



Multidisciplinary Approaches to Cancer Symposium

Relapsed/Refractory Follicular Lymphoma Treatment Updates

Benjamin Heyman, MD

Associate Clinical Professor

Division of Lymphoma

Department of Hematology/Hematopoietic Stem Cell Transplant

City of Hope

Disclosures

- Consultant for AbbVie, Eli Lilly, Guardant Health, Regeneron Pharmaceuticals, and Sobi
- Grant/Research Support from AstraZeneca, BeOne Medicines, Century Therapeutics, and Incyte

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.



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:

- *In this presentation, I plan to address how cultural, socioeconomic, and structural factors influence treatment access, shared decision making, and outcomes for patients with relapsed or refractory follicular lymphoma, with an emphasis on equitable delivery of emerging therapies.*
- *In this presentation, I plan to address how implicit biases may influence clinical judgment and treatment decisions in relapsed or refractory follicular lymphoma, and discuss strategies to promote more deliberate, consistent, and evidence-based care across diverse patient populations.*





NCCN Guidelines Version 3.2026

Classic Follicular Lymphoma

SUGGESTED TREATMENT REGIMENS^{a,b,c}

SECOND-LINE THERAPYⁱ

Preferred (in alphabetical order)

- Bendamustine^{d,j} + Obinutuzumab^{e,f} or Rituximab (not recommended if treated with prior Bendamustine)
- CHOP + Obinutuzumab^{e,f} or Rituximab
- CVP + Obinutuzumab^{e,f} or Rituximab

- Lenalidomide + Rituximab + Epcoritamab-bysp^{k,n} (category 1)
- Lenalidomide + Rituximab + Tafasitamab-cxix^{l,m} (≥1 prior systemic therapy including an anti-CD20 mAb) (category 1)

Other recommended (in alphabetical order)

- Lenalidomide (if not a candidate for anti-CD20 mAb therapy)
- Lenalidomide + Obinutuzumab or Rituximab
- Obinutuzumab
- Rituximab

SECOND-LINE THERAPY FOR OLDER OR INFIRM

(if none of the therapies are expected to be tolerable in the opinion of treating physician)

Preferred

- Rituximab (375 mg/m² weekly for 4 doses)

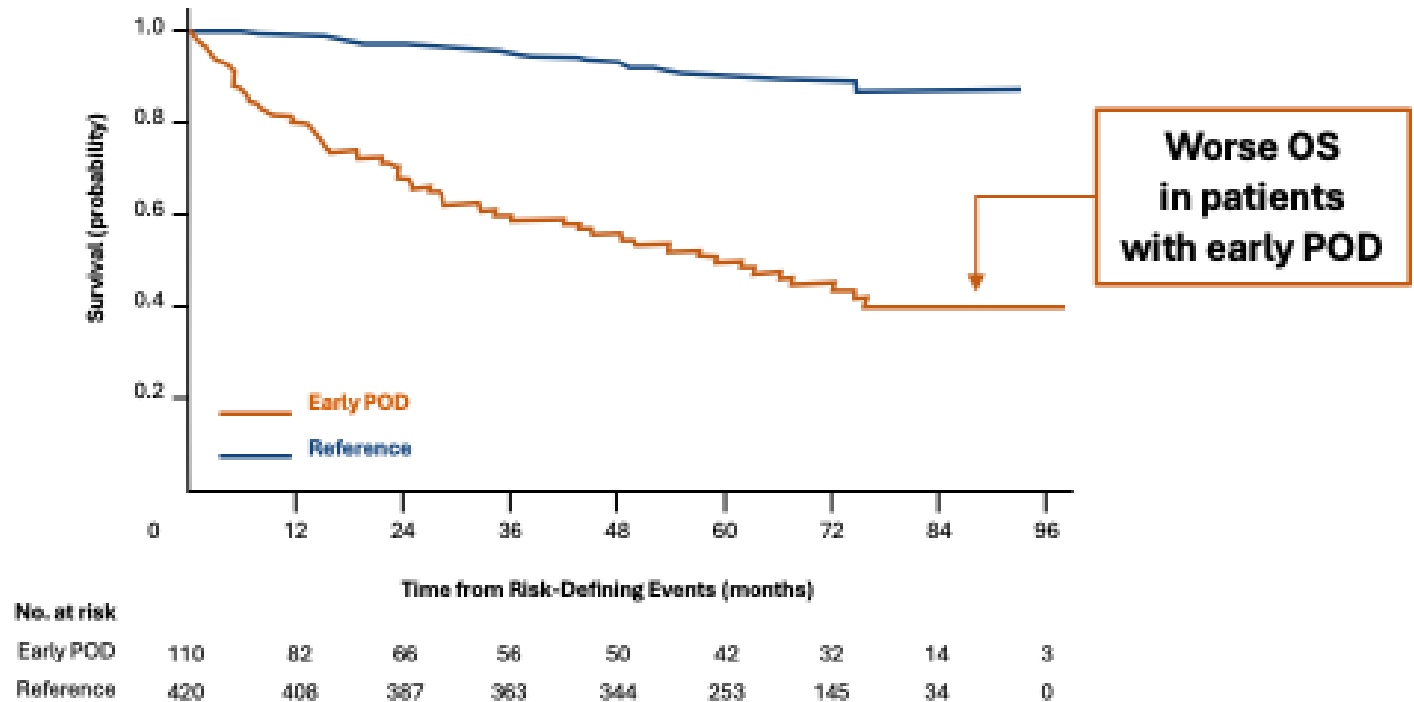
SECOND-LINE EXTENDED THERAPY (optional)

Preferred

- Rituximab maintenance 375 mg/m² one dose every 12 weeks for 2 years (category 1)
- Obinutuzumab maintenance for rituximab-refractory disease (1 g every 8 weeks for total of 12 doses)

Time to First Progression in FL is prognostic

- Biopsy recommended to detect histologic transformation of FL, which is reported to occur at a rate of **2% per year**¹
 - Higher rates among early relapse patients²
- Early progression of disease (≤ 2 years) after frontline chemoimmunotherapy (POD24) occurs in approximately **20% of patients**
 - Associated with inferior OS³
 - Represents a population requiring novel intervention



1. Link BK et al. *J Clin Oncol*. 2013;31(26):3272-3278. 2. Batlevi C et al. *European Journal of Cancer*. 2020;126:78-90.
3. Casulo C et al. *J Clin Oncol*. 2015;33(23):2516-2522.

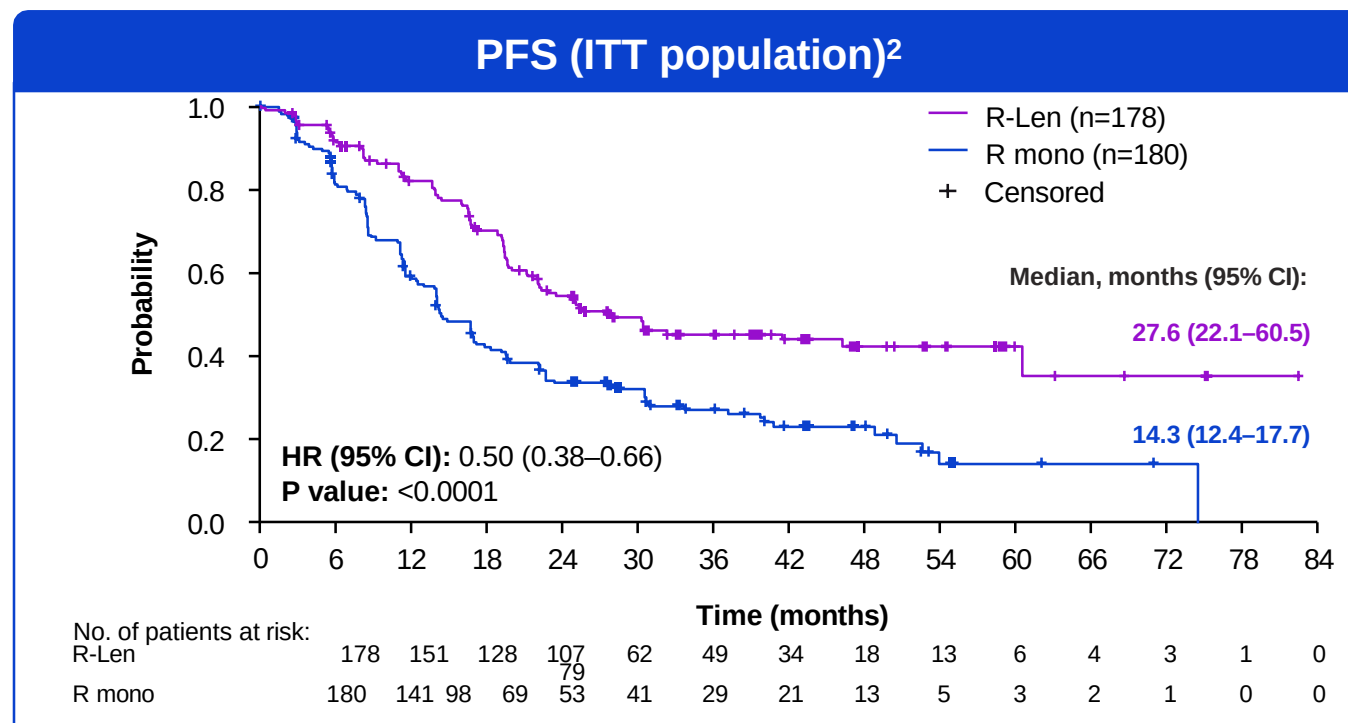


R-Len is an effective treatment option for R/R FL in the 2L+ setting^{1,2}

Phase III AUGMENT study of R-Len versus R mono in R/R indolent non-Hodgkin lymphoma

