



RELAPSED/REFRACTORY DLBCL: CAR-T CELLS, BISPECIFIC ANTIBODIES, AND EMERGING THERAPIES

ALEX F. HERRERA, MD

Chief, Division of Lymphoma
Professor, Department of Hematology and Hematopoietic Cell Transplantation
Director, Toni Stephenson Lymphoma Center
City of Hope
Duarte, California, USA

Disclosures



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KiTE Pharma/Gilead - consultancy

AstraZeneca –consultancy

ADC Therapeutics –consultancy

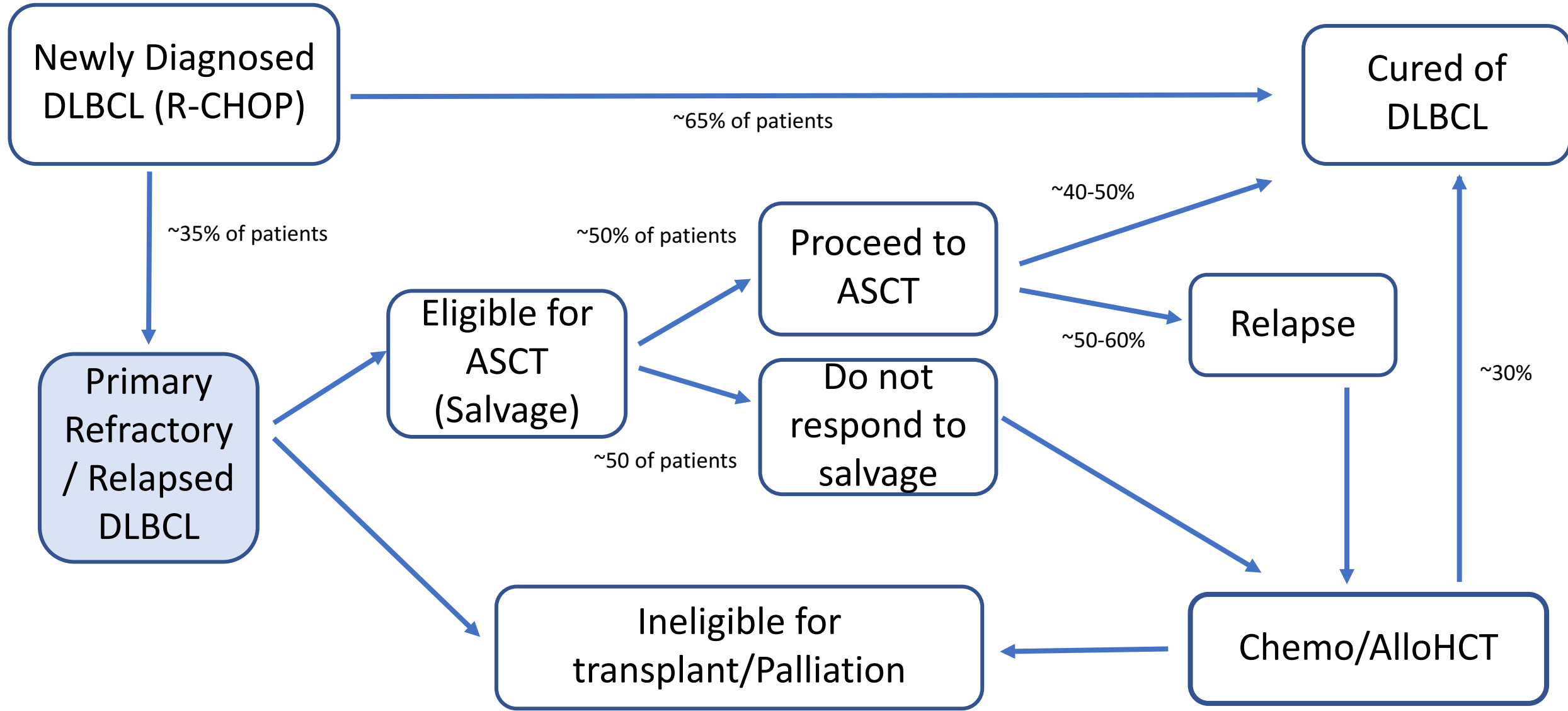
Genmab – consultancy

Allogene Therapeutics – consultancy

Eli Lilly and Company – consultancy

Incyte - consultancy

Historical Therapy of DLBCL



• Adapted from Maddocks K. *Hematology Am Soc Hematol Educ Program* (2020) 2020 (1): 101–106.

Relapsed/Refractory Aggressive B-cell Lymphoma

- ~1/3 of pts with aggressive B-NHL
- Historic Standard treatment:
 - Salvage/2L chemo-immunotherapy
 - Autologous stem cell transplantation (ASCT) for chemosensitive pts
- ASCT cured about half of pts

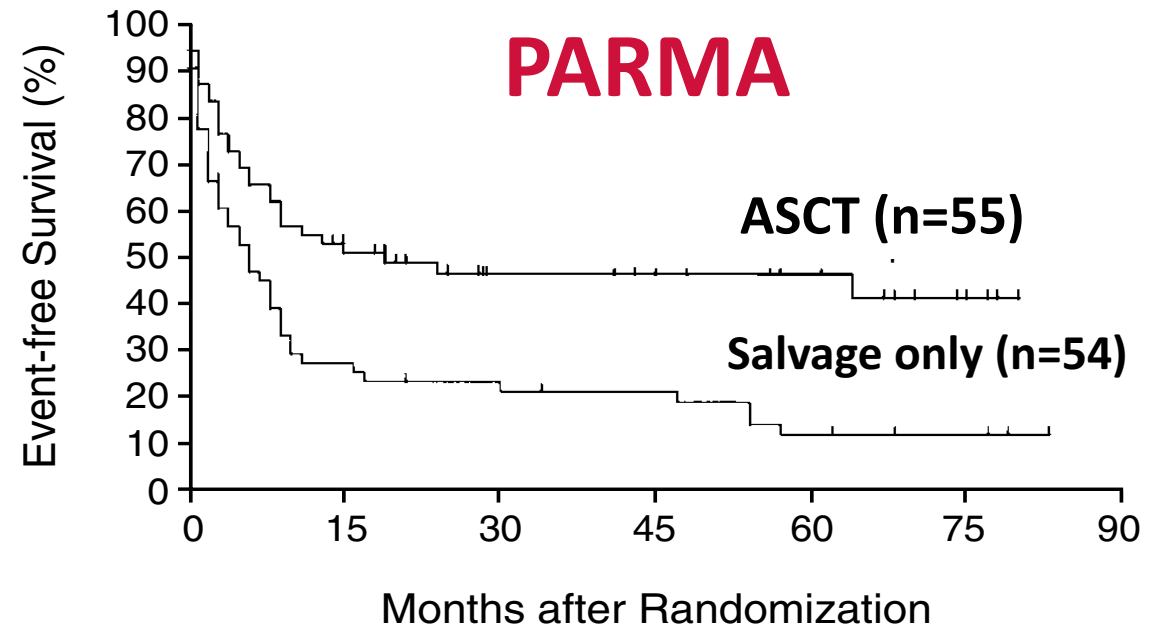


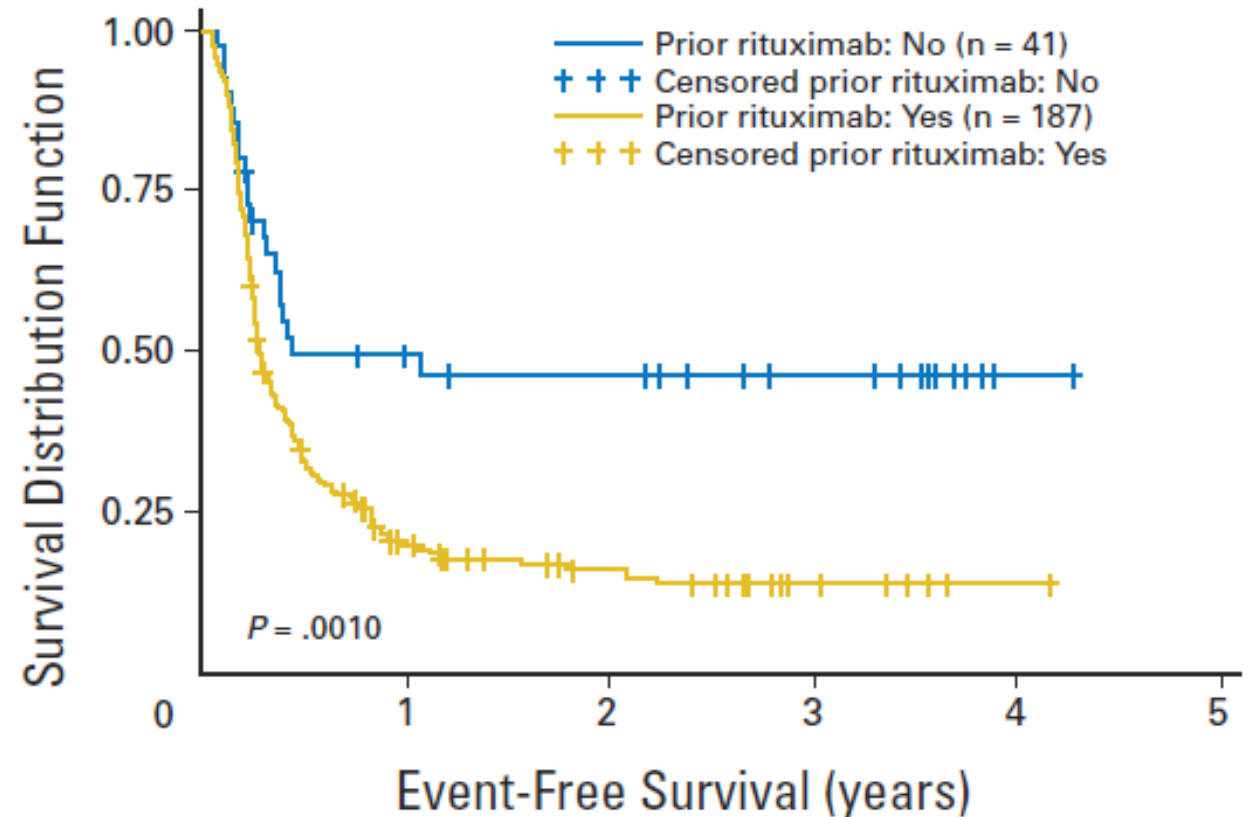
Figure 1. Kaplan–Meier Curves for Event-free Survival of Patients in the Transplantation and Conventional-Treatment Groups.

Early relapse after R-CHOP → dismal outcomes

1^o refractory/early relapse
after prior rituximab

- 2L salvage intent-to-transplant outcomes:
 - ORR 46%
 - 3y EFS 20%
 - 3y OS 39%

CORAL



CAR T-cells: A New Hope

CD19 Ab

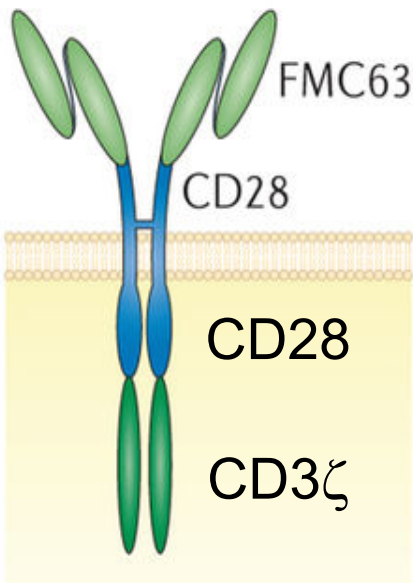
Hinge

Transmembrane

Signal 2

Signal 1

Gene transfer



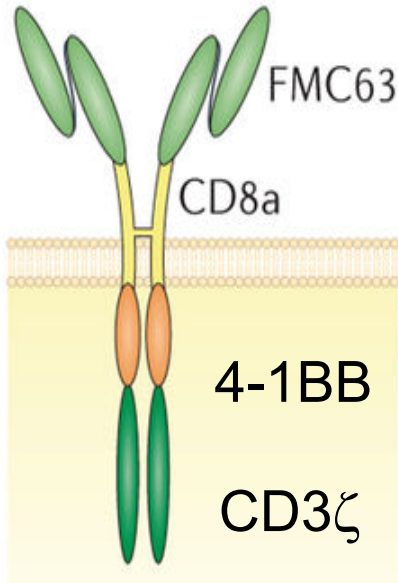
Retrovirus

Kite Pharma

KTE-C19

Axicabtagene ciloleucel

Axi-cel



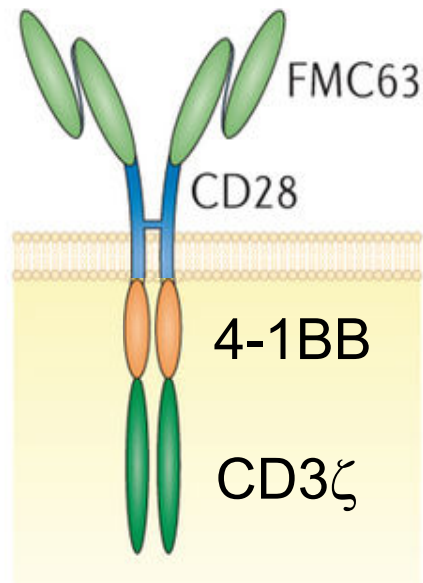
Lentivirus

Novartis

CTL-019

Tisagenlecleucel

Tisa-cel



Lentivirus

Juno Therapeutics

JCAR017 (CD4:CD8 = 1:1)

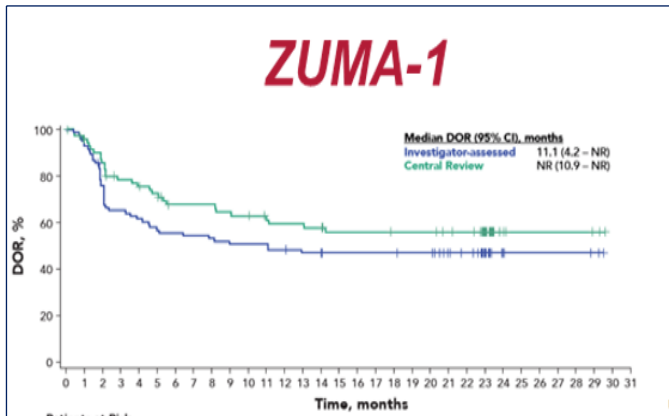
Lisocabtagene maraleucel

Liso-cel

CD19 CAR T-cells Yield Durable Remissions in ~30-40% of Patients

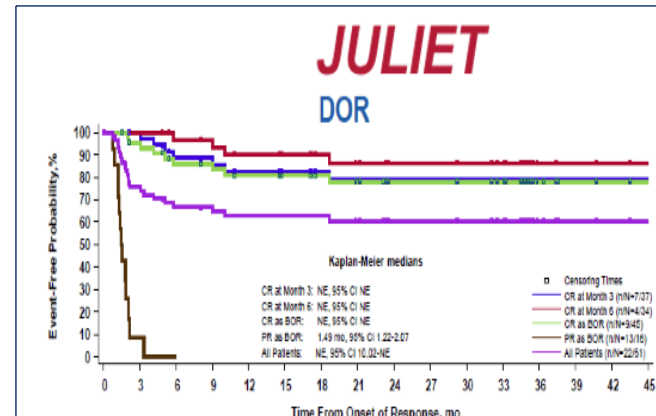
Kite – ZUMA-1

- N=101
- Refractory to last line of therapy
- Median follow-up 27.1m
 - Overall response rate 83%
 - Complete response rate 58%



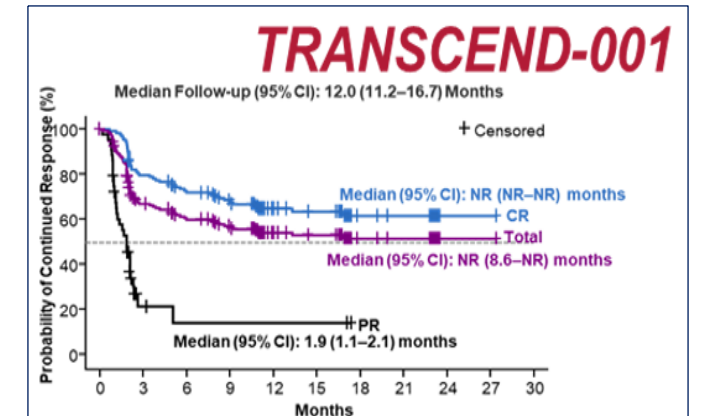
Novartis – JULIET

- N=111
- Relapsed or refractory
- Median follow-up 14 months
 - Overall response rate 52%
 - Complete response rate 40%



Juno - TRANSCEND

- N=255
- Relapsed or refractory
- Median follow-up 18.8 months
 - Overall response rate 73%
 - Complete response rate 53%



CAR T-cells vs Salvage Chemotherapy/Transplant

Aggressive B-NHL
Primary Refractory
Relapse \leq 12 mo of 1L

Bridging
chemo



ZUMA-7
Axi-cel

Bridging
chemo



BELINDA
Tisa-cel

Bridging
chemo

TRANSFORM
Liso-cel

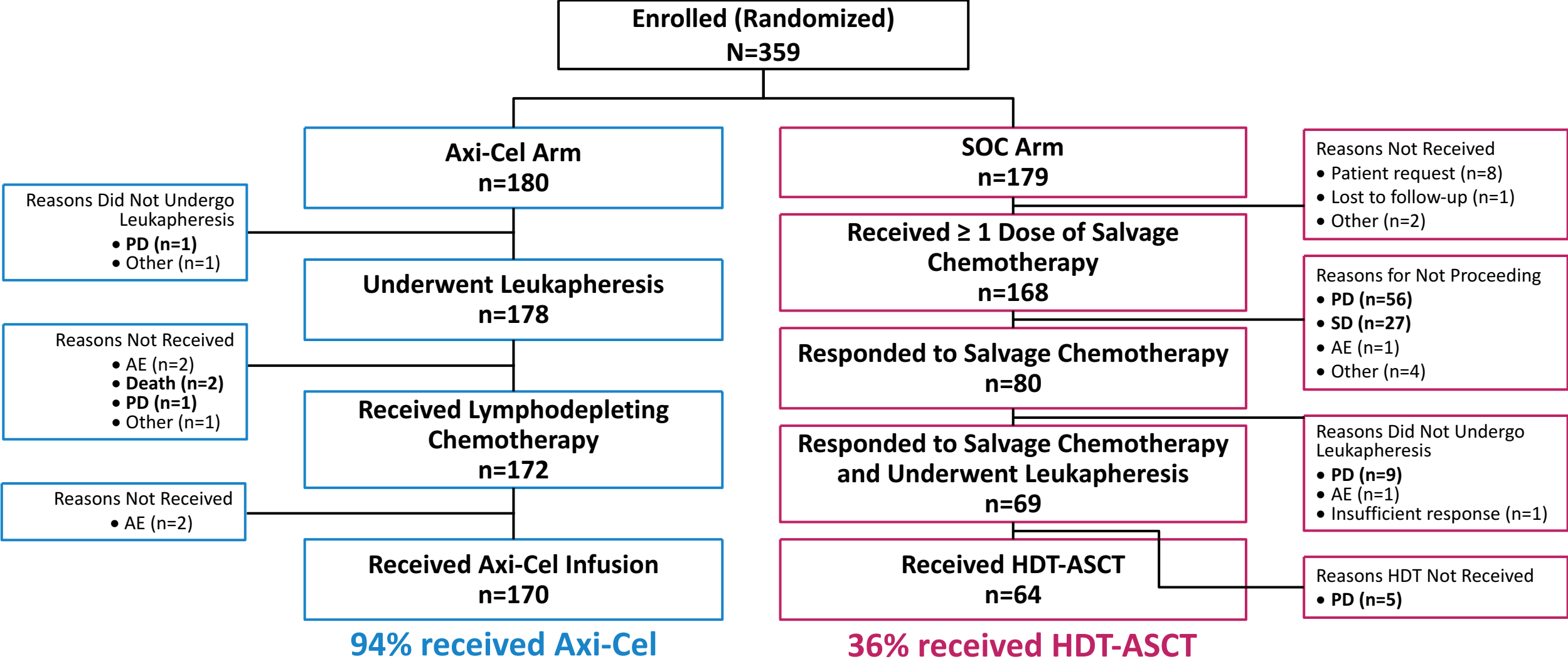
R
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E

1:1

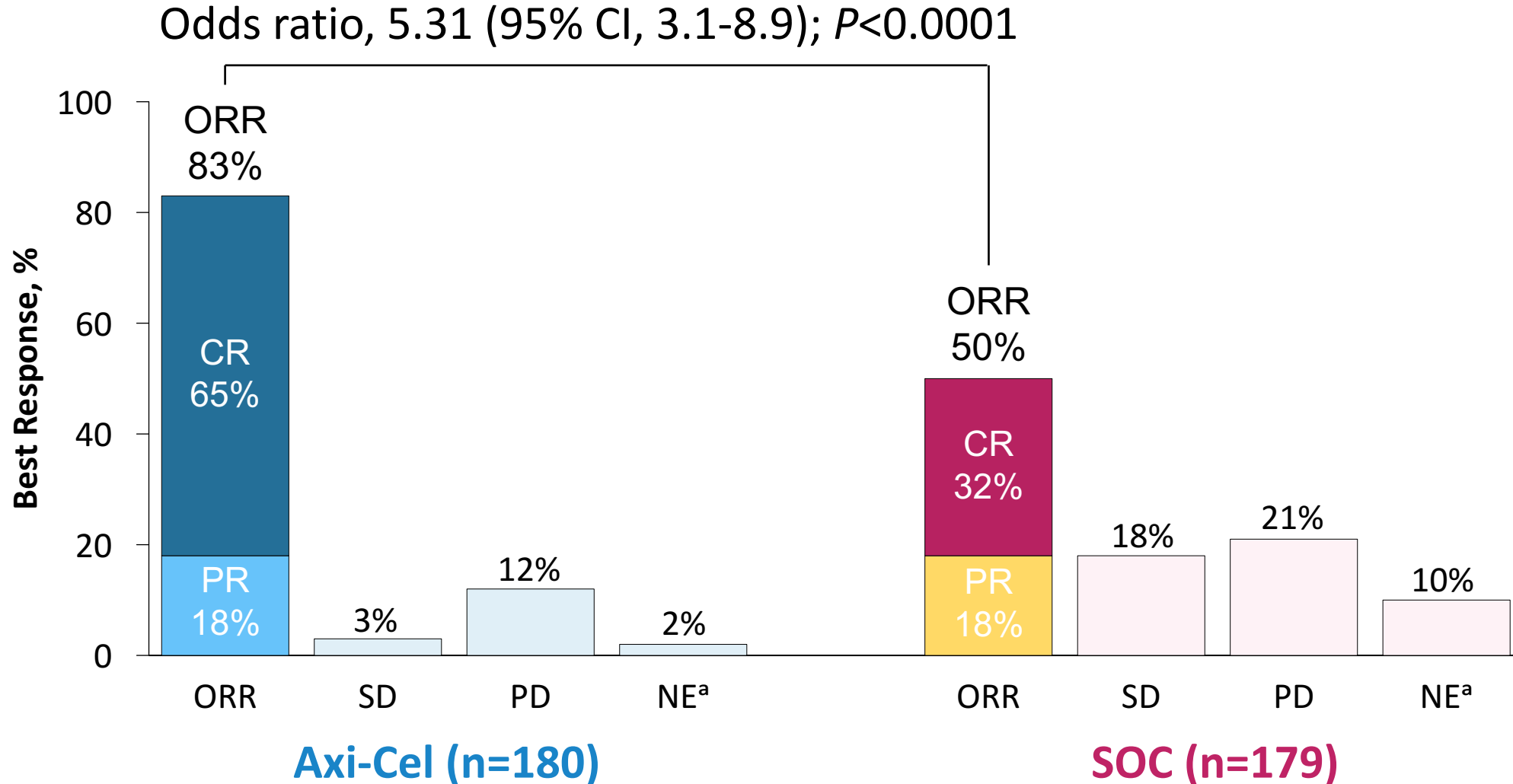
CAR T-cells

Salvage/ASCT

Zuma-7: Nearly 3x as Many Axi-Cel Patients Received Definitive Therapy Versus SOC Patients



