4th edition

Unmet challenges in high risk hematological malignancies: from benchside to clinical practice

Turin, March 26-27, 2026

Starhotels Majestic

Scientific board:
Marco Ladetto (Alessandria)
Umberto Vitolo (Candiolo-TO)

Paradigm shifts in the treatment of follicular lymphoma

Gilles Salles

Disclosures of Gilles SALLES

- Gilles Salles has received financial compensation in the last 12 months for consulting, participating in advisory boards or Data Monitoring Committees :

- *Abbvie, BeOne, BMS, Canopy, Daiichi Sankyo, EllipsesGenentech/Roche, Genmab, Janssen, Incyte, Ipsen, Kite/Gilead, Lilly, Merck, Novartis.*

- *He received research support from Abbvie, Daiichi Sankyo, Genentech, Genmab Janssen, Ipsen, which was managed by his institution.*

1. Newly diagnosed patients until now...

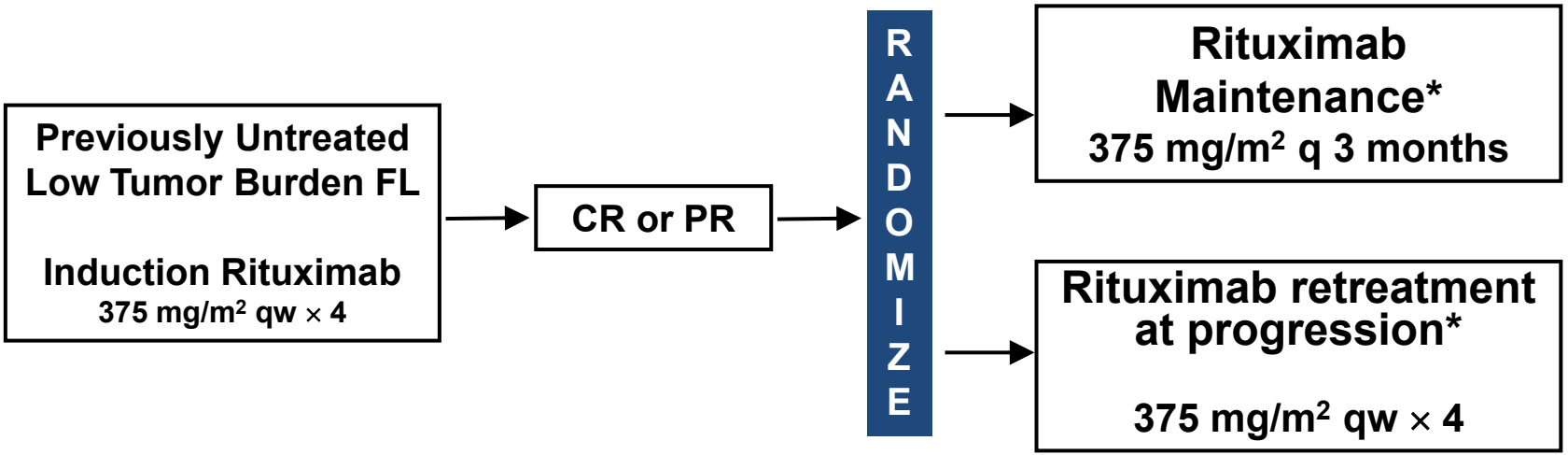
First line management of FL patients until 2026

1) In patients with localized disease:
   - Radiation therapy if single or contiguous nodes
   - Other cases: rituximab or watchful waiting

2) In patients with low tumor burden and/or asymptomatic disease
   - Watchful waiting remains the reference
   - Rituximab single agent: update on Resort and RWW studies

3) For other patients with high tumor burden in need of systemic treatment
   - *Rituximab (or obinutuzumab) – chemotherapy remains SoC*
   - *Update of the Relevance study (Rituximab-Lenalidomide vs. SoC)*

E4402 (RESORT) Schema



***Continue until treatment failure**

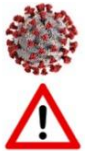
No response to retreatment or PD within 6 months of R

Initiation of cytotoxic therapy or Inability to complete planned R treatment

RESORT (E4402): Rituximab Maintenance versus Retreatment

Long Term Follow-up Conclusions

- ***No OS benefit for MR vs. RR***
- **Time to treatment failure**: no difference between RR and MR
- MR benefit for time to first cytotoxic therapy increased over time
  - …but 63% of patient on RR strategy remained chemo-free at 7 years
- Duration of response favored MR
  - …but 30% of RR patients remained in 1st remission at 10 years
- No long-term safety signals with prolonged MR (2nd CA, Ig levels)
- 4x less drug utilized with the RR strategy



Kahl BS, at al. JCO 2024

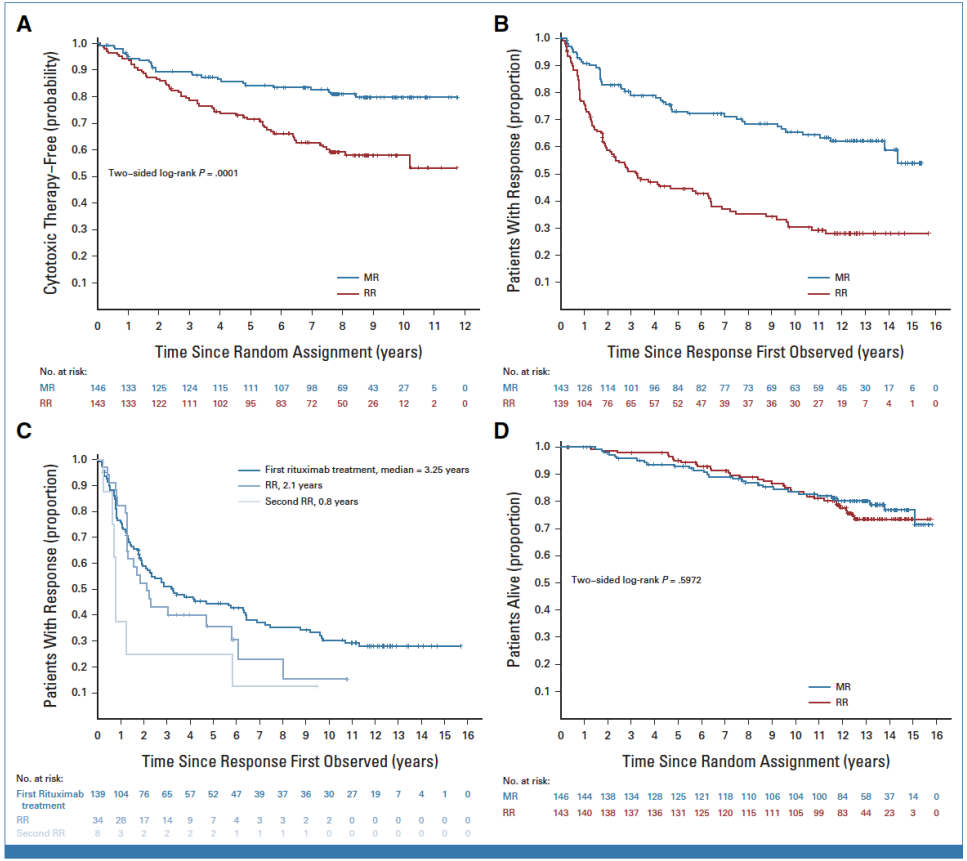
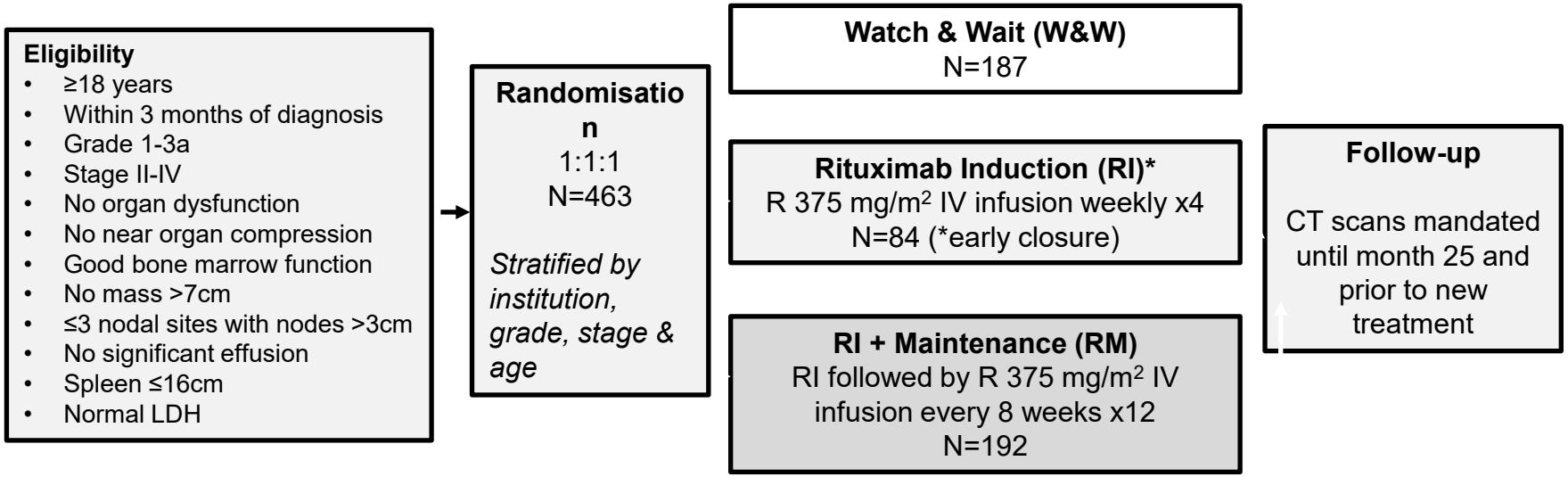


FIG 2. (A) KM estimate for time to first cytotoxic therapy. (B) KM estimate for duration of response. (C) KM estimate for duration of response for RR induction and first and second retreatment. (D) KM estimate for overall survival. KM, Kaplan-Meier; MR, maintenance rituximab; RR, retreatment rituximab.

The Rituximab versus Watchful Waiting study (RWW)

- Studies in the pre-rituximab era showed no benefit to early treatment of asymptomatic, low tumour burden follicular lymphoma (LTBFL) over a 'watch & wait' (W&W) approach
- The use of rituximab in this setting was assessed in the international, randomised phase 3 'W&W' study



Primary endpoints:

1. Time to initiation of new treatment (chemotherapy or radiotherapy)
2. Quality of life (QoL) at month 7

Northend M et al. Lancet Haematol, 2025

Early rituximab monotherapy versus watchful waiting for advanced stage, asymptomatic, low tumour burden follicular lymphoma: long-term results of a randomised, phase 3 trial

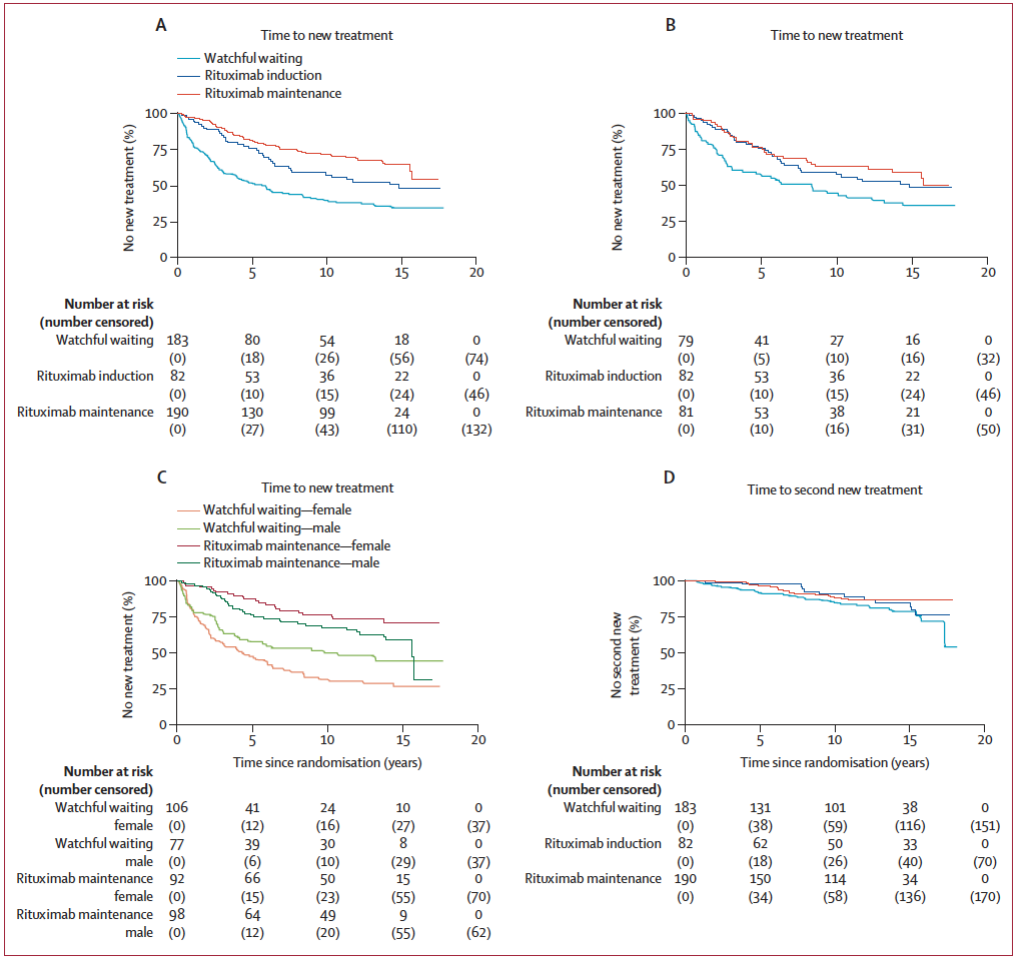
Michael Northend, William Wilson, Kushani Ediriwickrema, Laura Clifton-Hadley, Wendi Qian, Zaynab Rana, Tanya-Louise Martin, William Townsend, Moya Young, Fiona Miall, David Cunningham, Jan Walewski, Burhan Ferhanoglu, Kim Linton, Amanda Johnston, John F Seymour, David C Linch, Kirit M Ardeshna

Median Follow-up 14.7 y (IQR 13.3-15.6)

Median time to new treatment

Arm	Median and 95% CI
W&W	5.6 y (3.8-8.4)
RI	14.8 y (7.5 – not reached)
RM	not reached (15.6 – not estimable)

Arm	% patients free of new ttt at 15 yeras
W&W	65% (95%CI 56-72)
RI	48% (95% CI 36-60)
RM	34% (95% CI 27-42)



Northend M et al. Lancet Haematol, 2025

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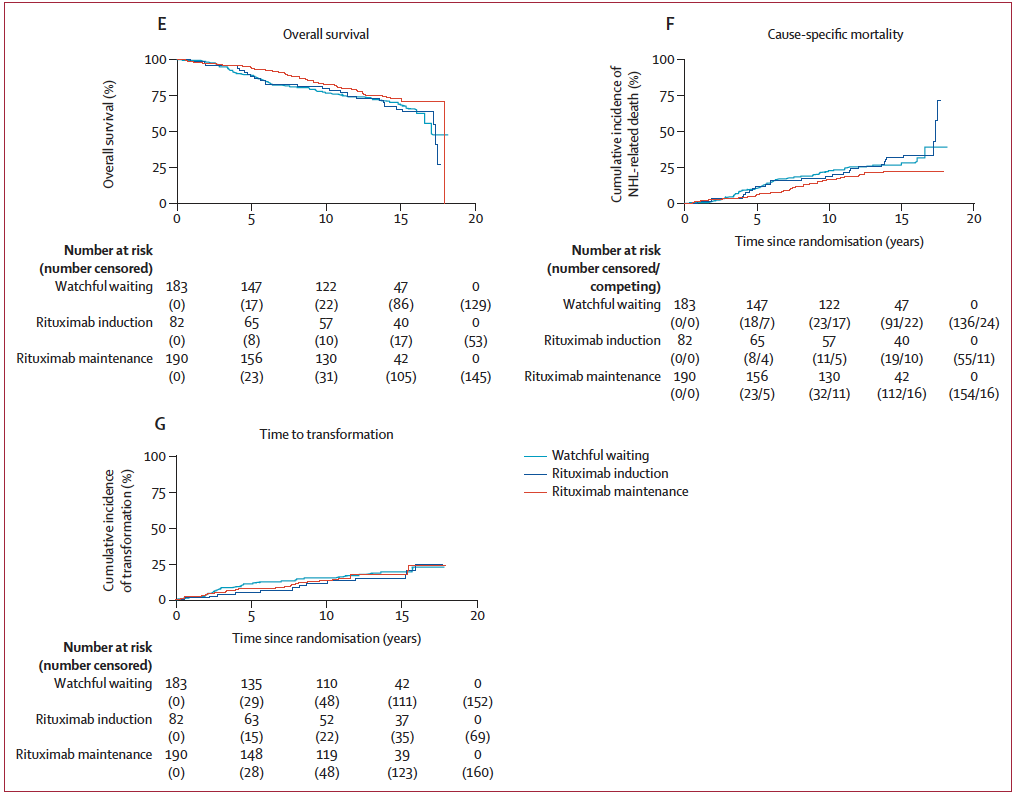
	Watchful waiting group (n=183)*	Rituximab induction group (n=82)*	Rituximab maintenance group (n=190)*
Median age, years	59	60	59
IQR	49–66	53–64	51–66
Range	27–82	33–85	26–86

