4th MEETING ON
INNOVATIVE IMMUNOTHERAPIES
FOR LYMPHOID MALIGNANCIES

Società Italiana di Ematologia

Presidents
Paolo Corradini
Marco Ruella
Pier Luigi Zinzani

Clinical results of bispecific antibodies in indolent NHL: what's next

Lorenzo Falchi, MD
Lymphoma Service Memorial Sloan-Kettering Cancer Center
New York

MILANO, STARHOTELS ROSA GRAND
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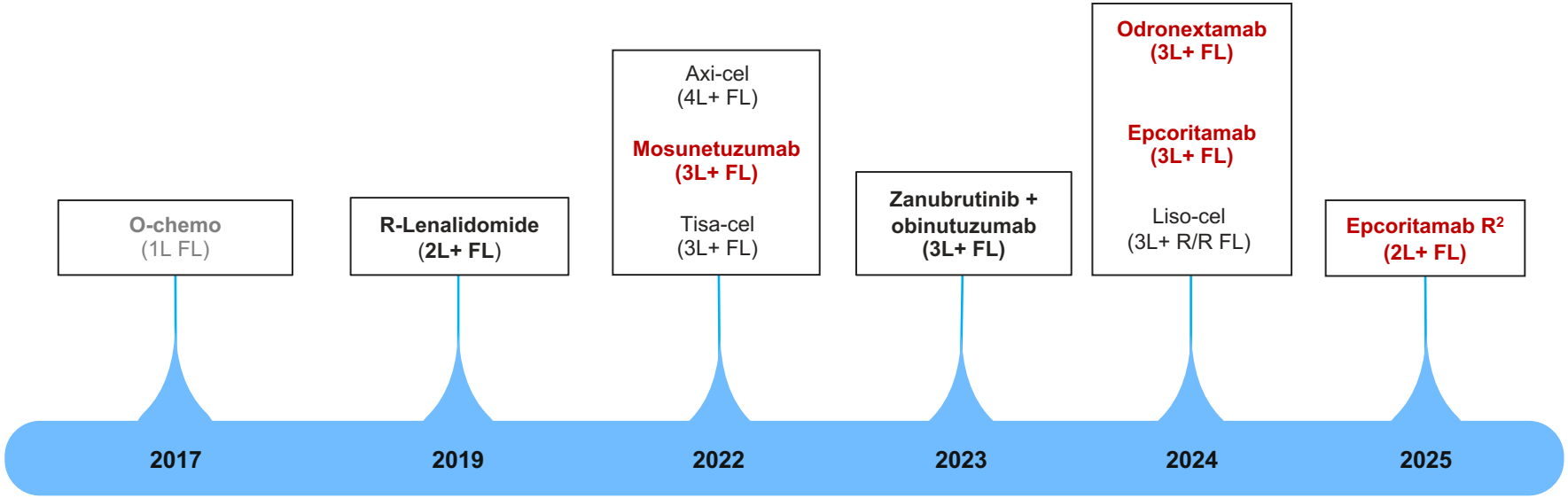
Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Travel support
Roche	x		x				x
Genentech	x		x			x	
Genmab	x		x			x	x
AbbVie	x		x			x	x
Innate Pharma	x						
BeOne medicines	x						
Astrazeneca	x		x				
Kite			x				x
Chugai			x			x	x
ADC therpeutics						x	
Johnson & Johnson						x	
Merck			x				
Sanofi	x		x				
Bristol Myers Squibb						x	
Regeneron						x	

Agenda:

- R/R iNHL: What's new/next?
  - Single-agent BsAb:
  - BsAb combinations
- 1L iNHL: What's new/next?
  - Single-agent BsAb
  - BsAb combinations

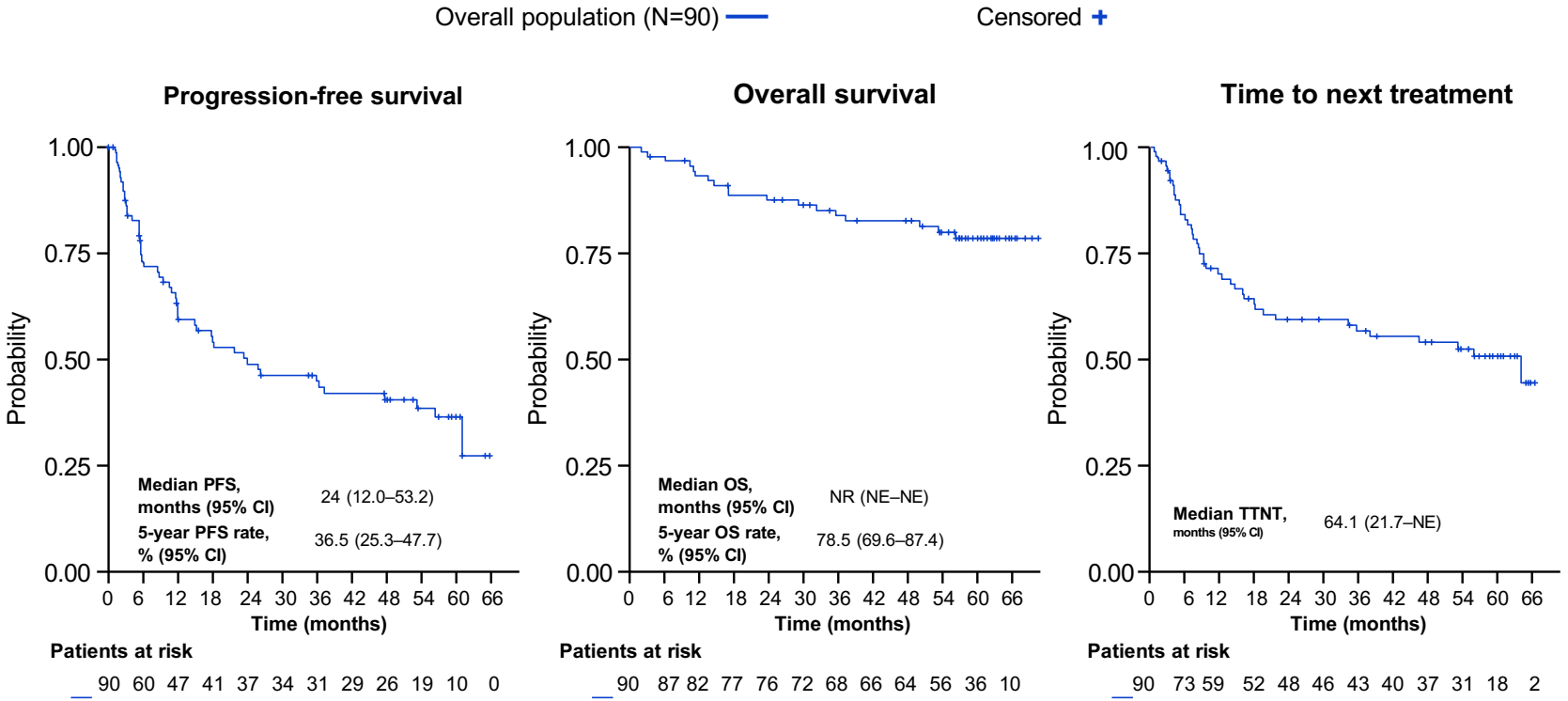
Evolution of treatments for R/R FL: A “chemo-free revolution”



Red font denotes bispecific antiboadies

L, line of therapy; FL, follicular lymphoma; R, rituximab; O, Obinutuzumab; axi-cel, axicabtagene ciloleucel; tisa-cel, tisagenlecleucel; liso-cel, lisocabtagene maraleucel

Long-term PFS and favorable OS are achievable with BsAb monotherapy: Mosunetuzumab in 3L+ FL



Budde E, et al. ASH 2025; abstract 5352

Bispecific antibody combination therapy in R/R FL

Regimen	Trial (Phase)	Patients (R/R FL cohorts)	Treatment duration and administration	Primary endpoint	Study status
Mosunetuzumab-Len	**CO41942** (Phase Ib/II)[1,2]	29[1]	**Mosunetuzumab** (IV/SC) 12 cycles **Len** (oral) 11 cycles[1,2]	Safety[1,2]	Active, not recruiting[2]
Mosunetuzumab-Len versus R-Len	**CELESTIMO** (Phase III)[3]	478[3]	**Mosunetuzumab** (IV) 12 cycles **Len** (oral) 12 cycles[3]	PFS (by IRC)[3]	Active, not recruiting[3]
Odronextamab-Len versus R-Len	**OLYMPIA-5** (Phase III)[4,5]	~352*[4]	**Odronextamab** (IV) 12 cycles **Len** (oral) 12 cycles[4,5]	Safety and PFS (by IRC)[4,5]	Recruiting[4]
Epcoritamab + R-Len	**EPCORE NHL-2** (Phase Ib/II)[6,7]	111[6]	**Epcoritamab** (SC) ≥2 years **Len** (oral) 12 cycles[6,7]	Safety and ORR[6,7]	Active, not recruiting[7]
Epcoritamab + R-Len versus R-Len	**EPCORE FL-1** (Phase III)[8]	549[8]	**Epcoritamab** (SC) 12 cycles **Len** (oral) 12 cycles[8]	ORR and PFS (by IRC)[8]	Active, not recruiting[8]

Results available

Products/indications are investigational and not approved. This slide is for educational purposes only

*Planned enrolment.

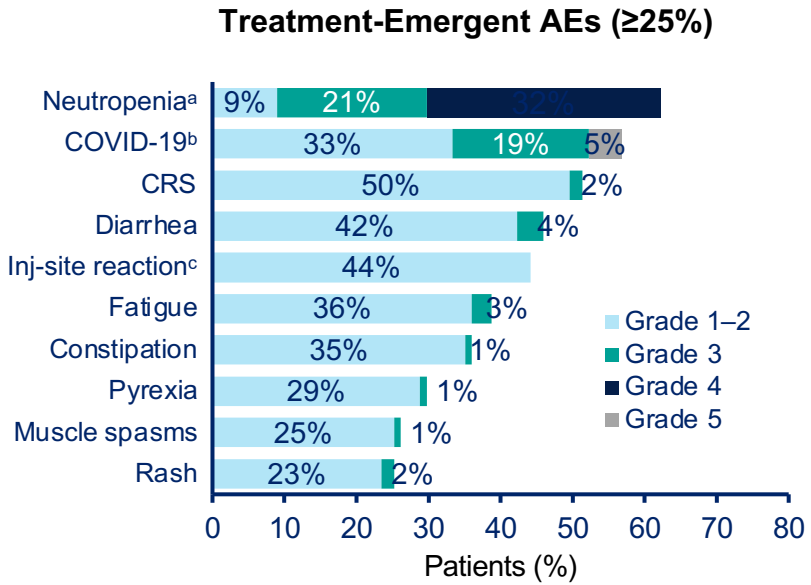
1. Morschhauser F, et al. ASH 2021; Oral presentation (abstract #129); 2. NCT04246086. Available at: https://clinicaltrials.gov/study/NCT04246086; 3. NCT04712097. Available at: https://clinicaltrials.gov/study/NCT04712097; 4. NCT06149286. Available at: https://clinicaltrials.gov/study/NCT06149286 5. Vitolo U, et al. ASCO 2023; Abstract (abstract #TPS7094); 6. Falchi L, et al. ASH 2024; Oral presentation (abstract #342); 7. NCT04663347. Available at: https://clinicaltrials.gov/study/NCT04663347; 8. NCT05409066. Available at: https://clinicaltrials.gov/study/NCT05409066.

