Eppur si muove...

La terapia nel MONDO LINFOMI

Studi RE-MIND e RE-MIND2

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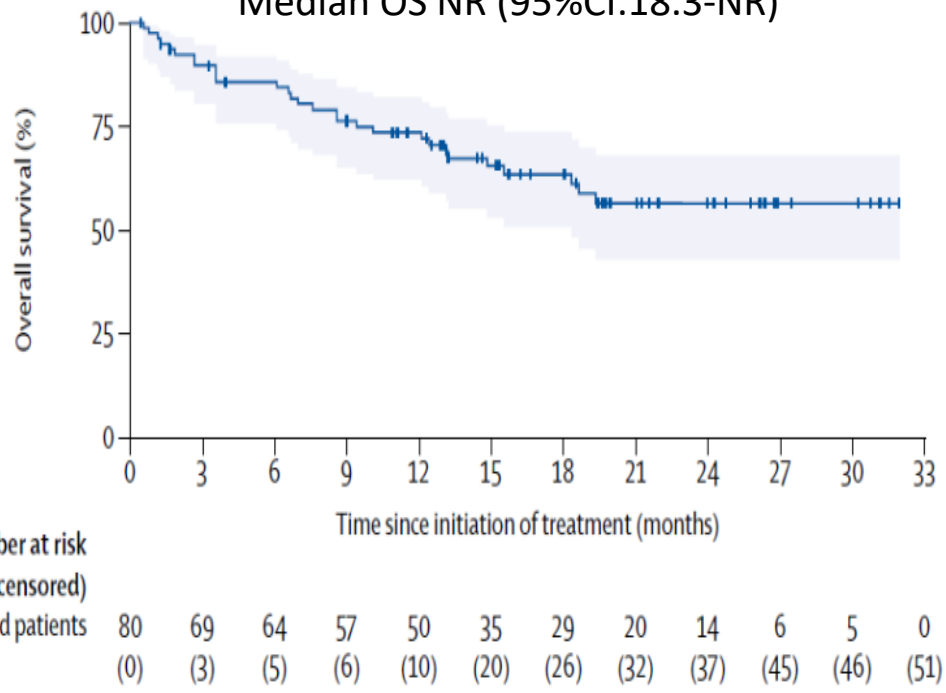
Tafasitamab + lenalidomide in R/R DLBCL

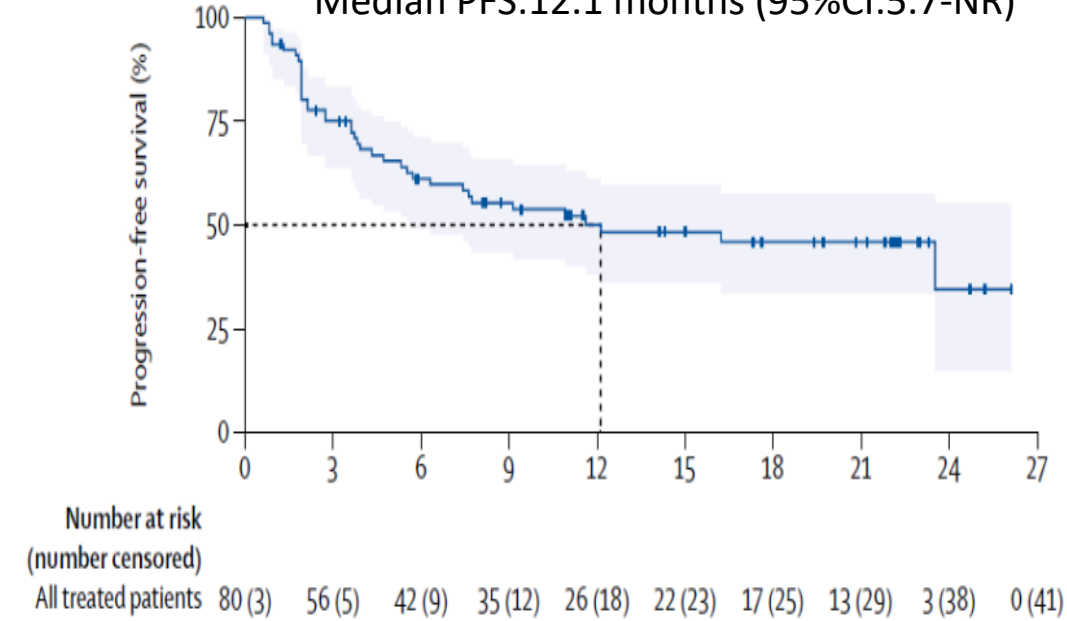
Single arm phase II study L-Mind

ORR	48 (60%; 48-71)

Median OS NR (95%CI:18.3-NR)



Median PFS:12.1 months (95%CI:5.7-NR)



Median follow-up:19.6 months

Salles G et al. Lancet Oncology 2020

RE- MIND STUDY

RE-MIND study: rationale

- delineate the **contribution of tafasitamab** to the efficacy of the combination with lenalidomide
- **real-world data** to generate a **matched control cohort** of lenalidomide monotherapy

Clin Cancer Res. 2021;27(22):6124-6134. doi:10.1158/1078-0432.CCR-21-1471

RE-MIND study: study design & patients

Study sites were selected according to

- geographic distribution in L-MIND (EU and United States)
- data completeness and number of available patients

Retrospective collection

- non–transplant-eligible R/R DLBCL pts treated with lenalidomide in real-world
- observational period of January 2005 to July 2019.