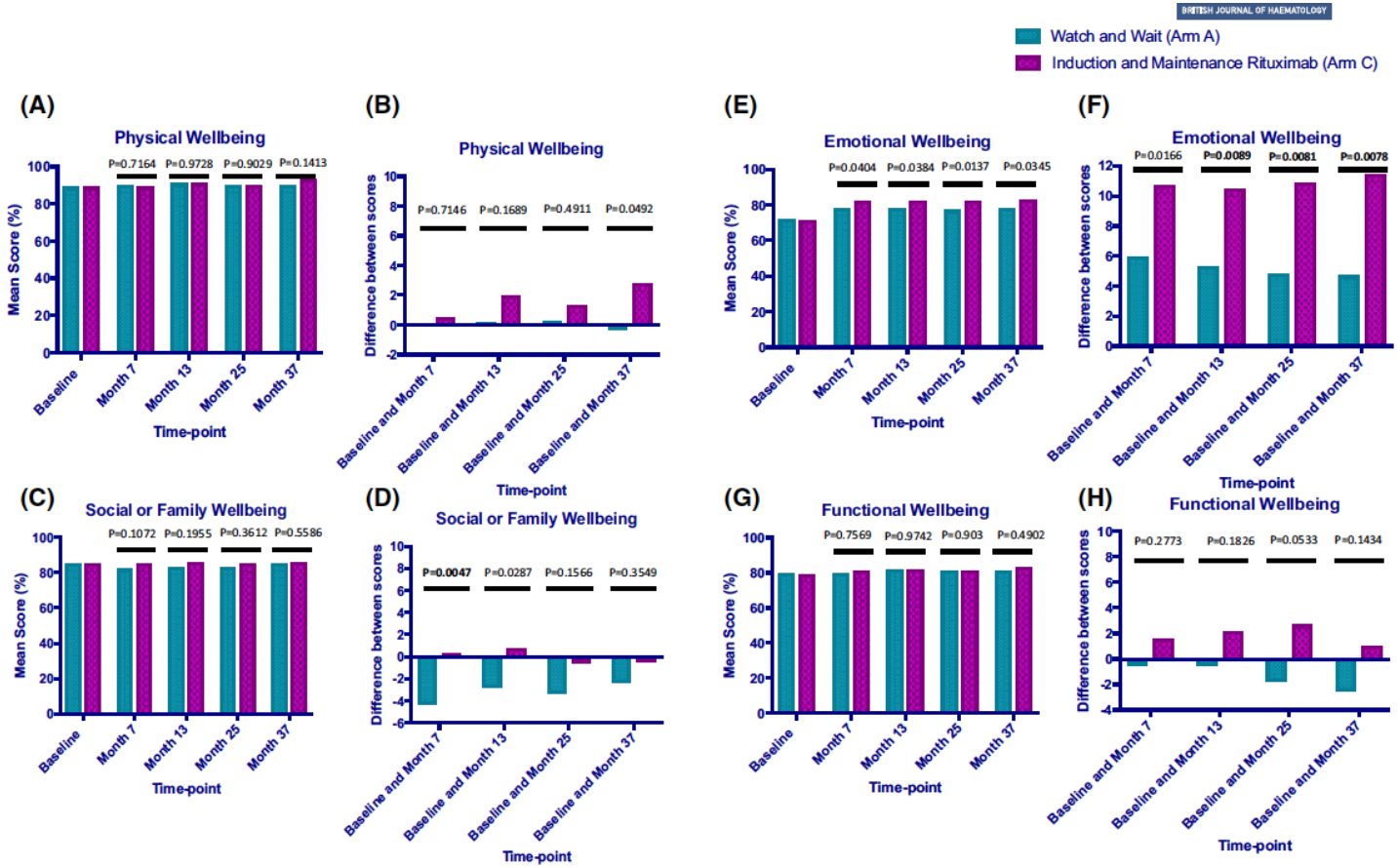


Overall Survival

Arm	10-year rate (95% CI)
W&W	76.5% (69.3-82.2)
RI	80.3% (69.4-87.6)
RM	82.1% (75.4-87.2)

Northend M et al. Lancet Haematol, 2025

QoL?



"… These results demonstrate improved QoL scores in the induction and maintenance rituximab arm, indicating that rituximab was not detrimental to QoL and resulted in an improved QoL in some domains."

Marzolini MAV et al. BJH, 2025;206:876–886.

R-chemo + R-maintenance (PRIMA): 10-year updated results

10-year PFS estimates

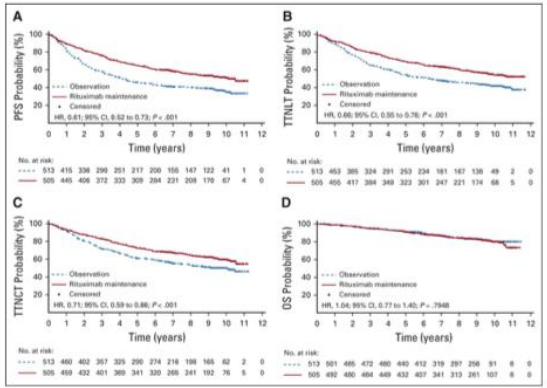
Observation 35%

R Maintenance 51%

Median time to new treatment initiation

Observation 6.1 y

R Maintenance > 10 y (not reached)



Bachy et al. JCO 2019

Luminari et al

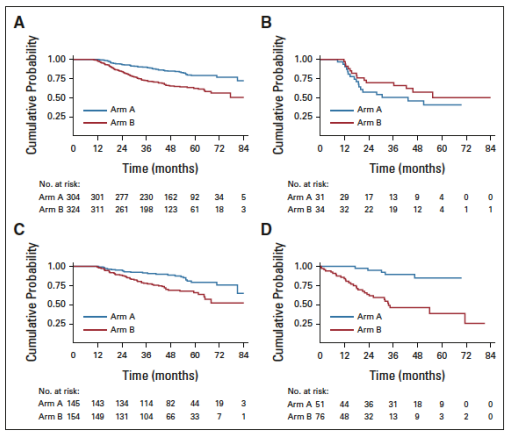
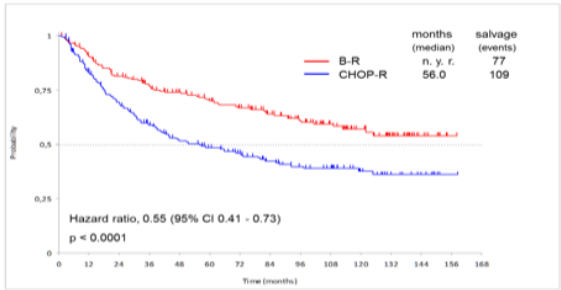


FIG 3. PFS for patients in CR/PR after EOI with reviewed PET and MRD: (A) EOT PET–, (B) EOT PET+, (C) EOT PET/MRD–/–, and (D) EOT PET– and MRD-positive at EOT or repositivized during follow-up. Arm A, reference arm; Arm B, experimental arm; CR, complete remission; EOI, end of induction; EOT, end of treatment; MRD, minimal residual disease; PET, positron emission tomography; PFS, progression-free survival; PR, partial remission.

10-year update of the StiL study

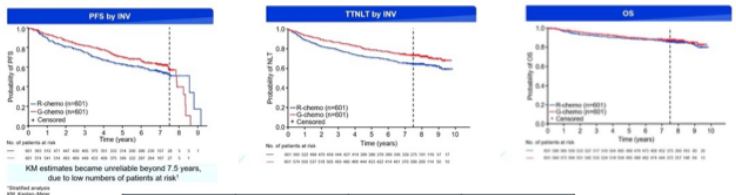
Median f-up 117 months – All histologic subtypes of iNHL

Used TNTT as a surrogate for PFS



ASCO 2017 Presented by Mathias Rummel

GALLIUM: obinutuzumab increased PFS and TTNT versus rituximab – 7 years follow-up



At 7-year	PFS % (95% CI)	TNTLT % (95% CI)	OS % (95% CI)
G-Chemo	63.4 (59.0-67.4)	74.1 (70.3-77.5)	88.5 (85.6-90.9)
R-Chemo	55.7 (51.3-59.9)	65.4 (61.4-69.2)	87.2 (84.1-89.7)
Hazard Ratio	*0.77 (0.64-0.93)*	*0.71 (0.58-0.87)*	*0.86 (0.63-1.18)*

Townsend W et al., Presented at: 2022 EHA Congress; June 9-12, 2022; Vienna, Austria. Abstract 5206

Lenalidomide plus rituximab for previously untreated advanced follicular lymphoma (FL): 10-year analysis of RELEVANCE trial

Context of Research

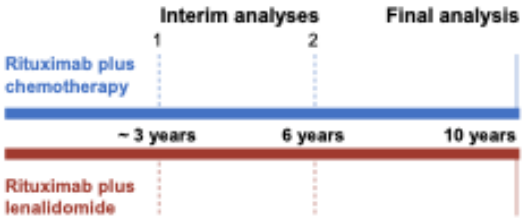
- The combination of rituximab and lenalidomide provides a chemo-free option for patients with follicular lymphoma (FL)
- Hence, follow-up to capture long-term efficacy and safety data is crucial

We report the final analysis at the 10-year follow-up of RELEVANCE Trial

Median follow-up: 9.8 years

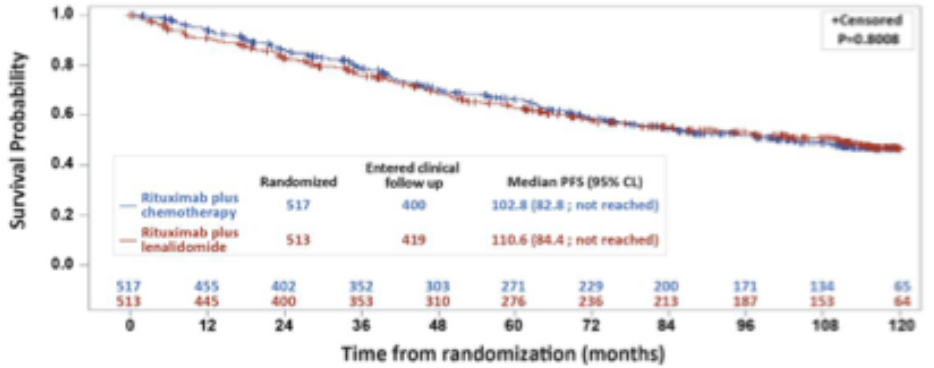
Patients and Methods

- Large, prospective, phase 3 trial in patients with previously untreated advanced FL



Co-primary efficacy endpoints:
Confirmed/unconfirmed response rate at 120 weeks and progression-free survival (PFS)

Main Outcomes: Comparable PFS benefit and safety profiles



CL, confidence limit; EMA, European Medicines Agency; IRC, Independent Review Committee; P, P-value; PFS, progression-free survival.

	Rituximab plus lenalidomide	Rituximab plus chemotherapy
Patients with SPM	79 (15.6%)	85 (16.9%)
Grade 5 TEAE	9 (1.8%)	6 (1.2%)
Deaths	87 (17.2%)	87 (17.3%)

IN PRESS – DO NOT POST

2. Newly diagnosed patients tomorrow?

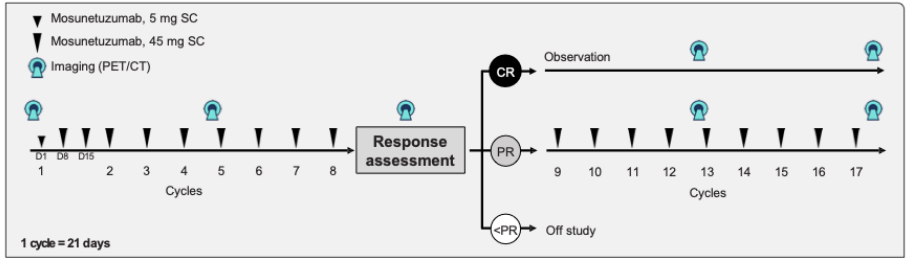
High Tumor Burden Follicular Lymphoma (1)

MITHIC-1 - Multicenter Phase 2 Study Overview

Endpoints:
- **Primary:** CR per Lugano
- **Secondary:** ORR, safety, PFS, DOR, TTNT, OS
- **Exploratory:** PD, ctDNA monitoring

Eligibility:
- ≥18 years; ECOG PS 0-2
- CD20+ previously untreated FL,
- G1-3A, stage II–IV
- **Need of therapy per GELF criteria**

Outpatient administration:
- Prophylaxis: Dexamethasone, anti H2, acetaminophen in C1 (and C2 if prior CRS)
- VZV and PJP prophylaxis and GCSF support per treating physician



Patients who experience progression at any time point were taken off study; CR, complete response; ORR, overall response rate; PFS, progression-free survival; DOR, duration of response; OS, overall survival; PD, progressive disease; ctDNA, circulating tumor DNA; CRS, cytokine release syndrome; VZV, varicella zoster virus; PJP, *Pneumocystis jirovecii* pneumonia; GCSF, granulocyte colony stimulating factor; PET/CT, positron emission tomography/computerized tomography; PR, partial response

4

Abstract #463

Combined Mosunetuzumab and Zanubrutinib for the Treatment of Patients with Newly Diagnosed High-Burden Follicular Lymphoma: First Results of the Multicenter Phase 2 MITHIC-FL2 Trial

Lorenzo Falchi[1], Clare Grieve[1], Christina Miah[1], Anastasia Martinova[1], Lauren Wood[1], Joanna Tortora[1], Joseph Roswarski[2], Alexander Boardman[1], Kevin David[1], Paola Ghione[1], Anita Kumar[1], Jennifer Lue[1], Efrat Luttwak[1], Ariela Noy[1], Colette Owens[1], Lia Palomba[1], Raphael Steiner[1], Robert Stuver[1], Pallawi Torka[1], Jasmine Zain[1], Andrew Zelenetz[1], Ayodeji Olukoya[2], Michelle Okwali[1], Honglei Zhang[3], Venkatraman Seshan[4], Pallavi Kanwar Galera[5], Ahmet Dogan[5], Santosha Vardhana[1], Kieron Dunleavy[2], Gilles Salles[1]

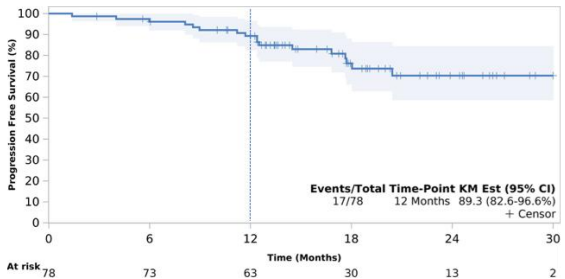
[1]Lymphoma Service, Memorial Sloan Kettering Cancer Center, New York, NY; [2]Lymphoma, Hematologic Malignancies Division, Lombardi Comprehensive Cancer Center, Washington, DC; 3 Radiology, Memorial Sloan Kettering Cancer Center, New York, NY; 4 Epidemiology-Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY; 5 Pathology and Laboratory Medicine, Memorial Sloan Kettering Cancer Center, New York, NY

Memorial Sloan Kettering Cancer Center

Presented at the 67th American Society of Hematology Annual Meeting and Exposition; December 6-9, 2025; Orlando, FL

Response type	Response evaluable (N=76)	Intention-to-treat (N=78)
Overall response	**95%**	92%
Complete response*	**82%**	79%
Partial response	13%	13%
Stable disease	3%	3%
Progressive disease	3%	3%
Non-evaluable	n/a	3%

