretation because progression on a clinical trial does not necessarily indicate a need to restart treatment.



DLBCL: Primary Treatment and Relapse

DR. MICHAEL JAIN
DR. INNA GONG

Dr. Jain reviewed how the rapidly expanding range of treatments for relapsed or refractory DLBCL, coupled with a lack of evidence on ideal sequencing, makes decisions challenging. He emphasized, however, that time to relapse remains the main guide to second-line treatment. Late relapses are associated with a wider range of mutations than early relapses and may therefore be biologically different from the original lymphoma and respond to another course of chemotherapy. Another consideration is that the number of prior lines of therapy affects both the patient and tumour, resulting in worsened T-cell function, systemic inflammatory alterations, and systemic metabolic and microbiome changes.

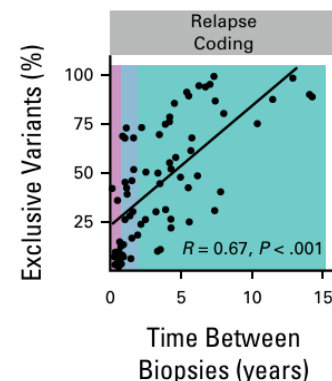
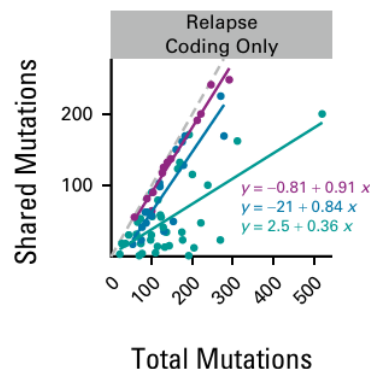
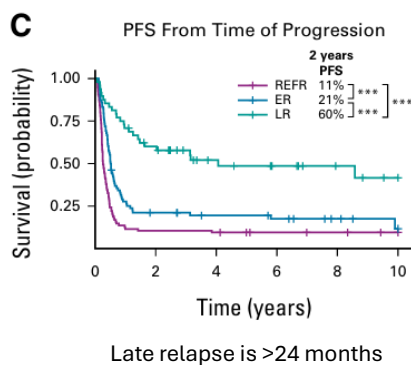
Patients whose disease progresses during first-line therapy and who are eligible for ASCT currently have access to axicel or lisocel. For those with relapsed or refractory disease in the third line or beyond, Health Canada-approved therapies include CAR T-cell therapy, glofitamab, epcoritamab, and loncastuximab tesirine, although the latter is not currently reimbursed. For those in the third-line setting or beyond who are not eligible for ASCT, options include pola-BR (reimbursed everywhere except Quebec), tafasitamab and lenalidomide (reimbursed in Quebec only) or glofitamab plus GemOx.

Discussing CAR T-cell therapy, Dr. Jain explained that patients may need holding therapy before leukapheresis and bridging therapy while their CAR T cells are manufactured. He said the optimal approach to bridging is unknown, although patients who respond well to bridging therapy have better outcomes after CAR T-cell therapy.

Bispecific antibodies can reduce tumour burden as holding or bridging therapy, but their 21-day step-up dosing may be inappropriate for patients with rapidly progressing disease. In his group's experience with 11-day accelerated step-up dosing, many patients required hospitalization for CRS and ICANS, and only 7 of 12 patients intended for CAR T-cell therapy ultimately received it. Combining a bispecific antibody with a treatment that reduces tumour burden more quickly may help, but this strategy needs further study.

Early results from a trial combining mosunetuzumab, polatuzumab, and axicel are encouraging. Among 24 patients who received axicel along with the combination therapy during bridging and consolidation, the 12-month PFS rate was 79%. He also discussed a Moffitt trial of comprehensive bridging radiation intended to bring patients as close as possible to a complete response before CAR T-cell infusion. Preliminary disease-control results were promising, but grade 3

The biology of early relapse is different than late



DR. MICHAEL JAIN, DR. INNA GONG



or higher ICANS occurred at a rate of 48%. Looking ahead, phase 3 trials are comparing dual-target CAR T-cell products, designed to recognize both CD19 and CD20, with established CAR T-cell therapies.

Dr. Jain emphasized that many questions remain in second-line DLBCL treatment, including the optimal intermediary therapy; what to use when CAR T-cell therapy is not an option; whether chemotherapy followed by ASCT or newer combinations are preferable for later relapses; and the most effective non-CAR T-cell combination therapies. His practical message was to consider the timing of relapse, the patient's condition, and the feasibility of delivering CAR T-cell therapy when choosing treatment.