Clin Cancer Res. 2021;27(22):6124-6134. doi:10.1158/1078-0432.CCR-21-1471

RE-MIND study: study design & patients

Retrospective collection of

- disease-specific medical history
- reasons for ASCT ineligibility
- dosing information
- treatment response
- and survival

comparable follow-up time

Clin Cancer Res. 2021;27(22):6124-6134. doi:10.1158/1078-0432.CCR-21-1471

RE-MIND study: study design & patients

Inclusion criteria

- age ≥18 years
- histologically confirmed DLBCL
- R/R after 1 to 3 prior systemic therapies
- not candidates for HDC + ASCT

Exclusion criteria

- CNS involvement
- lenalidomide in combination other anti-lymphoma therapy
- prior anti-CD19 therapy or IMIDs
- previous ASCT
- 'double/triple-hit' DLBCL
- a prior history of malignancies

Clin Cancer Res. 2021;27(22):6124-6134. doi:10.1158/1078-0432.CCR-21-1471

RE-MIND study: cohort balancing

Estimated propensity score (ePS)-based Nearest Neighbor 1:1 Matching methodology

- age (<70 vs ≥70 years)
- Ann Arbor stage (I/II vs III/IV)
- refractoriness to last therapy line
- number of prior lines of therapy (1 vs 2 or 3)
- history of primary refractoriness
- prior ASCT
- elevate LDH
- Neutropenia
- anemia

ECOG PS

Clin Cancer Res. 2021;27(22):6124-6134. doi:10.1158/1078-0432.CCR-21-1471

Outcomes

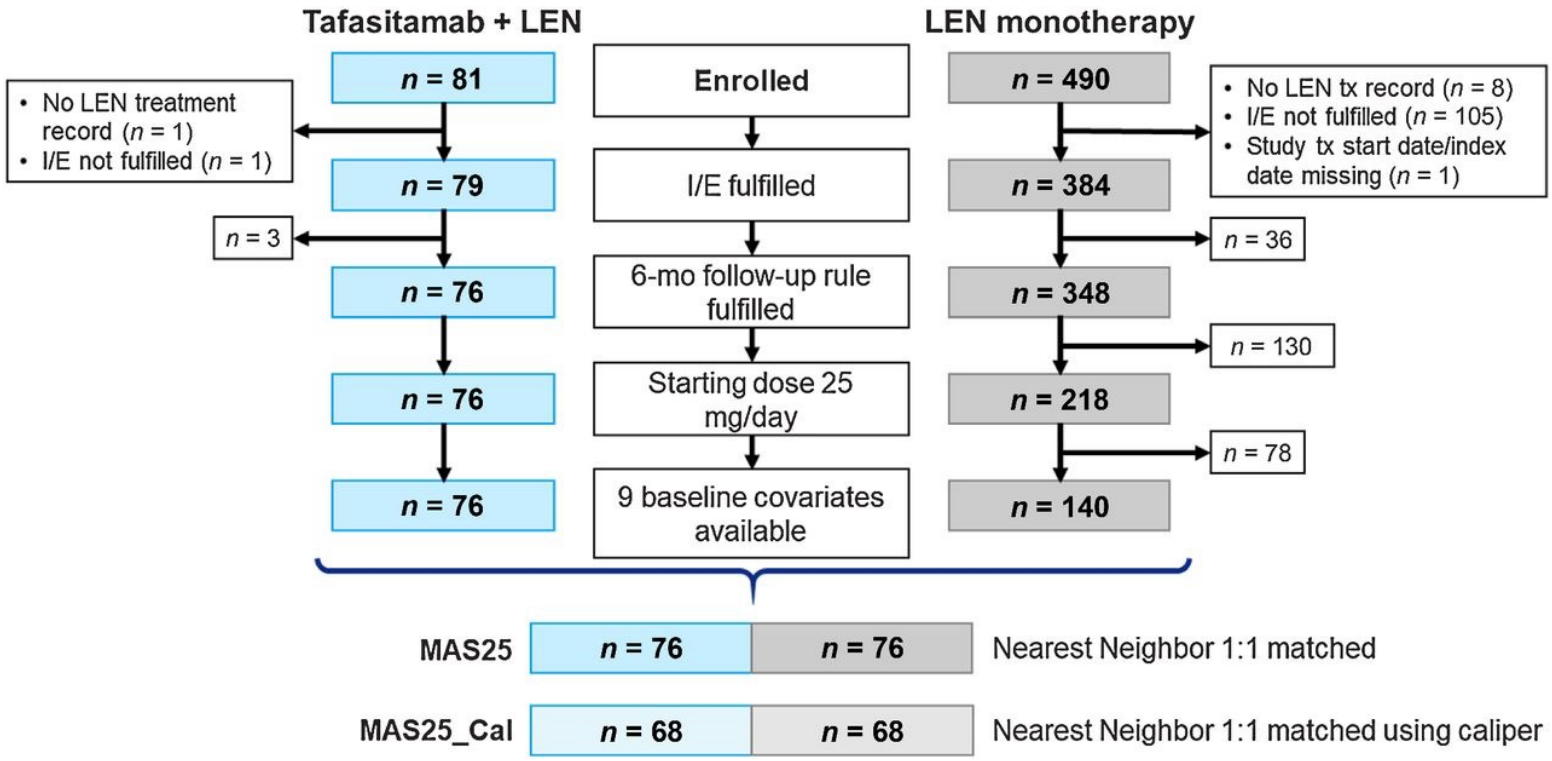
The **primary endpoint was best ORR** (CR or PR as best response) as assessed by the investigator

