City of Hope®

Multidisciplinary Approaches to Cancer Symposium

Novel Targeted Therapies, Bispecific Antibodies, and CAR T-Cell Therapy in Lymphoma

Focus: Bispecifics in Follicular Lymphoma

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Disclosures

- Consultant/Advisor for Abbvie & Ipsen
- Grant/Research Support from ADC-Therapeutics, Genmab, Genentech & Ipsen

This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

This presentation has been peer-reviewed and no conflicts were noted.

The off-label/investigational use of Odronextamab will be addressed.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

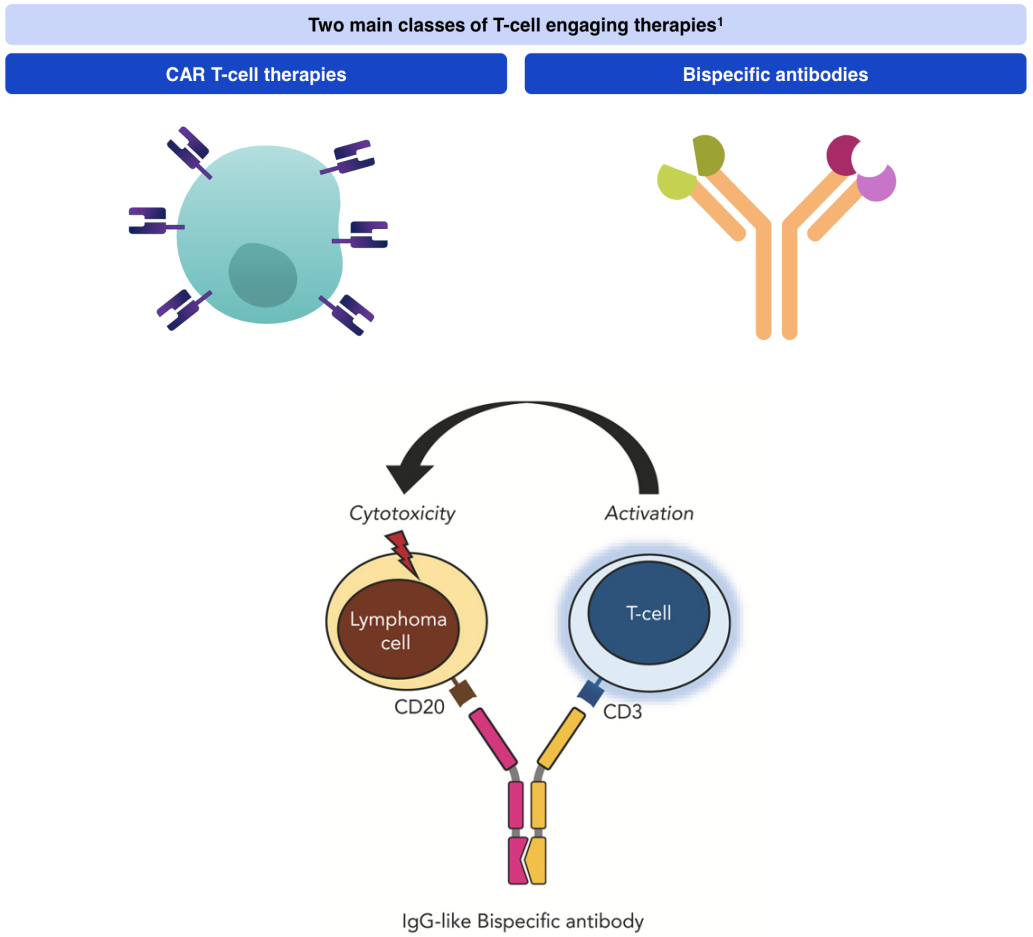
Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

The following CLC & IB components will be addressed in this presentation:

- *What are commonalities and differences among individuals in this patient population and access barriers to treatments.*
- *What are some populations and/or groups who frequently experience disparities in care.*

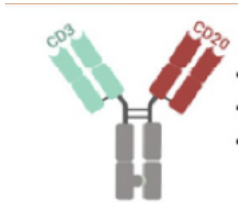
Introduction

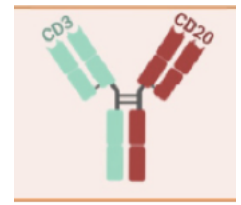
- T-cell engaging therapies have transformed treatment landscape of R/R FL
    - Three FDA approved CD19 directed CAR T-products: Axicabtagene ciloleucel, Tisagenlecleucel, Lisocabtagene maraleucel
    - Two FDA approved CD3/CD20 targeting bispecific antibodies (bsAb): Mosunetuzumab and Epcoritamab
- Goal of new therapies for R/R FL include improved durability of responses, higher survival rates, and manageable long-term and short-term safety profiles
- Focus of this talk will be on the C3/CD20 bispecific antibodies FDA approved and ongoing investigation in FL

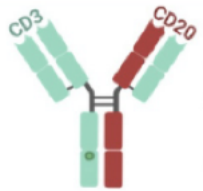


Bispecifics in 3L+ FL

Therapy	Structure	Formulation	Key Phase II study	Treatment schedule
Mosunetuzumab	Full-length, humanized IgG1 CD20:CD3 1:1[1]	IV or SC[2,3]	GO29781 (median follow-up: >36 months)[2,4,5]	**Fixed duration:** Q3W* for up to 17 cycles[2,4]
Epcoritamab†	Full-length, human IgG1 CD20:CD3 1:1[8]	SC[9]	EPCORE NHL-1 (median follow-up: 17.4 months)[10,11‡]	QW, C1–3; Q2W for six cycles (C4–9); Q4W* **until progression**[11]
Odronextamab†	Hinge-stabilized, fully human IgG4 CD20:CD3 1:1[13,14]	IV or SC[14]	ELM-2 (median follow-up: 20.1 months)[15,16]	QW, for four cycles;* Q2W **until progression**[16§]

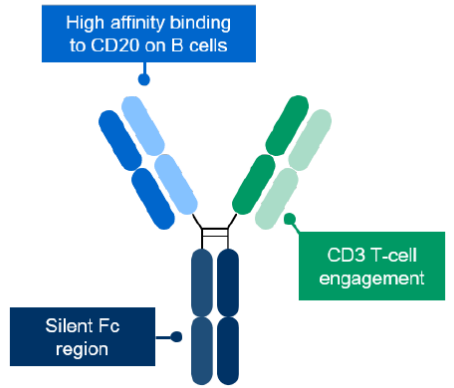






Mosunetuzumab in R/R FL

***Mosunetuzumab**:*
CD20xCD3 bispecific antibody[4]



Pivotal, single-arm, Phase II expansion study in patients with R/R FL and ≥2 prior therapies (NCT02500407)

Key inclusion criteria

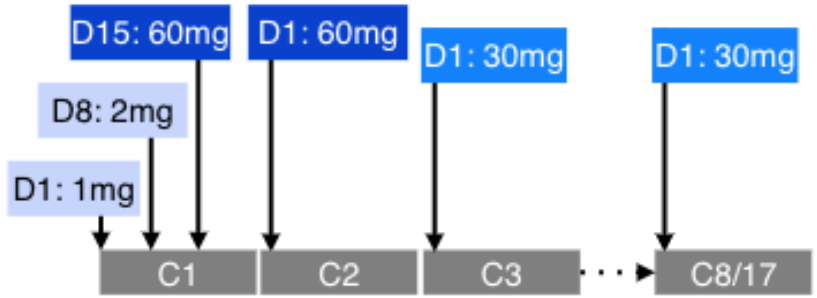
- FL Grade 1–3a
- ECOG PS 0–1
- ≥2 prior therapies including an anti-CD20 antibody and an alkylator

Data analysis

- Study met its primary endpoint: 60% CR rate versus 14% historic control ($p<0.0001$)[1,2]
- Updated efficacy and safety analysis with a median follow-up of 37.4 months

Mosunetuzumab administration

- IV mosunetuzumab administered in 21-day cycles with step-up dosing in C1
- Fixed-duration treatment: 8 cycles if CR after C8; 17 cycles if PR/SD after C8
- Retreatment with mosunetuzumab permitted at relapse for patients who achieved CR
- No mandatory hospitalization