DLBCL: Primary Treatment and Relapse

DR. MICHAEL JAIN

DR. INNA GONG

Dr. Gong reviewed current approaches to relapsed or refractory DLBCL in older or unfit patients. She emphasized that age alone should not determine whether a patient is considered for CAR T-cell therapy and that patients with primary refractory disease or early relapse should be referred for formal CAR T-cell assessment. The CAR T-cell team can help guide bridging treatment to enable suitable patients to proceed to CAR T-cell therapy.

In Ontario, access to second-line CAR T-cell therapy is tied to transplant eligibility, despite that appropriateness for CAR T-cell therapy may not align with appropriateness for ASCT. She noted that the median age of participants in DLBCL CAR T-cell trials is approximately 60 to 65 years. However, the ALYCANTE study evaluated axicel in transplant-ineligible patients, whose median age was 70 years. The PILOT study evaluated lisocel in patients who were not intended for transplant, with a median age of 74.

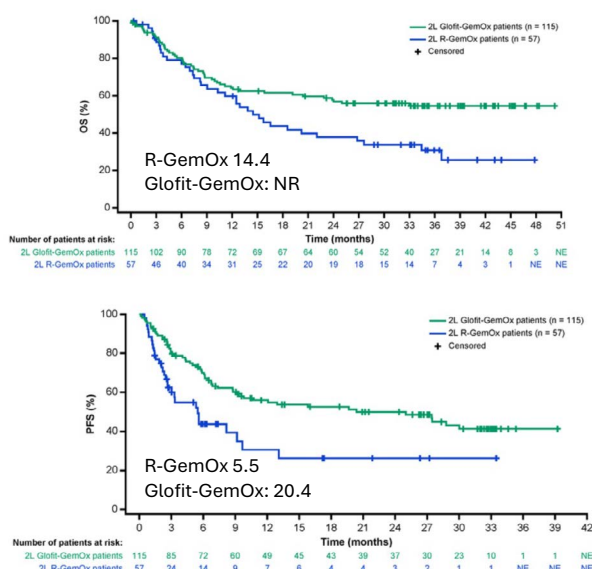
Phase 3 trials have not shown a consistent association between older age and worsened PFS or OS, although the U.S. consortium 5-year follow-up of real-world axicel outcomes found that while

age was not associated with worsened PFS or OS, it was associated with higher unadjusted non-relapse mortality with an odds ratio of 4.5. Princess Margaret Cancer Centre data suggest that disease burden and performance status, more than age, affected whether patients reach CAR T-cell infusion.

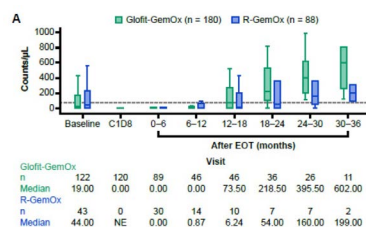
For patients who will not proceed to ASCT or CAR T-cell therapy, Dr. Gong highlighted that glofitamab plus GemOx may be an important second-line option. In the phase 3 STARGLO trial, the combination improved OS compared with R-GemOx in transplant-ineligible patients who had received at least one prior line of therapy. CRS occurred in 45% of patients, but this was largely grade 1 (32%) or grade 2 (10.5%), and 20% of patients in the treatment arm experienced grade 3 or higher infections. Dr. Gong also noted a subgroup analysis showing no apparent loss of benefit among patients older than 75 years. Dr. Gong cautioned that longer follow-up and real-world data are needed to demonstrate the long-term benefit of glofitamab plus GemOx. Ontario funds the glofitamab plus GemOx regimen for ASCT-ineligible patients who have received one prior line of therapy.

Other second-line options in development

Efficacy and safety of Glofit-GemOx in 2L setting



n (%),	Glofit-GemOx (n=172)	R-GemOx (n=88)
Any grade AE	172 (100)	85 (96.6)
Grade 3-4 AE	119 (69.2)	36 (40.9)
Grade 5 (fatal) AE	13 (7.6)	4 (4.5)
Serious AE	90 (52.3)	15 (17.0)
AE leading to discontinuation	13 (7.6)	3 (3.4)
CRS	77 (44.8)	0
Grade 1	55 (32.0)	0
Grade 2	18 (10.5)	0
Grade 3	4 (2.3)	0
Infections Grade 3-5	34 (19.8)	11 (12.5)



Abramson et al. Blood Adv 2026 2026 Aug 11;10(15):5367-5377.

DR. MICHAEL JAIN, DR. INNA GONG

include epcoritamab plus GemOx, epcoritamab monotherapy, mosunetuzumab and polatuzumab, and pola-R-GemOx. Dr. Gong presented early data showing promising results with these approaches.

On treatment sequencing considerations, Dr. Gong recommended avoiding bendamustine in CAR T-cell-eligible patients. She also recommended considering the potential effects of CD19-directed bispecific antibodies on future CAR T-cell therapy. Preliminary data suggests CD20-directed therapy may not affect future CAR T-cell efficacy, but real-world and immunologic data are still needed.