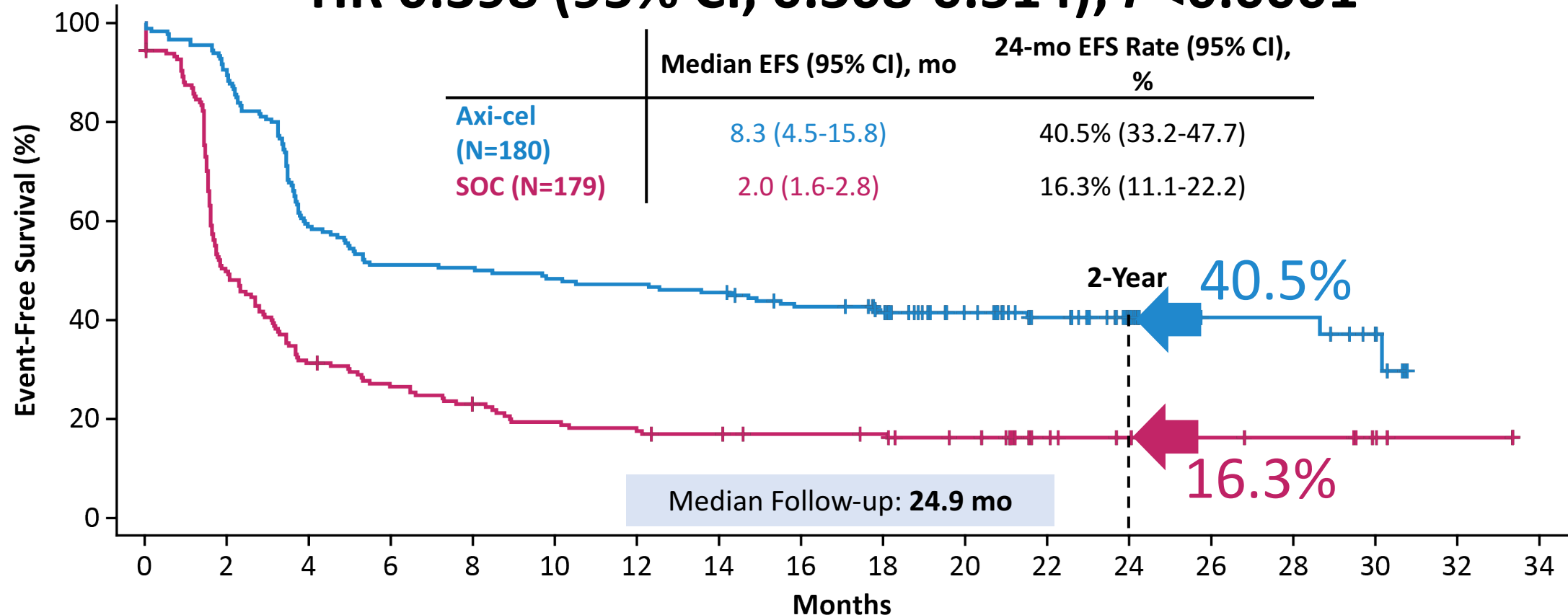
Zuma-7: ORR Significantly Higher in Axi-Cel Vs SOC



^a Not evaluable (NE): In the axi-cel arm, response assessments were not done for 4 patients. In the SOC arm, there were 4 patients with undefined disease and 14 who did not have response assessments done.

Primary EFS Endpoint: Axi-Cel Is Superior to SOC

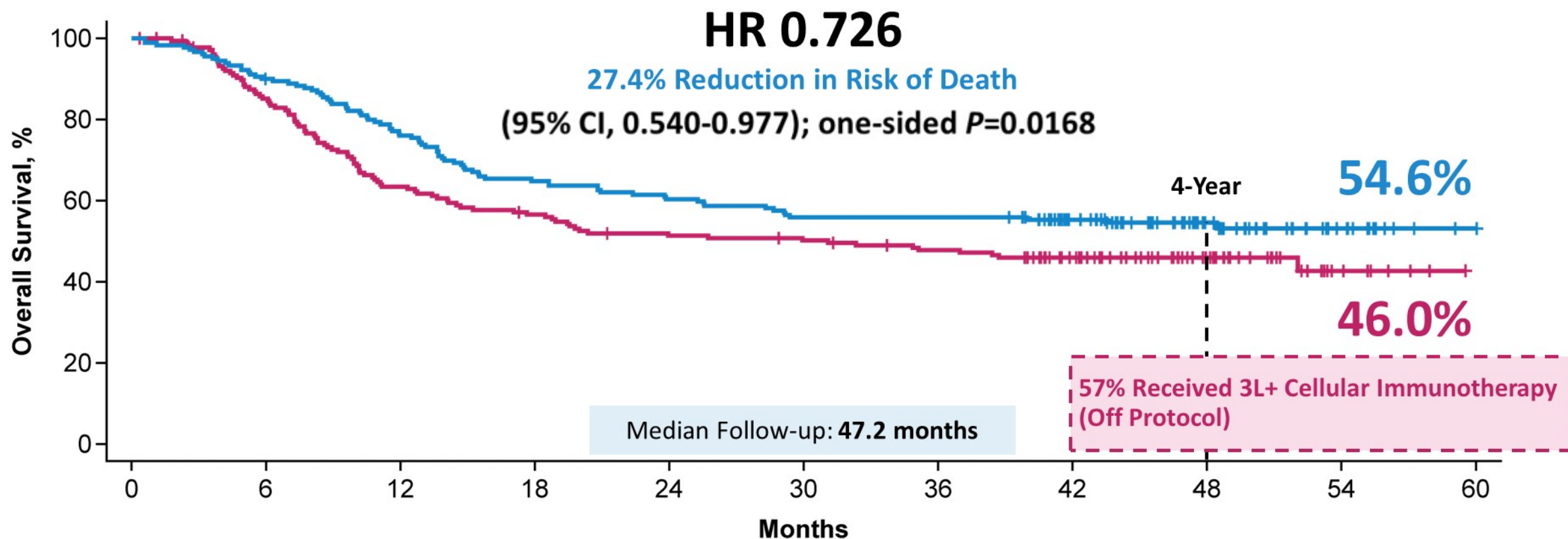
HR 0.398 (95% CI, 0.308-0.514); $P < 0.0001$



No. at Risk

Axi-cel	180	163	106	92	91	87	85	82	74	67	52	40	26	12	12	6		
SOC	179	86	54	45	38	32	29	27	25	24	20	12	9	7	6	3	1	0

Axi-Cel Improved Overall Survival Versus Standard of Care



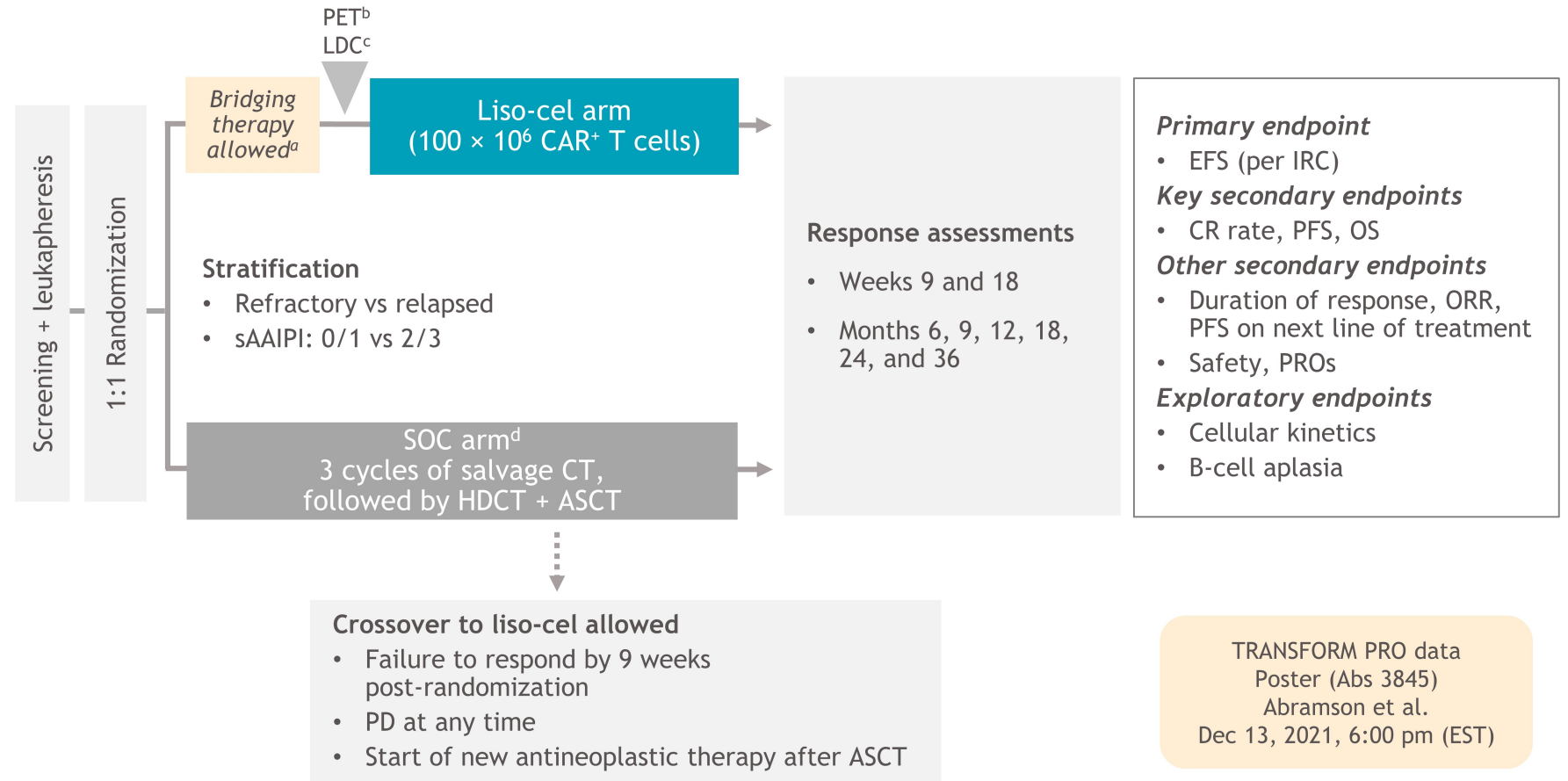
- 57% (n=102/179) of SOC patients received subsequent cellular immunotherapy (off protocol)
- Despite the increased survival in the SOC arm versus historical studies, axi-cel increased survival over SOC^{a,b}

^a Approximately 30% for early R/R LBCL in ORCHARRD (van Imhoff GW, et al. *J Clin Oncol.* 2017;35:544-551). ^b <40% for those with prior rituximab and early R/R LBCL in CORAL (Gisselbrecht C, et al. *J Clin Oncol.* 2010;28:4184-4190). 3L, third line; axi-cel, axicabtagene ciloleucel; HR, hazard ratio; LBCL, large B-cell lymphoma; R/R, relapsed/refractory; SOC, standard of care.

TRANSFORM study design

Key eligibility

- Age 18–75 years
- Aggressive NHL
 - DLBCL NOS (de novo or transformed from indolent NHL), HGBCL (double/triple hit) with DLBCL histology, FL3B, PMBCL, THRBCL
- Refractory or relapsed ≤ 12 months after 1L treatment containing an anthracycline and a CD20-targeted agent
- ECOG PS ≤ 1
- Eligible for HSCT
- Secondary CNS lymphoma allowed
- LVEF > 40% for inclusion
- No minimum absolute lymphocyte count



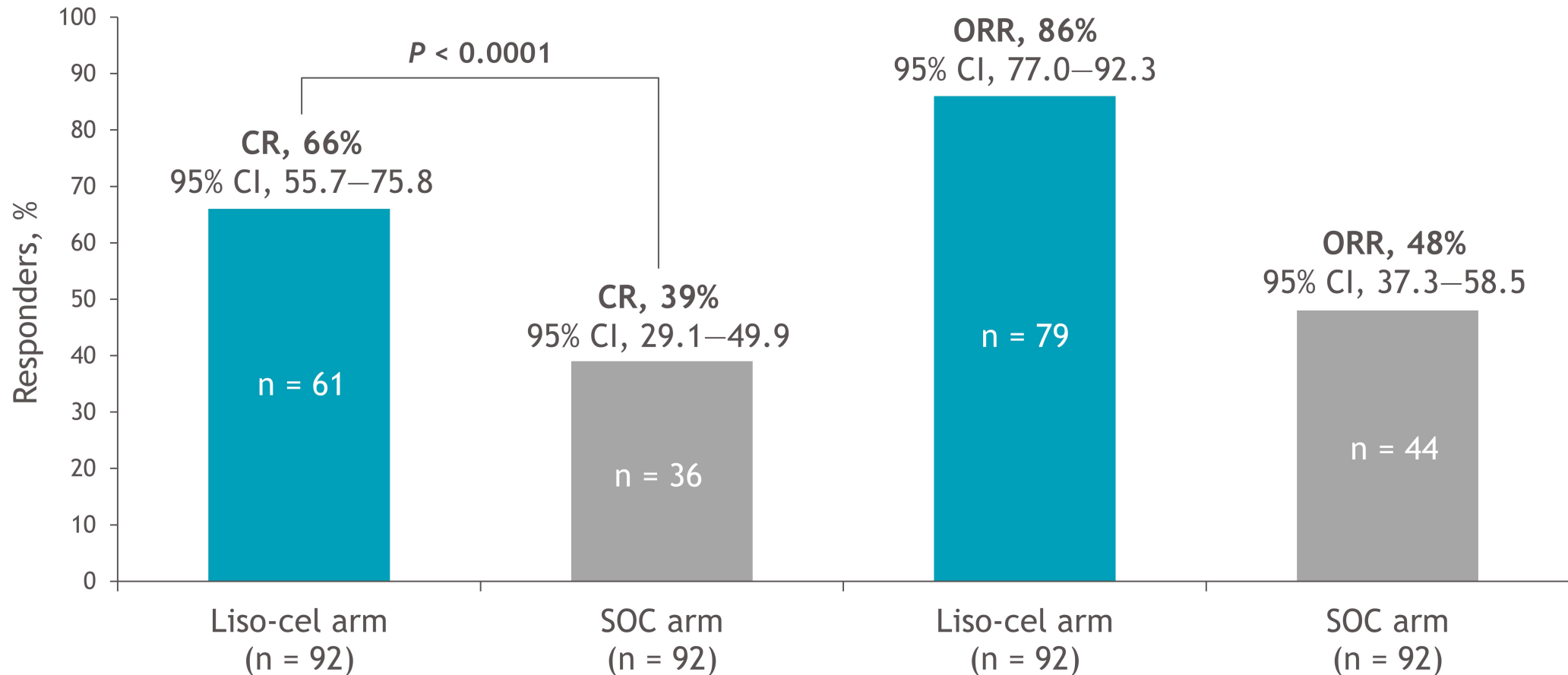
- **EFS is defined as time from randomization to death due to any cause, progressive disease, failure to achieve CR or PR by 9 weeks post-randomization, or start of a new antineoplastic therapy, whichever occurs first**

^aPatients may have received a protocol-defined SOC regimen to stabilize their disease during liso-cel manufacturing; ^bOnly for patients who received bridging therapy;

^cLymphodepletion with fludarabine 30 mg/m² and cyclophosphamide 300 mg/m² for 3 days; ^dSOC was defined as physician's choice of R-DHAP, R-ICE, or R-GDP.

DLBCL, diffuse large-B cell lymphoma; FL3B, follicular lymphoma grade 3B; HGBCL, high-grade B-cell lymphoma; IRC, independent review committee; LDC, lymphodepleting chemotherapy; NOS, not otherwise specified; PD, progressive disease; PMBCL, primary mediastinal large B-cell lymphoma; PRO, patient-reported outcome; sAAIPI, secondary age-adjusted International Prognostic Index; THRBCL, T-cell/histiocyte-rich large B-cell lymphoma.

TRANSFORM: Complete and objective response rates per IRC (ITT set)



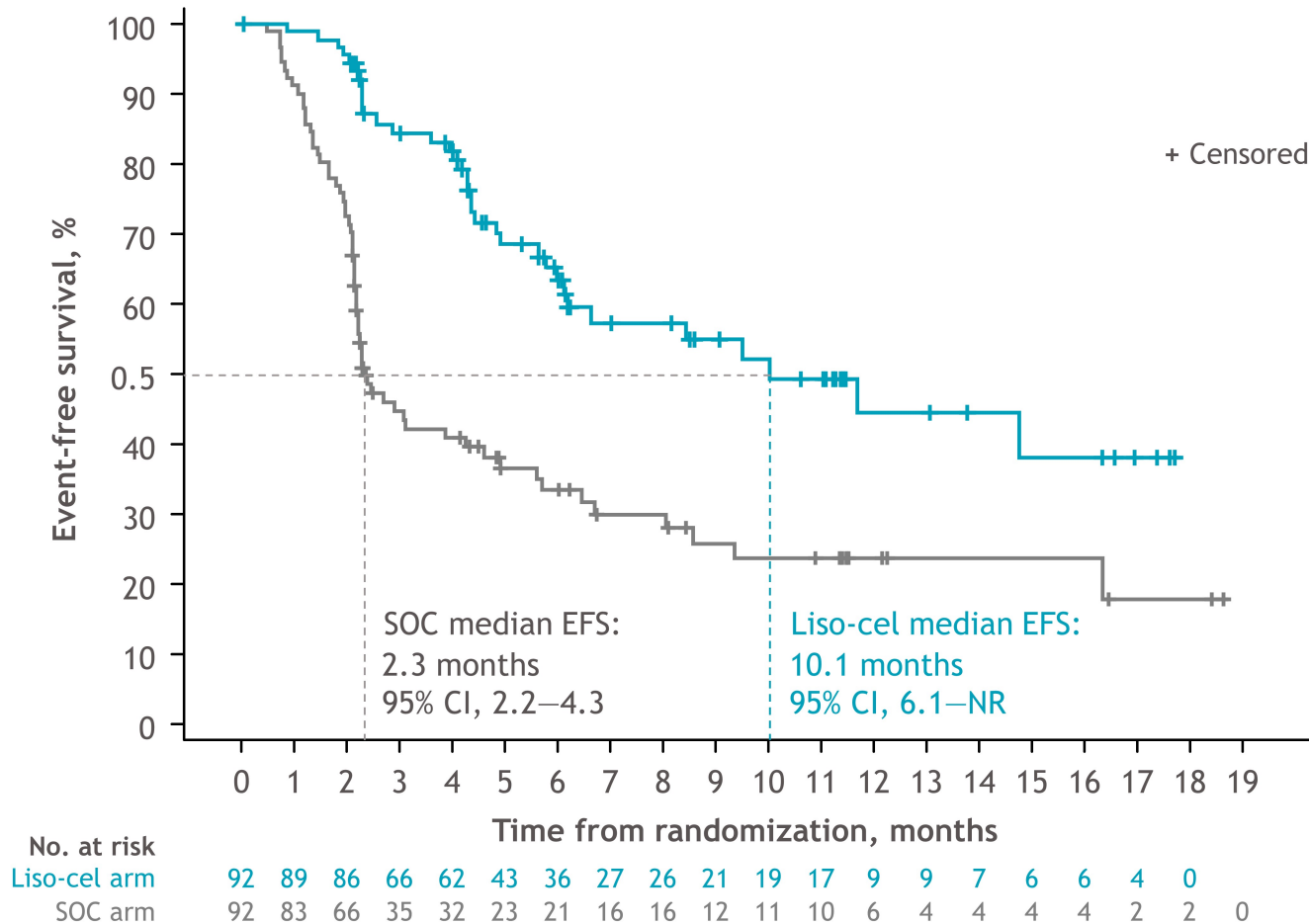
One-sided *P* value significance threshold to reject the null hypothesis was < 0.012

CR rate was defined as the proportion of patients achieving a best overall response of CR.

Kamdar M, et al. ASH 2021 [Abstract #91]

TRANSFORM: Event-free survival per IRC (ITT set; primary endpoint)

Median follow-up in both arms: 6.2 months



	Liso-cel arm (n = 92)	SOC arm (n = 92)
Patients with events, n	35	63
Stratified HR (95% CI)	0.349 (0.229–0.530)	
	<i>P</i> < 0.0001	
6-month EFS rate, % (SE)	63.3 (5.77)	33.4 (5.30)
Two-sided 95% CI	52.0–74.7	23.0–43.8
12-month EFS rate, % (SE)	44.5 (7.72)	23.7 (5.28)
Two-sided 95% CI	29.4–59.6	13.4–34.1

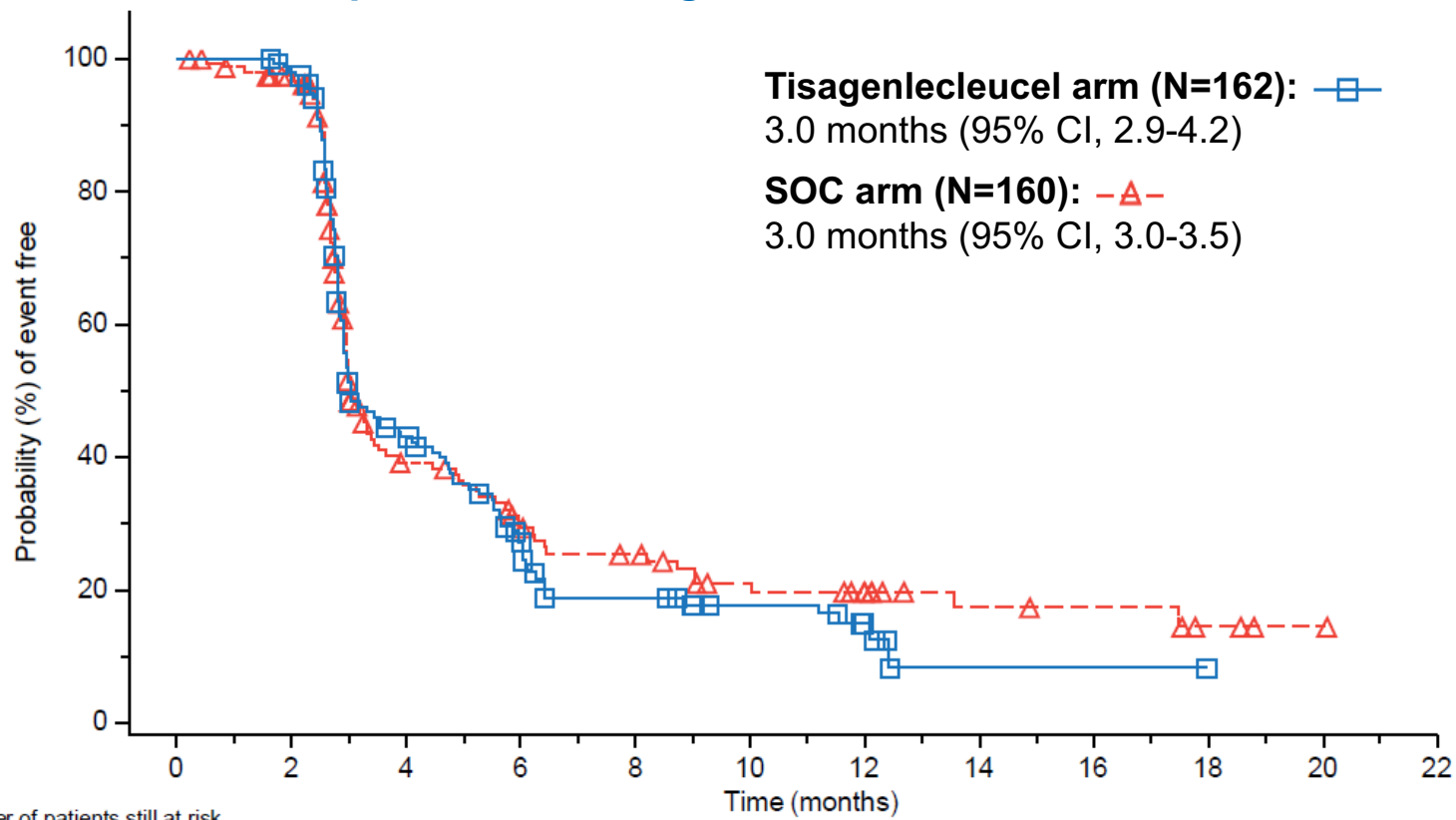
One-sided *P* value significance threshold to reject the null hypothesis was < 0.012

EFS is defined as the time from randomization to death due to any cause, progressive disease, failure to achieve CR or PR by 9 weeks post-randomization or start of a new antineoplastic therapy due to efficacy concerns, whichever occurs first.