Sample size calculation

- assumed difference of 23% in ORR (lena 35% vs tafa+lena 58%)
- minimal detecteble statistical difference in ORR of 17%
- power 80%

500 patients in the control cohort

RE-MIND: patient disposition



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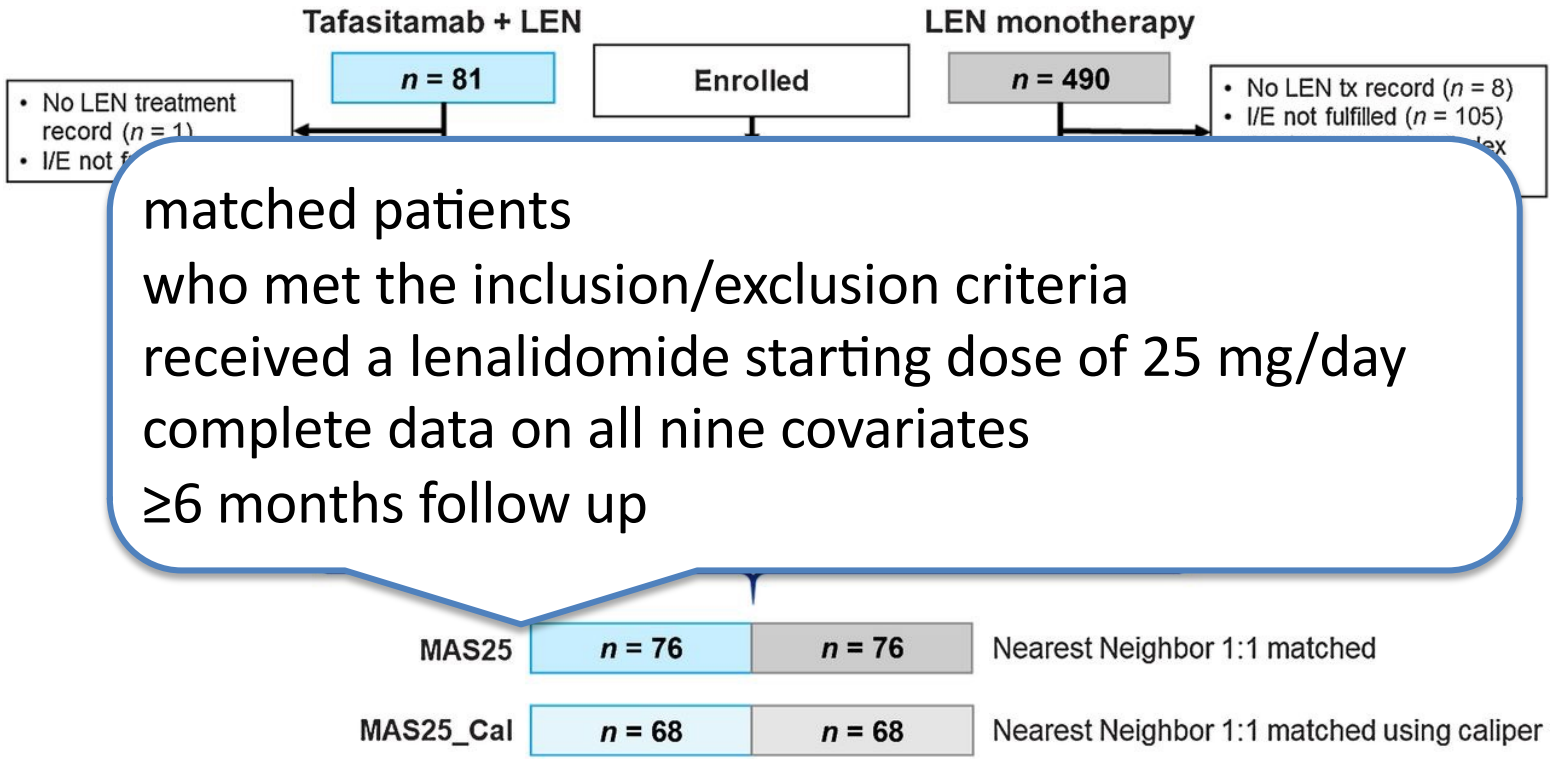
RE-MIND: patient disposition



