7th POSTGRADUATE

Lymphoma Conference

Real World Experience with Pola-BR, Tafa-Len and Loncastuximab Teserine

Bruce. D Cheson, M.D.

Lymphoma Research Foundation

Center for Cancer and Blood Disorders

Rome,
March 16-17 2022

VOI Donna Camilla Savelli Hotel

President:
P.L. Zinzani

Disclosures

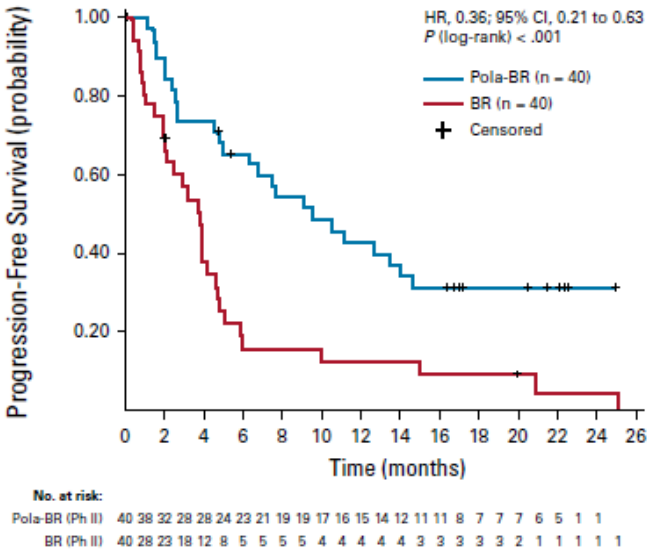
Disclosures of Name Surname

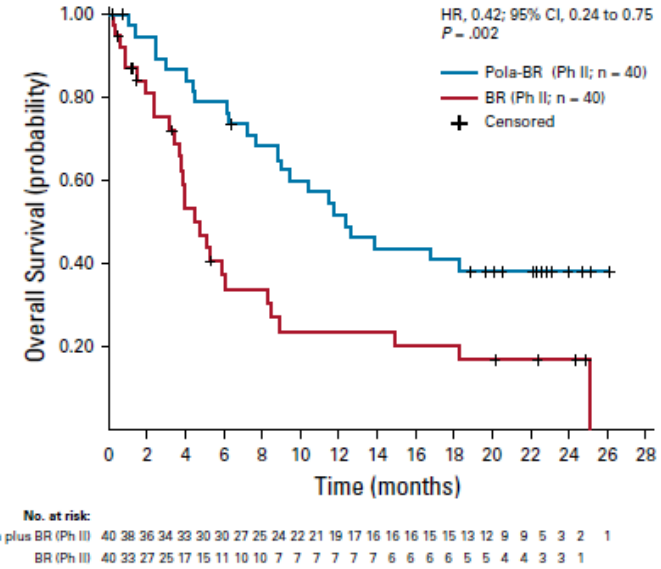
Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
ADC Therapeutics			x				
Morphosys			x		x	X	
Incyte					x		

Polatuzumab + BR vs BR: Phase 2 Trial Results

Efficacy

End of Treatment by IRC	Pola + BR (n=40)	BR (n=40)	Hazard Ratio
Overall Objective Response (ORR = CR+PR)	45.0%	17.5%	-
Complete Response	40.0%	17.5%	-
Partial Response	5.0%	0.0%	-
mDOR *(95% CI)*	12.6 (7.2, NE)	7.7 (4.0, 18.9)	0.47 (0.19, 1.14); *P* = ns
mPFS *(95% CI)*	9.5 (6.2, 13.9)	3.7 (2.1, 4.5)	0.36 (0.21, 0.63), *P* < 0.001
mOS *(95% CI)*	12.4 (9.0, NE)	4.7 (3.7, 8.3)	0.42 (0.24,0.75), *P* = 0.002





Median follow-up, 22.3 Months

Safety*

Adverse Events	Pola + BR (n=39)	BR (n=39)
Neutropenia (Grade 3-4)	46.2%	33.3%
Thrombocytopenia (Grade 3-4)	41.0%	23.1%
Anemia (Grade 3-4)	28.2%	17.9%
Peripheral neuropathy (All grades)	43.6%	7.7%
Diarrhea (All grades)	38.5%	28.2%
Fatigue (All grades)	35.9%	35.9%
Pyrexia (All grades)	33.3%	23.1%

- Fatal AEs occurred in 9 pola-BR patients and 11 BR patients, with infection being the most common adverse event (4 pola-BR; 4 BR)

*Select AEs with >30% in all grades

Sehn et al. Polatuzumab Vedotin in Relapsed or Refractory Diffuse Large B-Cell Lymphoma. *J Clin Oncol.* 2020;38:155-165.

RWE with Pola-Based Therapy: Italian Experience

Baseline Characteristics and Comparison Between the 2 Treatment Groups

	Total (n = 55)	PolaBR (n = 36)	PolaR (n = 19)	*P*
Sex, female/male, n(%)	26/29 (47.3/52.7)	17/19 (47.2/52.8)	9/10 (47.4/52.6)	ns
Age at diagnosis, y, median (range)	63.6 (29.2-84.2)	61.5 (29.2-84.2)	67.6 (30.4-81.8)	ns
Pathology classification at diagnosis, n (%)				ns
GCB	22 (40.0)	15 (41.7)	7 (36.7)	
ABC	6 (10.9)	5 (13.9)	1 (5.3)	
Non-GCB	17 (30.9)	11 (30.6)	4 (21.5)	
DLBCL-nos	10 (18.2)	8 (22.2)	2 (10.5)	
DLBCL subtypes, n (%)				ns
Double-hit	3 (5.5)	2 (5.6)	1 (5.3)	
Triple-hit	1 (1.8)	1 (2.8)	0 (0.0)	
Double expressor	3 (5.5)	2 (5.6)	1 (5.3)	
Ann Arbor stage, n (%)				ns
I	0	0	0	
II	11 (20.0)	6 (16.7)	5 (26.3)	
III	14 (25.5)	11 (30.6)	6 (31.6)	
IV	30 (54.5)	19 (52.8)	8 (42.1)	
Outcome first line, n (%)				ns
Relapsed	23 (41.8)	16 (44.4)	7 (36.8)	
Refractory	32 (58.2)	20 (55.6)	12 (63.2)	
Outcome last line, n (%)				ns
Relapsed	10 (18.2)	6 (16.7)	4 (21.1)	
Refractory	45 (81.8)	30 (83.3)	15 (78.9)	
Previous therapies, median (range)	3 (1–6)	3 (1–6)	3 (2–5)	ns

Argnani …Zinzani, et al, Hemasphere 6:e798, 2022

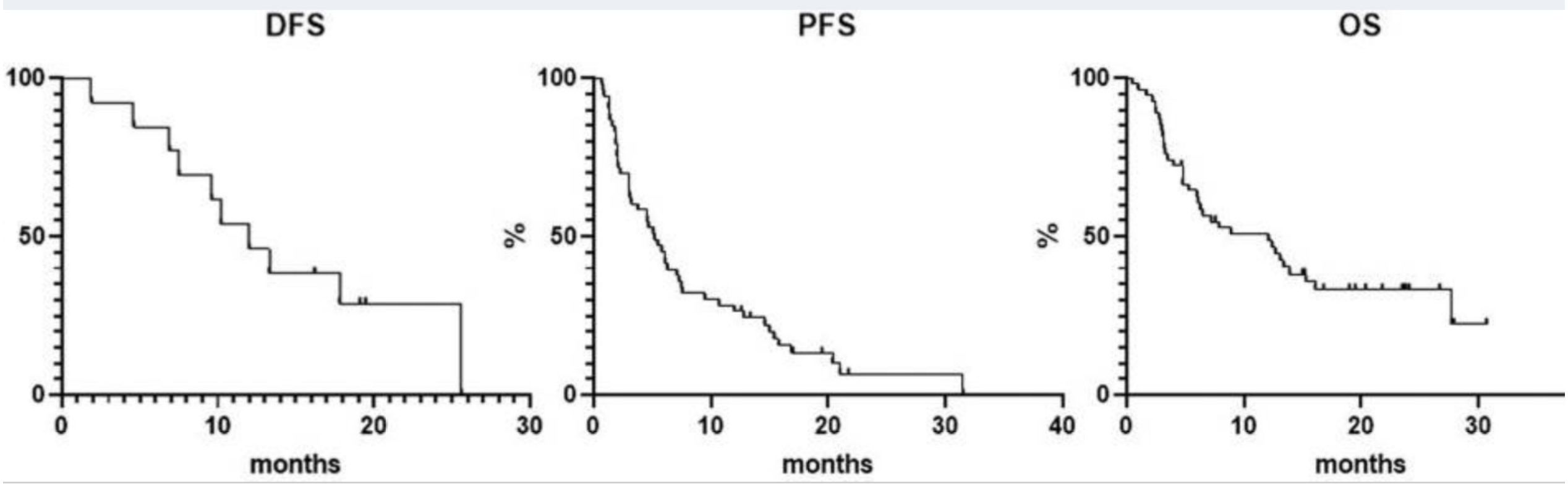
RWE with Pola-Based Therapy: Italian Experience

Response Rates and Comparison Between the 2 Treatment Groups

	Total (n = 55)	PolaBR (n = 36)	PolaR (n = 19)	*P*
ORR, %	32.7	30.6	36.9	ns
CR, n (%)	10 (18.2)	7 (19.4)	3 (15.8)	
PR, n	8	4	4	
Best response rate, %	49.1	47.2	52.6	ns
CR, n (%)	15 (27.3)	10 (27.8)	5 (26.3)	
PR, n	12	7	5	

Argnani,…Zinzani, et al, Hemasphere 6:(e798), 2022

P-(BR) in R/R DLBCL: RWE



Argnani…Zinzani, et al, Hemasphere 6:e798, 2022

Results of a UK real-world study of polatuzumab vedotin, bendamustine, and rituximab for relapsed/refractory DLBCL

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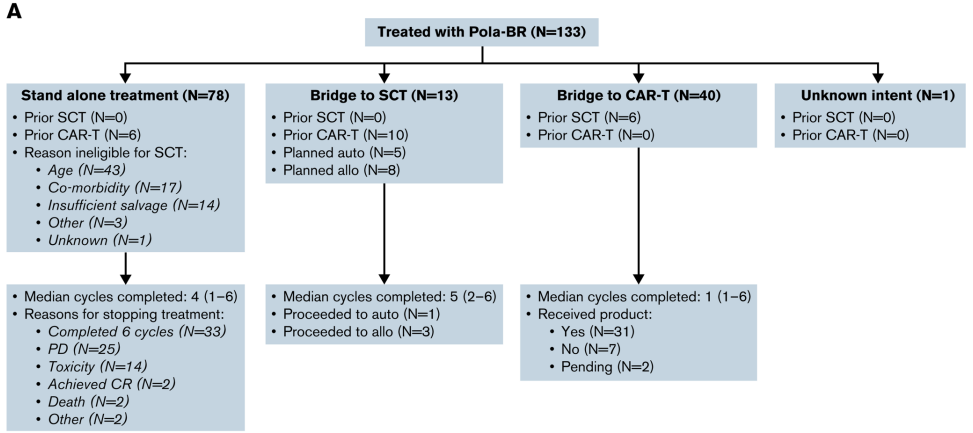