CI, confidence interval; HR, hazard ratio; NR, not reached; SE, standard error.

BELINDA: No Difference in EFS Between Treatment Arms

EFS per BIRC in Tisagenlecleucel and SOC Arms

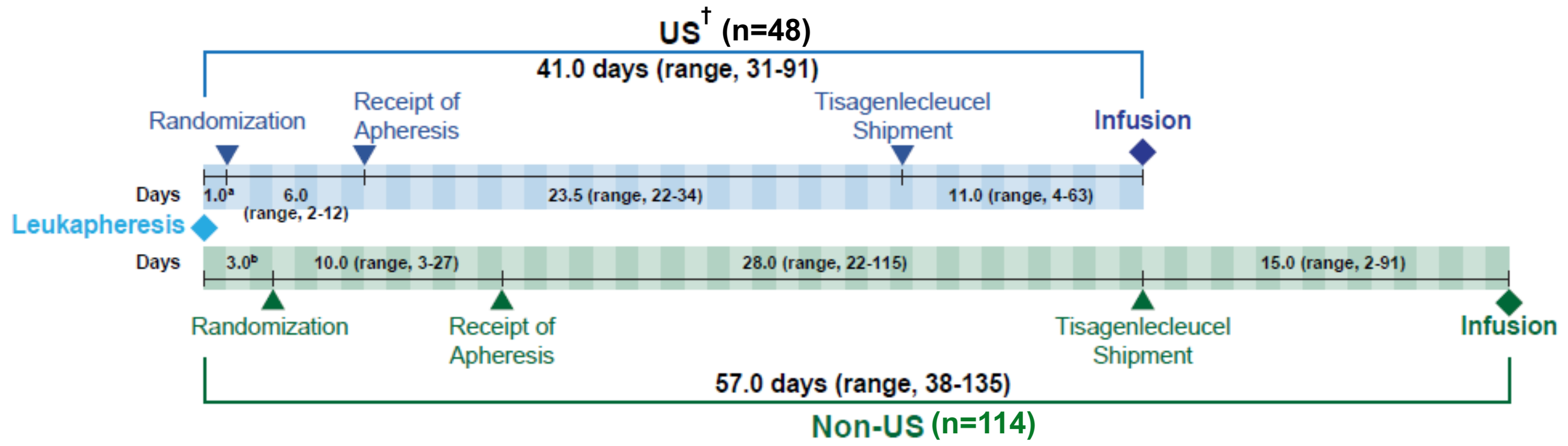


Number of patients still at risk	0	2	4	6	8	10	12	14	16	18	20	22
Tisagenlecleucel arm	162	156	57	32	19	13	6	1	1	0	0	0
SOC arm	160	148	45	31	25	17	12	7	6	3	1	0

- EFS^a was not significantly different between treatment arms
 - Primary analysis:
Stratified unadjusted HR: 1.07 (95% CI, 0.82-1.40, p^b=0.69)
 - Supportive analysis:
Stratified adjusted^c HR: 0.95 (95% CI, 0.72-1.25)
 - 6 patients responded to tisagenlecleucel infusion, but were captured as an EFS event due to SD/PD before or soon after infusion^d

Time to Tisagenlecleucel Infusion

- Median time to infusion for all patients on the Tisagenlecleucel arm was 52 days (range, 31-135)

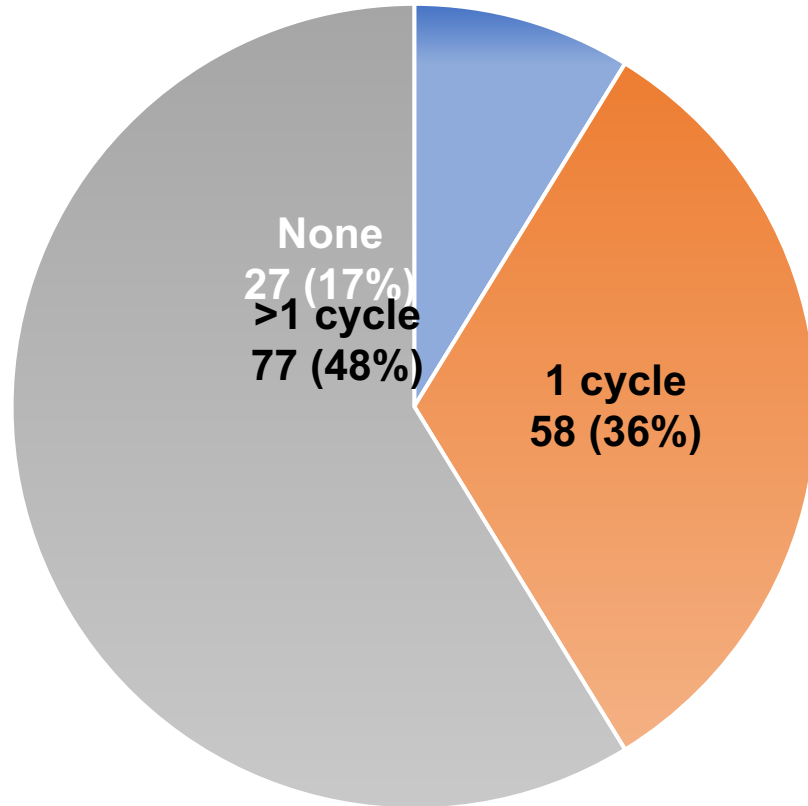


[†]North America was a stratification factor, and all enrolled patients in this group were from the United States (US).

^arange, 1-6 days. ^brange, 1-17 days

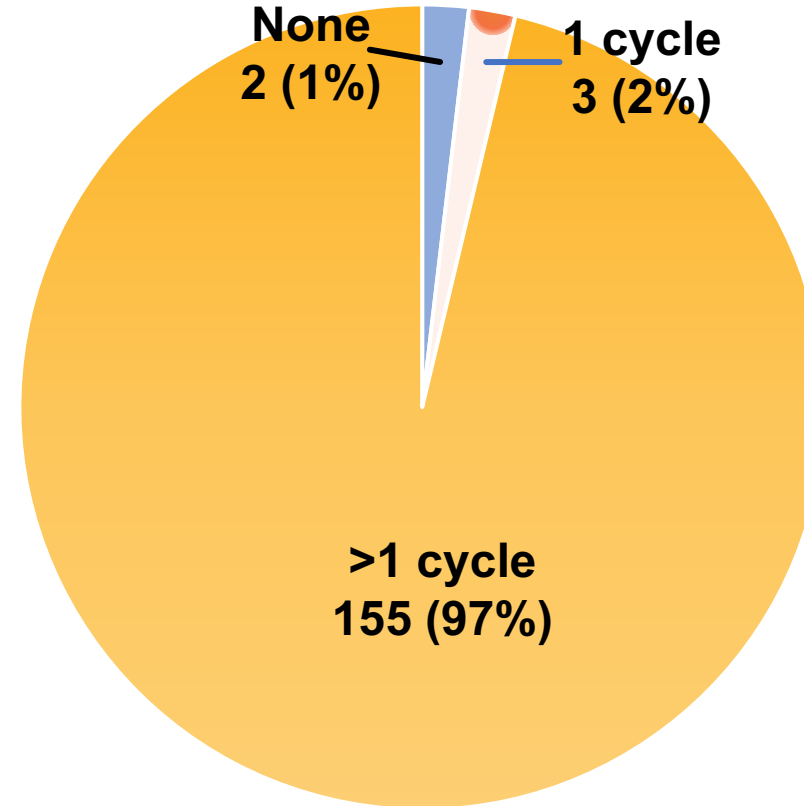
Platinum-based Immuno-Chemotherapy (PCT)

PCT Tisagenlecleucel Arm (n = 162)



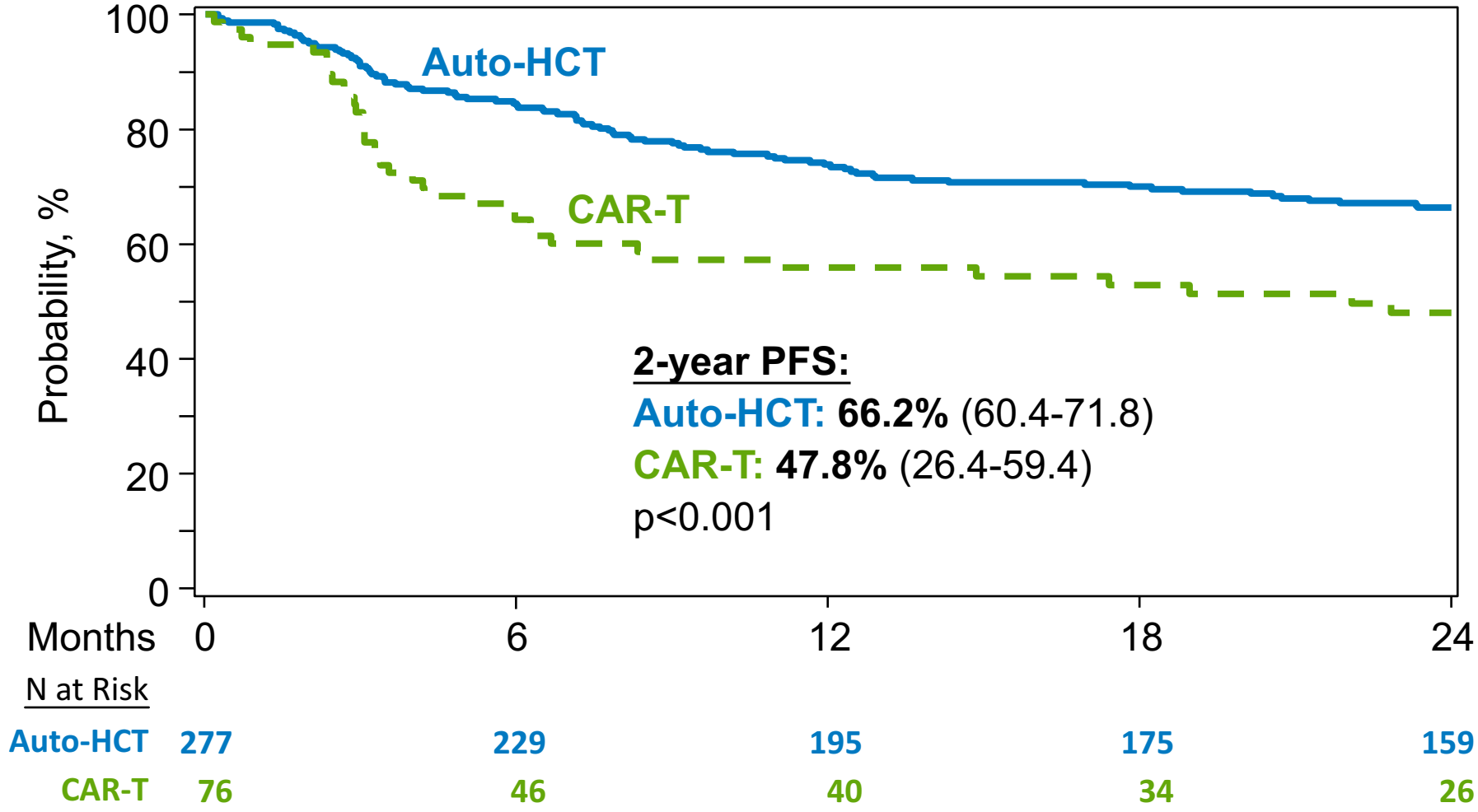
>1 cycle includes 20 (12%) patients who received a second PCT regimen

PCT SOC Arm (n= 160)



>1 cycle includes 86 (54%) patients who received a second PCT regimen

CIBMTR analysis of CART vs ASCT for pts in CR Progression-Free Survival



	N	Follow Up	ORR	CR	mPFS	mOS
ZUMA-1 ¹ (Axi-cel)	101	27.1 mo	83%	58%	5.9 mo	NR
JULIET ² (Tisa-cel)	111	14 mo	52%	40%	NR (responders)	12 mo
TRANSCEND ³ (Liso-cel)	255	18.8 mo	73%	53%	6.8 mo	21.1 mo

	Cytokine Release Syndrome		Neurologic Toxicity Syndrome (ICANS)	
	Any Grade	Severe	Any Grade	Severe
ZUMA-1 ¹ (Axi-cel)	93%	13%	64%	28%
JULIET ² (Tisa-cel)	58%	23%	21%	12%
TRANSCEND ³ (Liso-cel)	37%	1%	25%	15%



BISPECIFIC ANTIBODIES FOR RELAPSED/REFRACTORY DLBCL

Glofitamab Pivotal Phase II Study overview

Pivotal Phase II study in patients with R/R LBCL and ≥ 2 prior therapies

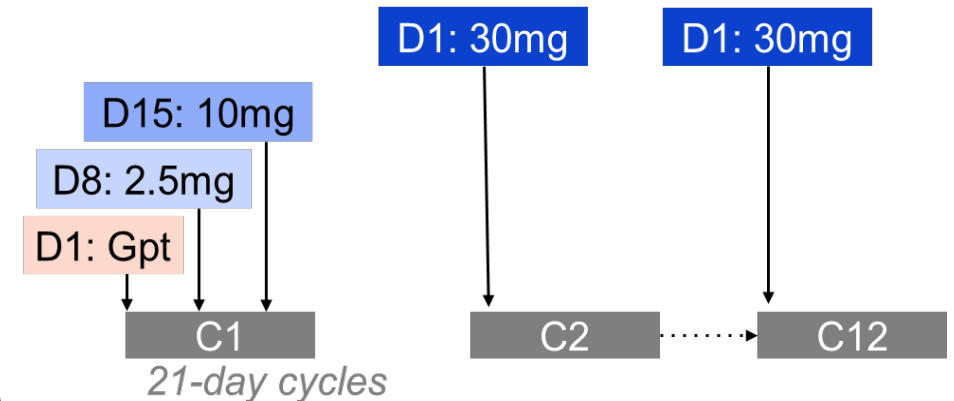
Key inclusion criteria

- DLBCL NOS, HGBCL, trFL, or PMBCL
- ECOG PS 0–1
- ≥ 2 prior therapies, including:
 - Anti-CD20 antibody
 - Anthracycline

Glofitamab IV administration

Fixed-duration treatment

- Maximum 12 cycles
- **CRS* mitigation:**
 - Obinutuzumab pre-treatment (1 x 1000mg)
 - C1 step-up dosing
 - Monitoring after first dose (2.5mg)



Endpoints

- **Primary:** CR rate (as best response) by IRC[†]
- **Key secondary:** ORR[‡], DoR, DoCR[‡], PFS, OS

Landmark analyses

- PFS and OS post-hoc analysis were performed by response (landmark at C3, or EOT)

*By American Society for Transplantation and Cellular Therapy criteria.¹ [†]By PET-CT (Lugano criteria²). [‡]By IRC and investigator. C, cycle; CRS, cytokine release syndrome; D, day; DLBCL NOS, diffuse large B-cell lymphoma not otherwise specified; DoCR, duration of complete response; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; EOT, end-of-treatment; Gpt, Obinutuzumab; HGBCL, high-grade B-cell lymphoma; IRC, independent review committee; IV, intravenous; ORR, overall response rate; OS, overall survival; PET-CT, positron emission tomography-computed tomography; PFS, progression-free survival; PMBCL, primary mediastinal large B-cell lymphoma; trFL, transformed follicular lymphoma.

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

2. Cheson BD, et al. J Clin Oncol 2014;32:3059–68.

Glofitamab in R/R DLBCL: Baseline characteristics

Glofitamab RP2D

n (%)*		N=155 [†]
Median age, years (range)		66.0 (21–90)
Male		101 (65)
ECOG PS	0	69 (45)
	1	84 (54)
Ann Arbor stage	I	10 (7)
	II	25 (16)
	III	31 (20)
	IV	85 (55)
NHL subtype	DLBCL	110 (71)
	trFL	29 (19)
	HGBCL	10 (7)
	PMBCL	6 (4)
Bulky disease	>6cm	64 (41)
	>10cm	19 (12)

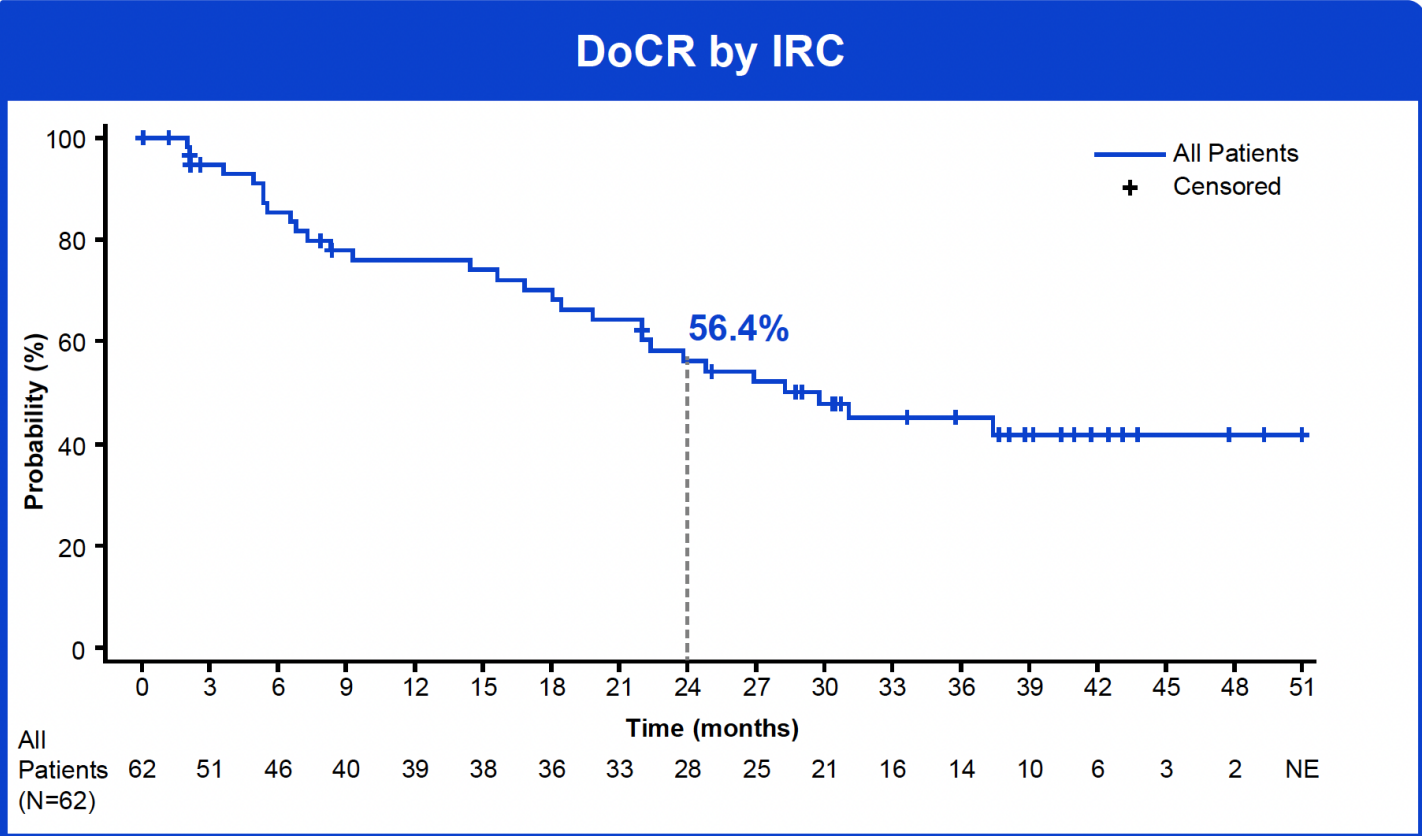
n (%)	N=155
Median no. of prior lines of therapy, n (range)	3 (2–7)
2 prior lines	61 (39)
≥3 prior lines	94 (61)
Prior anti-CD20 therapy	155 (100)
Prior anthracycline therapy	152 (98)
Prior CAR-T	52 (34)
Prior ASCT	29 (19)
Refractory to any prior therapy	139 (90)
Refractory to first prior therapy	91 (59)
Refractory to last prior therapy	131 (85)
Refractory to prior CAR-T	46/52 (88)
Refractory to any prior anti-CD20	129 (83)

The patient population was heavily pre-treated and highly refractory¹

Clinical cut-off date: Jan 16, 2023. *Unless otherwise specified. [†]Intent-to-treat population. ASCT, autologous stem cell transplant; CAR-T, chimeric antigen receptor T-cell; NHL, non-Hodgkin's lymphoma; RP2D, recommended Phase II dose.

