POST-ORLANDO 2025
Novità dal Meeting della Società Americana di Ematologia

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Torino
Centro Congressi Lingotto
19-21 febbraio 2026

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Abbvie			x			x	
Novartis			x				
BMS			x		x		
Kite			x		x		
Regeneron			x			x	
BeOne	x		x		x		

Novità dal Meeting della Società Americana di Ematologia

Torino, 19-21 Febbraio 2026

Abstract	IT	BsAb	CART	1L	2L+	vv
Mosunetuzumab with response-driven lenalidomide augmentation achieves high response rates and immune reprogramming in untreated follicular and marginal zone lymphoma: A multicenter Phase 2 trial		■		■		
Long term follow up of the response adapted FOLL12 trial for patients with advanced stage follicular lymphoma: A study by the fondazione italiana linfomi (FIL).	■			■		■
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		■		■		
Rituximab and epcoritamab as first-line therapy for patients with high-tumor burden follicular lymphoma: Results of a multicenter phase II trial		■		■		
Epcoritamab with rituximab + lenalidomide (R^2) and epcoritamab maintenance deliver deep and durable remissions in previously untreated (1L) follicular lymphoma (FL): 3-year outcomes from epcore NHL-2 arms 6 and 7		■		■		
Three-year follow-up of the Phase 1 first-in-human study investigating surovatamig, a novel CD19xCD3 T-cell engager, in patients with Relapsed/Refractory (R/R) follicular lymphoma (FL)		■			■	
Golcadomide (GOLCA), a potential, first-in-class, oral CELMoD™ agent, ± rituximab (R) in patients with Relapsed/Refractory follicular lymphoma (R/R FL): Phase 1/2 study extended follow-up Results	■				■	
Primary Phase 3 results from the epcore FL-1 trial of epcoritamab with rituximab and lenalidomide (R2) versus R2 for relapsed or refractory follicular lymphoma		■			■	
Three-Year Efficacy and Longitudinal Safety of Lisocabtagene Maraleucel (liso-cel) in Patients With Third-Line or Later (3L+) Follicular Lymphoma (FL) From TRANSCEND FL			■		■	
Clinical outcomes of tisagenlecleucel in patients with relapsed/refractory follicular lymphoma (r/r FL): Phase 2 ELARA 5-year update			■		■	
Outcomes in the 2nd decade following follicular lymphoma (FL) diagnosis: Long-term follow-up from the university of Iowa/Mayo Clinic SPORE molecular epidemiology resource (MER)						■
Are all GELF criteria created equal? utility of individual GELF criteria as guidance for treatment initiation in patients with advanced stage FL						■

MAYO CLINIC

Outcomes in the 2nd Decade Following Follicular Lymphoma Diagnosis

Long term follow up from the University of Iowa/
Mayo Clinic SPORE Molecular Epidemiology Resource

Jonathan R. Day, MD, PharmD, Melissa C. Larson, MS, Eric Mou MD, Urshila Durani MD, MPH, Carla Casulo, MD, Mazie Tsang, MD, Umar Farooq, MD, Patrizia Mondello, MD, PhD, J.C. Villasboas Bisneto, MD, Carrie A. Thompson, MD, Sergei Syrbu, MD, PhD, Andrew L. Feldman, MD, Christopher R. Flowers, MD, MS, Stephen M. Ansell, MD, PhD, Thomas E. Witzig, MD, Thomas M. Habermann, MD, James R. Cerhan, MD, PhD, Brian K. Link, MD, Yucai Wang, MD, PhD, Matthew J. Maurer, Sc.D. M.S.

ABSTRACT #1007

Knowledge Gap:

- What is OS in the second decade after diagnosis with FL?
- What is the risk of dying from lymphoma in 2nd decade?
- How does transformation risk change over time?
- Does progression risk change in 2nd decade?
  - Is FL curable?

Results

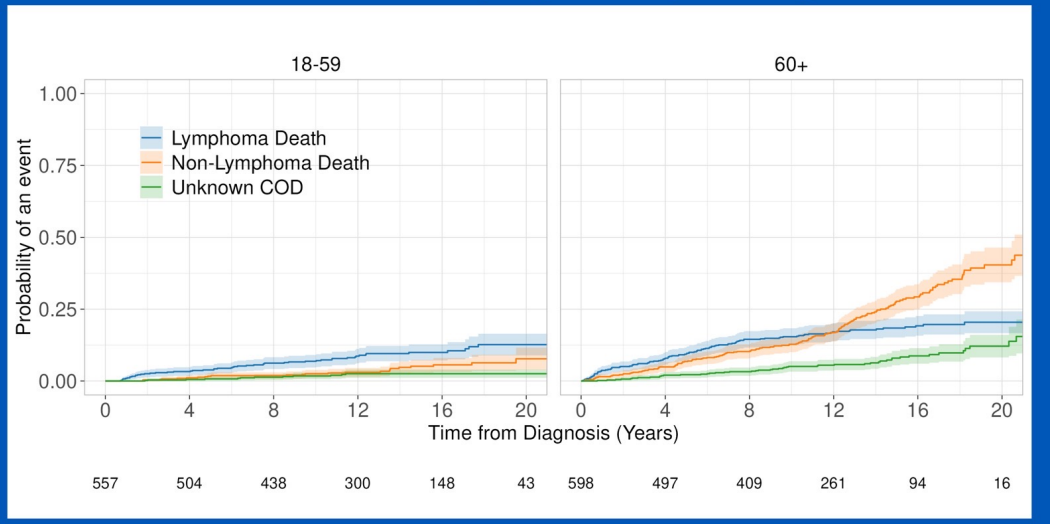
	N (%)
Overall	1155
Median Follow up	14 years (IQR 11-18 years)
Events	751
Deaths	402
Age at diagnosis	**Median = 60** (IQR 51-69)
60+	598 (52%)
Histology	
FL IIIA	12%
Stage	
III-IV	759 (67%)
FLIPI	
High	272 (27%)
FLIPI24	
High	280 (26%)

Initial Treatment
- **Observation** 403 (35%)
- **R-monotherapy** 139 (12%)
- **Immunochemotherapy (IC)** 453 (39%)
- **Radiation** (7%)
- **Other treatment** (7%)

IC type
- **R-CHOP** 195 (43%)
- **RCVP** 125 (28%)
- **BR** 121 (27%)

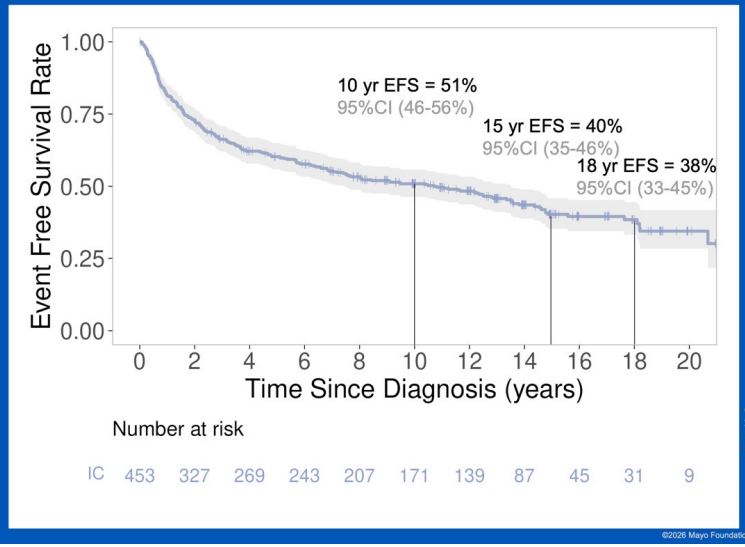
For additional cohort information: Cerhan JR, et al. Int J Epidemiol. 2017 Dec 1;46(6):1753-1754i.