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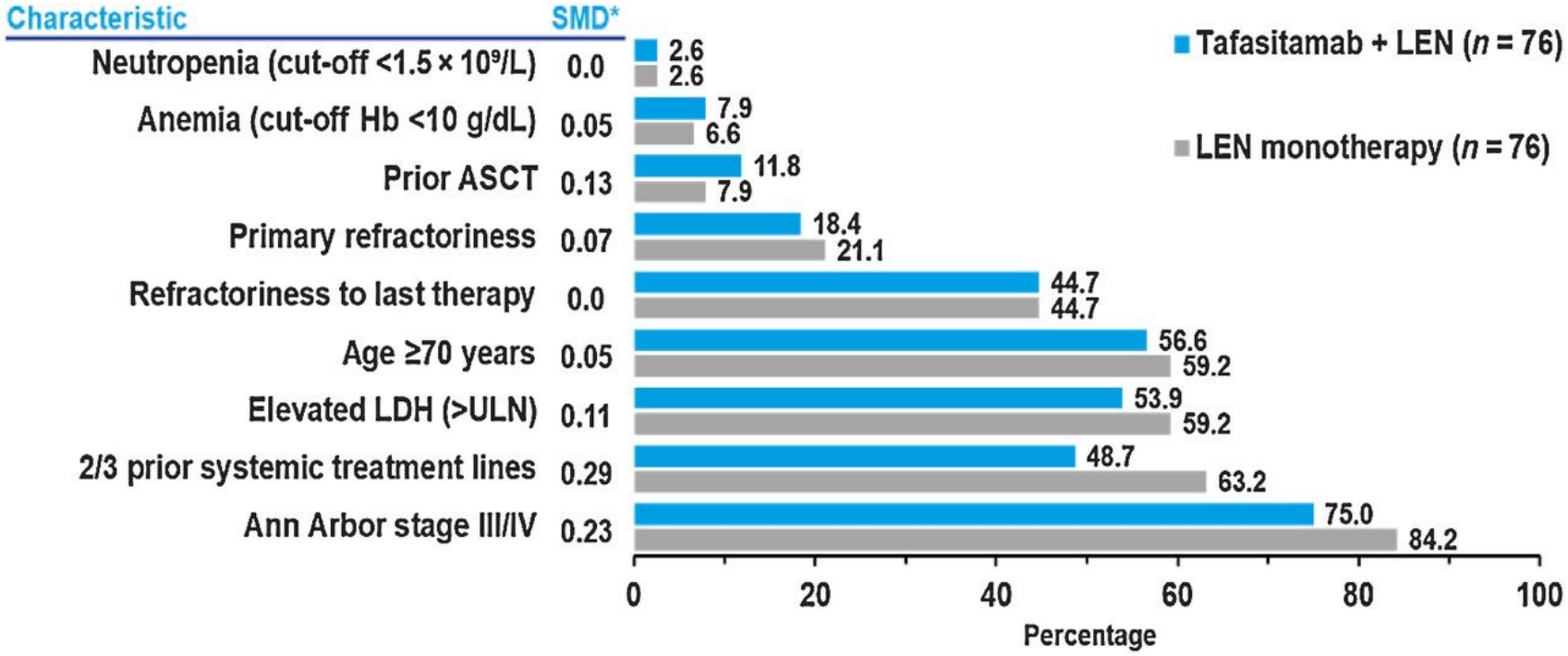
RE-MIND: baseline characteristics after cohort balancing (MAS25)

Baseline characteristics were well balanced across the two cohorts after the matching procedure