Complete responses remained durable following fixed-duration glofitamab treatment

	(N=155)*
CR rate, n (%) [95% CI]	62 (40) [32.2–48.2]
ORR, n (%) [95% CI]	80 (52) [43.5–59.7]
Median DoCR, months (95% CI)	29.8 (22.0–NE)
24-month DoCR, % (95% CI)	56.4 (42.9–69.8)
Ongoing CRs, n/N (%)	33/62 (53.2)
Median CR follow-up, months (range)	37.7 (0–51)



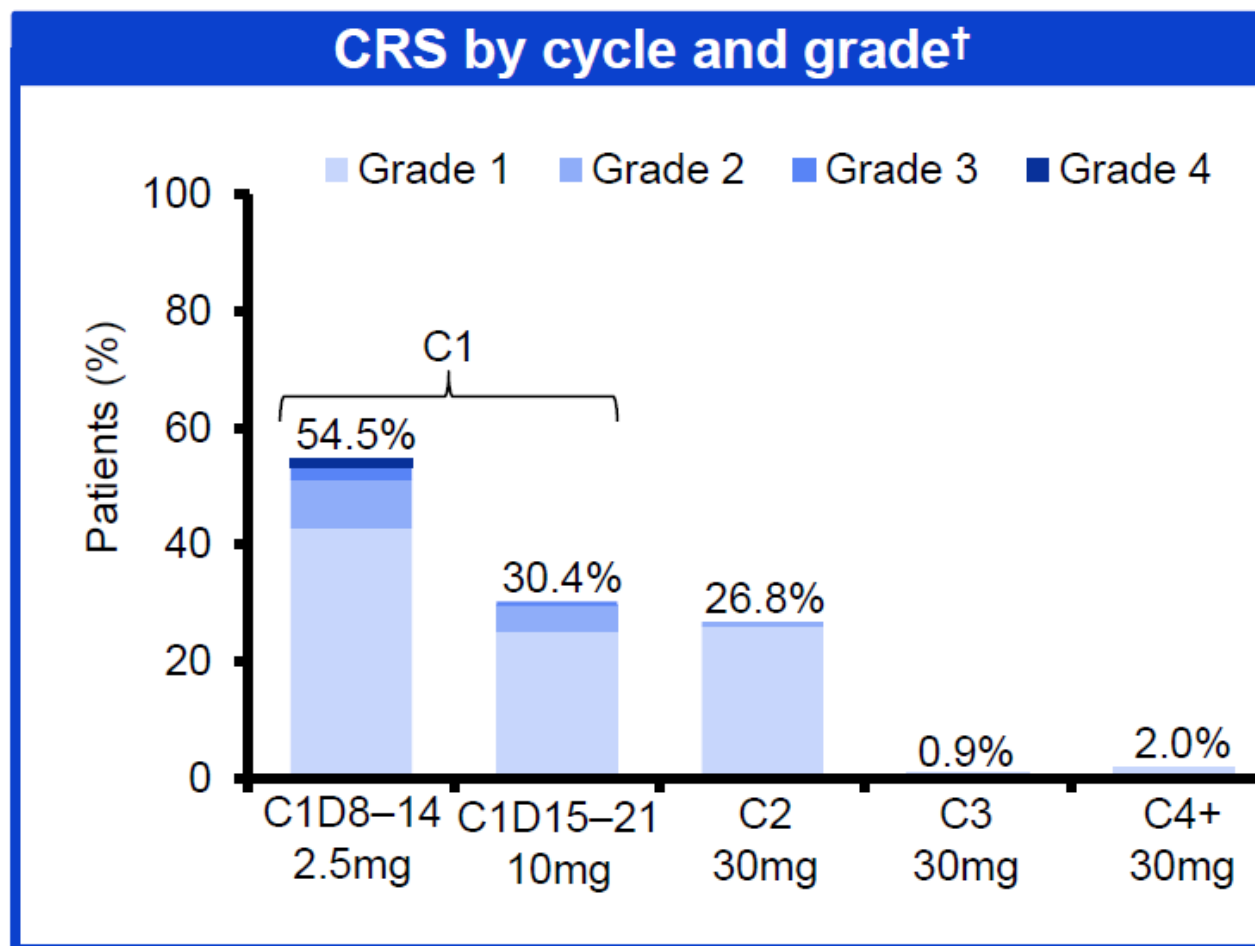
- Median time on study: 41.0 months (range: 0–52)

An estimated 56.4% of patients with a CR at any time remained in remission at 24 months

All responses in the table are based on the best overall response; *Intention-to-treat population; CI, confidence interval; NE, not estimable. Dickinson M, et al. ASH 2024.

Cytokine release syndrome

n (%)	N=154
CRS (any grade)*	97 (63.0)
Grade 1 (fever)	73 (47.4)
Grade 2	18 (11.7)
Grade 3	4 (2.6)
Grade 4	2 (1.3)
Median time to CRS onset from C1D8 dose, hours (range)	13.6 (6.2–51.8)
Corticosteroids for CRS management	27/97 (27.8)
Tocilizumab for CRS management	31/97 (32.0)



CRS was mostly low grade, time of onset was predictable, and most events occurred during C1

Epcoritamab



Prior Treatments	DLBCL & HGBCL, n=148	LBCL, N=157
Median time from initial diagnosis to first dose, mo	19	19
Median time from end of last therapy to first dose, mo	2.4	2.4
Median prior lines of therapy (range)	3 (2–11)	3 (2–11)
≥3 Lines of therapy, n (%)	104 (70)	110 (70)
Primary refractory ^b disease, n (%)	88 (59)	95 (61)
Refractory ^b to last systemic therapy, n (%)	122 (82)	130 (83)
Refractory ^b to ≥2 consecutive lines of therapy, n (%)	112 (76)	118 (75)
Prior ASCT, n (%)	27 (18)	31 (20)
Prior CAR T therapy, n (%)	58 (39)	61 (39)
Refractory ^b to CAR T therapy	43/58 (74)	46/61 (75)

Epcoritamab is effective in R/R DLBCL



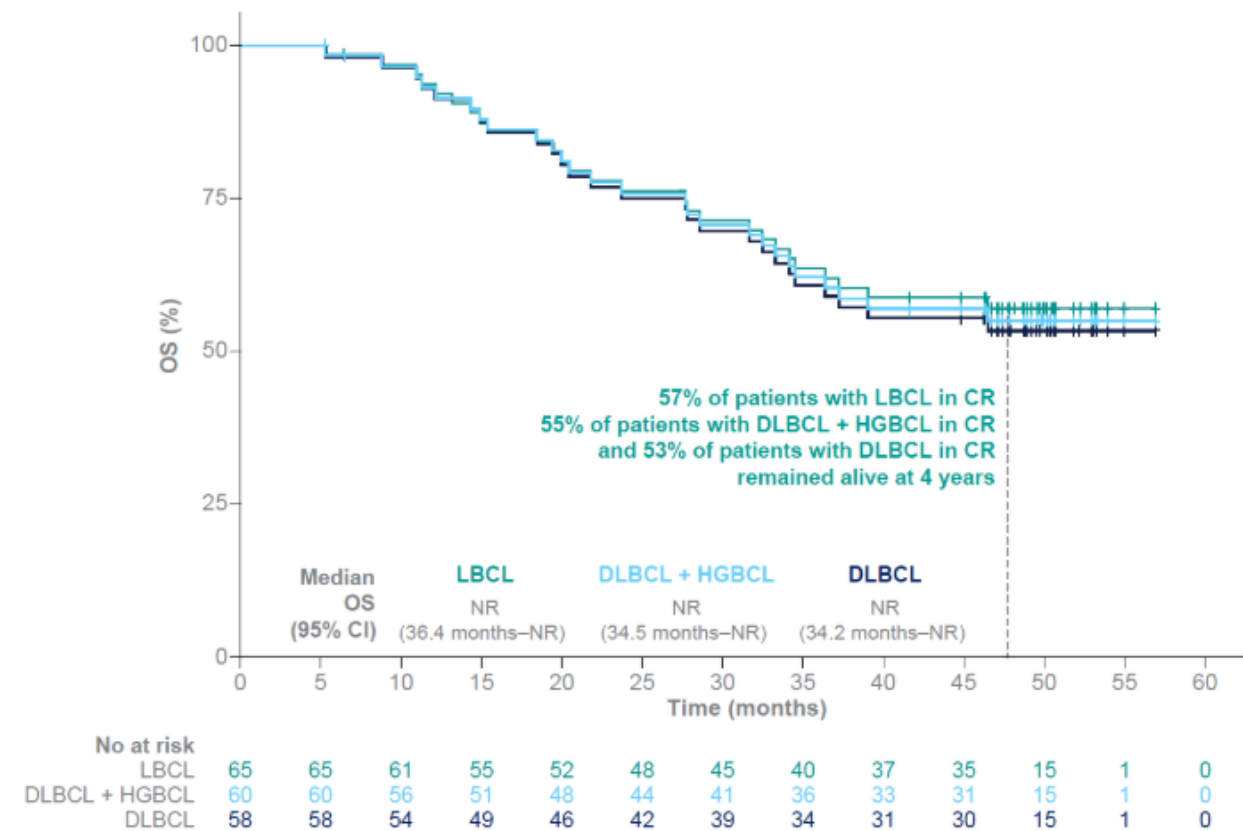
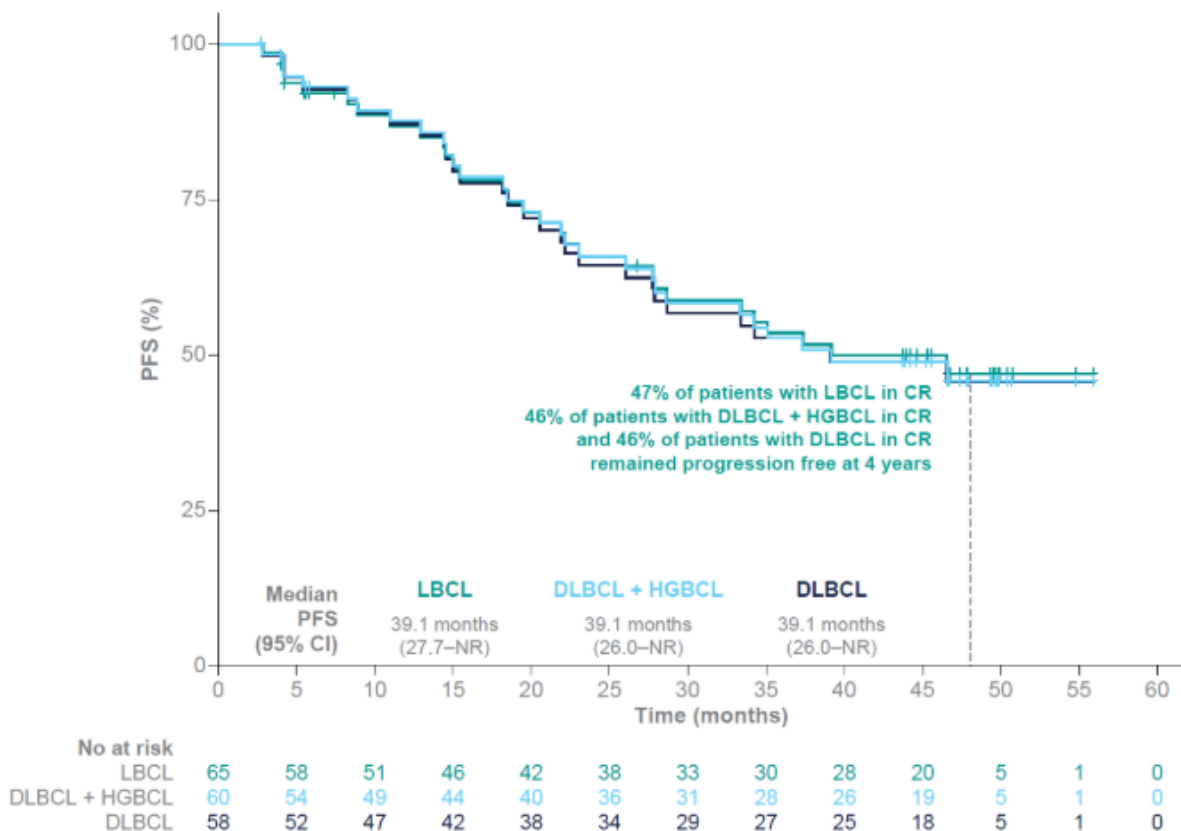
High Rates of Complete Response

Best Overall Response, n (%)	DLBCL & HGBCL, n=148 ^a	LBCL, N=157 ^a
Overall response	90 (61) [95% CI, 53–69]	99 (63) [95% CI, 55–71]
Complete response	57 (39) [95% CI, 31–47]	62 (39) [95% CI, 32–48]
Partial response	33 (22)	37 (24)
Stable disease	5 (3)	5 (3)
Progressive disease	37 (25)	37 (24)

Based on IRC per Lugano criteria. ^a16 patients were not evaluable.



Epcoritamab: Nearly half of CRs are durable at 4 years



- At the 4-year landmark, an estimated 32% of all patients and 57% of patients with a CR remained alive

Median follow-up time for PFS was 46.6 months (95% CI, 44.2–49.3) for patients in CR with LBCL (n = 65), 47.4 months (95% CI, 44.2–49.5) with DLBCL + HGBCL (n = 60), and 46.7 months (95% CI, 44.2–49.7) in DLBCL (n = 58). Median follow-up time for OS was 49.5 months (95% CI, 48.2–50.4) for patients in CR with LBCL (n = 65), 49.8 months (95% CI, 47.9–50.6) with DLBCL + HGBCL (n = 60), and 49.8 months (95% CI, 47.9–50.6) in DLBCL (n = 58). CI, confidence interval; CR, complete response; DLBCL, diffuse large B-cell lymphoma; HGBCL, high-grade B-cell lymphoma; LBCL, large B-cell lymphoma; NR, not reached; OS, overall survival; PFS, progression-free survival; R/R, relapsed or refractory.

Cytokine release syndrome after Epcoritamab



	LBCL N=157
CRS, n (%) ^a	80 (51)
Grade 1	50 (32)
Grade 2	25 (16)
Grade 3	5 (3)
Median time to onset after first full dose, h	20
Treated with anticytokine therapy, n (%)	23 (15)
Leading to treatment discontinuation, n (%)	1 (1)
CRS resolution, n/n (%)	79/80 (99)
Median time to resolution, d (range) ^b	2 (1–27)

^aGraded by Lee et al 2019 criteria.⁹ ^bMedian is Kaplan–Meier estimate based on longest CRS duration in patients with CRS.

STARGLO: GLOFIT+GEMOX

STARGLO: randomized Phase III trial in ASCT-ineligible patients with R/R DLBCL

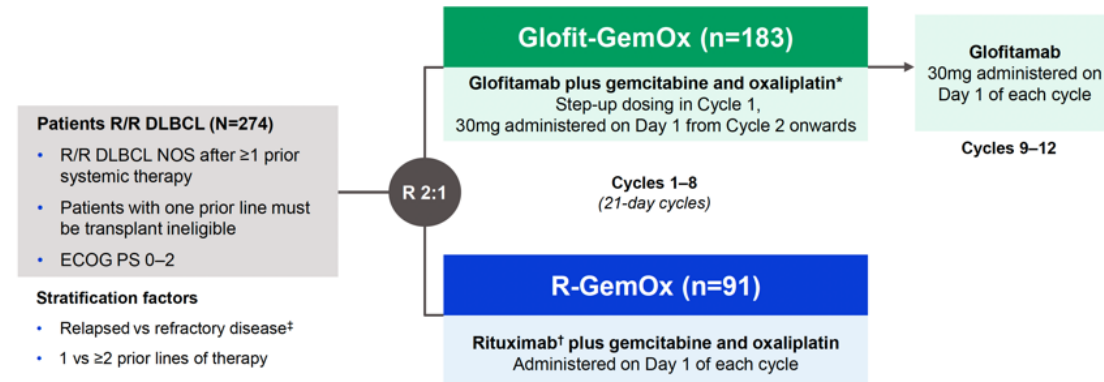


Table 2. Efficacy summary (intent-to-treat population).

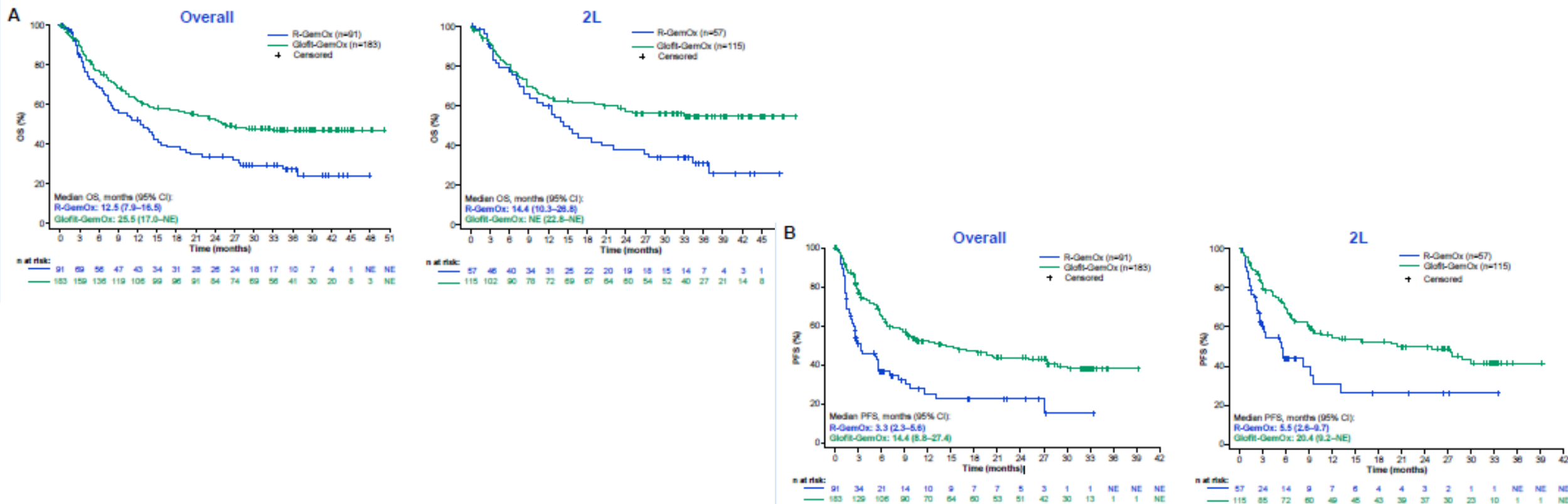
	Overall		2L	
	R-GemOx (n=91)	Glofit-GemOx (n=183)	R-GemOx (n=57)	Glofit-GemOx (n=115)
36-month OS, % (95% CI)	27.4 (17.3–37.5)	47.1 (39.5–54.6)	30.8 (17.7–44.0)	54.6 (45.2–64.0)
30-month PFS, % (95% CI)	15.2 (0.9–29.5)	38.1 (29.8–46.3)	26.3 (10.3–42.4)	41.5 (30.8–52.2)
ORR, n (%)	37 (40.7)	125 (68.3)	28 (49.1)	83 (72.2)
CR, n (%)	23 (25.3)	107 (58.5)	16 (28.1)	73 (63.5)
Median DoCR, months (95% CI)	24.2 (6.9–NE)	NE (27.2–NE)	NE (6.5–NE)	NE (24.8–NE)

ORR, overall response rate.

Glofit-GemOx in 2L: longer PFS and OS



Figure 2. Analysis of (A) OS and (B) PFS in the overall population and in the 2L setting.



Abramson J, et al ASH 2025

- In Glofit-GemOx-treated patients with a CR at end of treatment (EOT), median OS and PFS were not reached (**Figure 3**)
 - OS rate 24 months after EOT: 79.4% (95% CI: 70.3–88.4)
 - PFS rate 24 months after EOT: 74.2% (95% CI: 62.6–85.8).



Efficacy Results

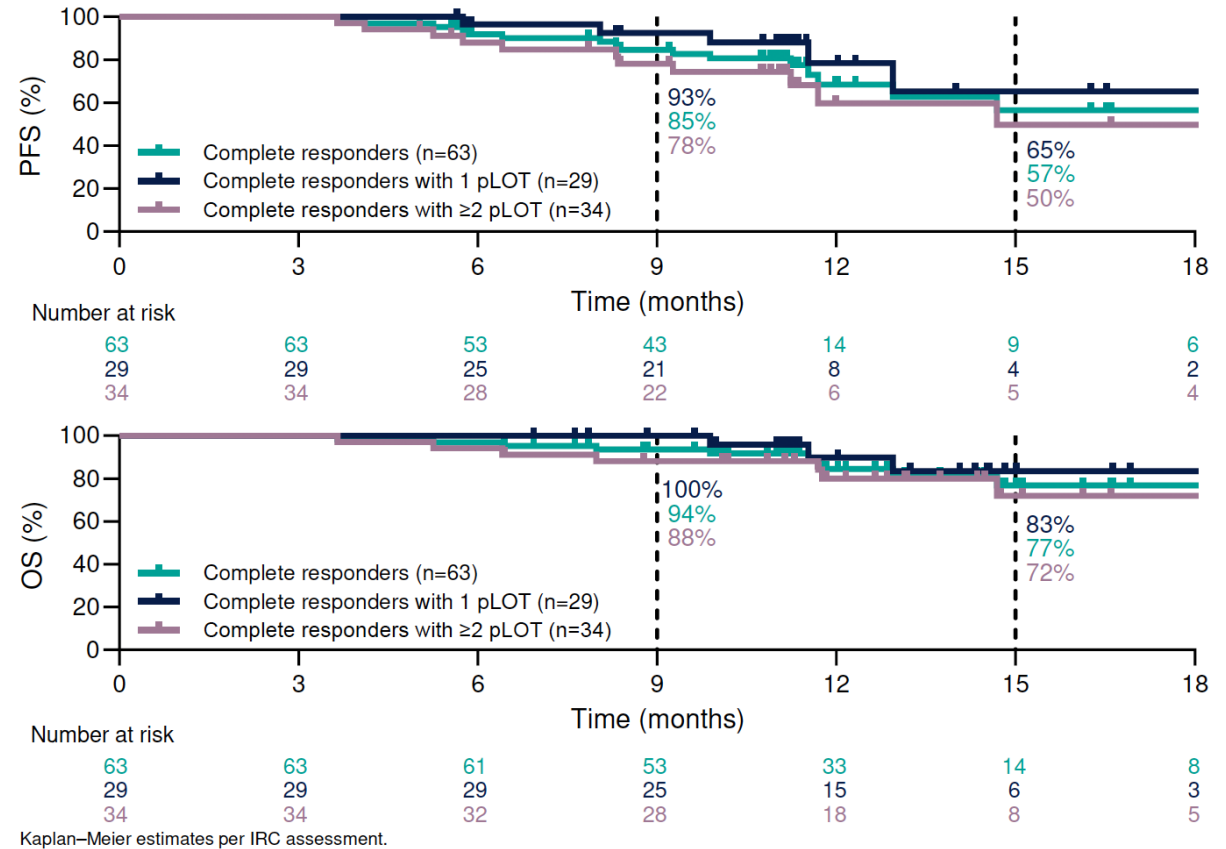
Responses Occurred Early and Rates Were High

Best Overall Response, n (%)	Investigator Assessment N=103 ^a	IRC Assessment N=103 ^b
Overall response rate	82 (80)	88 (85)
Complete response	60 (58)	63 (61)
Partial response	22 (21)	25 (24)
Median time to response (range), mo	1.5 (0.9–11.1)	1.5 (0.9–3.0)
Median time to complete response (range), mo	1.7 (1.3–10.7)	2.6 (1.3–22.1)

^aFive patients were not evaluable for response per investigator. ^bFour patients were not evaluable for response per IRC.