FL: Cause of Death by Age Group at Diagnosis



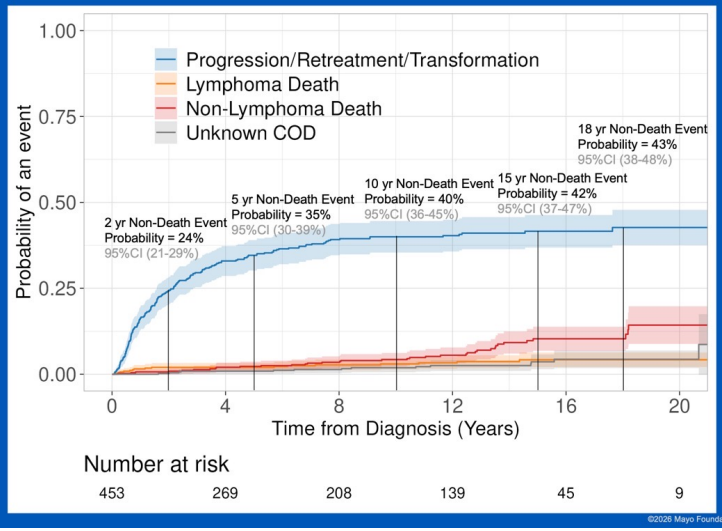
Median follow up 14 years: 18 year OS 55%

FL: EFS – Immunochemotherapy (IC) Treated Patients

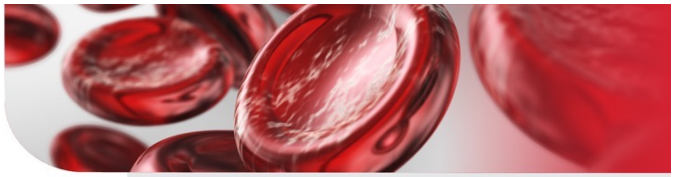


Comparisons Discussed:
Shadman M, et al. *J Clin Oncol.* 2018, Mar 1;36(7):697-703.
Bachy E, et al. *J Clin Oncol.* 2019 Nov 1;37(31):2815-2824.

Lymphoma Event Rate – IC treated patients



American Society of Hematology
Helping hematologists conquer blood diseases worldwide



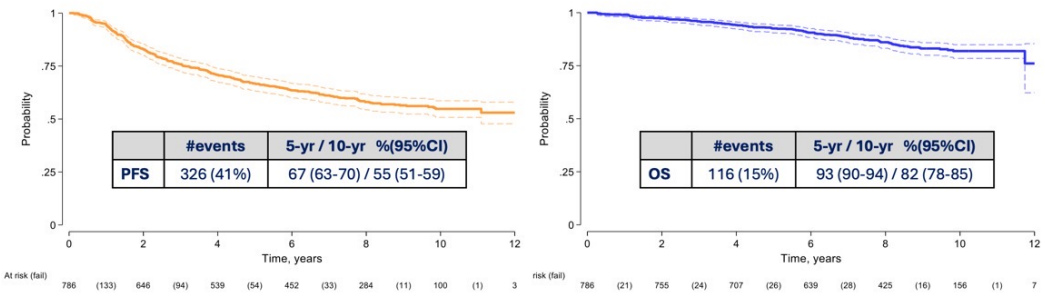
Long term follow up of the response adapted FOLL12 trial for patients with advanced stage follicular lymphoma: a study by the fondazione italiana linfomi (FIL).

Maria Elena Nizzoli, Antonella Anastasia, Carola Boccomini, Jacopo Olivieri, Ilaria Del Giudice, Simone Ferrero, Paolo Corradini, Gianluca Gaidano, Antonello Pinto, Benedetta Puccini, Marta Coscia, Marco Ladetto, Caterina Cecilia Stelitano, Francesca Ricci, Silvia Anna Maria Bolis, Alessia Bari, Annarita Conconi, Annalisa Arcari, Gerardo Musuraca, Annalisa Chiarenza, Dondi Alessandra, Vittoria Tarantino, Guido Gini, Filippo Ballerini, Sabrina Zoli, Sara Galimberti, Luigi Marcheselli, Luca Arcaini, Massimo Federico, ***Stefano Luminari***

Aim of the long term follow up analysis

- Reassess primary and secondary study endpoints
- Reevaluate the role of prognostic factors
- Analyze survival after first relapse
- Assess late events

Updated PFS and OS [n=786]



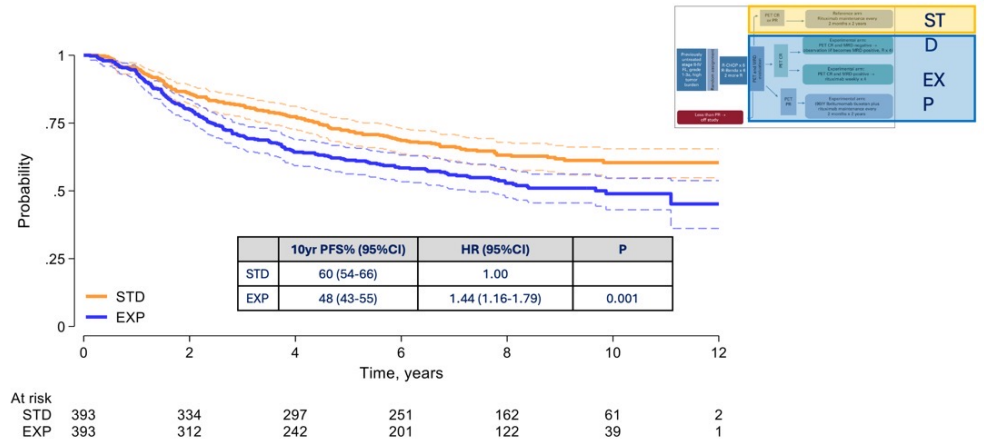
	#events	5-yr / 10-yr %(95%CI)
PFS	326 (41%)	67 (63-70) / 55 (51-59)

	#events	5-yr / 10-yr %(95%CI)
OS	116 (15%)	93 (90-94) / 82 (78-85)

Median follow-up: 8.8 yrs (range 0.1-12.5 yrs)

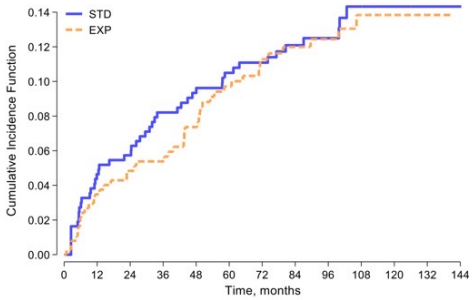
53 additional months of mFUP, 129 additional events for PFS and 86 for OS vs JCO paper

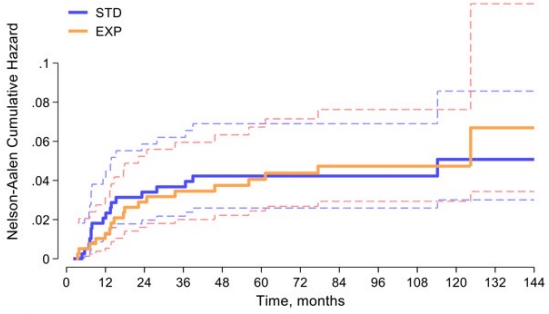
Updated PFS by STD and EXP arm - All patients (N=786)