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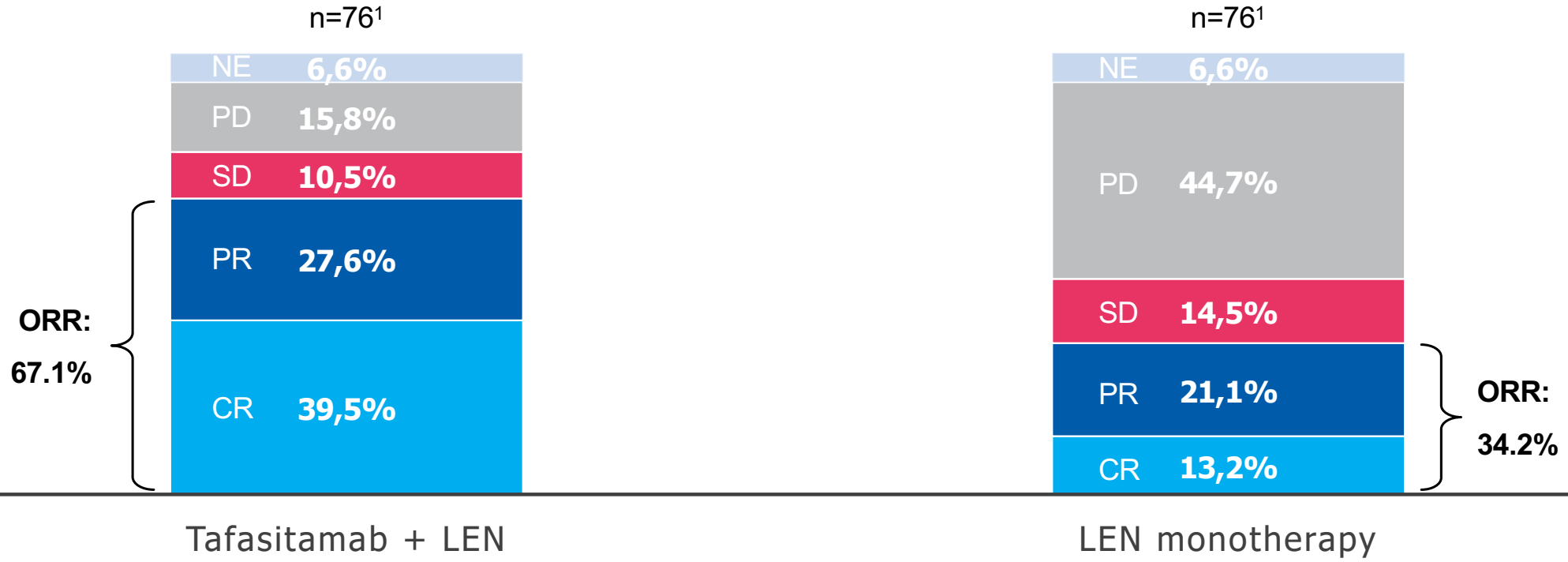
RE-MIND: primary endpoint – best ORR



Odds ratio (95% CI)	3.9 (1.9–8.1); P<0.0001

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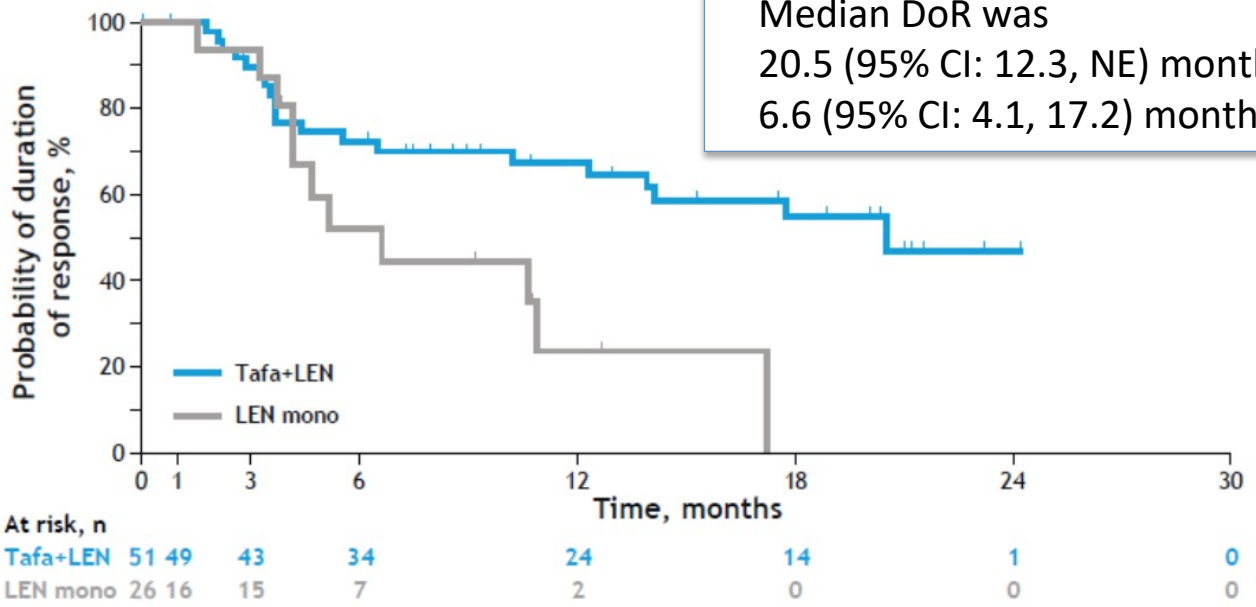
RE-MIND: secondary endpoint – DoR



Median DoR was
20.5 (95% CI: 12.3, NE) months in the tafa+LEN cohort
6.6 (95% CI: 4.1, 17.2) months in the LEN-mono cohort.