Baseline characteristic (ITT population), % ^{1,2}	R-Len n=178	R mono n=180
ECOG PS 0	65	71
FLIPI high risk	39	30
Refractory to last therapy	17	14
Prior therapies ≥3	25	23
High-tumor burden per GELF criteria	54	48

82% of patients had FL^{1,2}



R-Len is superior versus R mono, but most patients will relapse

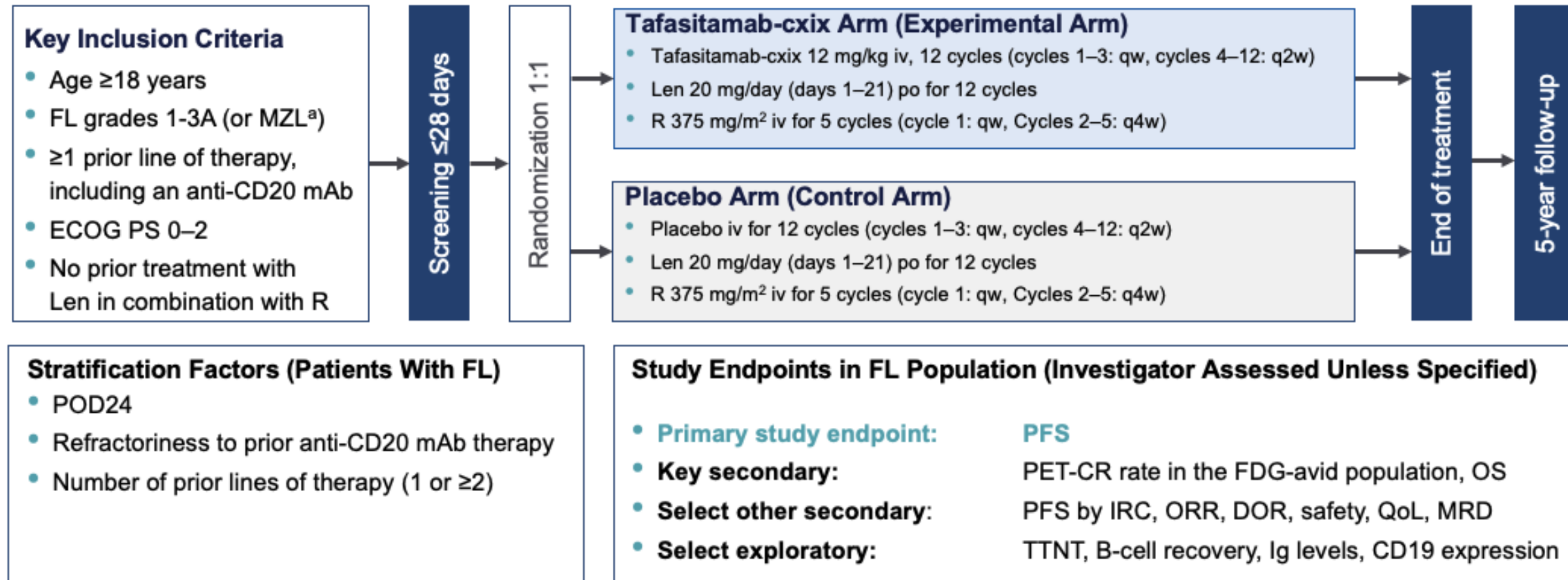
Median follow-up was 65.9 months.

GELF, Groupe d'Etude des Lymphomes Folliculaires; HR, hazard ratio; ITT, intention-to-treat; mono, monotherapy.

1. Leonard JP, et al. J Clin Oncol 2019;37:1188–99;

2. Leonard JP, et al. ASH December 2022; Oral presentation (abstract #230).

inMIND Phase 3 Study of Tafa + Len + R in R/R FL



inMIND Efficacy - Response

84% vs 72%

Overall response rate

45% vs 34%

Complete response

OR 2.0

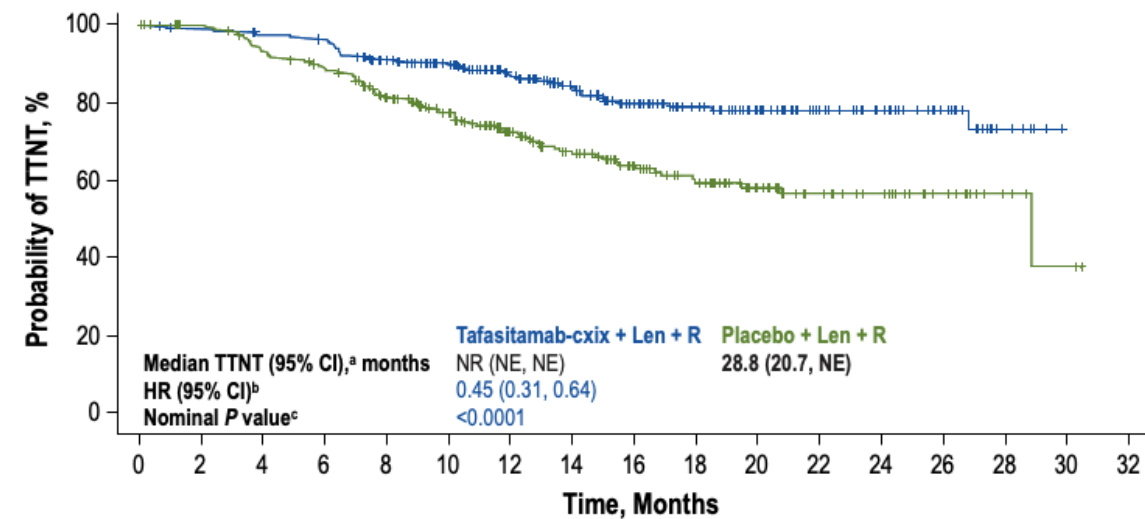
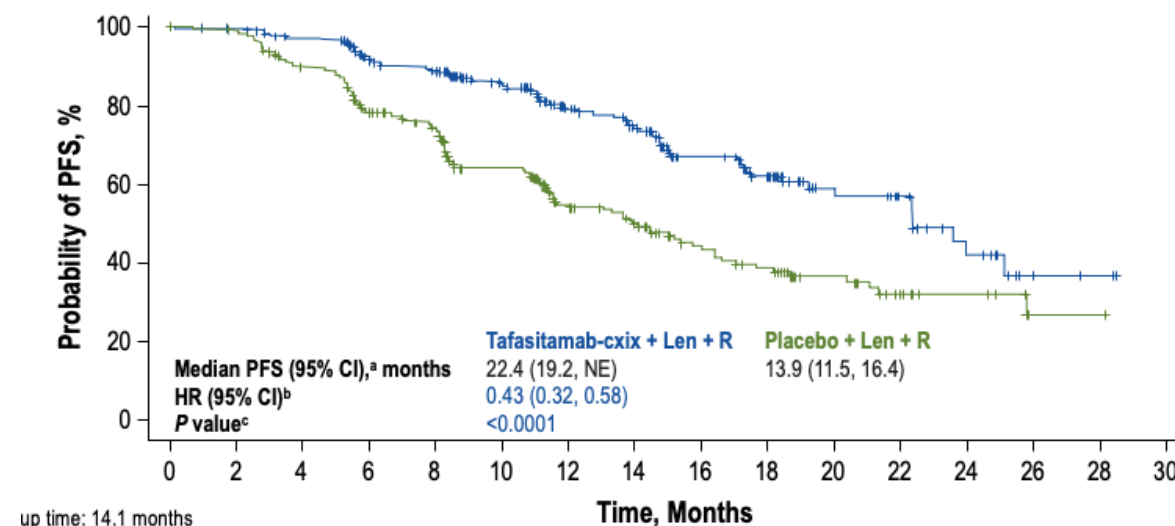
95% CI 1.30–3.02; p=0.0014

