



8th Annual

LEAD 2026

LEADERSHIP
EMPOWERMENT
DEVELOPMENT

Enriching Experiences for Leaders in Hematology and Oncology

SEPT
18-19,
2026

Updates in Non-Hodgkin Lymphoma

Meryl Colton, MD MSc

Kaiser Permanente Medical Group / East Bay Leukemia and
Lymphoma Center of Excellence

 mcolton_2

 Bio Ascend™
A Vaniam Group Company

 University of Nebraska
Medical Center

Disclosures

Advisor: Genmab, Pfizer

UPDATES IN

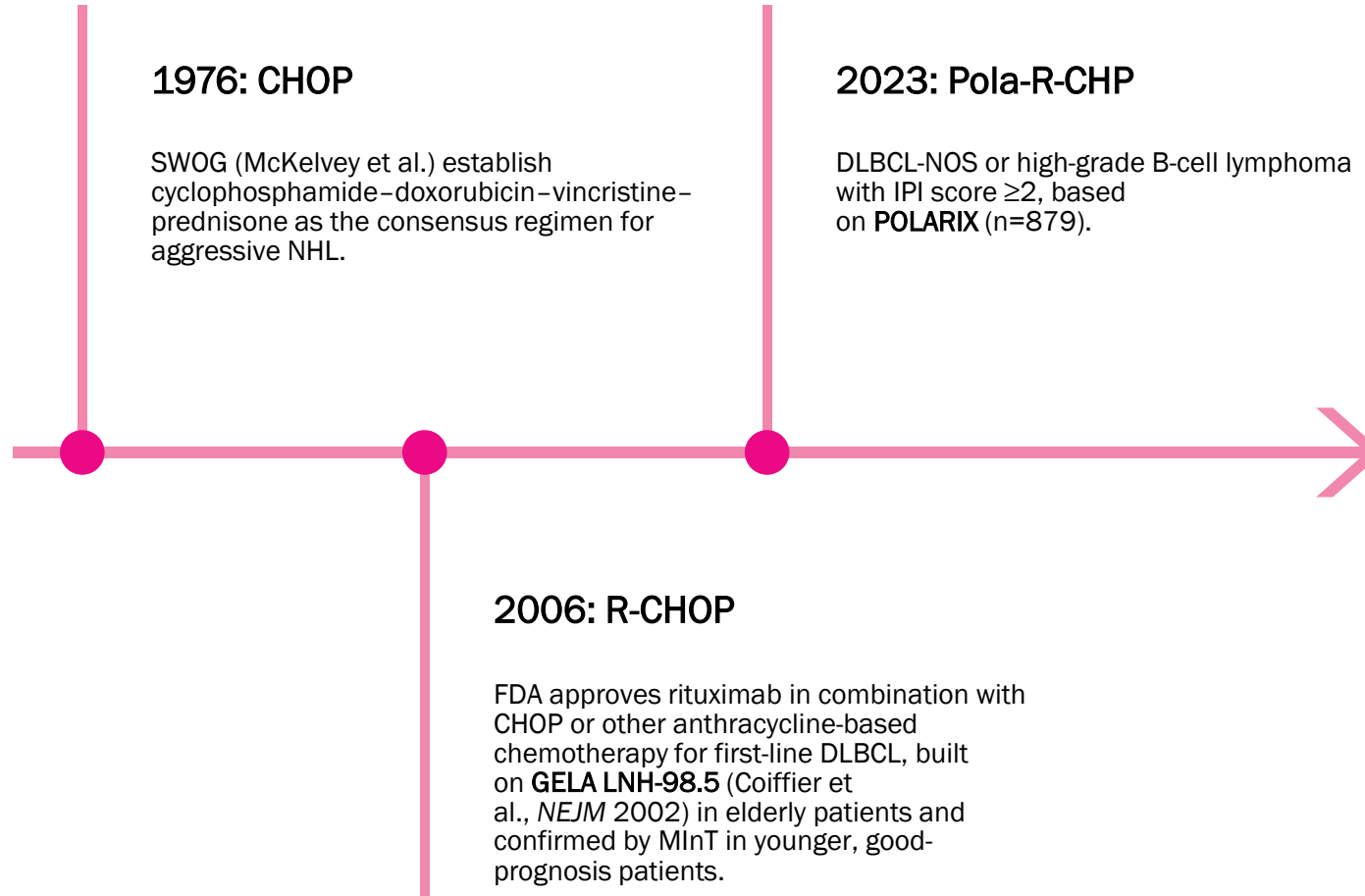
Diffuse Large B-Cell
Lymphoma

Mantle Cell Lymphoma

Follicular Lymphoma

Diffuse Large B-Cell Lymphoma

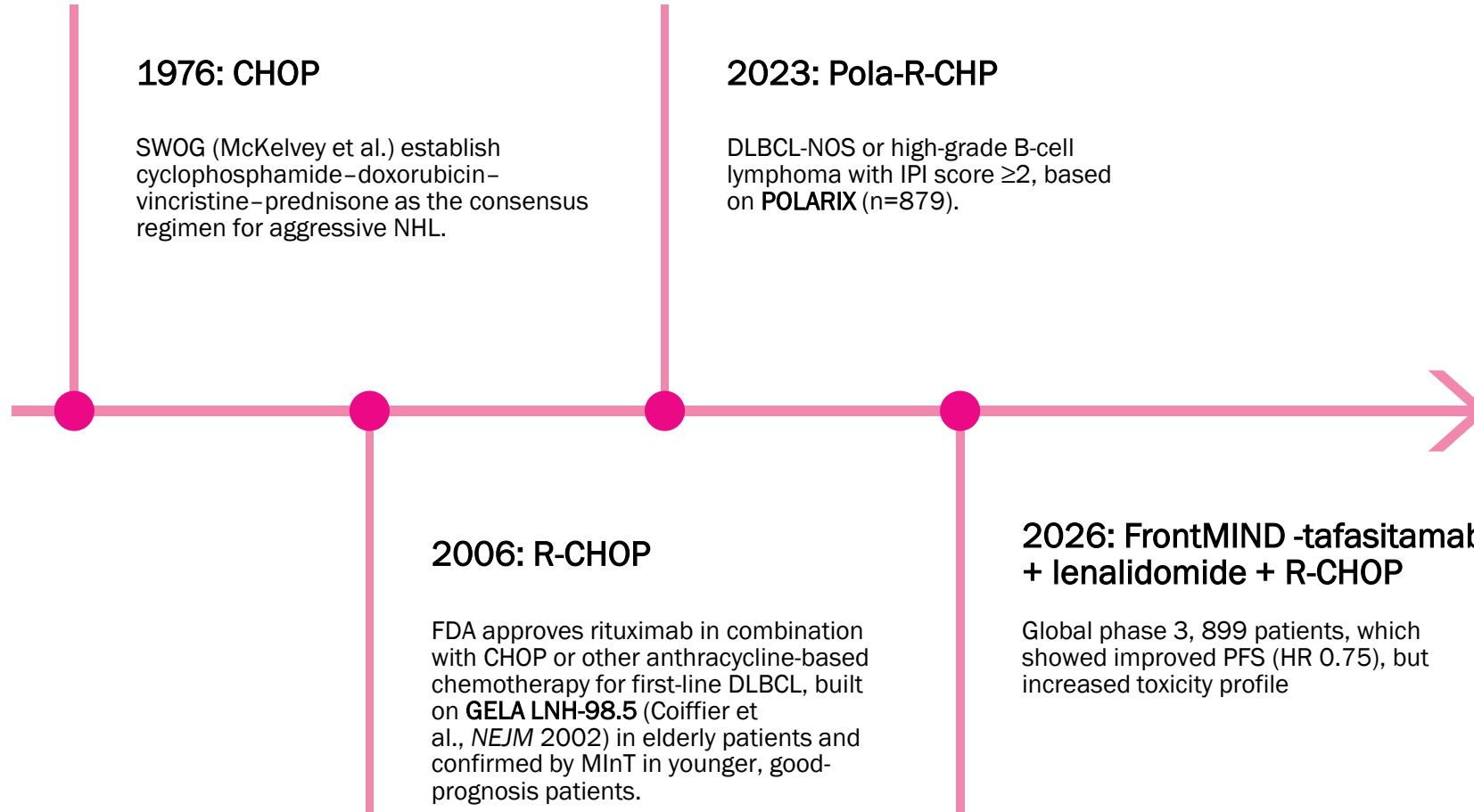