SQ dosing 5 mg (C1D1), 45 mg (C1D8), 45 mg C1D15 until EOT

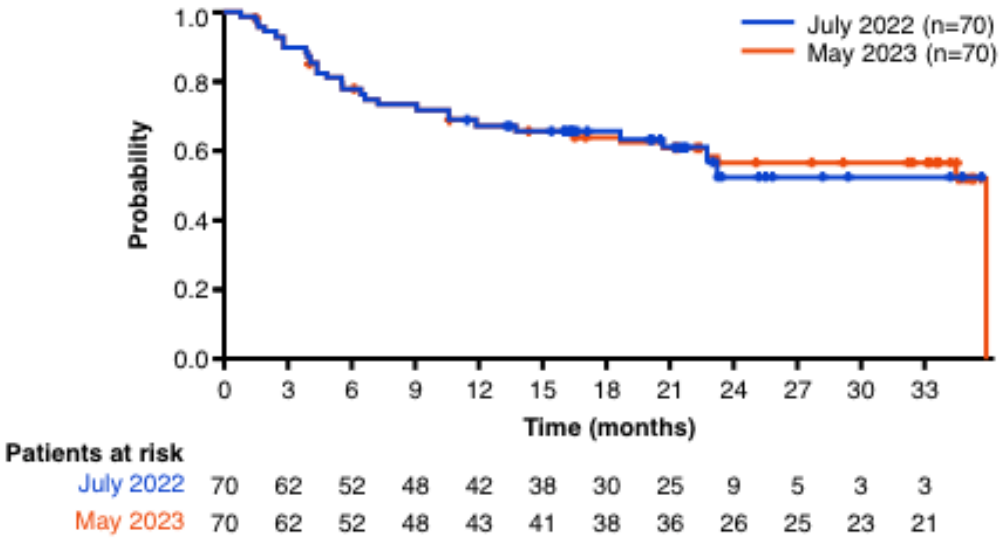
Schuster et al ASH 2023

Mosunetuzumab R/R FL Efficacy

Efficacy

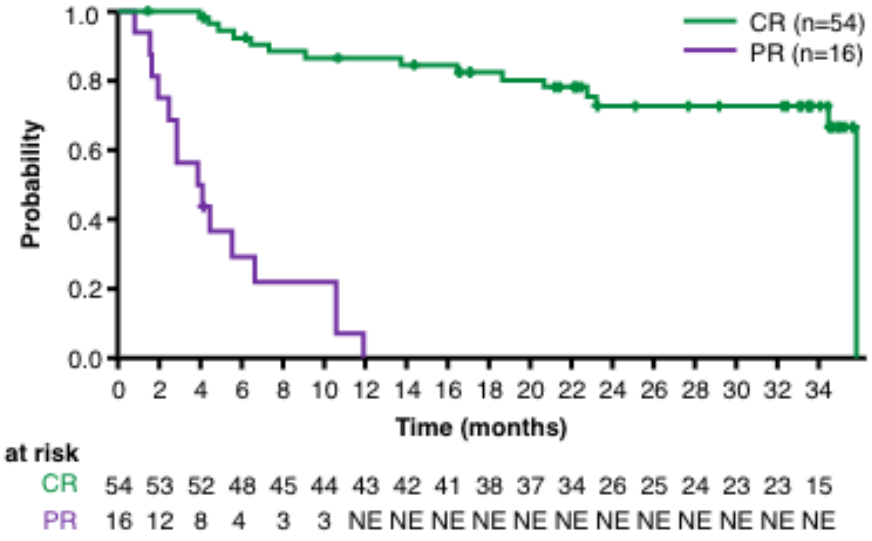
-**CR rate: 60%** (95% CI: 49-70) by both IRC and INV
-**ORR rate: 80%** (95% CI: 70-88) by IRC and 78% (95% CI: 68-66) by INV
-Consistent benefit in patients with double refractory disease and POD24

DOR (July 2022 vs May 2023 data cut-off)



	n=70
Median DOR, months (95% CI)*	35.9 (20.7–NE)
30-month DOR rate, % (95% CI)†	56.6% (44.2–68.9)

DOR for CR vs PR (May 2023 data cut-off)



Median DOR in patients with CR, months (95% CI); n=54*	35.9 (NE–NE)
Median DOR in patients with PR, months (95% CI); n=16*	4.0 (2.5–6.7)

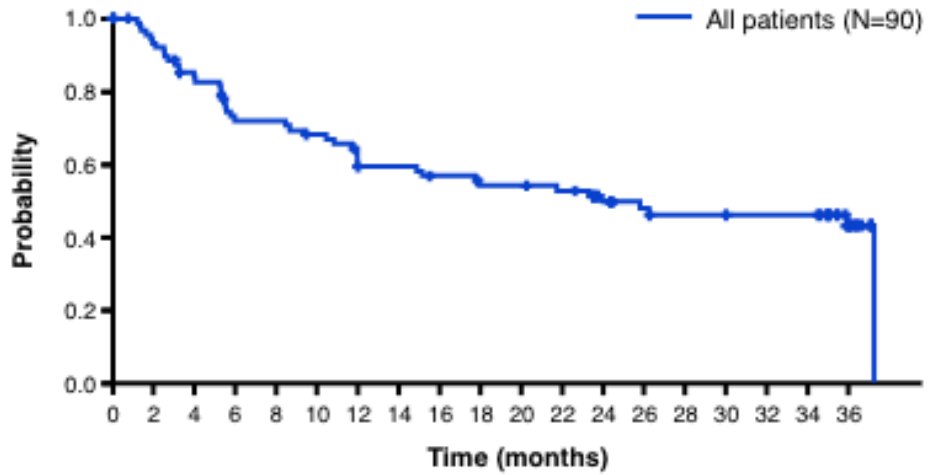
72.7% (95% CI: 60.8–86.8) of patients with a CR are estimated to remain alive and progression-free 30 months after their first response

Schuster et al ASH 2023

Mosunetuzumab R/R FL Efficacy

PFS and OS: median follow-up > 36 months

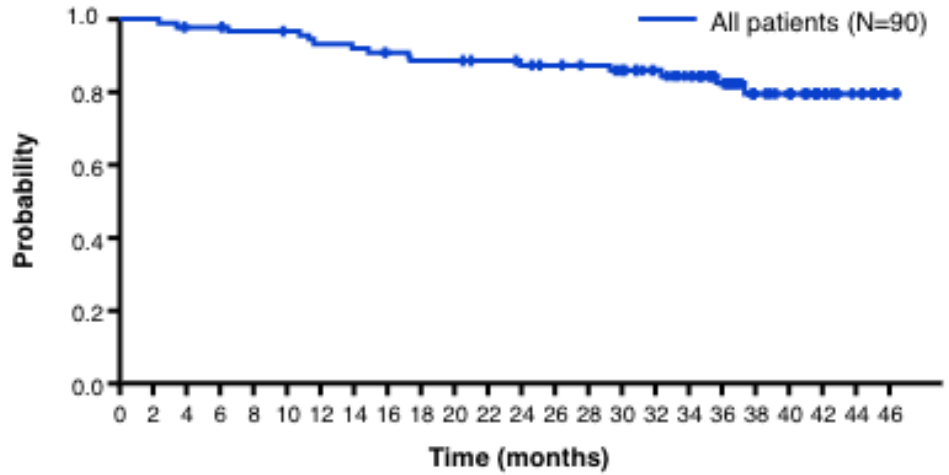
PFS



Patients at risk 90 81 72 60 59 55 47 46 43 40 40 38 30 27 25 25 24 24 13

	N=90
Median PFS, months (95% CI)	**24.0** (12.0–NE)
36-month PFS, months (95% CI)	**43.2%** (31.3–55.2)

OS



Patients at risk 90 89 87 86 85 84 81 80 78 76 76 74 72 70 68 62 56 51 39 26 21 14 8 1

	N=90
Median OS, months (95% CI)	**NR** (NE–NE)
36-month OS, months (95% CI)	**82.4%** (73.8–91.0)

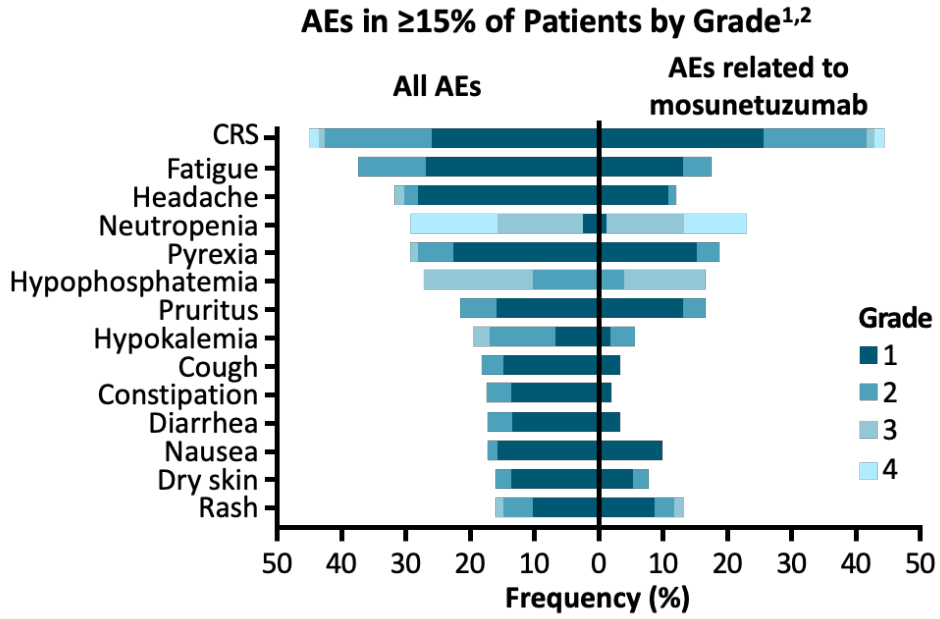
Robust and stable progression-free and overall survival rates at 3 years

Schuster et al. ASH 2023

Mosunetuzumab R/R FL Safety

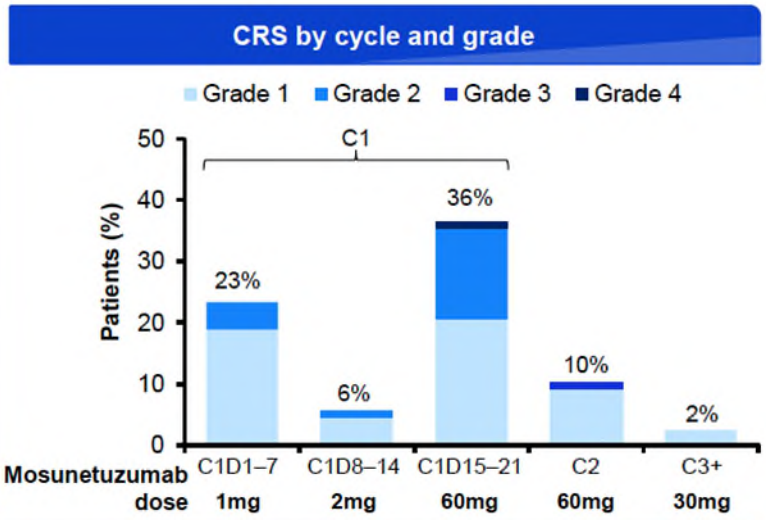
Adverse events (AEs)	N=90
AE	100%
Mosunetuzumab related	92%
Grade 3/4 AE	70%
Mosunetuzumab related	51%
Serious AE	47%
Mosunetuzumab related	33%
Grade 5 (fatal) AE	2%*
Mosunetuzumab related	0
AE leading to treatment discontinuation	4%†
Mosunetuzumab related	2%

Safety Profile



CRS Summary

CRS by ASTCT criteria[1]	N=90
CRS (any grade)	44%
Grade 1	26%
Grade 2	17%
Grade 3	1%
Grade 4	1%
Median time to CRS onset, hours (range)	
C1D1	5.2 (1.2–24)
C1D15	27 (0.1–391)
Median CRS duration, days (range)	3 (1–29)
Corticosteroids for CRS management	11%
Tocilizumab for CRS management	8%
Events resolved	100%



CRS was predominantly low grade and during Cycle 1
All CRS events resolved; no new events were reported with 10 months of additional follow-up

Single Agent Mosun in Frontline FL

Response, %	Patients (N = 45)
Overall response	96
• Complete response	76
• Partial response	20
Stable disease	2
Progressive disease	2