Epcoritamab + R2 Results in 2L+ FL: Deep Responses with a Manageable Safety Profile

Best Response, n (%)[a]	N=111
Overall response	**107 (96)**
Complete response	**97 (87)**
Partial response	10 (9)
Progressive disease	2 (2)

MRD Negativity, n/n (%)	MRD Evaluable
MRD negativity at any time[b]	**66/75 (88)**
MRD negative and complete response[c]	63/68 (93)
MRD negativity in high-risk subgroups	
POD24 (1L CIT)	26/30 (87)
Primary refractory	25/28 (89)
Double refractory	23/27 (85)

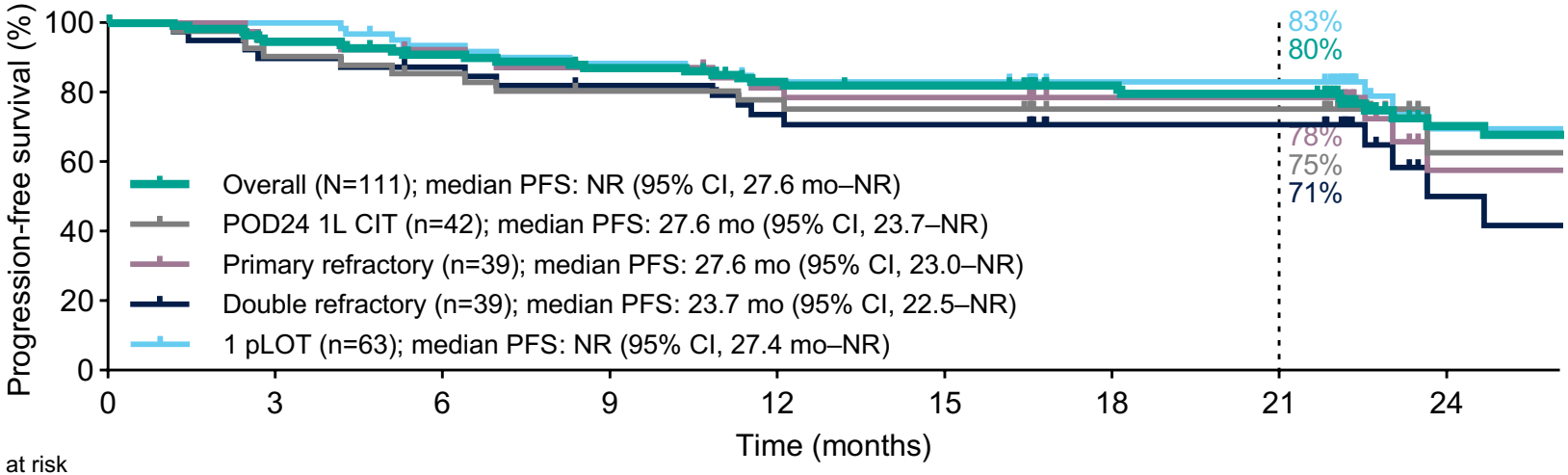
[a]Two patients were not evaluable for response. [b]MRD negative at any time point with an assay cutoff of 10^{-6} (PBMC assay; clonoSEQ). [c]One patient became MRD positive at a subsequent assessment (C5D1); patient later experienced radiographic PD.



[a]Combined term includes neutropenia and decreased neutrophil count. [b]Combined term includes COVID-19, COVID-19 pneumonia, and post-acute COVID-19 syndrome. [c]Combined term includes injection-site reaction, erythema, pain, pruritus, rash, and swelling

Falchi et al. *Blood*. 2025 Nov 27;146(22):2629-2640

Progression-Free Survival and Duration of Response



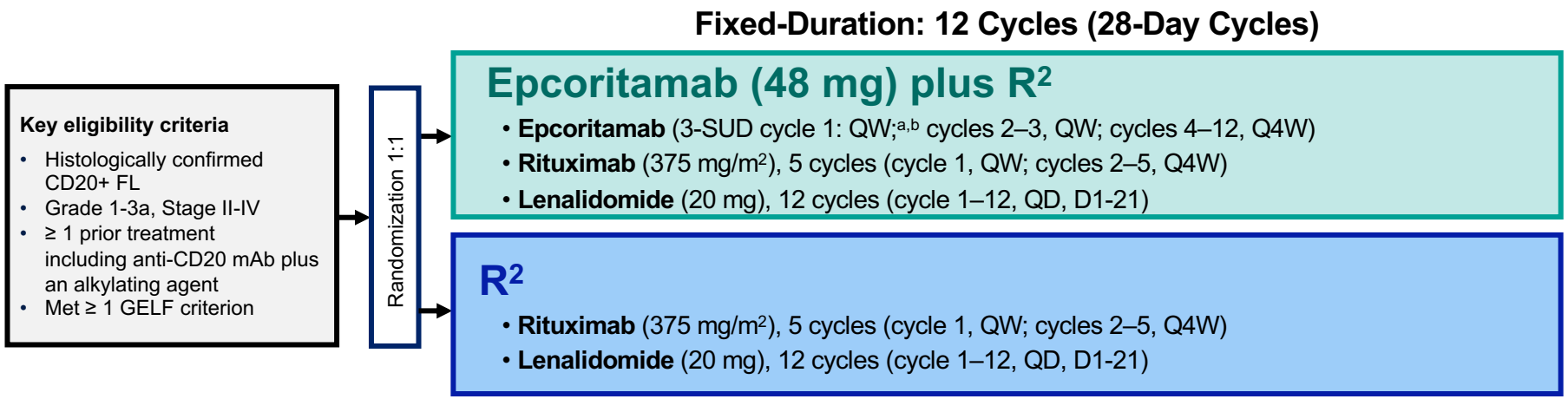
Patients at risk									
Overall	111	102	95	90	82	80	68	66	29
POD24 1L CIT	42	37	34	31	30	29	21	21	5
Primary refractory	39	37	35	32	28	27	22	22	7
Double refractory	39	35	33	30	26	25	18	18	6
1 pLOT	63	61	55	52	45	45	38	38	13

PFS in MRD- vs. MRD+ patients: 86% vs 44% at 21 months*

Data cutoff: May 15, 2024. PFS is among the full analysis population. Median follow-up for PFS: 22.3 months.

Falchi et al. *Blood* (2024) 144 (Supplement 1): 342 and Blood, online, ahead of print

EPCORE FL-1: Phase 3, Global, Randomized, Open-Label Study



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 R2 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

Baseline Demographics and Disease Characteristics Were Generally Balanced

Characteristic	Epcoritamab+R² (N = 243)	R² (N = 245)	Overall (N = 488)
Median age, y (range)	60 (30, 84)	63 (24, 89)	61 (24, 89)
≥ 65, n (%)	88 (36)	106 (43)	194 (40)
Male, n (%)	139 (57)	138 (56)	277 (57)
Race, n (%)			
Asian	63 (26)	54 (22)	117 (24)
Black	6 (2)	2 (< 1)	8 (2)
White	168 (69)	184 (75)	352 (72)
Ethnicity, n (%)			
Hispanic	29 (12)	28 (11)	57 (12)
ECOG, n (%)			
0	166 (68)	170 (69)	336 (69)
1-2	77 (32)	75 (31)	152 (31)
Ann Arbor stage, n (%)			
II	37 (15)	44 (18)	81 (17)
III-IV	206 (85)	201 (82)	407 (83)
FLIPI score, n (%)			
0–1	63 (26)	56 (23)	119 (24)
2	79 (33)	76 (31)	155 (32)
3–5	100 (41)	113 (46)	213 (44)
Bulky disease (≥ 7 cm), n (%)	47 (19)	61 (25)	108 (22)

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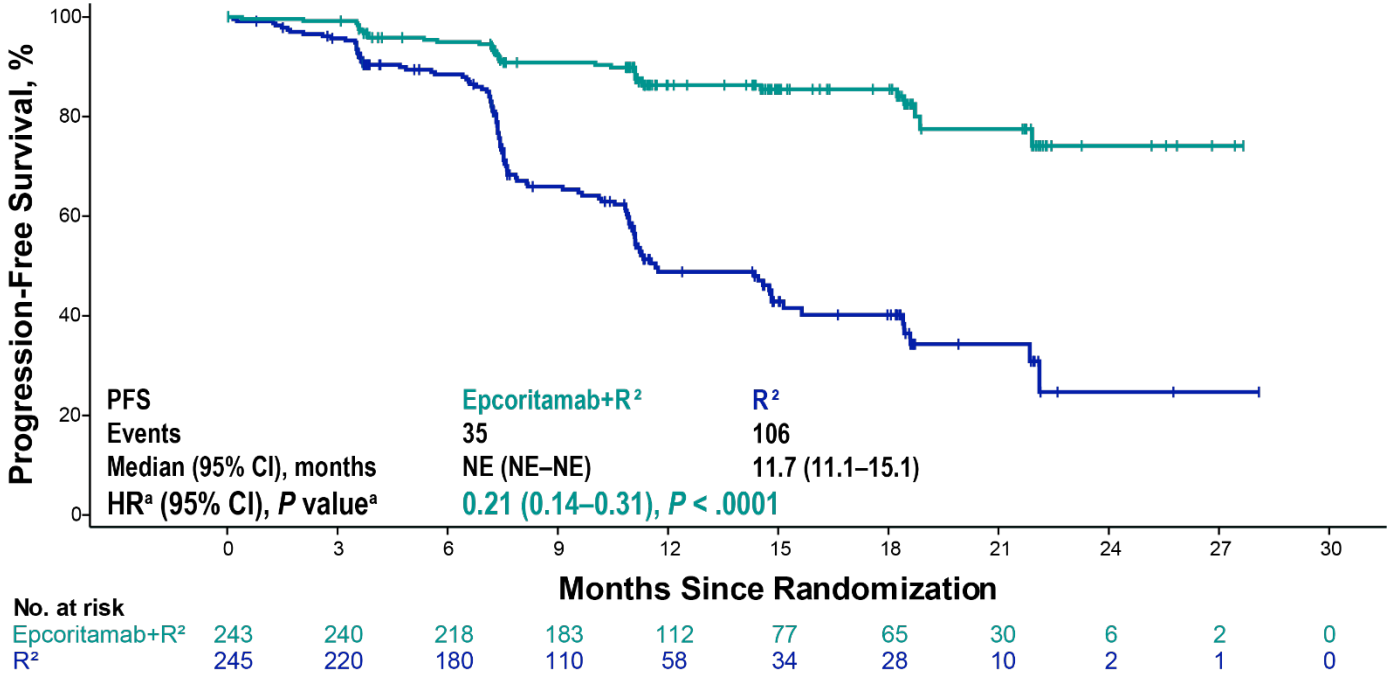
Treatment History Was Generally Balanced Across Epcoritamab+R^2 and R^2

	Epcoritamab+R^2 (N = 243)	R^2 (N = 245)	Overall (N = 488)
Median time from initial diagnosis to randomization, years (range)	4.5 (0.2, 30.3)	5.3 (0.1, 43.0)	5.0 (0.1, 43.0)
Number of prior lines of therapy, median (range)	1 (1, 7)	1 (1, 6)	1 (1, 7)
1, n (%)	145 (60)	141 (58)	286 (59)
2, n (%)	58 (24)	61 (25)	119 (24)
≥ 3, n (%)	40 (16)	43 (18)	83 (17)
Prior anti-CD20 antibody, n (%)	243 (100)	245 (100)	488 (100)
Prior anti-CD20 antibody containing chemotherapy, n (%)	239 (98)	240 (98)	479 (98)
Prior bendamustine in last line, n (%)	53 (22)	47 (19)	100 (20)
Prior R^2, n (%)	8 (3)	9 (4)	17 (3)
POD24,[a] n (%)	106 (44)	93 (38)	199 (41)
Refractory to 1L therapy, n (%)	86 (35)	81 (33)	167 (34)
Refractory to anti-CD20 antibody, n (%)	104 (43)	103 (42)	207 (42)
Refractory to last line of therapy, n (%)	84 (35)	82 (33)	166 (34)
Double refractory[b]	91 (37)	91 (37)	182 (37)

[a]POD24 is defined as progression of disease ≤ 2 years from the date of initiation of frontline therapy. [b]Double refractory is refractory to prior anti-CD20 therapy and prior alkylator therapy.