History of frontline DLBCL therapy



Lenz et al, Lancet, 2026

LEAD 2026: Leadership, Empowerment, and Development

History of frontline DLBCL therapy

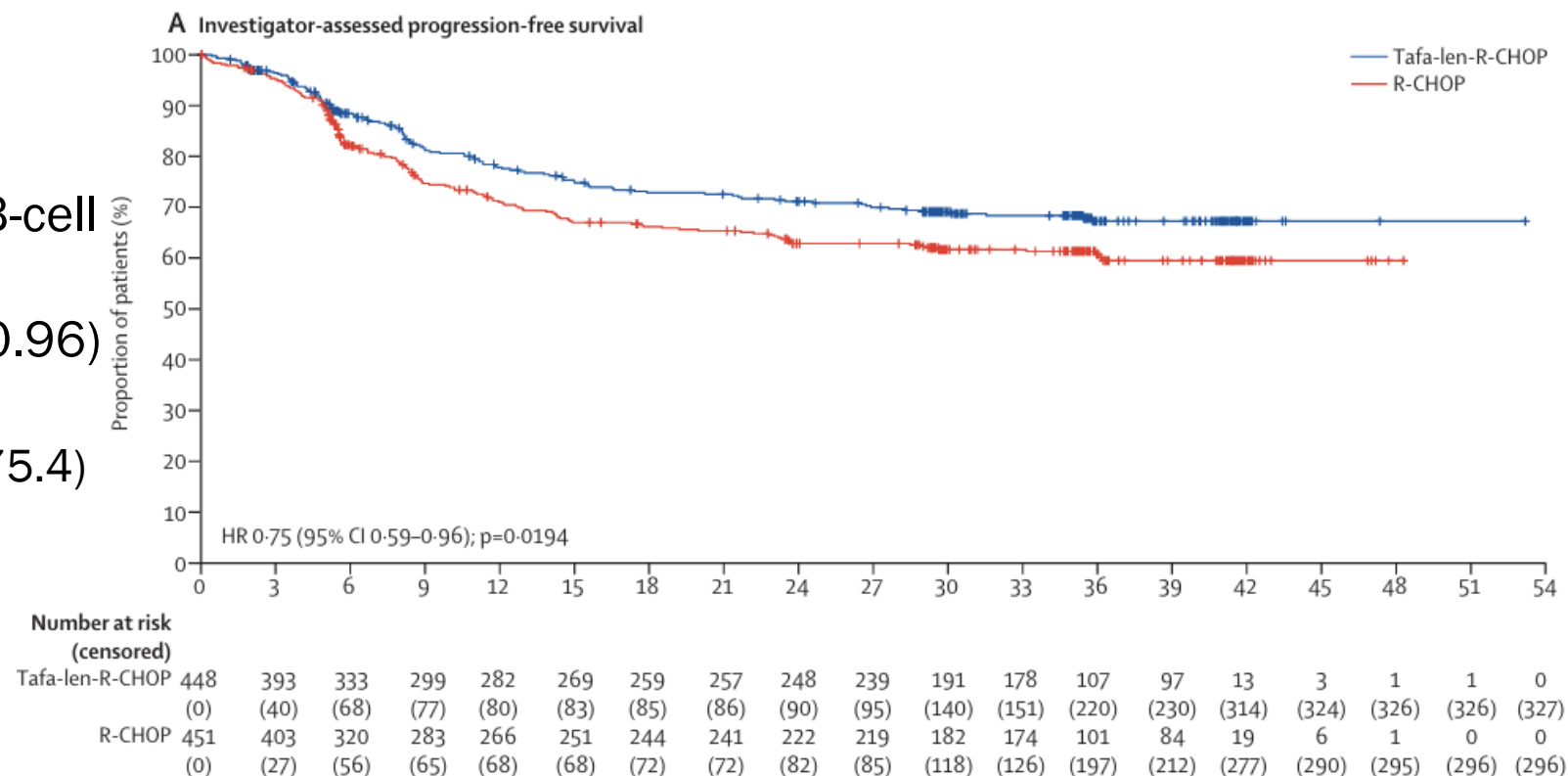


Lenz et al, Lancet, 2026

LEAD 2026: Leadership, Empowerment, and Development

In patients with newly diagnosed DLBCL, Tafasitamab+lenalidomide + RCHOP vs. RCHOP showed improved PFS, but increased toxicity

- Global phase 3 trial
- 899 patients
- High risk DLBCL (IPI 3-5), high grade B-cell
- Improved PFS
 - Overall HR (95% CI): **0.75 (0.59, 0.96)**
 - 2-year PFS
 - Tafa-len-RCHOP: **71.1% (66.3-75.4)**
 - RCHOP: **62.9% (57.9-67.5)**