CI, confidence interval; DoR, duration of response; LEN, lenalidomide; MAS25, matched analysis set

25; mo, month; NR, not reached

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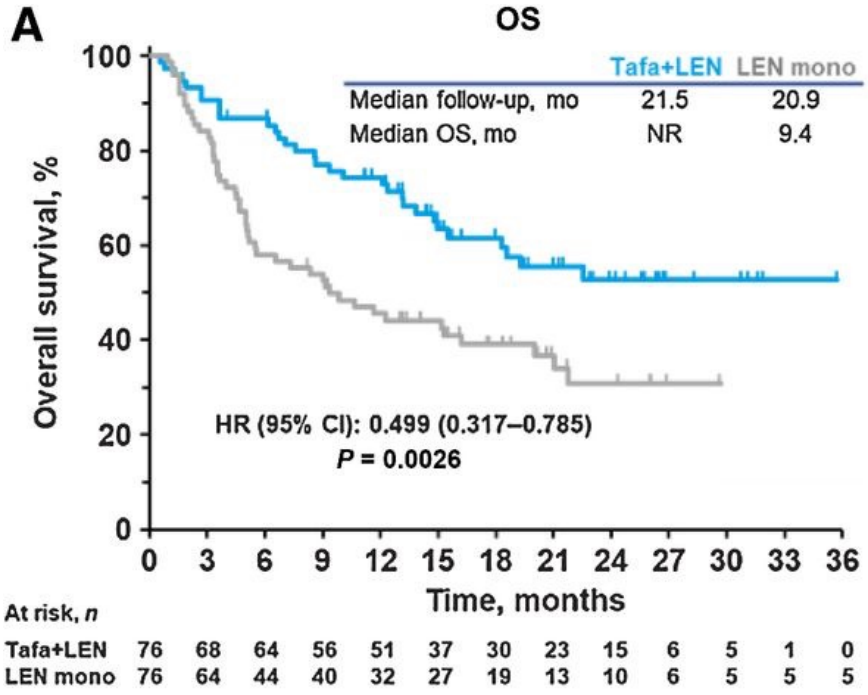
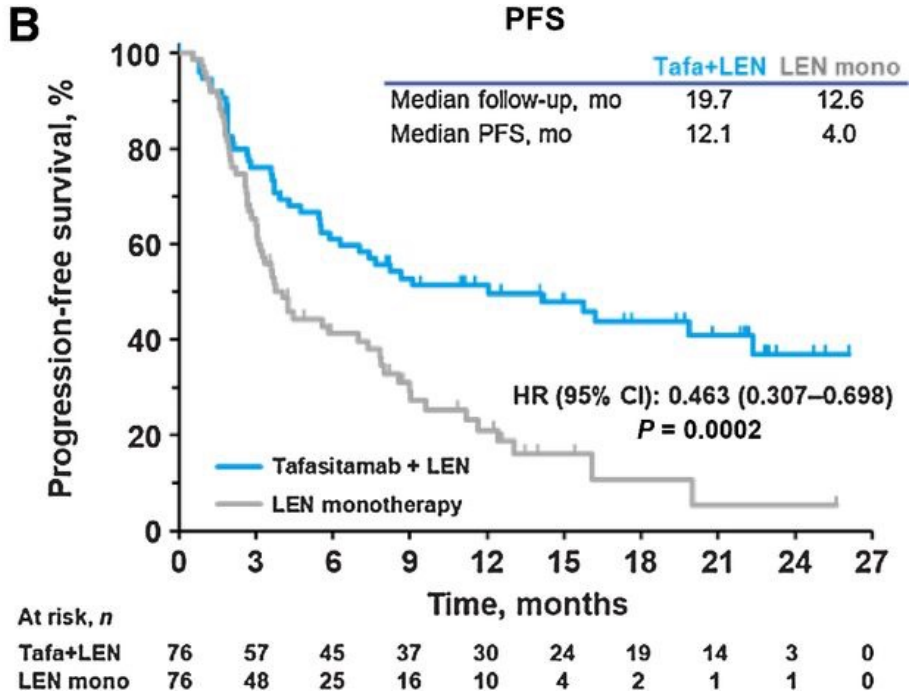
RE-MIND: secondary endpoint – OS & PFS