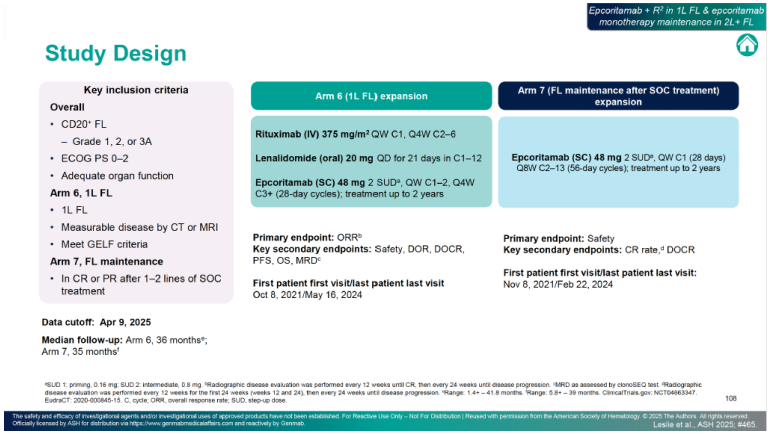
Progression-Free Survival

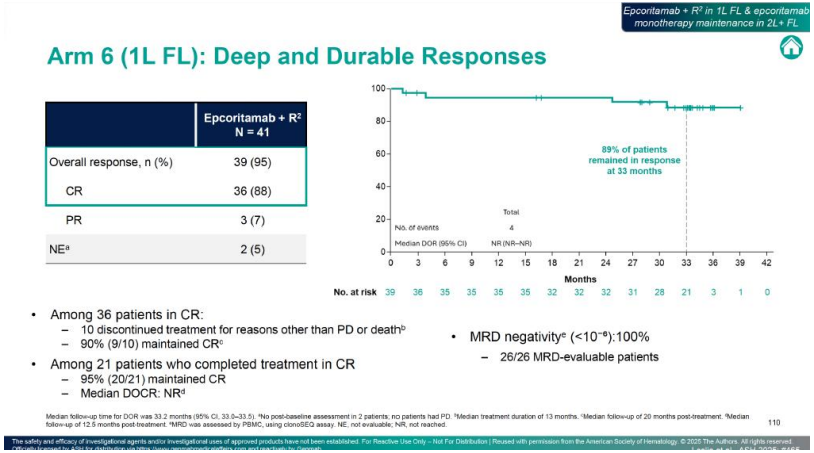


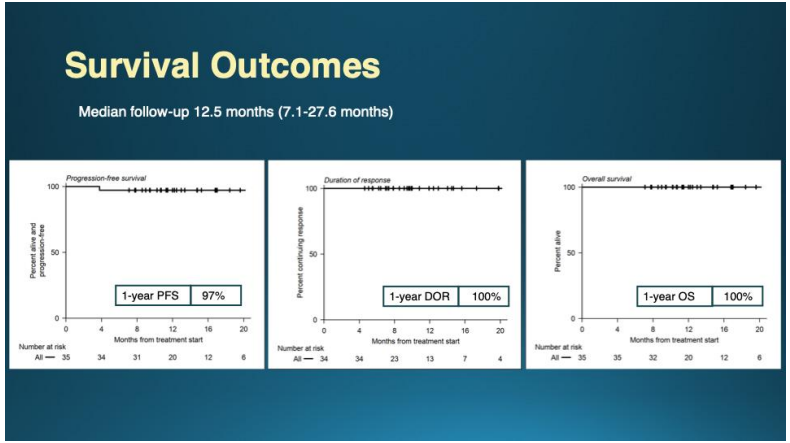
Response Type	Response Evaluable (n=51)
Overall Response	47 (92%)
Complete Response	**42 (82%)**
Partial Response	5 (10%)
Stable Disease	1 (2%)
Progressive Disease	3 (6%)

Falchi L et al., ICML 2025 ; ASH 2025

High Tumor Burden Follicular Lymphoma (2)



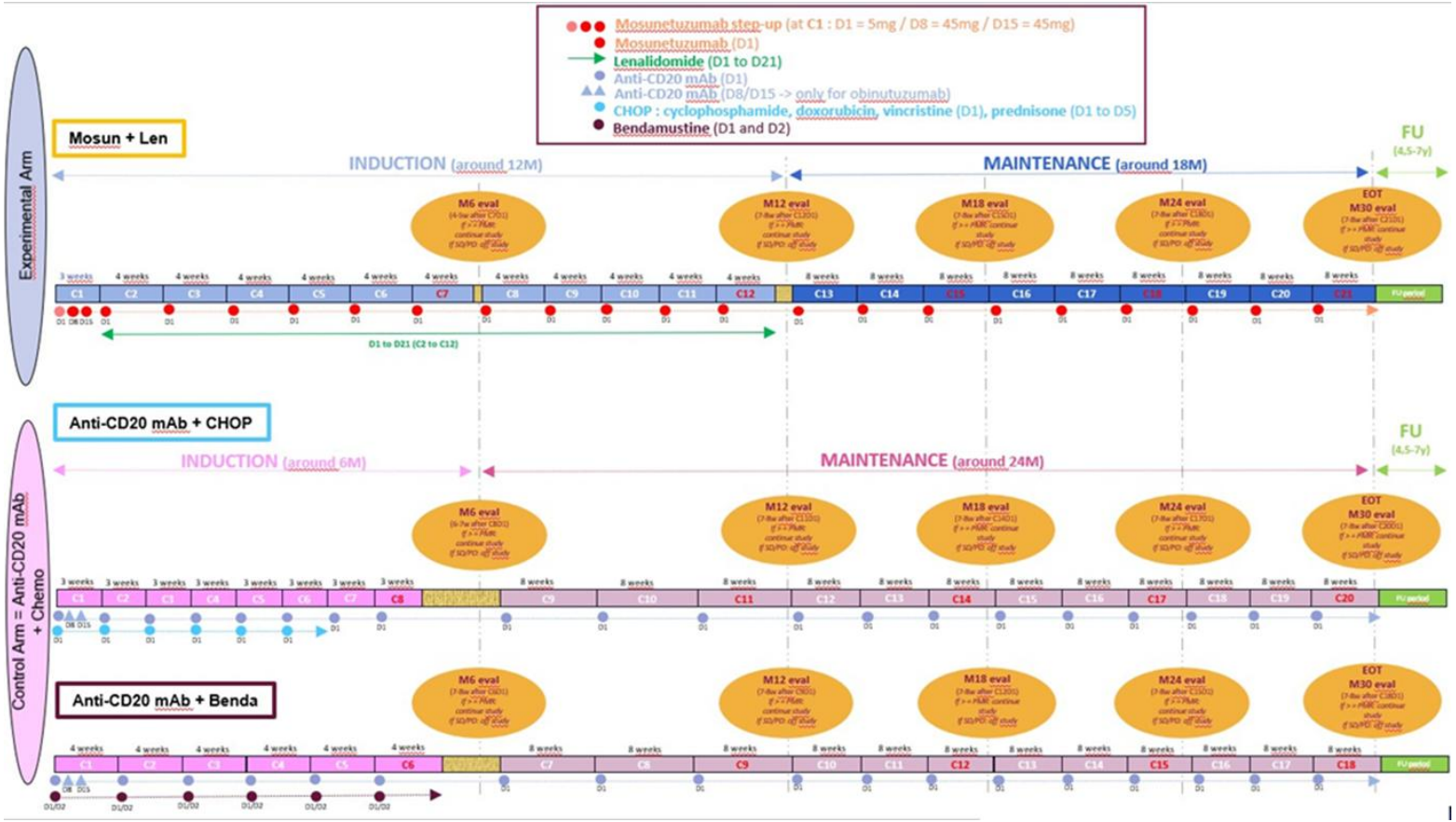




Leslie L et al., ASH 2025 ; Merryman R et al, ASH 2025

MorningLYte

High Tumor Burden Follicular Lymphoma (3)



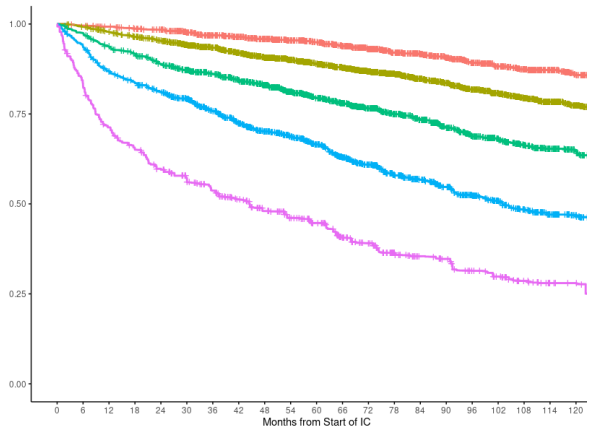
FLIPI24: An Improved International Prognostic Model Developed on Early Events in Follicular Lymphoma

Variable	Input Range	Effect	HR
Age	18-90	Non-linear	1.01 per year (60-75] 1.05 per year (75-90)
LDH/ULN	0.5-5	Linear	1.44 per unit
B2M	1-10	Linear	1.17 per unit
HGB	8-17	Linear	0.92 per unit
WBC	4-11	Linear	1.08 per unit

@MaurerStats

Online calculator at rtools.mayo.edu

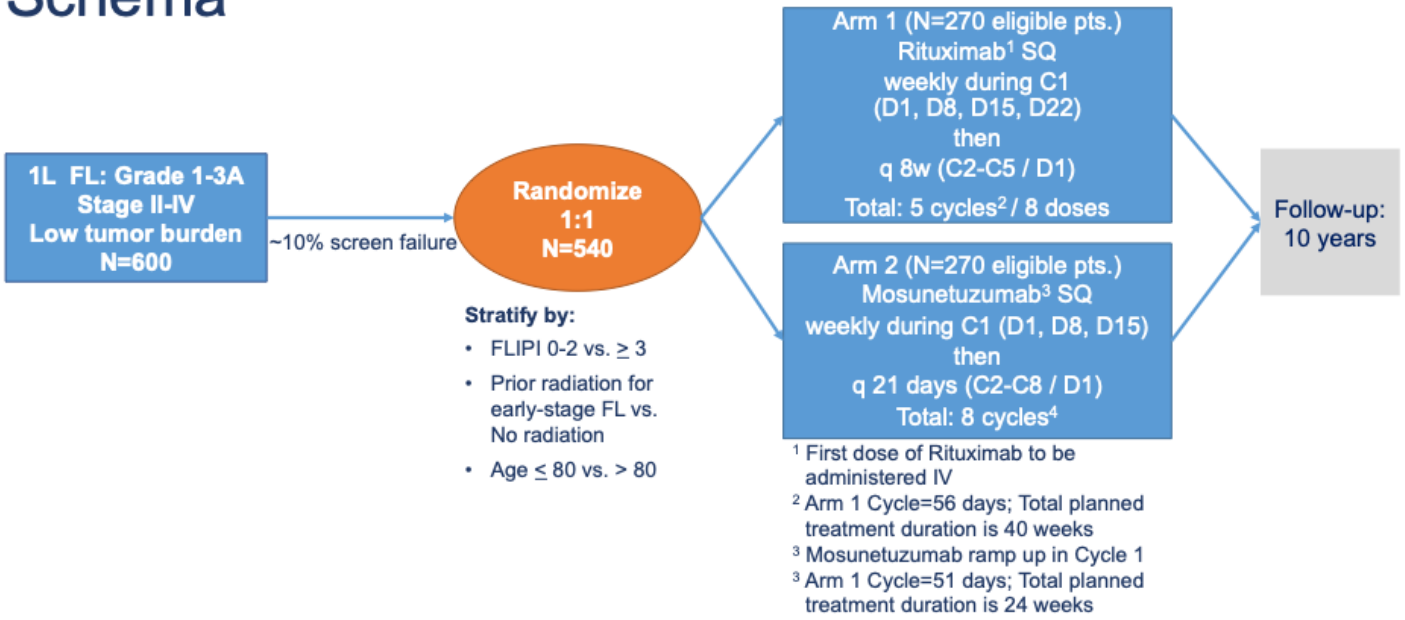
Risk group	FLIPI24 Score	% of pts	EFS24	10-year OS
Low	<10%	25%	92%	86%
Low-Avg	10-15%	40%	85%	77%
Avg	15-20%	16%	75%	65%
High	20-40%	15%	62%	47%
Very High	>40%	4%	41%	28%



Maurer M et al. JCO 2025

S2308: Randomized Phase III Study of Mosunetuzumab vs Rituximab in Low Tumor Burden Follicular Lymphoma

Schema



Mosunetuzumab and Rituximab are provided by the study

3. Patients with relapsed or refractory disease...

Is there a standard in patients with R/R disease?

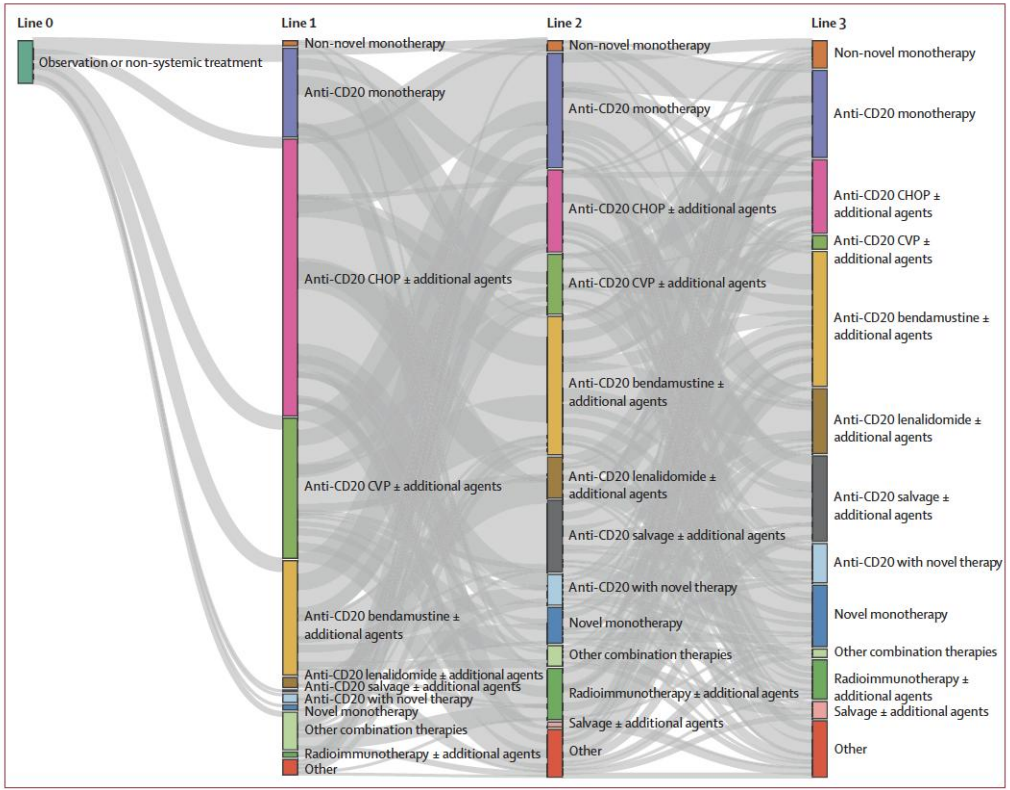


Figure 1: **Sankey plot of treatment patterns across lines of therapy**
CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisolone. CVP=cyclophosphamide, vincristine, and prednisolone.

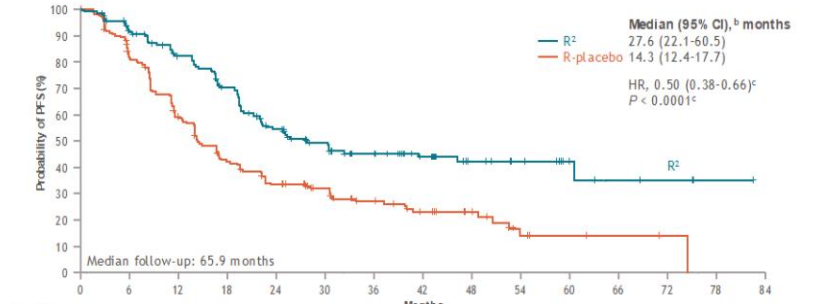
After a median follow-up of 71 months from index therapy, 5-year overall survival was:

75% (95% CI 70-79)

Casulo C, et al. Lancet Haematol. 2022 Apr;9(4):e289-e300.

AUGMENT 5-year results: lenalidomide plus rituximab versus rituximab plus placebo in patients with relapsed/refractory indolent non-Hodgkin lymphoma

Progression-free survival[a] (ITT population)



- Median PFS was 27.6 months for R² versus 14.3 months for R-placebo (HR, 0.50; *P* < 0.0001)

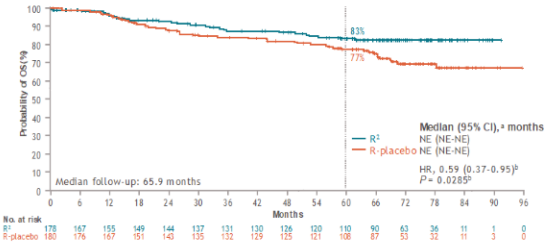
[a]PFS per 2007 IWG criteria as assessed by IRC is the primary endpoint, but the follow-up period is by investigator. Censoring rules were based on FDA guidance; [b]Median estimate was from Kaplan-Meier analysis; [c]The *P* value was from a log-rank test stratified by previous rituximab treatment (yes/no), time since last antilymphoma therapy (≤ 2/> 2 years), and disease histology (FL/MZL). The HR was calculated using a Cox proportional hazard model adjusted using the same stratification factors.