Lenz et al, Lancet, 2026

Toxicity

	Tafa-len-R-CHOP group (n=443)				R-CHOP group (n=447)			
	Any grade	Grade 3	Grade 4	Grade 5 (death)	Any grade	Grade 3	Grade 4	Grade 5 (death)
Number of treatment-emergent adverse events	437 (99%)	95 (21%)	263 (59%)	26 (6%)	434 (97%)	97 (22%)	226 (51%)	17 (4%)
Treatment-emergent serious adverse events	222 (50%)	107 (24%)	63 (14%)	26 (6%)	174 (39%)	79 (18%)	59 (13%)	17 (4%)
Treatment-related treatment-emergent adverse events	423 (95%)	87 (20%)	264 (60%)	8 (2%)	407 (91%)	82 (18%)	217 (49%)	8 (2%)
Treatment-emergent adverse events leading to discontinuation of all study drug components	23 (5%)	5 (1%)	9 (2%)	1 (<1%)	24 (5%)	13 (3%)	3 (1%)	4 (1%)
Most common treatment-emergent adverse event								
Neutropenia	313 (71%)	55 (12%)	251 (57%)	0	267 (60%)	51 (11%)	208 (47%)	0
Anaemia	205 (46%)	101 (23%)	4 (1%)	0	154 (34%)	71 (16%)	2 (<1%)	0
Thrombocytopenia	172 (39%)	58 (13%)	62 (14%)	0	119 (27%)	30 (7%)	32 (7%)	0
Constipation	152 (34%)	0	0	0	126 (28%)	0	0	0
Nausea	117 (26%)	8 (2%)	0	0	140 (31%)	5 (1%)	0	0
Diarrhoea	109 (25%)	10 (2%)	2 (<1%)	0	74 (17%)	6 (1%)	0	0
Hypokalaemia	96 (22%)	27 (6%)	6 (1%)	0	65 (15%)	15 (3%)	3 (1%)	0
Fatigue	95 (21%)	9 (2%)	0	0	86 (19%)	8 (2%)	0	0
COVID-19	90 (20%)	15 (3%)	1 (<1%)	4 (1%)	104 (23%)	12 (3%)	2 (<1%)	1 (<1%)
Leukopenia	82 (19%)	18 (4%)	47 (11%)	0	57 (13%)	18 (4%)	31 (7%)	0
Pyrexia	82 (19%)	4 (1%)	0	0	54 (12%)	1 (<1%)	1 (<1%)	0
Febrile neutropenia	74 (17%)	44 (10%)	28 (6%)	1 (<1%)	57 (13%)	39 (9%)	18 (4%)	0
Infusion-related reaction	71 (16%)	3 (1%)	0	0	50 (11%)	1 (<1%)	0	0
Neuropathy peripheral*	70 (16%)	4 (1%)	0	0	74 (17%)	4 (1%)	0	0
Oedema peripheral	52 (12%)	1 (<1%)	0	0	41 (9%)	0	0	0
Alopecia	51 (12%)	0	0	0	50 (11%)	1 (<1%)	0	0
Peripheral sensory neuropathy*	50 (11%)	5 (1%)	0	0	42 (9%)	0	0	0
Asthenia	49 (11%)	7 (2%)	0	0	54 (12%)	5 (1%)	0	0
Insomnia	48 (11%)	2 (<1%)	0	0	57 (13%)	1 (<1%)	0	0
Stomatitis	47 (11%)	2 (<1%)	0	0	41 (9%)	3 (1%)	0	0
Vomiting	43 (10%)	6 (1%)	0	0	50 (11%)	3 (1%)	0	0

≥ Grade 3
86% vs 77%

Fatal AE
6% vs 4%

Lenz et al, Lancet, 2026

FrontMIND conclusions

- Clear PFS benefit: 2 year PFS 71.1% vs. 62.9% [HR **0.75** (0.59, 0.96)]
- Consistent benefit across ABC and GCB subtypes and in double-hit lymphoma.
- R-CHOP dose intensity and discontinuation rates were preserved.
- Higher grade ≥ 3 toxicity (86.7% vs 76.1%), more infections.
- Added infusion-visit burden (Tafasitamab is dosed weekly)
- RCHOP control arm (vs. R-Pola-CHP)
- Does tafasitamab upfront diminish effectiveness of CD19 CART at relapse?

Will another regimen take down RCHOP/R-Pola-CHP?

Study	Phase	Comparison	Comments
SKYGLO	III	Glofitimab added to Pola-R-CHP vs. Pola	still accruing, no data yet.
EPCORE DLBCL-2	III	Epcoritamab + R-CHOP vs. R-CHOP	still accruing, no data yet.
waveLINE-010	III	Zilovetamab vedotin (an anti-ROR1 antibody-drug conjugate) + R-CHP vs. R-CHOP	targeting ~1,046 patients, actively recruiting
OLYMPIA-3	III	Odronextamab + CHOP vs. rituximab + CHOP	still in the dose-optimization phase, though early data from the first part showed high response rates and manageable toxicity.
Zuma-23	III	Axicabtagene ciloleucel vs SOC	High risk DLBCL. Still accruing

Last note on DLBCL....

FDA issued Complete Response Letters (CRLs) for **Glofitimab + chemo (R/R DLBCL combo)** and **odronextamab (R/R FL and DLBCL)**.

Odronextamab's FL BLA has since been resubmitted and accepted for review.

Mantle Cell Lymphoma

Historic Frontline Mantle Cell Framework: “The Three Course Meal”

1. Induction
Chemotherapy

(best if includes Cytarabine)