	10yr PFS% (95%CI)	HR (95%CI)	P
STD	60 (54-66)	1.00	
EXP	48 (43-55)	1.44 (1.16-1.79)	0.001

Second primary malignancies – Cumulative Incidence Function by Arm

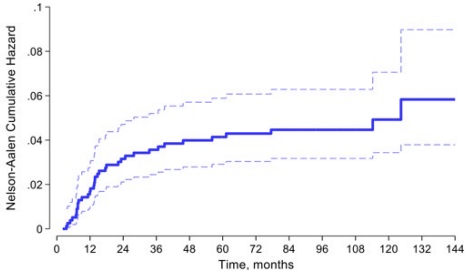


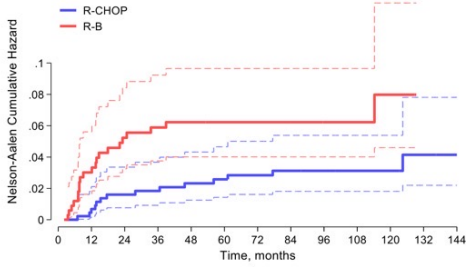


Group	n (#sec. neo.)	5-yr CIF % (95%CI)	sHR (95%CI)	P-value
All	744 (92)	10.1 (8.0-12.4)	-	
STD	368 (47)	10.5 (7.6-13.9)	Ref.	
EXP	376 (45)	9.7 (6.9-13.0)	0.95 (0.63-1.43)	0.816
	Adj. by Age cont., Sex, FLIPI2, Induction		0.96 (0.64-1.44)	0.839

Group	n (#tFL)	5-yr Cum. Haz. % (95%CI)	HR (95%CI)	P-value
All	786 (35)	4.1 (2.9-5.9)	-	
STD	393 (17)	4.2 (2.6-6.9)	Ref.	
EXP	393 (18)	4.0 (2.4-6.7)	1.08 (0.56-2.10)	0.819
	Adj. By Age cont., Sex, FLIPI2, Induction		1.14 (0.59-2.23)	0.690

tFL – from start of induction (n=786, tFL=35)





Group	n (#tFL)	5-yr Cum. Haz. % (95%CI)	HR (95%CI)	P-value
All	786 (35)	4.1 (2.9-5.9)	-	
RCHOP	445 (13)	2.6 (1.4-4.7)	Ref.	
RB	341 (20)	6.2 (4.0-9.6)	2.20 (1.11-4.36)	0.024
	Adj. By Age cont., Sex, FLIPI2, Arm		2.32 (1.15-4.68)	0.019

Cum. Haz.: cumulative hazard rate according to Nelson-Aalen estimation.

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

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 R²

- **Epcoritamab** (3-SUD cycle 1: QW;[a,b] cycles 2–3, QW; cycles 4–12, Q4W)
- **Rituximab** (375 mg/m²), 5 cycles (cycle 1, QW; cycles 2–5, Q4W)
- **Lenalidomide** (20 mg), 12 cycles (cycle 1–12, QD, D1-21)

R²

- **Rituximab** (375 mg/m²), 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 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.

Baseline Demographics and Disease Characteristics Were Generally Balanced

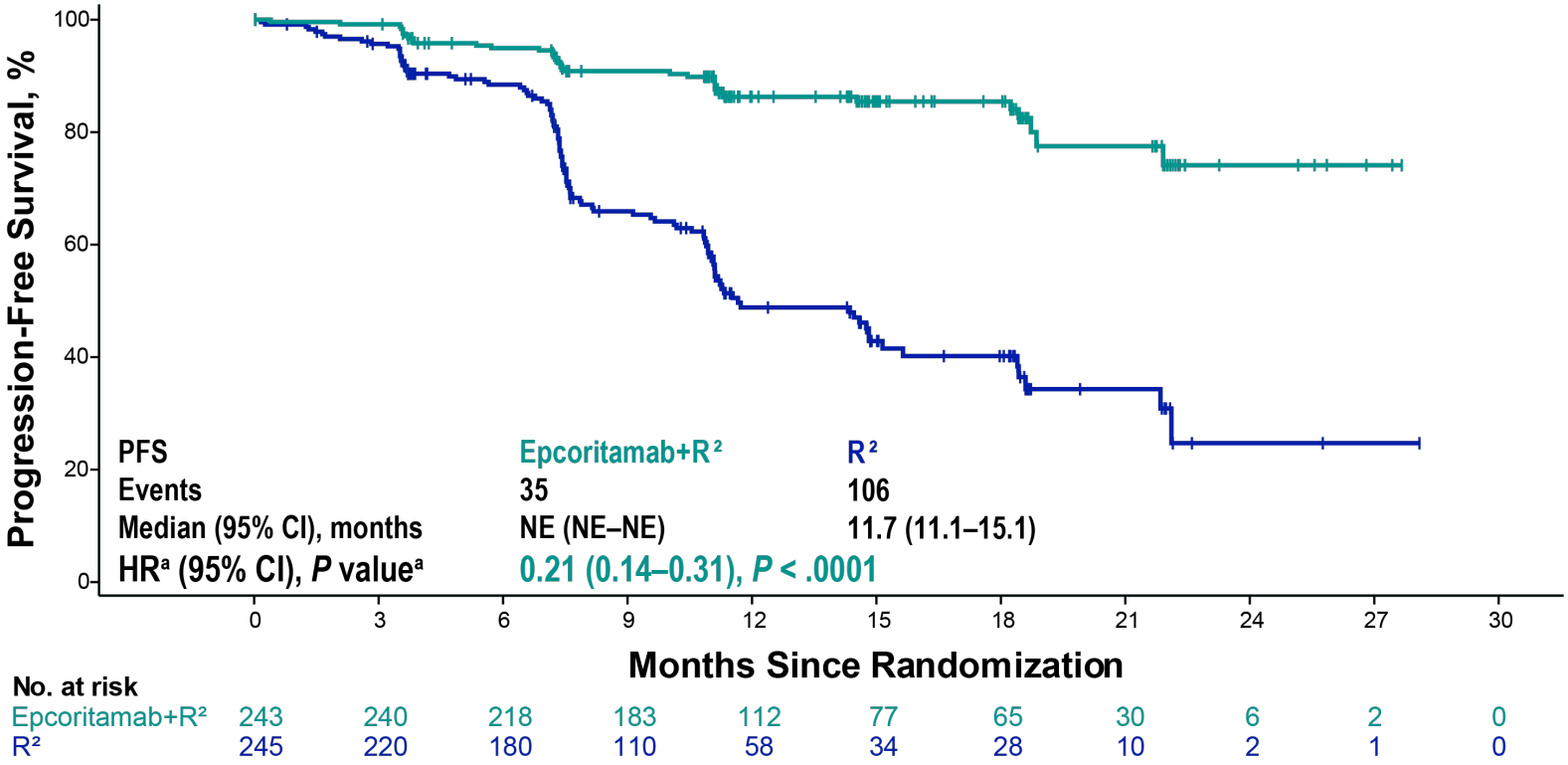
Characteristic	Epcoritamab+R^2 (N = 243)	R^2 (N = 245)	Overall (N = 488)
Median age, y (range)	60 (30, 84)	63 (24, 89)	61 (24, 89)
≥ 65, n (%)	88 (36)	106 (43)	194 (40)
Male, n (%)	139 (57)	138 (56)	277 (57)
Race, n (%)			
Asian	63 (26)	54 (22)	117 (24)
Black	6 (2)	2 (< 1)	8 (2)
White	168 (69)	184 (75)	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)

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.