	Tafasitamab plus lenalidomide plus rituximab	Placebo plus lenalidomide plus rituximab
Overall response rate (intention-to-treat population)		
Patients	273	275
Best response*		
Complete response	124 (45%)	94 (34%)
Partial response	104 (38%)	105 (38%)
Stable disease	28 (10%)	46 (17%)
Progressive disease	7 (3%)	20 (7%)
Not evaluable	2 (1%)	0
Not done	8 (3%)	10 (4%)
Complete response (radiographic)†	141 (52%)	110 (40%)
Overall response rate‡, % (95% CI)§	84% (78.6–87.7)	72% (66.7–77.6)
Odds ratio¶ (95% CI)§	2.0 (1.30–3.02)	..
Nominal p value	0.0014	..

inMIND - Survival

Time-to-event endpoints

Endpoint	Tafasitamab-cxix + Len + R	Placebo + Len + R	HR (95% CI)
Median PFS, months	22.4 (19.2, NE)	13.9 (11.5, 16.4)	0.43 (0.32, 0.58)
Median DOR, months	21.2 (19.5, NE)	13.6 (12.4, 18.6)	0.47 (0.33, 0.68)
Median TTNT, months	NR (NE, NE)	28.8 (20.7, NE)	0.45 (0.31, 0.64)
Median OS, months	NR (27.9, NE)	NR (NE, NE)	0.59 (0.31, 1.13)



inMIND - Safety

Key safety takeaways

Rates of High-Grade AEs were comparable between both arms

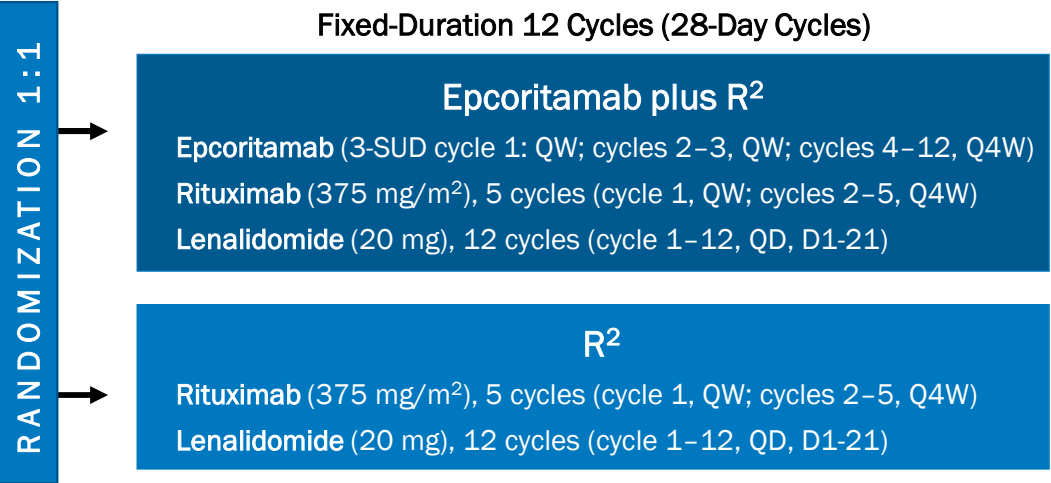
Lenalidomide dose interruptions or discontinuation were similar between both arms

Most Common Grade 3 or 4 TEAEs (≥5% in Any Group)			
Preferred Term, n (%)	Tafasitamab-cxix + Len + R (n=274) ^a	Placebo + Len + R (n=272) ^b	Total (n=546)
Neutropenia	109 (40)	102 (38)	211 (39)
Pneumonia	23 (8)	14 (5)	37 (7)
Thrombocytopenia	17 (6)	20 (7)	37 (7)
Decreased neutrophils	16 (6)	18 (7)	34 (6)
Anemia	12 (4)	16 (6)	28 (5)
COVID-19	16 (6)	6 (2)	22 (4)
COVID-19 pneumonia	13 (5)	3 (1)	16 (3)

EPCORE FL-1 Phase 3 Study of Epcoritamab + R² vs R² in Patients With R/R FL: Study Design and Patients

Key Inclusion Criteria

- Histologically confirmed FL and CD20+
- Grade 1-3a, Stage II-IV
- ≥ 1 prior treatment (anti-CD20 mAb plus chemotherapy)
- Met ≥ 1 GELF criterion



Dual primary endpoints: ORR per IRC and PFS per IRC
Secondary endpoints: CR rate, OS, and MRDc
Additional secondary endpoints: DOR, DOCR, TTNLT, safety, and PRO assessments

Patient Characteristics		Epcoritamab+R ² (N = 243)	R ² (N = 245)	Overall (N = 488)
Median age (range), years		60 (30, 84)	63 (24, 89)	61 (24, 89)
ECOG PS, %	0	166 (68)	170 (69)	336 (69)
	1-2	77 (32)	75 (31)	152 (31)
	3-5	100 (41)	113 (46)	213 (44)
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)
Prior anti-CD20 antibody, n (%)		243 (100)	245 (100)	488 (100)
Prior anti-CD20 antibody containing chemo, n (%)		239 (98)	240 (98)	479 (98)
POD24, n (%)		106 (44)	93 (38)	199 (41)
Refractory to 1L therapy, n (%)		86 (35)	81 (33)	167 (34)
Double refractory		91 (37)	91 (37)	182 (37)
Number of prior lines of therapy, median (range)		1 (1, 7)	1 (1, 6)	1 (1, 7)

EPCORE FL-1 Efficacy: Response

Epcoritamab + R² vs R²

95% vs 79%

Overall response rate

83% vs 50%

Complete response

89% vs 49%

12-month duration of response (KM estimate)

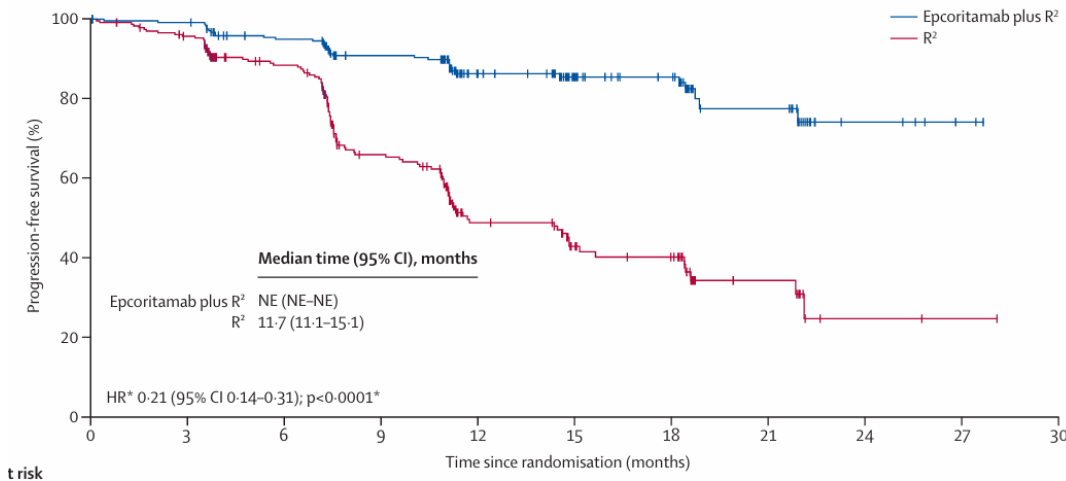
	Epcoritamab plus R ² (n=243)	R ² (n=245)
Median follow-up, months, median (95% CI) [IQR]	14·8 (13·96–16·23) [12·0–19·3]	14·6 (13·57–15·64) [10·2–18·6]
Overall response rate, n (% [95% CI])*	231 (95% [92–97])	194 (79% [74–84])
Complete response, n (% [95% CI])*	201 (83% [77–87])	122 (50% [43–56])
Partial response	30 (12%)	72 (29%)
Stable disease	1 (<1%)	17 (7%)
Progressive disease	7 (3%)	16 (7%)
NE†	4 (2%)‡	18 (7%)‡
Duration of response		
Median, months§	NE (NE–NE)	11·5 (8·5–18·6)
12-month Kaplan–Meier estimate, %	89·2% (83·6–93·0)	48·5% (38·8–57·5)
Duration of complete response		
Median, months§	NE (NE–NE)	18·6 (11·1–NE)
12-month Kaplan–Meier estimate, %	91·2% (84·5–95·0)	56·0% (42·4–67·6)