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

Epcoritamab+R² Resulted in Superior PFS per IRC With 79% Risk Reduction



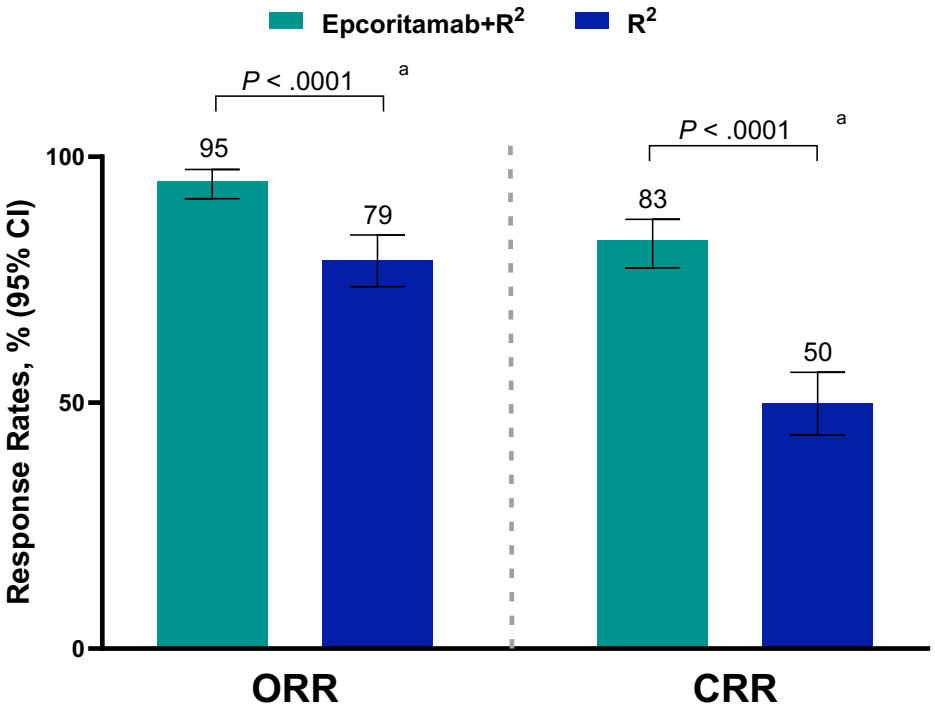
- Concordance rate was 94% for PFS between IRC and investigator assessment
- The estimated 16-month PFS was 85.5% (95% CI: 79.7, 89.7) for epcoritamab+R² and 40.2% (95% CI: 31.8, 48.4) for R²

Median follow-up for PFS: epcoritamab+R² (14.4m), R² (11.5m). The first planned interim analysis (January 10, 2025) achieved statistical significance on PFS, HR 0.21 (95% CI 0.13, 0.33) $P < 0.0001$, with a 1-sided significance level of 0.0023.

[a]Nominal *P* value is based on stratified log-rank test. Hazard ratio is estimated using stratified Cox proportional hazards model. This analysis was performed on the 78% information fraction.

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

Epcoritamab+R^2 Resulted in Higher Response Rates Versus R^2



	Epcoritamab+R^2 (N = 243)	R^2 (N = 245)
ORR, n (%)	231 (95)	194 (79)
CRR, n (%)	201 (83)	122 (50)
PR, n (%)	30 (12)	72 (29)
SD, n (%)	1 (< 1)	17 (7)
PD, n (%)	7 (3)	16 (7)
NE,[b] n (%)	4 (2)	18 (7)

The first planned interim analysis (January 10, 2025) achieved statistical significance for ORR (N = 232; 95.7% vs 81.0%; *P* < 0.0001, with a 1-sided significance level of 0.005) and CR (74.5% vs 43.3%; *P* < 0.0001, with a 1-sided significance level of 0.025).

[a]Nominal *P* value by stratified Cochran-Mantel-Haenszel method. [b]Patients with no post-baseline disease assessment were also included.

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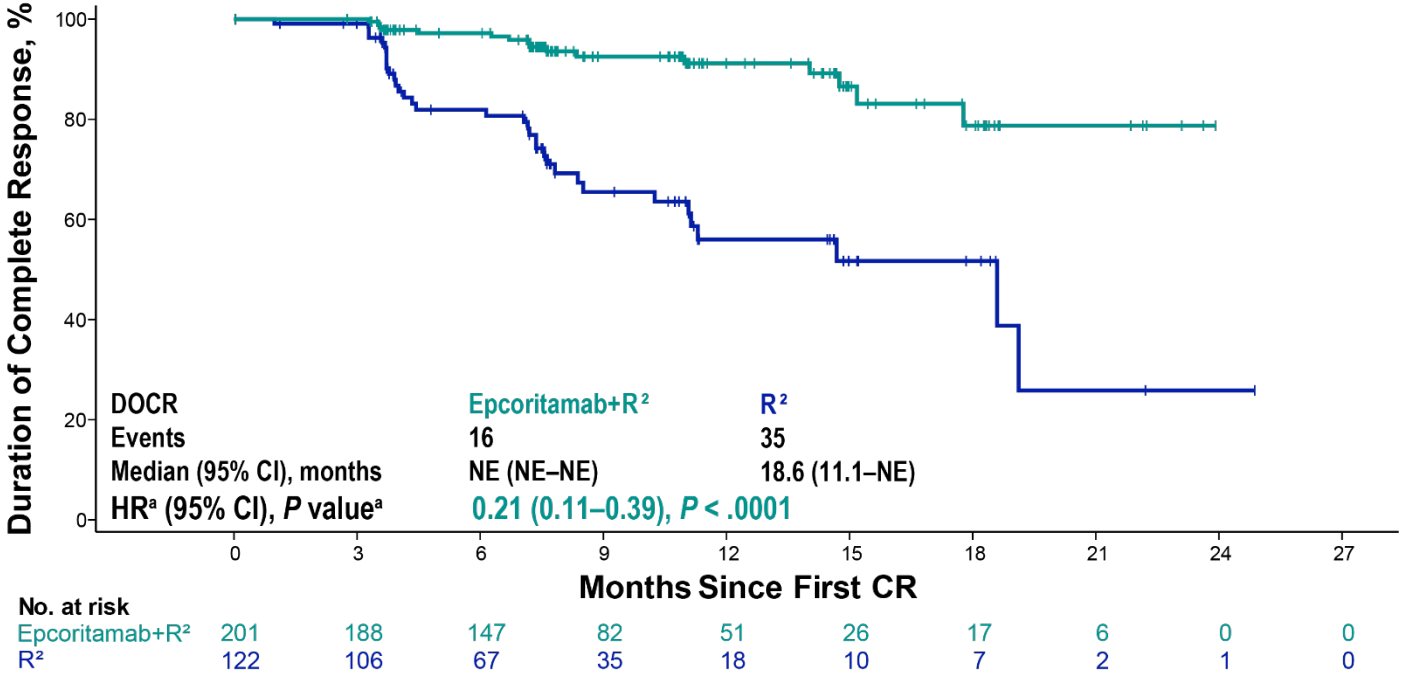
Epcoritamab+R^2 Resulted in Deep and Durable Complete Responses



- Improvement in DOCR was seen with epcoritamab+R^2

Median follow-up for DOCR: epcoritamab+R^2 (7.9m), R^2 (7.6m). DOCR results are for descriptive purposes only.
[a]Nominal *P* value is based on stratified log-rank test. Hazard ratio is estimated using stratified Cox proportional hazards model.

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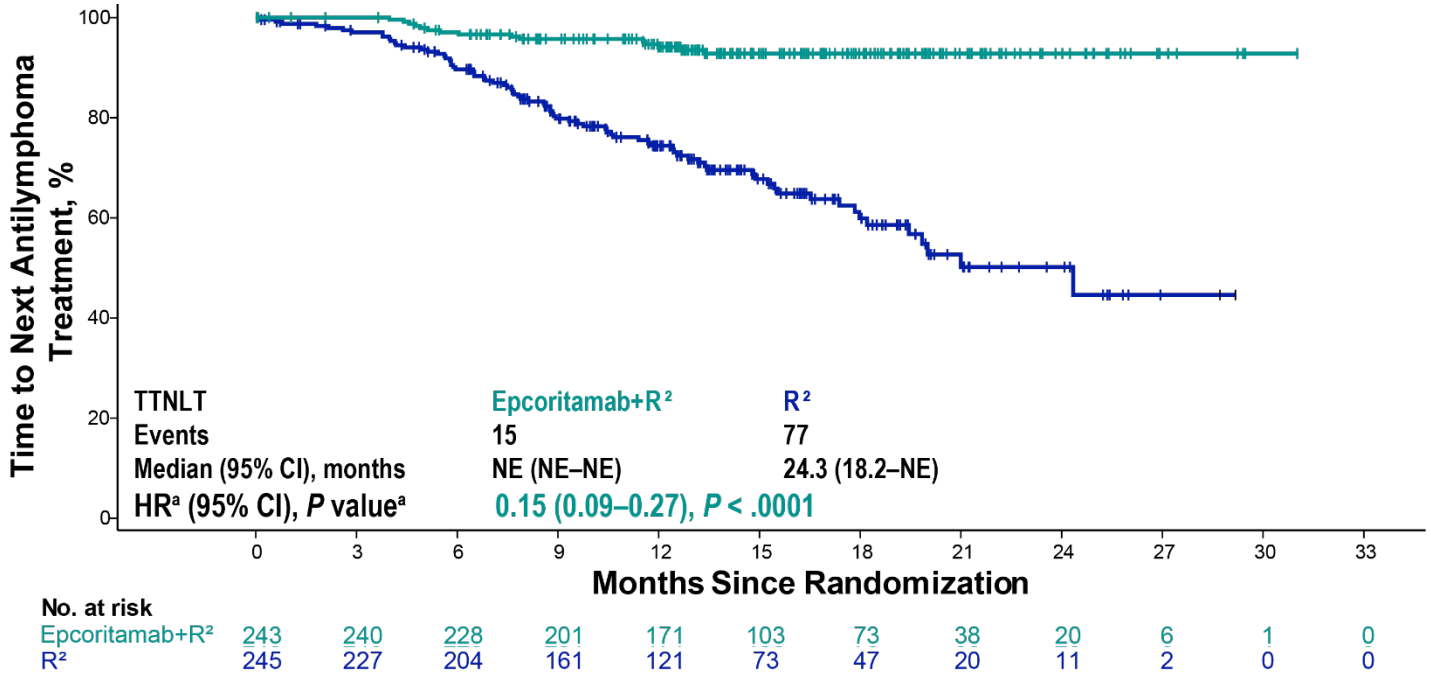
Epcoritamab+R^2 Extended Time to Next Treatment



- 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

Median follow-up for TTNLT: epcoritamab+R² (14.6m), R² (14.1m). TTNLT results are for descriptive purposes only.
[a]Nominal *P* value is based on stratified log-rank test. Hazard ratio is estimated using stratified Cox proportional hazards model.