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

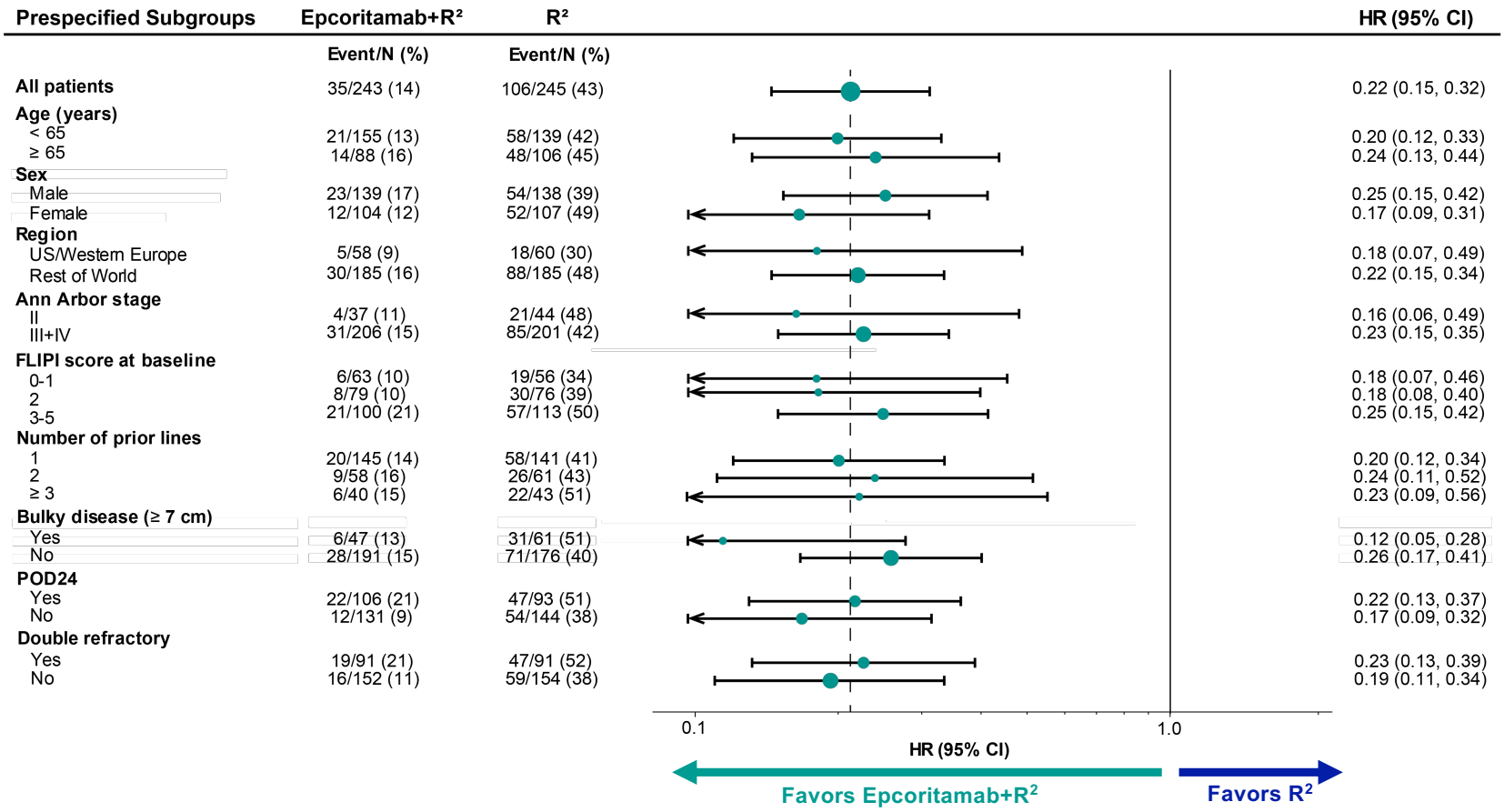


- Concordance rate was 94% for PFS between IRC and investigator assessment
- The estimated 16-month PFS was 85.5% (95% CI: 79.7, 89.7) for epcoritamab+R² and 40.2% (95% CI: 31.8, 48.4) for R²

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.

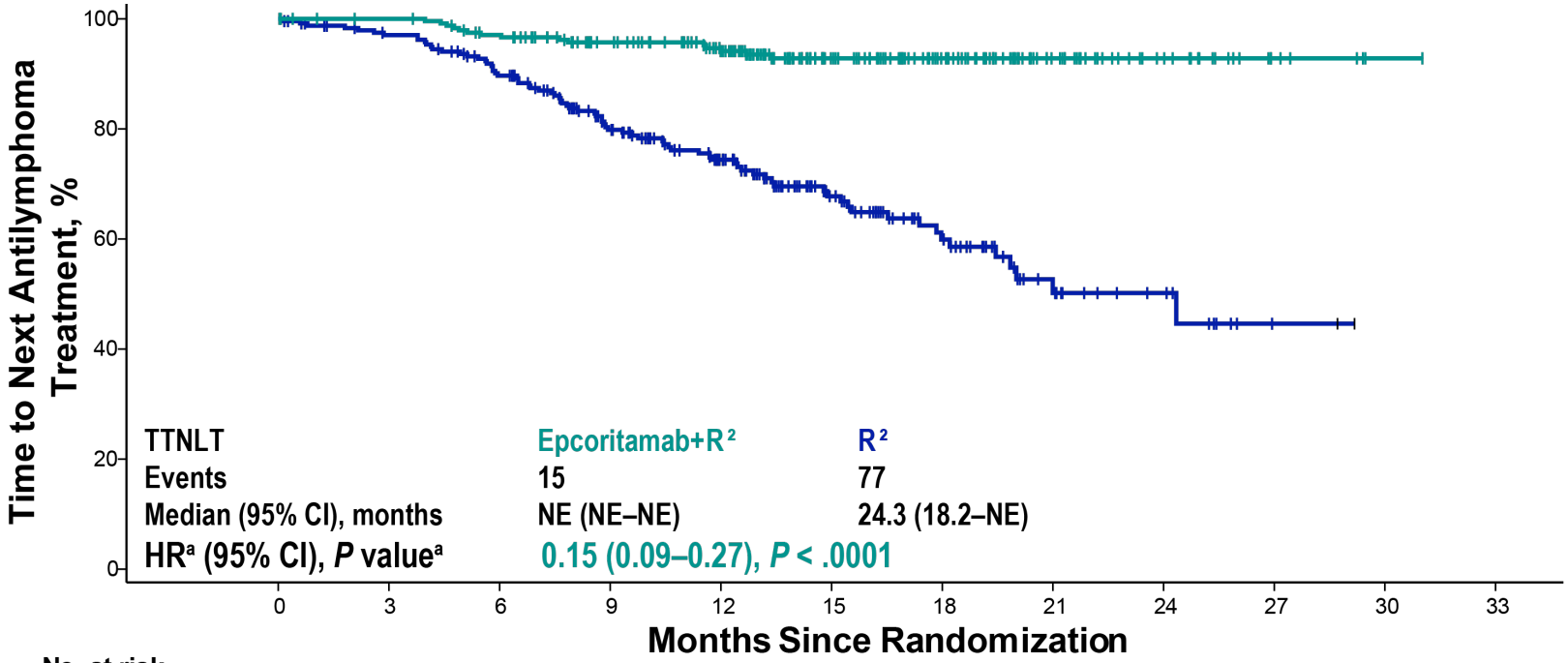
Epcoritamab+R² Demonstrated Favorable PFS Across a Broad R/R FL Population



- Trends in favor of epcoritamab+R² were shown for all prespecified subgroups and ORR, CR, and DOR endpoints

N represents the total number of patients within each category in each arm. Arrows indicate that the confidence interval is extended more than current range. 95% CI is by unstratified Cox proportional hazard model.