Response Across Risk Groups, %	Complete Response	Partial Response
All patients (N = 45)	76	20
Grade		
• 1-2 (n = 34)	76	21
• 3A (n = 11)	73	18
Bulky disease (>7 cm)		
• No (n = 31)	74	19
• Yes (n = 14)	79	21
SUV_{max}		
• <13 (n = 33)	79	18
• ≥13 (n = 12)	67	25

Median follow-up: 5.8 months

Falchi et al. ASH 2023. Abstract 604

Epcoritamab in R/R FL: Pivotal EPCORE NHL-1 Study

Dose expansion

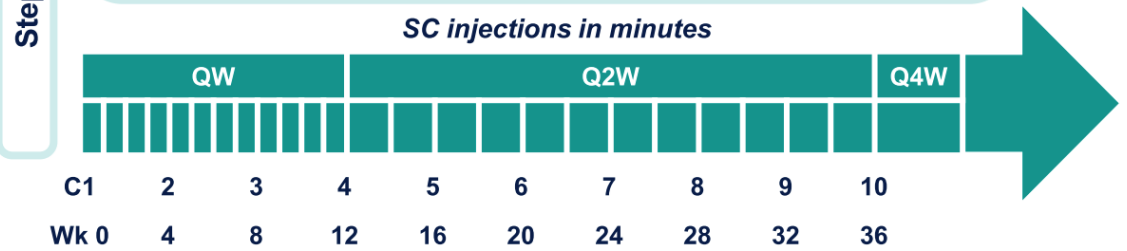
Key inclusion criteria[a]:

- R/R CD20+ mature B-cell neoplasm
- ECOG PS 0–2
- ≥2 prior lines of antineoplastic therapy, including ≥1 anti-CD20 mAb
- Prior treatment with an alkylating agent or lenalidomide
- FDG-avid disease by PET/CT
- Prior CAR T allowed

Data cutoff: April 21, 2023
Median follow-up: 17.4 mo

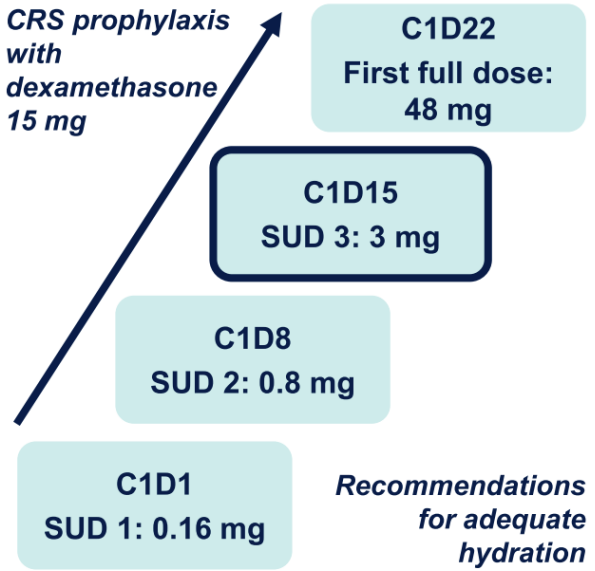
Step-up dosing[b]

Epcoritamab SC RP2D 48 mg
Treatment until PD[c] or unacceptable toxicity
R/R FL grade 1–3A expansion cohort, N=128



- **Primary endpoint:** ORR by independent review committee (IRC)
- **Key secondary endpoints:** MRD[d], DOR, TTR, PFS, OS, CR rate, and safety/tolerability

C1 optimization



- Hospitalization not mandated in this setting
- **Primary objective:** Assess impact on risk and severity of CRS

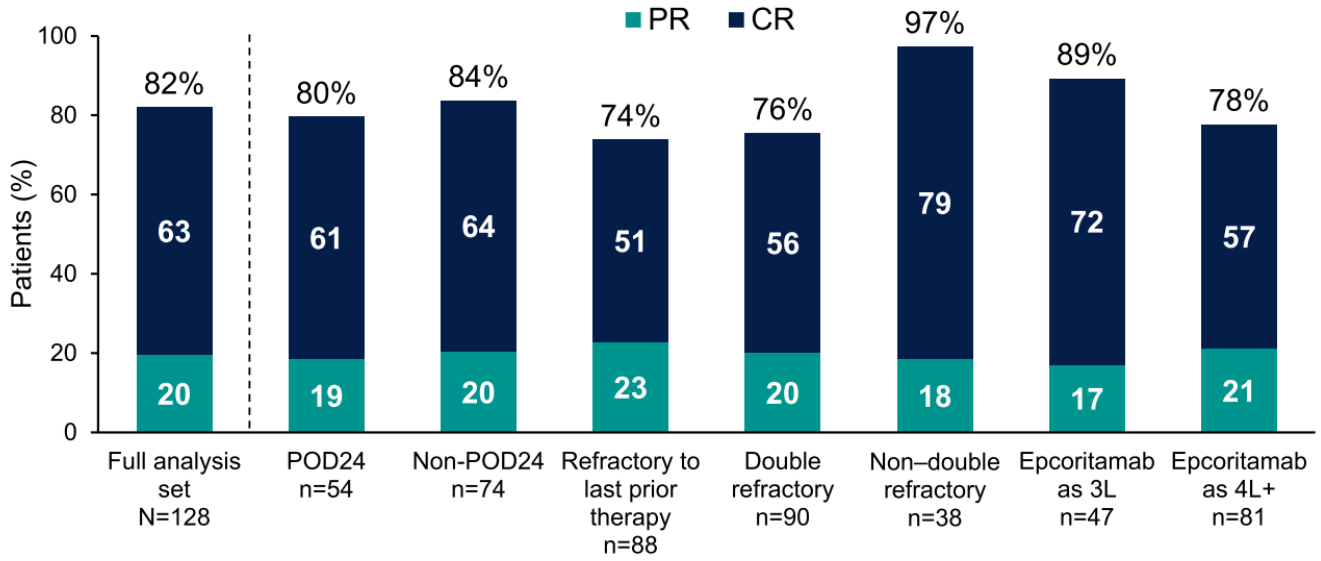
Cycle 1 Step-Up Dosing*

*With prednisolone prophylaxis.
To mitigate CRS.
*Hospitalization mandated for 24 hr following first full dose

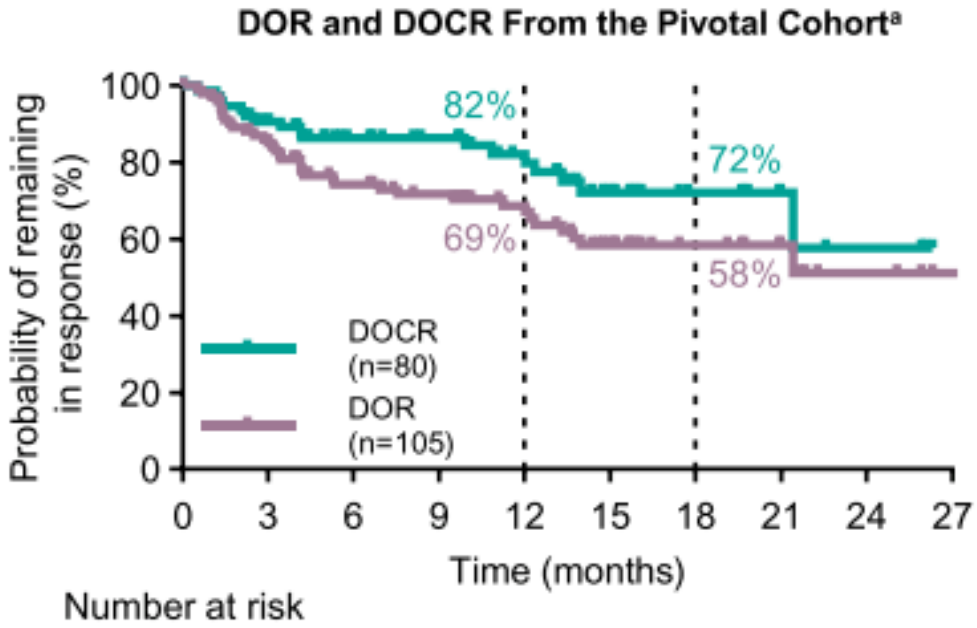
Epcoritamab SC
D1: 0.16 mg
D8: 0.8 mg
D15: 48 mg
D22: 48 mg