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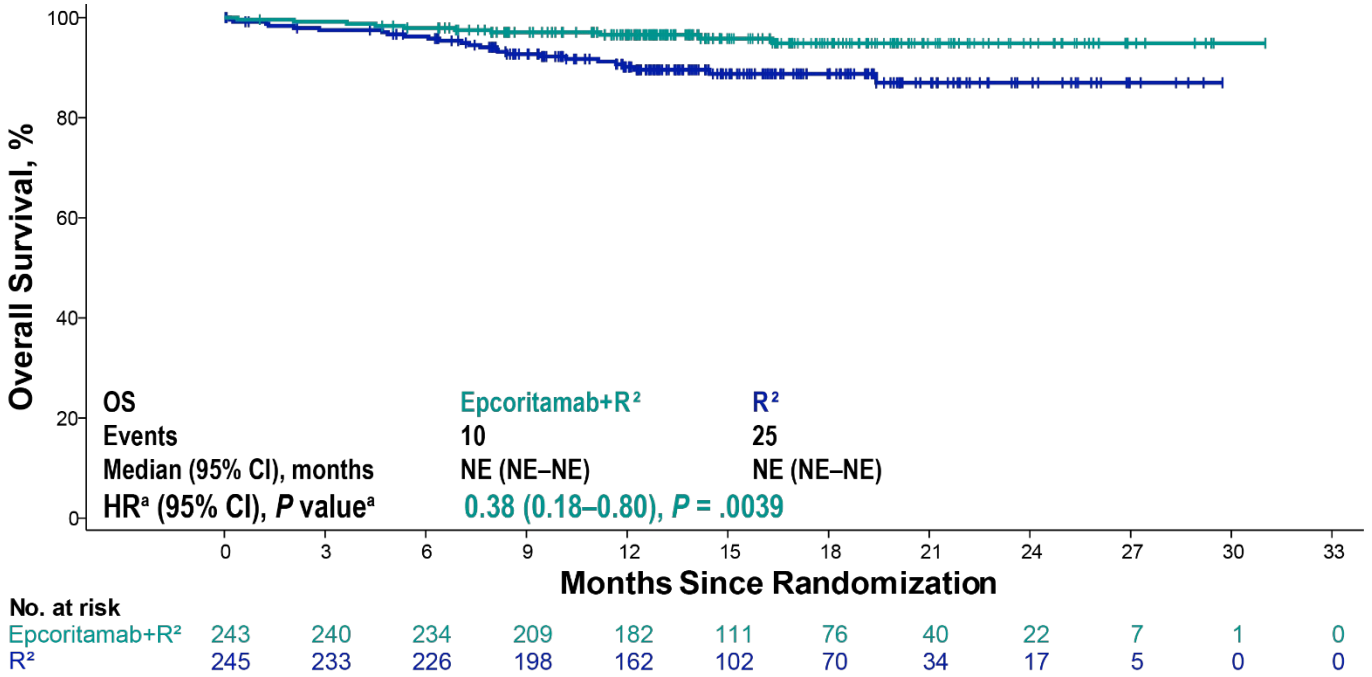
Positive Trend for Overall Survival With Epcoritamab+R²



- The 16-month estimate for OS was 95.8% with epcoritamab+R² and 88.8% with R²

Median follow-up for OS: epcoritamab+R² (14.8m), R² (14.6m). The OS data is based on the 24% (35/146 events) information fraction and has not yet reached statistical significance; additional analyses are forthcoming.
[a]*P* value is based on stratified log-rank test with 1-sided significance level of 0.000005. Hazard ratio is estimated using stratified Cox proportional hazards model.

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Manageable AEs With No New Safety Signals

Adverse Event, n (%)	Epcoritamab+R² (N = 243)		R² (N = 238)	
	Any Grade	Grade ≥ 3	Any Grade	Grade ≥ 3
Any adverse event	242 (100)	219 (90)	235 (99)	161 (68)
Serious adverse event	135 (56)	-	69 (29)	-
Adverse event leading to treatment discontinuation	46 (19)	-	29 (12)	-
Epcoritamab	21 (9)	-	-	-
Rituximab	7 (3)	-	12 (5)	-
Lenalidomide	45 (19)	-	29 (12)	-
Adverse event of clinical interest > 20%[a,b]				
Infections[c]	188 (77)	81 (33)	125 (53)	37 (16)
Neutropenia	180 (74)	167 (69)	123 (52)	100 (42)
Cytokine release syndrome	85 (35)	-	1 (< 1)	-
Anemia	68 (28)	19 (8)	41 (17)	11 (5)
Thrombocytopenia	67 (28)	23 (9)	44 (18)	15 (6)
Pyrexia	58 (24)	1 (< 1)	33 (14)	3 (1)
Rash	58 (24)	19 (8)	53 (22)	9 (4)
COVID-19	54 (22)	7 (3)	32 (13)	4 (2)

- Neutropenia was manageable and few patients discontinued any study drug (epcoritamab+R², 3%; R², 2%)
  - Incidence of febrile neutropenia: epcoritamab+R², 6%; R², 3%
- Infections were manageable and few patients discontinued any study drug (epcoritamab+R², 6%; R², 1%)
- Fatal adverse events were rare (epcoritamab+R², 2%; R², 4%)
- Despite higher rates of AEs in the epcoritamab+R² arm, most patients completed the prescribed regimen (median relative dose intensity ≥ 90% for epcoritamab+R²)

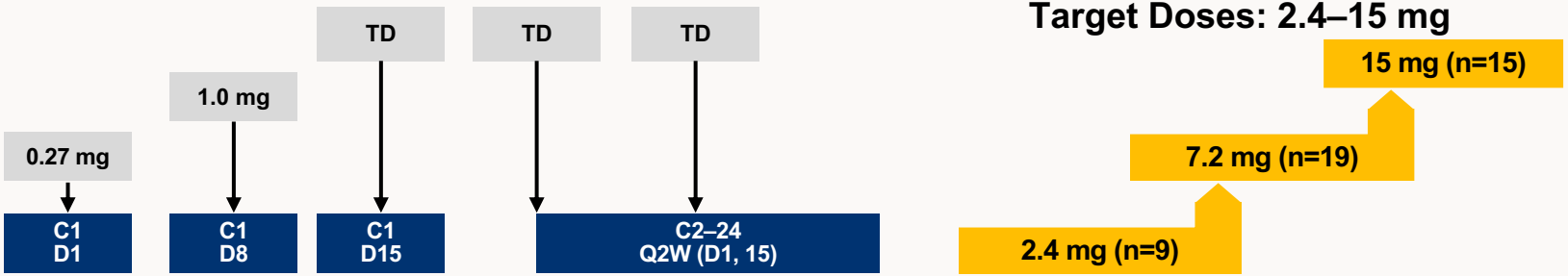
[a]Neutropenia, anemia, pyrexia, rash and COVID-19 are grouped terms comprising multiple clinically related Preferred Terms. [b]This includes the AESI of CRS. [c]Events were in the MedDRA system organ class "Infections and Infestations." No grade 5 infections were reported.

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

Surovatamig Phase 1 Study Design

Dosing Regimen

Double SUD (n=43)

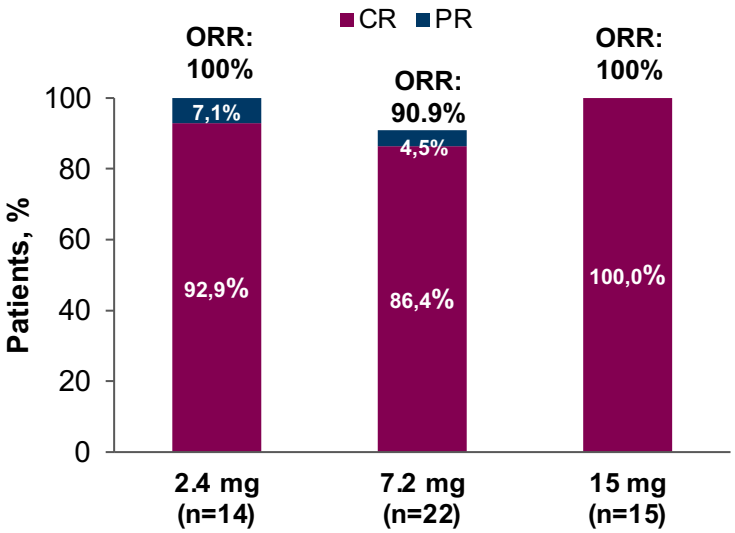


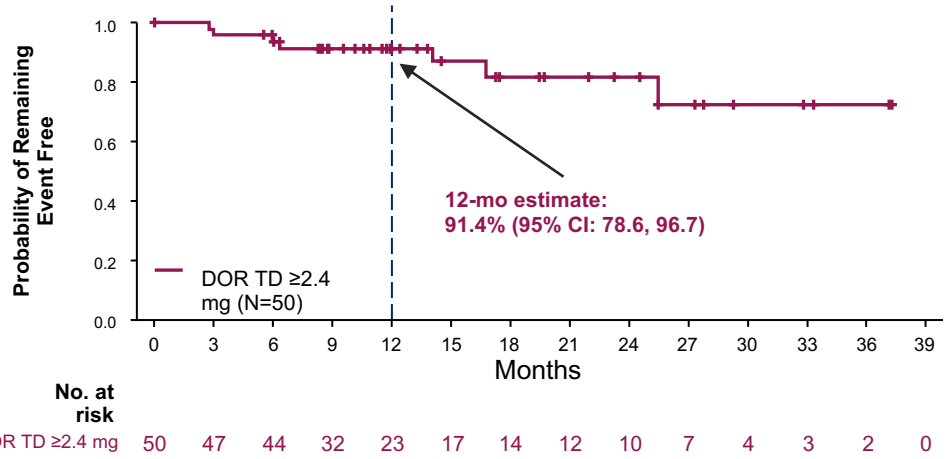
Surovatamig Treatment

- Surovatamig is administered intravenously in fixed-dose escalation, 1SUD, or 2SUD
- Treatment is delivered in 28-day cycles up to 2 years
  - Cycle 1 doses were inpatient
- Patients with CR on 2 consecutive scans may receive surovatamig every 4 weeks after C6
- Premedication with dexamethasone included two 10-mg doses prior to cycle 1 surovatamig doses