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MCL: Evolving Approaches to Treatment in 2026

DR. NIRAV SHAH

DR. MARY-MARGARET KEATING

Dr. Shah began his presentation by describing MCL as a highly heterogeneous disease. Approximately 10% to 15% of patients have indolent disease and typically benefit from relatively well-tolerated treatment for many years. The more common classical/nodal MCL requires more aggressive therapy, while blastoid or pleomorphic MCL, including *TP53*-mutated disease, is especially challenging to treat.

In the U.S., two CAR T-cell products are approved for relapsed MCL. In the ZUMA-2 trial, brexucel led to an ORR of 93% and a median PFS of 26 months. However, among patients achieving a complete response with brexucel, the median PFS was 48 months, raising the possibility of long-term disease control. Toxicity is a major concern, however, as 15% of patients experienced grade 3 or higher CRS and 31% of patients experienced grade 3 or higher ICANS. In a real-world cohort of patients with MCL treated with brexucel, in which 79% of patients would not have met ZUMA-2 eligibility criteria, the ORR was 90%

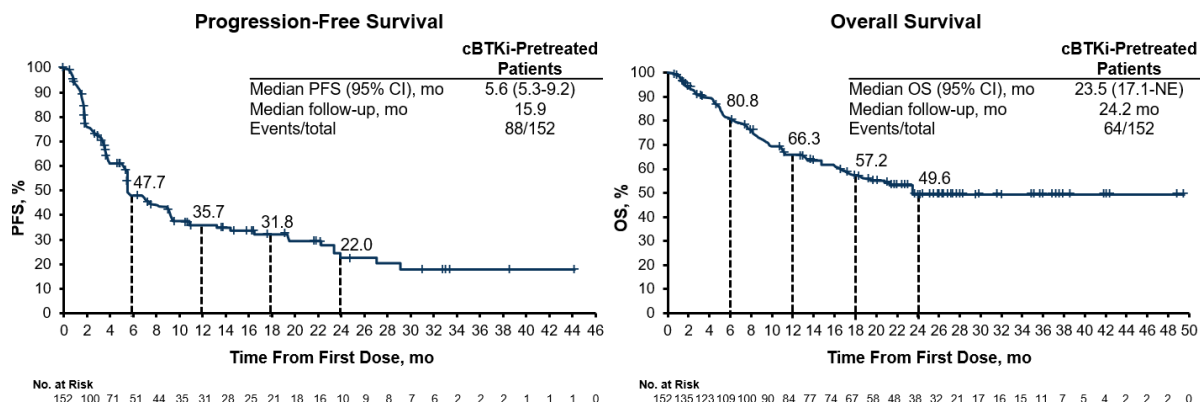
and the median PFS was 16 months; 20% of patients required ICU-level care and one-year non-relapse mortality was 10% (Wang et al, 2023).

Lisocel is significantly less toxic, with grade 3 or higher CRS and ICANS occurring at rates of 1% and 9% respectively in the TRANSCEND-NHL trial. However, efficacy outcomes are not as robust as with brexucel; the median PFS in patients with MCL was approximately 15 months. Based on these results, Dr. Shah explained that he would prefer lisocel for older, less fit patients while he would choose brexucel for fit patients with controlled disease.

Dual-targeted CAR T-cell therapies may improve these outcomes, as MCL is characterized by consistent CD19 expression as well as “bright” CD20 expression. Dr. Shah described his group’s phase 1/2 study of LV20.19, a CAR T-cell therapy targeting both CD19 and CD20. All 17 patients responded, despite extensive prior treatment and a 47% rate of *TP53* aberrations among enrolled patients. The complete response rate was 88% at a median follow-up of

Pirtobrutinib Efficacy in MCL post BTKi

Median DOR was 21.6 months



Median PFS 5.6 months and Median OS 23.5 months in
cBTKi pretreated patients

Wang et al ASH 2025

15 months (Shah, 2025). There were no cases of grade 3 or higher CRS, while two patients developed severe ICANS, and three fatal infections occurred. Dr. Shah highlighted a trial testing dual-targeted CAR T-cell therapy earlier in high-risk MCL, with sites in Edmonton and Toronto.

For patients needing treatment while awaiting CAR T-cell therapy, or those who cannot receive CAR T-cell therapy, Dr. Shah highlighted pirtobrutinib. In patients with MCL previously exposed to covalent BTKis, its ORR was approximately 50% and the median PFS was 6 months, although some patients experienced much longer benefit. Its favourable tolerability, including very low rates of atrial fibrillation and bleeding events associated with covalent BTKis, makes it useful as a bridge to either CAR T-cell or bispecific therapy.