Epcoritamab in R/R FL: Response

ORRs and CR Rates Were High Regardless of Subgroup

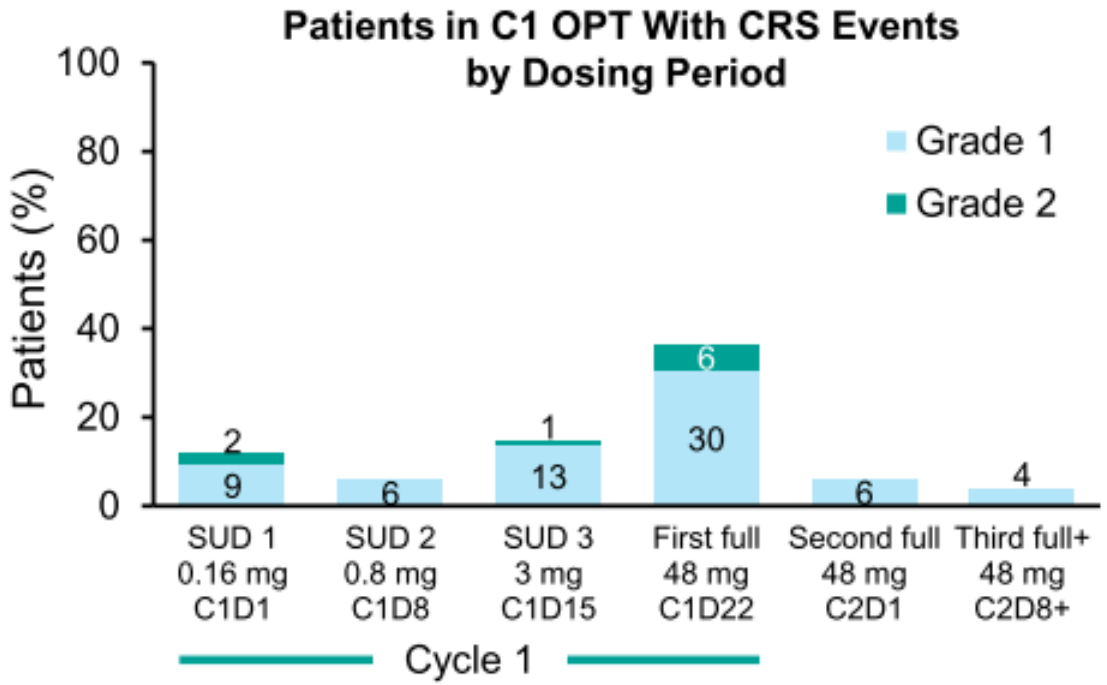


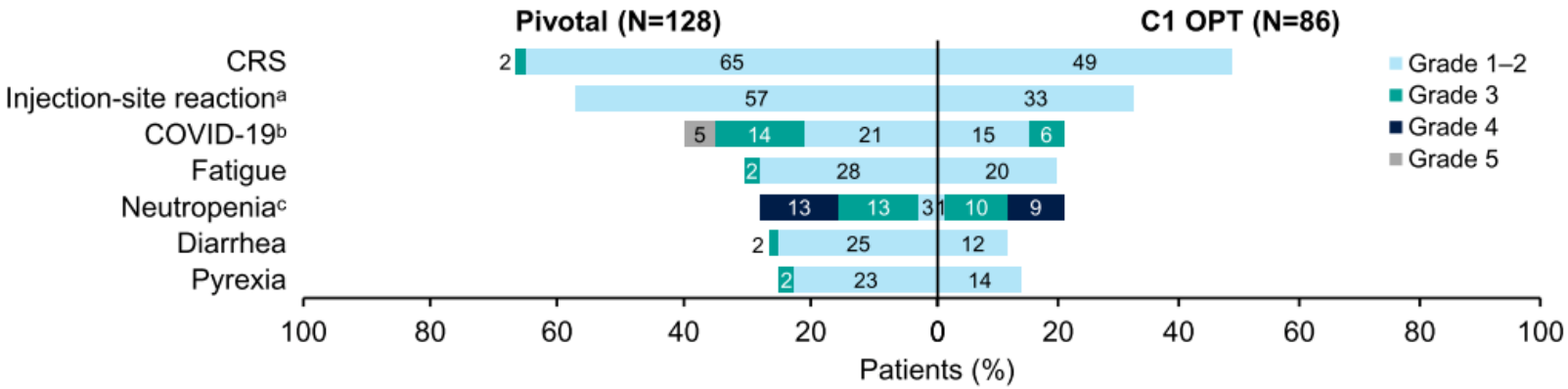
Median follow-up of 17.4 mos
Median PFS: 15.4 months
Median OS: not reached



Epcoritamab in R/R FL: Safety

	Pivotal N=128	C1 OPT N=86
CRS,[a] n (%)	85 (66)	42 (49)
Grade 1	51 (40)	34 (40)
Grade 2	32 (25)	8 (9)
Grade 3	2 (2)	0
Treated with tocilizumab, n (%)	31 (24)	10 (12)
Leading to epcoritamab discontinuation, n (%)	**0**	**0**
CRS resolution, n/n (%)	**85/85 (100)**	**42/42 (100)**
Median time to resolution, d (range)	2 (1–54)	2 (1–14)
ICANS, n (%)	8 (6)[b]	0



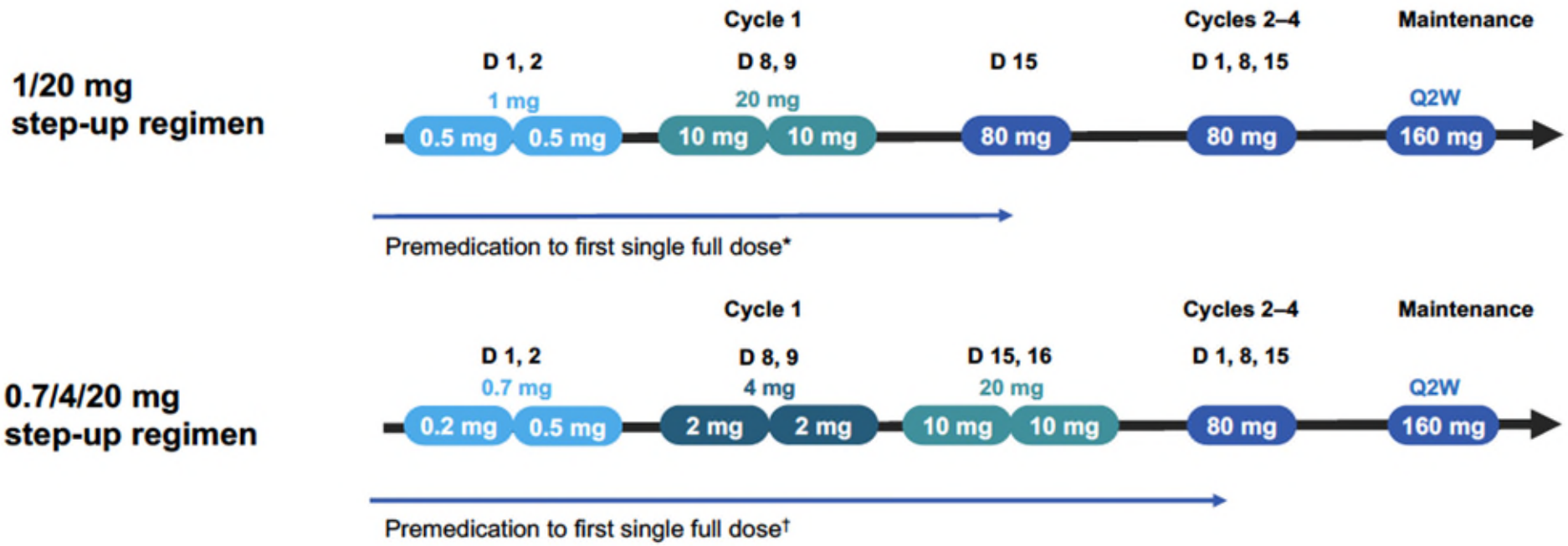


- Linton et al. ASH 2023, Vose ASCO 2024

Odronextamab FL Dosing

Cycle 1 step-up regimen optimized during the course of the study to further mitigate the risk for cytokine release syndrome

- The study initiated with a Cycle 1 step-up regimen of 1/20/80 mg
- This was modified to 0.7/4/20 mg during Cycle 1 to further mitigate the risk of CRS



Kim. ASH 2022. Abstr 949. NCT03888105.

Odronextamab R/R FL: Efficacy

Best overall response	Independent central review N=121*	Investigator evaluation N=121*
Objective response rate (ORR)†	**81.8%** [95% CI: 73.8–88.2%]	81.8% [95% CI: 73.8–88.2%]
Complete response	**75.2%**	70.2%
Partial response	6.6%	11.6%
Stable disease	5.8%	2.5%
Progressive disease	4.1%	5.8%

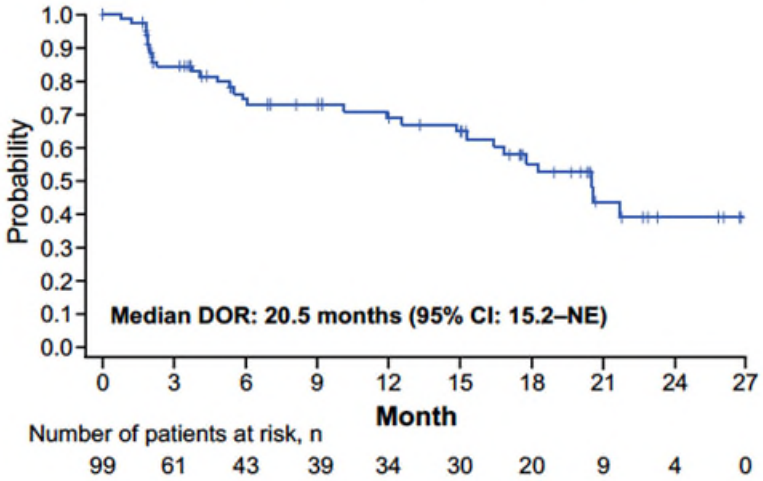
Week 12 response assessment by independent central review	1/20 step-up regimen N=68	0.7/4/20 step-up regimen N=53
ORR	72.1% [95% CI: 59.9–82.3%]	75.5% [95% CI: 61.7–86.2%]
Complete response	61.8%	71.7%

- Majority of R/R FL patients achieved a complete response
- 92% of responders were complete responders
- Consistent efficacy observed at Week 12 regardless of Cycle 1 step-up regimen

Kim. ASH 2022. Abstr 949. .

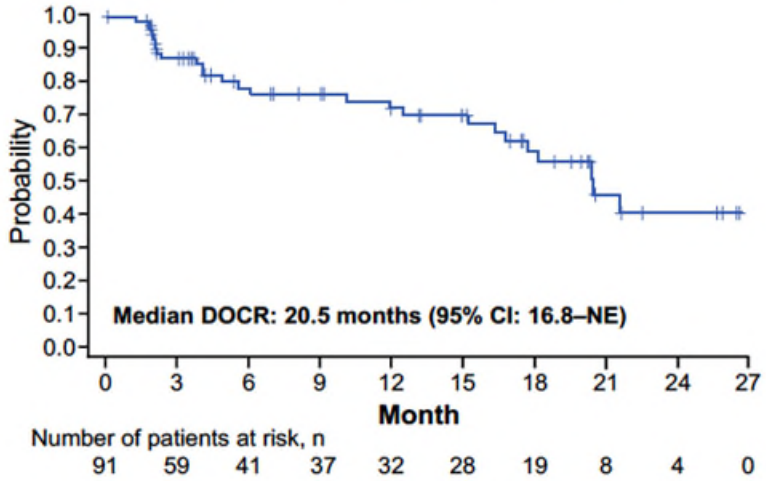
Odronextamab R/R FL: Efficacy

Duration of response – Independent central review



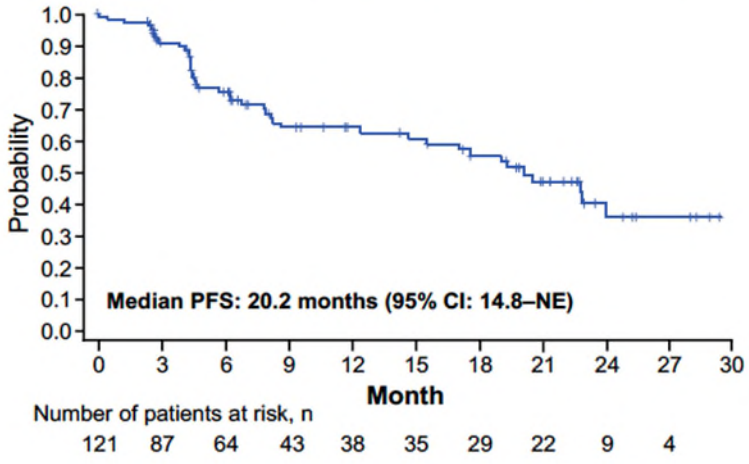
- 12-month DOR: 68.8% (95% CI: 55.9–78.7)
- 18-month DOR: 55.0% (95% CI: 40.6–67.3)

Duration of complete response – Independent central revie



- 12-month DOCR: 72.2% (95% CI: 58.7–81.9)
- 18-month DOCR: 59.1% (95% CI: 43.6–71.6)

Progression-free survival – Independent central review



- 12-month PFS rate: 64.0% (95% CI: 52.7–73.3)
- 18-month PFS rate: 55.3% (95% CI: 43.1–65.8)

Data cut-off date: Sep 15, 2022

Median follow-up 22.4 months (range: 2.6-33.0)

Kim. ASH 2022. Abstr 949. .