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Summary

Clinical trials

Clinical trials

Observational national studies

	L-MIND (n 81)	RE-MIND (n 76)	Wiernik et al (n 49)	Witzig et al (n 108)	Broccoli et al (n 153)	Mondello et al (n 123)
	Tafa + Lena	Tafa+lena vs Lena	Lena	Lena	Lena	Lena
ORR	**59%**	**67% vs 34%**	**35%**	**28%**	**29%**	**37%**
CR	41%	39% vs 12%	12%	7%	23%	21%
PR	17%	27% vs 22%	23%	21%	6%	16%
mOS	31.6 m	NR vs 9.4 m	Not reported	Not reported	12 m	Not reported

Salles et al, Lancet Onc 2020
Zinzani et al. Cli Cancer Res 2021
Wiernik et al. J Clin Oncol 2008
Broccoli et al, The Oncologist 2019
Mondello et al, The Oncologist 2016

RE-MIND: conclusions (*i*)

Tafa + lena leads to improved outcomes

ORR	(67.1% vs. 34.2%; odds ratio 3.89; P < 0.0001)
CR	(39.5% vs. 13.2%)
median DoR	(20.5 months vs. 6.6 months)
median PFS	(12.1 months vs 4 months)
median OS	(NR vs. 9.4 months; HR, 0.499; P= 0.00269)

RE-MIND outcomes for LENA monotherapy are comparable to those published for LENA monotherapy in clinical trials

Clin Cancer Res. 2021;27(22):6124-6134. doi:10.1158/1078-0432.CCR-21-1471

RE-MIND: conclusions (*ii*)

Within the limitations of non-randomised trials, ePS-based 1:1 matching allows for a robust estimation of the additional treatment effect attributable to tafasitamab when added to LEN as in the L-MIND trial

Tafa plus lena, followed by tafa monotherapy = additional option in R/R DLBCL not eligible for ASCT

- FDA approval
- NCCN guidelines
- EMA approval

Clin Cancer Res. 2021;27(22):6124-6134. doi:10.1158/1078-0432.CCR-21-1471

RE- MIND2 STUDY

RE-MIND2 study: rationale

- compare **tafasitamab + lenalidomide** to commonly administered systemic therapies for ASCT-ineligible R/R DLBCL
- **real-world data** to generate a **matched control cohort** of NCCN/ESMO recommended therapies for ASCT-ineligible R/R DLBCL

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RE-MIND2 study: study design & methods

Study sites were selected from

- academic and public hospitals, private practices in North America, Europe and Asia Pacific

Retrospective collection

- non–transplant-eligible R/R DLBCL pts treated with
  - Gemcitabine + oxaliplatin + rituximab (R-GemOx)
  - rituximab + bendamustine (BR)
  - polatuzumab vedotin + bendamustine + rituximab (pola-BR)
  - rituximab + LEN (R2)
  - CD19 CAR-T therapies (CAR-T)
  - pixantrone

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RE-MIND2 study: study design & methods

Inclusion criteria (based on L-MIND study)

- patients aged ≥18 years with histologically confirmed DLBCL
- ≥2 systemic therapies for DLBCL (including ≥1 anti-CD20 therapy)

Primary endpoint

- overall survival (OS)

Secondary endpoints

- objective response rate (ORR)
- complete response rate (CR)
- progression-free survival (PFS)
- duration of response (DoR)

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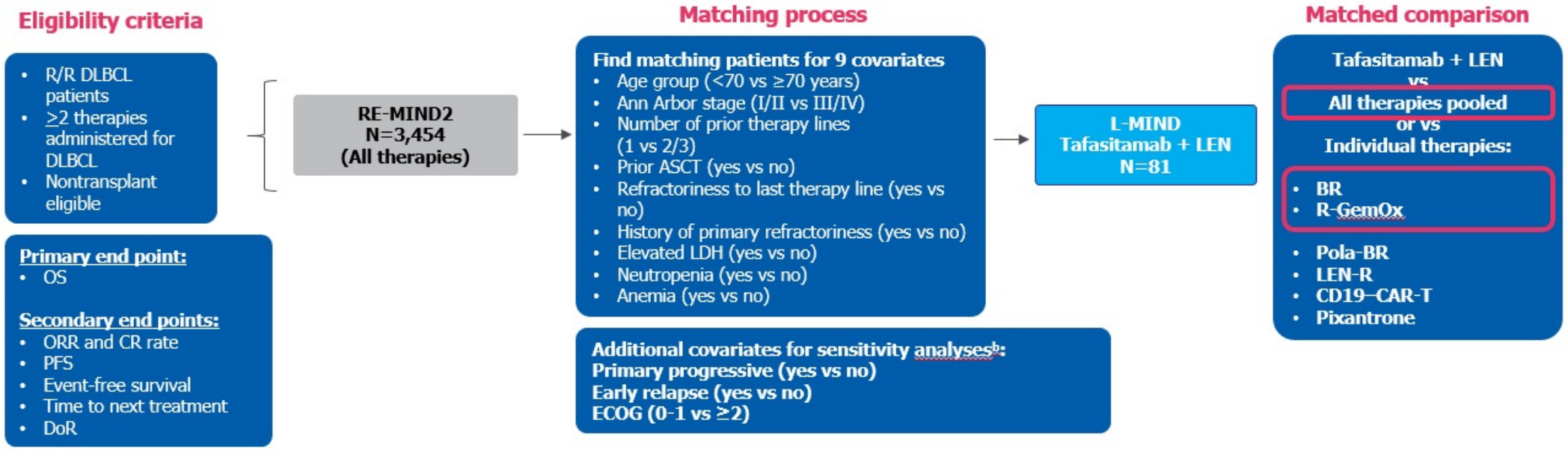
RE-MIND2 study: study design & methods