EPCORE FL-1 Efficacy: Survival

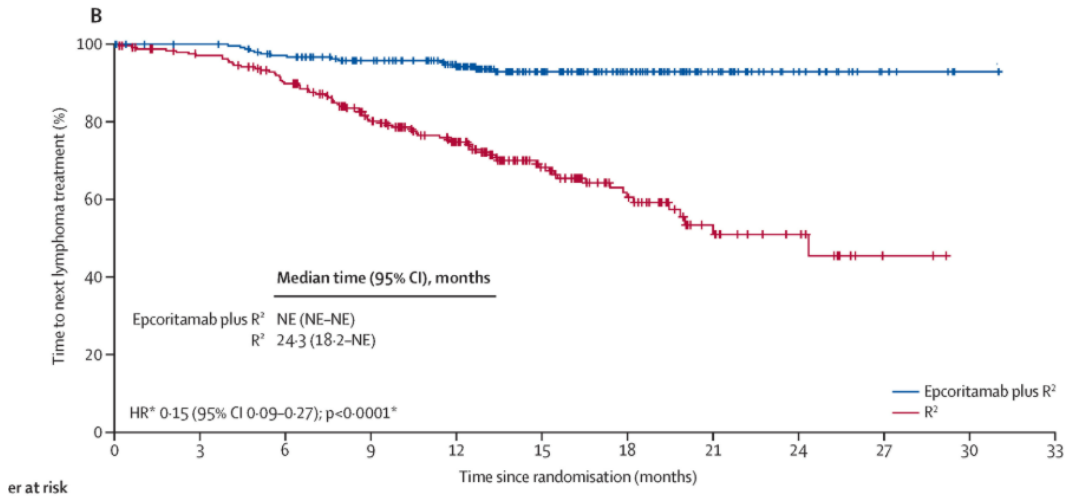
Time-to-event endpoints

Endpoint	Epcoritamab + R ²	R ²	HR (95% CI)
Median PFS, months	NE (NE-NE)	11.7 (11.1–15.1)	0.21 (0.14–0.31)
Median TTNT, months	NE (NE-NE)	24.3 (18.2–NE)	0.15 (0.09–0.27)
Median OS, months	NE (NE-NE)	NE (NE-NE)	—

16-mo PFS
85.5%
vs 40.2%



16-mo TTNT
92.8%
vs 64.9%



EPCORE FL-1 Efficacy: Survival

Consistent benefit across subgroups

14/14

subgroups favoured epcoritamab + R²

0.12–0.29

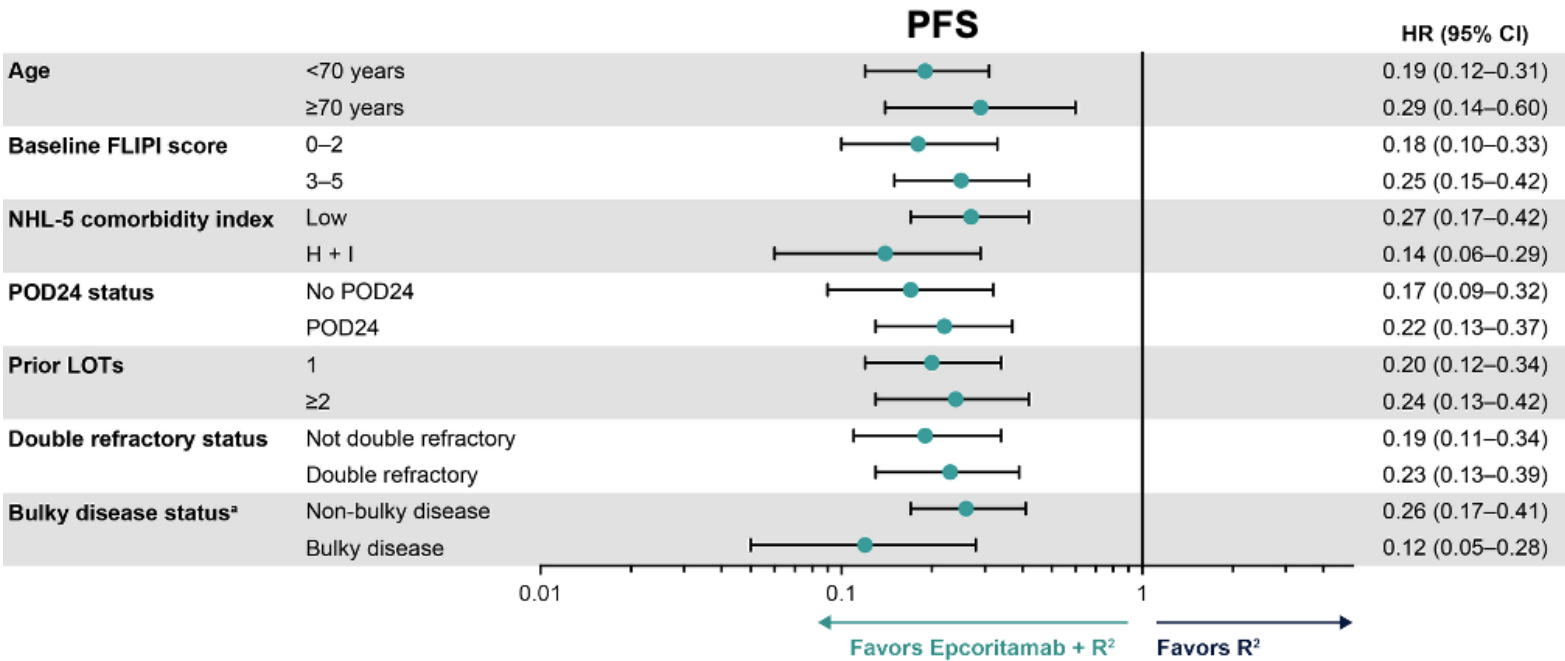
HR range across all subgroups

0.22

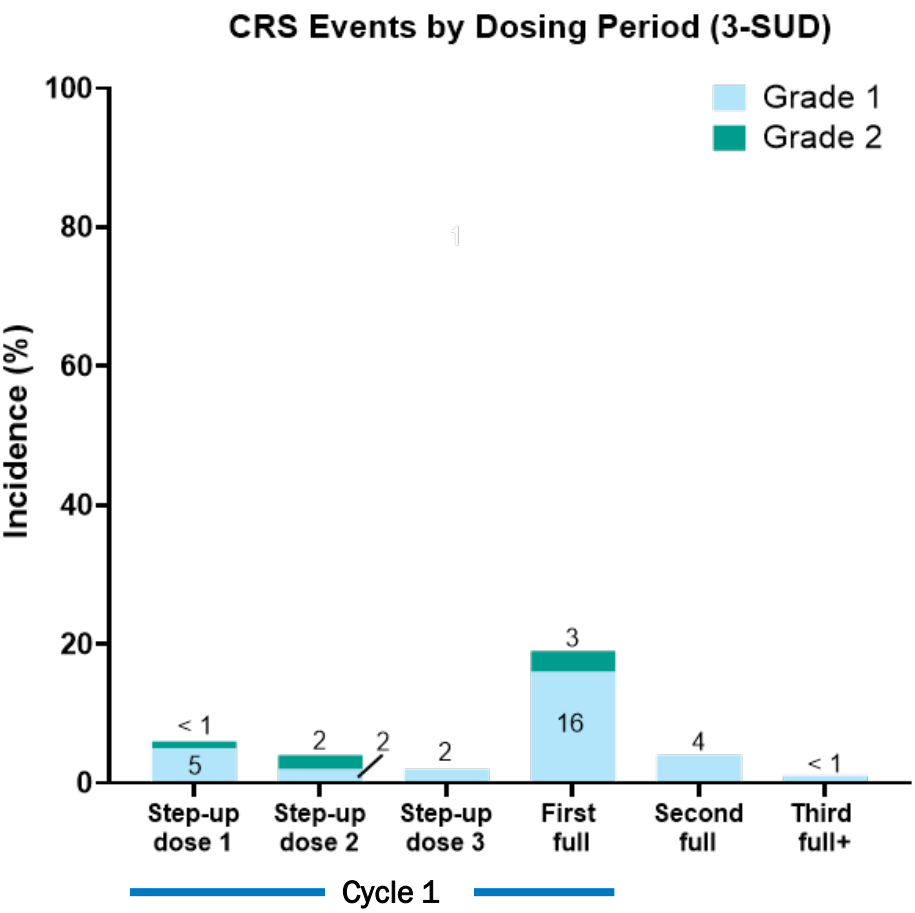
HR in the POD24 high-risk subgroup

- Both low and high risk clinically relevant subgroups showed improved PFS with Epcor-R2 vs R2

PFS by Prespecified Relevant Subgroups



EPCORE FL-1 : CRS



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

Approach to 3L+ FL



National
Comprehensive
Cancer
Network®

PLEASE NOTE that use of this NCCN Content is governed by the End-User License Agreement, and you MAY NOT distribute this Content or use it with any artificial intelligence model or tool.
Printed by Loretta Nastoupil on 3/23/2026 8:54:02 PM. Copyright © 2026 National Comprehensive Cancer Network, Inc. All Rights Reserved.