Odronextamab in R/R FL: Safety

n, (%)	1/20 regimen (N=68)	0.7/4/20 regimen (N=63)
CRS any Grade	38 (55.9%)	36 (57.1%)
Grade 1	22 (32.4%)	28 (44.4%)
Grade 2	12 (17.6%)	7 (11.1%)
Grade 3	4 (5.9%)	1 (1.6%)
Grade 4	0	0
Grade 5	0	0
Received corticosteroids	11 (16.2%)	17 (27.0%)
Received tocilizumab	9 (13.2%)	12 (19.0%)
Received vasopressors	4 (5.9%)	1 (1.6%)

- 0.7/4/20 mg step-up regimen reduced the incidence of grade 2 and grade 3 CRS
- Approximately half of patients with R/R FL had CRS, mostly grade 1
- Only 1 case of grade 3 CRS with 0.7/4/20 mg step-up regimen and no grade 4 or higher CRS events
- All CRS events resolved with a median time to resolution of 2 days (range 1–51)
- No patients required mechanical ventilation or ICU admission for the management of CRS

n (%)	1/20 regimen (N=68)	0.7/4/20 regimen (N=63)	All patients (N=131)
ICANS, any grade	1 (1.5%)	0	1 (0.8%)
Grade ≥3	0		0
Infusion related reaction, any grade	21 (30.9%)	16 (25.4%)	37 (28.2%)
Grade ≥3	4 (5.9%)	2 (3.2%)	6 (4.6%)
Infection, any grade	51 (75.0%)	35 (55.6%)	86 (65.6%)
Grades 1–2	23 (33.8%)	21 (33.3%)	44 (33.6%)
Grades 3–4	19 (27.9%)	11 (17.5%)	30 (22.9%)
Grade 5	9 (13.2%)	3 (4.8%)	12 (9.2%)
Tumor lysis syndrome, any grade	1 (1.5%)	0	1 (0.8%)
Grade ≥3	1 (1.5%)		1 (0.8%)

Building On the Benefits of Monotherapy

Monotherapy with bispecific antibodies[1–4]

- High response rates
- Manageable safety profiles

Can we further optimize the efficacy and safety of these therapies?

Potential benefits of combination therapy

Increased efficacy through synergistic/additive effects[5,6]

Targeting multiple pathways minimizes drug resistance[5,6]

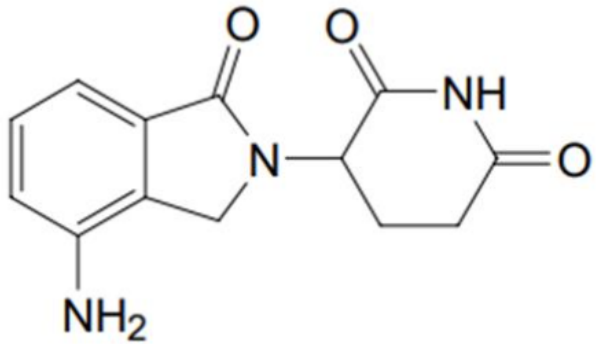
Rationale for Combinations with Lenalidomide

Lenalidomide has **additive/synergistic activity** with anti-CD20 antibodies in preclinical lymphoma models and in patients with R/R FL[1,2]

Lenalidomide is a potent **immunomodulatory** agent:[1]

- Activates CD28 and enhances T-cell responses[3]
- Leads to **cytokine production**[1]
- Has direct **anti-proliferative activity** against lymphoma cells[1]

Lenalidomide: oral immune modulator[1,4]



▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

1. Gribben JG, et al. J Clin Oncol 2015;33:2803–11; 2. Morschhauser F, et al. Blood 2021;138(S1):129; 3. Kotla V, et al. J Hematol Oncol 2009;2:36; 4. Reddy LM, et al. E-J Chem 2011;9:1165–74; 5. Sun LL, et al. Sci Transl Med 2015;7:287ra70.

Bispecific Antibody Combination Therapy in R/R FL

Therapy	Trial (Phase)	Regimen	Patients (R/R FL cohorts)	Treatment duration and administration	Primary endpoint
Mosunetuzumab	**CO41942** (Phase Ib/II)[1,2]	Mosun-Len	187	**Mosun** (IV/SC) 12 cycles: C1 SUD; C2–12 Q4W **Len** (oral) 11 cycles: C2–12	Safety
	CELESTIMO (Phase III)[3,4]	Mosun-Len versus R-Len*	~400†	**Mosun** (IV) 12 cycles: C1 SUD; C2–12 Q4W **Len** (oral) 11 cycles: C2–12	PFS (by IRC)
Epcoritamab	**EPCORE NHL-2** (Phase I/II)[5,6]	Epcoritamab + R-Len	111	**Epcoritamab** (SC) 12 cycles: C1–3 QW (SUD); C4–9 Q2W; C10–12 Q4W OR C1–2 QW; C3 onwards Q4W for up to 2 years **R** (IV) plus **Len** (oral) 12 cycles	Safety
	EPCORE FL-1 (Phase III)[7,8]	Epcoritamab + R-Len versus R-Len‡	~520†	**Epcoritamab** (SC) 12 cycles: C1 SUD; C2–3 QW; C4–12 Q4W **R** (IV) 5 cycles plus **Len** (oral) 12 cycles	PFS (by IRC)
Odronextamab	**OLYMPIA-5** (Phase III)[9,10]	Odronextamab-Len versus R-Len‡	~352†	**Odronextamab** (IV) 12 cycles: C1 SUD; C2–3 QW; C4–6 Q2W; C7–12 Q4W **Len** (oral) 12 cycles	PFS (by IRC)

Investigational drug/indications, not authorized.
*R-Len: R (IV) 6 cycles plus Len (oral) 12 cycles. †Planned enrolment.
‡R-Len: R (IV) 5 cycles plus Len (oral) 12 cycles.
IRC, Independent Review Committee; Mosun, mosunetuzumab.

1. Morschhauser F, et al. ASH 2021; Oral presentation (abstract #129); 2. NCT04246086. Available at: https://clinicaltrials.gov; 3. Nastoupil L, et al. ASCO 2022; Poster presentation (abstract #TPS7588); 4. NCT04712097. Available at: https://clinicaltrials.gov; 5. Merryman R, et al. ASCO 2023; Oral presentation (abstract #7506); 6. NCT04663347. Available at: https://clinicaltrials.gov; 7. Falchi L, et al. ASH 2023; Oral presentation (abstract #3053); 8. NCT05409066. Available at: https://clinicaltrials.gov; 9. Vitolo U, et al. ASCO 2024 (abstract #TPS7094); 10. NCT06149286. Available at: https://clinicaltrials.gov.

Phase 1b CO41942 Trial of Mosun-Len in R/R FL

Study overview

Key inclusion criteria

- CD20+ FL Grade 1–3a
- R/R to ≥1 prior chemo-immunotherapy regimen including an aCD20 antibody; prior lenalidomide allowed
- ECOG PS 0–2

Objectives

- Primary: safety and tolerability of M-Len
- Other: efficacy (response, durability of response) and pharmacokinetics

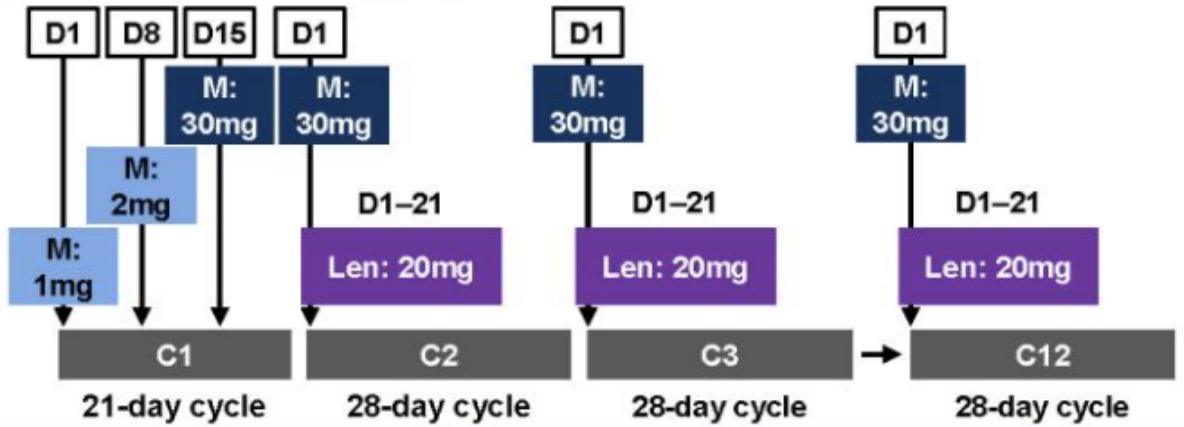
M-Len administration

Mosunetuzumab

- IV administration for 12 cycles (C1: Q3W; C2–12: Q4W)
- C1 step-up dosing (CRS mitigation)
- No mandatory hospitalization