Pola-BR treatment subgroups according to treatment intent

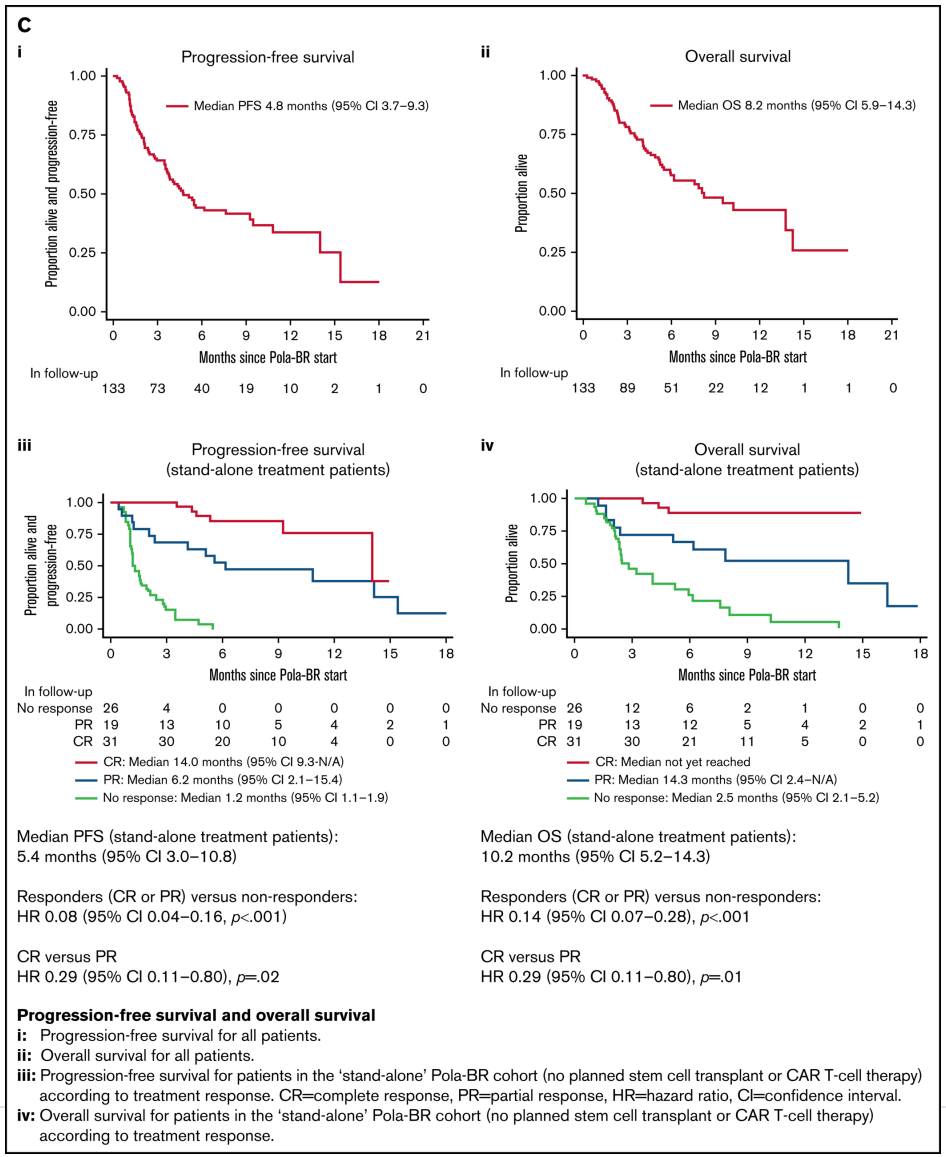
B

Best response to Pola-BR	All patients (N=133)	Prior CAR-T (N=16)	Double/ triple hit lymphoma (N=14)	Transformed lymphoma (N=31)	Stand alone treatment (N=78)	Bridge to CAR-T (N=40)	>1 prior lines of treatment (N=86)	Refractory to most recent treatment (N=91)	Bulk (N=36)
CR	42 (31.6%)	3 (18.8%)	3 (21.4%)	11 (35.5%)	31 (39.7%)	7 (17.5%)	21 (24.4%)	16 (17.6%)	9 (25.0%)
PR	31 (23.3%)	4 (25.0%)	2 (14.3%)	10 (32.3%)	19 (24.4%)	9 (22.5%)	19 (22.1%)	22 (24.2%)	3 (8.3%)
SD	13 (9.8%)	3 (18.8%)	2 (14.3%)	2 (6.5%)	5 (6.4%)	6 (15.0%)	11 (12.8%)	9 (9.9%)	6 (16.7%)
PD	42 (31.6%)	6 (37.5%)	6 (42.9%)	7 (22.6%)	21 (26.9%)	16 (40.0%)	32 (37.2%)	39 (42.9%)	15 (41.7%)
Missing	5 (3.8%)	0 (0.0%)	1 (7.1%)	1 (3.2%)	2 (2.6%)	2 (5.0%)	3 (3.5%)	5 (5.5%)	3 (8.3%)
ORR (95% CI)	57.0% (48.0%–65.7%)	43.8% (19.8%–70.1%)	38.5% (13.9%–68.4%)	70.0% (50.6%–85.3%)	65.8% (54.0%–76.3%)	42.1% (26.3%–59.2%)	48.2% (37.1%–59.4%)	44.2% (33.5%–55.3%)	36.4% (20.4%–54.9%)
p-value*	–	.3	.1	.1	.02	.02	.01	<.001	.002

Response rates to Pola-BR. p-values are from a chi-squared test comparing ORR in the following subgroups: Prior CAR-T vs N prior CAR-T; Double/triple hit vs No double/triple hit; Transformed lymphoma vs de novo high grade lymphoma; Stand alone treatment vs all other treatment intention; >1 prior lines of treatment vs 1 prior line; Refractory to most recent vs Not refractory to most recent; Bulk vs No bulk. Patients with missing information on a subgroup are excluded from that comparison.

Northend, Blood Adv 6(9), 2022

Results of a UK real-world study of polatuzumab vedotin, bendamustine, and rituximab for relapsed/refractory DLBCL



Median PFS (stand-alone treatment patients):
5.4 months (95% CI 3.0–10.8)

Responders (CR or PR) versus non-responders:
HR 0.08 (95% CI 0.04–0.16, $p<.001$)

CR versus PR
HR 0.29 (95% CI 0.11–0.80), $p=.02$

Median OS (stand-alone treatment patients):
10.2 months (95% CI 5.2–14.3)

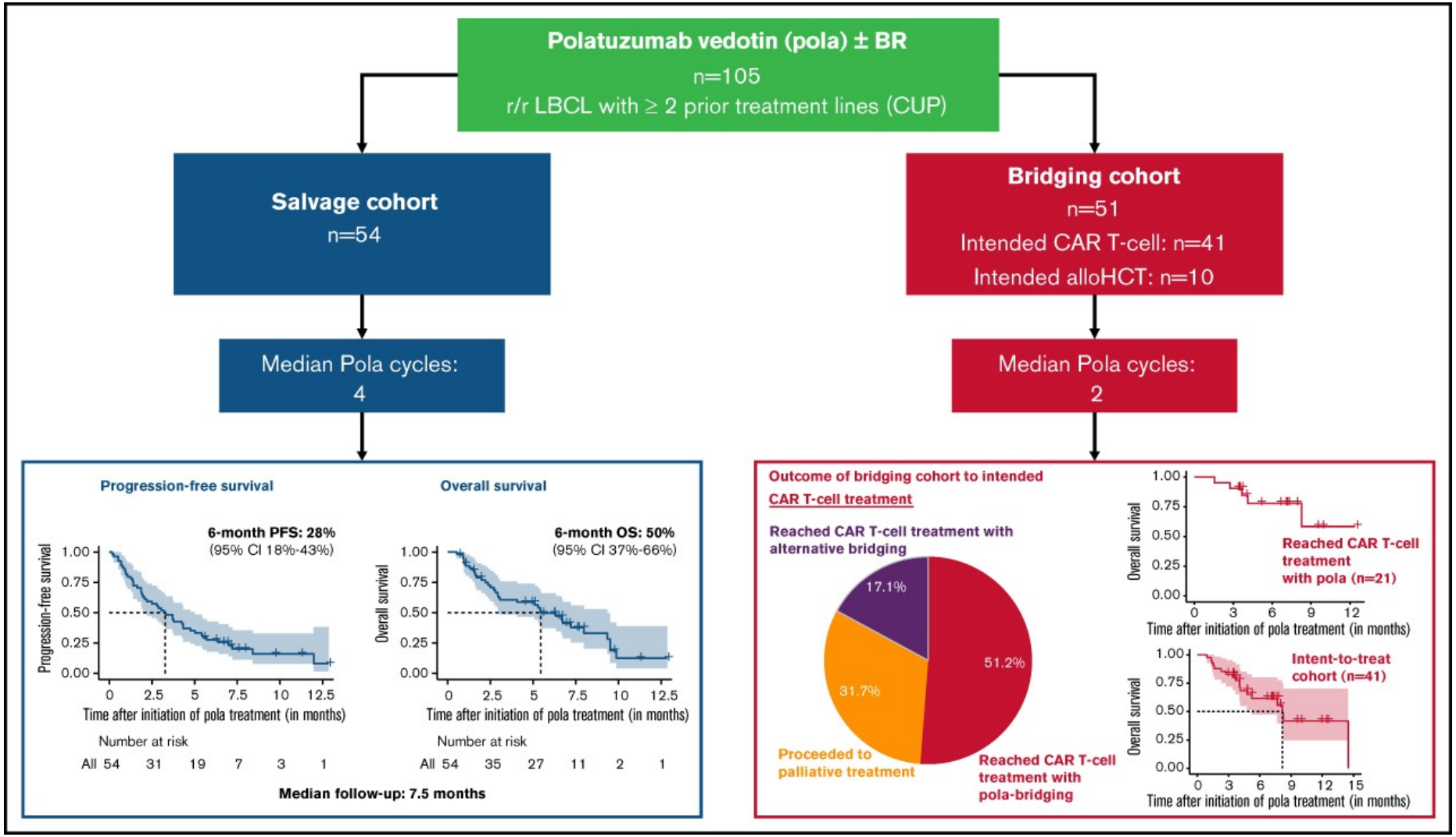
Responders (CR or PR) versus non-responders:
HR 0.14 (95% CI 0.07–0.28), $p<.001$

CR versus PR
HR 0.29 (95% CI 0.11–0.80), $p=.01$

Progression-free survival and overall survival
i: Progression-free survival for all patients.
ii: Overall survival for all patients.
iii: Progression-free survival for patients in the 'stand-alone' Pola-BR cohort (no planned stem cell transplant or CAR T-cell therapy) according to treatment response. CR=complete response, PR=partial response, HR=hazard ratio, CI=confidence interval.
iv: Overall survival for patients in the 'stand-alone' Pola-BR cohort (no planned stem cell transplant or CAR T-cell therapy) according to treatment response.

Northend, Blood Adv 6(9), 2022

Polatuzumab vedotin as salvage and bridging treatment in R/R large B-cell lymphomas: German Experience



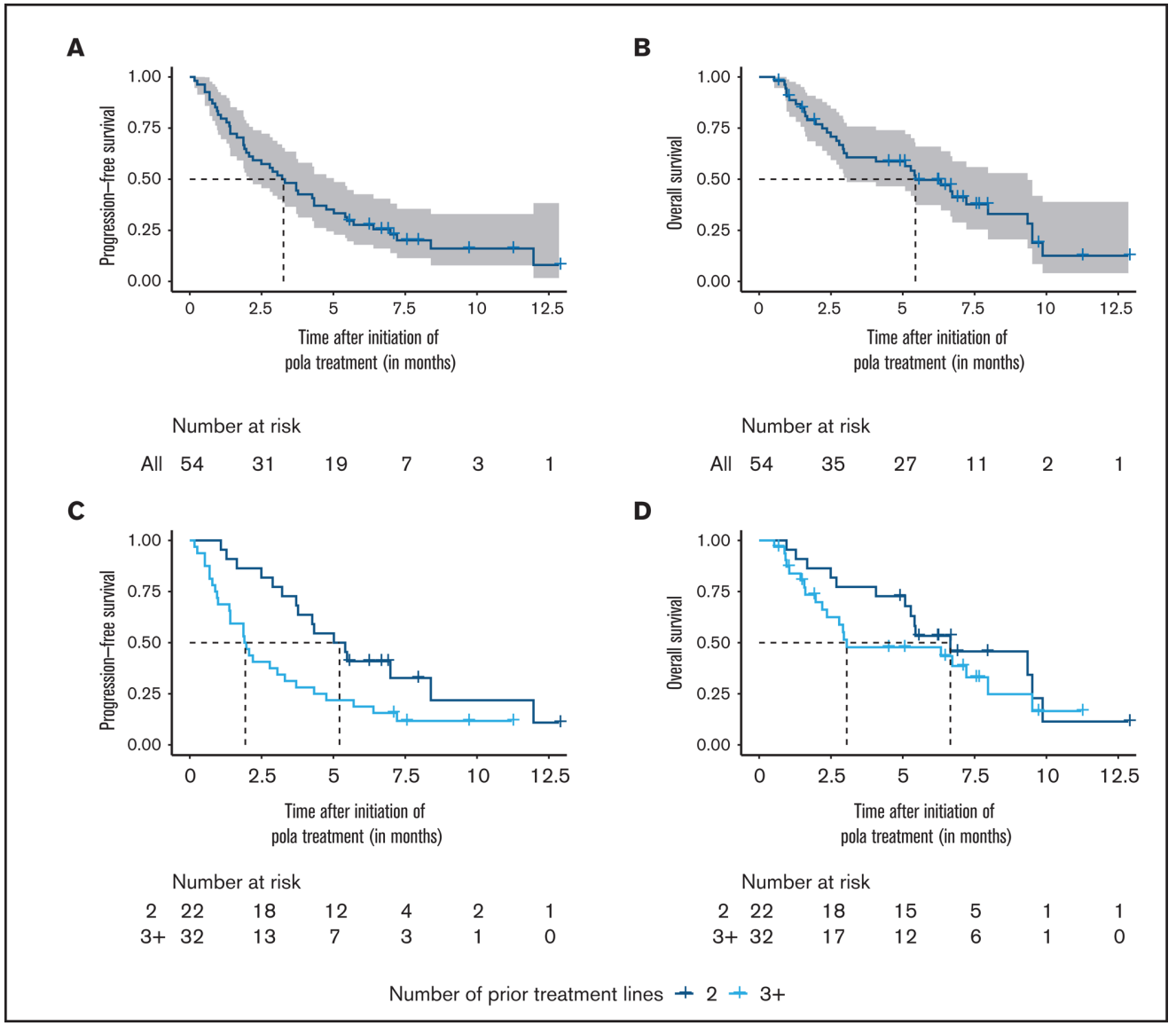
Liebers, et al Blood Adv, 2021,

Responses to polatuzumab vedotin in the salvage cohort

Best response	Salvage cohort (n = 54)
OR rate*	26 (48.1)
CR	8 (14.81)
PR	15 (27.78)
Clinical response	3 (5.56)
Nonresponse rate	28 (51.9)
SD	4 (7.41)
MR	3 (5.56)
PD	11 (20.37)
Clinical progression	10 (18.52)