NCCN Guidelines Version 3.2026 Classic Follicular Lymphoma

[NCCN Guidelines Index](#)
[Table of Contents](#)
[Discussion](#)

SUGGESTED TREATMENT REGIMENS^{a,b,c}

THIRD-LINE AND SUBSEQUENT THERAPY	
Second-line therapy regimens (FOLL-B 2 of 6) that were not previously given can also be used as options for third-line and subsequent therapy	
<u>Preferred (in alphabetical order)</u> • T-cell mediated therapy^k ▶ Bispecific antibody therapy^l ◇ Epcoritamab-bysp ◇ Mosunetuzumab-axgb (IV or SC)^m ▶ Chimeric antigen receptor (CAR) T-cell therapy^{n,o} ◇ Axicabtagene ciloleucel (CD19-directed) ◇ Lisocabtagene maraleucel (CD19-directed) ◇ Tisagenlecleucel (CD19-directed)	<u>Other recommended</u> • BTK inhibitor (BTKi) ▶ Zanubrutinib^l + Obinutuzumab • Loncastuximab tesirine-lpyl^{l,n} + Rituximab (category 2B)

THIRD-LINE CONSOLIDATION THERAPY
<u>Useful in Certain Circumstances</u> • Allogeneic hematopoietic cell transplantation (HCT) in selected cases^p

Bispecific antibodies in R/R FL after ≥ 2 prior therapies

Therapy	Formulation	Key Phase II study	Treatment schedule	Status
Mosunetuzumab	IV or SC ¹	GO29781 (median follow-up: >49.4 months) ^{1,2}	Fixed duration: Q3W* for eight cycles if CR is achieved, or up to 17 cycles ¹	Approved in R/R FL after ≥ 2 prior therapies by the EMA and FDA ^{3,4}
Epcoritamab	SC ⁵	EPCORE NHL-1 (median follow-up: 17.4 months) ^{5†}	QW, C1–3*; Q2W for six cycles (C4–9); Q4W until progression ⁵	Approved in R/R FL after ≥ 2 prior therapies by the FDA and EMA ^{3,4}
Odronextamab	IV ⁶	ELM-2 (median follow-up: 28.3 months) ⁶	QW, for four cycles;* Q2W until progression ^{6‡}	Approved in R/R FL after ≥ 2 prior therapies by the EMA ⁷

1. Shadman et al. ASH 2024
2. Hess et al. EHA June 2025
3. US PI www.accessdata.fda.gov/scripts/cder/daf/
4. EU SmPC. www.ema.europa.eu/en/medicines

5. Linton KM et al. Lancet Hematology 2024
6. Jagadeesh D et al. ASCO May 2025
7. Ordspono EMA. www.ema.europa.eu

Phase II G029781 study of mosunetuzumab in 3L+ FL

Key inclusion criteria^{1,2}

- Histologically confirmed FL (Grade 1–3a)
- ECOG PS 0 or 1
- ≥2 prior regimens, including an anti-CD20 antibody and an alkylator

Endpoints^{1,2}

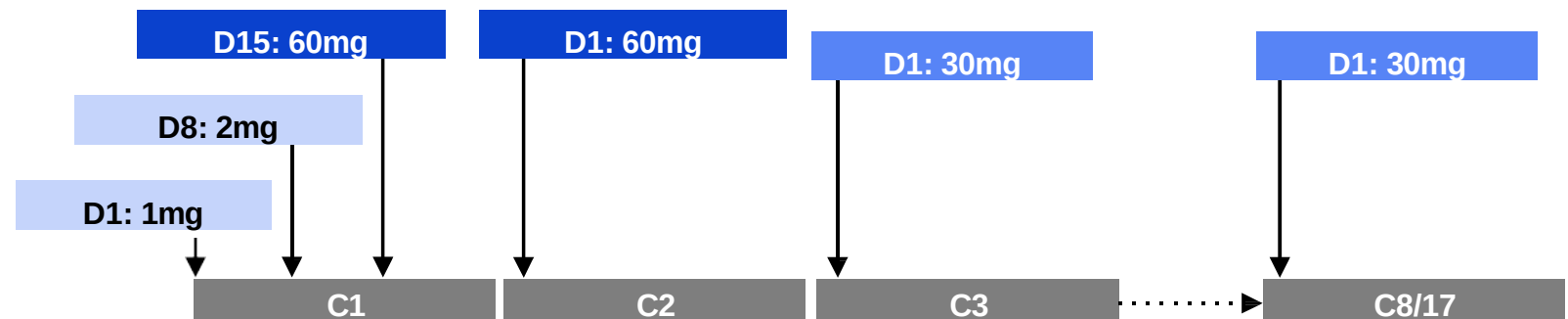
- Primary: CR (best response) rate by IRC*
- Secondary: ORR, OS, DOR, PFS, safety and tolerability

Mosunetuzumab administration^{1,2}

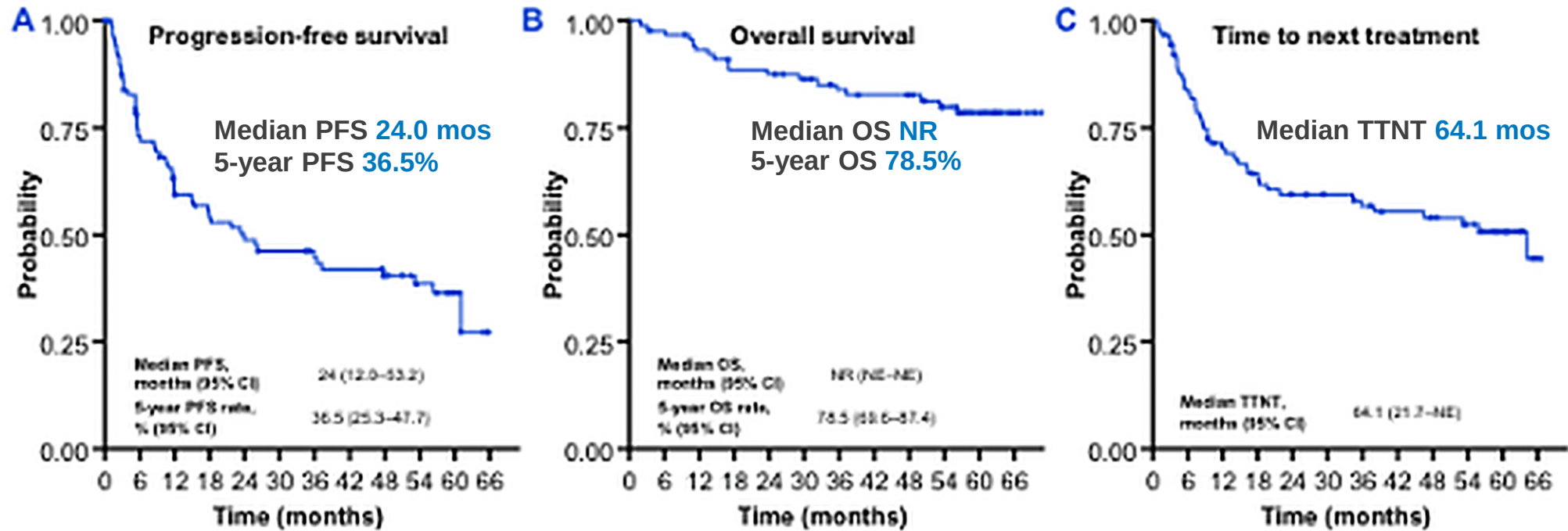
- Q3W IV administration
- **Fixed-duration treatment**
 - Eight cycles if CR after C8
 - 17 cycles if PR/SD after C8
- **No mandatory hospitalization**
- Retreatment permitted at relapse for patients who achieved a CR

CRS mitigation

- Step-up dosing during C1
- Corticosteroid premedication during C1 and C2, optional from C3 onwards