NCT04594642; data cutoff: May 19, 2025

High Response Rates Observed at All Target Doses



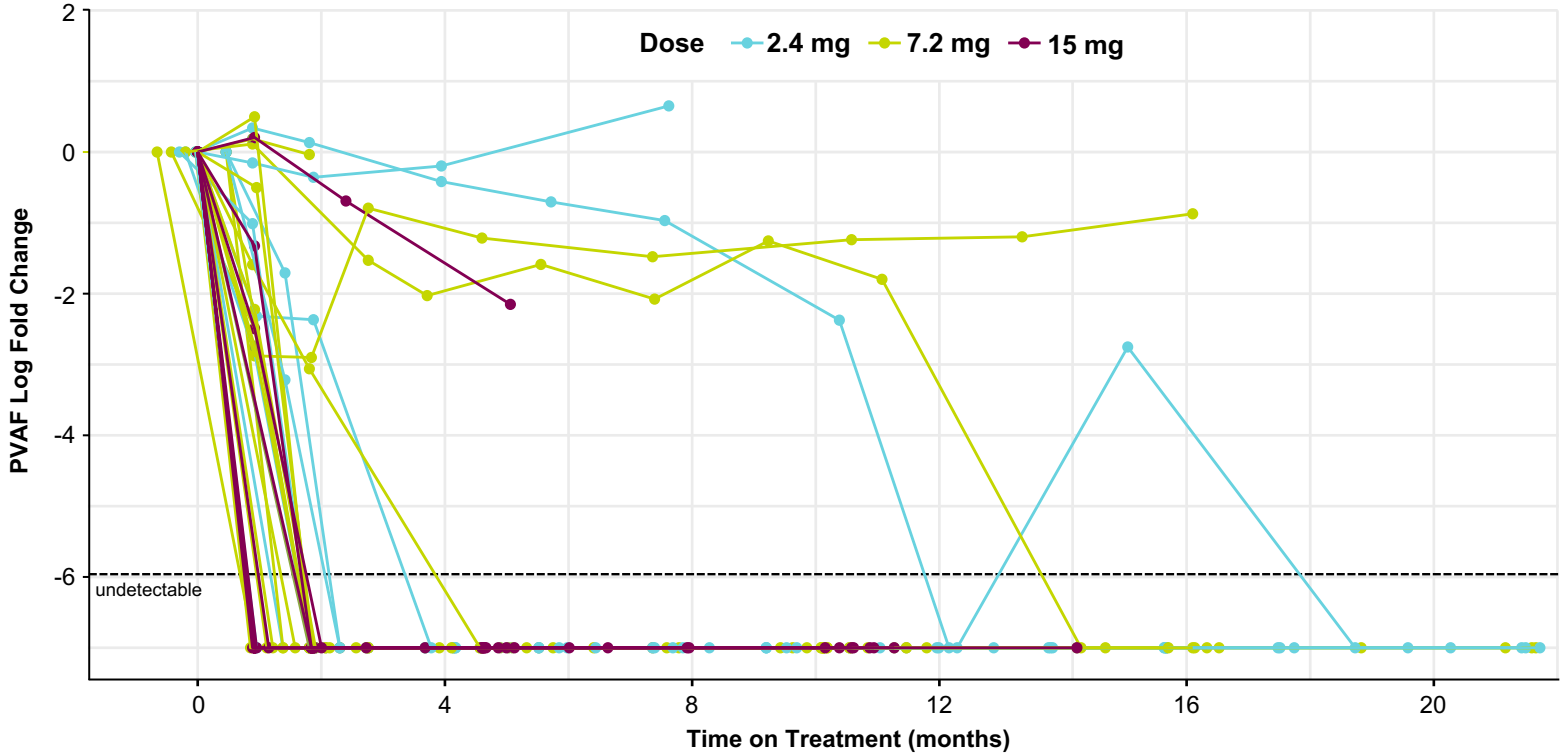


- ORR/CR rate for patients who received ≥2.4 mg was 96%/92%
- In the ITT population, ORR/CR rates were 100%/93%, 87%/83% and 100%/100% in the 2.4-mg, 7.2-mg and 15-mg cohorts, respectively[a]

[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

Rapid Clearance of ctDNA in MRD Responders



ctDNA assessed by PhasED-Seq

Mosun / glofit + golcadomide in R/R B-NHL: Study design

Key inclusion criteria

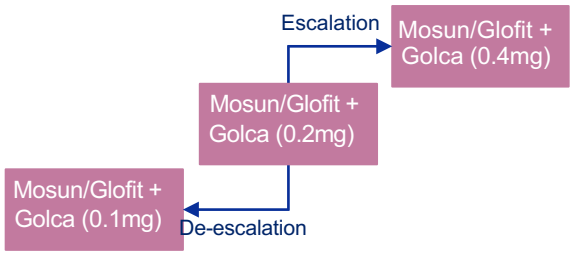
- R/R DLBCL, trFL, or FL Grade 1–3a
- ≥2 prior lines of therapy for dose escalation and ≥1 prior line of therapy for dose expansion
- CAR T-cell therapy ineligible

Endpoints

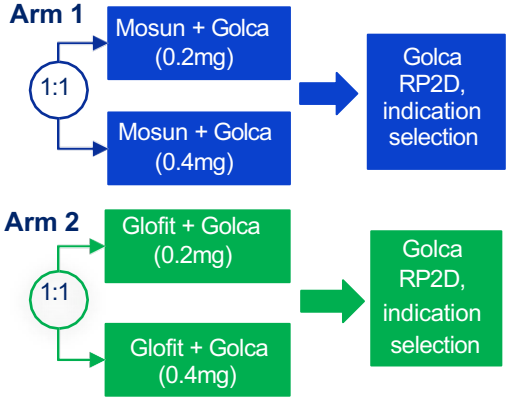
- **Primary**: Safety, DLTs, and Golca RP2D selection
- **Key secondary**: Investigator-assessed best ORR and CR rate (by Lugano 2014 criteria[1])

Study treatment administration

Dose escalation: 3L+ R/R NHL (n=3–9 in each cohort)



Dose expansion: 2L+ R/R FL, R/R DLBCL (n=20 in each cohort)



Mosun SC
- Fixed-duration treatment (5/45/45mg)*
- CRS† mitigation: C1 SUD (5mg on C1D1, 45mg on D8 and 15; 21- or 28-day cycle)
- No mandatory hospitalization

Glofit IV
- Fixed-duration treatment (2.5/10/30mg)‡
- CRS† mitigation: obinutuzumab pretreatment on C1D1 and C1 SUD (2.5mg on C1D8, 10mg on C1D15; 21-day cycle)
- Hospitalization was required 24 hours after first dose (C1D8) of Glofit

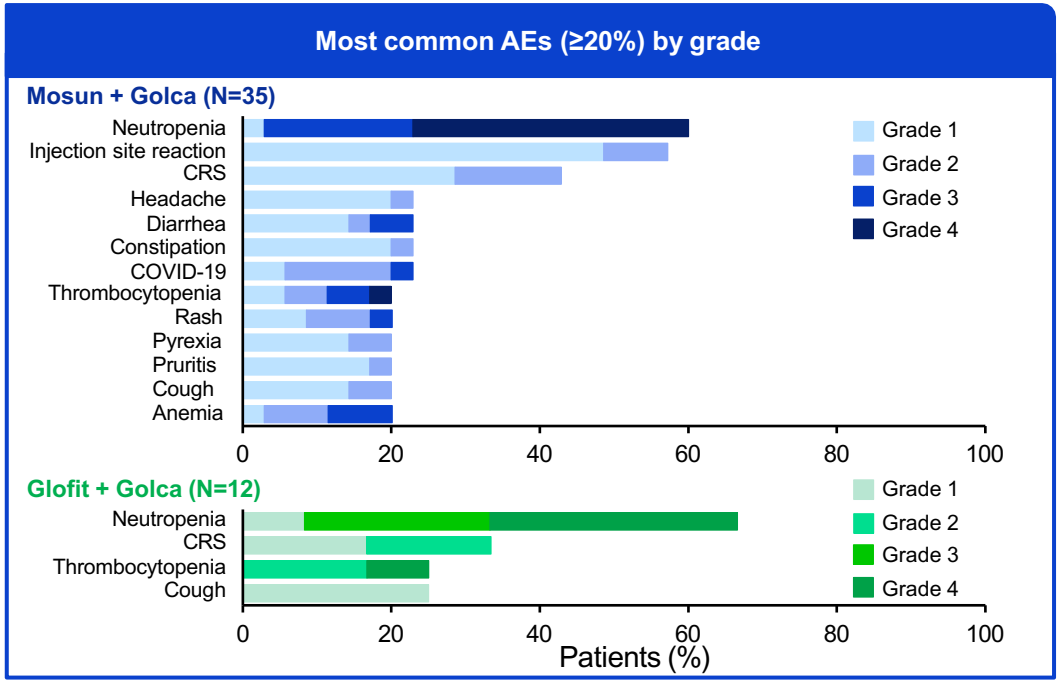
Golca oral§
- Arm 1: given daily from D1–14 in C1 or C2 onwards
- Arm 2: given daily from D1–10 in C2 or C3 onwards

*Mosun was administered with SUD during C1 and at 45mg on D1 of C2–12 (28-day cycle). †CRS events were graded by American Society for Transplantation and Cellular Therapy criteria.[2] ‡Glofit was administered with SUD during C1 and at the target dose (30mg) on D1 of C2–12 (21-day cycles). §The initial Golca dose was 0.2mg.
2L+, second-line or later; 3L+, third-line or later; C, cycle; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; D, day; DLT, dose limiting toxicity; IV, intravenous; ORR, overall response rate; RP2D, recommended Phase 2 dose; SC, subcutaneous; SUD, step-up dosing; trFL, transformed follicular lymphoma.

1. Cheson BD, et al. J Clin Oncol 2014;32:3059–68;
2. Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625–38.

Safety overview

n (%) unless otherwise stated	Mosun + Golca (N=35)	Glofit + Golca (N=12)
AE	35 (100)	12 (100)
Grade 3/4 AE	26 (74.3)	8 (66.7)
Serious AE	23 (65.7)	6 (50.0)
AESI*	13 (37.1)	4 (33.3)
Grade 5 (fatal) AE	0	0
AE leading to treatment discontinuation	6 (17.1)†	0
AE leading to dose modification/ interruption	19 (54.3)‡	6 (50.0)§

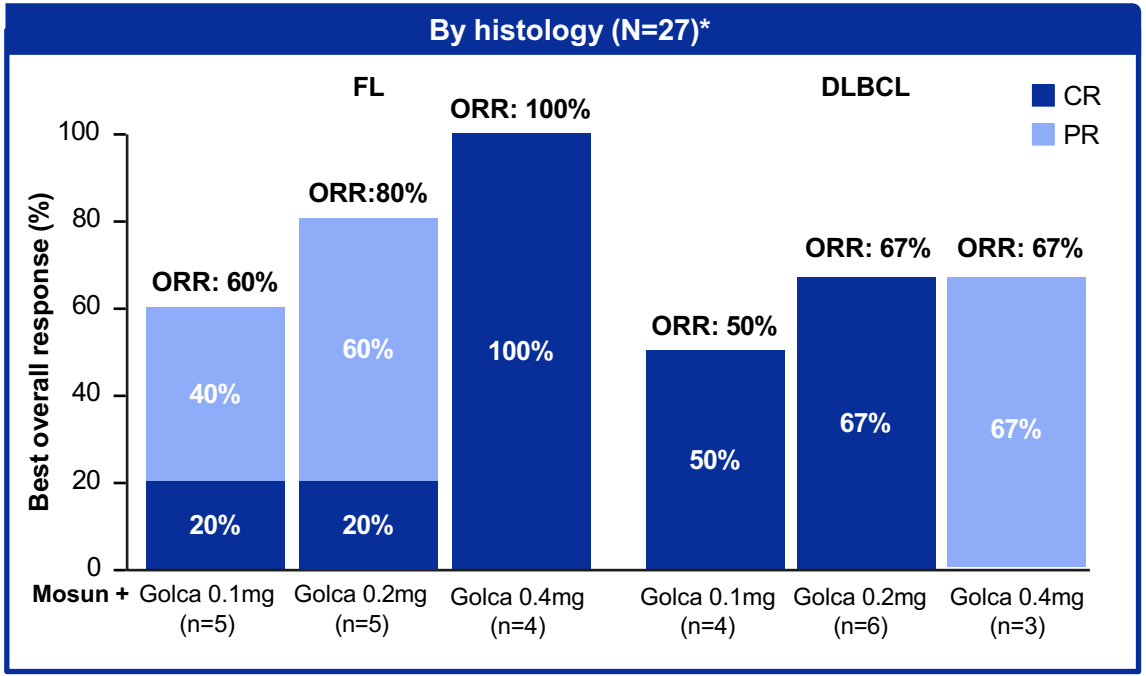


The safety profile was manageable with low rates of AEs leading to treatment discontinuation; neutropenia was the most common AE

*Protocol defined AESIs. †Neutropenia (n=4), thrombocytopenia (n=1), anemia (n=1) and disseminated intravascular coagulation (n=1). ‡Infections including COVID-19 (n=7), neutropenia (n=6), febrile neutropenia (n=2), pneumonia (n=1), folliculitis (n=1), bronchospasm (n=1), CRS (n=1), injection site reaction (n=1), chest pain (n=1), influenza (1), atrial fibrillation (n=1) and supraventricular tachycardia (n=1). §Neutropenia (n=1), febrile neutropenia (n=1), sinusitis (n=1) and nausea (n=1). AE, adverse event; AESI, AEs of special interest.