Treatment-emergent adverse events (safety population)

Patients with TEAE, n (%)	R² (n = 176)	R-placebo (n = 180)
Any-grade TEAE	174 (99)	173 (96)
Any-grade TEAE related to lenalidomide or placebo	159 (90)	118 (66)
Any-grade TEAE related to rituximab	134 (76)	105 (58)
Grade 3/4 TEAE[a]	121 (69)	58 (32)
Grade 3/4 TEAE related to lenalidomide or placebo	101 (57)	38 (21)
Grade 3/4 TEAE related to rituximab	57 (32)	20 (11)
Grade 5 TEAE[a,b]	2 (1)	2 (1)
Serious any-grade TEAE	45 (26)	25 (14)
Any-grade TEAE related to lenalidomide or placebo	23 (13)	8 (4)
Any-grade TEAE related to rituximab	13 (7)	4 (2)

- Grade 3/4 TEAEs were more common in patients who received R² versus R-placebo (69% vs 32%); the most common was neutropenia (R², 50%; R-placebo, 13%)

Overall survival (ITT population)



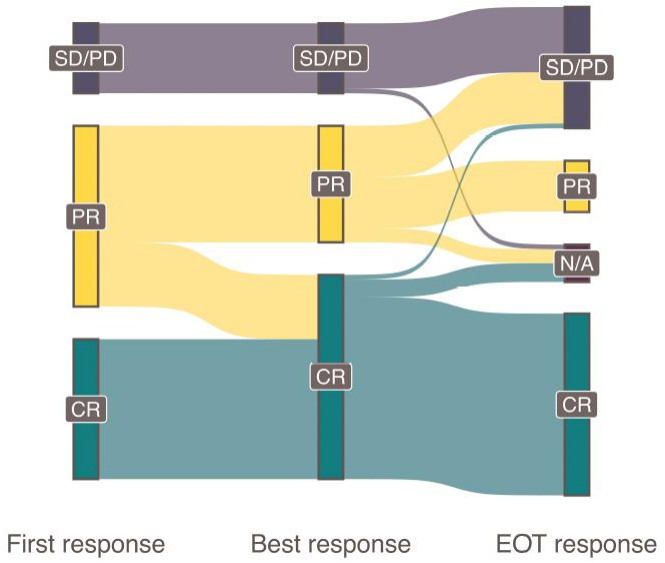
- Although median OS was not reached for either arm, there was an improvement in OS with R² compared with R-placebo (HR, 0.59; *P* = 0.0285)
  - 5-year OS rates for R² versus R-placebo were 83.2% and 77.3%, respectively

[a]Median estimate was from Kaplan-Meier analysis; [b]The *P* value was from a log-rank test stratified by previous rituximab treatment (yes/no), time since last antilymphoma therapy (≤ 2/> 2 years), and disease histology (FL/MZL). The HR was calculated using a Cox proportional hazard model adjusted using the same stratification factors.

	POD 24 (n=147)	No POD24 (n=148)
R2 – median PFS	30.4 (16.8-NR)	39.4 (22.9-NR)
R- placebo – median PFS	13.8 (6.7-16.9)	13.9 (11.2-16.6)

Leonard J et al. ASH2022, abstract 230

R2: real life data at MSK



Cassanello G et al., Haematologica 2024

R2 as a new SoC…

Symphony 1: R2 +/- Tazemetostat (NCT04224493)

EPCORE FL-1 (NCT05409066)

InMIND: R2 +/- Tafasitamab (NCT04680052)

Mohagany: R2 vs. Obin-Zanubrutinib (NCT05100862)

Celestimo: R2 vs. Mosunetuzumab-Len (NCT04712097)

OLYMPIA-5: R2 vs. Odronextamab (NCT06149286)

LEDA: Tisagenlecleucel vs. SOC (inc. R2) (NCT05888493)

ZUMA-22: Axi-cell vs. SOC (inc. R2) (NCT05371093)

EPCORE FL-1: Epcoritamab with Rituximab + Lenalidomide (R^2) vs. R^2 for R/R FL

Fixed-Duration: 12 Cycles (28-Day Cycles)

Key eligibility criteria

- Histologically confirmed CD20+ FL
- Grade 1-3a, Stage II-IV
- ≥ 1 prior treatment including anti-CD20 mAb plus an alkylating agent
- Met ≥ 1 GELF criterion

Randomization 1:1

Epcoritamab (48 mg) plus R^2

- **Epcoritamab** (3-SUD cycle 1: QW;[a,b] cycles 2–3, QW; cycles 4–12, Q4W)
- **Rituximab** (375 mg/m^2), 5 cycles (cycle 1, QW; cycles 2–5, Q4W)
- **Lenalidomide** (20 mg), 12 cycles (cycle 1–12, QD, D1-21)

R^2

- **Rituximab** (375 mg/m^2), 5 cycles (cycle 1, QW; cycles 2–5, Q4W)
- **Lenalidomide** (20 mg), 12 cycles (cycle 1–12, QD, D1-21)

Stratification factors

- Disease status:
  - 2L: > or ≤ 2 years since last therapy
  - 3L+: > or < 6 months since last therapy
- Region: US/EU vs Rest of World

- **Dual primary endpoints: ORR per IRC and PFS per IRC**
- Key secondary endpoints: CR rate per IRC, OS, and MRD[c]
- Additional secondary endpoints: DOR, DOCR, TTNLT, safety, and PRO assessments

Data cutoff: May 24, 2025; median follow-up: 14.8 months[d]
Enrollment period: October 2022 - January 2025

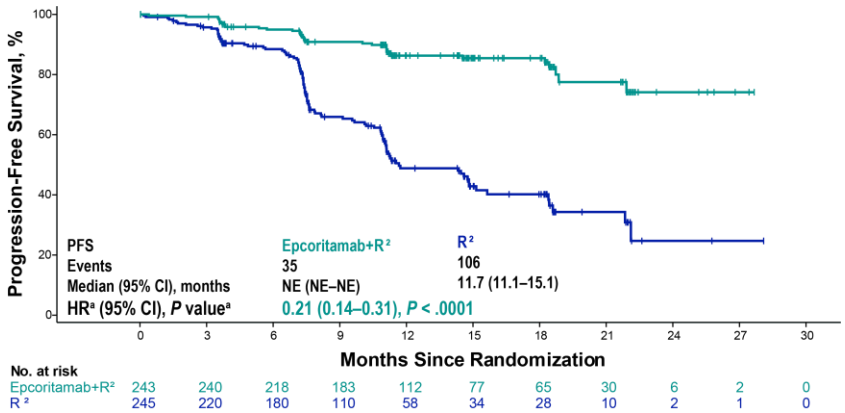
[a]Two step-up dosing (SUD) regimens during cycle 1 to mitigate the risk of cytokine release syndrome: either a 2-SUD (0.16 mg on cycle 1 day 1, 0.8 mg on cycle 1 day 8), or 3-SUD (0.16 mg on cycle 1 day 1, 0.8 mg on cycle 1 day 8, 3 mg on cycle 1 day 15) regimen, followed by full dose 48 mg. The 3-SUD regimen was implemented after reduced CRS severity and incidence had been observed in the EPCORE NHL-1 FL trial (NCT03625037).[1] [b]The 24 mg epcoritamab plus R^2 arm was closed to enrollment based on the superior efficacy for the 48 mg dose from EPCORE NHL-2.[2] Only the data for the optimal dose explored (48 mg) are presented here. [c]Minimal residual disease data are forthcoming in a future analysis. [d]The data presented here are from the second planned interim analysis (May 24, 2025) after 78% Information Fraction for PFS had occurred.

1. Vose J, et al. *J Clin Oncol.* 2024;42(16_suppl):7015–7015. 2. Falchi L, et al. *Blood*. 2024;144(Supplement 1):342–342.

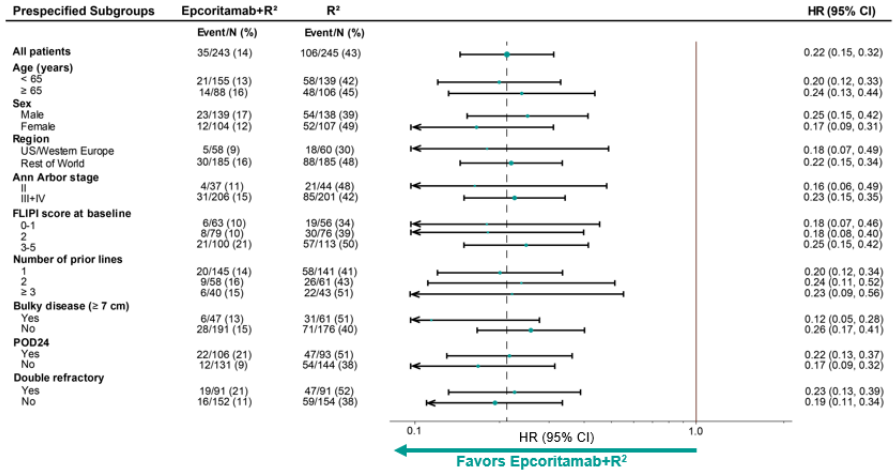
Falchi L, et al. *Lancet.* 2026 Jan 10;407(10524):161-173

Primary Results From the EPCORE FL-1 Phase 3 Study of Epcoritamab + R^2 vs R^2 in Patients With R/R FL: PFS

PFS in ITT Population



PFS by Prespecified Subgroups

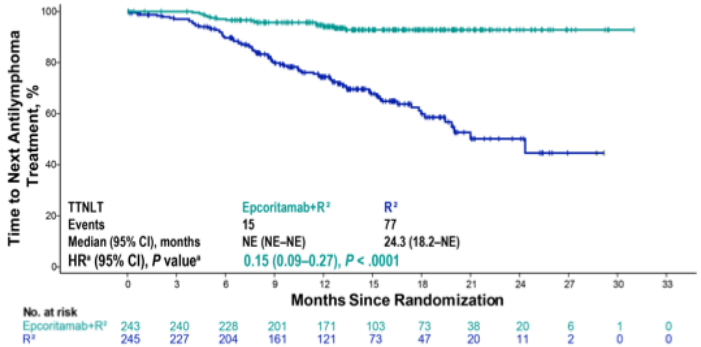


- Median follow-up for PFS: epcoritamab+R^2 (14.4m), R^2 (11.5m).
- Concordance rate was 94% for PFS between IRC and investigator assessment
- The estimated 16-month PFS was 85.5% (95% CI: 79.7, 89.7) for Epcor + R^2 and 40.2% (95% CI: 31.8, 48.4) for R^2

Falchi L, et al. *Lancet.* 2026 Jan 10;407(10524):161-173.

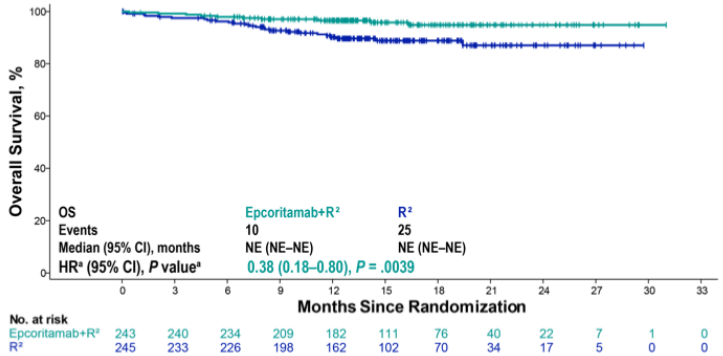
EPCORE FL-1: Epcoritamab with Rituximab + Lenalidomide (R^2) vs. R^2 for R/R FL – secondary endpoints

Epcoritamab+R^2 Extended Time to Next Treatment



- At 16 months, 92.8% of patients treated with epcoritamab+R^2 remained free from new antilymphoma treatment compared with 64.9% of patients treated with R^2

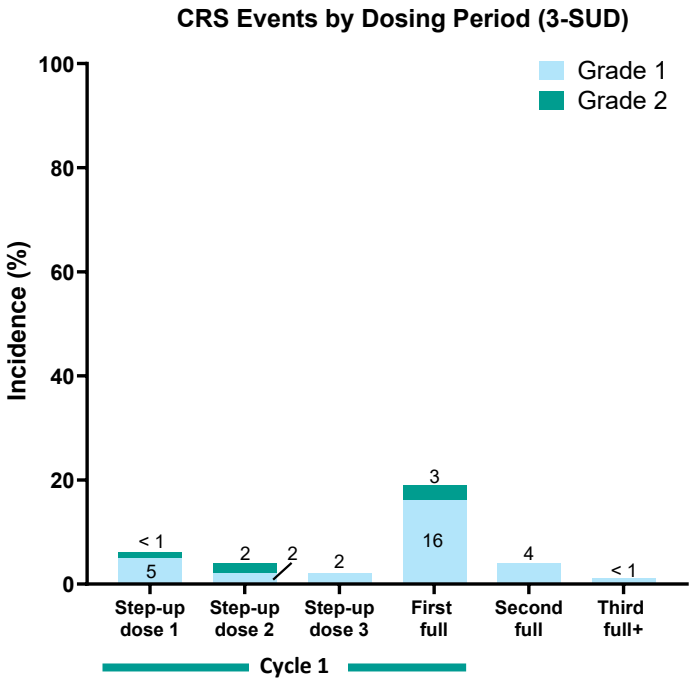
Positive Trend for Overall Survival With Epcoritamab+R^2



- The 16-month estimate for OS was 95.8% with epcoritamab+R^2 and 88.8% with R^2

Falchi L, et al. *Lancet.* 2026 Jan 10;407(10524):161-173

EPCORE FL-1 Phase 3 Study of Epcoritamab + R^2 vs R^2 in Patients With R/R FL: Safety

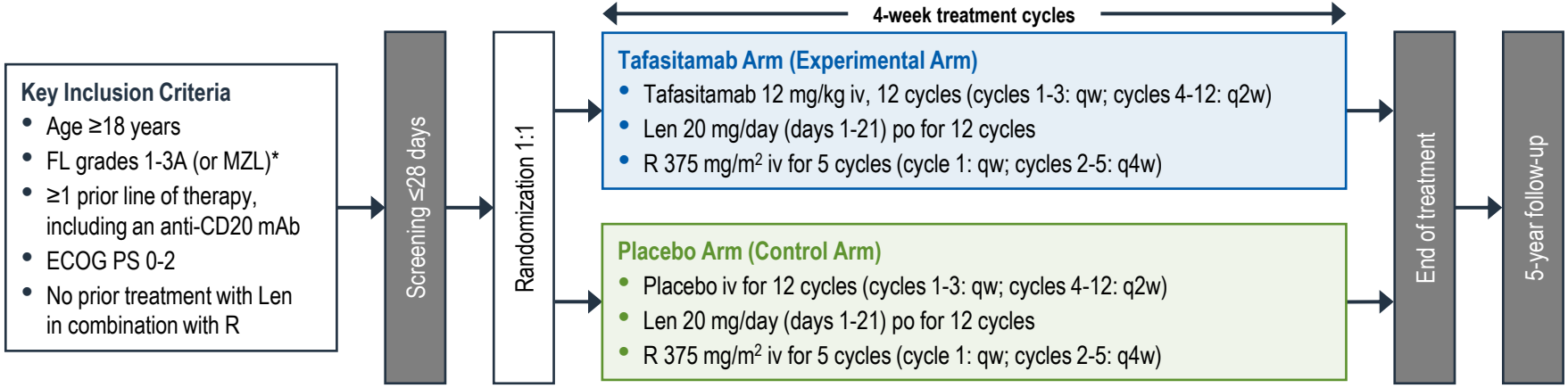


	Epcoritamab+R^2 2-SUD N = 110	Epcoritamab+R^2 3-SUD N = 133
CRS, n (%)	50 (45)	35 (26)
CRS grade, n (%)		
1	40 (36)	28 (21)
2	10 (9)	7 (5)
CRS signs and symptoms, n (%)[a]		
Fever	49 (98)	33 (94)
Hypotension	9 (18)	6 (17)
Hypoxia	1 (2)	2 (6)
Time to first CRS onset from first full dose, days, median (range)	1 (< 1, 6)	1.5 (< 1, 10)
Time to CRS resolution, days, median (range)	1 (< 1, 12)	1 (< 1, 26)
CRS interventions, n (%)[a]		
Treated with tocilizumab	12 (24)	9 (26)
Treated with corticosteroid	23 (46)	13 (37)

[a]Of patients who had CRS.