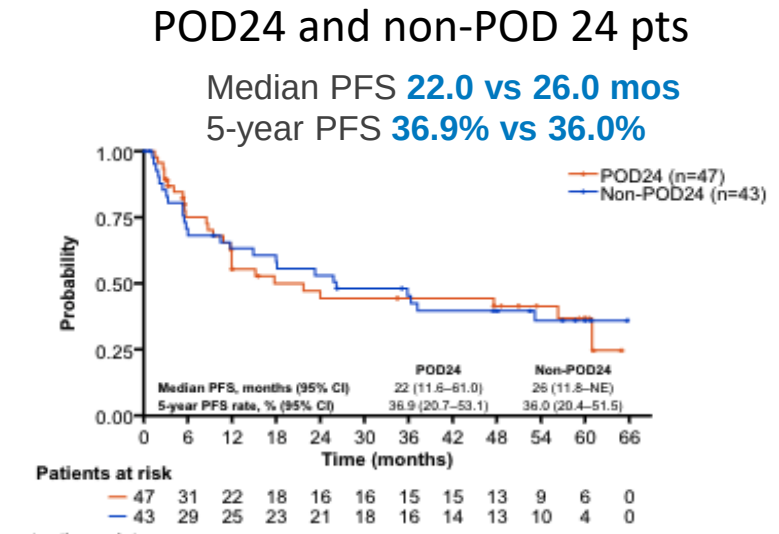
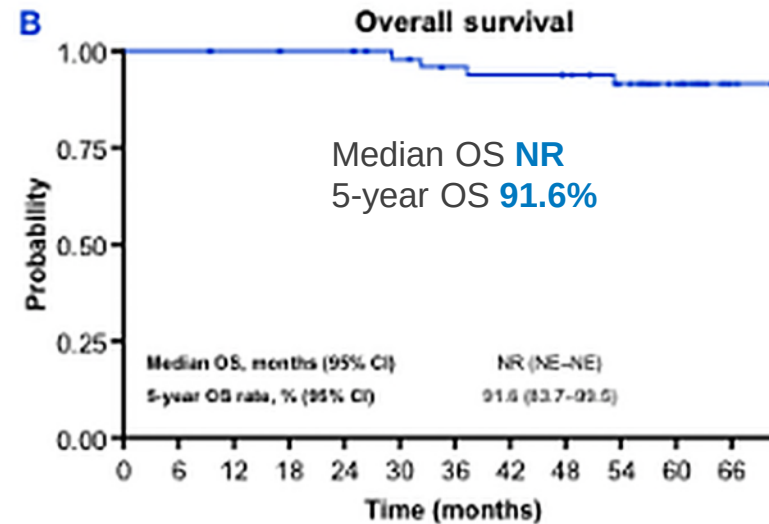
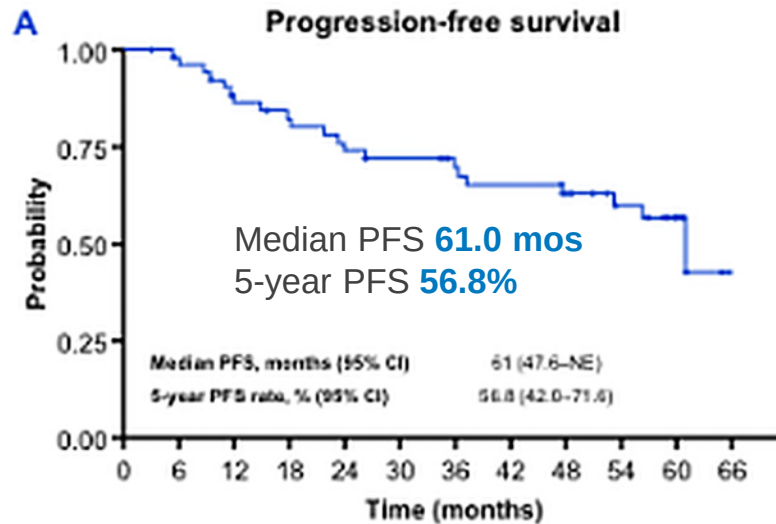


Mosun phase II study in R/R FL: 5-year follow up



- ORR and CRR were 78% and 60%
- Median DOCR was NR, 5-year DOCR was 52%
- More than half of pts did not require new anti-lymphoma txt at 5-year landmark

Mosun phase II study in R/R FL: 5-year follow up subgroups



- In those who achieved CR, 5-year PFS 56.8% and 5-year OS 91.6%
- In POD24 vs non-POD24, 5-year PFS 36.9% vs 36.0%

Single-Agent Mosunetuzumab: Safety in R/R FL

Summary of AEs

n (%) patients with ≥1 AE	N=90
Number of patients with at least one AE	90 (100)
Grade 3/4 AE	62 (68.9)
Serious AEs	43 (47.8)
Grade 5 AEs*	2 (2.2)
AEs leading to treatment discontinuation	4 (4.4)
Infections	45 (50.0)
Serious infections	18 (20.0)
Grade 3/4 infections	15 (16.7)
Infection AEs leading to treatment withdrawal	1 (1.1)†