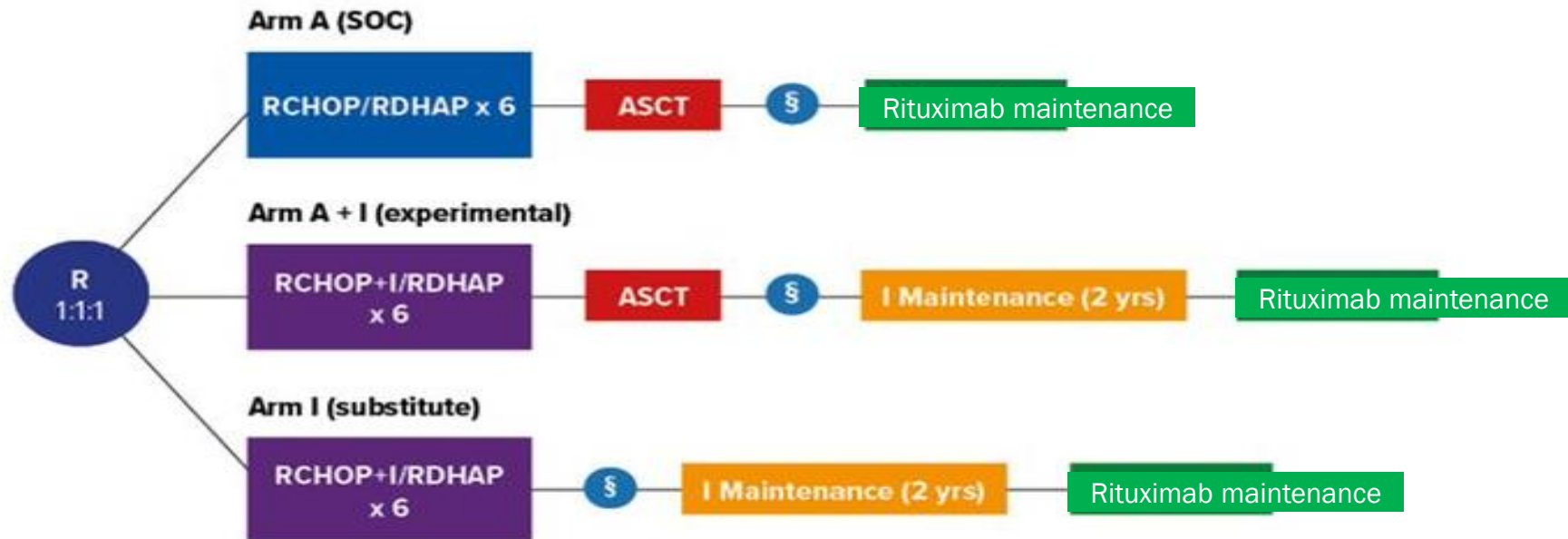
2. Autologous
Transplant

3. Rituximab
maintenance

Historic Mantle Cell Framework: “The Three Course Meal”