- High concordance (90%) between investigator and IRC assessment
- By IRC assessment, median duration of response among complete responders was 25.4 mo (range, 2.2 to 31.9+)

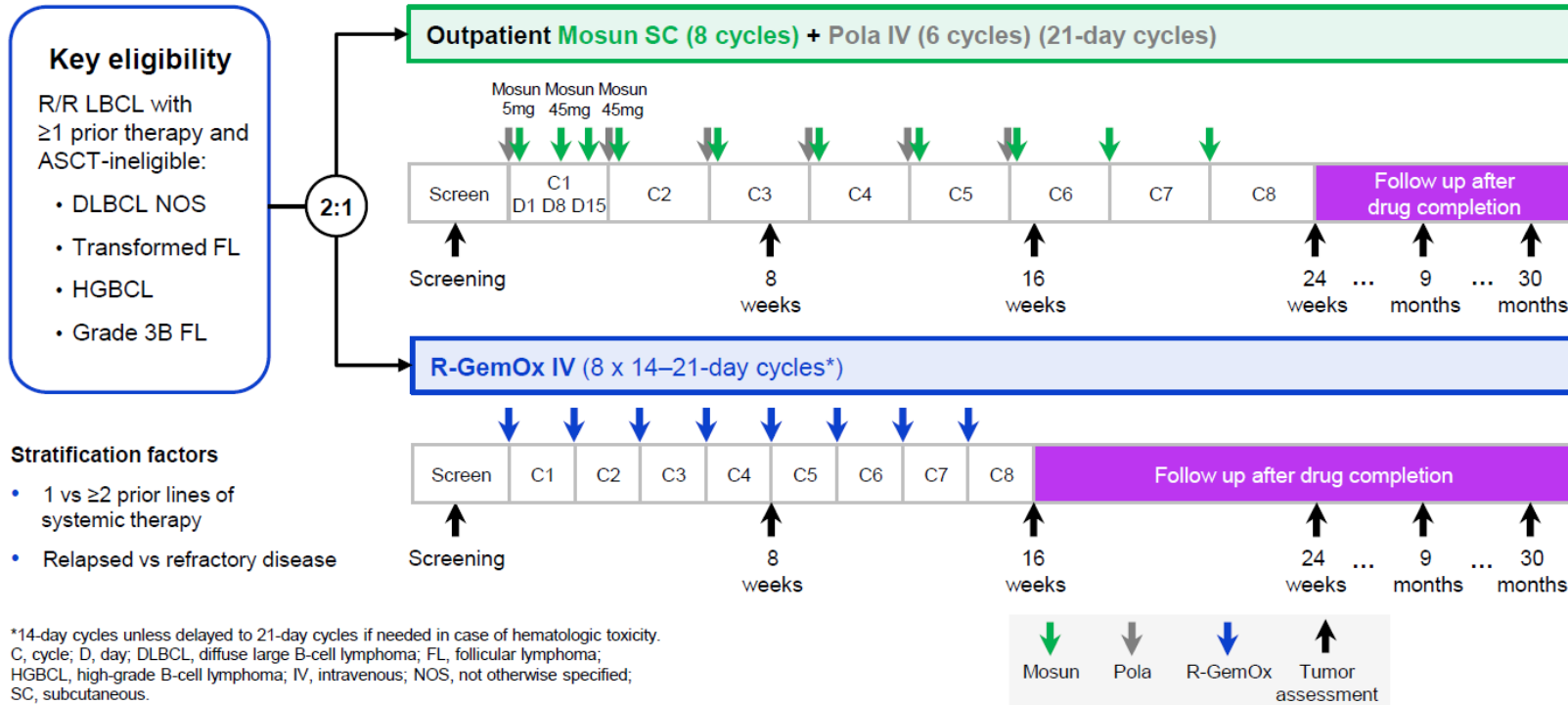
High Rates of Progression-Free and Overall Survival Among Complete Responders



SUNMO: Mosun-Pola vs R-GemOx



Study design

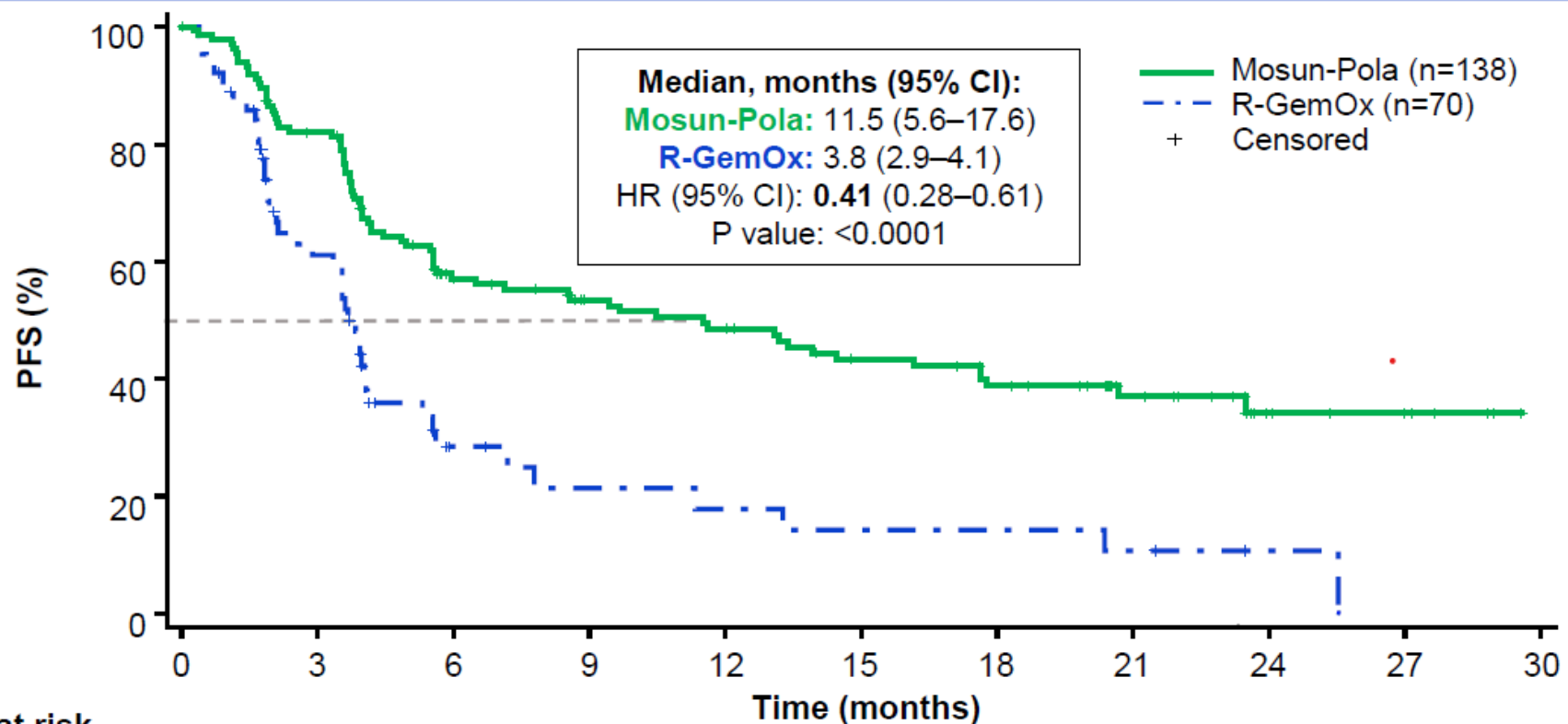


	ORR	CR
Mosun-Pola	70%	51%
R-GemOx	40%	24%

Mosun-Pola
ORR 70% vs 40%
CR 51% vs 24%

Mosun-Pola significantly prolonged progression-free survival versus R-GemOx

Primary endpoint: Progression-free survival by IRC

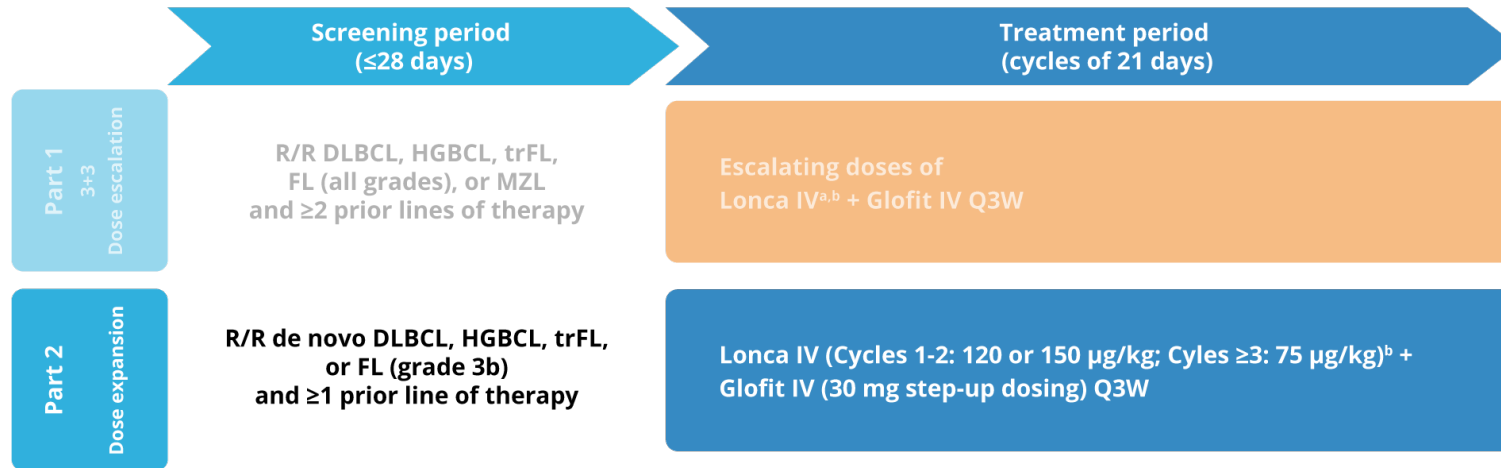


Mosun-Pola demonstrates a 59% risk reduction for progression or death compared with R-GemOx

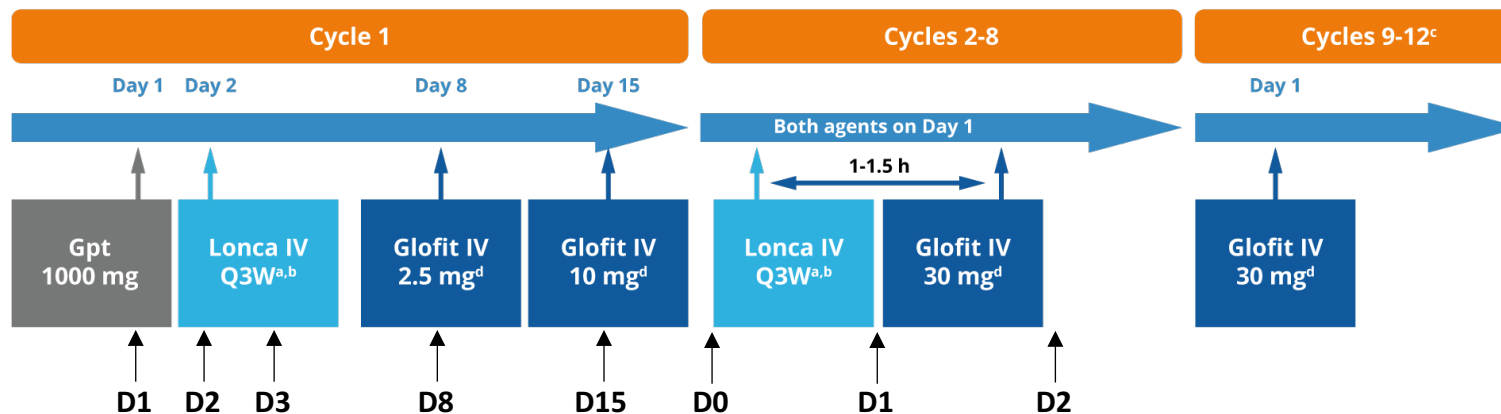
n at risk		0	3	6	9	12	15	18	21	24	27	30
Mosun-Pola	138	108	65	54	49	40	34	20	8	5	NE	NE
R-GemOx	70	33	9	6	5	4	4	3	1	NE	NE	NE

Clinical cut-off date: 17 February, 2025. PFS is censored at earliest of NALT or two or more missing tumor assessments, whichever occurred first. CI, confidence interval; HR, hazard ratio; NALT, new anti-lymphoma therapy; NE, non estimable.

Glofit-Lonca: LOTIS-7 Study Design & Patient Population



Lonca + Glofit treatment sequence



Study population

- Patients with 3L+ R/R B-NHL (part 1) and 2L+ R/R LBCL (part 2)
- ECOG PS score of 0-2
- Prior autologous SCT (>100 days) or CAR-T therapy (>100 days) is allowed
- Measurable disease (per 2014 Lugano Classification)
- Excludes patients with clinically significant third-space fluid accumulation

Endpoints

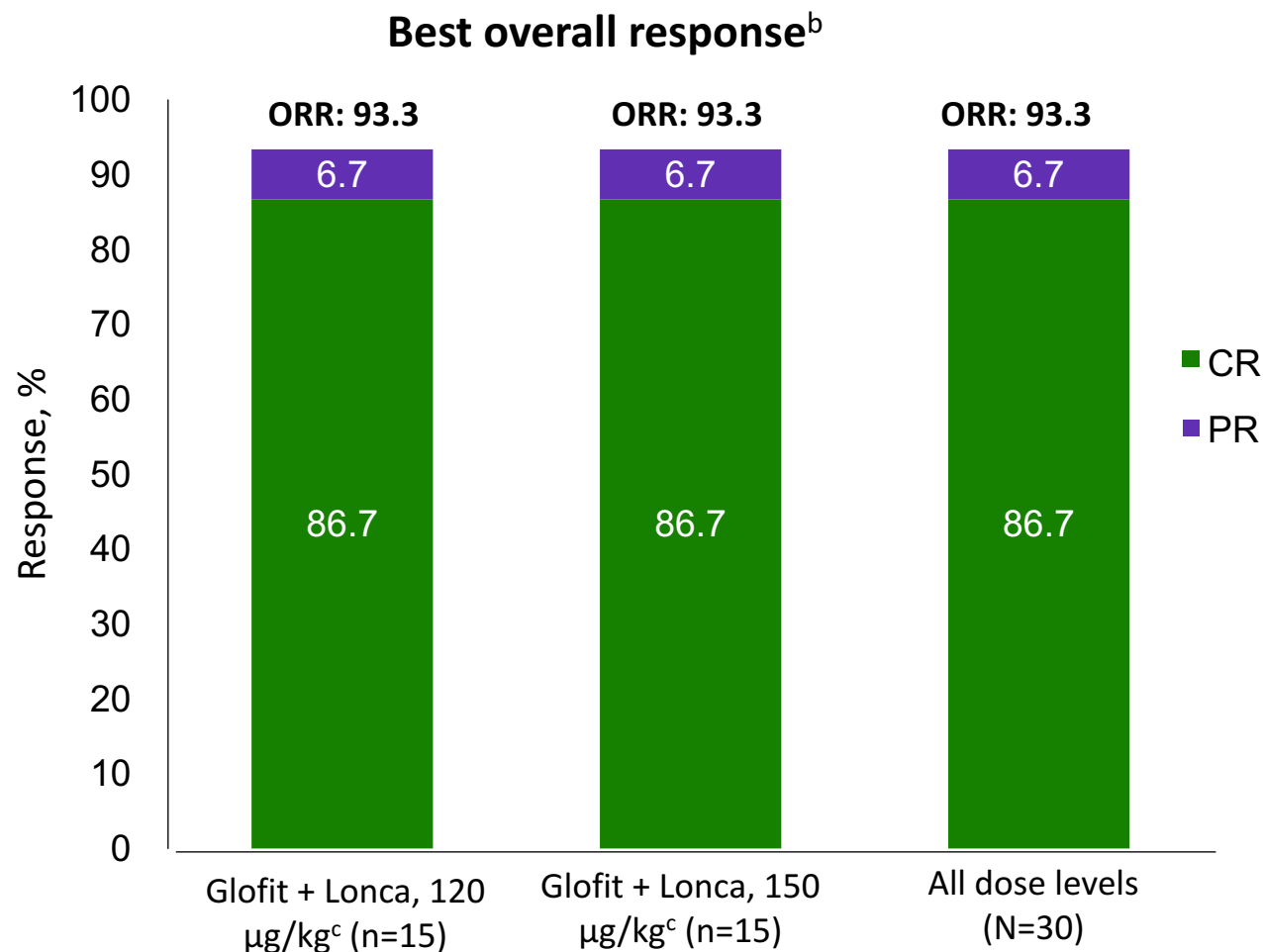
- **Primary:** safety and tolerability; MTD and/or RDE
- **Secondary:** ORR, DOR, CR rate, PFS, RFS, and OS; PK and immunogenicity
- **Exploratory:** Glofit concentration in circulation; biomarker and PK correlations with clinical outcomes

2L+, second line or later; 3L+, third line or later; B-NHL, B-cell non-Hodgkin lymphoma; CAR-T, chimeric antigen receptor T cell; CR, complete response; CRS, cytokine release syndrome; D, day; Dex, dexamethasone; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; FL, follicular lymphoma; Glofit, glofitamab; Gpt, obinutuzumab; HGBCL, high-grade B-cell lymphoma; IV, intravenous; Lonca, loncastuximab tesirine; MTD, maximum tolerated dose; MZL, marginal zone lymphoma; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; PK, pharmacokinetic; Q3W, every 3 weeks; RDE, recommended dose for expansion; RFS, relapse-free survival; R/R, relapsed or refractory; SCT, stem cell transplant; trFL, transformed follicular lymphoma.

^aDose level 1, 90 µg/kg; dose level 2, 120 µg/kg; and dose level 3, 150 µg/kg. ^bIf the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3 per label. ^cParticipants may continue Glofit up to 12 cycles and may continue lonca up to 8 cycles (or until disease progression, unacceptable toxicity, or other discontinuation criteria, whichever occurs first). The follow-up period is for ≤2 years from the end of treatment. ^dThe first dose of Glofit on Cycle 1, Day 8 has a 24-hour mandatory hospitalization; subsequent doses require hospitalization if grade ≥2 CRS occurs.

Glofit-Lonca: Best Overall Response & Duration of Response

EFFICACY EVALUABLE POPULATION (N=30)^a



Duration of response

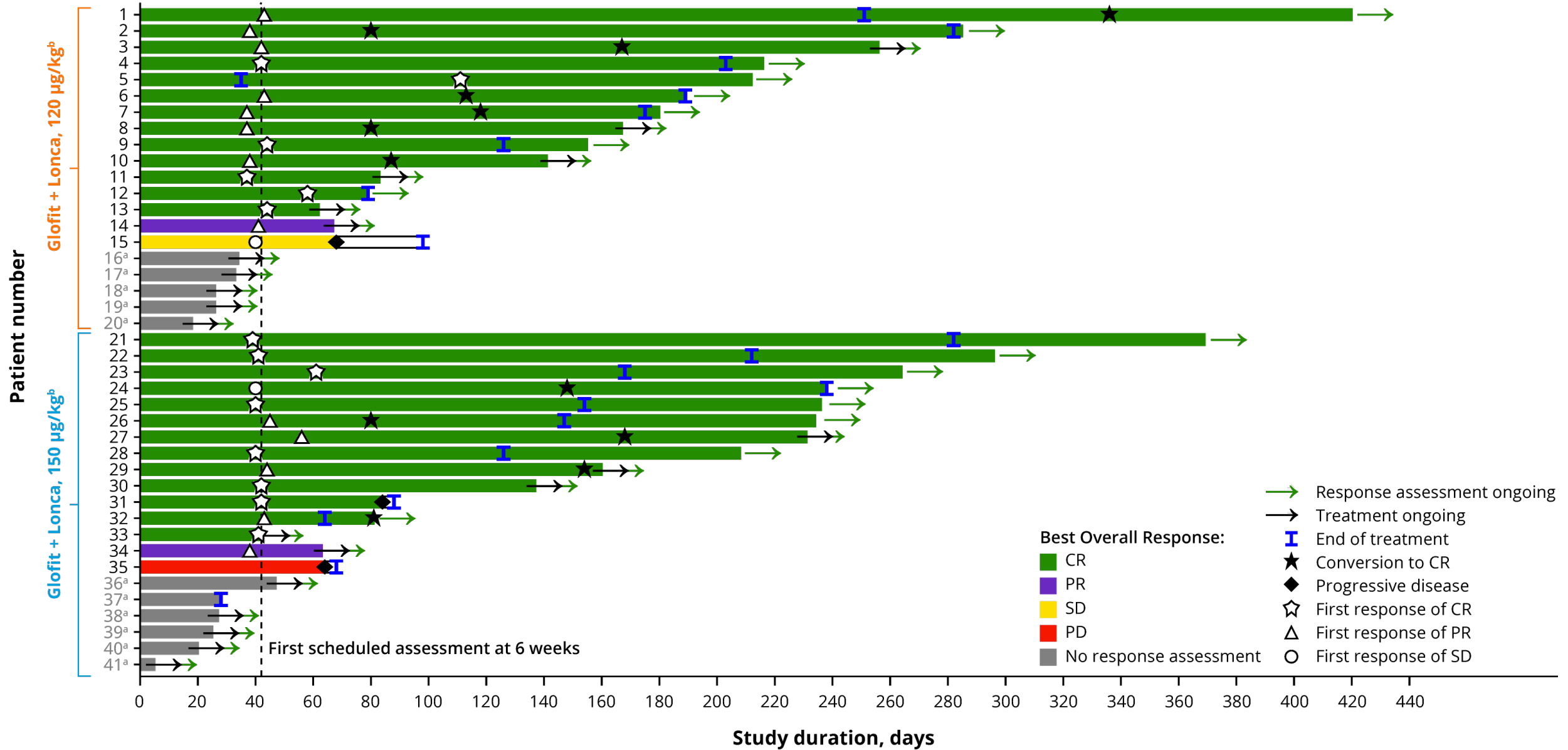
Characteristic, n (%)	Glofit + Lonca, 120 µg/kg ^c (n=15)	Glofit + Lonca, 150 µg/kg ^c (n=15)	All dose levels (N=30)
DOR^d Median	(n=14) NE	(n=14) NE	(n=28) NE
Time to first response (CR or PR) Median, days	(n=14) 42.0	(n=14) 42.0	(n=28) 42.0
Time to first CR Median, days	(n=13) 80.0	(n=13) 42.0	(n=26) 70.5

Data cutoff: April 14, 2025.

CR, complete response; DOR, duration of response; Glofit, glofitamab; Lonca, loncastuximab tesirine; NE, not estimable; ORR, overall response rate; PR, partial response.

^aThe efficacy evaluable population (N=30) included all patients who received ≥1 dose of the study drug with a valid baseline and ≥1 valid postbaseline disease assessment. Patients who did not have a postbaseline assessment owing to early clinical progression or death were also included. ^bPercentages do not add up to total due to rounding. ^cWhen the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3. ^dIn the efficacy evaluable population, the DOR and probability of maintaining an event-free response were evaluated in responders (n=28), including all patients who had a best response of CR or PR.