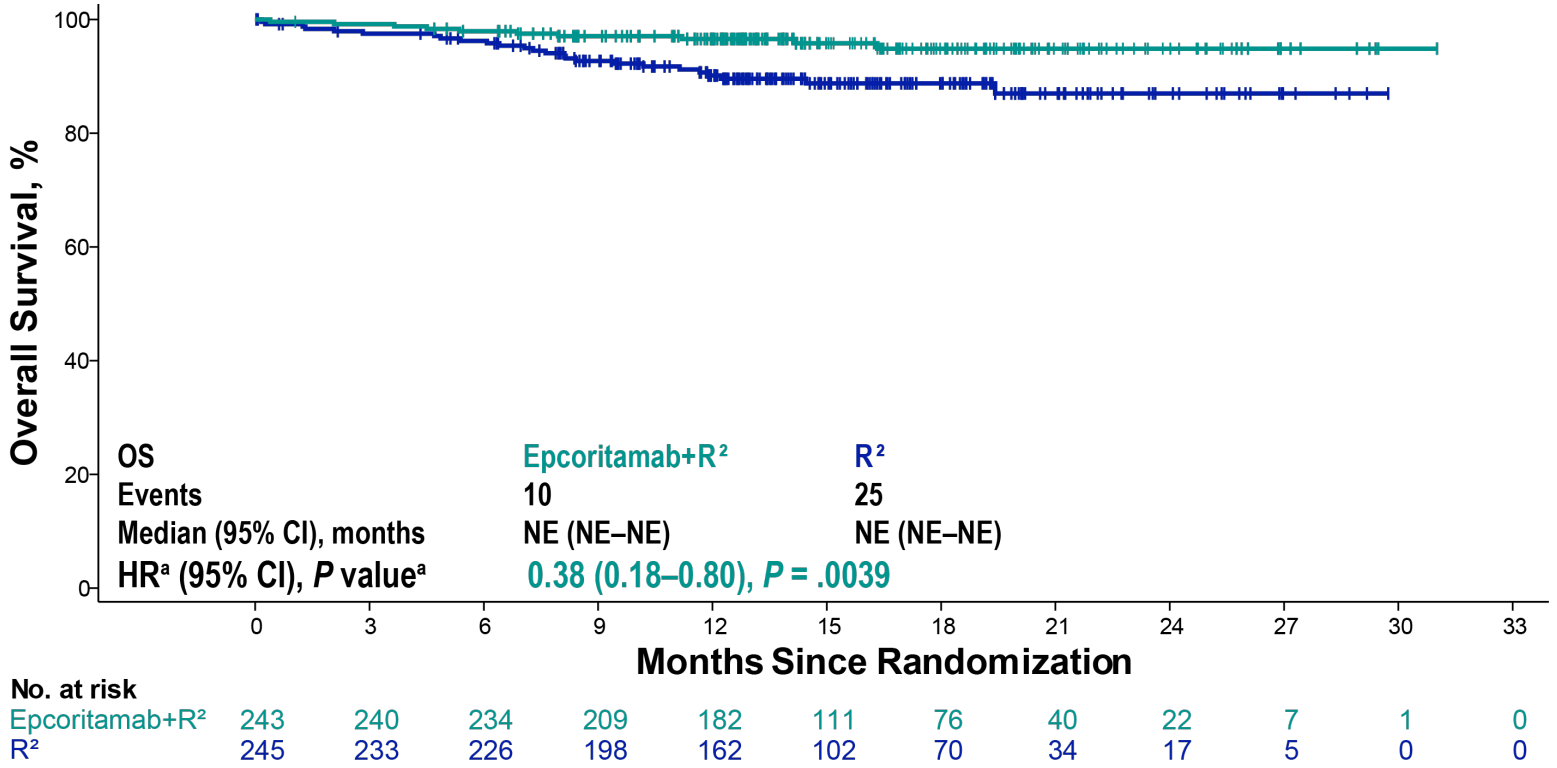
Epcoritamab+R² Extended Time to Next Treatment



- At 16 months, 92.8% of patients treated with epcoritamab+R² remained free from new antilymphoma treatment compared with 64.9% of patients treated with R²

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.

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.

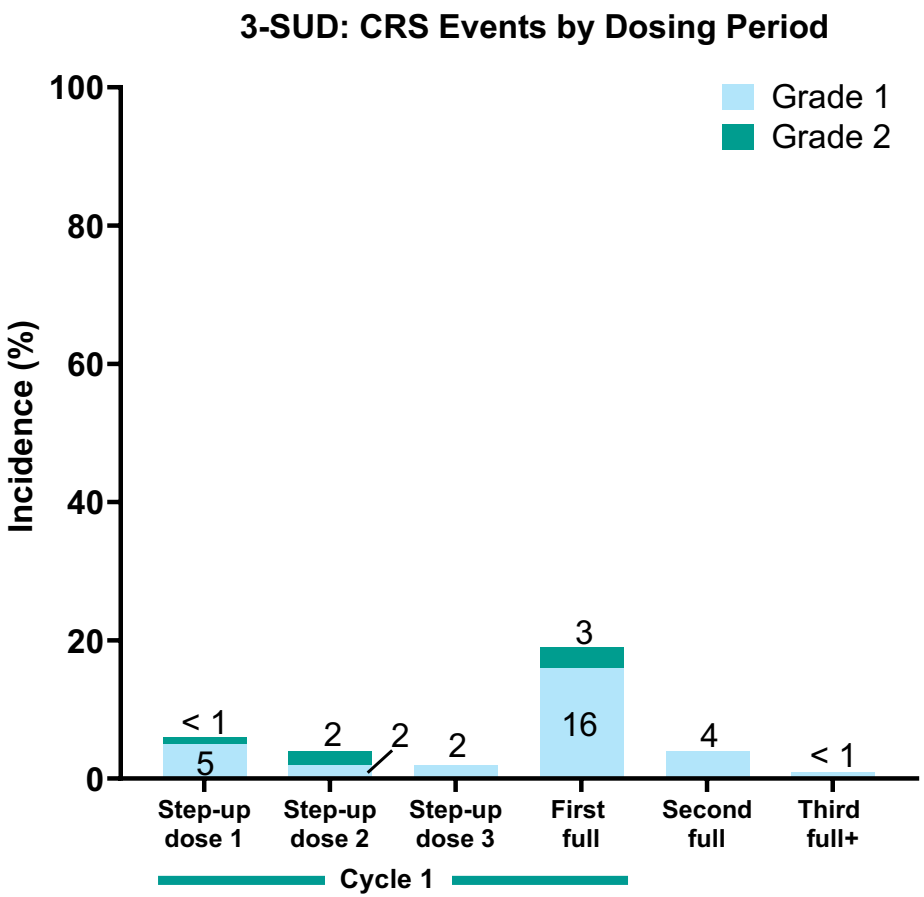
Manageable AEs With No New Safety Signals

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)

[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.

- 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)

CRS Was Low Grade and Predictable With Epcoritamab+R²



	Epcoritamab+R² 2-SUD N = 110	Epcoritamab+R² 3-SUD[a] 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 (%)*		
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 (%)*		
Treated with tocilizumab	12 (24)	9 (26)
Treated with corticosteroid	23 (46)	13 (37)

*Of patients who had CRS

- Hydration and dexamethasone were utilized for CRS prophylaxis
- One event of ICANS was observed and was grade 1
- No discontinuations due to CRS and ICANS. All events resolved.
- No events of CTLS were reported

[a]The 3-SUD regimen was implemented based off the EPCORE NHL-1 FL trial (NCT03625037).[1]

[1]Vose J, et al. *J Clin Oncol* 2024; 42 (suppl 16): 7015.