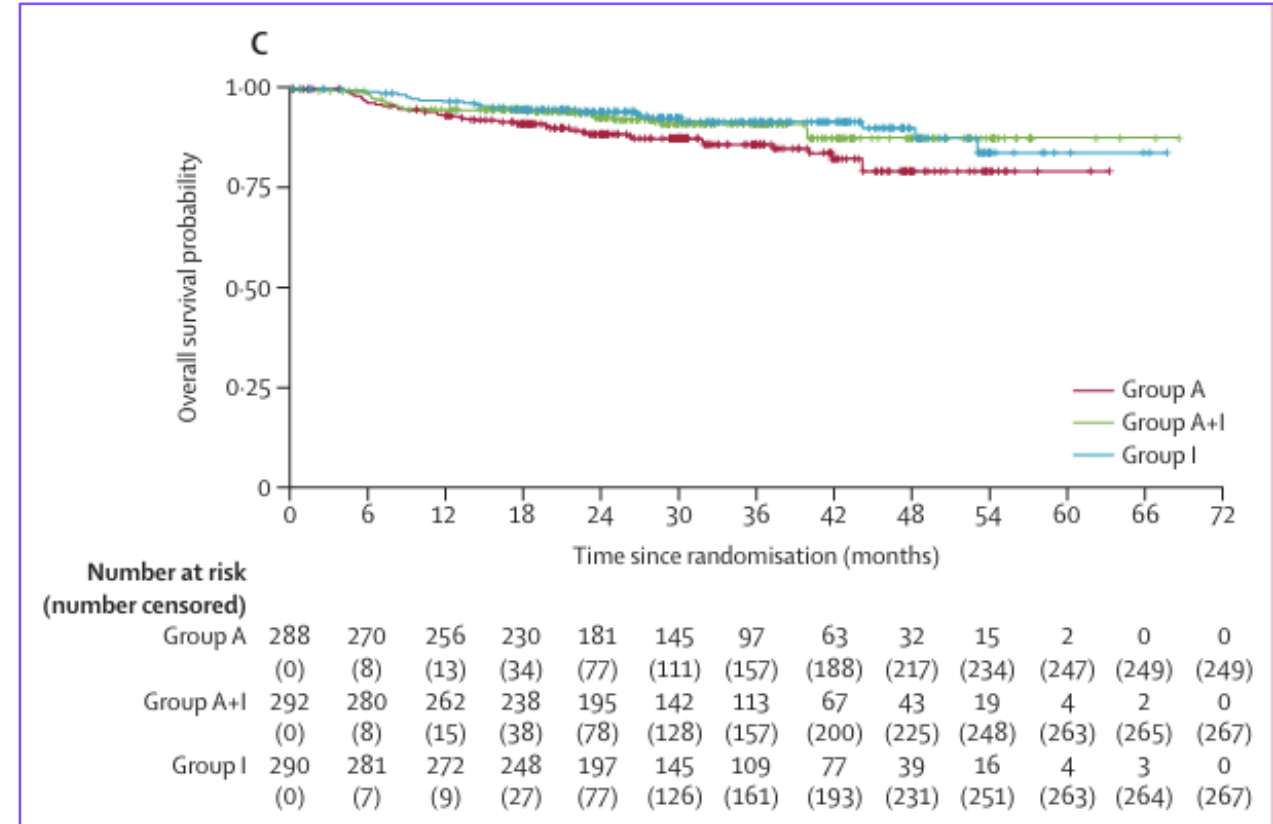


The Triangle Study

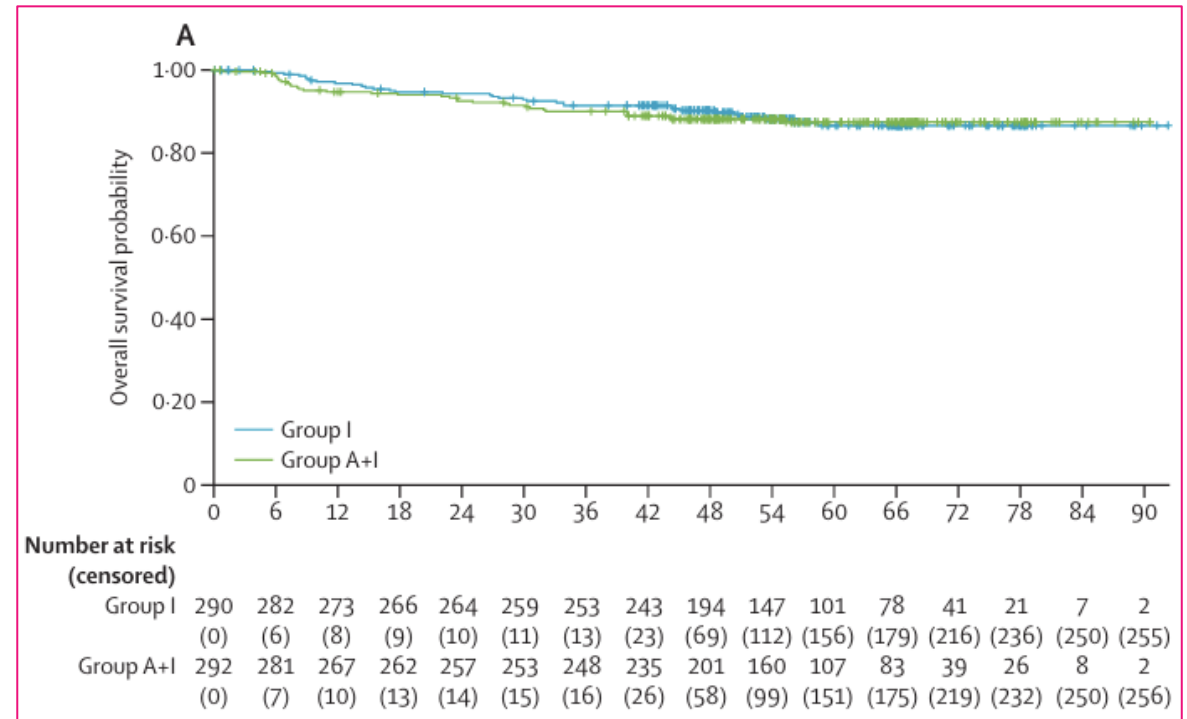
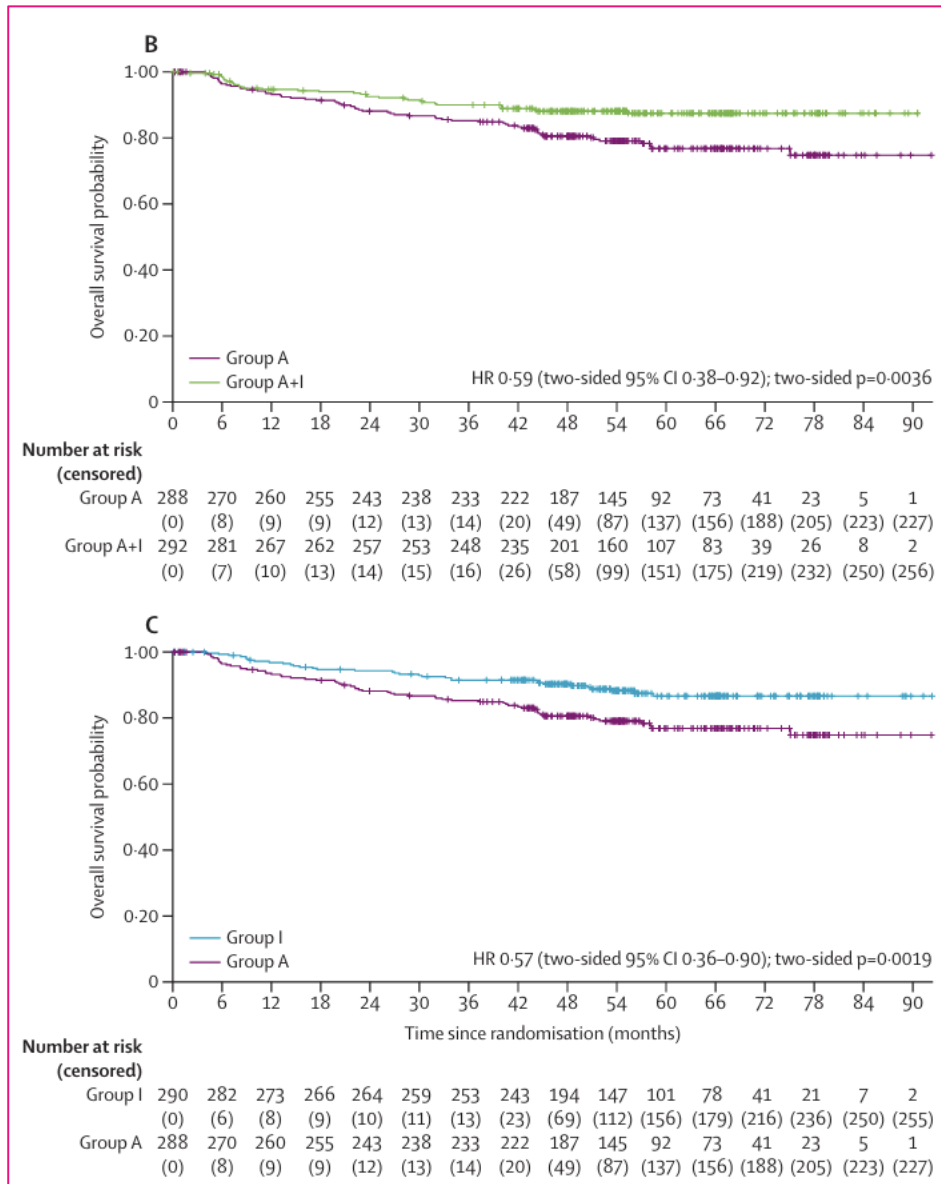


The Triangle Study showed early improvement in FFS for both BTKi treatment groups compared to control

	FFS (95% CI)	HR (one-sided 98.3% CI)
<u>A</u> : Chemoimmunotherapy + ASCT	72% (67–79)	
<u>A+I</u> : Chemoimmunotherapy + ibrutinib + ASCT	88% (84–92)	0.52 (0–0.86)
<u>I</u> : Chemoimmunotherapy+ ibrutinib	86% (82–91)	1.77 (0–3.7)



TRIANGLE 4.5-year follow-up confirms OS benefit for adding ibrutinib and supports omitting autologous stem-cell transplant.