Andreadis et al. ASH 2025

Best overall response in Arm 1: Mosun + Golca



- Median time to first response for all patients (N=27)*: 2.6 months (range: 2–4)
- Response in patients who received prior CAR T-cell therapy (n=8):
  - Overall, 5 patients achieved a CR
    - Two patients had FL and one achieved CR
    - Six patients had DLBCL and four achieved a CR

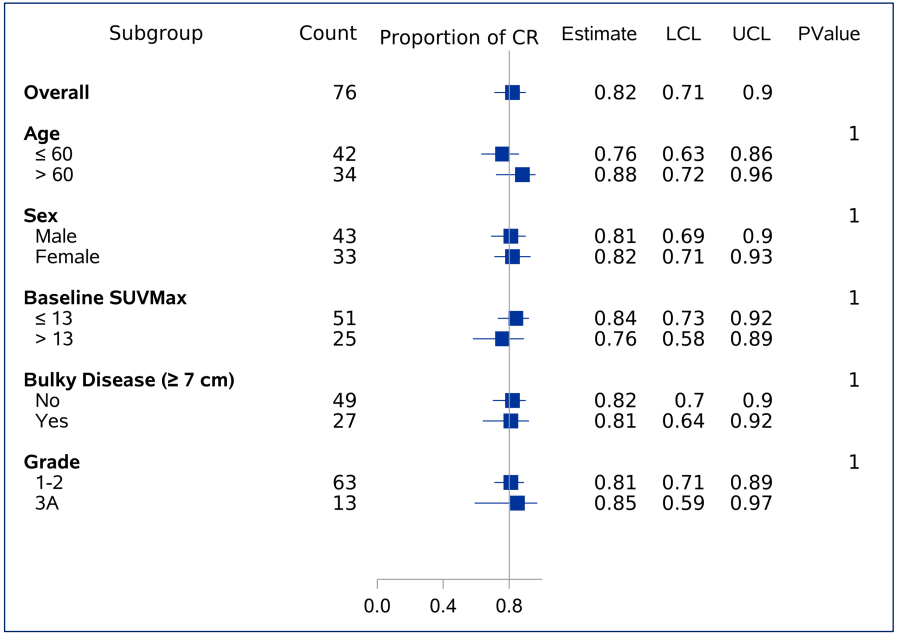
High response rates were observed in patients with FL and DLBCL including those who received prior CAR T-cell therapy

*Efficacy-evaluable population. PR, partial response.

Andreadis et al. ASH 2025

SC mosunetuzumab monotherapy in 1L FL: MITHIC-FL1

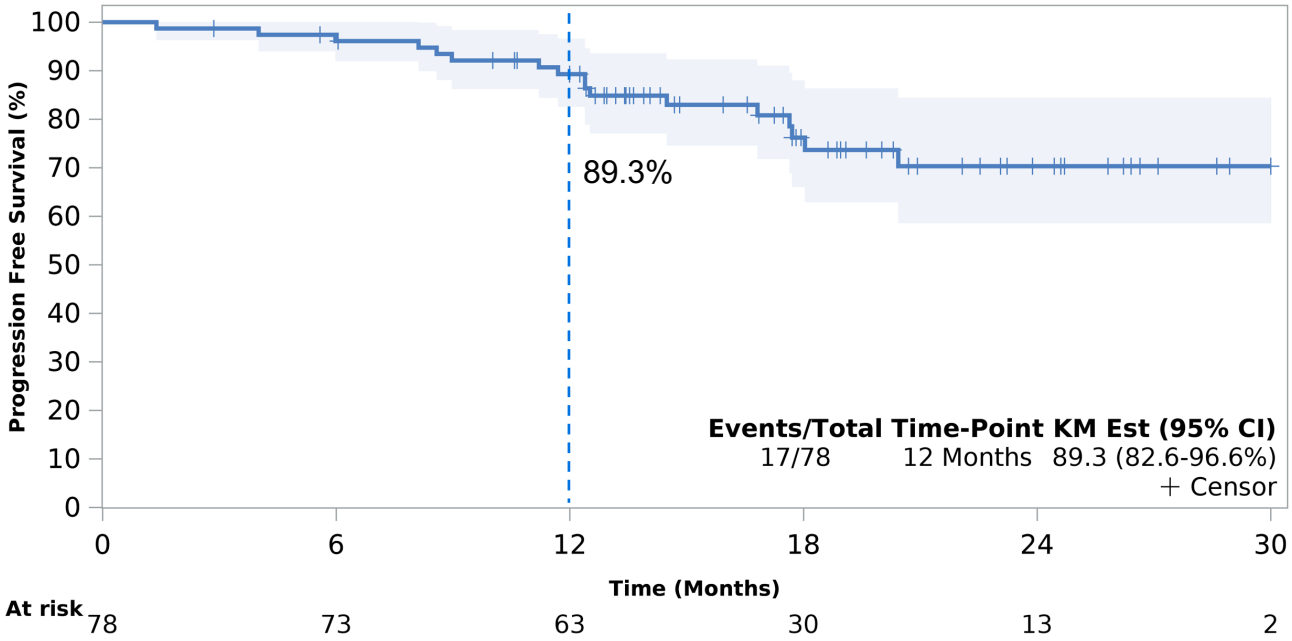
Response type	Response evaluable (N=76)	Intention-to-treat (N=78)
Overall response	**95%**	92%
Complete response*	**82%**	79%
Partial response	13%	13%
Stable disease	3%	3%
Progressive disease	3%	3%
Non-evaluable	n/a	3%



Intention-to-treat group includes all patients who received at least one dose of mosunetuzumab. Response evaluable population includes all patients who had at least one radiographic response evaluation. *One patient's end-of-treatment response adjudication was updated from a partial response to a complete response after biopsy of the only persistent FDG-avid lesion after treatment demonstrated Schwannoma; this patient received a total of 17 mosunetuzumab cycles

Falchi et a. ICML 2025

Progression-Free Survival

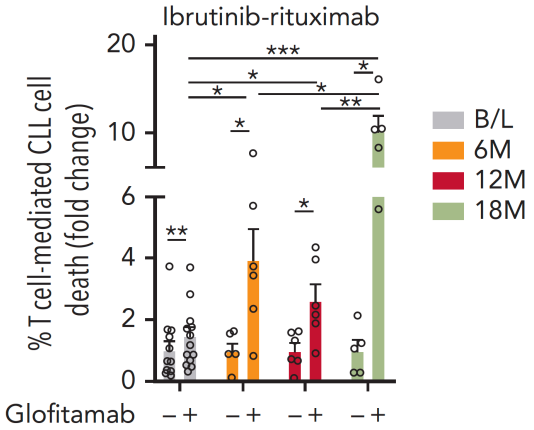


- 13 Patients experienced PD:
  - 7 are on observation
  - 2 received radiation to a single site of PD
  - 4 had transformation and were treated with R-CHOP (all in continued CR)
- CD20 status by IHC at PD:
  - 8 CD20+
  - 3 CD20-
  - 2 not biopsied

Falchi et a. ICML 2025

Zanubrutinib as Rational Combination Partner for Mosunetuzumab

- Second generation, covalent Bruton Tyrosine kinase inhibitor (BTKi) FDA approved for 3L+ FL in combination with obinutuzumab[1]
- *In vitro*, treatment with BTKi, including zanubrutinib, downregulated T-cell PD-1 expression.[2,3]
- BTKi increased the number of CD8+ T-cell immune synapses in patients with B-cell lymphoid malignancies[4]
- Co-culture of a BsAb and BTKi resulted in increased BsAb-mediated target cell killing.[4]



HYPOTHESIS: Adding zanubrutinib to mosunetuzumab may mitigate or reverse T-cell exhaustion, increase mosunetuzumab-mediated tumor killing, and improve clinical results.

1. Zinzani PL et al. J Clin Oncol J Clin Oncol 41:5107-5117; **2.** Zou YX, et al. Hematol Oncol. 2019;37(4):392-400; **3.** Svanberg R et al, haematologica 2021; 106(9); **4.** Papazoglou D et al Blood 2024 Jan 4;143(1):57-63.

Multicenter Phase 2 Study Overview

Eligibility:

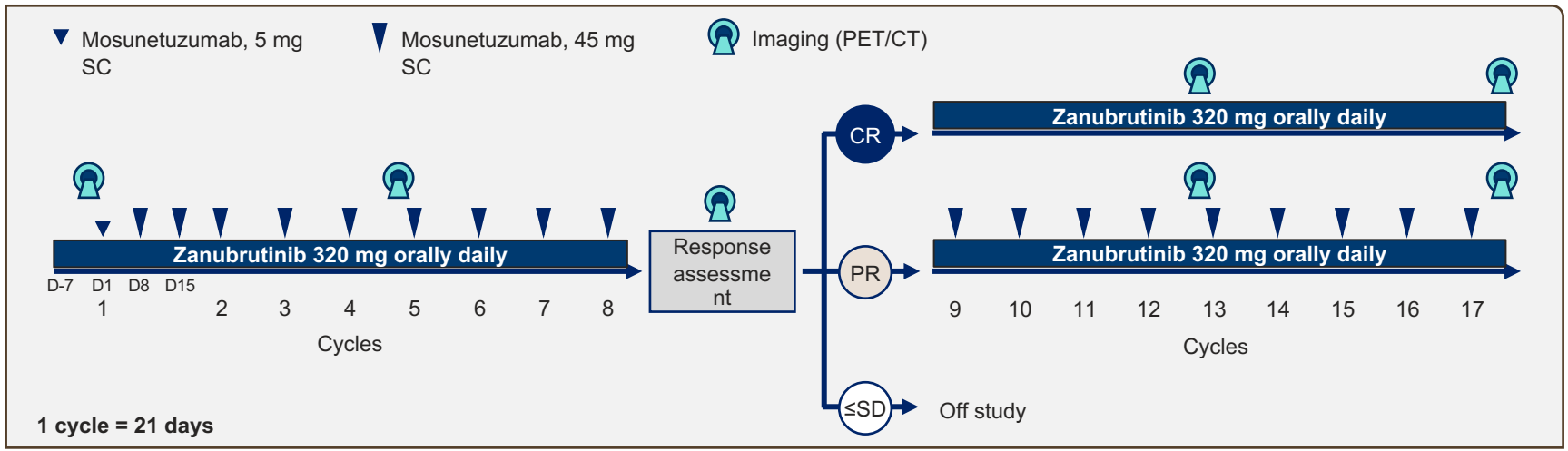
- ≥18 years; ECOG PS 0-2
- CD20+ previously untreated FL
- G1-3A, stage II–IV
- **In need of therapy per GELF criteria**