Liebers, et al Blood Adv, 2021

Polatuzumab vedotin as salvage in R/R large B-cell lymphomas



Liebers, et al Blood Adv, 2021

Responses to polatuzumab vedotin in the bridging cohort

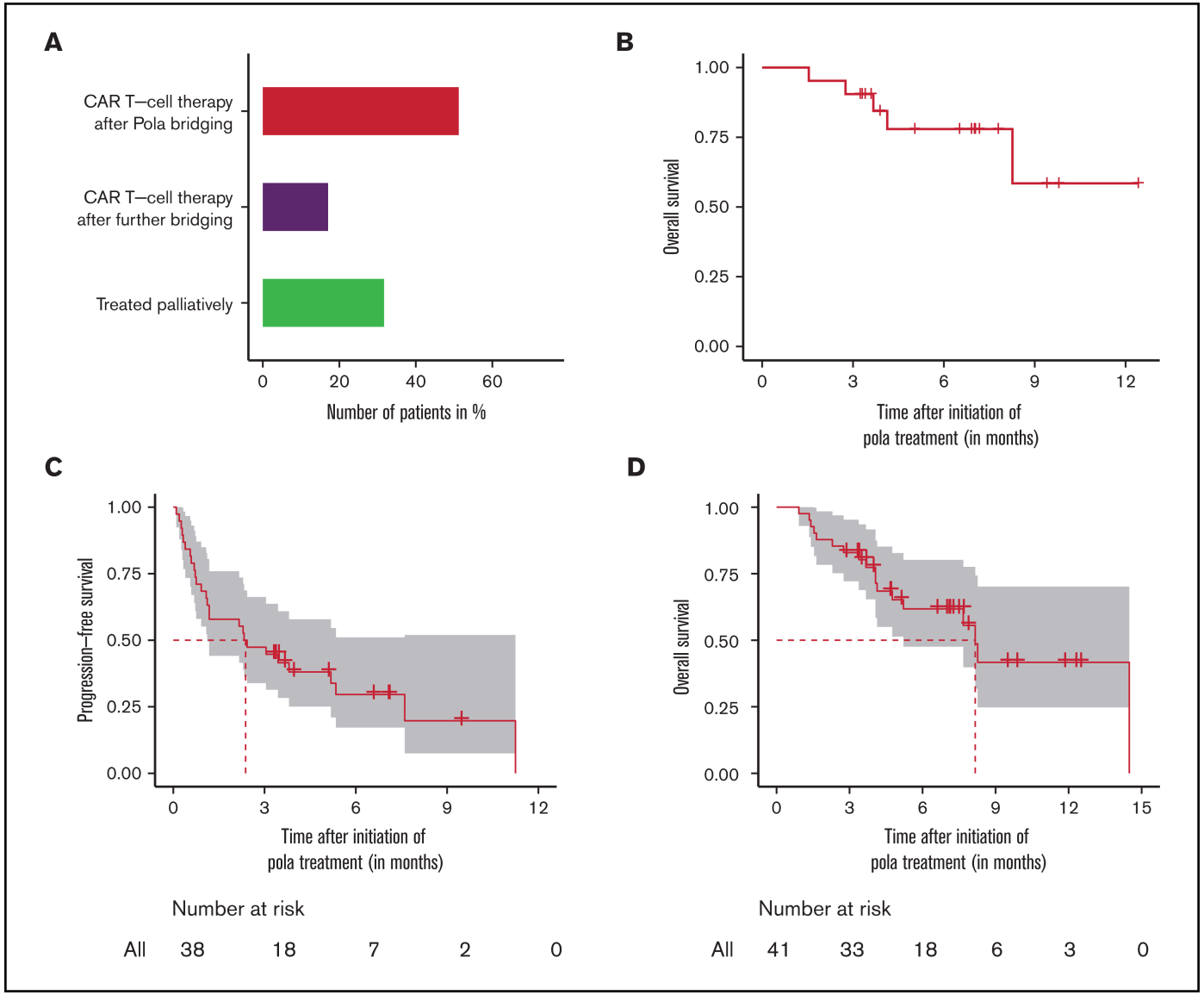
Best responses polatuzumab vedotin	n
Intended CAR T-cell therapy, n = 41	
Proceeded to CAR T-cell therapy after pola bridging, n = 21 (51.2%)	
CR	0
PR	5
Clinical response	2
SD/clinical stable disease	7
MR	2
PD/clinical progression	5
Proceeded to CAR T-cell therapy after alternative bridging, n = 7 (17.1%)	
PD/clinical progression	7

Liebers, et al Blood Adv, 2021

Treated palliatively, n = 13 (31.7%)	
CR*	1
Clinical response†	2
MR	1
PD/clinical progression	6
Not evaluable	3
Intended alloHCT, n = 10	
Proceeded to alloHCT after pola bridging, n = 5	
CR	1
PR	3
SD	1

Liebers, et al Blood Adv, 2021

Polatuzumab vedotin as bridging in R/R large B-cell lymphomas



Liebers, et al Blood Adv, 2021.

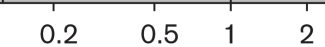
Polatuzumab vedotin as salvage and bridging treatment in R/R large B-cell lymphomas

A

Variable		N	Hazard ratio	p
Age		54	0.98 (0.95, 1.01)	0.121
Diagnosis	DLBCL	49	Reference	
	HGBCL	5	0.60 (0.18, 2.06)	0.420
Backbone treatment pola	Pola–(R)–Chemo	34	Reference	
	Pola–R	20	1.14 (0.62, 2.12)	0.675
Response pretreatment	Response	27	Reference	
	No response	27	2.44 (1.28, 4.62)	0.007
Prior treatment lines	2	22	Reference	
	3+	32	2.25 (1.14, 4.44)	0.019

B

Variable		N	Hazard ratio	p
Age		54	1.02 (0.98, 1.06)	0.36
Diagnosis	DLBCL	49	Reference	
	HGBCL	5	0.64 (0.15, 2.76)	0.55
Backbone treatment pola	Pola–(R)–Chemo	34	Reference	
	Pola–R	20	0.86 (0.40, 1.83)	0.69
Response pretreatment	Response	27	Reference	
	No response	27	2.12 (1.04, 4.30)	0.04
Prior treatment lines	2	22	Reference	
	3+	32	1.77 (0.84, 3.74)	0.13



Liebers, et al Blood Adv, 2021

Efficacy of POLA-(BR) Regimens:RWE

Study	Pts	Refractory (%)	OS mo	PFS mo	CR (%)	ORR (%)	mFU mo
Argnani (‘22)	55	81.8	9.0	4.9	27.3	49.1	11
Vodicka (‘22)	21	76.2	8.7	3.8	23.8	33.3	6.8
Dimou (‘21)	49	78.0	8.5	4.0	20	35	10.8
Segman (‘21)	47	23.0	8.3	5.6	40	61	6.8
Northend (‘22)	133	68.4	8.2	4.8	31.6	57	7.7
Terui (‘21)	35	66.0	NR	5.2	42.9	71.4	5.4
Dal (‘22)	71	49.3	5	NA	<32.4	47.9	5

Toxicity of POLA-(BR) Regimens

Study	Pts	Neutropenia, gr 3-4 (%)	Thrombocytopenia, gr 3-4 (%)	Neuropathy, all grades (%)
Sehn (‘20)	40	46.2	41.0	43.6
Argnani (‘22)	55	25.0	8.3	8.3
Liebers (‘21)	105	38.5	32.7	21.2
Terui (‘21)	35	31.4	20.0	19.7
Dal (‘22)	71	33.8	29.5	32.4

Subgroup Receiving 1 Prior Line of Therapy (2L patients) Responded Durably to Tafasitamab-cxix + LEN*

Long-term Outcomes From L-MIND: Tafasitamab-cxix + LEN in R/R DLBCL (Phase 2)**

*Combination of Tafasitamab +LEN is administered for a maximum of 12 cycles, followed by Tafasitamab as monotherapy until disease progression or unacceptable toxicity

	35-Month Analysis: 2L Patients	35-Month Analysis: 3L+ Patients
	N=40	N=40
ORR (95% CI), %	67.5 (50.9, 81.4)	47.5 (31.5, 63.9)
CR, % (N)	47.5 (N=19)	32.5 (N=13)
PR, % (N)	20 (N=8)	15 (N=6)
mDoR (95% CI), months	43.9 (9.1-NR)	NR (15-NR)
mPFS (95% CI), months	23.5 (7.4-NR)	7.6 (2.7-NR)
mOS (95% CI), months	45.7 (24.6-NR)	15.5 (8.6-NR)

The USPI includes efficacy data on a subset of patients with centrally confirmed diagnoses of DLBCL[3]: N=71; ORR=55%; mDoR=21.7 months after 12-Month analysis

2L = second-line; 3L = third-line; NR = Not Reached

1. Data on file:EMA_MOR208C203_Tables_22JUL2020. MorphoSys US Inc.; 2. Data on file: IA_MOR208C203_Overall_Tables_24FEB2021, MorphoSys US Inc;
3. MONJUVI (tafasitamab-cxix) Prescribing Information

Tafasitamab plus lenalidomide versus Pola-BR, R2, and CAR-T: comparing outcomes from RE-MIND2, an observational, retrospective cohort study in relapsed/refractory diffuse large B-cell lymphoma

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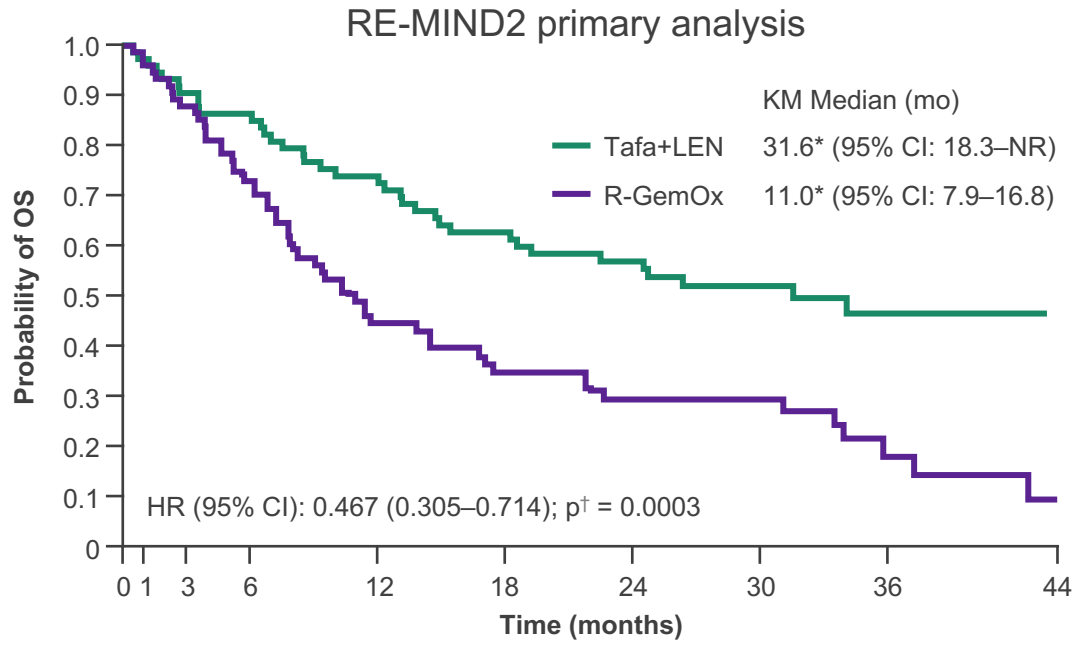
*Presenting author.
†Was an employee at time of study conduct.