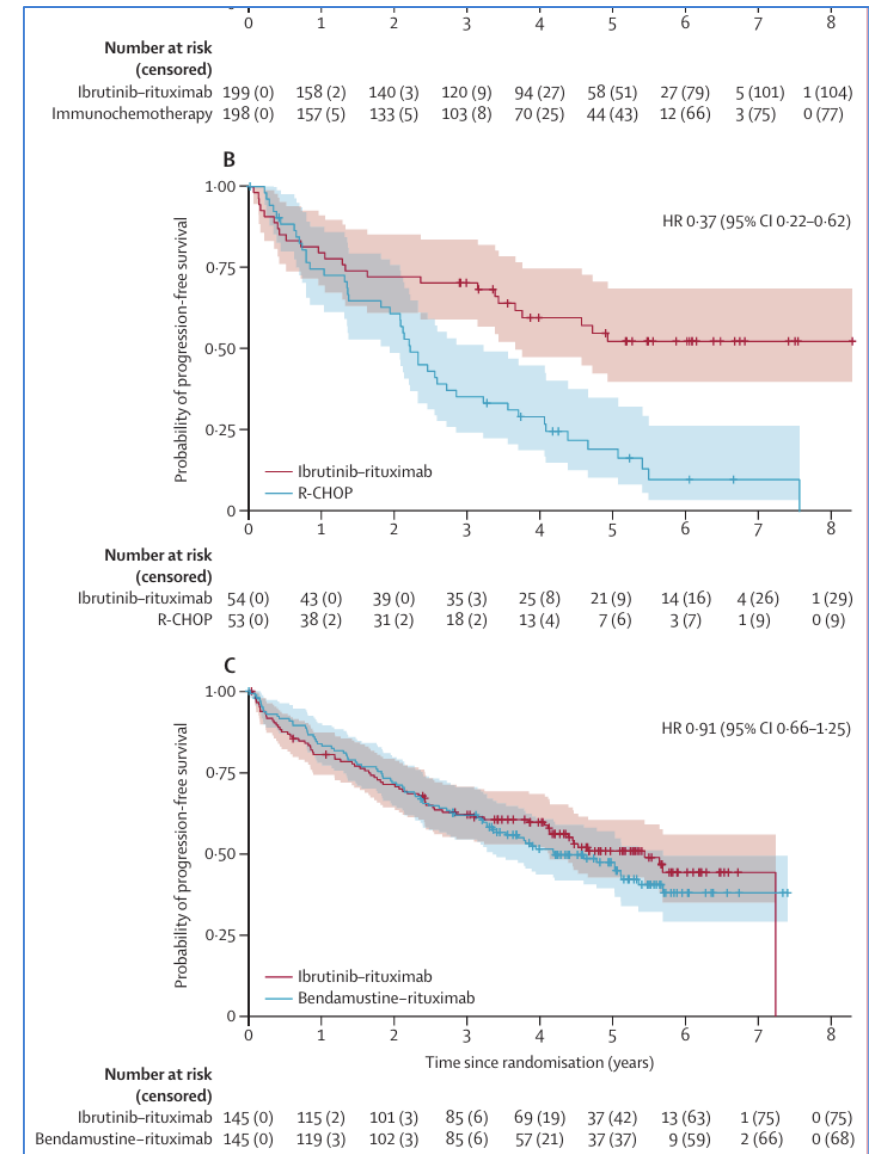


ASCT → 3% Mortality
Poor ibrutinib tolerance:

- Increased toxicity
- Increased infections

ENRICH established chemotherapy-free BTKi–rituximab as an option for older patients.

- 397 patients ≥ 60 yo with newly diagnosed mantle cell lymphoma
- Median progression-free survival of ibrutinib-rituximab was superior to immunochemotherapy hazard ratio (
 - HR: **0.69** (95% CI 0.52-0.90); **p=0.0034**.
- In subgroup analysis, there was **no statistical difference** between ibrutinib-rituximab and BR



Other evidence for chemo-free options in the frontline setting

Trial	Phase / Design	Regimen(s)	Population (n)	Key results
MANGROVE	Phase 3, randomized	Zanubrutinib + rituximab (indefinite, chemo-free) vs. bendamustine-rituximab ×6	Previously untreated, transplant-ineligible MCL (n=510)	PFS HR 0.57 (95% CI 0.43–0.76, P<.0001) favoring the chemo-free arm; OS immature but trending favorable; no new safety signals
TrAVeRse	Phase 2, single-arm	Acalabrutinib + venetoclax + rituximab	Treatment-naive MCL (n=21)	ORR 100%, CR 71.4%; 2-yr PFS 63.2%, 2-yr OS 75.2%
BOVen (TP53-mutant cohort)	Phase 2, single-arm, fixed-duration/MRD-driven	Zanubrutinib + obinutuzumab + venetoclax	Treatment-naive, TP53-mutated MCL (n=25)	ORR 96%, CR 88%; undetectable MRD in 100% of evaluable patients at end of treatment; 2-yr PFS 72% (primary endpoint met)
OAsIs (Cohort C)	Phase 1/2, single-arm	Ibrutinib + obinutuzumab + venetoclax	Treatment-naive, intermediate/high-MIPi MCL (n=15)	5-yr data: ORR 93%, CR 87%; 5-yr PFS 80%, 5-yr OS 93%
Window-2	Phase 2, single-arm, risk-adapted	Ibrutinib + rituximab + venetoclax (IRV) induction, then either observation (if MRD-negative/low-risk) or short-course R-HyperCVAD/MTX (if high-risk)	Young, previously untreated MCL	
AVO / MAVO	Phase 1/2, single-arm	Acalabrutinib + venetoclax + obinutuzumab	Combined R/R and treatment-naive cohorts	

Other evidence for chemo-free options in the frontline setting

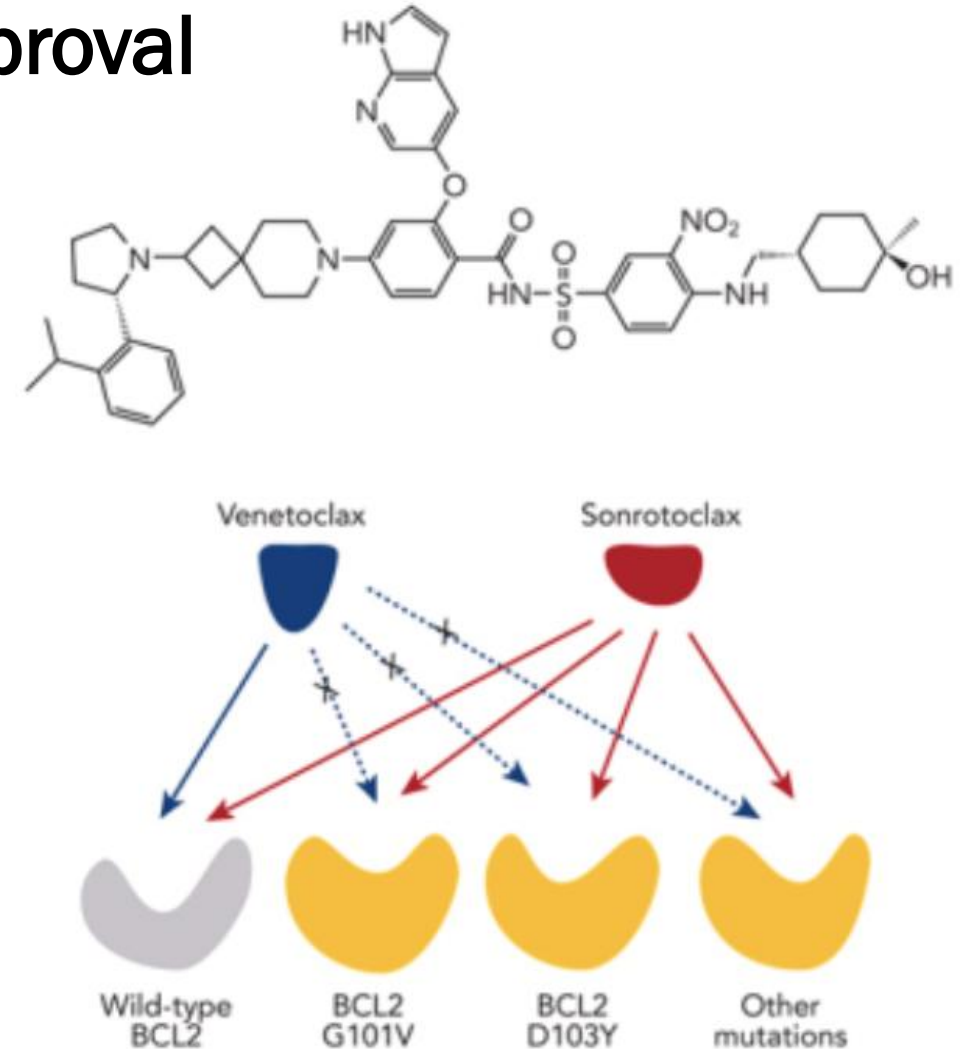
Trial	Phase / Design	Regimen(s)	Population (n)	Key results
BOVen (TP53-mutant cohort)	Phase 2, single-arm, fixed-duration/MRD-driven	Zanubrutinib + obinutuzumab + venetoclax	Treatment-naïve, TP53-mutated MCL (n=25)	ORR 96%, CR 88%; Undetectable MRD in 100% of evaluable patients at end of treatment; 2-yr PFS 72% (primary endpoint met)

Now included in NCCN guidelines for TP53 mut disease!