Glofit-Lonca: Efficacy over time (N=41)

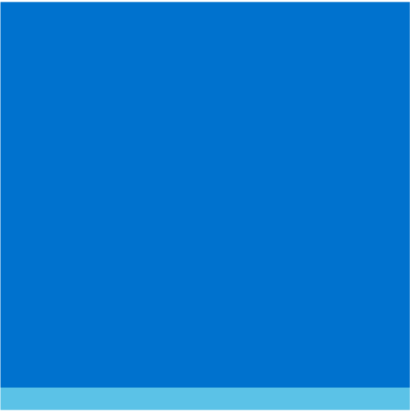


Data cutoff: April 14, 2025.

Each bar represents 1 patient in the study. Response was determined by an independent reviewer.

CR, complete response; Glofit, glofitamab; Lonca, loncastuximab tesirine; PD, progressive disease; PR, partial response; SD, stable disease.

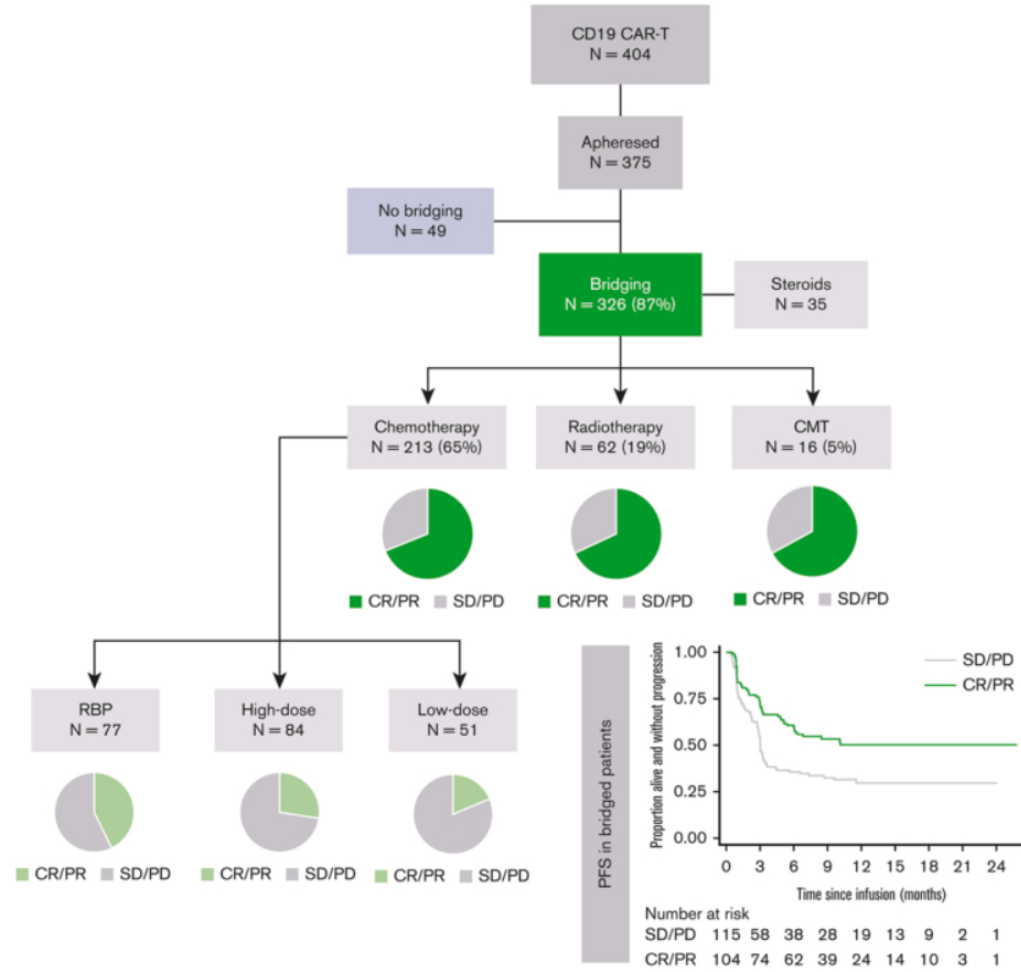
^aPatients were not yet efficacy evaluable because they had not reached the 6-week assessment (n=10) or had withdrawn before any assessment (Patient 39).^bWhen the starting dose of Lonca is 120 µg/kg or 150 µg/kg, the dose will be reduced to 75 µg/kg for Cycles ≥3.



BRIDGING BEFORE CAR-T

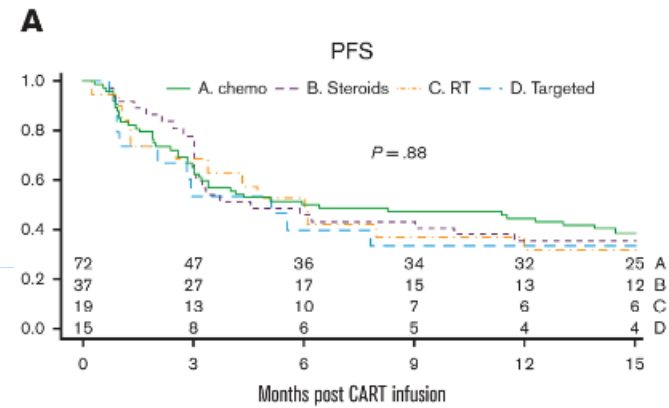
Bridging prior to CART

Response to bridging associated with improved CART outcomes vs lack of response

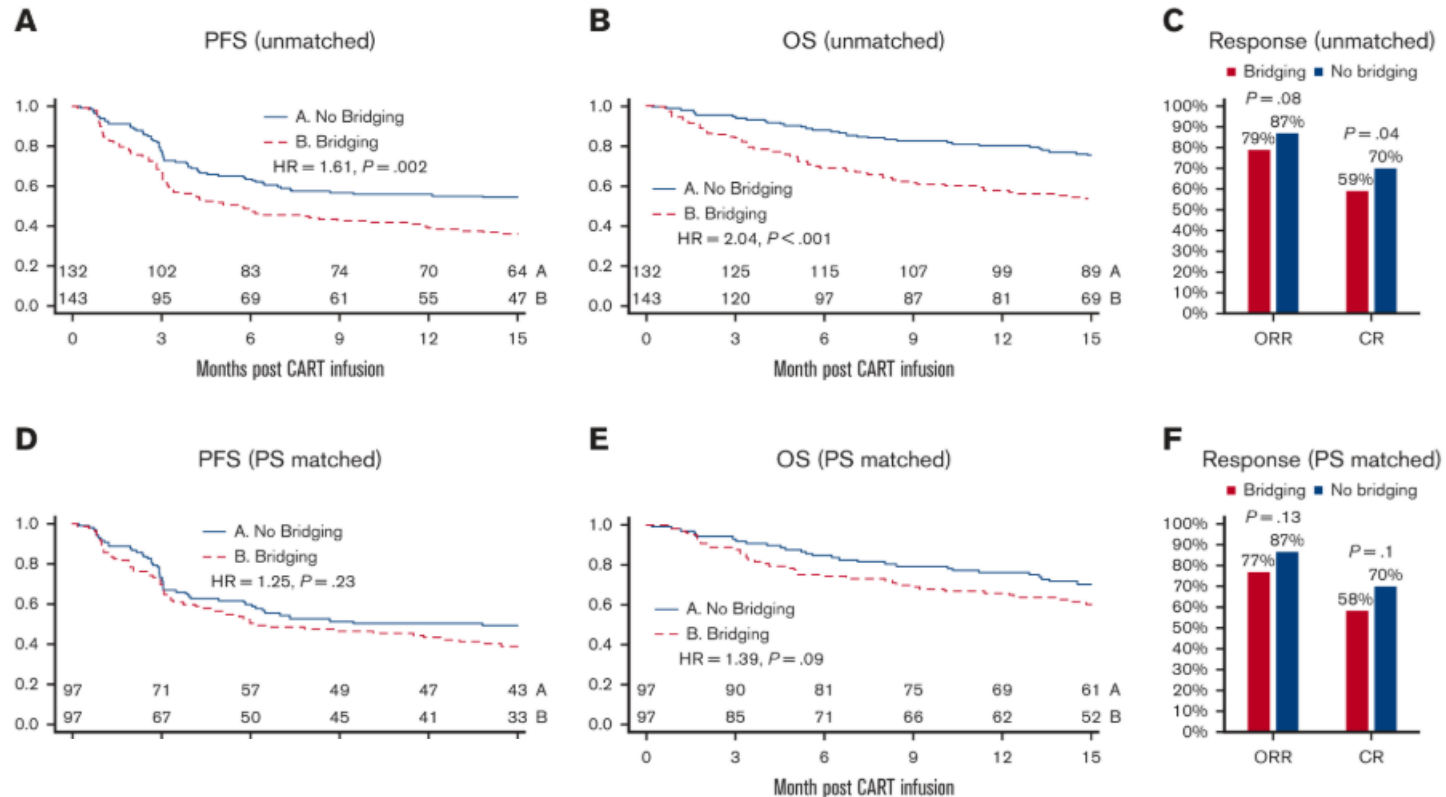


Conflicting evidence re: bridging tx type

- Pola-based regimens favored
- Radiation esp for limited stage dz

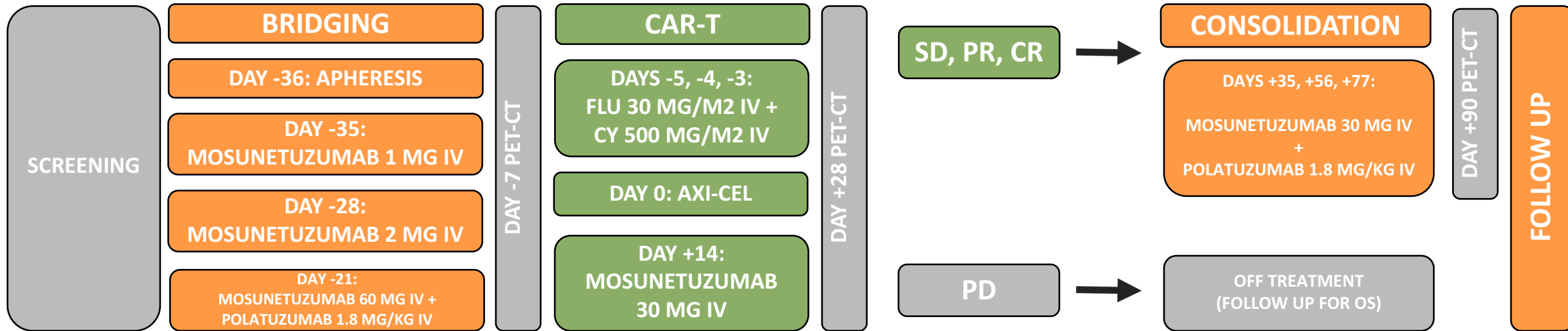


Need for bridging tracks with poor prognosis however propensity matching renders difference non-significant



Total Therapy Approach: Mosun-Pola + Axi-cel

ClinicalTrials.gov: NCT05260957



KEY INCLUSION CRITERIA:

- Age ≥18
- **ELIGIBLE DIAGNOSES:** DLBCL (NOS), PMBCL, TFL, HGBL, FL grade 3B
- **DISEASE STATUS:** ≥ 1 lines of therapy
- ECOG PS 0-2; CrCl ≥30, LVEF ≥45%, ANC ≥1000, Plt ≥75k, Hgb ≥8

KEY EXCLUSION CRITERIA:

- **ACTIVE CNS INVOLVEMENT.** Prior CNS involvement allowed
- **PRIOR CD19 CAR-T THERAPY**

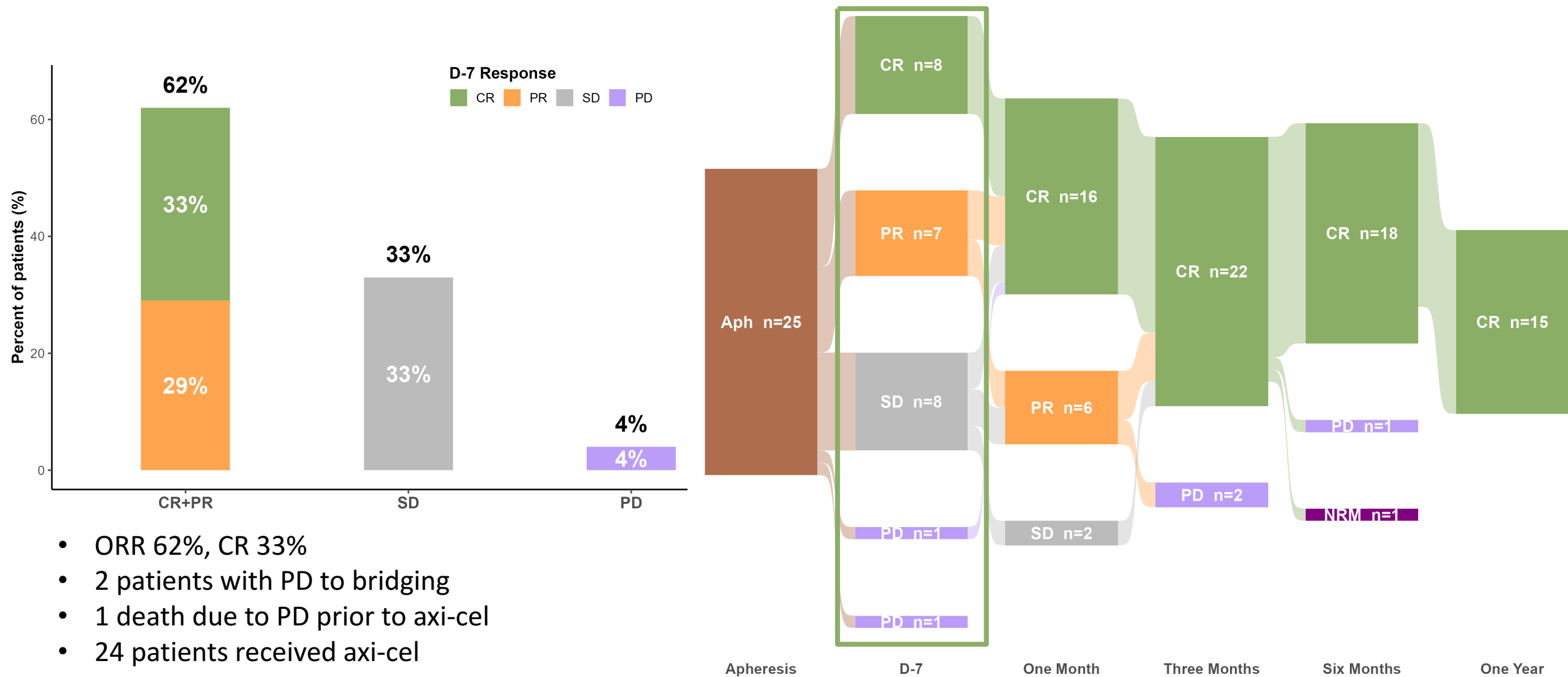
PRIMARY ENDPOINT:

- CR at D90 post CAR-T infusion

SECONDARY ENDPOINTS:

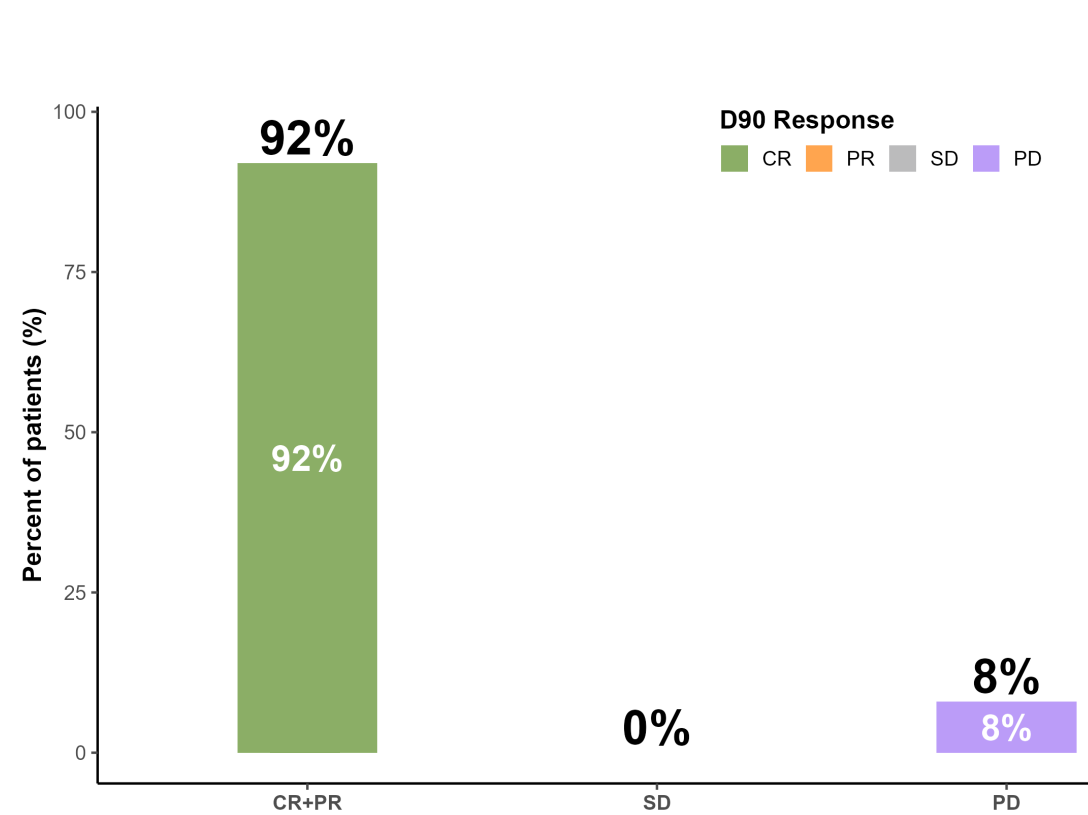
- OS, PFS, DOR
- Safety
- ctDNA for MRD

Mosun-Pola Bridging Results in 33% CR rate

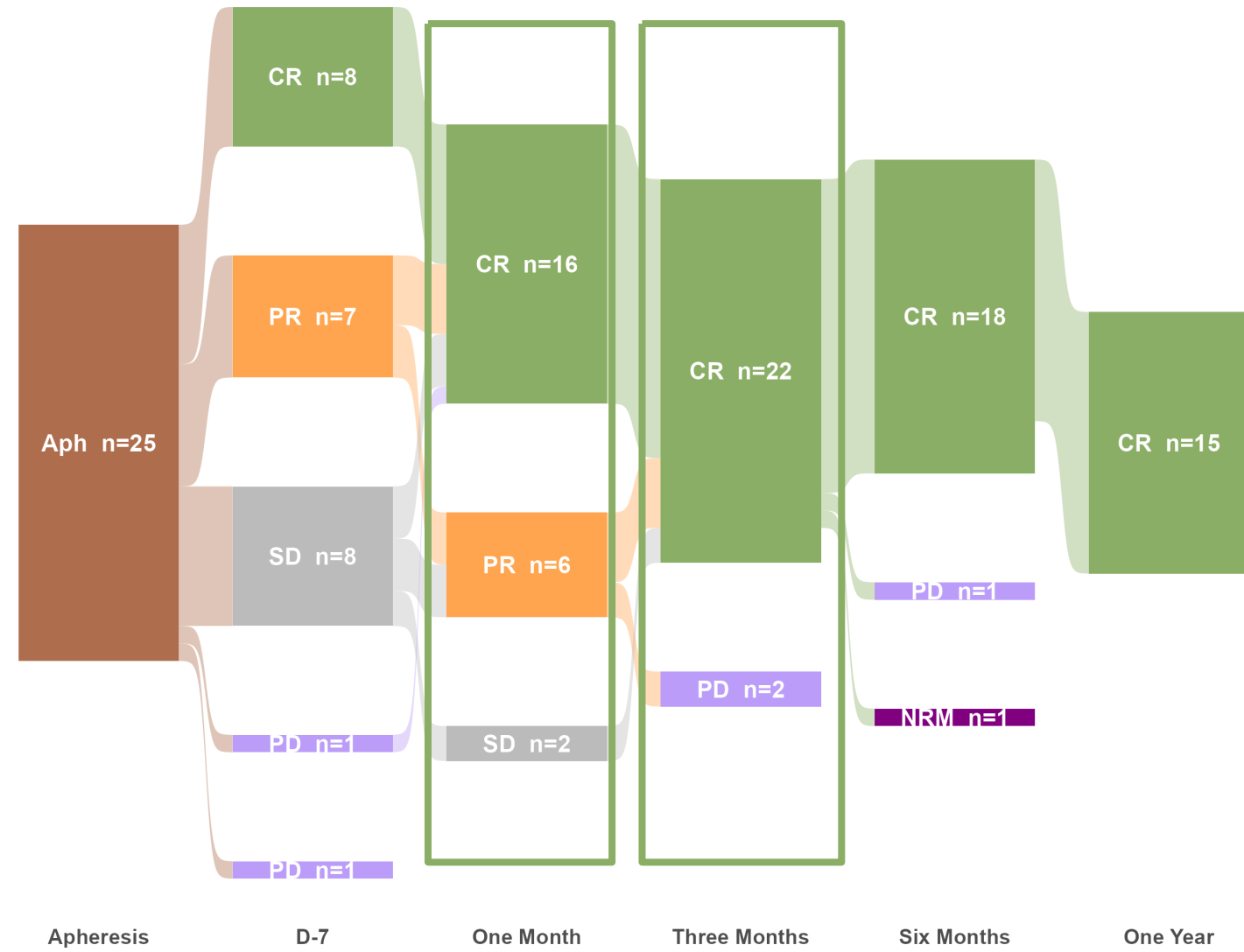


- ORR 62%, CR 33%
- 2 patients with PD to bridging
- 1 death due to PD prior to axi-cel
- 24 patients received axi-cel