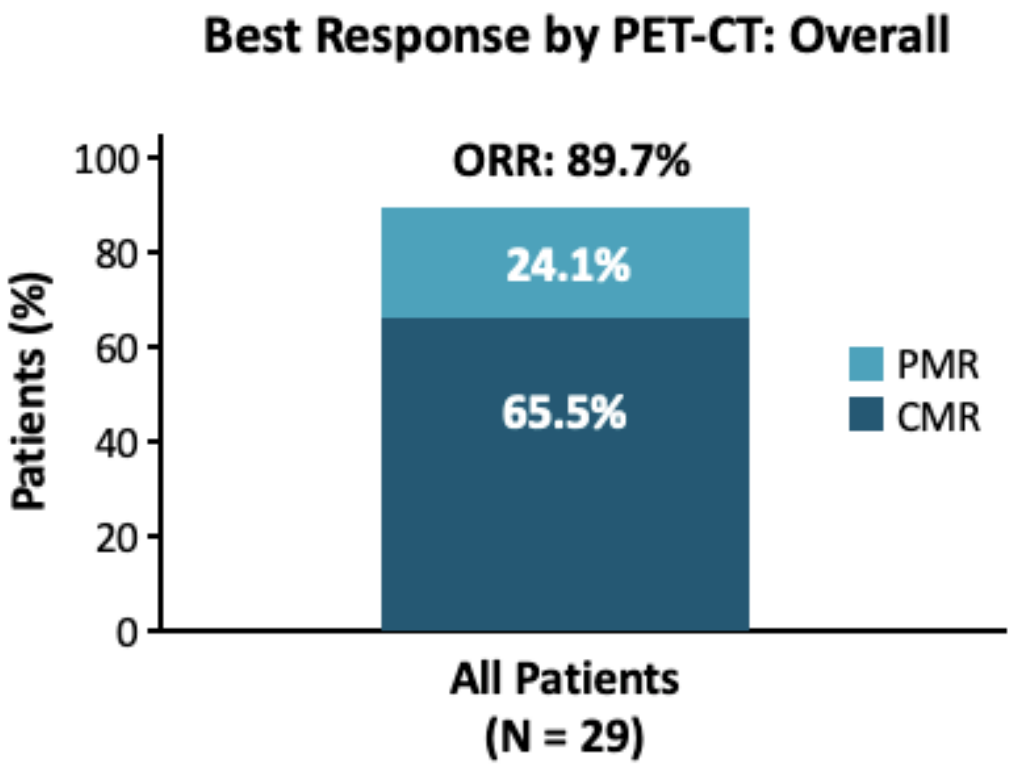
Lenalidomide

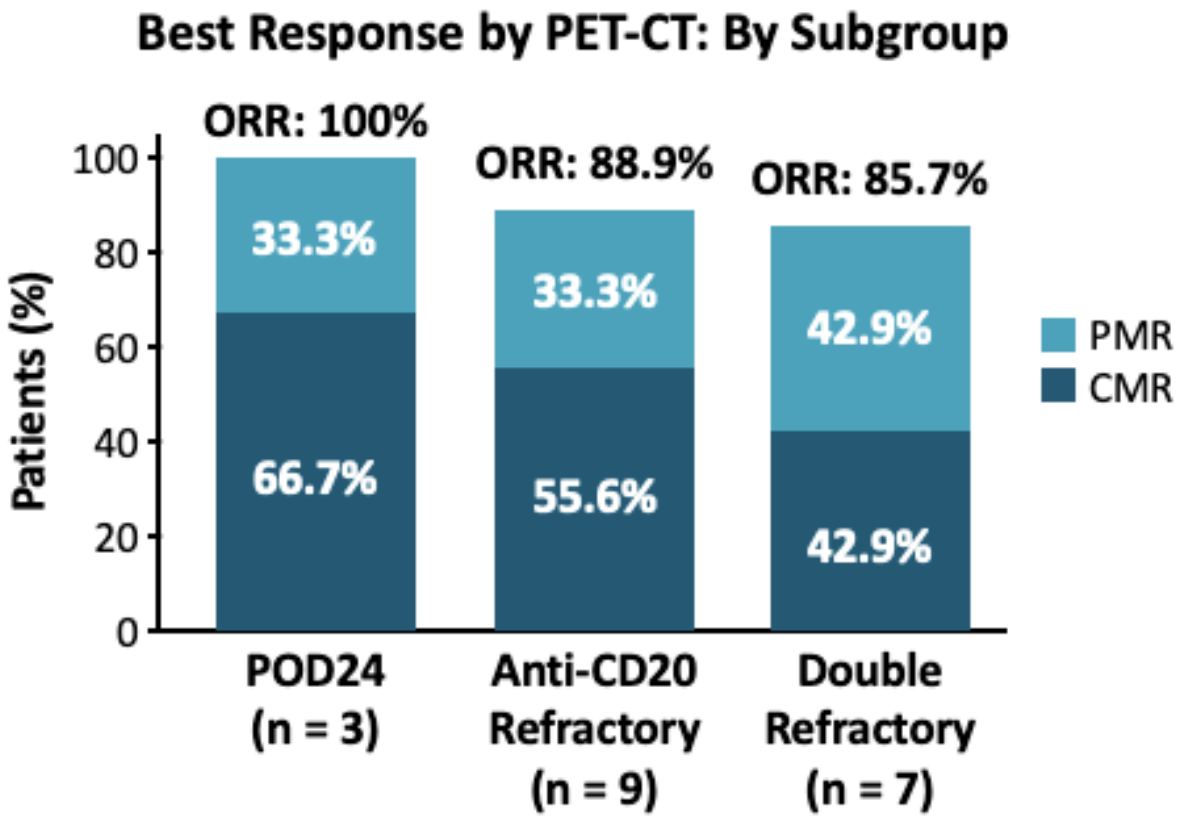
- Oral administration for 11 cycles (C2–12)



C, Cycle; CRS, cytokine release syndrome; D, Day; IV, intravenous; Q3W, once every 3 weeks; Q4W, once every 4 weeks

Mosun-Len in R/R FL: Efficacy





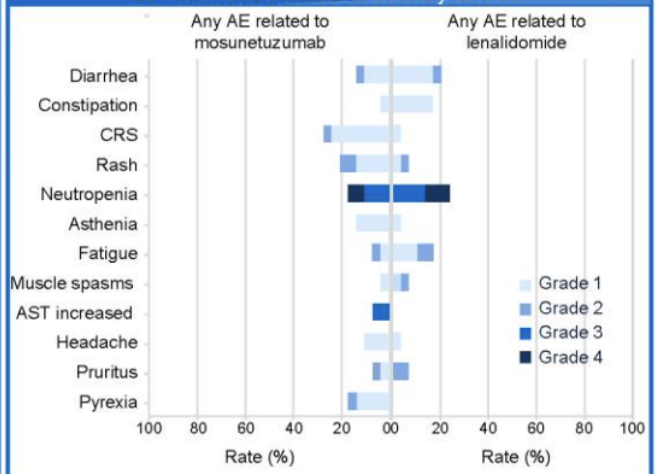
- Median time to first/best response: 2.5 mo (range: 1.4-5.3)/2.5 mo (range: 1.4-10.7)
- High ORR and CMR rate in overall population, including those with high-risk disease

Mosun-Len in R/R FL: Safety

- Median duration of follow-up: 5.4 months (range: 3–12)

	N=29
AE Related to mosunetuzumab / lenalidomide	29 (100%) 27 (93.1%) / 23 (79.3%)
Grade 3–4 AE Related to mosunetuzumab / lenalidomide	13 (44.8%) 1 (3.4%) / 1 (3.4%)
Serious AE Related to mosunetuzumab / lenalidomide	9 (31.0%) 6 (20.7%) / 1 (3.4%)
Grade 5 (fatal) AE	0
AE leading to mosunetuzumab / lenalidomide discontinuation	0 / 1 (3.4%)
AE leading to mosunetuzumab dose delay	6 (20.7%)
AE leading to lenalidomide dose reduction	2 (6.9%)
AE leading to lenalidomide temporary dose interruption	6 (20.7%)
AE leading to lenalidomide dose reduction AND temporary dose interruption	4 (13.7%)

AEs with ≥15% incidence overall and corresponding rates of treatment-related events by Grade



- **M-Len had a favorable safety profile. No AEs led to mosunetuzumab discontinuation.**

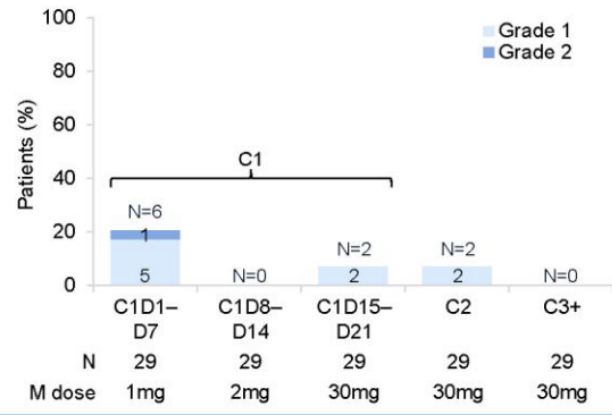
AE, adverse event; AST, aspartate aminotransferase

Adverse Event Summary

Cytokine Release Syndrome

	N=29
CRS (any Grade)*	8 (27.6%)
Grade 1	7 (24.1%)
Grade 2	1 (3.4%)†
Grade ≥3	0
Serious AE of CRS (any Grade)	4 (13.8%)‡
Median time to first CRS onset, days (range)	1 (1–28)
Median CRS duration, days (range)	3 (2–5)
Corticosteroids for CRS management	0
Tocilizumab for CRS management	0
CRS leading to mosunetuzumab discontinuation	0
CRS resolved	8 (100%)

Patients (%) with CRS by Cycle and Grade



- **CRS was low Grade and confined to C1–2. No increase in rate or severity with addition of lenalidomide.**

*assessed using ASTCT criteria[1]; †patient with WBC of 108k/uL at treatment initiation and circulating FL; patient had fever and hypoxia that required 2L nasal cannula oxygen; ‡Grade 1: 3 patients (10.3%); Grade 2: 1 patient (3.4%)

1. Lee et al. Biol Blood Marrow Transplant 2019;25:625–38

Mosun + Len in Frontline FL

Study Design

Key inclusion criteria

- CD20+ FL Grade 1–3a
- Previously untreated and require systemic therapy*
- ECOG PS 0–2