Falchi L, et al. ASH 2025. Abstract 466. Falchi L, et al. *Lancet*. 2025: Online. https://doi.org/10.1016/S0140-6736(25)02360-8.

inMIND: Phase 3, Double-Blind, Placebo-Controlled, International, Multicenter Randomized Study



Stratification Factors (Patients With FL)

- POD24
- Refractoriness to prior anti-CD20 mAb therapy
- Number of prior lines of therapy (1 or ≥2)

Study Endpoints in FL Population (Investigator Assessed Unless Specified)

- **Primary study endpoint:** PFS
- **Key secondary:** PET-CR rate in the FDG-avid population, OS
- **Select other secondary:** PFS by IRC, ORR, DOR, safety, QoL, MRD
- **Exploratory:** TTNT, B-cell recovery, Ig levels, CD19 expression

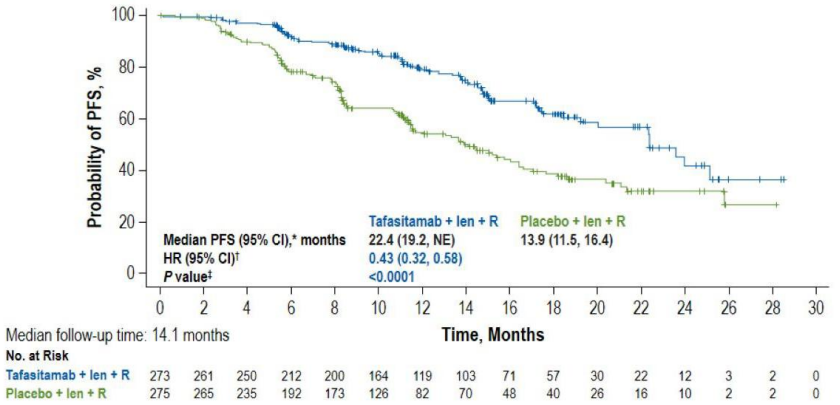
- Powered to assess PFS in the FL population, triggered when 174 investigator-assessed events occurred
- OS analysis planned after 5 years of follow-up

*Limited number of patients with MZL were enrolled but the study was not powered for this population; data for patients with MZL will be presented separately. DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FDG, fluorodeoxyglucose; FL, follicular lymphoma; Ig, immunoglobulin; IRC, independent review committee; iv, intravenous; Len, lenalidomide; mAb, monoclonal antibody; MRD, minimal residual disease; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PET-CR, positron emission tomography-complete response; PFS, progression-free survival; po, orally; POD24, disease progression within 24 months of initial diagnosis; QoL, quality of life; qw, weekly; q2w, every 2 weeks; q4w, every 4 weeks; R, rituximab; TTNT, time to next treatment.

inMIND: Results

PET-CR (FDG-Avid Population)	Tafasitamab + Len + R	Placebo + Len + R
Patients with FDG-avid disease at baseline	251	254
Patients with postbaseline PET assessments, n (%)*	201/251 (80.1)	205/254 (80.7)
Best metabolic response based on PET, n (%)†		
CMR	124 (49.4)	101 (39.8)
PMR	37 (14.7)	39 (15.4)
NMR/SD	19 (7.6)	12 (4.7)
PMD	19 (7.6)	51 (20.1)
Not done	50 (19.9)	46 (19.3)
PET-CR rate, % (95% CI)	**49.4** (43.1, 55.8)	**39.8** (33.7, 46.1)
Odds ratio (95% CI)	**1.5 (1.04, 2.13)**	
Nominal *P* value	**0.0286**	

Primary Endpoint: PFS by Investigator Assessment

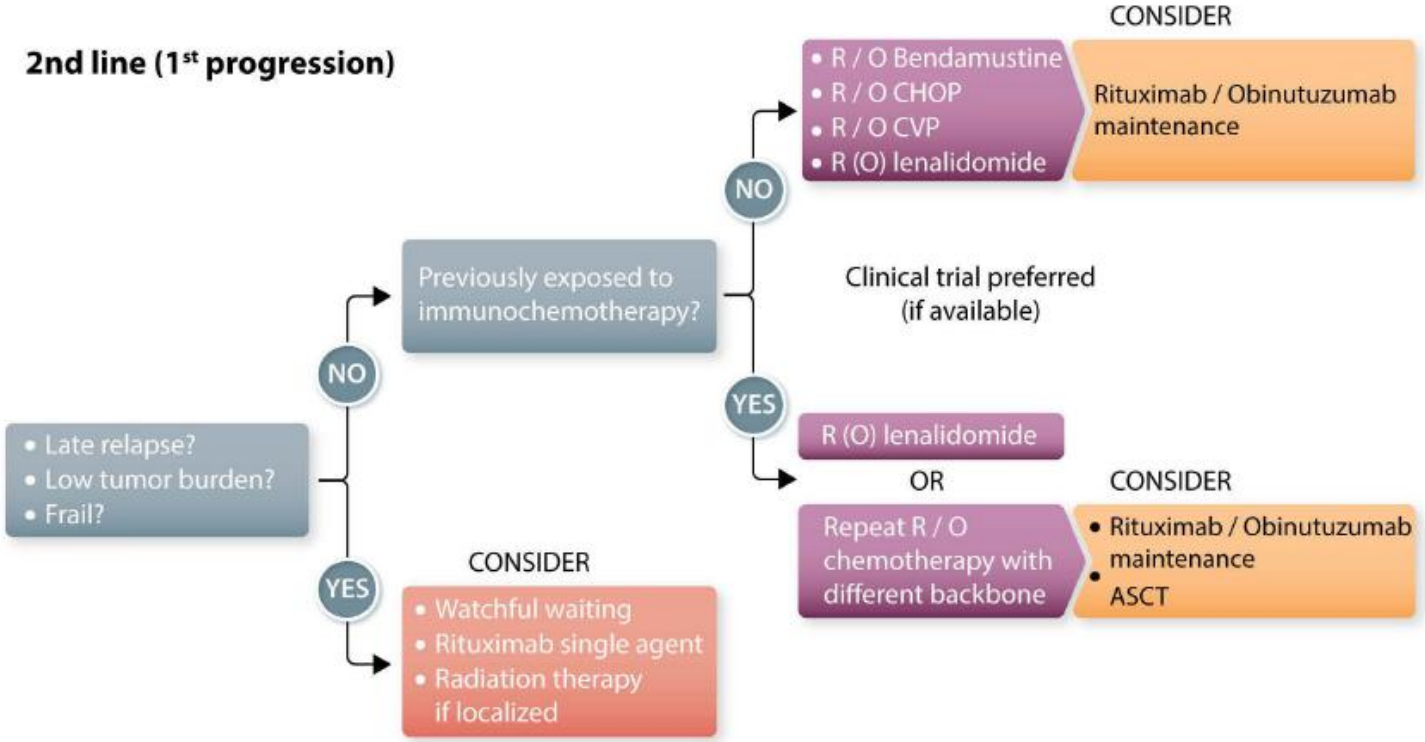


Significant improvement in PFS was observed with tafasitamab

Subgroup analyses indicated that the benefit of Tafasitamab was observed across different difficult-to-treat categories (POD24, >1 previous line, rituximab refractoriness)

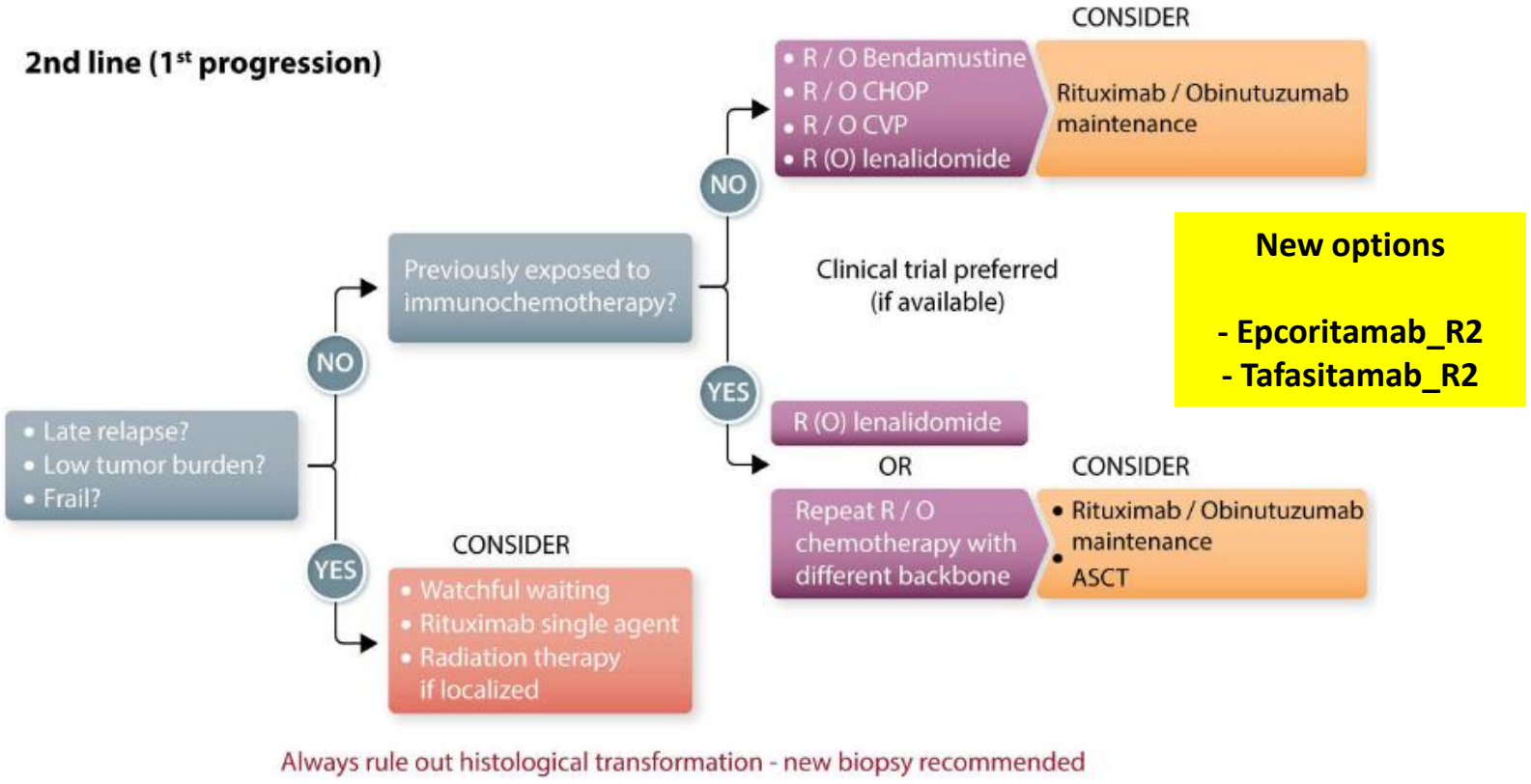
Sehn LH et al, 66th ASH Annual Meeting & Exposition • San Diego, CA, USA • December 7-10, 2024 (Abstract #LBA-1) ; Sehn et al, ICML 18th

Options at first progression



Qualls D & Salles G, Haematologica 2022

Options at first progression



New options

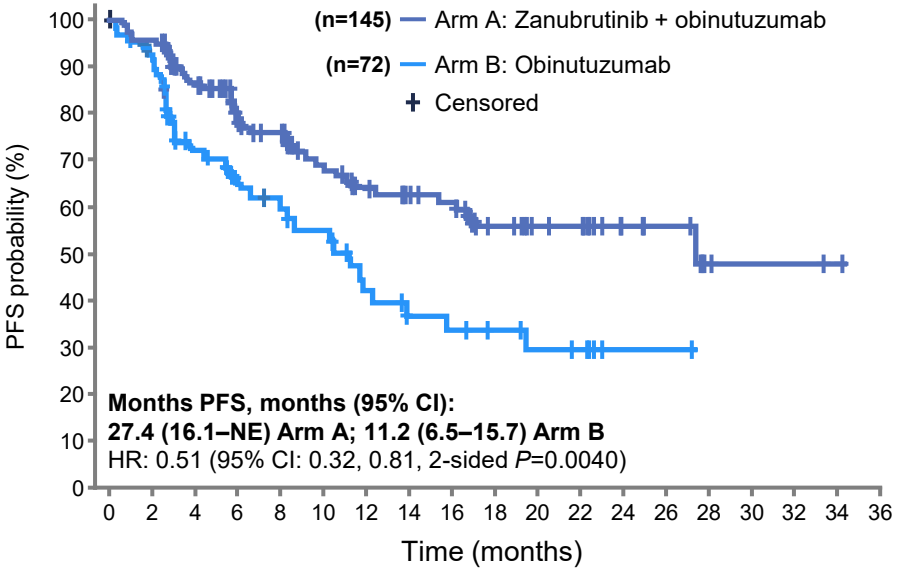
- Epcoritamab_R2
- Tafasitamab_R2

Qualls D & Salles G, Haematologica 2022

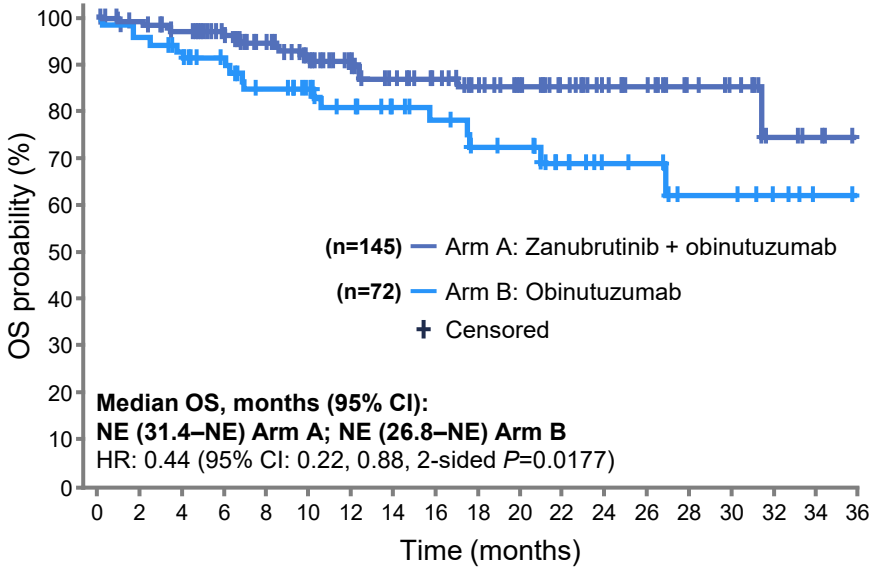
Adding Zanu to Obin improves response and survival in R/R FL

ROSEWOOD: Primary analysis of phase 2 randomized study in patients with ≥2 prior LOT (N=217)

PFS (by IRC)



OS (by IRC)



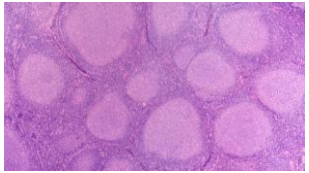
ZO demonstrated superior efficacy to O and had a favorable benefit-risk profile;

ORR (ZO vs O): 45.8% vs 68.3% and CR rate 19.4% vs 37.2%

* Not powered to detect difference in OS

Zinzani PL *et al, JCO* 2022; **40**(16):7510–7510

BsAb CD3 x CD20 in patients with R/R follicular lymphoma (updated 2025)



Patients' characteristics might differ among studies.