Primary Outcome: 90% CR at D90

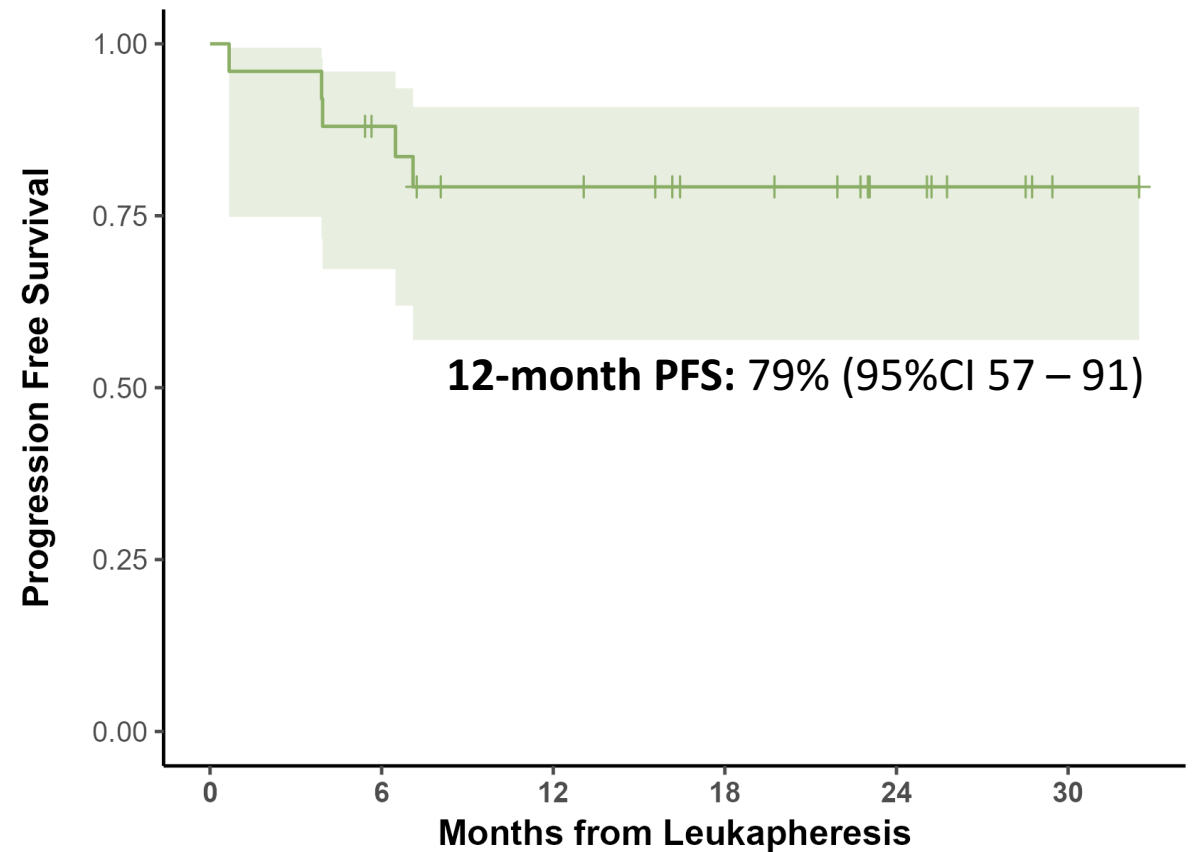
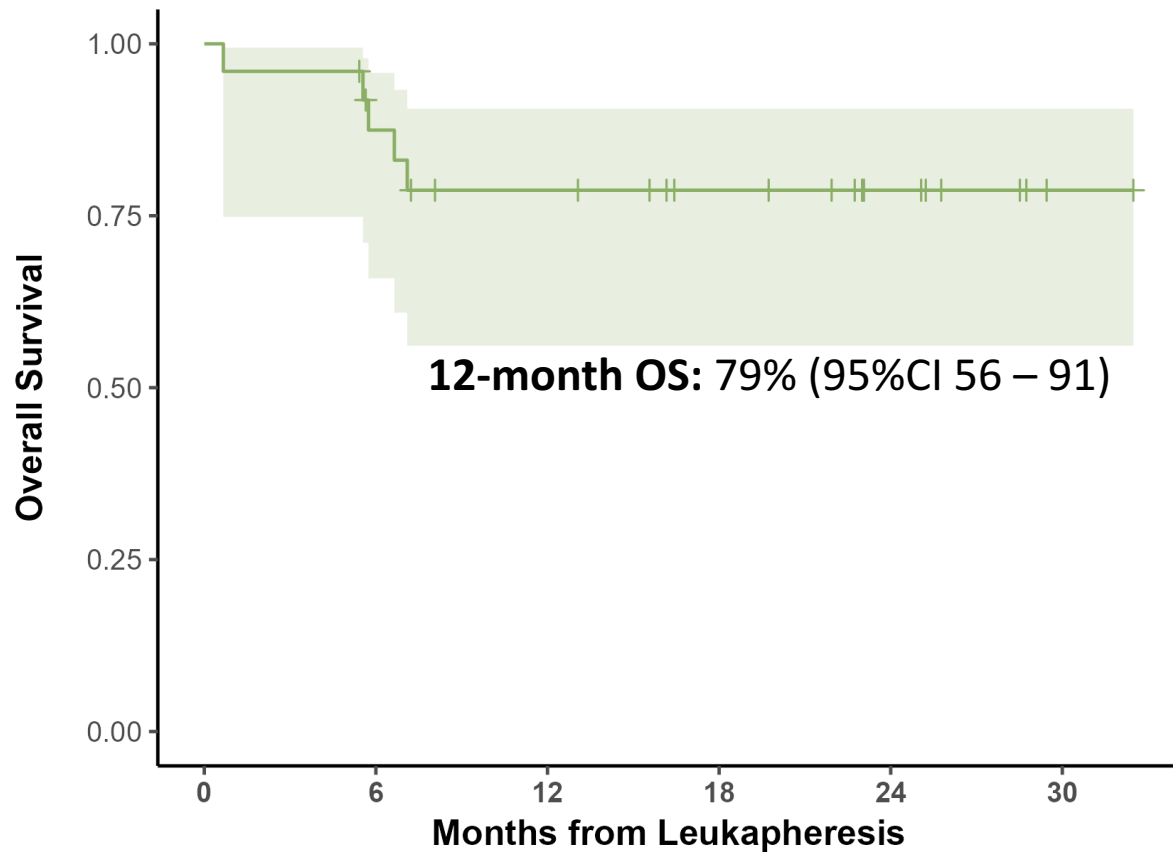


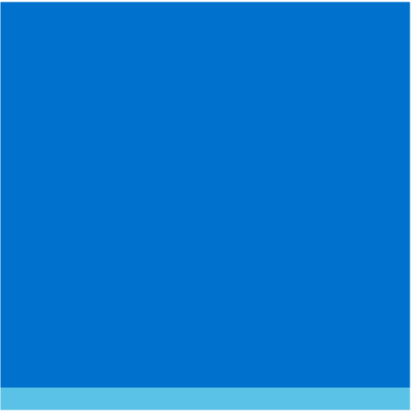
- CR% at D28 was 67%, no PD – all eligible for consolidation dosing of mosun-pola
- By D+90, CR rate improved to 92%



Mosun-Pola-Axi-cel Demonstrates High Durability of Response

Median follow-up: 22.7 months





AFTER CAR-T AND BISPECIFICS: EMERGING THERAPIES FOR RELAPSED/REFRACTORY DLBCL

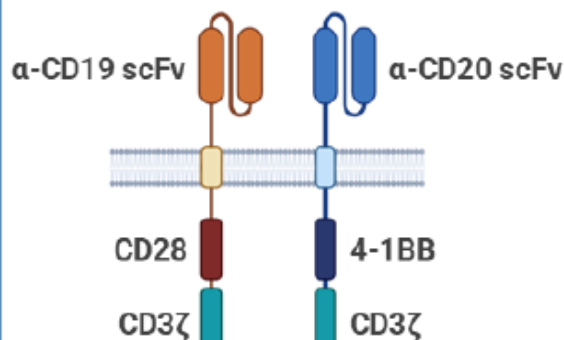
KITE-363 and KITE-753 CAR Design Enables Two Independent CARs to Work Synergistically

Smart Targeting With Synergistic Signaling

Independently Targets CD19 and CD20

CD19 CAR

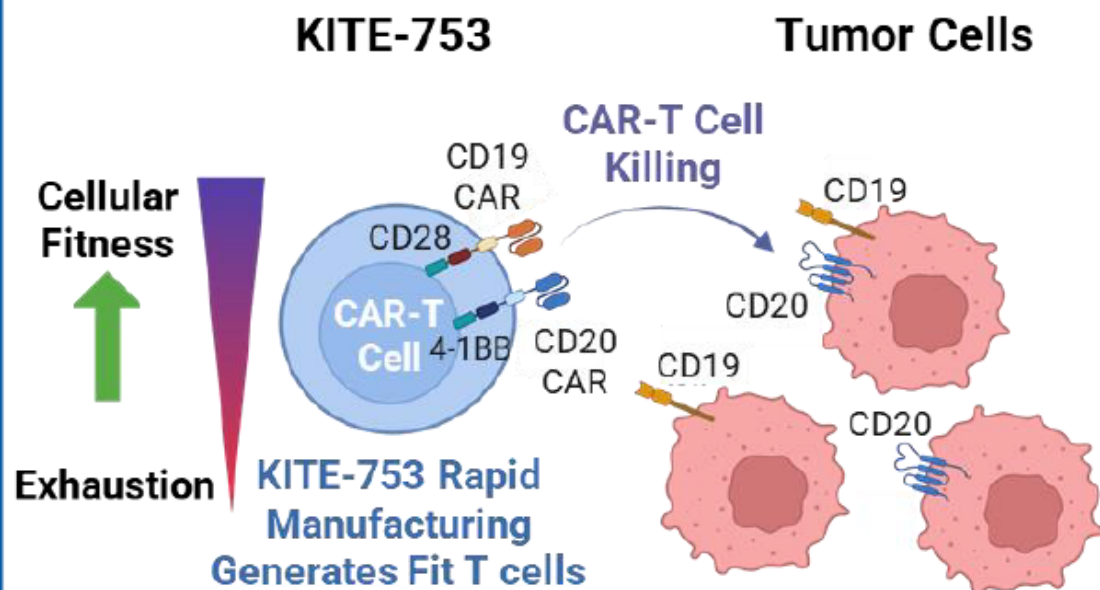
CD20 CAR



Cytolytic activity
Cytokine release
Proliferation

Dual Costimulation With CD28 and 4-1BB Boosts CAR T-Cell Performance

KITE-753 Mechanism of Action



Unmet Need

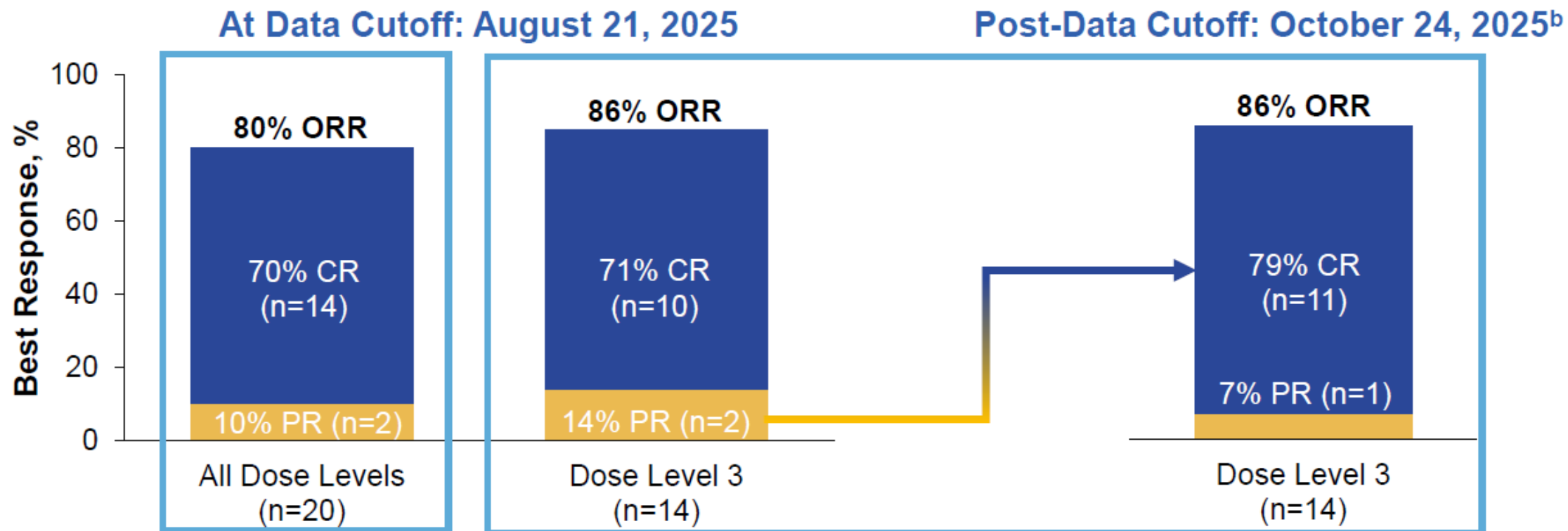
- Although CD19 CAR T-cell therapies have been transformational in R/R LBCL, there is an opportunity for further improvement
 - e.g., In ZUMA-7, EFS rate at 48 months with axi-cel was 36.5% for patients with primary refractory LBCL vs 46.1% for early relapsed LBCL¹

KITE DuoCore™ Construct

- KITE-363 and KITE-753 are investigational, **bicistronic, CAR T-cell therapies with synergistic signaling** designed to prevent antigen escape
- KITE-753 uses a **rapid manufacturing process that preserves naive and stem cell memory T cells**
- Here we report the initial safety and preliminary efficacy of KITE-753 and updated results of KITE-363 (NCT04989803)

1. Westin JR, et al. TCT 2025. Abstract 244. scFv, single-chain variable fragment.

High ORR and CR Rate With KITE-753 in CAR-Naive Patients^a



- Median time to first response among all patients (N=30) was 29 days
- In CAR-naive patients in dose level 3, 9 of the 11 patients with CRs had a CR at their 1-month assessment; the remaining 2 patients had a CR by their 3-month assessment (1 after the data cutoff)
- In patients with prior CAR exposure (n=10), 3 achieved a CR and 2 had a PR

^a One non-responder had T-cell histiocyte-rich LBCL. ^b Median follow-up was 4.0 months (range, 1.1-21.6). One patient had an additional assessment after the data cutoff date of August 21, 2025.

KITE-363 Update^a: No DLTs or Pausing Criteria; Durable Responses With Dose Level 3 in Highly Refractory CAR-Naive LBCL

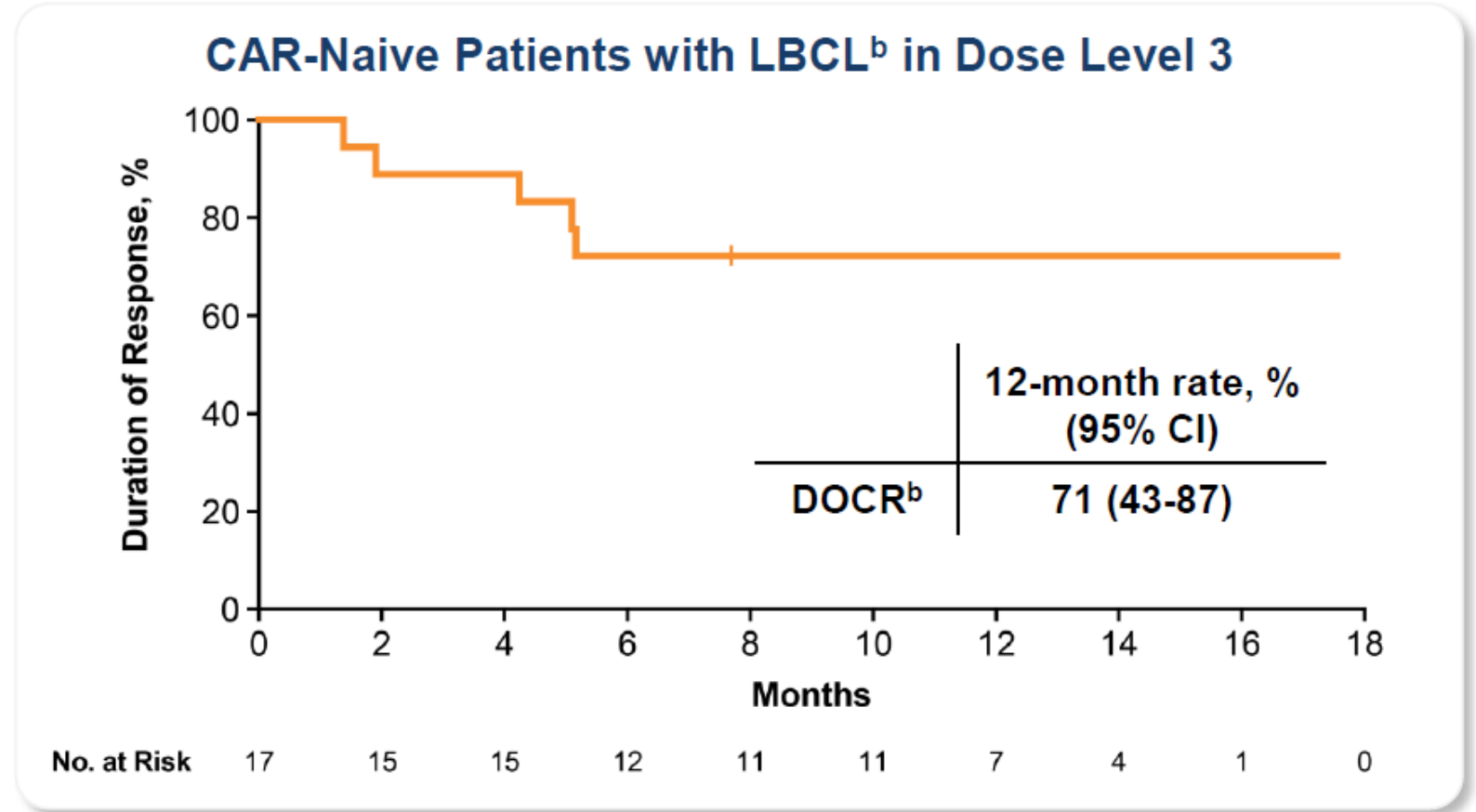
- Median follow-up: 17.5 months (range, 11.2-44.3); N=37
- In CAR-naive patients with LBCL in dose level 3 (N=22), 68% were primary refractory and 73% had elevated baseline LDH

Safety Update

- CRS and ICANS events that occurred with KITE-363 were primarily Grade 1 or 2
- No Grade 4 or 5 CRS or ICANS events occurred

Efficacy Update

- ORR: 87% (CR rate: 78%) among CAR-naive patients in dose level 3
- Median DOCR^c: Not yet reached, with a plateau appearing near Month 6

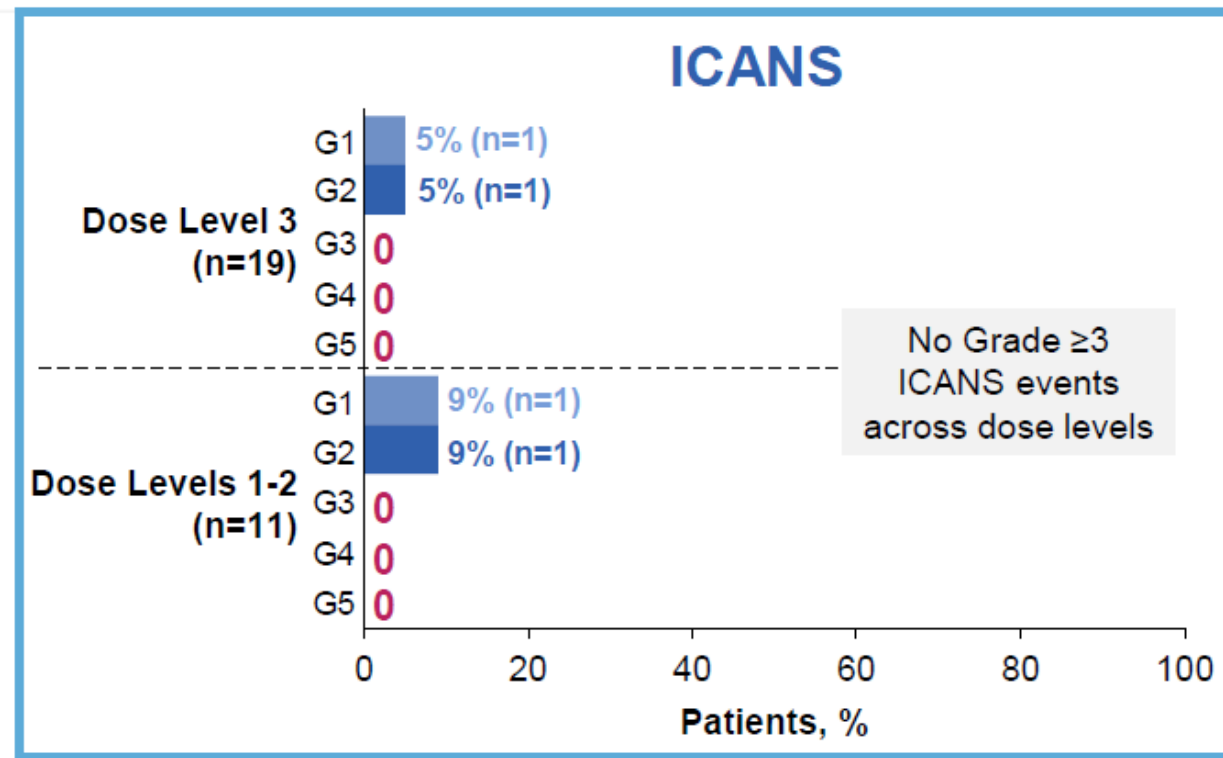
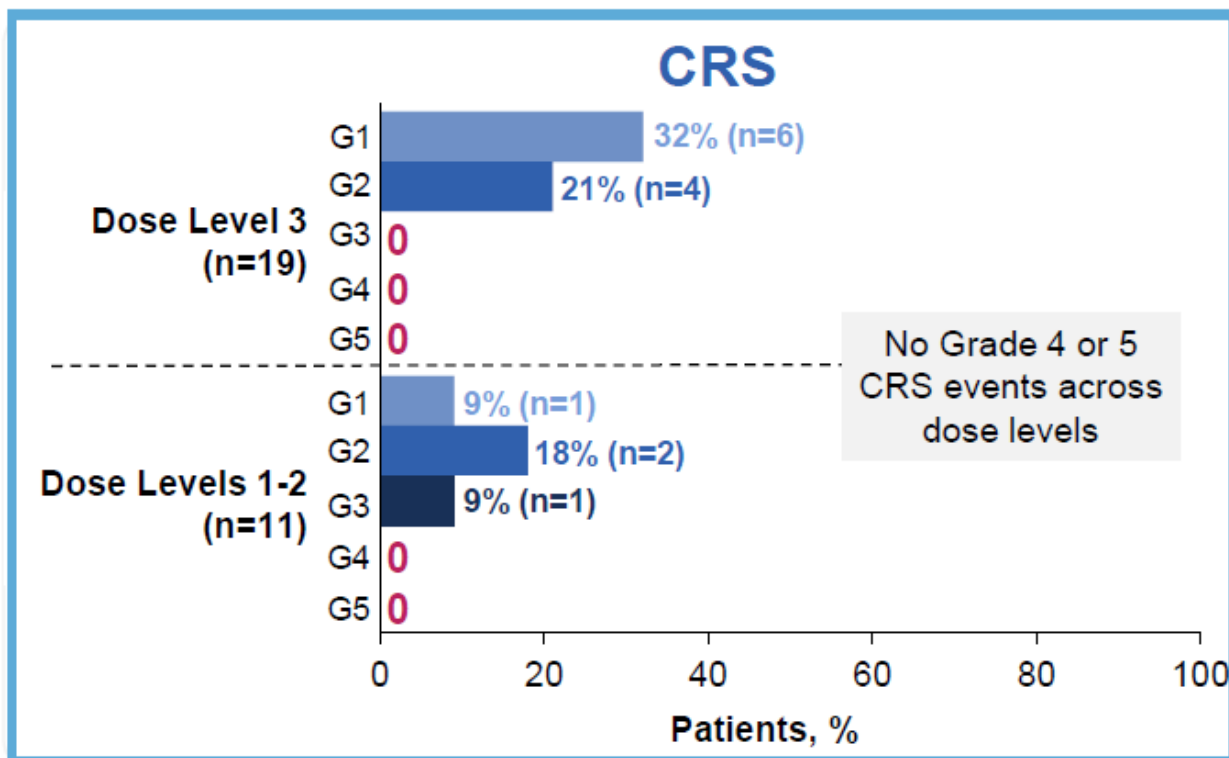


*The censoring observed was not due to loss to follow-up or withdrawal but due to the observation window ending before an event occurred and indicates that patients were event-free up to the data cutoff. At the time of data cutoff, all but 1 censored patients remained in response

^a Initial KITE-363 safety and efficacy data were previously reported.¹ ^b One CAR-naive patient with nodular lymphocyte predominant Hodgkin lymphoma was excluded. ^c DOCR was defined as DOR among all patients who achieved a best response of CR.