CELESTIMO (GO42909): Study design

Randomised, open-label, multicentre Phase III study of mosunezutumab (IV) and lenalidomide compared with rituximab and lenalidomide in patients with R/R FL

Eligibility

- Age ≥18 years
- Grade 1–3a CD20+ FL
- ECOG PS 0–2
- ≥1 prior systemic anti-lymphoma therapy
- Target enrolment (Randomised cohort): 400

Stratification factors

- POD 24 status
- Prior lines of therapy (1 vs ≥2)
- Refractoriness to anti-CD20 therapy

Randomised 1:1*

Arm A

Mosunetuzumab + lenalidomide

- Mosunetuzumab IV on C1 [D1 (1 mg), D8 (2 mg), D15 (30 mg)] q3w and C2–12 D1 (30 mg) q4w
- Lenalidomide on C2–12 D1-21 (20 mg)

Arm B

Rituximab + lenalidomide

- Rituximab IV on C1 D1/D8/D15/22 and C3, 5, 7, 9. 11 D1 (375 mg/m²) q4w
- Lenalidomide on C1–12 D1-21 (20 mg)

Arm C

Mosunetuzumab + lenalidomide
(US extension cohort, n=54 pts)

1º endpoint

PFS (IRC-assessed) in ITT

Efficacy follow-up: 5 years from time of randomisation

Secondary and other endpoints†

- PFS (INV-assessed) in ITT, CR rate (by PET-CT), ORR, OS, DOR, DOCR, time to deterioration in physical functioning and fatigue by EORTC QLQC30, safety, PK, immunogenicity, biomarker

IRC, Independent Review Committee.

https://clinicaltrials.gov/study/NCT04712097#study-plan
Nastoupil L, et al. EHA 2022; Poster presentation (#P1125)

Non-randomized single arm US extension of CELESTIMO

Key inclusion criteria

- CD20+ FL Grade 1–3a
- ≥1 prior systemic therapy for FL
- ECOG PS 0–2

Endpoints

- Preliminary efficacy of Mosun-Len: INV-assessed ORR and CR (Lugano criteria[1])
- Safety: incidence and severity of AEs and CRS according to CTCAE v5.0 and ASTCT[2] criteria, respectively

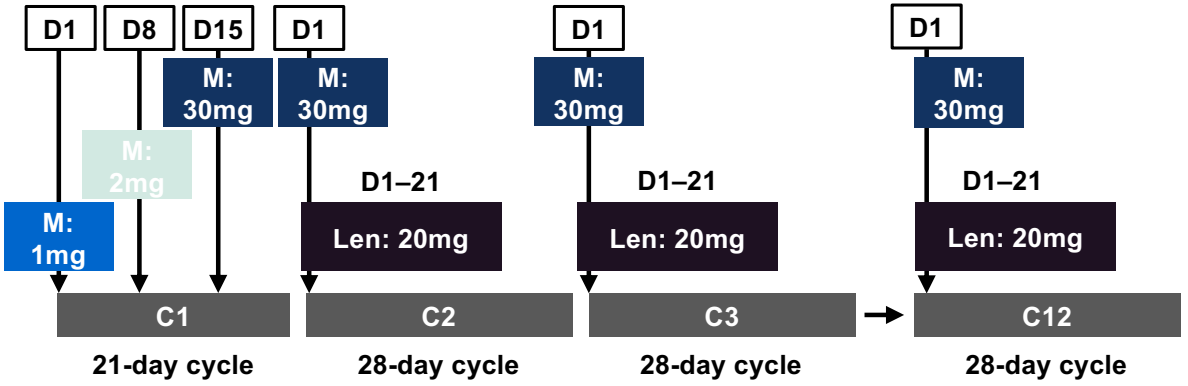
Mosun-Len administration

Mosunetuzumab

- IV administration for 12 cycles (C1: QW; C2–12: D1 of each cycle)
- C1 step-up dosing (CRS mitigation)
- No mandatory hospitalization

Lenalidomide

- Oral administration for 11 cycles (C2–12)



AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; C, Cycle; CR, complete response; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; D, Day; ECOG PS, Eastern Oncology Group performance status; INV, investigator; IV, intravenous; M, mosunetuzumab; ORR, objective response rate; QW, weekly.

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.

Baseline characteristics

n (%), unless otherwise stated		2L+ FL US cohort (n=54)
Age, years	Median (range)	62.0 (37–82)
Sex	Male	32 (59.3)
Race	Asia Black or African American White Multiple* Unknown	3 (5.6) 2 (3.7) 47 (87.0) 1 (1.9) 1 (1.9)
Ethnicity	Hispanic or Latino Not Hispanic or Latino	12 (22.2) 42 (77.8)
ECOG PS	0 1 2	40 (74.1) 13 (24.1) 1 (1.9)
Ann Arbor stage	I/II III/IV	9 (16.7) 45 (83.3)

n (%)		2L+ FL US cohort (n=54)
FLIPI score	0/1 2 3 4 5	n=52† 13 (25.0) 18 (34.6) 17 (32.7) 3 (5.8) 1 (1.9)
FL grade	1/2 3a	n=47† 28 (59.6) 19 (40.4)
POD24	Yes	16 (29.6)
Number of prior lines of therapy	1 ≥2	30 (55.6) 24 (44.4)
Refractory to prior CD20 therapy	Yes	n=48† 19 (39.6)
Relapsed after prior CD20 therapy	Yes	n=48† 17 (35.4)
Double refractory	Yes	n=53† 9 (17.0)

Data cut-off: June 9, 2025. *American Indian or Alaska Native, White. †Missing or partial data.
2L+, at least one prior therapy; FLIPI, Follicular Lymphoma International Prognostic Index; POD24, progressive disease within 24 months of first systemic therapy.

Sano D, et al. ASH 2025; Poster presentation (abstract #1800).

Mosun-Len achieved high response rates in patients with R/R FL

n (%)	2L+ FL US cohort (n=54)
ORR	52 (96.3)
CR	47 (87.0)
PR	5 (9.3)
Stable disease	0
Progressive disease	2 (3.7)

The **median duration of follow-up** was **12.7 months** (range: 5–20)

Data cut-off: June 9, 2025.
PR, partial response.

Sano D, et al. ASH 2025; Poster presentation (abstract #1800).

Mosun-Len had manageable safety

n (%)	2L+ FL US cohort (n=54)
Any grade AE	54 (100)
Mosunetuzumab related	48 (88.9)
Lenalidomide related	50 (92.6)
AE leading to discontinuation of mosunetuzumab	6 (11.1)
AE leading to discontinuation of lenalidomide	10 (18.5)
Grade 3/4 AE	31 (57.4)
Grade 5*	1 (1.9)
Serious AE	15 (27.8)
Mosunetuzumab related	9 (16.7)
Lenalidomide related	4 (7.4)

n (%)	2L+ FL US cohort (n=54)
CRS by ASTCT grading	15 (27.8)
Grade 1	12 (22.2)
Grade 2	2 (3.7)
Grade 3	1 (1.9)
Infections†	31 (57.4)
Grade 1	2 (3.7)
Grade 2	24 (44.4)
Grade 3	3 (5.6)
Grade 4	1 (1.9)
Grade 5	1 (1.9)
Neutropenia/neutrophil count decreased	22 (40.7)
Grade 3/4	18 (33.3)
Febrile neutropenia (Grade 3)	2 (3.7)

CRS events were mainly low grade and all resolved

- Median duration of CRS: 4.0 days (range: 1.0–23.0)
- Median time to onset of first CRS event: 2.0 days (range: 1.0–27.0)

The most common AEs (any grade, by preferred term) were fatigue (57.4%), maculo-papular rash (42.6%), and constipation (42.6%)

Data cut-off: June 9, 2025. *Pneumonia, considered to be mosunetuzumab related. †The most common infections were: COVID-19, 20.4%; sinusitis, 18.5%; and upper respiratory tract infection, 16.7%; which were mainly Grade 2 (44.4%) in severity.