Objectives

- Primary: Safety and tolerability of Mosun-Len
- Other: Efficacy (response assessed every 3 cycles,† durability of response), biomarkers, and PK

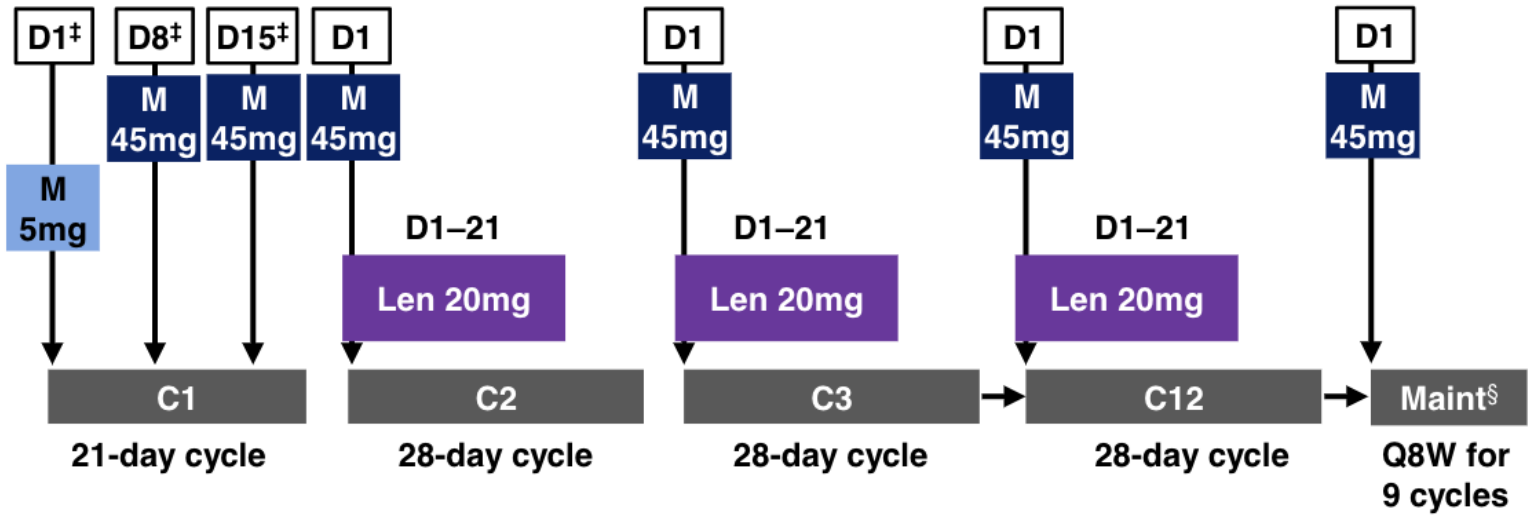
Mosun-Len administration

Mosun

- SC administration for 12 cycles (C1: Q3W; C2–12: Q4W)
- C1 step-up dosing (CRS mitigation)
- No mandatory hospitalization

Len

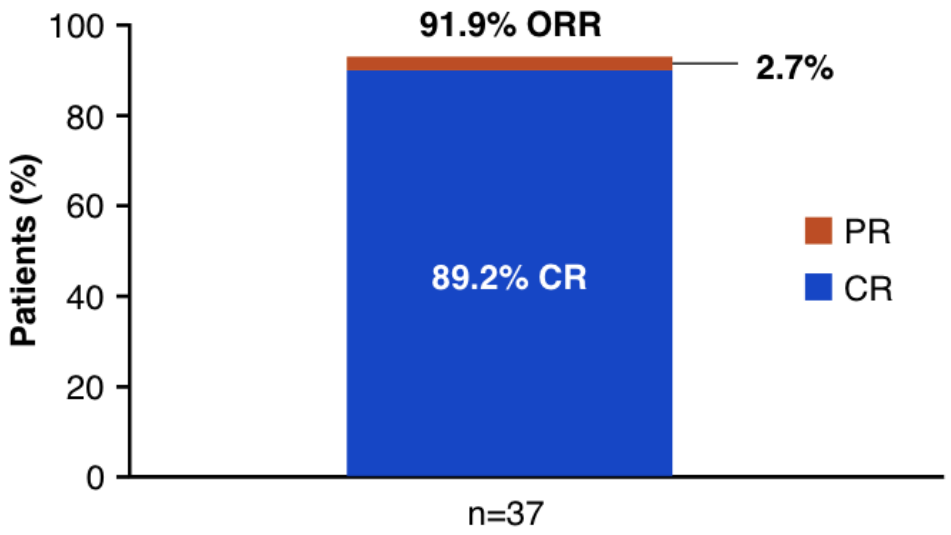
- Oral administration for 11 cycles (C2–12)



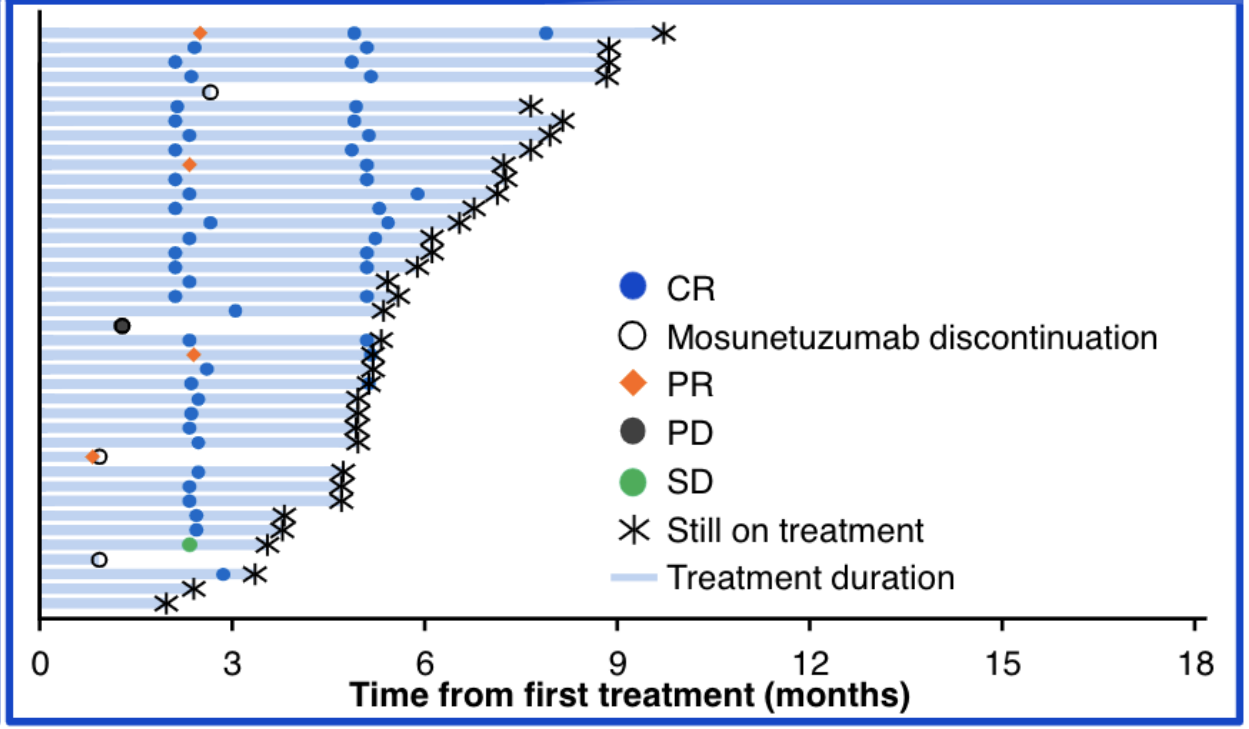
Mosun + Len in Frontline FL: Efficacy

- Median duration of follow-up: 5.2 months (range: 1–10); most patients (95%) had 3–9 months of follow-up at CCOD

Best overall response*



Response timing and duration†



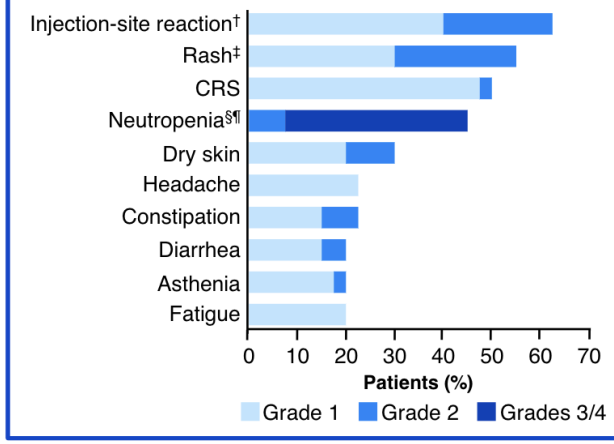
ORR and CR rates were high. All patients who responded were still in response at the CCOD

Mosun+ Len in Frontline FL: Safety

- 29 patients (72.5%) received at least six cycles of treatment at CCOD

	N=40; n (%)
AEs Related to Mosun/Len	40 (100) 38 (95.0) / 33 (82.5)
Serious AEs Related to Mosun/Len	13 (32.5) 9 (22.5) / 3 (7.5)
Grade 3/4 AEs	22 (55.0)
Serious Grade 3/4 AEs Related to Mosun/Len	3 (7.5) 2 (5.0) / 1 (2.5)
Grade 5 AEs	0
AE leading to dose reduction/modification Mosun Len	 0 9 (22.5)
AE leading to dose delay/interruption Mosun Len	 11 (27.5) 17 (42.5)
AE leading to any treatment discontinuation	2 (5.0)*

Most common AEs (≥20% incidence)



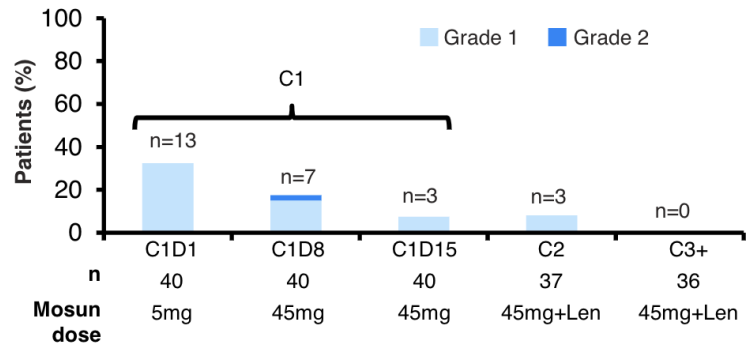
Mosun-Len had a manageable safety profile