Sonrotoclax granted accelerated approval

(May, 2026)

- First next-gen BCL2 inhibitor
- R/R MCL after ≥ 2 lines including a BTKi
- Based on single-arm BGB-11417-201 (n=103)
 - ORR 52%
 - median DOR 15.8 mo.
 - Dosing requires a 4-week TLS ramp-up to 320 mg daily.



Eyre et al, 2026
Lieu et al, Blood 2024

Follicular Lymphoma

There has not been a uniform consensus on the treatment order of follicular lymphoma

Options include:

First Line	Second Line	Third Line
BR (or BO)	BR (or BO)	T-cell engager: - Epcoritamab - Mosunetuzumab
RCHOP (or OCHOP)	RCHOP (or OCHOP)	
R-CVP (O-CVP)	R-CVP (O-CVP)	
Lenalidomide + Revlimid (R2)	Lenalidomide + Revlimid (R ²)	CART: - Axi-cel - Liso-cel - Tisa-cel
Lenalidomide monotherapy	Tafasitamab-cxix + R ²	

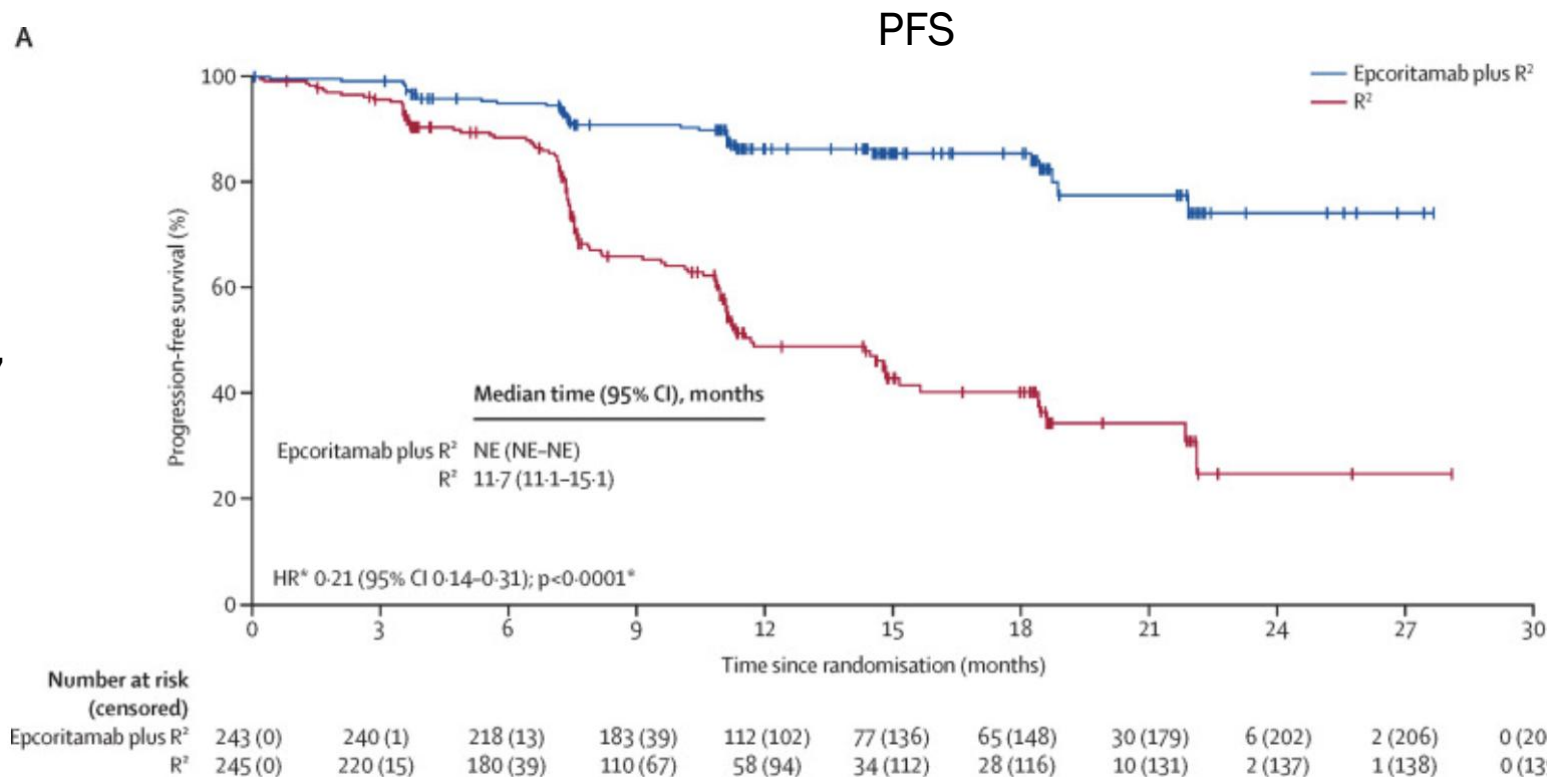
Ref: NCCN 2025

LEAD 2026: Leadership, Empowerment, and Development

EPCORE FL-1 introduced first bispecific to second line options

- 488 patients with follicular lymphoma
 - Enriched for high risk:
 - 41% FLIPI 3-5, 33% FLIPI 2
- ORR
 - 95% with epcoritamab + R²
 - 79% with R² p<0.0001)
- PFS: Longer with epcoritamab plus R²
 - Hazard Ratio 0.21 (95% CI 0.14–0.31), p<0.0001
- Grade 3 or higher adverse:
 - 90% with epcoritamab plus R²
 - 68% with R²

Now included in NCCN guidelines
2nd line treatment of FL!