	Mosunetuzumab [1]	Odronextamab [2]	Epcoritamab [3]
Patients	n=90	n=128	n=127/149
Overall Response Rate	78%	80%	85%
Complete Response Rate	60%	73%	67%
Median Progression-Free Survival	24 months	21 months	~ 18 months
Duration - of Response / - of Complete Response	36 m. / 52 m.	23 m. / 25 m.	NA / NR

1. Sehn LH et al, Blood 2025 ; Cheah CY, ICML2025, abstract #236
2. Kim TM et al. Ann Oncol 2024
3. Linton K et al, Lancet Haem 2024; Vitolo U, EHA 2025, PF881

At 18 m., 58% and 72% of patients maintained their response or complete response, respectively

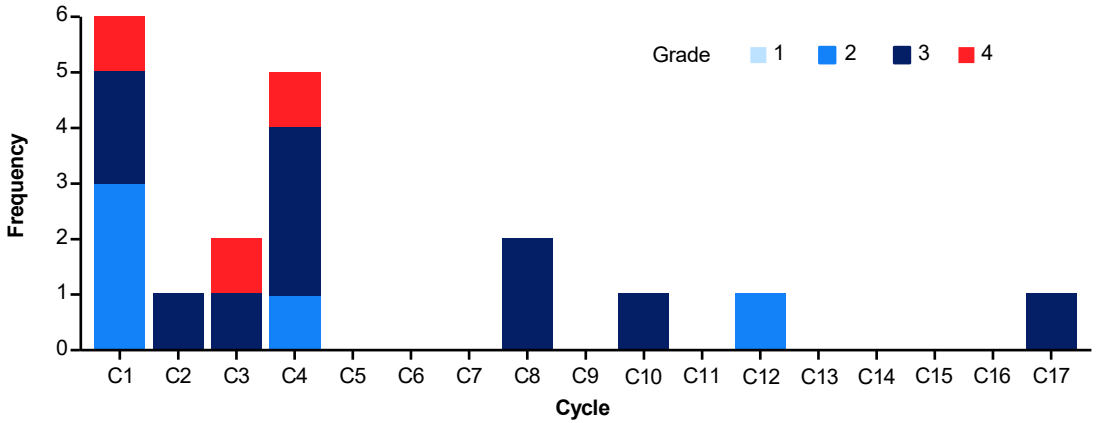
NR = Not Reached; NA = not available ; m.=months

Mosun: Efficacy summary: duration of response

Efficacy endpoints*	Overall population (N=90)	POD24 status		Line of therapy		Age	
		Non-POD24 (n=43)	POD24 (n=47)	3L therapy (n=35)	4L+ therapy (n=55)	<65 years (n=60)	≥65 years (n=30)
Median DOR,† months (95% CI)	35.9 (18.7–NE)	35.9 (20.7–NE)	NR (10.6–NE)	NR (11.9–NE)	34.5 (16.5–NE)	NR (16.5–NE)	35.9 (13.7–NE)
30-month DOR, (95% CI)	56% (43.3–67.8)	61% (43.9–78.5)	50% (33.2–67.4)	62% (43.9–79.7)	51% (34.0–67.0)	56% (41.2–71.8)	55% (35.5–75.0)
Median DOCR,‡ months (95% CI)	NR (33.0–NE)	NR (31.5–NE)	NR (18.7–NE)	NR (NE)	33.0 (18.7–NE)	NR (33.0–NE)	NR (18.7–NE)
30-month DOCR, (95% CI)	71% (58.2–84.0)	75% (56.5–92.6)	67% (48.8–86.1)	77% (59.3–94.9)	66% (48.5–84.5)	73% (56.7–89.2)	69% (48.1–89.6)
Median TTNT, months (95% CI)	NR (19.4–NE)	NR (16.0–NE)	NR (16.2–NE)	NR (18.1–NE)	NR (13.9–NE)	19.4 (9.7–NE)	NR (NE)

*By investigator assessment. †The median duration of objective response was assessed only among patients who had a complete or partial response.
‡The median duration of complete response was assessed only among patients with a complete response.
CI, confidence interval; DOCR, duration of complete response; NE, not evaluable; NR, not reached; TTNT, time-to-next-treatment.

Mosun: Serious infection by cycle



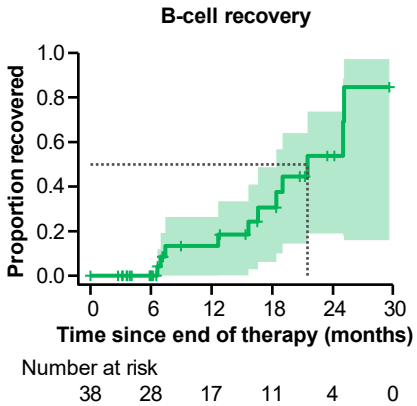
	C1	C2	C3	C4	C5	C6	C7	C8	C9	C10	C11	C12	C13	C14	C15	C16	C17
n=	90	87	83	81	76	71	69	69	16	15	13	13	12	12	11	11	11
Grade:																	
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	3	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0
3	2	1	1	3	0	0	0	2	0	1	0	0	0	0	0	0	1
4	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0

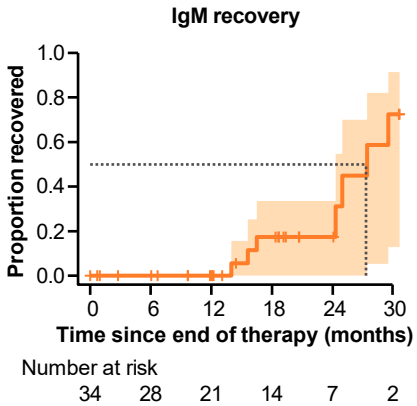
- **Most common (≥2%) Grade ≥3 serious infections:**
  - Urinary tract infection (3%)
  - Pneumonia (2%)
  - Septic shock (2%)
  - COVID-19 (2%)
  - Epstein–Barr viremia (2%)
- **Serious infections concurrent with neutropenia were rare (1%)**
- **Majority of serious infections resolved (19/21)***

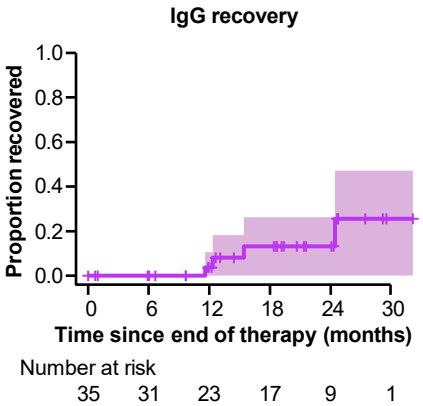
Most serious infections (14/19 [74%]) occurred in the first four cycles; only three events were reported beyond C8

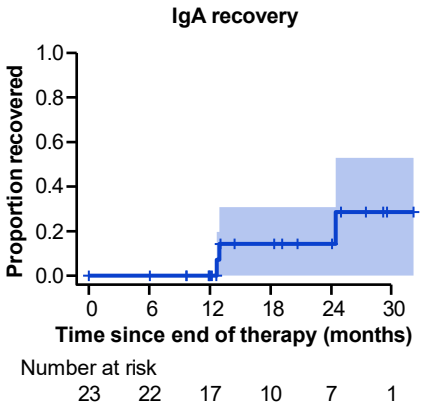
*Serious infections were not resolved in two patients: Grade 2 Herpes zoster, unrelated to study treatment and was reported to be recovering/resolving (n=1); Grade 3 *Klebsiella* infection, unrelated to study treatment and patient did not recover by the time of fatal disease progression (n=1).

Mosun: B-cell levels and immunoglobulin changes over time







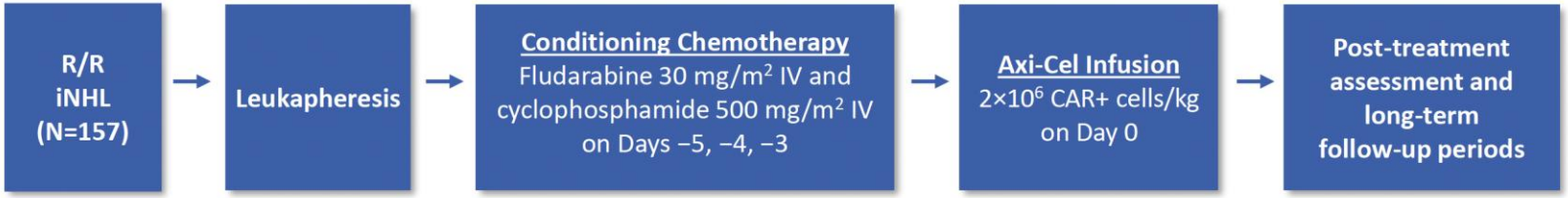


- Recovery of B cells and immunoglobulins were evaluated after completion of treatment in patients with a CR
- Immunoglobulin treatment was used in 9% of all patients

B-cell and immunoglobulin recovery were observed in patients with a CR after completion of fixed-duration treatment

Thresholds for recovery: B cells, ≥70 cells/μL; IgG, ≥8g/L; IgM, ≥0.5g/L; IgA, ≥1g/L.
IgA, immuglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M.

ZUMA-5: Study Schema



Key ZUMA-5 Eligibility Criteria

- R/R FL (Grades 1–3a) or MZL (nodal or extranodal)[a]
- ≥2 Prior lines of therapy that must have included an anti-CD20 mAb combined with an alkylating agent[b]

Primary Endpoint

- ORR (IRRC assessed per the Lugano classification[1])

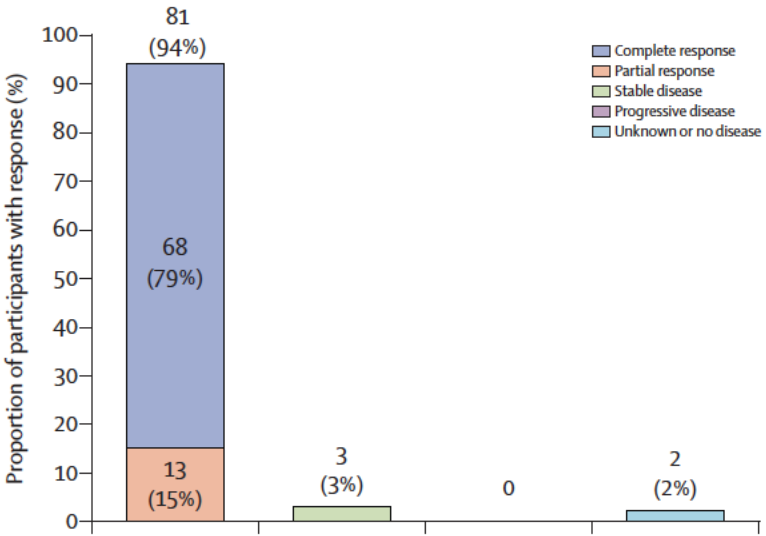
Key Secondary Endpoints

- CR rate (IRRC assessed)
- Investigator-assessed ORR[a]
- DOR, PFS, OS
- AEs
- CAR T-cell and cytokine levels

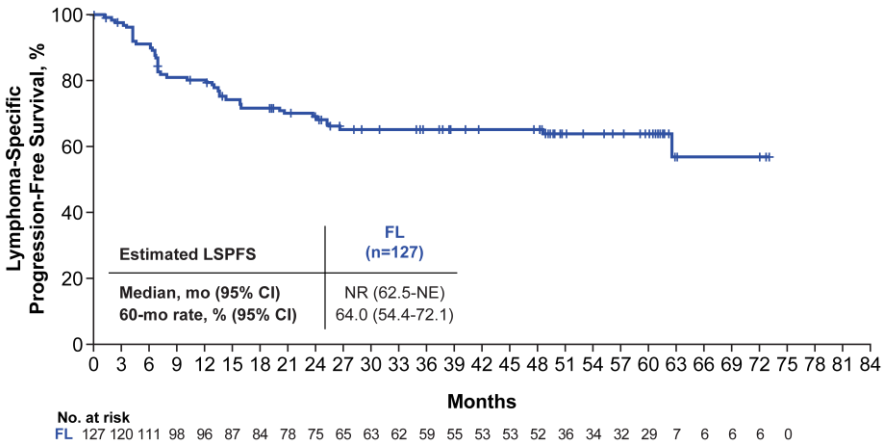
Cellular therapies: CAR-T cell

example: Axicabtagene-Ciloleucel (Zuma-5 study)

High response rates



Prolonged duration of response



Jacobson C et al, Lancet Onc 2021; Neelapu SS et al., ASH 2024

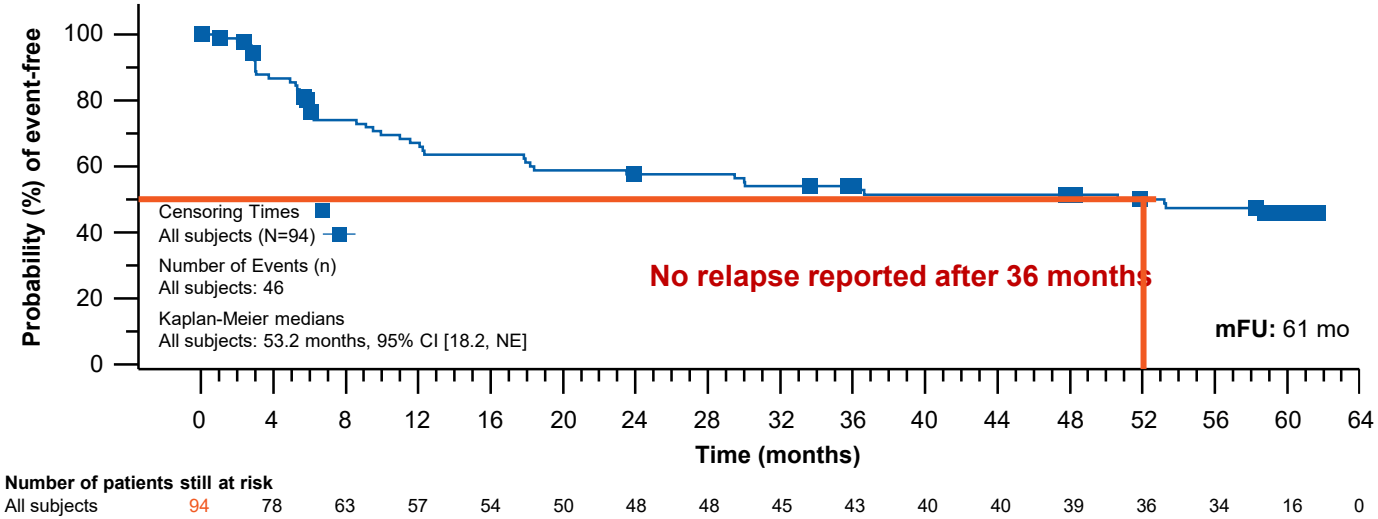
Tisa-Cel, ELARA: Consistent Response Rate Was Reported in All Patients and High-risk Subgroups

Response rate, all patients and high-risk subgroups	ORR, % (n/N)	CRR, % (n/N)
All patients (efficacy analysis set[a])	86.2 (81/94)	68.1 (64/94)
Patients with high-risk characteristics		
High FLIPI (3-5 risk factors)	80.7 (46/57)	61.4 (35/57)
POD24[b]	82.0 (50/61)	59.0 (36/61)
Bulky disease[c]	85.5 (53/62)	64.5 (40/62)
Double refractory	84.6 (55/65)	66.2 (43/65)

CRR, complete response rate; FLIPI, Follicular Lymphoma International Prognostic Index; ORR, objective response rate; POD24, progression of disease within 2 years of frontline systemic therapy.
[a]Efficacy analysis set includes all patients who have received tisagenlecleucel and had measurable disease at baseline per IRC. [b]POD24 from first anti-CD20 mAb-containing therapy or rituximab monotherapy.
[c]Bulky disease defined as 1 lesion >7 cm or at least 3 lesions >3 cm.

Schuster SJ. et al, ASH2025

ELARA:Median PFS Was 53.2 Months



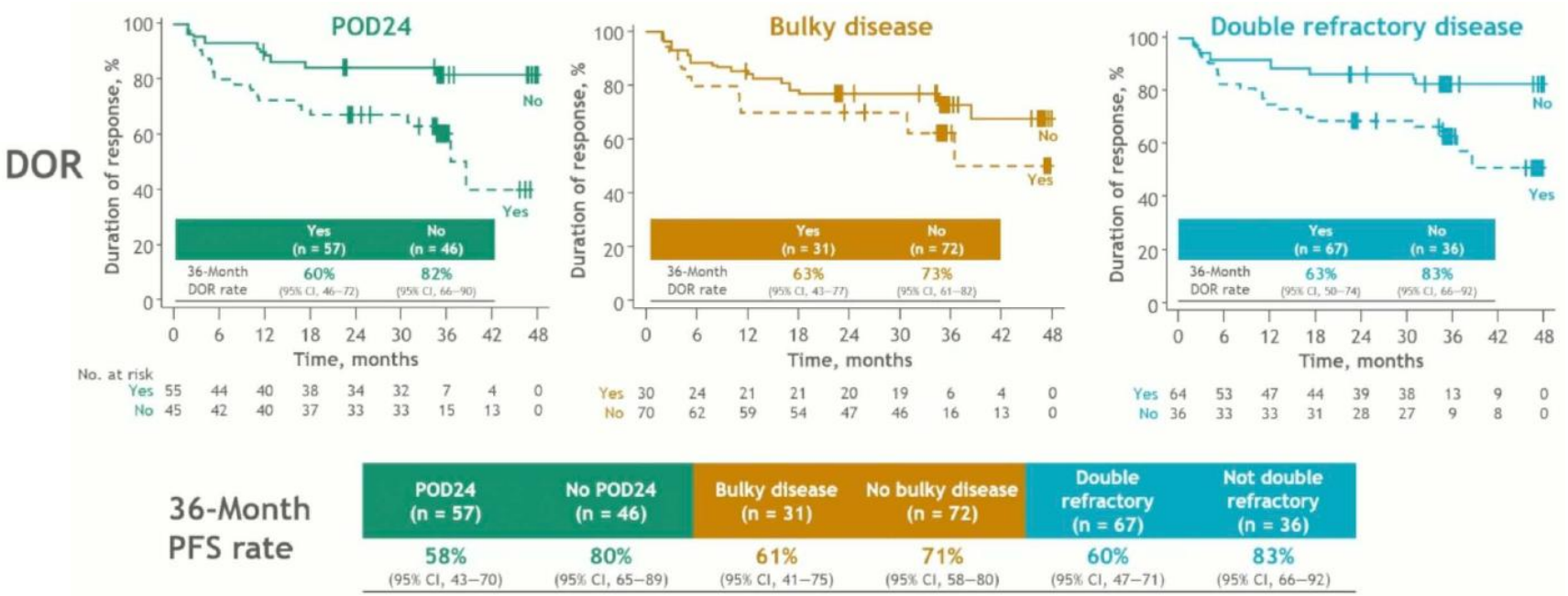
- **The 60-month PFS rate was 46% in all patients, and 59.8% in patients who experienced CR[1]**

CI, confidence interval; CR, complete response; mFU, median follow-up; mo, month; NE, not estimable; PFS, progression-free survival.