Sano D, et al. ASH 2025; Poster presentation (abstract #1800).

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

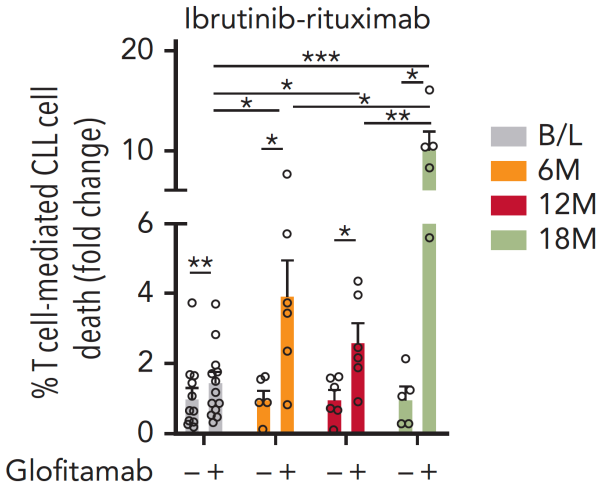
Lorenzo Falchi[1] , Clare Grieve[1], Christina Miah[1], Anastasia Martinova[1], Lauren Wood[1], Joanna Tortora[1], Joseph Roswarski[2], Alexander Boardman[1], Kevin David[1], Paola Ghione[1], Anita Kumar[1], Jennifer Lue[1], Efrat Luttwak[1], Ariela Noy[1], Colette Owens[1], Lia Palomba[1], Raphael Steiner[1], 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

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

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:

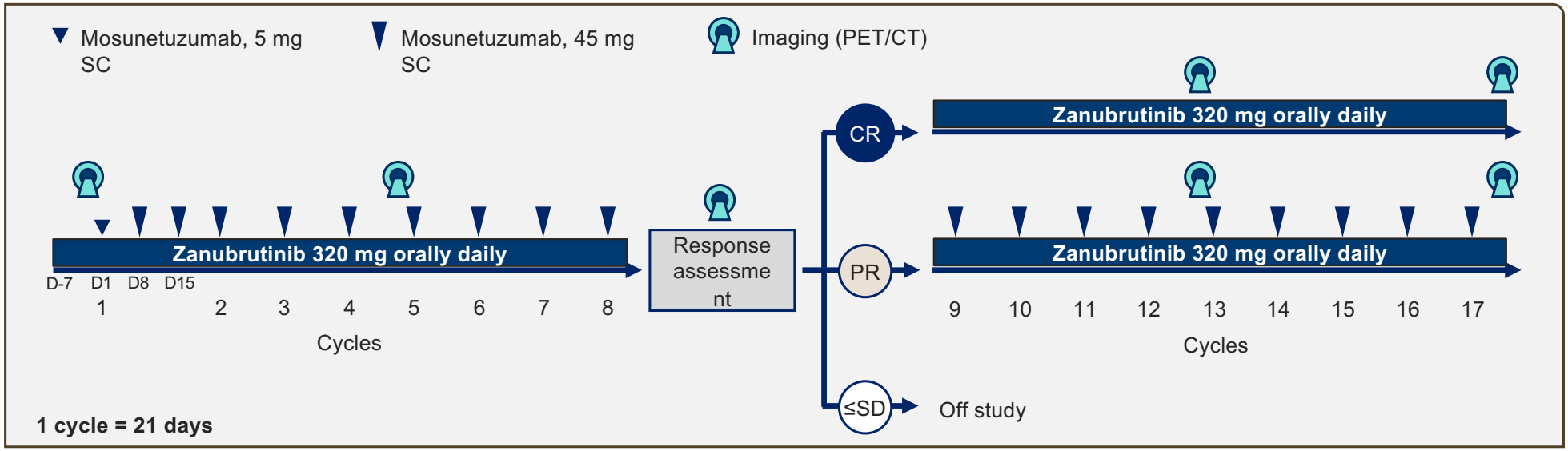
- ≥18 years; ECOG PS 0-2
- CD20+ previously untreated FL
- G1-3A, stage II–IV
- **In need of therapy per GELF criteria**

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

Patient Characteristics

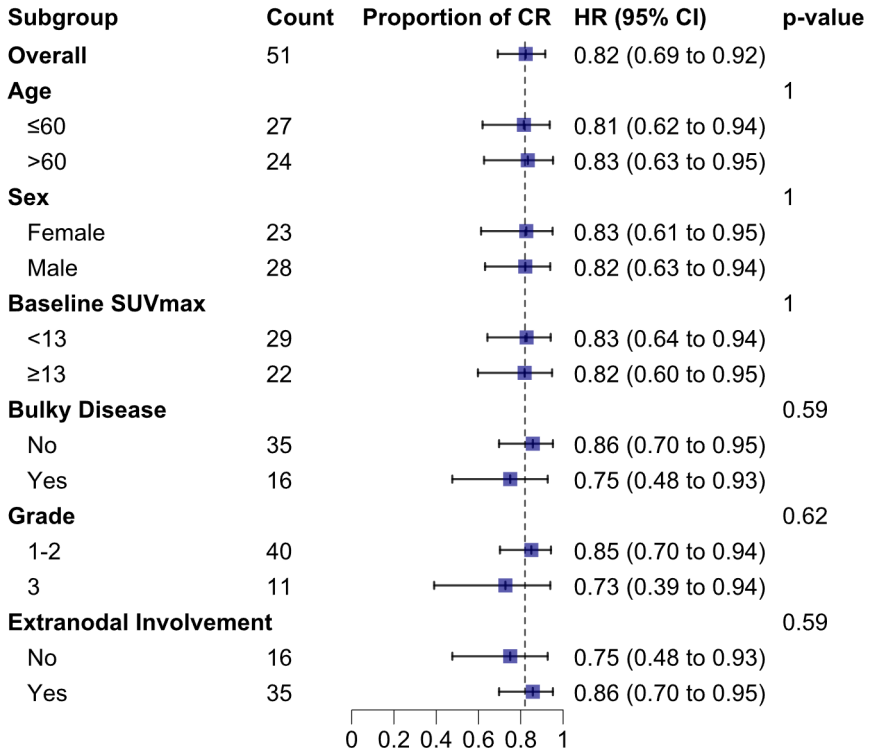
Characteristic	Safety-Evaluable Patients (N=54)
Median Age, years (range)	59 (25 - 79)
Female	26 (48%)
Race	
White	41 (76%)
Asian	6 (11%)
Black	4 (7.4%)
Other	3 (5.6%)
Ethnicity	
Non-Hispanic	46 (85%)
Hispanic	6 (11%)
Unknown	2 (3.7%)
ECOG Status	
0	38 (70%)
1	16 (30%)
Grade	
1-2	42 (78%)
3a	12 (22%)
Lugano Stage	
II	6 (11%)
III	18 (33%)
IV	30 (56%)

Characteristic	Safety-Evaluable Patients (N=54)
Elevated LDH	9 (17%)
Median ALC (range)	1.11 (0.34 - 22.00)
Met GELF criteria	54 (100%)
GELF Criteria	
>3x3cm Nodes	30 (56%)
Mass-Related Symptoms	30 (56%)
Mass > 7cm	23 (43%)
Splenomegaly	20 (37%)
B Symptoms	9 (17%)
Pleural Effusion	5 (9.3%)
Lymphocytosis	3 (5.6%)
Cytopenia	2 (3.7%)
FLIPI Risk Level	
Low (0-1)	16 (30%)
Intermediate (2)	28 (52%)
High (3-5)	10 (19%)
Median SUV_{max} (range)	12.2 (5.6 - 33.6)