Background

- Treatment options for R/R DLBCL have increased in recent years[1]
- Assessing comparative effectiveness of novel treatments in randomized head-to-head studies is time-consuming and costly and may delay patient access to new treatment options[2]
- Real-world data can be used to generate external comparators to complement single-arm clinical trials[3,4]
- The RE-MIND2 (NCT04697160) primary analysis, compared patient outcomes from L-MIND with matched patient populations treated with R-GemOx, BR and pooled systemic NCCN/ESMO recommended therapies for ASCT ineligible patients with R/R DLBCL[5]
- Here, we present results from an expanded analysis of RE-MIND2 comparing tafasitamab plus LEN versus Pola-BR, R2, and CAR-T therapies



Tafa+LEN (n=74)										
At risk	74	72	66	63	53	44	37	24	14	0
Event(s)	0	2	7	10	19	27	31	34	36	36
Censored	0	0	1	1	2	3	6	16	24	38
R-GemOx (n=74)										
At risk	74	73	65	53	29	21	15	12	5	0
Event(s)	0	1	9	20	40	46	49	49	53	55
Censored	0	0	0	1	5	7	10	13	16	19

*Patients received ≥2 prior systemic therapies for R/R DLBCL (including ≥1 anti-CD20 therapy); †Log rank test.

ASCT, autologous stem cell transplant; BR, bendamustine and rituximab; CAR-T, CD19 chimeric antigen receptor T-cell; CI, confidence interval; DLBCL, diffuse large B-cell lymphoma; ESMO, European Society of Medical Oncology; HR, hazard ratio; KM, Kaplan-Meier; LEN, lenalidomide; NCCN, National Cancer Care Network; OS, overall survival; Pola-BR, polatuzumab vedotin plus bendamustine and rituximab; R2, rituximab plus lenalidomide; R-GemOx, rituximab plus gemcitabine and oxaliplatin; R/R, relapsed/refractory; Tafa, tafasitamab.

1.Cheson BD, et al. Blood Can J 2021;11:68.
2. Mullard A. Nat Reviews 2018;17:81–5.
3. FDA. https://www.fda.gov/media/124795/download.
4. Przepiorka D, et al. Clin Can Res 2015;21:4035–4039
5. Nowakowski GS, et al. Poster ABCL-346. SOHO 2021. https://epostersonline.com/soho2021/node/99.

RE-MIND2 expanded analysis study design

Eligibility criteria

- R/R DLBCL patients
- ≥2 therapies administered for DLBCL
- Transplant ineligible

RE-MIND2
N=3,454
(All therapies)

Matching process

Find matching patients for 6 covariates*

- Age group (<70 years vs ≥70 years)
- Number of prior therapy lines (1 vs 2/3)
- Prior ASCT (yes vs no)
- History of primary refractoriness (yes vs no)
- Refractoriness to last therapy line (yes vs no)
- ECOG (0–1 vs ≥2)

Matched comparison

L-MIND
Tafasitamab + LEN
N=81
Cut-off date: November 2019

Tafasitamab + LEN vs

- Pola-BR
- R2
- CAR-T

Primary endpoint:

- OS

Key secondary endpoints:

- ORR and CR rate
- DoR
- PFS

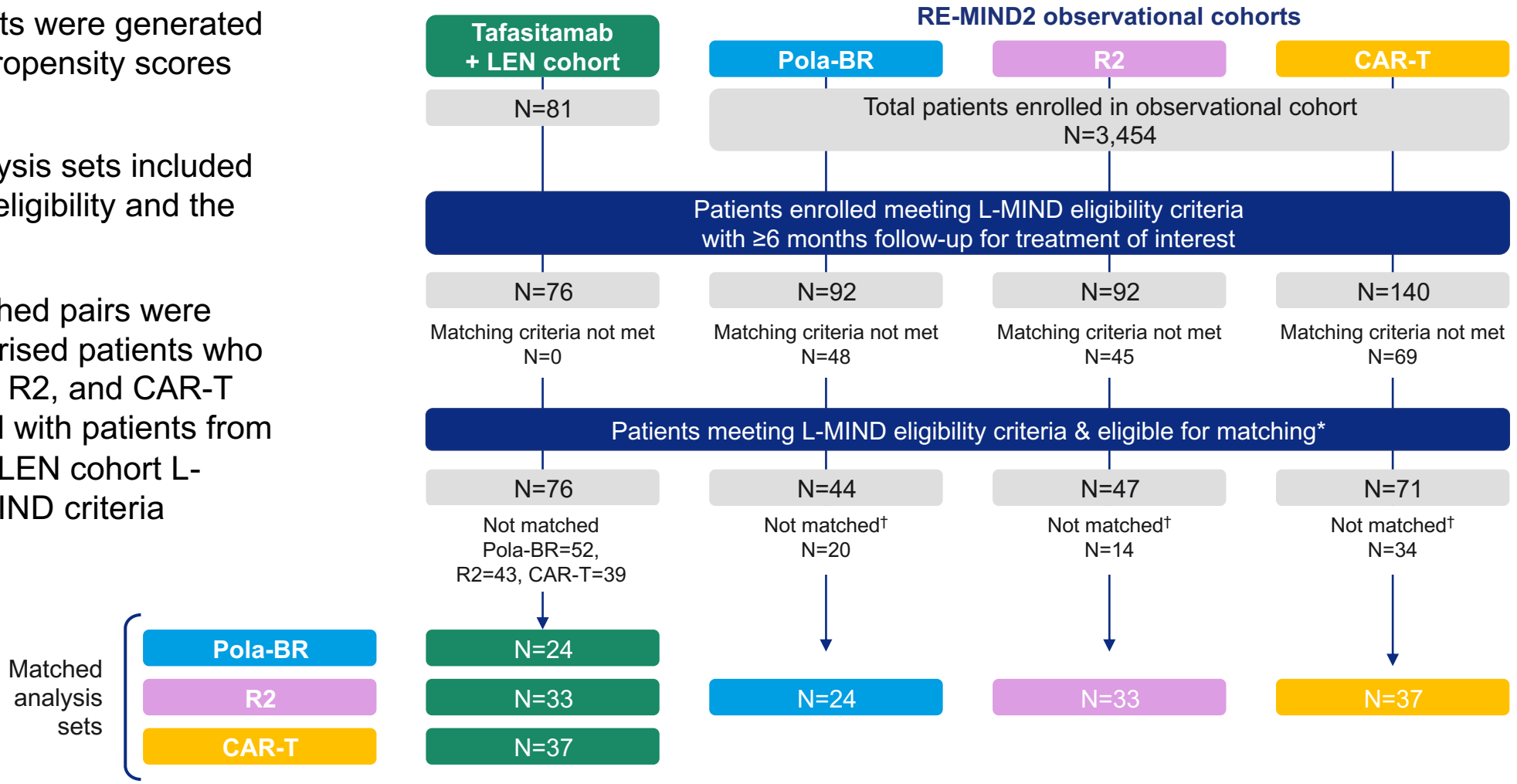
Sensitivity analyses

- Performed using inverse probability of treatment weighting
- Matching on 9 covariates with multiple imputation, to account for missing data

* 9 covariates were used for the primary analysis; ASCT, autologous stem cell transplant; CAR-T, CD19 chimeric antigen receptor T-cell therapies; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; ECOG, Eastern Cooperative Oncology Group performance status; LEN, lenalidomide; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Pola-BR, polatuzumab vedotin plus bendamustine and rituximab; R2, rituximab plus lenalidomide; R/R, relapsed/refractory.

Analysis populations

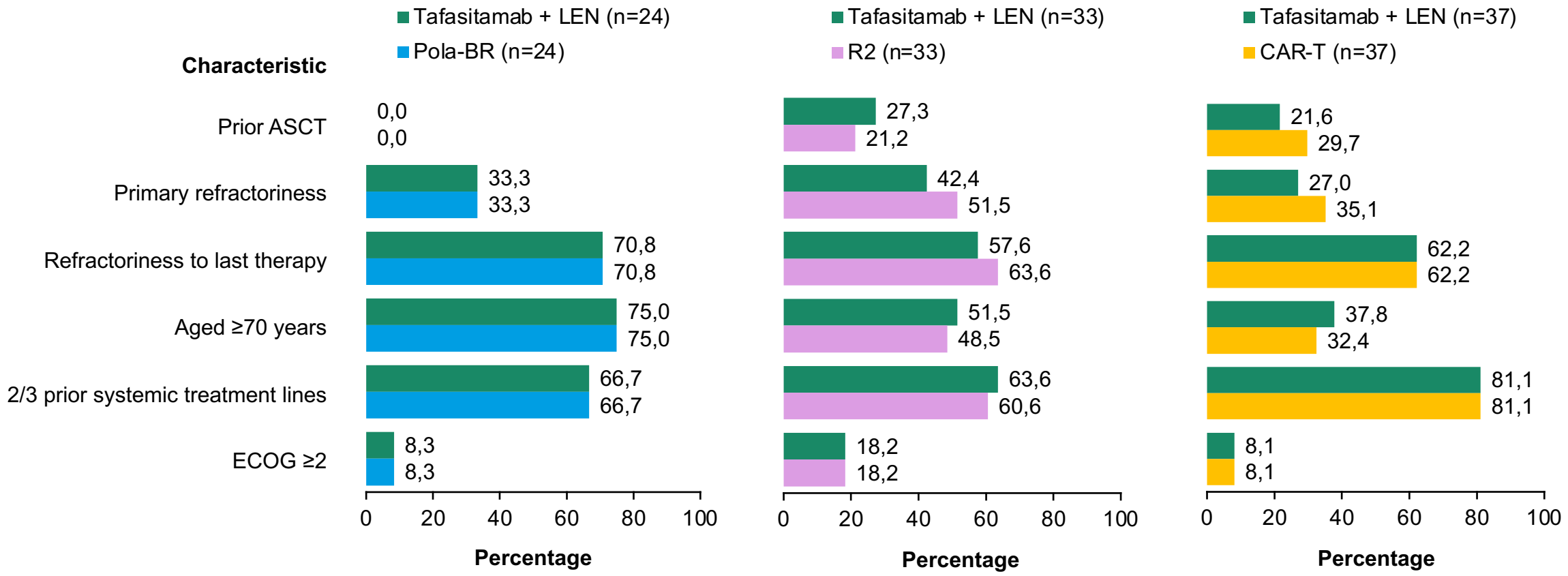
- Comparator cohorts were generated using estimated propensity scores and 1:1 matching
- The resulting analysis sets included patients who met eligibility and the matching criteria
- Patient-level matched pairs were created and comprised patients who received Pola-BR, R2, and CAR-T therapies matched with patients from the tafasitamab + LEN cohort L-MIND criteria L-MIND criteria



*With complete data for six matching covariates, Based on 1:1 nearest neighbor propensity score.
CAR-T, CD19 chimeric antigen receptor T-cell therapies; LEN, lenalidomide; Pola-BR, polatuzumab vedotin plus bendamustine and rituximab; R2, rituximab plus lenalidomide; R/R, relapsed/refractory.