Endpoints:

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

Outpatient administration:

- Administration: Zanubrutinib PO; mosunetuzumab SC
- Prophylaxis: Dexamethasone, anti H2, acetaminophen in C1 (and C2 if prior CRS)
- VZV and PJP prophylaxis and GCSF support per treating physician

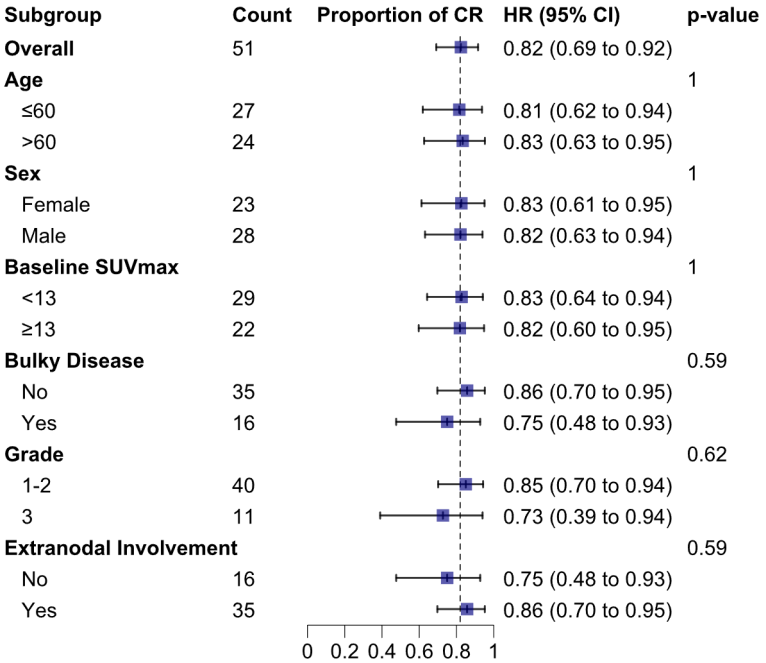


Patients who experience progression at any time point were taken off study; CR, complete response; ORR, overall response rate; PFS, progression-free survival; DOR, duration of response; TTNT, time to next treatment; OS, overall survival; PD, progressive disease; ctDNA, circulating tumor DNA; ECOG, Eastern Cooperative, Study Group; FL, follicular lymphoma; GELF, Groupe d'etudes des lymphomes folliculaires; PO, oral; SC, subcutaneous; 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; SD, stable disease

Falchi et a. ASH 2025: Abstract 463

Mosunetuzumab + Zanubrutinib Induced Deep Responses in Most Patients

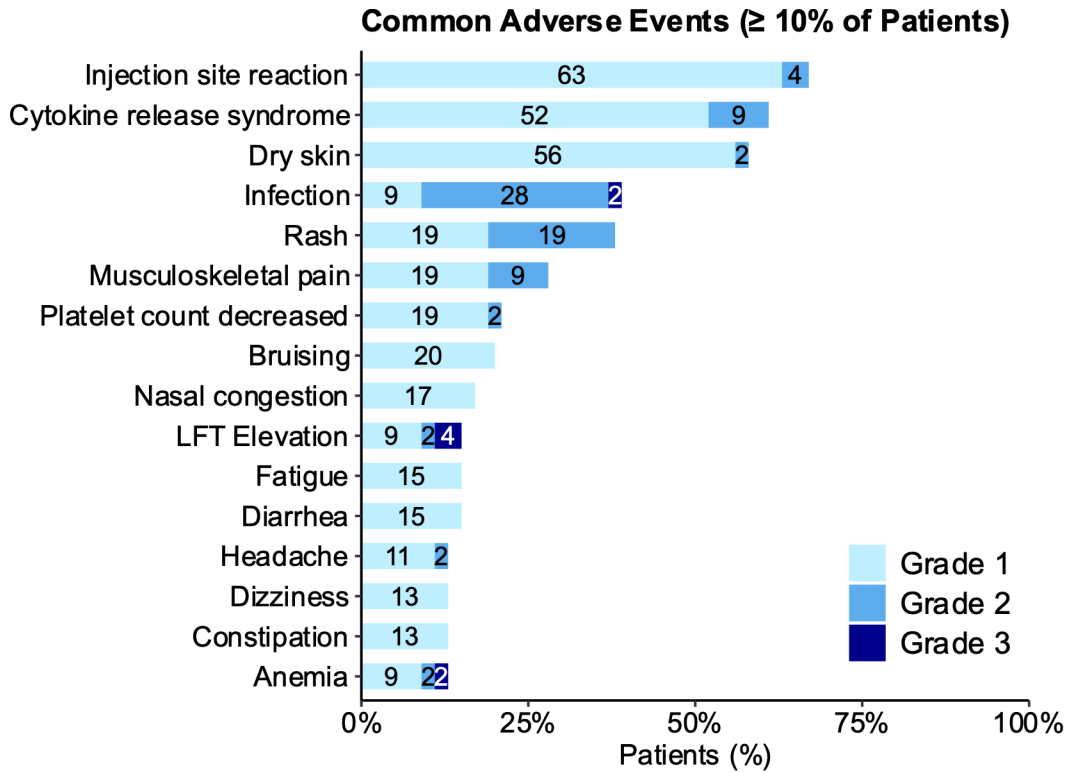
Response Type	Response Evaluable (n=51)
Overall Response	47 (92%)
Complete Response	**42 (82%)**
Partial Response	5 (10%)
Stable Disease	1 (2%)
Progressive Disease	3 (6%)



Data cutoff: November 14, 2025; response assessed per the 2014 Lugano criteria and integrated with the 2016 LYRIC criteria; evaluable = patients who received at least one dose of study drug and underwent at least one response assessment

Falchi et a. ASH 2025: Abstract 463

Most Adverse Events Were Low-Grade



- No safety signals were observed for mosunetuzumab or zanubrutinib
- Most AEs were grade 1-2
- No patient discontinued treatment due to AEs
- No neurotoxicity, clinical tumor lysis syndrome, or tumor flare reaction
- 11 patients had bruising (22%), all grade 1
- 2 patients had epistaxis (4%), all grade 1
- No episodes of atrial fibrillation
- One patient developed G5 EBV-associated HLH during Cycle 1. This patient had negative EBER staining on baseline biopsy and did not have detectable EBV viral load at baseline.

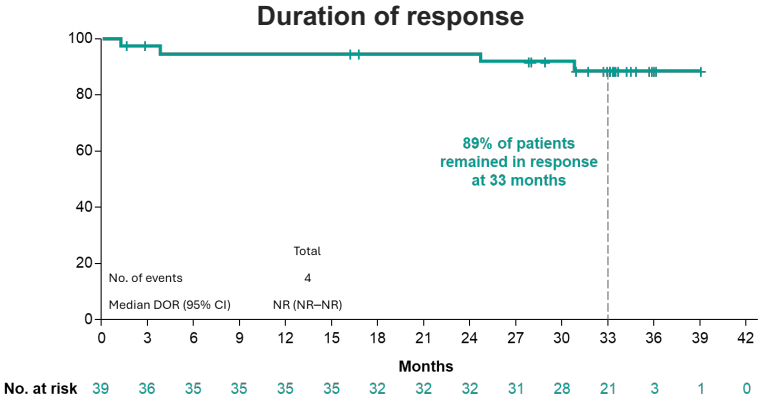
Other AEs of interest: 3 Patients had G3 (1) or G4 (2) neutropenia; 1 had G3 febrile neutropenia; 1 had G3 acute kidney injury in the setting of tumor ureteral compression; 1 had prostate cancer (G3), and 1 had G3 syncope

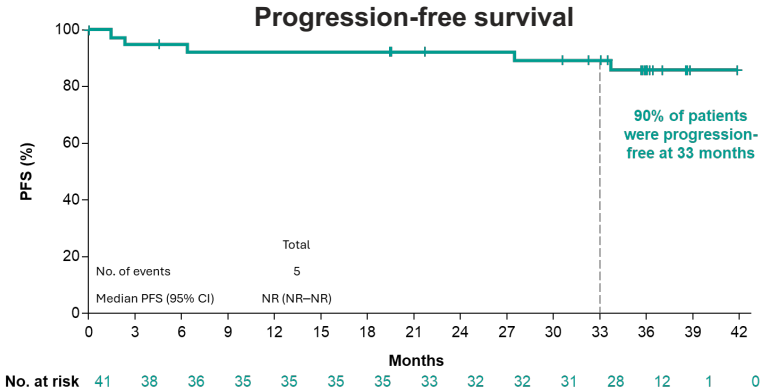
Falchi et a. ASH 2025: Abstract 463

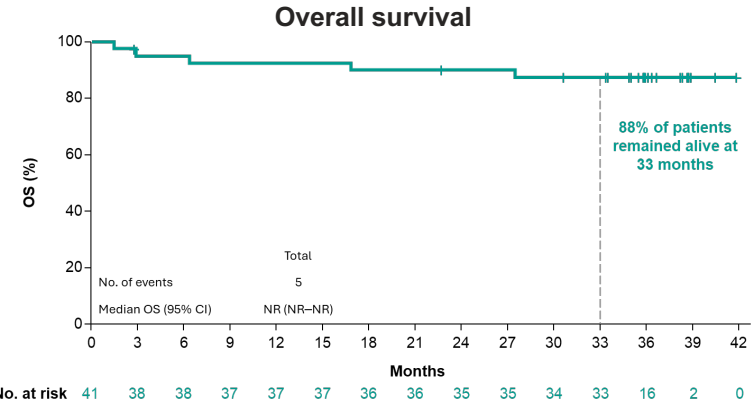
Epcoritamab + R2 1L FL: Deep and Durable Responses

	Epcoritamab + R² N = 41
Overall response, n (%)	39 (95)
CR	36 (88)
PR	3 (7)
NE[a]	2 (5)

- Among 36 patients in CR, 9/10 who discontinued treatment for reasons other than PD or death[b] maintained CR[c]
- MRD negativity[e] (<10^{-6}):100% (26/26 MRD-evaluable patients



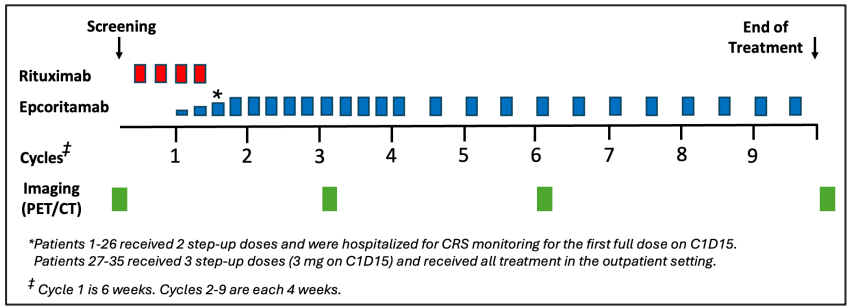




Median follow-up time for DOR was 33.2 months (95% CI, 33.0–33.5). [a]No post-baseline assessment in 2 patients; no patients had PD. [b]Median treatment duration of 13 months. [c]Median follow-up of 20 months post-treatment. [d]Median follow-up of 12.5 months post-treatment. [e]MRD was assessed by PBMC, using clonoSEQ assay. NE, not evaluable; NR, not reached.