Reference: 1. Thieblemont C et al. Blood. 2024;144(suppl 1):3034

Schuster SJ. et al, ASH2025

3-Year Results From the TRANSCEND FL Study of Lisocabtagene Maraleucel in Patients With 3L+ FL: DOR and PFS Across Subgroups



36-Month PFS rate

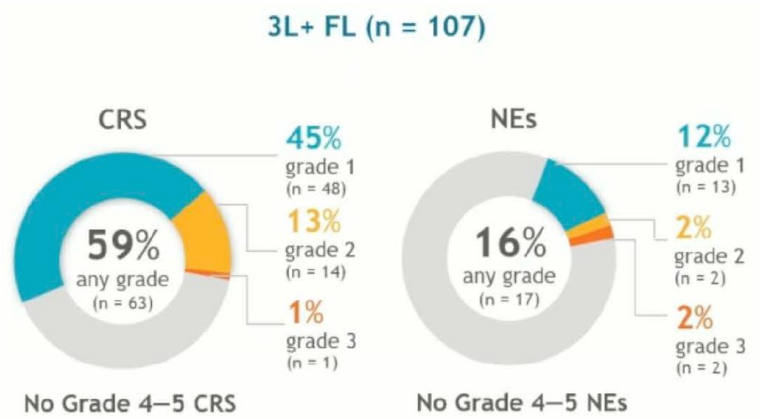
POD24 (n = 57)	No POD24 (n = 46)	Bulky disease (n = 31)	No bulky disease (n = 72)	Double refractory (n = 67)	Not double refractory (n = 36)
58% (95% CI, 43–70)	80% (95% CI, 65–89)	61% (95% CI, 41–75)	71% (95% CI, 58–80)	60% (95% CI, 47–71)	83% (95% CI, 66–92)

- Responses were durable with high PFS rates among patients with high-risk disease
- Of the evaluated subgroups, median DOR was only reached among those with POD24

POD24, progressive disease ≤24 mo from initial immunochemotherapy.

Ahmed S, et al. ASH 2025. Abstract 467.

3-Year Results From the TRANSCEND FL Study of Lisocabtagene Maraleucel in Patients With 3L+ FL: Safety and Summary



	3L+ FL (n=107)
Grade ≥3 infection, n (%)	**13 (12)**
TE period	7 (7)
Post-TE period	8 (7)
Second primary malignancy, n (%)	**11 (10)**
Non-hematologic	7 (7)
Hematologic	4 (4)
Secondary T-cell malignancy, n (%)	0 (0)
Grade ≥3 cytopenia at Day 90 visit, n (%)	**23 (21)**
Recovered to Grade ≤2 by Day 365, n/N (%)	18/19 (95)

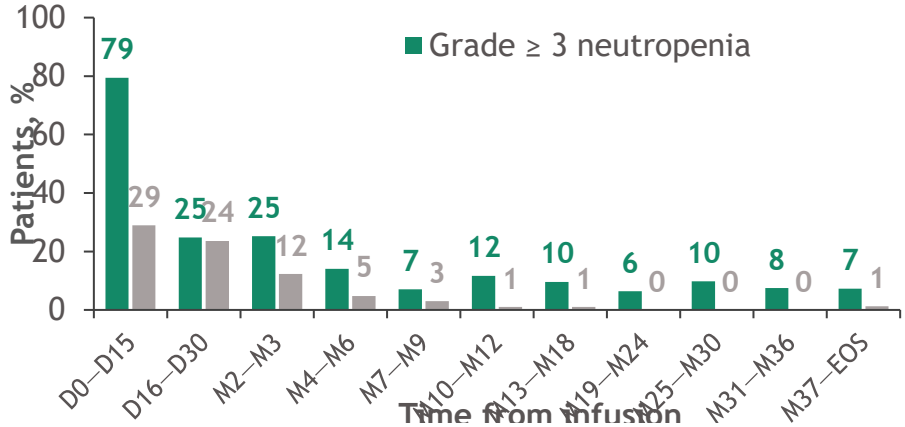
- No new safety signals observed with longer follow-up
- Most cases of CRS and NEs were Grades 1-2
- Incidence of Grade ≥3 neutropenia and use of growth factors was consistently low after Month 4
- >50% of patients had persistent B-cell aplasia or hypogammaglobulinemia at 1-y after infusion; despite this, incidence of infections was consistently low in long-term follow-up

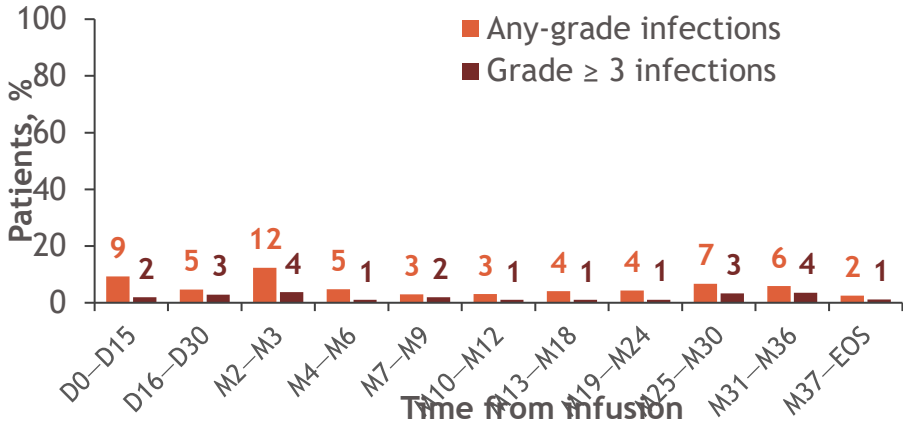
Authors' Conclusions

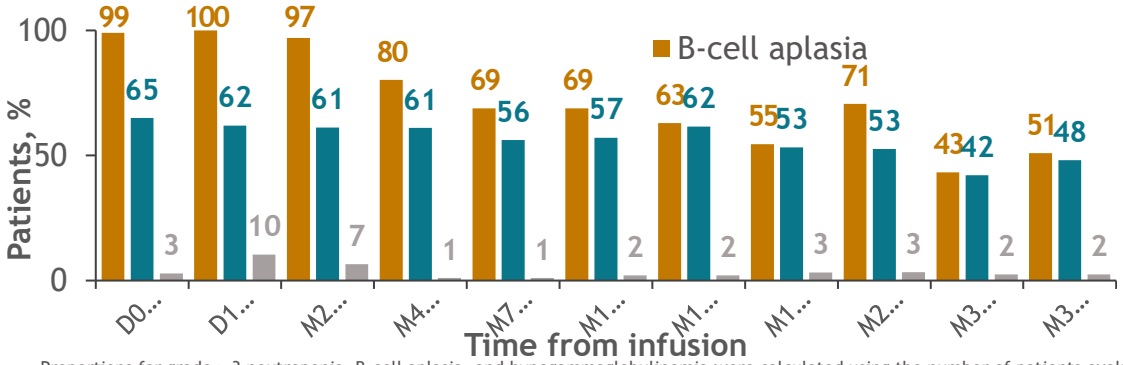
- Liso-cel showed high rates of deep (CR rate, 94%) and durable responses (36-mo DOR, 70%) with sustained survival (36-mo OS, 86%) in 3L+ R/R FL
- Consistently high efficacy was seen across subgroups, even among patients with high-risk characteristics (POD24, bulky disease, double-refractory disease)
- Longitudinal analyses demonstrated favorable long-term safety

POD24, progressive disease ≤24 mo from initial immunochemotherapy; TE, treatment emergent.
Ahmed S, et al. ASH 2025. Abstract 467.

Liso-cel showed favorable long-term safety (1/2)







- Incidences of grade ≥ 3 neutropenia and use of growth factors remained consistently low from Month 4 onward
- Incidences of infections were consistently low across all time periods despite persistent B-cell aplasia or hypogammaglobulinemia in > 50% of patients at 1 year after infusion

Proportions for grade ≥ 3 neutropenia, B-cell aplasia, and hypogammaglobulinemia were calculated using the number of patients evaluated for each laboratory parameter in each time period as the denominator. From M25—M36, > 50% of patients on study had missing values for laboratory parameters. Proportions for infections and growth factor use were calculated using the number of patients on study in each time period: D0—D15, n = 107; D16—D30, n = 106; M2—M3, n = 106; M4—M6, n = 105; M7—M9, n = 100; M10—M12, n = 97; M13—M18, n = 97; M19—M24, n = 94; M25—M30, n = 90; M31—M36, n = 85; M37—EOS, n = 81. Monthly ranges start on the first day of the first month and end on the last day of the last month. Each patient is counted once in each time period but is counted again if having an event in another time period. Results are consistent when patients who started subsequent antilymphoma therapy were excluded at the initiation of subsequent therapy. D, Day; M, Month; IVIG, intravenous immunoglobulin G.

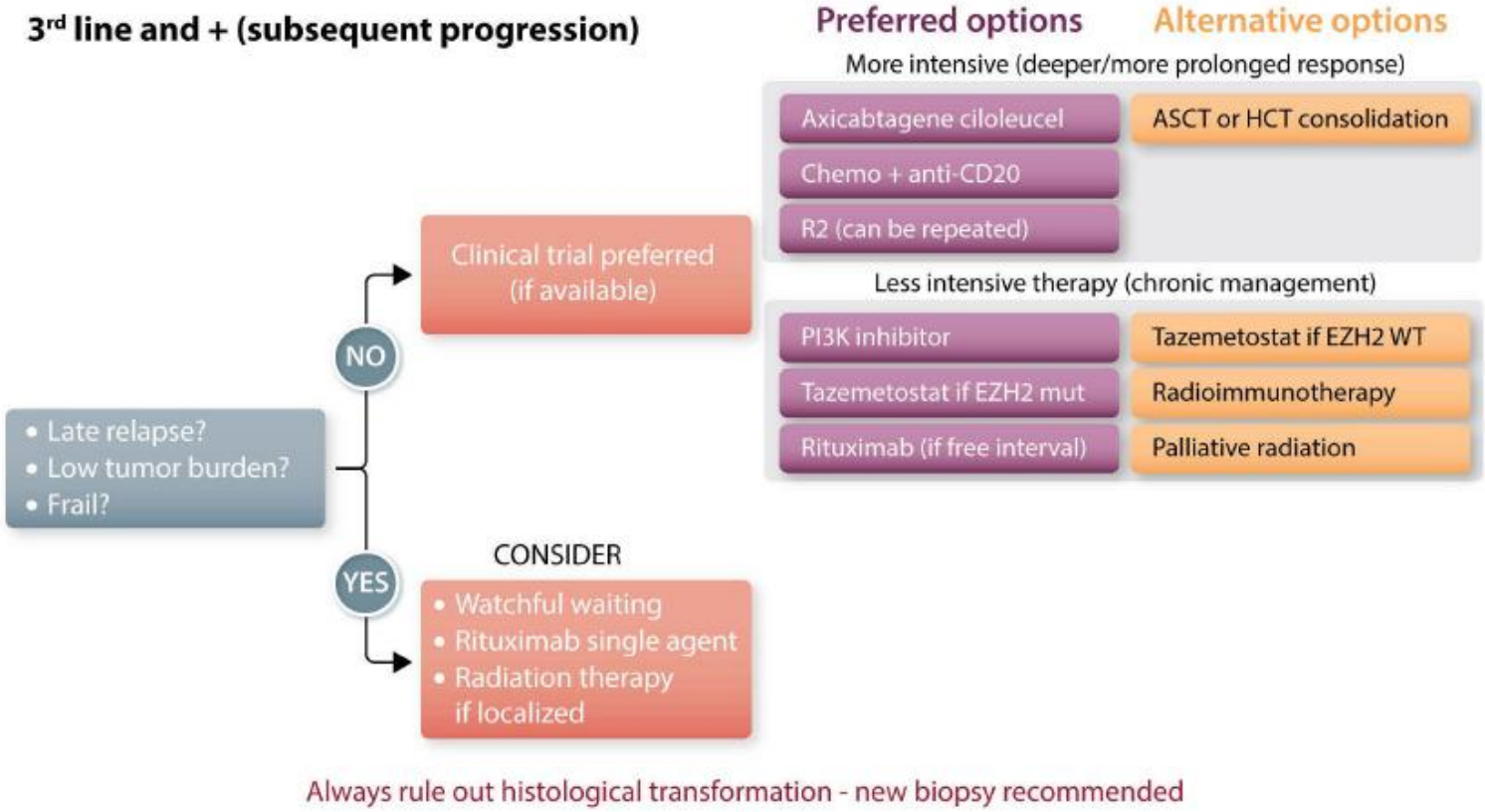
Ahmed S, et al. ASH 2025 [Abstract #467]

CAR T-cell: comparison of Phase 2 R/R FL Data

	ZUMA-5 Jacobsen, et al Lancet 2022	ELARA Fowler N, et al, Nat Med 2022	TRANSCEND FL Morschhauser F, et al. ICML 2023
Product (costim)	Axi-cel (CD28)	Tisa-cel (4-1BB)	Liso-cel (4-1BB)
N	148 (total), 124 (FL)	97	237 (FL)
POD24	55%	63%	55%
Refractory	68%	78%	67%
Bridging therapy	4%	45%	39%
Median follow up	17.5 months	16.6 months	16.6 months
FL ORR	94%	86%	97%
FL CRR	79%	68%	94%
Any Grade CRS/NE	78% / 56%	48.5% / 37%	58% / 15%
Grade >=3 CRS/NE	6% / 15%	1% / 3%	1% / 2%

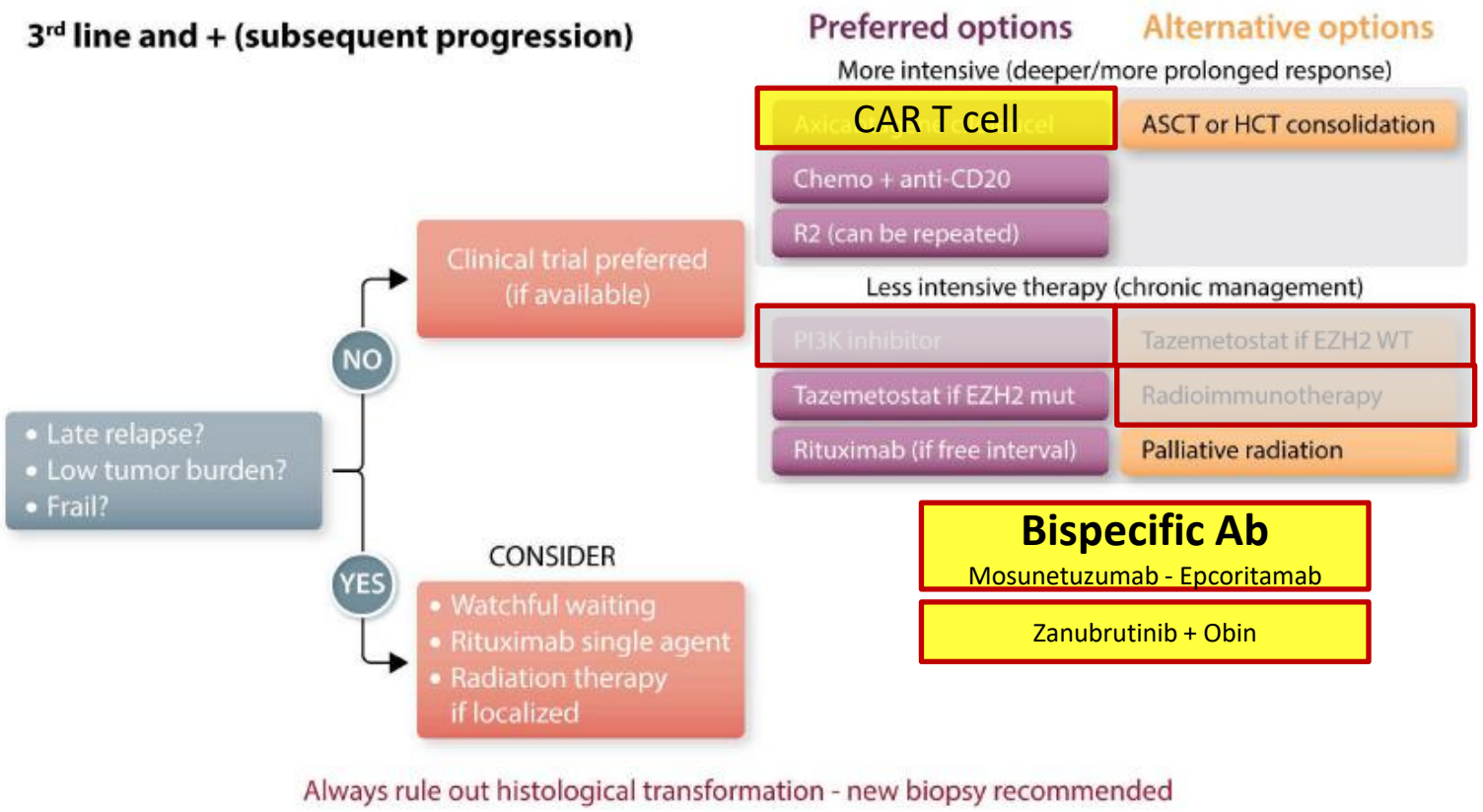
Alec Boardman

Options at later lines (3+)