Results: Baseline characteristics for tafasitamab + LEN versus Pola-BR, R2, and CAR-T

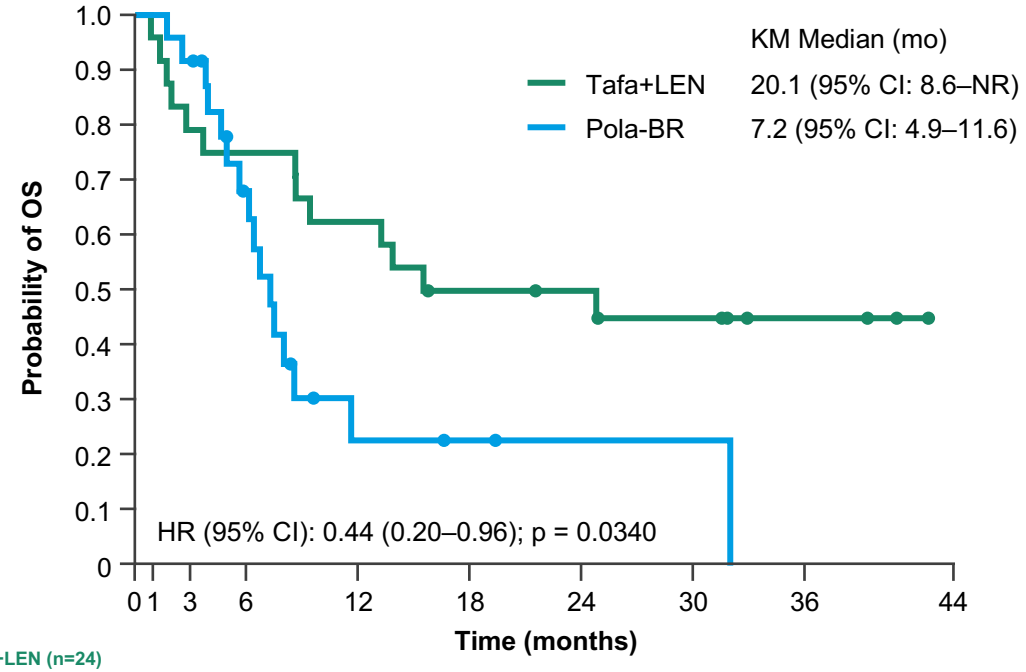
- A high degree of covariate balance was achieved between the tafasitamab plus LEN and comparator therapy cohorts



ASCT, autologous stem-cell transplant; CAR-T, CD19 chimeric antigen receptor T-cell therapies; ECOG, Eastern Cooperative Oncology Group; LEN, lenalidomide; Pola-BR, polatuzumab vedotin plus bendamustine plus rituximab; R2, rituximab plus lenalidomide.

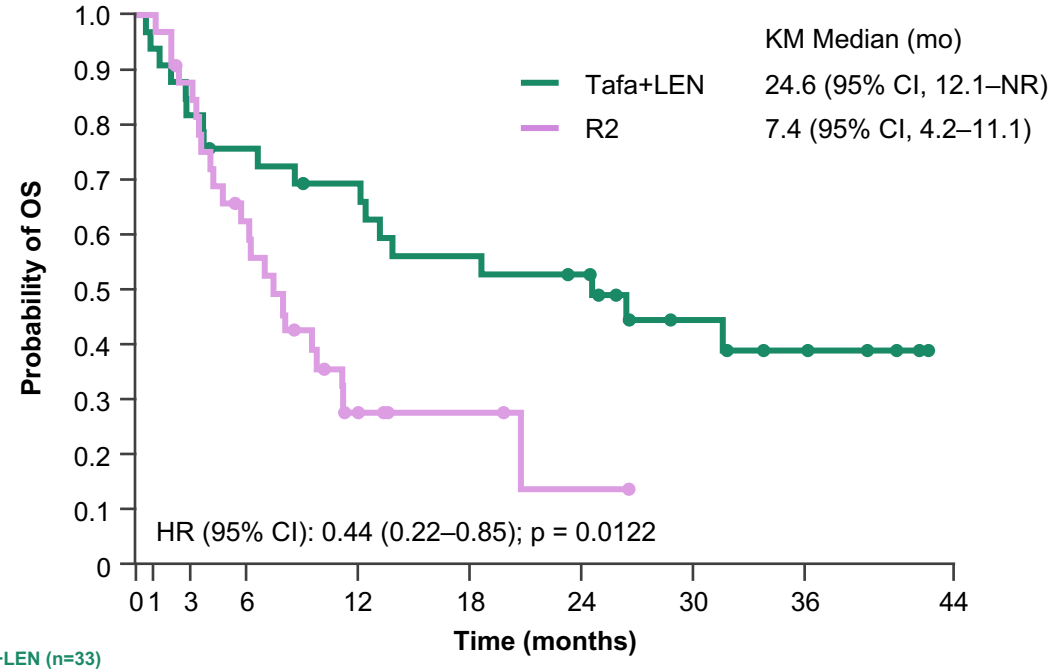
Primary endpoint: OS

- Tafasitamab + LEN was associated with statistically significant improvements in OS versus Pola-BR and versus R2



Tafa+LEN (n=24)										
At risk	24	23	19	18	15	11	10	8	4	0
Event(s)	0	1	5	6	9	12	12	13	13	13
Censored	0	0	0	0	0	1	2	3	7	11
Pola-BR (n=24)										
At risk	24	24	22	13	3	2	1	1	0	0
Event(s)	0	0	2	7	15	15	15	15	16	16
Censored	0	0	0	4	6	7	8	8	8	8

Median duration of follow-up: tafasitamab plus + LEN: 32 mo; Pola-BR: 16.6 mo



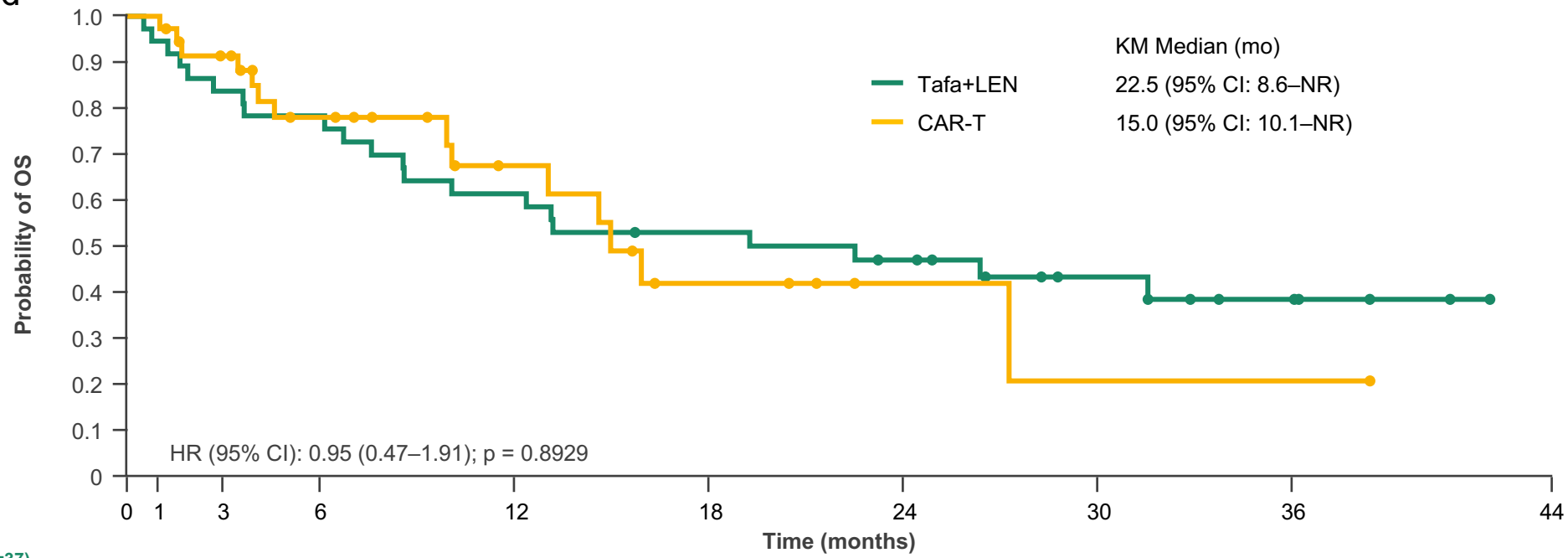
Tafa+LEN (n=33)										
At risk	33	31	27	24	21	17	15	8	5	0
Event(s)	0	2	6	8	10	14	15	17	18	18
Censored	0	0	0	1	2	2	3	8	10	15
R2 (n=33)										
At risk	33	33	28	19	5	3	1	0	0	0
Event(s)	0	0	4	12	22	22	23	23	23	23
Censored	0	0	1	2	6	8	9	10	10	10

Median duration of follow-up: tafasitamab plus + LEN: 32; mo; R2: 13.4 mo

CI, confidence interval; KM, Kaplan-Meier; LEN, lenalidomide; mo, month; NR, not reached; Pola-BR, polatuzumab vedotin plus bendamustine plus rituximab; OS, overall survival; R2, rituximab plus lenalidomide; Tafa, tafasitamab. P values were calculated using Log-rank test.

Primary endpoint: OS

- A comparable OS benefit with tafasitamab + LEN versus CAR-T (22 versus 15 months), without statistical significance, was observed



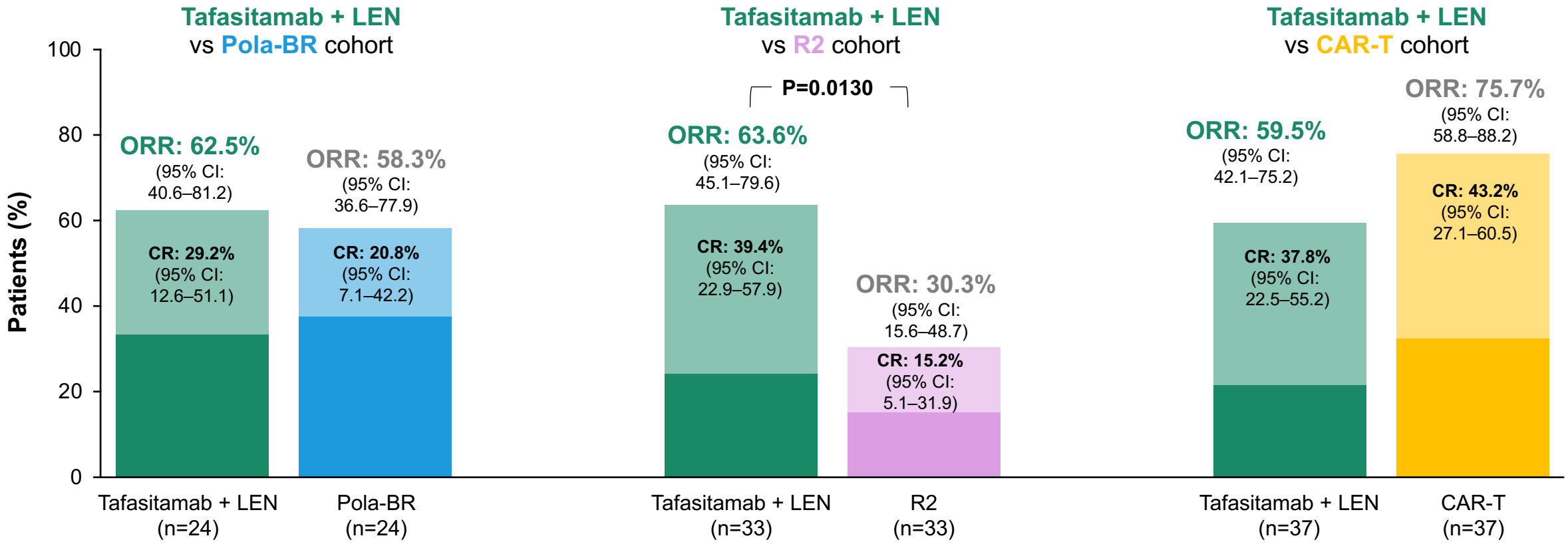
Tafa+LEN (n=37)										
At risk	37	35	31	28	22	18	15	9	5	0
Event(s)	0	2	6	8	14	17	19	20	21	21
Censored	0	0	0	1	1	2	3	8	11	16
CAR-T (n=37)										
At risk	37	37	30	22	11	5	2	1	1	0
Event(s)	0	0	3	7	9	13	13	14	14	14
Censored	0	0	4	8	17	19	22	22	22	23

Median duration of follow-up: tafasitamab plus + LEN: 32 mo; CAR-T: 10.2 mo

CAR-T, CD19 chimeric antigen receptor T-cell; CI, confidence interval; KM, Kaplan-Meier; LEN, lenalidomide; mo, month; NR, not reached; OS, overall survival; Tafa, tafasitamab.