20.0%

of patients had a serious infection

0

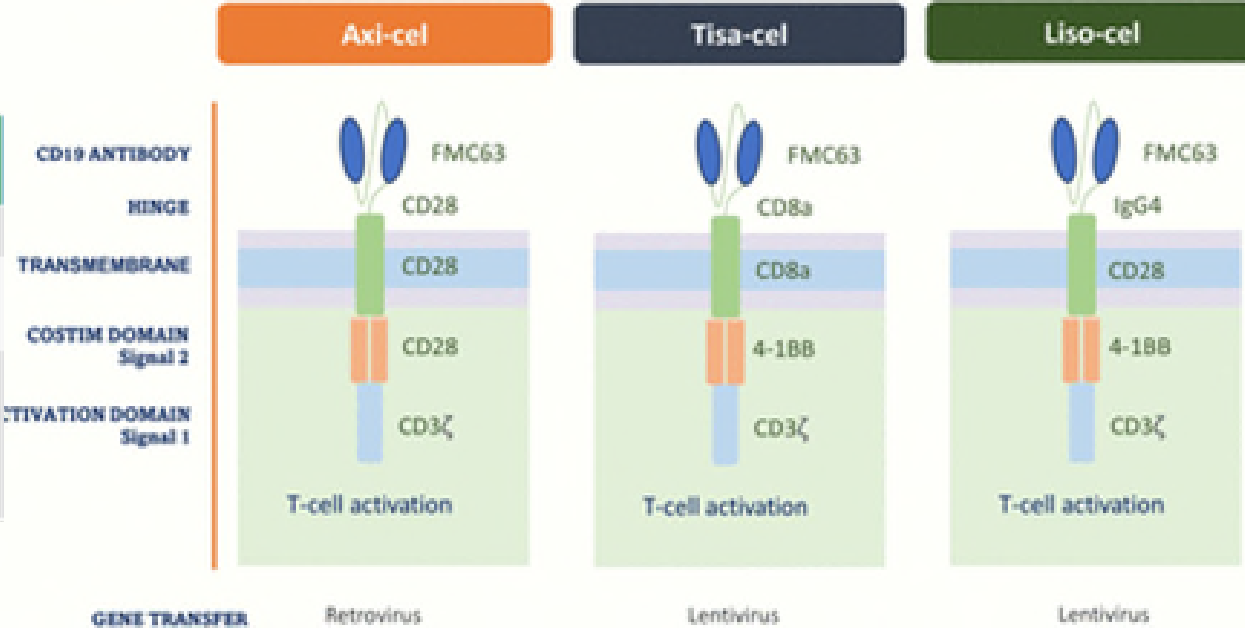
infectious deaths

73.7%

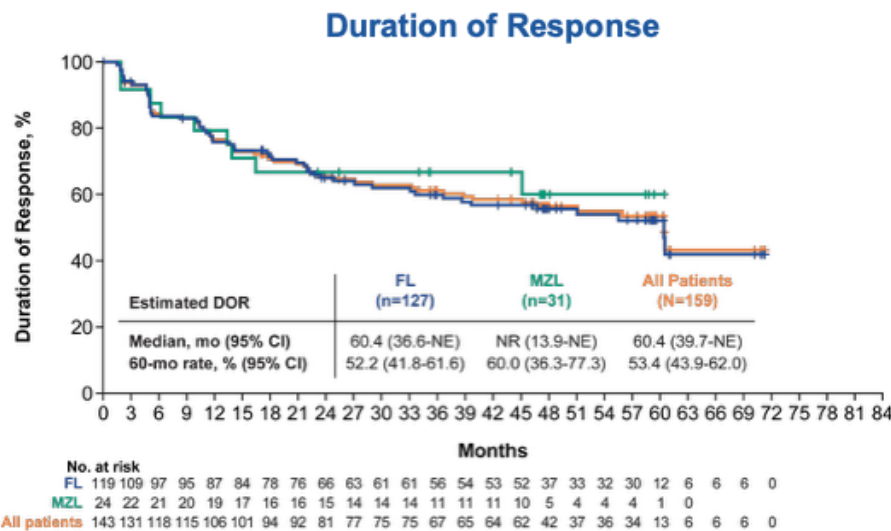
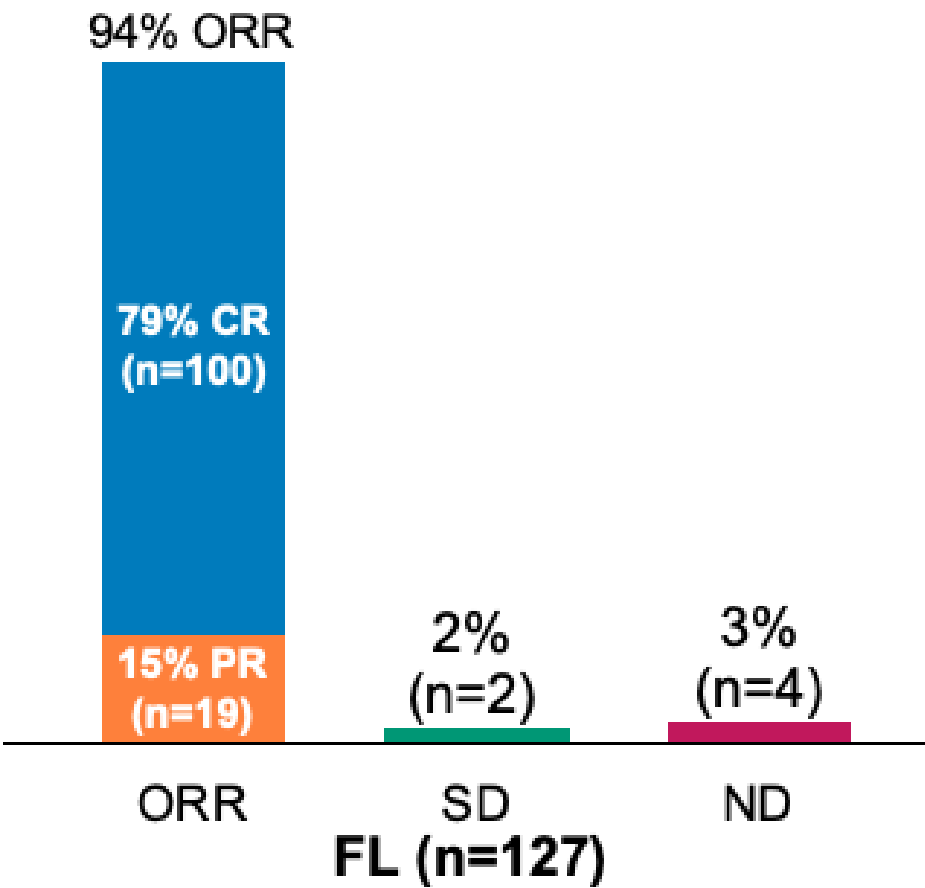
of serious infections in the first 4 cycles

CAR T in R/R FL after ≥ 2 prior therapies

	Axicabtagene Ciloleucel ¹	Tisagenlecleucel ²	Lisocabtagene Maraleucel ³
Construct	Anti-CD19- CD28 -CD3z	Anti-CD19- 41BB -CD3z	Anti-CD19- 41BB -CD3z
Dose	$2 \times 10^6/\text{kg}$ (max 2×10^8)	$0.6\text{--}6.0 \times 10^8/\text{kg}$	In 2L: $90\text{--}110 \times 10^6$ In 3L+: $50\text{--}110 \times 10^6$
Lympho-depletion	Flu/Cy 30/500 mg/m^2 x 3 days	Flu/Cy 25/250 mg/m^2 x 3 days, or bendamustine x 2 days	Flu/Cy 30/300 mg/m^2 x 3 days