1. Dahiya S, et al. ASCO 2025. Abstract 7003.

No Grade ≥ 3 CRS or ICANS Occurred With Dose Level 3 of KITE-753



CRS		Dose Level 1-2 (n=11)	Dose Level 3 (n=19)
Median time to onset (range), days		9.5 (7-11)	6.0 (3-8)
Median duration of event (range), days		6.5 (2-8)	5.0 (2-7)
AE management, n (%)	Tocilizumab	3 (27)	9 (47)
	Corticosteroids	2 (18)	8 (42)
	Anakinra	0	0

ICANS		Dose Level 1-2 (n=11)	Dose Level 3 (n=19)
Median time to onset (range), days		12.5 (11-14)	10.0 (10-10)
Median duration of event (range), days		6.5 (2-11)	2.0 (2-2)
AE management, n (%)	Tocilizumab	0	0
	Corticosteroids	2 (18)	2 (11)
	Anakinra	0	2 (11)

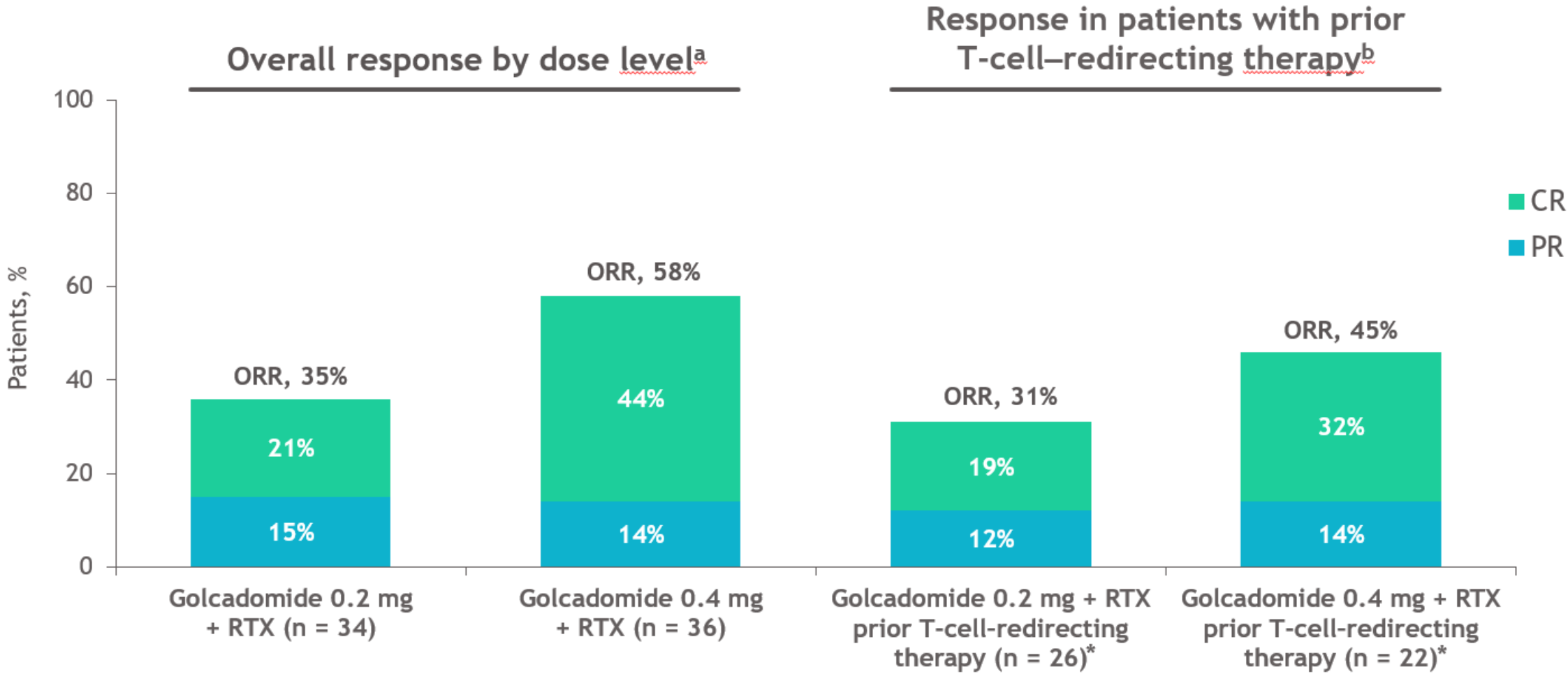
No prophylactic steroids and/or tocilizumab were used on study

Golcadomide, a Potential, First-In-Class, Oral CELMoD™ Agent, ± Rituximab in Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma: Phase 1/2 Study Extended Follow-Up Results

[Marc S. Hoffmann](#),¹ [Julio Chavez](#),² [Jason R. Westin](#),³ [Judit Mészáros Jørgensen](#),⁴ [Javier Munoz](#),⁵ [Cecilia Carpio Segura](#),⁶ [Guilherme Fleury Perini](#),⁷ [Emmanuel Bachy](#),⁸ [Victoria Campbell](#),⁹ [Caroline Riley](#),¹⁰ [Franck Morschhauser](#),¹¹ [Daniel Morillo](#),¹² [Alev Akyol](#),¹³ [Berengere de Moucheron](#),¹⁴ [Michael Pourdehnad](#),¹⁵ [Akshay Sudhindra](#),¹³ [Soraya Carrancio](#),¹⁶ [Jessica Voetsch](#),¹⁷ [Gang Yang](#),¹⁸ [Serena Perna](#),¹³ [Jean-Marie Michot](#)¹⁹

¹The University of Kansas Medical Center, Kansas City, KS, USA; ²Moffitt Cancer Center, Tampa, FL, USA; ³The University of Texas MD Anderson Cancer Center, Houston, TX, USA; ⁴Aarhus University Hospital, Aarhus, Denmark; ⁵Mayo Clinic, Phoenix, AZ, USA; ⁶University Hospital Vall d'Hebron, Experimental Hematology, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; ⁷Hospital Israelita Albert Einstein, São Paulo, Brazil; ⁸Lyon Sud Hospital, Lyon, France; ⁹NHS Lothian - Western General Hospital, Edinburgh, Scotland; ¹⁰Rigshospitalet University Hospital, Copenhagen, Denmark; ¹¹University of Lille, Centre Hospitalier Universitaire de Lille, Lille, France; ¹²START Madrid - FJD Early Phase Unit, Fundación Jiménez Díaz University Hospital, Madrid, Spain; ¹³Late Clinical Development, Hematology/Oncology and Cell Therapy, Bristol Myers Squibb, Madison, NJ, USA; ¹⁴Center for Innovation and Translational Research Europe (CITRE), Bristol Myers Squibb, Seville, Spain; ¹⁵Early Clinical Development, Hematology/Oncology and Cell Therapy, Bristol Myers Squibb, San Francisco, CA, USA; ¹⁶Oncogenesis (ONC) Thematic Research Center (TRC), Bristol Myers Squibb, San Diego, CA, USA; ¹⁷Translational Informatics and Predictive Sciences, Bristol Myers Squibb, Lawrenceville, NJ, USA; ¹⁸Global Biometrics & Data Sciences, Bristol Myers Squibb, Madison, NJ, USA; ¹⁹Gustave Roussy Institute of Cancer, Département d'Innovation Thérapeutique et d'Essais Précoces (DITEP), Villejuif, France

Golcadomide 0.4 mg + RTX achieves a high ORR and CRR in a heavily pretreated patient population, including patients with prior T-cell–redirecting therapy



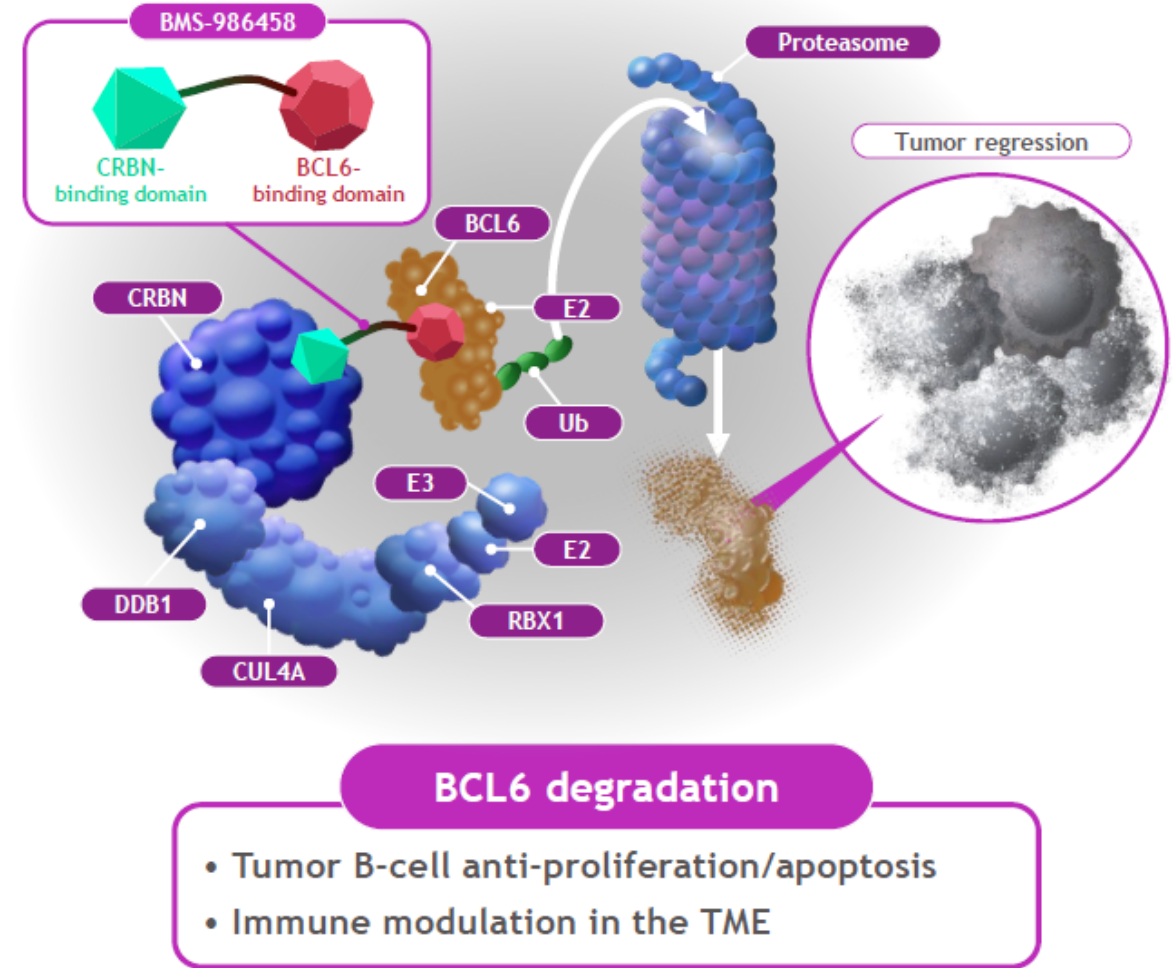
Data cutoff: 15 September 2025.

^aEfficacy-evaluable population consisting of patients who completed ≥ 1 cycle of golcadomide (taking $\geq 75\%$ of assigned doses) and having a baseline and ≥ 1 postbaseline tumor assessment.; ^bCAR T and/or bispecific antibody treatment.

^{*}11 and 14 patients had both CAR-T and bispecifics in the 0.2mg and 0.4mg, respectively; CAR, chimeric antigen receptor; CR, complete response; CRR, complete response rate; ORR, overall response rate; PR, partial response; RTX, rituximab.

BMS-986458 is a first-in-class, highly selective, BCL6 degrader¹

- BMS-986458-mediated BCL6 degradation occurs through recruitment of the CRBN E3 ligase, ubiquitination, and subsequent proteolytic processing by the proteasome
- BMS-986458-mediated degradation of BCL6 leads to anti-proliferation and apoptosis of tumor B cells, and immune modulation
 - In vitro, BMS-986458 phenotypically modulates Tfh and Treg cells without affecting cell viability

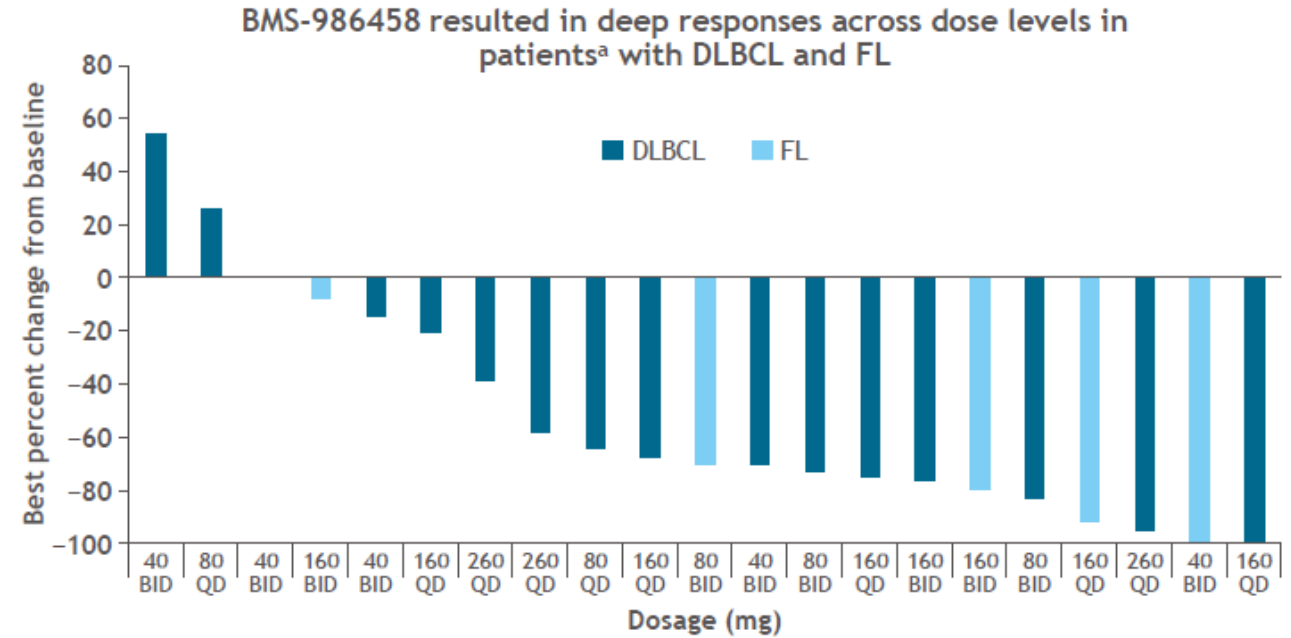


BCL6, B-cell lymphoma 6; CRBN, cereblon; CUL4A, cullin 4A; DDB1, DNA damage-binding protein 1; RBX1, RING-box protein 1; Tfh, T follicular helper cells; TME, tumor microenvironment; Treg, regulatory T cells; Ub, ubiquitin.

1. Grocock L, et al. Oral presentation at the American Society of Hematology (ASH) Annual Meeting 2024; December 5-10, 2024; San Diego, CA. Abstract 957.

BMS-986458 induces deep and rapid antitumor activity

- ORR = 81.0% (17/21), CR = 23.8% (5/21), PR = 57.1% (12/21)
 - One patient with triple-hit status achieved a CR
 - In patients with DLBCL, ORR = 80% (12/15), CR = 7% (1/15)
 - In patients with FL, ORR = 83% (5/6), CR = 67% (4/6)
- Among responders, the median (range):
 - Time to first objective response = 1.77 (1.6-2.4) months
 - Duration of response = 3.71 (1.15-NR) months



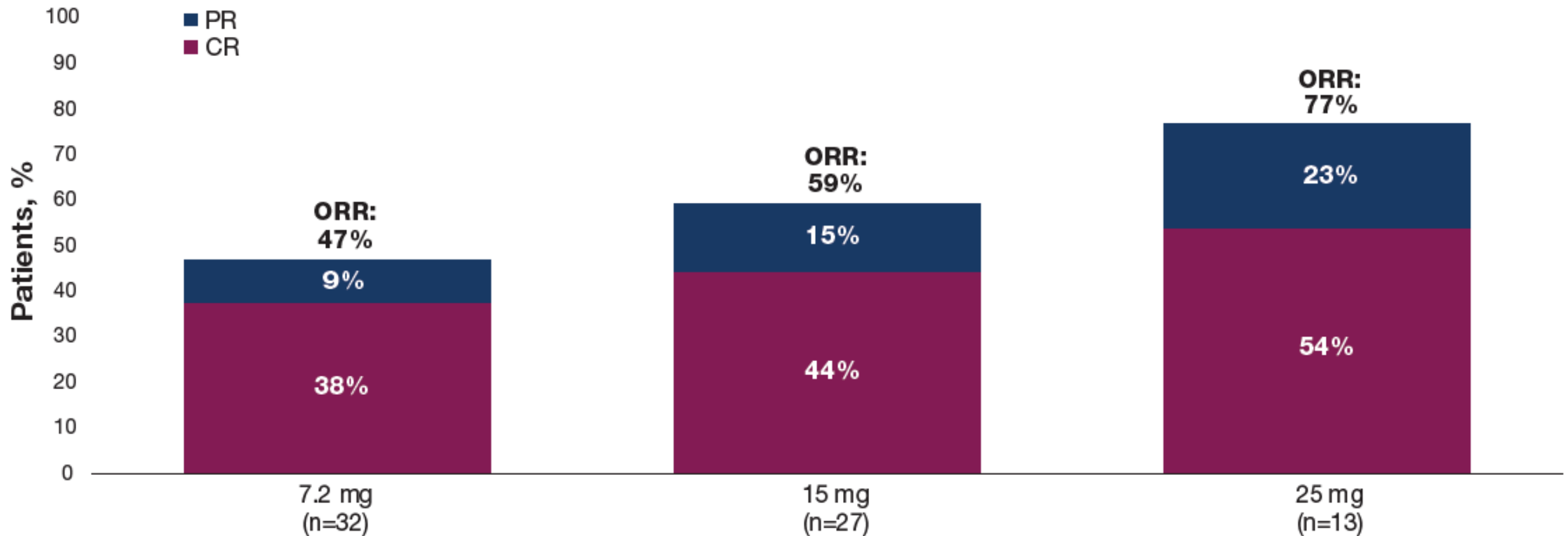
Skin tumor lesions showed rapid clinical response in a patient with CR^b



^aEfficacy-evaluable population. ^bThe images come from a 66-year-old male diagnosed with high-grade B-cell lymphoma (MYC+/BCL2+/BCL6+), GCB, transformed from prior FL, stage IV, IPI 4-5. Prior treatments for high-grade B-cell lymphoma were ibrutinib + venetoclax, CAR T cell therapy, epcoritamab + venetoclax + ibrutinib + lenalidomide, and loncastuximab. BOR was PR. The patient received BMS-986458 160mg BID, at C1D8 clinical improvement of skin lesions, and at C3D1 partial metabolic response. Cutoff date: April 10, 2025. BCL6, B-cell lymphoma 6; BID, twice daily; BOR, best overall response; C, cycle; D, day; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; GCB, germinal center B-cell-like; IPI, International Prognostic Index; NR, not reached; ORR, objective response rate; PR, partial response; QD, once daily.

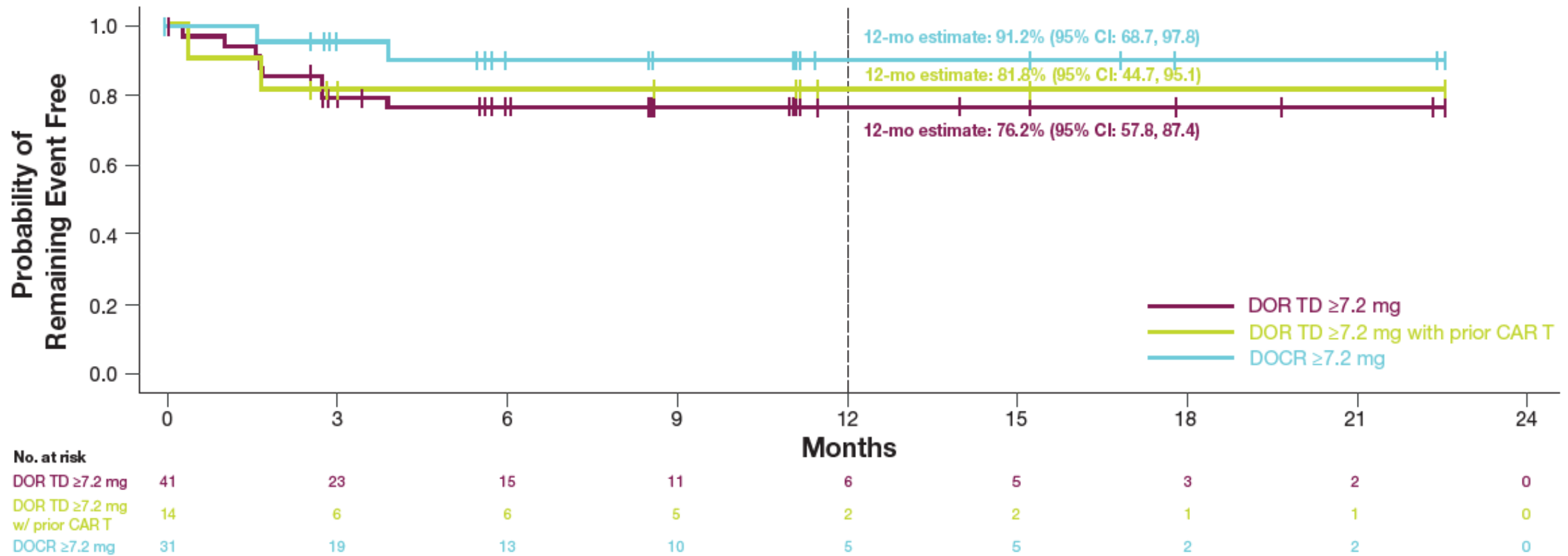
Surovatamig CD19xCD3 BsAb: Response by Dose Level

Figure 1. Response Rates by Target Dose (≥ 7.2 mg) in Efficacy-Evaluable Patients



Surovatamig CD19xCD3 BsAb DOR

Figure 3. DOR and DOCR for TD ≥ 7.2 mg Among All Patients and DOR for TD ≥ 7.2 mg Among Patients With Prior CAR T



Conclusions



- CAR T-cells improves survival as 2nd line therapy for primary refractory/early relapsed DLBCL
- Bispecific antibodies are highly effective with favorable toxicity profile
 - Bispecific combinations promising efficacy
- Bridging therapy prior to CART – response = more favorable prognosis
- Emerging therapies promising results even in patients with prior CART/BsAb