Secondary endpoint: ORR and CR rate

- ORR and CR rate were statistically significantly higher with tafasitamab + LEN versus R2
- Statistical differences versus Pola-BR and CAR-T were not detected with the sample sizes in the matched cohorts



CAR-T, CD19 chimeric antigen receptor T-cell; CI, confidence interval; CR, complete response; LEN, lenalidomide; ORR, overall response rate; Pola-BR, polatuzumab vedotin plus bendamustine plus rituximab; R2, rituximab plus lenalidomide.

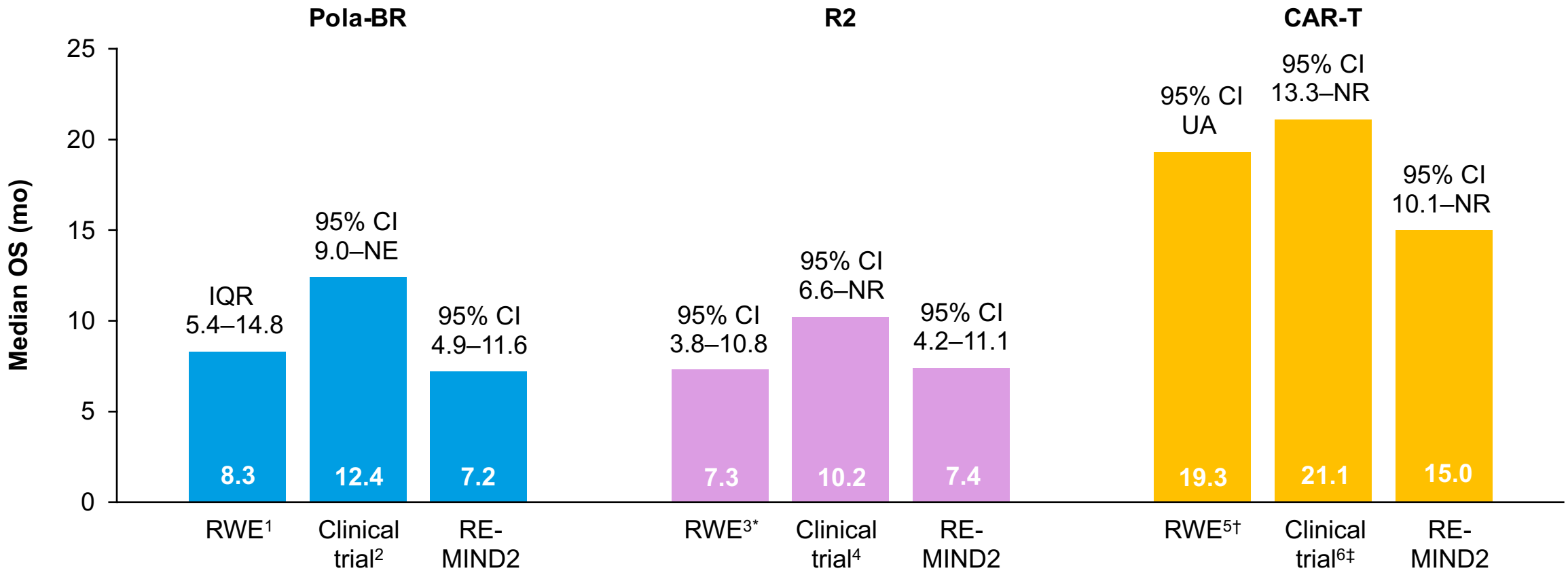
Secondary endpoints: PFS and DoR

- Tafasitamab + LEN was associated with statistical and clinically meaningful improvements in PFS versus R2
  - Improvements in PFS were observed versus Pola-BR and versus CAR-T
- A low number of patients with tumor assessment data precluded comparative analysis of DoR

	Tafa + LEN (n=24)	Pola-BR (n=24)	Tafa + LEN (n=33)	R2 (n=33)	Tafa + LEN (n=37)	CAR-T (n=37)
Median **PFS**, mo (95% CI)	8.0 (1.9–19.9)	5.0 (2.5–5.6)	5.9 (3.6–36.7)	2.8 (2.0–5.8)	6.3 (3.6–22.5)	4.0 (3.1–12.8)
HR (95% CI) p* value	0.482 (0.217–1.073) 0.0689		0.511 (0.281–0.927) **0.0252**		0.612 (0.302–1.240) 0.1696	
Median **DoR**, mo (95% CI)	17.7 (3.6–34.8)	2.3 (0.3–6.1)	34.8 (3.6–34.8)	12.4 (2.7–19.3)	26.1 (4.4–NR)	5.9 (2.0–10.0)

CAR-T, CD19 chimeric antigen receptor T-cell; CI, confidence interval; DoR, duration of response; KM, Kaplan-Meier; LEN, lenalidomide; mo, months; PFS, progression-free survival; Pola-BR, polatuzumab vedotin plus bendamustine plus rituximab; R2, rituximab plus lenalidomide; tafa, tafasitamab.
*Calculated using Log-rank test.

RE-MIND2 versus literature reported outcomes for comparator therapies



CAR-T, CD19 chimeric antigen receptor T-cell; CI, confidence interval; mo, month; IQR, interquartile range; NE, not-evaluable; NR, not reached; Pola-BR, polatuzumab vedotin plus bendamustine plus rituximab; R2, rituximab plus lenalidomide; RWE, real-world evidence; UA, unavailable to report.

*Includes 21 patients with R/R DLBCL and 3 patients with transformed follicular lymphoma.

†Tisagenlecleucel or axicabtagene ciloleucel.

‡Lisocabtagene maraleucel.

1.Segman Y, et al. Leuk Lymphoma 2020;62:118–24.
2.Sehn L, et al. J Clin Oncol 2019;38:155–65.
3.Lee Y-P, et al. Cancer Manag Res 2021;13:4241–50.
4.Wang M, et al. Leukemia 2013;27(9):1902–9.
5.Sermer D, et al. Blood Adv 2020;4:4669–78.
6.Abramson JS, et al. Lancet 2020;396(10254):839–52.

Conclusions

- The primary endpoint was met for comparisons with tafasitamab + LEN compared with Pola-BR and R2
  - Statistically significant improvements in median OS were observed
  - Median OS was comparable with tafasitamab + LEN relative to CAR-T therapies
- Numerical differences, favoring tafasitamab + LEN, were observed for the secondary endpoints
- Sensitivity analyses which confirmed the main analysis were performed
- The RE-MIND2 study design used strict patient-level matching to compare real-world and clinical trial populations
  - This allows a contextualization of outcomes with different treatments in the absence of head-to-head trials
- Due to the recent approval of the comparator treatments, these data may inform treatment decisions in the context of emerging therapies for R/R DLBCL

CAR-T, CD19 chimeric antigen receptor T-cell; DLBCL, diffuse large B-cell lymphoma;
LEN, lenalidomide; OS, overall survival; Pola-BR, polatuzumab vedotin plus bendamustine plus rituximab; R2, rituximab plus lenalidomide; R/R relapsed/refractory; RWD, real-world data.

Real-World Assessment of Combination Tafasitamab and Lenalidomide (TL) in Relapsed or Refractory DLBCL

David Qualls[1], Loretta Nastoupil[2], Nicholas Lambert[3], Paolo Caimi[4], Mwanasha Merrill[5], Jennifer Crombie[5], David Bond[6], Kami Maddocks[6], Sarah Rutherford[7], Graham Wehmeyer[7], Jason Romancik[8], Behzad Amoozgar[9], Brad Kahl[9], Lori Leslie[10], Jeremy S. Abramson[11], Michelle Okwali[1], Phuong Dao[1], Michael Buege[1], Venkatraman Seshan[1], Connie Batlevi[1,12], Gilles Salles[1]

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[4]Taussig Cancer Institute, Cleveland Clinic Foundation, Cleveland, OH
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[6]The Ohio State University, Columbus, OH
[7]Meyer Cancer Center, Weill Cornell Medicine and New York Presbyterian Hospital, New York, NY
[8]Winship Cancer Institute at Emory University, Atlanta, GA
[9]Washington University School of Medicine, St. Louis, MO
[10]John Theurer Cancer Center, Hackensack University Medical Center, Hackensack, NJ
[11]Massachusetts General Hospital, Boston, MA
[12]Current affiliation: Genentech, San Francisco, CA

Patients

Patient and Disease

Characteristic	TLOC cohort	L-MIND trial
Number of patients	157	81
Female sex	51%	46%
Age (yrs), median (range)	75 (26-94)	72 (41-86)
Race		
White, all ethnicity	89%	89%
Asian	6%	2%
Other/Unknown	5%	1%
Diagnosis		
DLBCL, NOS	59%	89%
Transformed	23%	9%
HGBCL (Double/Triple Hit)	15%	2%
Other	3%	0%
Cell of Origin (Hans)		
GCB	57%	47%
non-GCB	34%	26%
Unknown	10%	27%
Risk (IPI)		
0-2	28%	49%
3-5	72%	51%
Ann Arbor Stage		
I-II	10%	25%
III-IV	90%	75%

Prior Treatment

Characteristic	TLOC	L-MIND
Prior lines of therapy for DLBCL		
Median (range)	2 (0-11)	2 (1-4)
0	4%*	0%
1	29%	49%
2	30%	43%
3	16%	6%
4	6%	1%
≥5	16%	0 (0)
Primary Refractory	51%	18%
Refractory to last therapy	66%	44%
Prior SCT	13%	11%
Prior CAR T	28%	0%

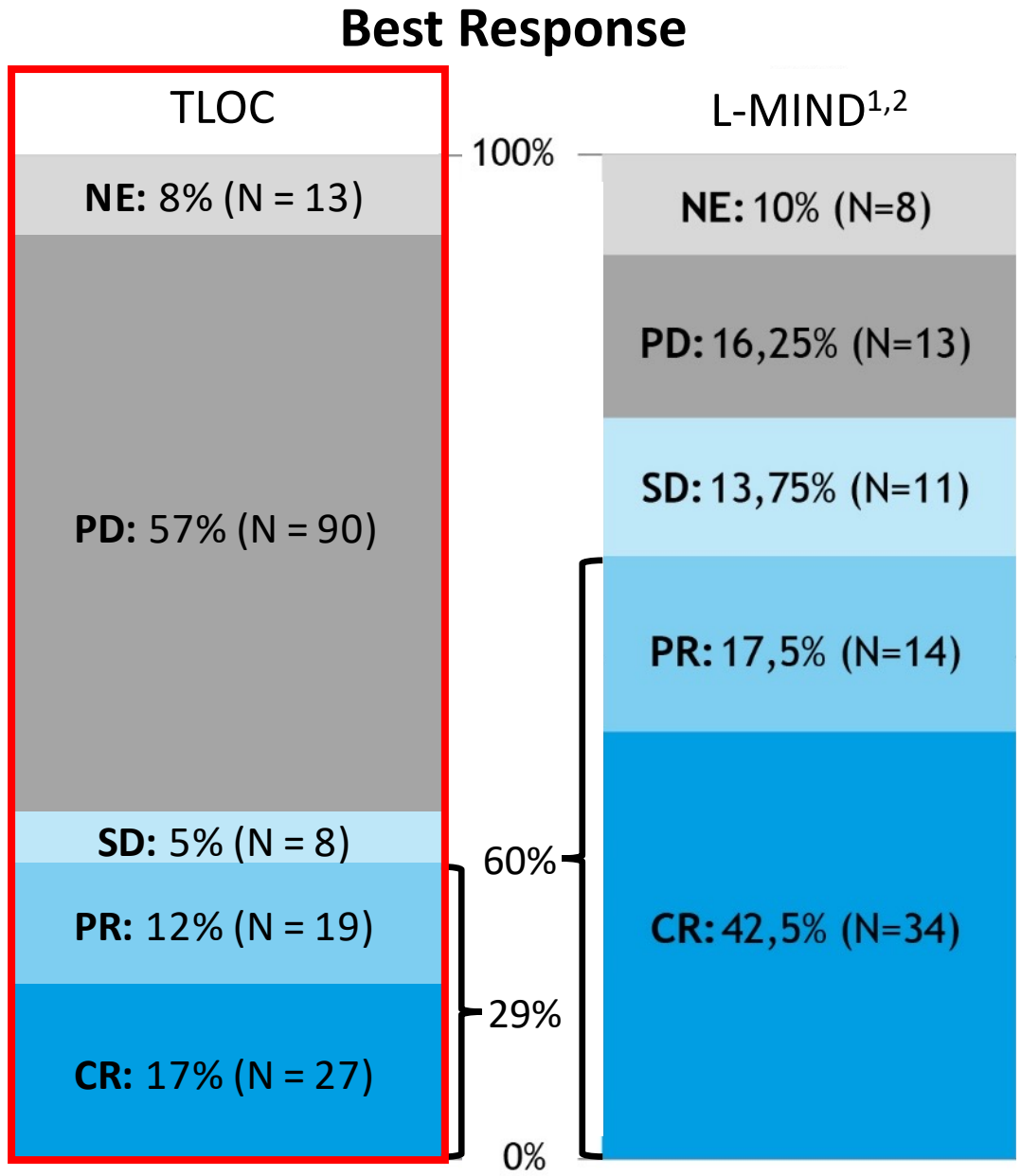
L-MIND Eligible: 11%

Reasons for L-MIND ineligibility:

- EGFR < 60 ml/min 33%
- Prior anti-CD19 therapy 28%
- >3 prior lines of therapy 23%
- ECOG PS 3-4 18%
- High-grade B cell lymphoma 15%

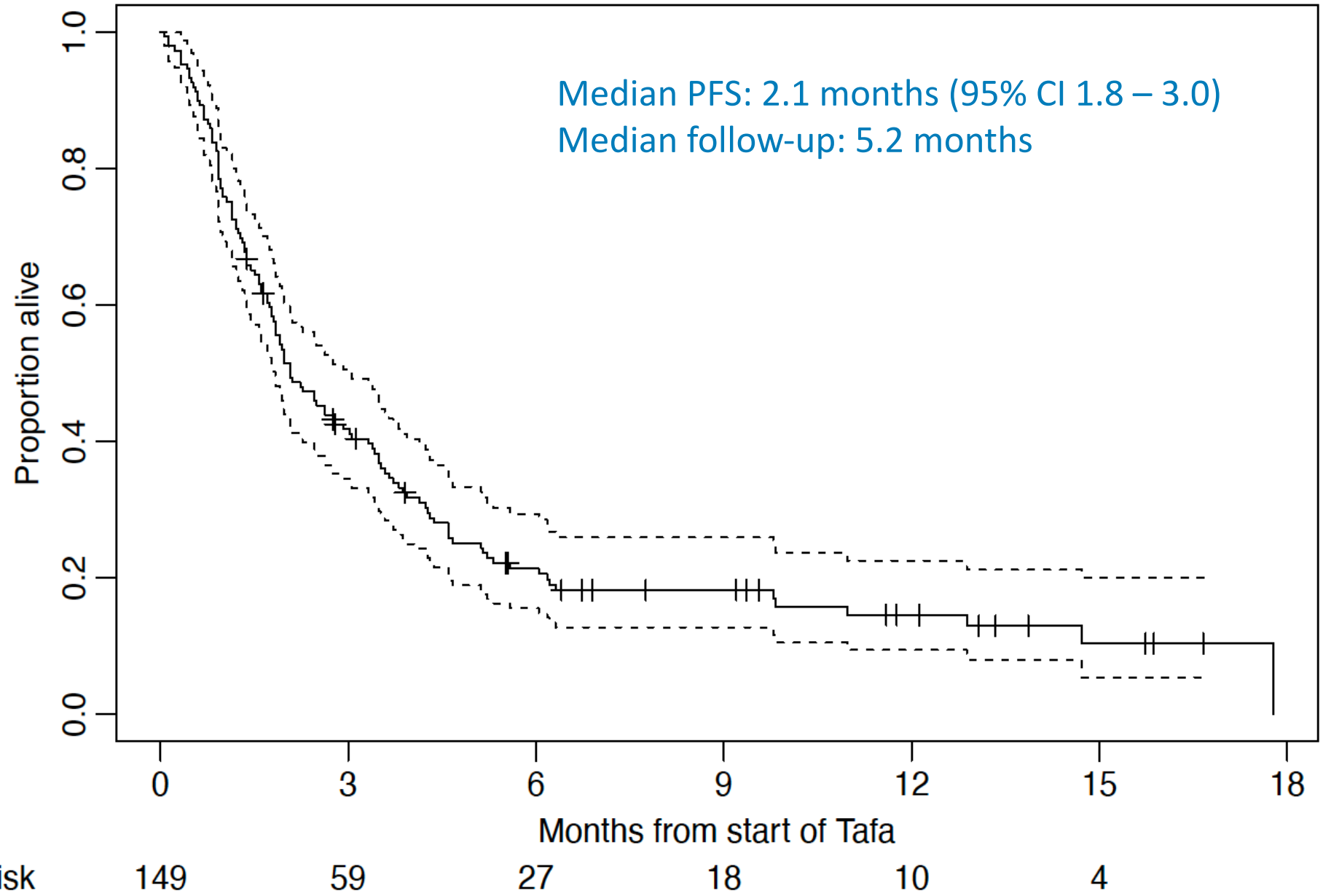
Treatment exposure and responses

Treatment	
Time on treatment	
Median (IQR), days	59 (28 - 118)
Lenalidomide treatment timing	
Patients with delay in initiation	46%
Median delay time, days (IQR)	7 (4-20)
Starting daily lenalidomide dose (L-MIND: 25 mg)	
Patients with dose reduction at initiation	66%
Median starting dose, mg (IQR)	20 (10-25)
Reasons for initial lenalidomide reduction	
Frailty/Performance status	43%
Renal dysfunction	35%
Cytopenias	10%
Other/unknown	12%