Summary of Adverse Events

Cytokine Release Syndrome

	N=40; n (%)*
CRS† (any grade) Grade 1 Grade 2	20 (50.0) 19 (47.5) 1 (2.5)
Serious AE of CRS‡ (any grade)	6 (15.0)
Median time to first CRS onset,§ days (range)	2.5 (1–27)
Median CRS duration, days (range)	2.0 (1–26)
CRS resolved	20 (100)
Corticosteroids for CRS management	0
Tocilizumab for CRS management	2 (5.0)¶
CRS leading to Mosun discontinuation	0

Patients with CRS† by cycle and grade



CRS occurred in 50% of patients (predominantly Grade 1 with one Grade 2 event) and was confined to C1–C2
None of the CRS cases required vasopressors, supplemental oxygen, or ICU admission
All events resolved

EPCORE NHL-2: Epcoritamab + R^2 in Follicular Lymphoma

- Multicenter, open-label phase Ib/II trial (current analysis reported data from arm 6 and arm 2b)

Median Follow-up: 8.1 Mo (1.4+ to 10.7)

Patients with untreated CD20+ FL; grade 1-3A; treatment needed based on symptoms or disease burden per GELF criteria; measurable disease by CT/MRI; adequate organ function; ECOG PS 0-2
(N = 41)[1]

→

Arm 6:
Epcoritamab 48 mg SC*
QW for C1-2, Q4W for C3+ up to 2 yr
+
R^2 for C1-12†

→

- **Primary endpoints:** antitumor activity (ORR), safety
- **Key secondary endpoint:** DoR

Median Follow-up: 6.4 Mo

Patients with R/R CD20+ FL; grade 1-3A; stage II-IV; treatment needed based on symptoms or disease burden per GELF criteria; measurable disease by CT/MRI; adequate organ function; ECOG PS 0-2
(N = 76)[2]

→

Arm 2b:
Epcoritamab 48 mg SC*
QW for C1-2, Q4W for C3+ up to 2 yr
+
R^2 for C1-12†

→

- **Primary endpoints:** safety, antitumor activity

*Epcoritamab administered in 28-day cycles, with step-up dosing comprising priming and intermediate doses prior to first full dose, along with corticosteroid as CRS prophylaxis. †Rituximab 375 mg/m^2 IV QW for C1, Q4W for C2-6 (arm 6) or C2-5 (arm 2b); lenalidomide 20 mg PO QD x 21 days for C1-12.

1. Falchi. ASH 2022. Abstr 611. 2. Falchi. ASH 2022. Abstr 609.

EPCORE NHL-2: Response

Best Overall Response, %	1L FL (n = 36)	R/R FL (n = 66)
ORR	94	95
▪ CMR	86	80
▪ PMR	8	15
SD	NR	3
PD	3	2

- Responses were observed early at first assessment in both arms
- Median duration of response was not reached in either arm
- In the R/R FL arm, deep responses were observed across high-risk subgroups, including both primary and double-refractory disease, POD24, and those refractory to last therapy
- Median PFS was not reached in patients with R/R FL, 12-month PFS 78%
- 18-month PFS and OS was 90%, DOR 88%, and DOCR 95% in frontline arm

Falchi. ASH 2022. Abstr 611. Fachi. ASH 2022. Abstr 609.

EPCORE NHL-2: CRS Events

CRS Outcome, n (%)	1L FL (N = 41)	R/R FL (N = 76)
CRS ▪ Grade 1 ▪ Grade 2	22 (54) 16 (39) 6 (15)	33 (43) 25 (33) 8 (11)
Median time to onset after first full dose, days (range)	3 (1-6)	2 (1-9)
CRS resolution	22 (100)	33 (100)
Median time to resolution, days (range)	4 (1-10)	2 (1-23)
CRS leading to tx d/c	0	0
Tocilizumab use	4 (10)	8 (11)

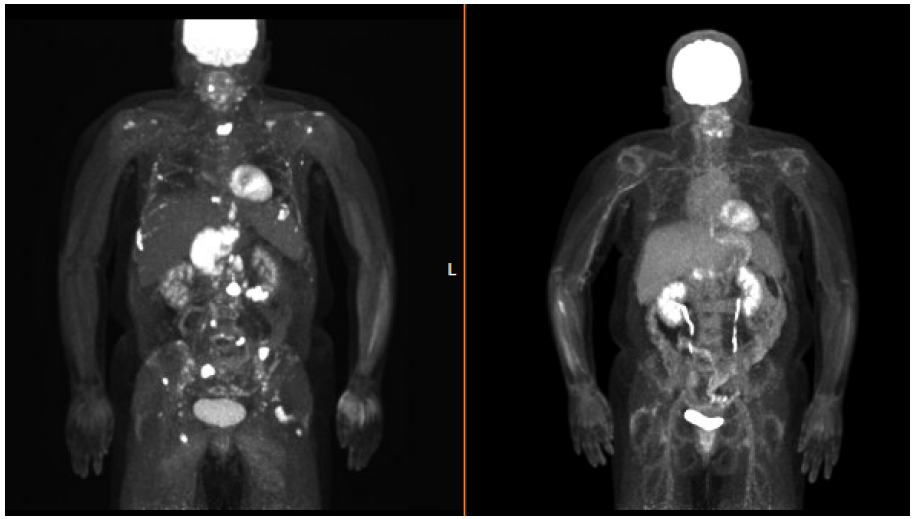
CRS Events by Dosing Period, %	1L FL (N = 41)		R/R FL (N = 76)	
	Gr 1	Gr 2	Gr 1	Gr 2
Priming C1D1	5	0	3	3
Intermediate C1D8	2	0	0	0
First full C1D15	32	15	32	9
Second full C1D22	3	0	1	0
Third full+ C2D1+	10	0	3	0

- No grade ≥3 CRS events were observed
- CRS timing was predictable; most cases occurred following first full dose

Falchi. ASH 2022. Abstr 611. Fachi. ASH 2022. Abstr 609.

Ongoing FL Bispecific Combination Trials at COH

- Epcoritamab + Lenalidomide in frontline FL IRB 22509 (PI: Dr. Thiruvengadam)
  - Stage 1 just completed accrual, Stage 2 now open
- Mosunetuzumab + Polatuzumab in R/R FL IRB 23003 (PI: Dr Mei)
  - Currently in safety lead-in
- Epcoritamab + Tazemetostat in R/R FL IRB 23820 (PI: Dr. Thiruvengadam)
  - Planned to open soon



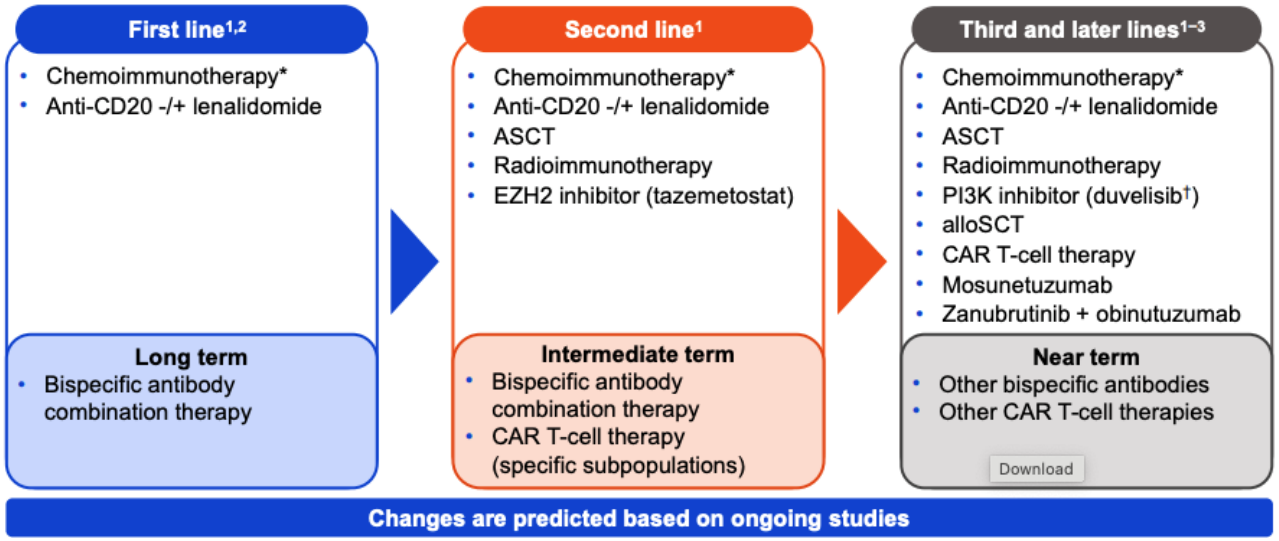
Pre-Treatment

Post 4 cycles Epcor-Len Treatment

Conclusion

- BsAb appear to be among the most active agents available for 3L+ FL with possible exception of CAR T-cell therapy
- BsAb have some practical advantages over CAR T-cell therapy in terms of tolerability, administration, availability, and less toxicity
- BsAb may still incur serious adverse events including cytopenias and infections, and major issue remains CRS risk during SUD
- BsAb are being moved into earlier lines of therapies in FL and being evaluated in novel combinations in all lines of treatment
- Optimal sequencing of T-cell engaging therapies remains a current and future challenge

FL Treatment Landscape



Questions that Remain for Bispecifics in FL….

- Durability of responses observed with bsAb and are we curing some patients (time will tell…)
- How to sequence bsAb with CAR T-cell therapy and which patients to select for one txt approach vs the other
- How to choose between the bsAb available
  - Factors to consider include route of administration, dosing schedule, fixed vs indefinite, disease factors such as concern for transformation, and provider comfort/experience
- How to mitigate toxicity of bsAb and integrate into smaller community practice settings

Lymphoma Center at COH

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- Tanya Siddiqi MD
- Matt Mei MD
- Elizabeth Budde MD, PhD
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- Tycel Phillips MD
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- CRNs and CRCs

Thank you for your attention!

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