Finally, Dr. Shah reviewed emerging bispecific approaches. Glofitamab resulted in an ORR of 85% and complete response rate of 78% in a phase 1/2 clinical trial, although only approximately half of patients were exposed to BTKi therapy and responses were lower in BTKi-exposed patients. The median duration of complete response was 15 months and the median PFS was 17 months. CRS occurred in 70% of patients, and 12% of these events were grade 3 or higher, while neurologic events occurred in 7 of 61 treated patients. Mosunetuzumab plus polatuzumab also showed promising activity in a more heavily treated population, with an ORR of 81% and a median PFS of 18.6 months. There were no cases of grade 3 or higher CRS; one patient experienced grade 2 ICANS.

Dr. Shah concluded that T-cell-directed approaches have improved outcomes in relapsed or refractory MCL after BTKi therapy and earlier application of these modalities may result in durable remissions.



MCL: Evolving Approaches to Treatment in 2026

DR. NIRAV SHAH

DR. MARY-MARGARET KEATING

Dr. Keating reviewed how frontline treatment choices for MCL are changing. In the TRIANGLE study, adding ibrutinib to R-CHOP and R-DHAP improved 4-year failure-free survival and OS by approximately 10% compared with the regimen without ibrutinib. As a result, the TRIANGLE regimen has challenged the routine use of ASCT in transplant-eligible patients.

For older or less fit patients, BR followed by rituximab maintenance remains an established option. More recent trials have asked whether adding a BTKi improves outcomes with this regimen. In SHINE, adding ibrutinib improved median PFS (81 months versus 53 months), but the toxicity of prolonged first-generation BTKi treatment limited its appeal. ECHO tested acalabrutinib with BR in patients aged 65 or older and also met its PFS endpoint: median PFS was 66 months versus 50 months with BR alone. It did not show an OS difference, however, Dr. Keating noted that many patients crossed over from the placebo arm to receive treatment. Dr. Keating said the unresolved

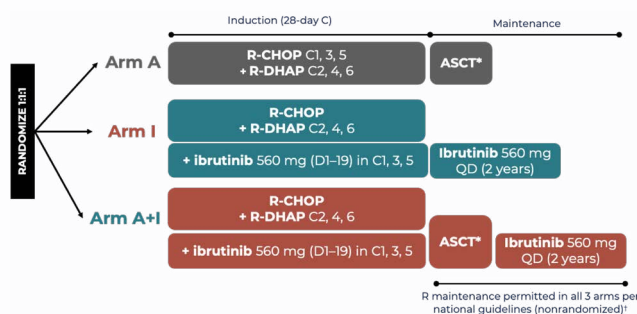
question is whether every older patient should receive a BTKi upfront or whether some can receive BR first and a BTKi at relapse. She pointed to a retrospective study published earlier this year that evaluated the latter approach and found that EFS2 with BTKi reserved for second-line treatment was similar to outcomes reported in ECHO and SHINE.

The ENRICH study examined a chemotherapy-free alternative, ibrutinib plus rituximab, in frontline MCL treatment. Although PFS favoured ibrutinib over R-CHOP, outcomes with ibrutinib were similar to those with BR. Dr. Keating interpreted the study as support for a chemotherapy-free option, rather than evidence that it is superior to BR.

Dr. Keating then turned to *TP53*-mutated MCL, which accounts for approximately 10% to 15% of cases and responds poorly to conventional approaches, including intensive chemotherapy. SHINE showed that adding a BTKi did not greatly improve outcomes in this high-risk population, resulting in a median PFS of 29 months. Dr. Keating

TRIANGLE: Does ASCT still add benefit in the BTKi era?

Phase III | Untreated MCL | Age ≤ 65 | n=870



4-year FFS

Arm A: 70%

Arm I: 82%

Arm A+I: 81%

A+I vs I HR 0.86; p=0.21

4-year OS: 81% | 88% | 90%

☐ Adding ASCT to an ibrutinib-containing regimen did not improve FFS and increased toxicity

TRIANGLE studied fit patients ≤65 receiving cytarabine-based induction

Dreyling M et al. Lancet 2024; Dreyling M et al. Lancet 2026

DR. NIRAV SHAH, DR. MARY-MARGARET KEATING

A woman with long dark hair is speaking at a podium. She is wearing a black top and a blue lanyard. A microphone is positioned in front of her. The background is dark with vertical red and blue light streaks.

highlighted early studies of novel-agent combinations: in the BOVen study of 25 patients with untreated *TP53*-mutated MCL, zanubrutinib, obinutuzumab and venetoclax produced high response rates, with a 2-year PFS rate of 72%. TrAVeRse is testing an MRD-guided combination of acalabrutinib, venetoclax, and rituximab in a broader population, approximately 16% of whom had *TP53*-mutated MCL. Patients who were MRD-negative were randomized to receive acalabrutinib until progression or observation. Initial results are encouraging, with a 6-month PFS of 97%, but follow-up is too short to establish durability.



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