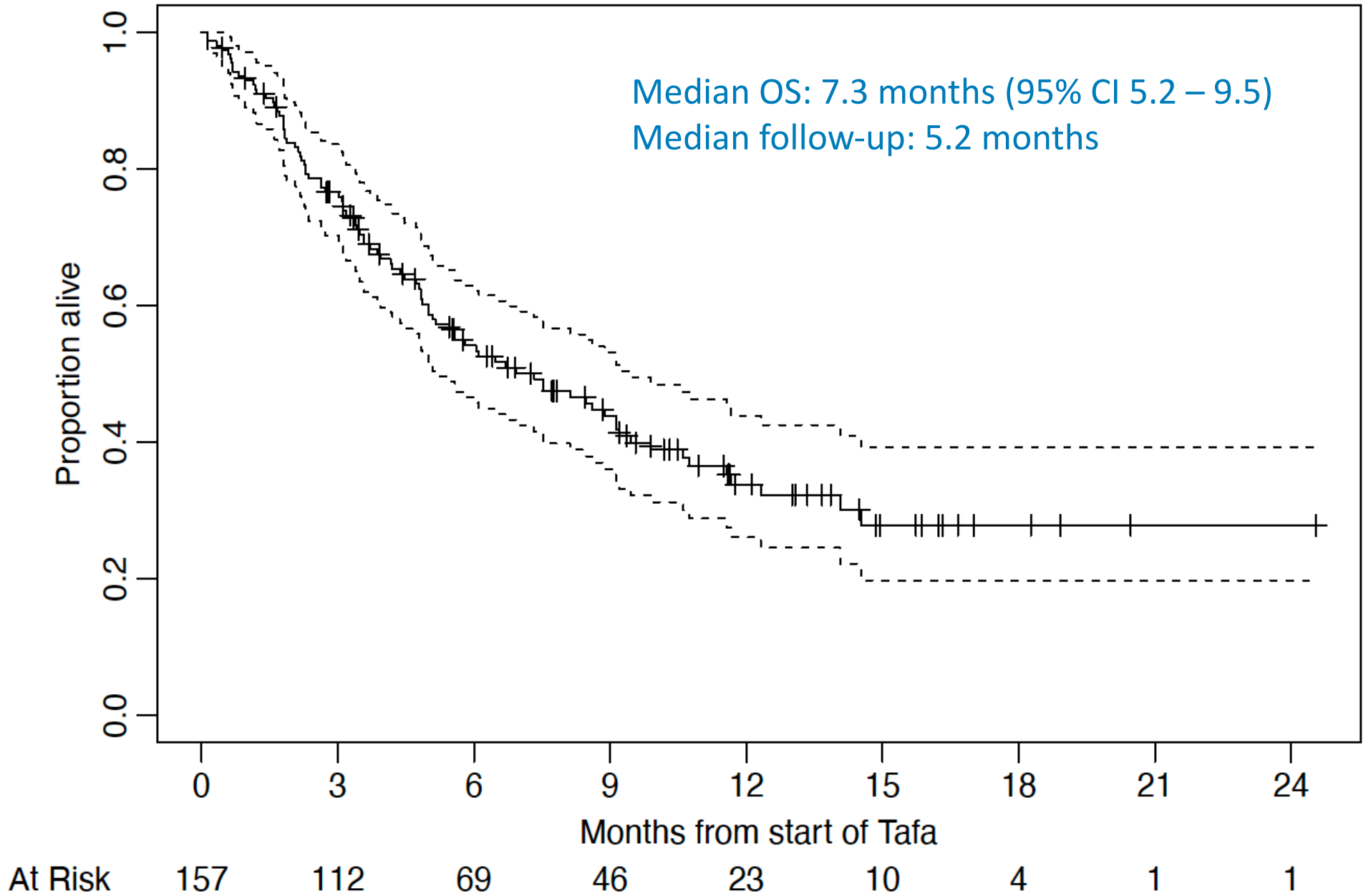


[1]Duell J et al., Haematologica 2021
[2]Duell J et al., presented at ASCO 2021

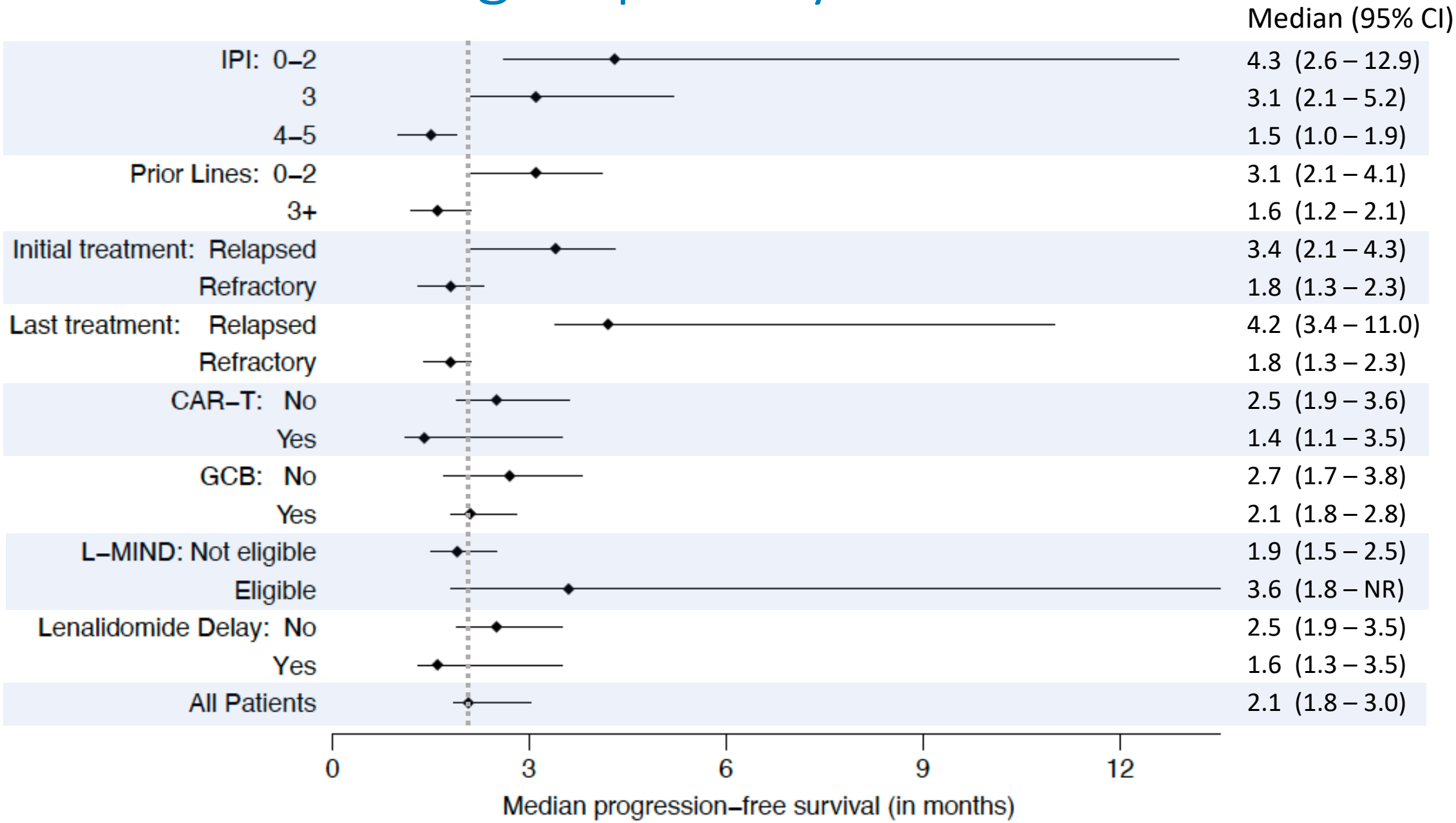
Progression-Free Survival



Overall Survival



Subgroup Analysis of PFS

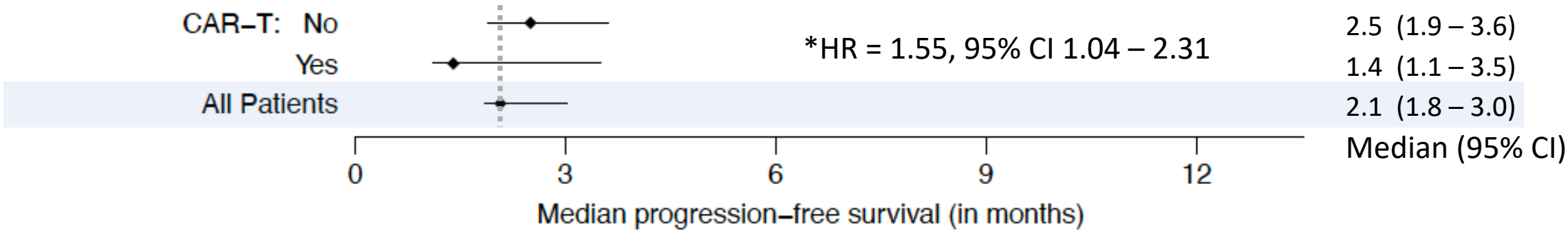


TL after CD19-directed CAR T cell therapy

- 42 patients (28%) had CAR T before TL
- 19 with biopsy recorded after CAR T
  - 15/19 confirmed CD19 expression
  - 4/19 CD19 expression not reported

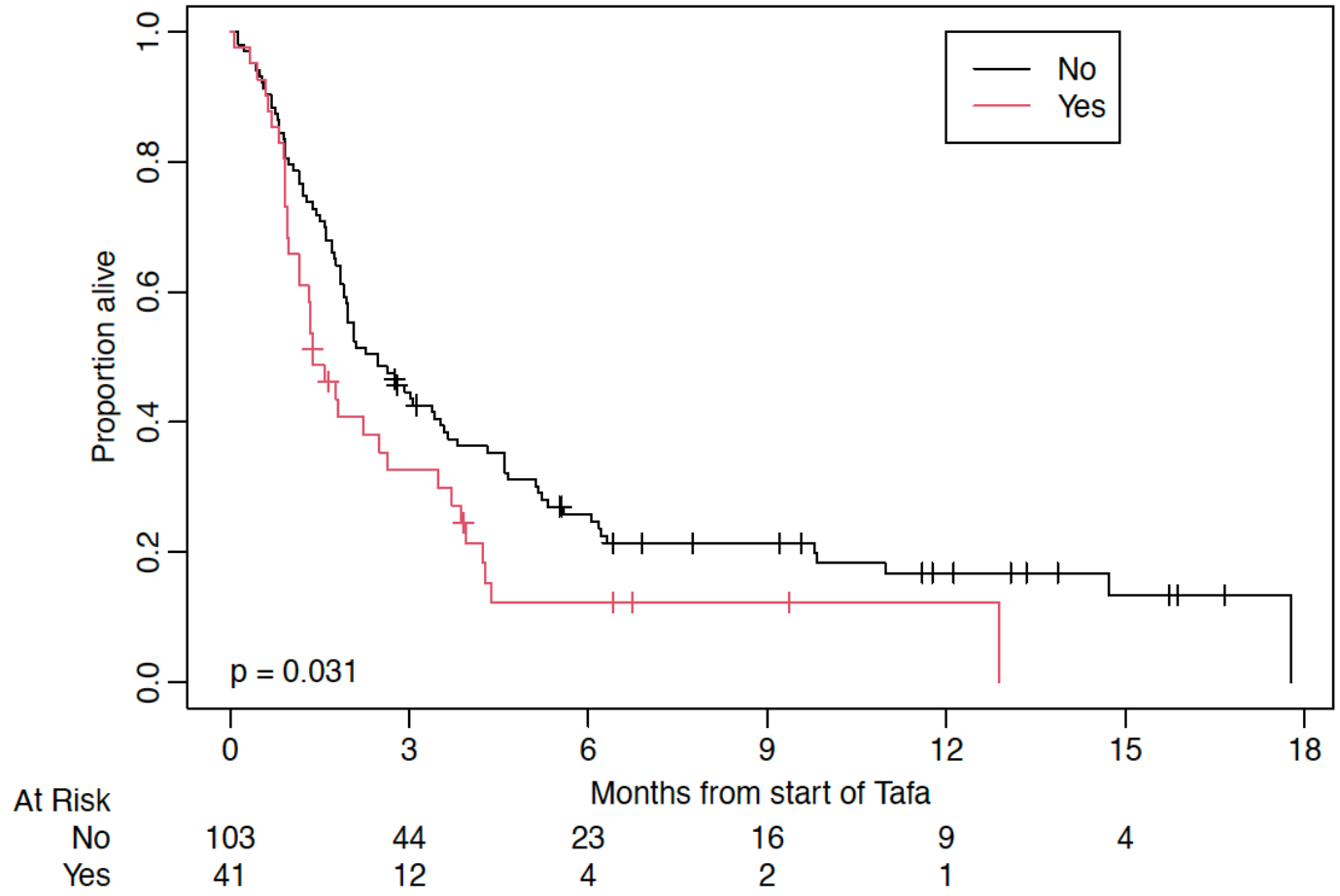
Response to TL according to CAR T Response

DOR after CAR T	≥ 6 months (N = 11)	< 6 months (N = 15)
ORR	36%	7%
CRR	36%	7%



TL after CAR T cell therapy

- 42 patients received anti-CD19 CAR T therapy before TL
- 19 with biopsy recorded after CAR T
  - 15/19 confirmed CD19 expression
  - 4/19 CD19 expression not reported



Median PFS

Prior CAR: 1.4 months (95% CI 1.1 - 3.5)

No prior CAR: 2.5 months (95% CI 1.9 – 3.6)

HR = 1.55, 95% CI 1.04 – 2.31

Adverse event profile similar to L-MIND

Clinically significant adverse events: resulting in dose reduction, treatment delay, treatment discontinuation, hospitalization, or death

Event	Proportion affected (%)
Hematological (All)	38
Neutropenia	28
Anemia	15
Thrombocytopenia	15
Febrile Neutropenia	8

*Other: autoimmune hemolysis (1), neuropathy (1), MDS, bowel obstruction/perf, AKI, pruritis, hypotension (2), pleural effusions, transaminase/bili elevations (2), myalgias, constipation, hematuria, cognitive decline, cough

Event	Proportion affected (%)
Infection	16
COVID-19	3
Asthenia	13
Decreased appetite	9
Fevers	7
Diarrhea	4
Rash	3
Peripheral Edema	3
DVT/PE	3
Other*	13

Treatment discontinued: 137 patients (POD 80%, Toxicity 13%, Death 3%, Other 13%)
Deaths: 91 patients (POD 85%, Toxicity 1%, Unrelated 5%, Unknown 9%)

Conclusions

- Limited overlap between TLOC and L-MIND cohorts (11% L-MIND eligible)
- Treatment delays and dose reductions with lenalidomide were common
- Median PFS was 2.1 months (L-MIND: median PFS 12.1 months)
- Worse PFS seen in patients with refractory disease, ≥3 lines of therapy therapy, higher IPI

TL may be optimally suited for patients with fewer prior lines of therapy and non-refractory disease, reflecting the L-MIND clinical trial population

Loncastuximab tesirine: Phase 2 Lotis-2 Trial Results

Efficacy Parameter	Loncastuximab (N=145)
Overall Response Rate, % (95% CI)	48.3% (39.9, 56.7)
Complete Response Rate	24.1% (17.4, 31.9)
Partial Response Rate	24.1% (17.4, 31.9)
Duration of Overall Response	(N=70)
Median (95%CI), Months	10.3 (6.9, NE)

NE=Not Estimatible

Adverse Events in ≥10% of Patients (N=145)	All Grades	Grade ≥3
Fatigue	38%	1%[a]
Edema	28%	3%
Rash	30%	2%
Pruitis	12%	0%
Photosensitivity Reaction	10%	2%
Nausea	23%	0%
Diarrhea	17%	2%
Abdominal Pain	14%	3%
Vomiting	13%	0%
Constipation	12%	0%
Musculoskeletal Pain	23%	1%
Decreased Appetite	15%	0%
Dyspnea	13%	1%
Pleural Effusion	10%	2%
Upper Respiratory Tract Infection	10%	<1%

[a] No Grade 4 adverse reactions occurred

Select Laboratory Abnormalities in ≥10% of Patients*	All Grades	Grade ≥3
Platelet Decreased	58%	17%
Neutrophil Decreased	52%	30%
Hemoglobin Decreased	51%	10%
GGT Increased	57%	21%
Glucose Increased	48%	8%
AST Increased	41%	<1%[a]
Albumin Decreased	37%	<1%[a]
ALT Increased	34%	3%

*The denominator used to calculate the rate varied from 143 to 145 based on the number of patients with a baseline value and at least one post-treatment value

[a] No Grade 4 adverse reactions occurred

1. Zynlonta Prescribing Information. Murray Hill, NJ: ADC Therapeutics America

Long-term Registry of Patients Treated With Loncastuximab Tesirine

ClinicalTrials.gov Identifier: NCT05160064

Recruitment Status : Withdrawn (Sponsor administrative decision)
First Posted : December 16, 2021
Last Update Posted : June 22, 2022

View this study on Beta.ClinicalTrials.gov

Sponsor:
ADC Therapeutics S.A.

Information provided by (Responsible Party):
ADC Therapeutics S.A.

Study Details | Tabular View | No Results Posted | Disclaimer | How to Read a Study Record

CAR T-cell therapy in DLBCL patients failing CD19-directed treatment

	Patients (N = 14)
CD19 expression on lymphoma cells after loncastuximab tesirine therapy, n (%)	
Positive	10 (71)
Not checked	4 (29)
Median interval between loncastuximab tesirine and CAR T-cell therapy (range), d	120 (22-600)
Additional therapy between loncastuximab tesirine and CAR T-cell therapy, n (%)	
Yes*	6 (43)
No	8 (57)
Disease status before CAR T-cell therapy, n (%)	
Refractory disease	5 (36)
Progressive disease	8 (57)
Partial remission	1 (7)

Thapa et al, Blood Adv 4 (16), 2020

CAR-T Following Loncastuximab Teserine

CAR T-cell therapy in DLBCL patients failing CD19-directed treatment

	Patients (N = 14)
CD19 expression on lymphoma cells after loncastuximab tesirine therapy, n (%)	
Positive	10 (71)
Not checked	4 (29)
Median interval between loncastuximab tesirine and CAR T-cell therapy (range), d	120 (22-600)
Additional therapy between loncastuximab tesirine and CAR T-cell therapy, n (%)	
Yes*	6 (43)
No	8 (57)
Disease status before CAR T-cell therapy, n (%)	
Refractory disease	5 (36)
Progressive disease	8 (57)
Partial remission	1 (7)
Best response to CAR T-cell therapy, n (%)	
Complete response	6 (43)
Partial response	1 (7)
Refractory disease	7 (50)

Thapa et al, Blood Adv 4 (16), 2020

Outcome of CAR-T Patients

- Median interval between Lonca and CAR-T was 120 d (22-600)
- 6 received additional therapy prior to CAR-T
- 5/6 CRs ongoing at 6 mo
- 1 relapse after 11 months
- 6/7 < CR died at a median of 5 mo

Thapa et al, Blood Adv 4 (16), 2020

Conclusions

- Efficacy of RWE studies is generally inferior to published data:
  - Trials included highly selected patients
  - RWE patients generally ineligible for studies
  - RWE more often in community settings
  - Quality of care varies
- Safety data appear similar
  - Not as carefully collected
  - Retrospective analysis
- RWE data suggest how a regimen might fare in general practice
- Putting inappropriate patients on a regimen will limit enthusiasm for appropriate patients