EPCORE FL-1 Conclusions

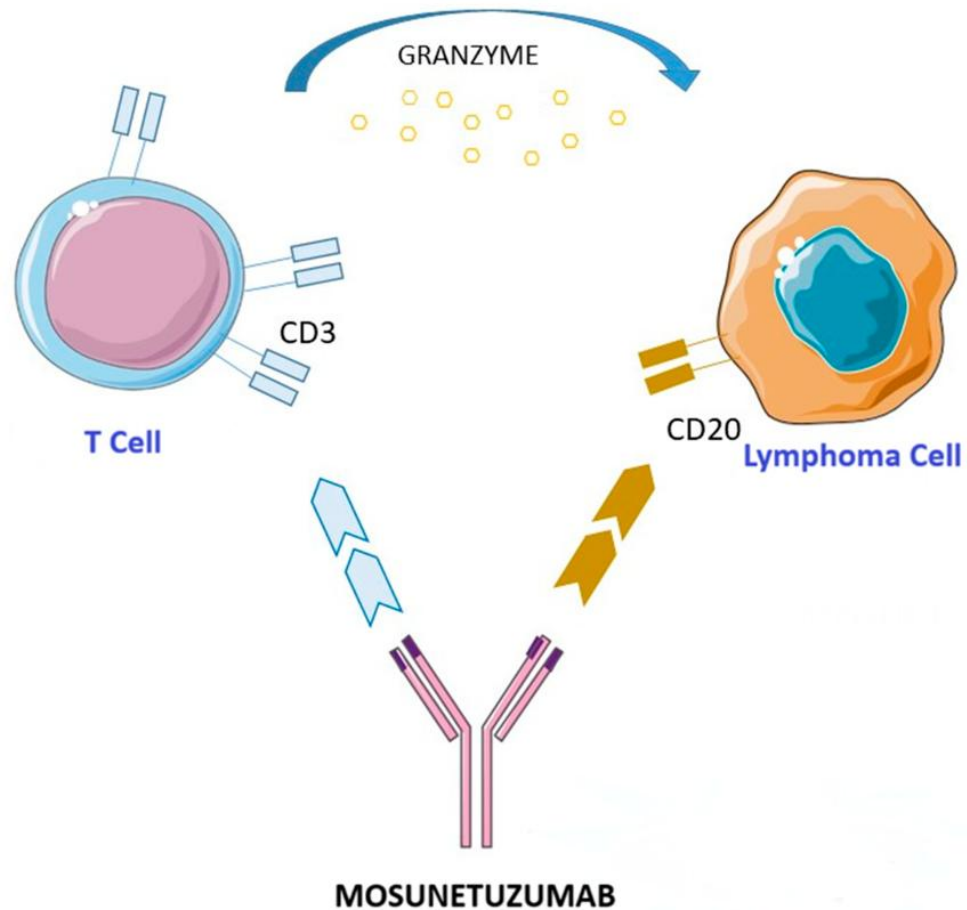
- Epcoritamab + R² is a highly effective 2nd line treatment option for patients with FL
- This treatment can be delivered outpatient
- There are significant risks most notably neutropenia and infection

Ongoing questions

- Is epcoritamab + R² superior to sequential R² and epcoritamab?
- Epcoritamab vs tafasitamab + R² ?
- What are best practices to manage infection risk
- Will single agent bispecific, CART, novel agent (CELMOD?) outperform current second line options?

Subcutaneous mosunetuzumab approved!

(Dec 21, 2025)



- PK-noninferiority-based approval of a ~1-minute SC injection
- R/R follicular lymphoma supporting cohort:
 - ORR 74.5%
 - CRR 58.5%

Thank you!

References

BeOne Medicines announces positive phase 3 results for BRUKINSA in frontline mantle cell lymphoma. News release. BeOne Medicines. June 30, 2026. Accessed June 30, 2026. <https://ir.beonemedicines.com/news/beone-medicines-announces-positive-phase-3-results-for-brukinsa-in-frontline-mantle-cell-lymphoma/44597eac-a44b-451f-a021-48d345cdb85e>

Dreyling M, Doorduijn J, Giné E, et al; European Mantle Cell Lymphoma Network. Addition of autologous stem-cell transplantation to an ibrutinib-containing first-line treatment in patients aged 18-65 years with mantle cell lymphoma (TRIANGLE): 4.5-year follow-up of a three-arm, randomised, open-label, phase 3 superiority trial of the European MCL Network. *Lancet*. 2026 May 16;407(10542):1953-1967.

Eyre, Toby et al. Phase I/II Study of Sonrotoclax (BGB-11417) Monotherapy in Patients With Mantle Cell Lymphoma Previously Treated With Anti-CD20 Therapy and a Bruton Tyrosine Kinase Inhibitor. *J Clin Oncol* **44**, 2233-2243(2026).

Falchi L, Nijland M, Huang H et al. Epcoritamab, lenalidomide, and rituximab versus lenalidomide and rituximab for relapsed or refractory follicular lymphoma (EPCORE FL-1): a global, open-label, randomised, phase 3 trial. *The Lancet*, 2026; 407, 161-173

Genentech, Inc. FDA Approves Genentech's Lunsumio VELO™ for Subcutaneous Use in Relapsed or Refractory Follicular Lymphoma [press release]. South San Francisco, CA: Genentech; December 21, 2025. <https://www.gene.com/media/press-releases/15095/2025-12-21/fda-approves-genentechs-lunsumio-velo-fo>

Kumar A, Soumerai J, Abramson JS, et al. Zanubrutinib, obinutuzumab, and venetoclax for first-line treatment of mantle cell lymphoma with a TP53 mutation. *Blood*. 2025 Jan 30;145(5):497-507.

Lenz G, Trněný M, Burke JM, et al; frontMIND Study Investigators. Tafasitamab plus lenalidomide and R-CHOP versus R-CHOP for first-line treatment of patients with high-risk diffuse large B-cell lymphoma (frontMIND): a global, phase 3, randomised, double-blind, placebo-controlled trial. *Lancet*. 2026 Jun 20;407(10547):2528-2541. Epub 2026 May 30.

Lewis DJ, Jerkeman M, Sorrell L, et al; ENRICH investigators. Ibrutinib and rituximab versus immunochemotherapy in patients with previously untreated mantle cell lymphoma (ENRICH): a randomised, open-label, phase 2/3 superiority trial. *Lancet*. 2025 Oct 25;406(10514):1953-1968. doi: 10.1016/S0140-6736(25)01432-1. Epub 2025 Oct 3.

Liu J, Li S, Wang Q, et al. Sonrotoclax overcomes BCL2 G101V mutation-induced venetoclax resistance in preclinical models of hematologic malignancy. *Blood*. 2024 May 2;143(18):1825-1836.

Tavarozzi, R., Maher, N., Catania, G. et al. Evolving therapeutic strategies in mantle cell lymphoma: advancements and future directions. *Leukemia* **40**, 857–871 (2026).