LDH, lactate dehydrogenase; ALC, absolute lymphocyte count; FLIPI, follicular lymphoma international prognostic index; GELF, Groupe d'etudes des lymphomes folliculaires; SUV, standardized uptake value

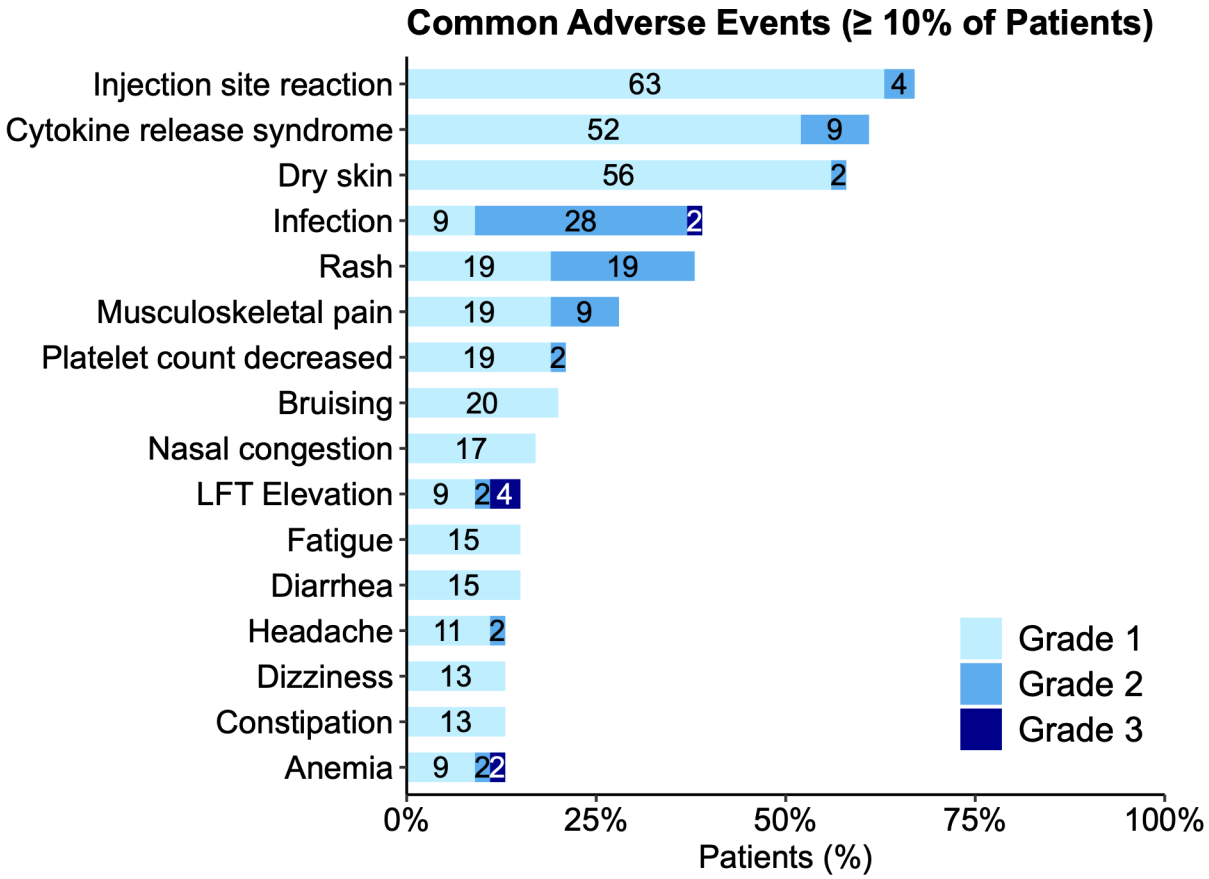
Mosunetuzumab + Zanubrutinib Induced Deep Responses in Most Patients

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

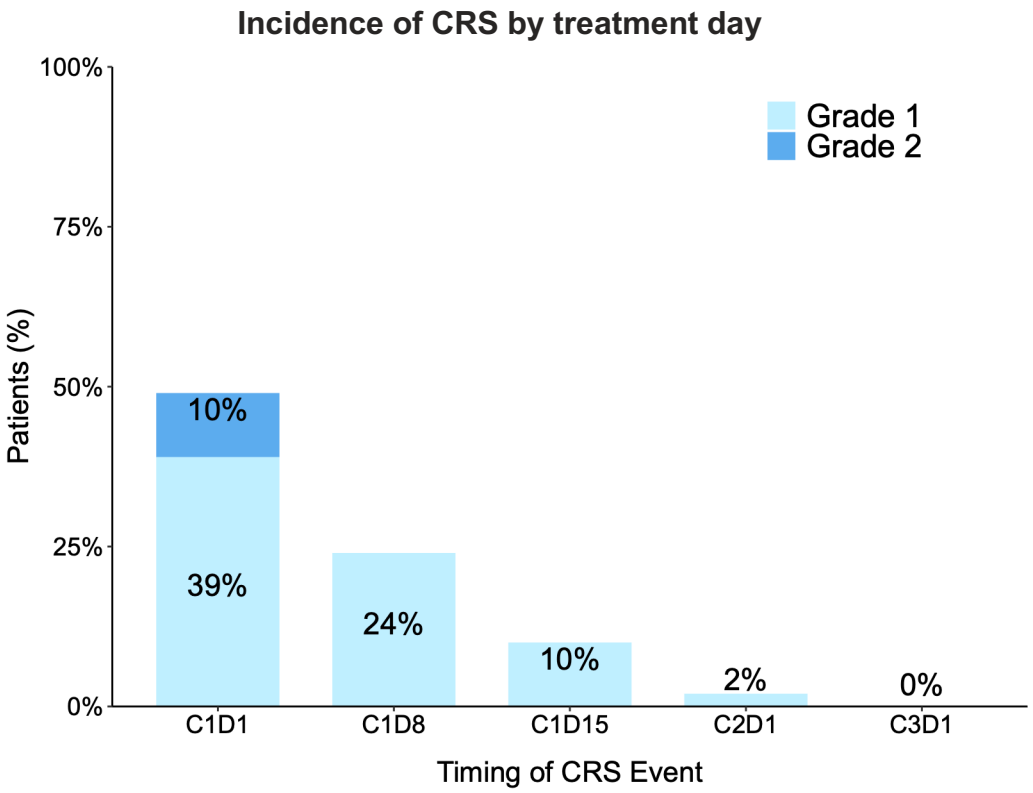
Most Adverse Events Were Low-Grade



- No safety signals were observed for mosunetuzumab or zanubrutinib
- Most AEs were grade 1-2
- No patient discontinued treatment due to AEs

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

CRS was Predictable and Mostly Grade 1



CRS[1]	Safety-evaluable patients (n=54)
Incidence	33 (61%)
Grade 1	28 (52%)
Grade 2	5 (9%)
n. unique CRS episodes	43
Resolved	43 (100%)
Corticosteroid use	21 (39%)
Tocilizumab use	4 (7%)
CRS reported as SAE	5 (9%)

- 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.

[1]Graded per Lee et al. Biol Blood Marrow Transplant 2019 Apr;25(4):625-638

ORAL Abstract Sessions

Conclusions

Long term FUP analyses

- Excellent outcomes with currently available therapies
- Competing events are key determinants in the long term

Relapsed refractory FL

We have a new standard for 2L therapy (Epco- R2)
Mosu Len likely to follow (CELESTIMO)

First Line therapy

BsAbs Combo are highly promising, but…

Sunday, December 7, 09:30 AM - 11:00 AM EST

Monday, December 8, 04:30 PM - 06:00 PM EST