ZUMA 5 Axi-cel in FL Efficacy

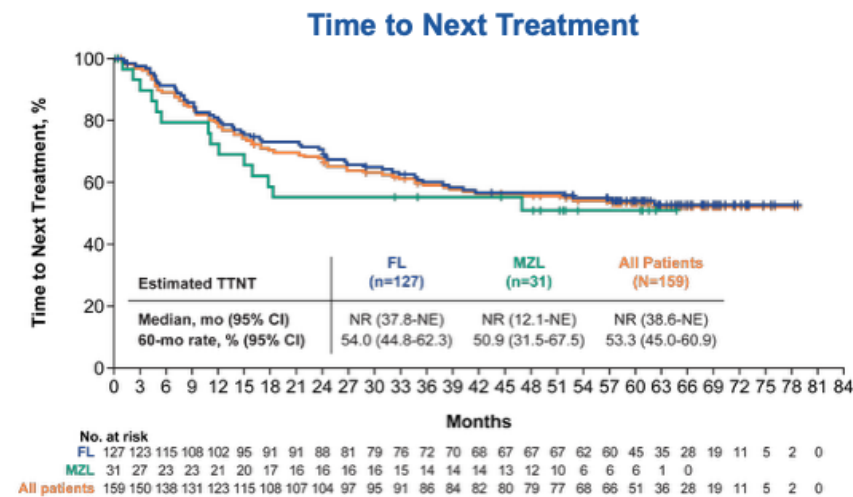


Median DOR

60.4 mo

60-mo DOR 52.2%

43% ongoing response

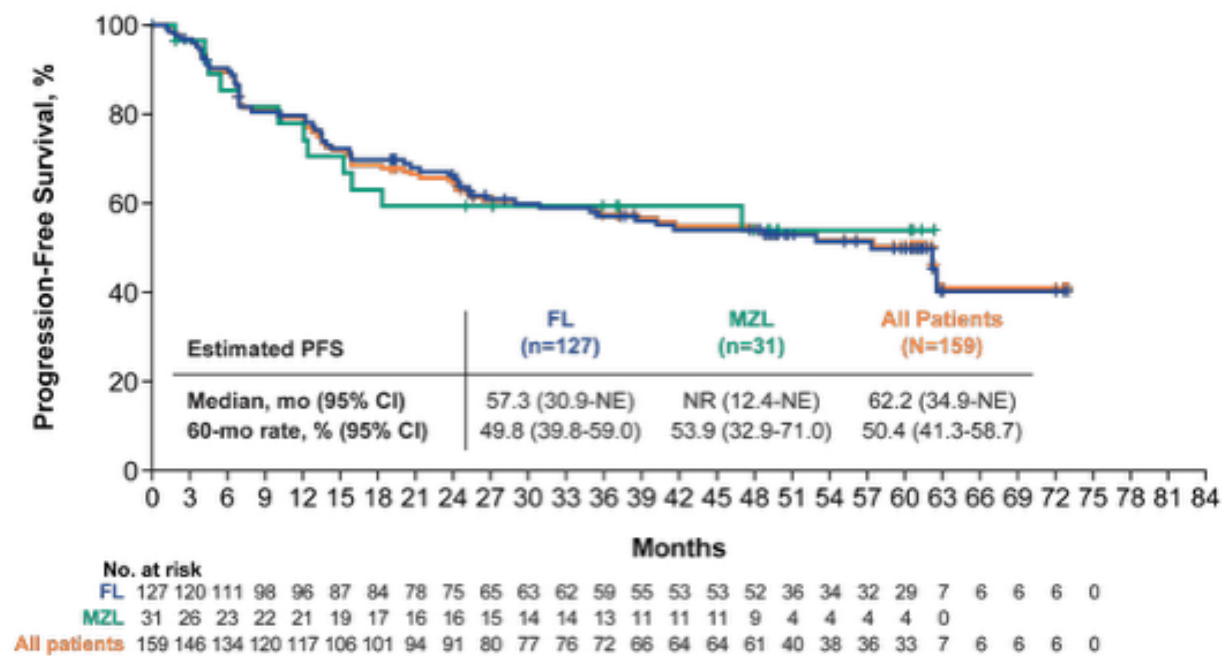


Median TTNT

Not reached

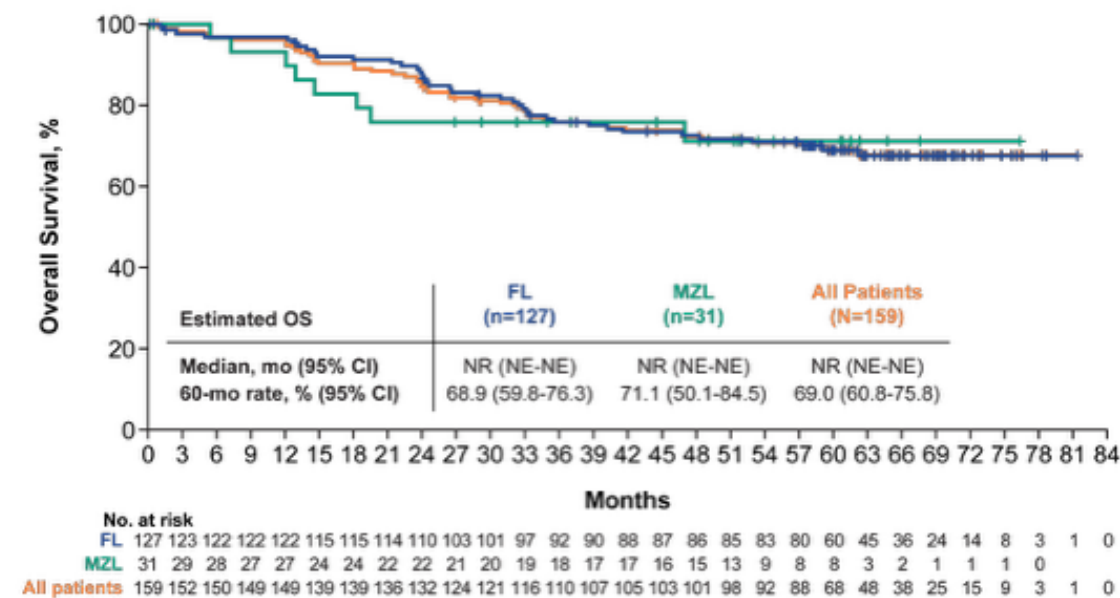
ZUMA 5 Axi-cel Survival Outcomes

Progression-Free Survival^a



Median PFS 57.3 mos; 60-month PFS rate 49.8%

Overall Survival



Median OS not reached; 60-month OS rate 68.9%

ZUMA 5 Axi-cel Safety

Adverse Events	FL (n = 124)	MZL (n = 22)	All (N = 148)
Any AE, %	99	100	99
▪ Any grade infection	52	63	53
Grade ≥3 AEs, %	85	96	86
▪ Neutropenia	60	67	61
▪ Anemia	23	29	24
▪ Thrombocytopenia	23	21	23
▪ Infection	15	29	18
Serious AEs, %	46	71	50
CRS, %	78	100	82
▪ Grade ≥3	6	8	7
Neurologic events, %	56	71	59
▪ Grade ≥3*	15	38	19
▪ Median duration, days (IQR)	14 (5-43)	10 (5-28)	—

70%

Grade ≥3
cytopenias

18%

Grade ≥3
infections

1

Unresolved
CRS event

- Grade ≥3 infections included pneumonia (n = 10), opportunistic (n = 4), URTI (n = 1)
- All CRS events resolved except 1 event of multisystem organ failure in a patient with FL and bulky disease
- No new treatment related safety signals observed in 3 and 5-yr follow-up analysis

BsAb vs CAR T Efficacy in R/R FL

Agent	ORR (%)	CR (%)	DoR (%)	PFS	OS
Mosunetuzumab ¹	78	60	54 mo 46% (5-yr 52% DOCR)	5-year 37%	5-yr 79%
Epcoritamab ²	82	63	18 mo 72% (DOCR)	1.5 year 49%	1.5-yr 70%
CAR T-cell therapy					
Axi-cel ⁴	94	79	5-yr 52%	5-yr 50%	3-yr 69%
Tisa-cel ⁵	86	68	4-yr 61%	5-yr 46%	5-yr 74%
Liso-cel ⁶	97	94	3-yr 70%	3-yr 68%	3-yr 86%

CR (avg)
CAR T ~80%
BsAb ~65%

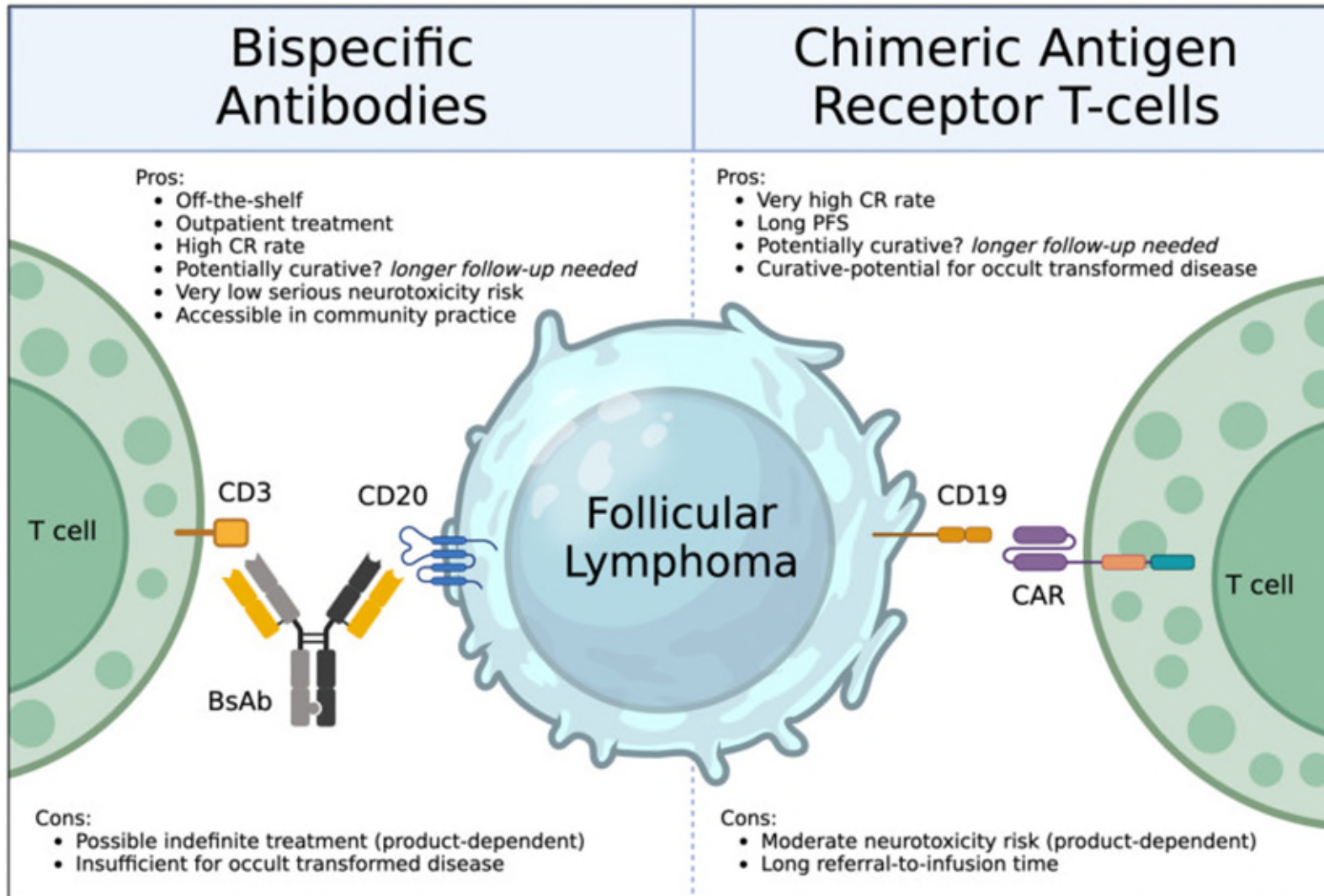
DoCR (avg)
CAR T ~74% at 24 mos
BsAb ~65% at 28 mos

PFS plateau?
CAR T ~51% at 5-yr
BsAb ~39% at 5-yr

BsAb vs CAR T Safety in R/R FL

Agent	CRS Rate		Neurotoxicity Rate		Grade 3+ Infections	Tocilizumab Required
	Any Grade	Grade 3+	Any Grade	Grade 3+		
Mosun	44%	2%	5%	2%	13%	8%
Epcor	49%	0%	0%	0%	22%	12%
CAR T-cell therapy						
Axi-cel	78%	6%	56%	18%	15%	50%
Tisa-cel	49%	0%	23%	1%	9%	34%
Liso-cel	58%	1%	15%	2%	5%	25%

BsAb vs CAR T



Thank You

Questions?

cityofhope.org



Question 1

In the EPCORE FL-1 trial, the addition of epcoritamab to R² provided superior efficacy, and a higher incidence of adverse events, compared with R² alone.

A. True

B. False

Question 2

In the InMind trial; the addition of tafasitamab to lenalidomide and rituximab resulted in improvement in progression-free survival; without a clinically significant increase in adverse event

A. True

B. False