Qualls D & Salles G, Haematologica 2022

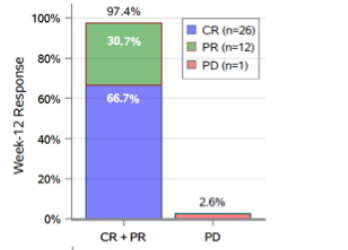
Options at later lines (3+)

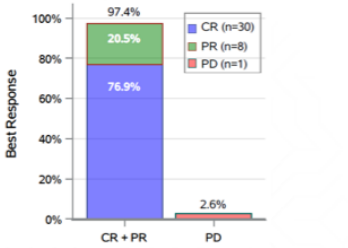


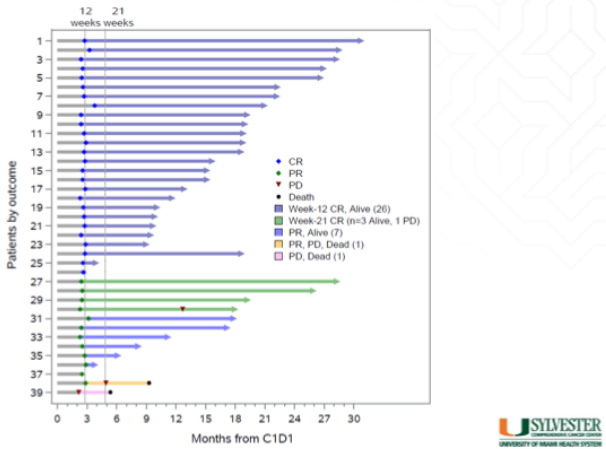
Qualls D & Salles G, Haematologica 2022

Stay tuned…

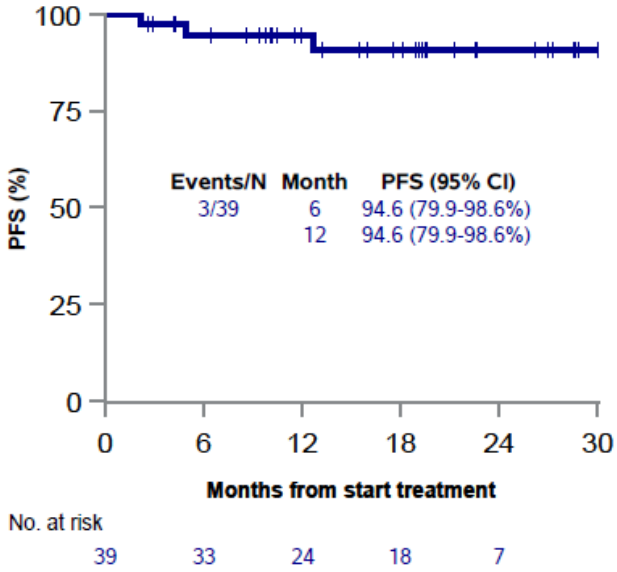
Loncastuximab-Rituximab in R/R FL - Efficacy







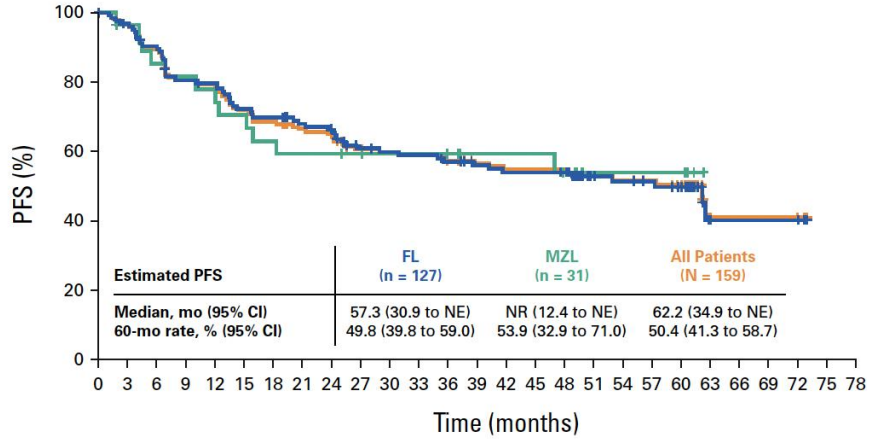
The null hypothesis was rejected (one-sided p<0.0001)



Aldreruccio JP et al., Lancet Haem 2025

ZUMA-5: 5-year follow up indicates possible cure in FL

PFS

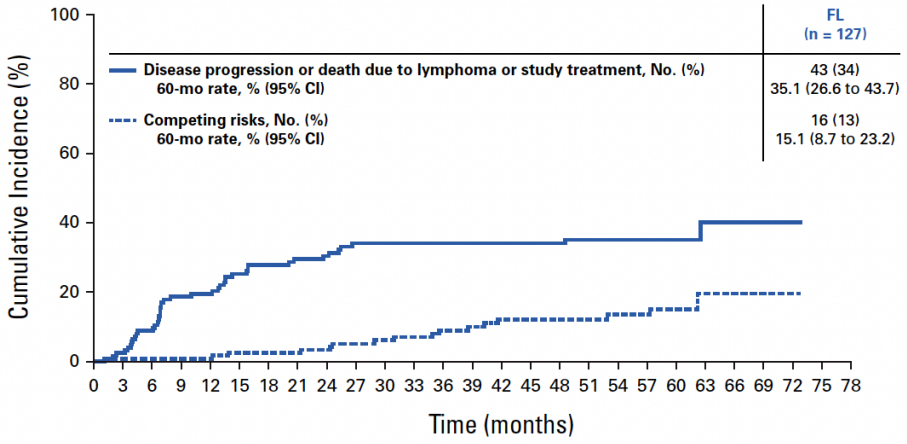


Estimated PFS	FL (n = 127)	MZL (n = 31)	All Patients (N = 159)
Median, mo (95% CI)	57.3 (30.9 to NE)	NR (12.4 to NE)	62.2 (34.9 to NE)
60-mo rate, % (95% CI)	49.8 (39.8 to 59.0)	53.9 (32.9 to 71.0)	50.4 (41.3 to 58.7)

Number at risk:

FL	127	120	111	98	96	87	84	78	75	65	63	62	59	55	53	53	52	36	34	32	29	7	6	6	6	0
MZL	31	26	23	22	21	19	17	16	16	15	14	14	13	11	11	11	9	4	4	4	4	0				
All patients	159	146	134	120	117	106	101	94	91	80	77	76	72	66	64	64	61	40	38	36	33	7	6	6	6	0

Cumulative Incidence of Relapse

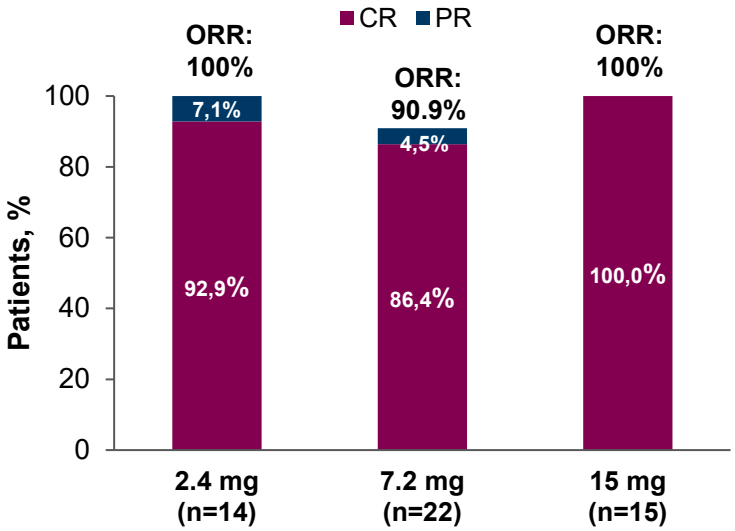


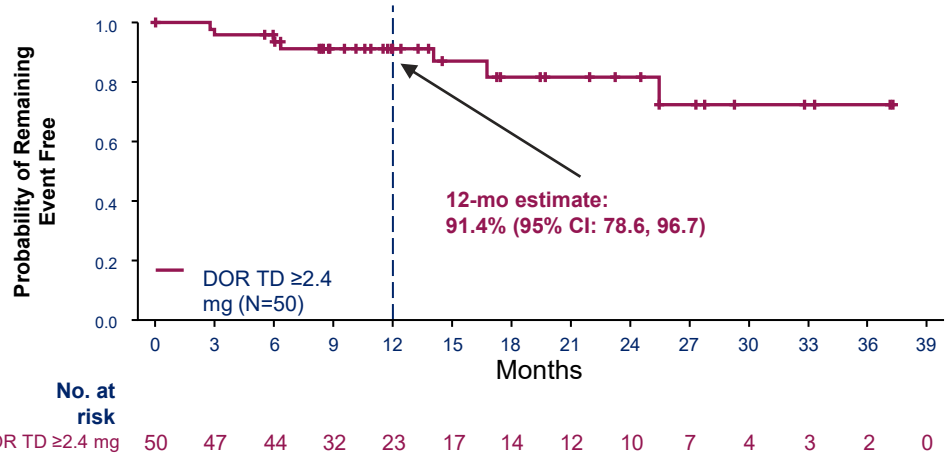
Number at risk:

FL	127	120	111	98	96	87	84	78	75	65	63	62	59	55	53	53	52	36	34	32	29	7	6	6	6	0

Neelapu et al. JCO 2025

Surovatamig, CD3 × CD19 BsAb Phase 1 Study in B-NHL





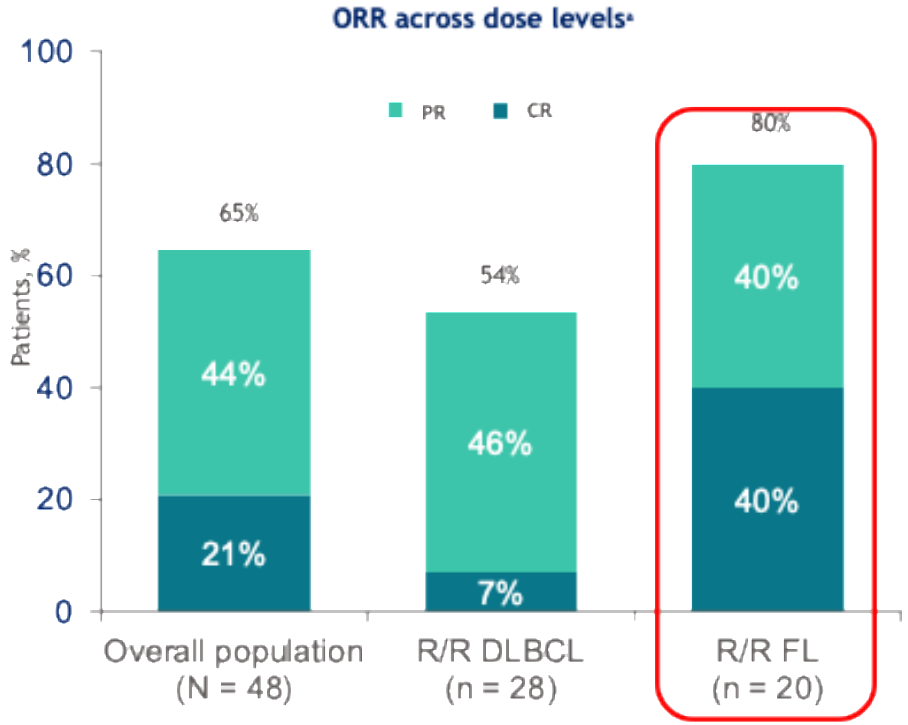
- ORR/CR rate for patients who received ≥2.4 mg was 96%/92%
- In the ITT population, ORR/CR rates were 100%/93%, 87%/83% and 100%/100% in the 2.4-mg, 7.2-mg and 15-mg cohorts, respectively[a]

[a]ITT population includes 1 additional patient who discontinued prior to response assessment due to AE at 7.2 mg TD

- All 8 patients with prior CD20 TCE therapy and/or CD19 CAR T who achieved CR with surovatamig remain in CR
- All 11 patients who completed surovatamig treatment remain in CR off treatment

Hou J, et al. Blood. 2025;146:1005.

BMS-986458, a bifunctional, cereblon-dependent ligand-directed BCL6 degrader in patients with R/R NHL: Phase 1 update



- Median follow-up 4.29 months
- **Median n. of lines of therapy: 5 (2-12)**
  - **Prior CART = 62%**
  - **Prior BsAb/TrAb = 58%**
  - **Prior CART + BsAb/TrAb = 37%**
- Among responders, the median (range):
  - Time to first response: 1.8 months (1.0–2.4)
  - Duration of response: 5.8 months (0–11.7)
  - Duration of CR: NR (0–11.7)
- Responses were observed across subgroups of interest, including Prior CAR-T cell therapy, HGBCL, tDLBCL, GCB/non-GCB, and BCL6 expression

Cutoff date: November 6, 2025. [a]Efficacy-evaluable patients.
BCL6, B-cell lymphoma 6; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; FL, follicular lymphoma; GCB, germinal center B-cell-like; HGBCL, high-grade B-cell lymphoma; NR, not reached; ORR, objective response rate; PR, partial response; R/R, relapsed/refractory; tDLBCL, transformed DLBCL.

Morschhauser F, et al. ASH 2025 Abstract 480.

Is cure of patients with FL achievable?

R-CHOP: 15-year update

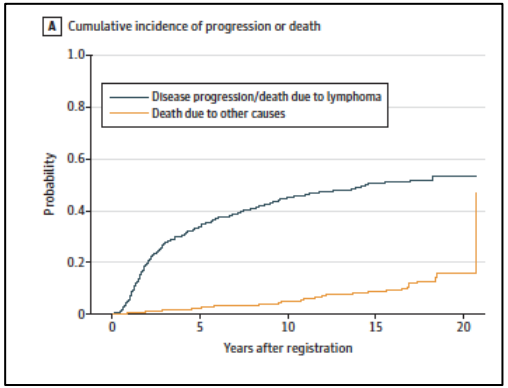
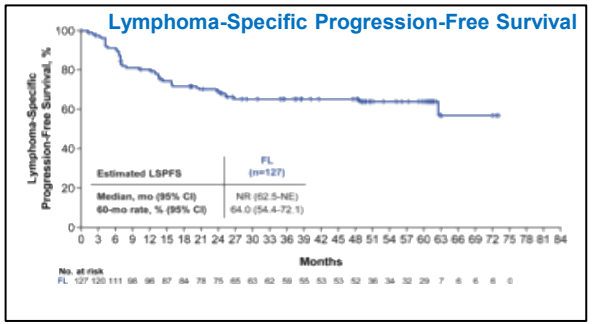


Table 2. Cure Rate Estimates

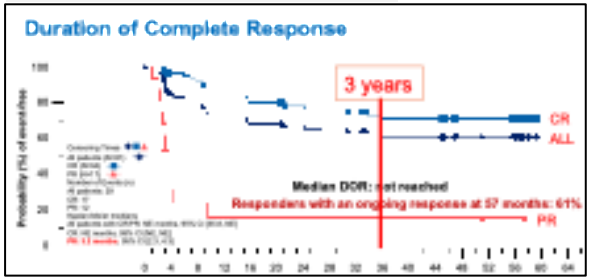
Characteristic	Cure estimate, % (95% CI)
Overall	42 (33-52)
FLIPI score	
Low (0-1)	47 (30-65)
Intermediate (2)	46 (33-60)
High (3-5)	30 (17-48)
β2M	
Low	55 (44-66)
High	31 (20-46)

Abbreviations: β2M, β 2 microglobulin; FLIPI, Follicular Lymphoma International Prognostic Index.

Axi-cel: 5-year update



Tisa-cel: 5-year update



- How do we define cure?
  - Lack of detectable disease (how to detect?)
  - "functional cure"
- Long term responses exist after
  - Immunochemotherapy without or with maintenance
  - Auto- and Allo-SCT
  - CAR T cell therapy (?)
  - BsAb combinations??

Neelapu S et al, ASH 2024 ; Shadman M et al, JAMA Onc, 2026

Thank you for your attention

Memorial Sloan Kettering Cancer Center™

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