Leslie L et a. ASH 2025: Abstract 465

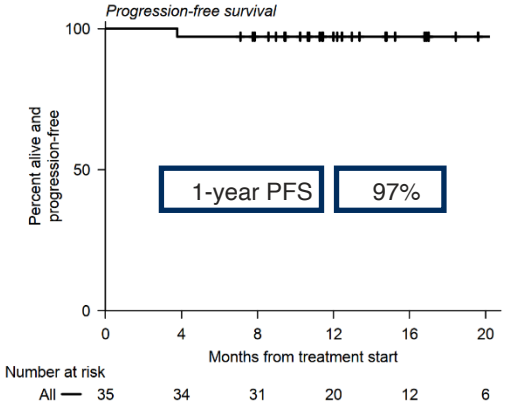
R-epcoritamab in 1L high-burden FL: Phase 2 trial (DFCI)

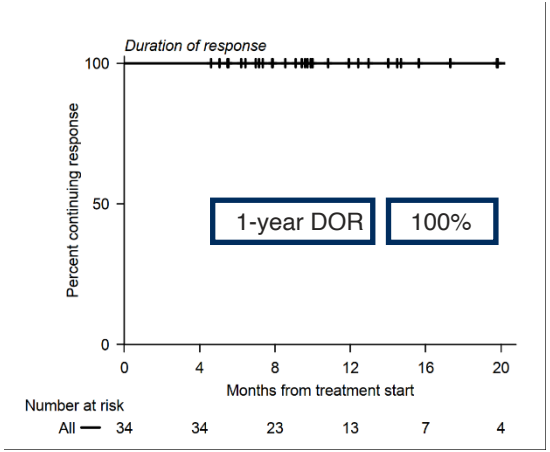


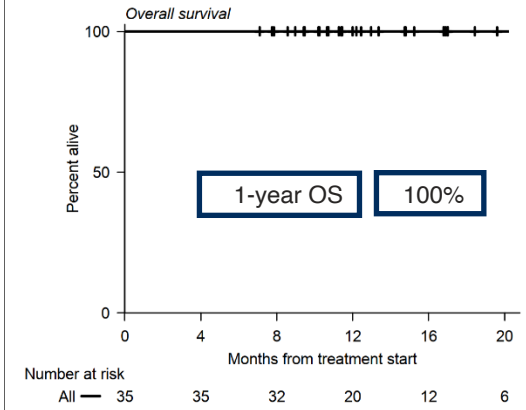
*Patients 1-26 received 2 step-up doses and were hospitalized for CRS monitoring for the first full dose on C1D15. Patients 27-35 received 3 step-up doses (3 mg on C1D15) and received all treatment in the outpatient setting.

‡ Cycle 1 is 6 weeks. Cycles 2-9 are each 4 weeks.

	C3D1	EOT*	Best Response
N	35	30	35
ORR	97%	97%	97%
CMR	86%	93%	94%







Merryman R et a. ASH 2025: Abstract 464

Ongoing randomized studies of bispecific antibody combinations in 1L FL

Regimen	Trial (Phase)	Patients (1L FL cohorts)*	Treatment duration and administration	Primary endpoint	Study status
Mosunetuzumab-Len versus R- / G-chemo	**MorningLyte** (Phase III)[1]	790[1]	**Mosunetuzumab** (SC) 21 cycles **Len** (oral) 11 cycles[1]	PFS (by IRC)[1]	Recruiting[1]
Odronextamab-chemo versus R-chemo	**OLYMPIA-2** (Phase III)[2]	733[2]	**Odronextamab** (IV) **CHOP/CVP** (IV)[2]	Part 1: DLTs and safety Part 2: CR30 (by ICR)[2]	Recruiting[2]
Epcoritamab-R-Len versus R- / G-chemo	**EPCORE FL-2** (Phase III)[3]	1095[3]	**Epcoritamab** (SC) **R** (IV) **Len** (oral)†[3]	CR30 (by IRC) PFS (by IRC)[3]	Recruiting[3]
Surovatamig plus R versus R-chemo	**SOUNDTRACK-F1** (Phase III)[4]	975[4]	**R-surovatamig** (IV) 7 cycles alone (arm A) or + maintenance (ie, 17 cycles) (arm B)	Safety run-in: RP3D safety Phase III: PFS by IRC[4]	Recruiting[4]

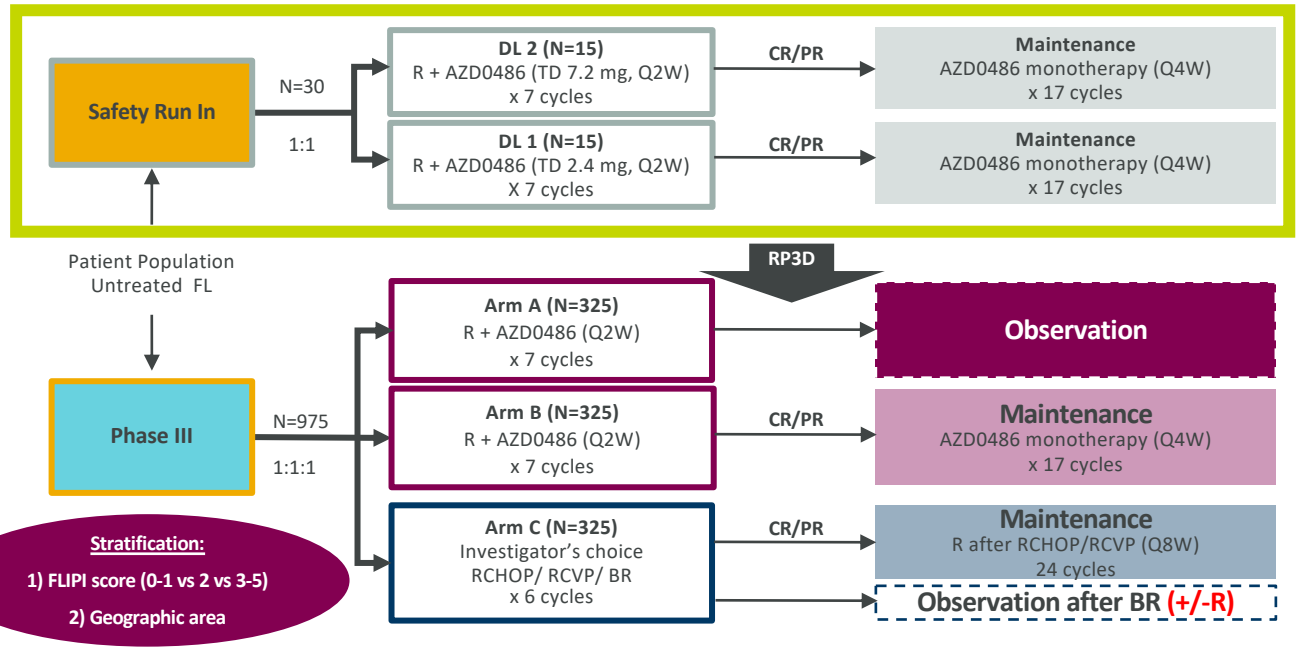
Products/indications are investigational and not approved. This slide is for educational purposes only

*Estimated enrollment. †120-week treatment duration

CR30, complete response at 30 months; CVP, cyclophosphamide, vincristine and prednisone; DLT, dose-limiting toxicity; BICR, blinded independent central review; ICR, independent central review; RP3D, recommended Phase III dose.

1. NCT06284122. Available at: https://clinicaltrials.gov/study/NCT06284122;
2. NCT06097364. Available at: https://clinicaltrials.gov/study/NCT06097364;
3. NCT06191744. Available at: https://clinicaltrials.gov/study/NCT06191744;
4. NCT06549695. Available at: https://clinicaltrials.gov/study/NCT06549595.

SOUNDTRACK F1: Phase III Study Design with Safety Run-In



Target population:

- Treatment naïve FL
- Meet GELF criteria

Endpoints:

- **Primary:**
  - Safety Run-in: Safety and tolerability of AZD0486 + R and RP3D determination
  - Phase III: PFS assessed by IRC based on Lugano Response Criteria
- **Secondary:**
  - Safety Run-in: Efficacy (ORR, CRR, CR@EOI, CR30, DoR, PFS, OS), PK/PD/Immunogenicity
  - Phase III: Efficacy (**CR@EOI (Key secondary)**, ORR, CRR,, CR30, DoR, PFS, TTNT, OS), safety, PK/Immunogenicity, PRO, MRD-ve CR rate

B: Bendamustine; CNS: Central nervous system; CR: complete response; CR30: complete response at 30 months; DL: Dose level; DoR: Duration of Response; EOI: end of induction; FL: Follicular Lymphoma; MRD: Minimal residual diseaseORR: Overall response rate; PB: peripheral blood; OS: Overall survival; PFS: progression free survival; PR; partial response; PRO: Patient reported outcome; QxW: every x weeks; R: rituximab; RP3D: recommended Ph3 dose; SOC= standard of care; TD= target dose; TTNT: Time to next treatment

Bispecific antibodies in iNHL: Take home messages

1. Bispecific antibodies are transformative drugs for patients with iNHL (FL)

- High efficacy, regardless of risk factors, with manageable safety profile
- More accessible than CAR-T

2. In R/R iNHL (FL) BsAb combinations are the path forward

- Epcoritamab + R2 is a new standard 2L+ therapy
- Surovatamig data are compelling (CD19 more stable than 20?)

3. In 1L BsAb monotherapy (or + R) may have a role, combinations are being developed

- Benefit potentially comparable with CIT but better tolerability (and acceptance)
- MRD monitoring as a tool to shorten treatment duration?

4. Critical shortage of data on non-FL iNHL!

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Robert N. Stuver, MD
Ariela Noy, MD
Andrew D. Zelenetz, MD, PhD
Gilles A. Salles, MD, PhD

Clinical Team:

Anastasia Martinova, RN
Lauren Wood, MSN, RN, OCN
Joanna Tortora, RN
Jason Brecher RN, OCN
Kate Doyle, RN
Merissa Manos, RN
Jayrol Mock, RN
Dianna Tyznar, RN
Taylor Sipos, RN
Jennifer Howgate-Klingaman, RN
Merissa Manos, RN

Study Research Team:

Clare Grieve, MPH
Michelle Okwali, MPH
Christina Miah, BA
Sherin Uralil, MBBS
Mia Catillo, MPH
Natalie Slupe, BA
Walter Ramos-Amador, MPH, MS
Kareem McKenzie, AS
DeVona Reese, MS
Vanessa Petillo, AS
Amelia Pfiffer, BS
Abigail Boswell, BA
Maria Chabowska, BS
Alexandra Lopez Ferreira, BS
Honglei Zhang
Venkat Seshan, PhD

Translational Science Team:

Santosha Vardhana, MD, PhD
Philipp Berning, MD
Ya-Hui (Nicole) Lin, MS

Pallavi Galera, MD
Ahmet Dogan, MD, PhD

Collaborators

Lombardi CCC:

Joseph Roswarski, MD
Kieron Dunleavy, MD
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