Matching criteria and estimated propensity score (ePS)-based method

Efficacy outcomes comparison: L-MIND cohort vs the observational cohort RE-MIND2 database



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RE-MIND2 study: study design & methods

Three matched analysis sets (MAS) comprising cohorts receiving **tafasitamab + LEN** versus cohorts of **systemic therapies pooled for R/R DLBCL**, **BR**, and **R-GemOx**

Table 1. Demographics and baseline characteristics

		MAS for systemic therapies pooled		MAS for BR		MAS for R-GemOx	
Matching characteristics		Tafasitamab + LEN (n=76)	Systemic therapies pooled (n=76)	Tafasitamab + LEN (n=75)	BR (n=75)	Tafasitamab + LEN (n=74)	R-GemOx (n=74)
Age, n (%)	Age <70 years	33 (43.4)	31 (40.8)	33 (44.0)	33 (44.0)	31 (41.9)	26 (35.1)
	Age ≥70 years	43 (56.6)	45 (59.2)	42 (56.0)	42 (56.0)	43 (58.1)	48 (64.9)
Ann Arbor stage, n (%)	I+II	19 (25.0)	19 (25.0)	18 (24.0)	19 (25.3)	18 (24.3)	15 (20.3)
	III+IV	57 (75.0)	57 (75.0)	57 (76.0)	56 (74.7)	56 (75.7)	59 (79.7)
Refractoriness to last prior therapy, n (%)	Yes	34 (44.7)	35 (46.1)	33 (44.0)	32 (42.7)	33 (44.6)	29 (39.2)
	No	42 (55.3)	41 (53.9)	42 (56.0)	43 (57.3)	41 (55.4)	45 (60.8)
Number of prior systemic treatment lines, n (%)	1	39 (51.3)	39 (51.3)	39 (52.0)	39 (52.0)	39 (52.7)	41 (55.4)
	2	32 (42.1)	32 (42.1)	31 (41.3)	22 (29.3)	30 (40.5)	26 (35.1)
	3	5 (6.6)	5 (6.6)	5 (6.7)	14 (18.7)	5 (6.8)	7 (9.5)
History of primary refractoriness, n (%)	Yes	14 (18.4)	12 (15.8)	14 (18.7)	19 (25.3)	14 (18.9)	14 (18.9)
	No	62 (81.6)	64 (84.2)	61 (81.3)	56 (74.7)	60 (81.1)	60 (81.1)
Prior ASCT, n (%)	Yes	9 (11.8)	10 (13.2)	9 (12.0)	14 (18.7)	8 (10.8)	8 (10.8)
	No	67 (88.2)	66 (86.8)	66 (88.0)	61 (81.3)	66 (89.2)	66 (89.2)
Elevated LDH (>ULN), n (%)	Yes	41 (53.9)	44 (57.9)	41 (54.7)	37 (49.3)	41 (55.4)	48 (64.9)
	No	35 (46.1)	32 (42.1)	34 (45.3)	38 (50.7)	33 (44.6)	26 (35.1)
Neutropenia (cut-off <1.5 x 109/L), n (%)	Yes	2 (2.6)	2 (2.6)	2 (2.7)	4 (5.3)	2 (2.7)	5 (6.8)
	No	74 (97.4)	74 (97.4)	73 (97.3)	71 (94.7)	72 (97.3)	69 (93.2)
Anemia (cut-off hemoglobin <10 g/dL), n (%)	Yes	6 (7.9)	5 (6.6)	6 (8.0)	5 (6.7)	6 (8.1)	5 (6.8)
	No	70 (92.1)	71 (93.4)	69 (92.0)	70 (93.3)	68 (91.9)	69 (93.2)
Other characteristics							

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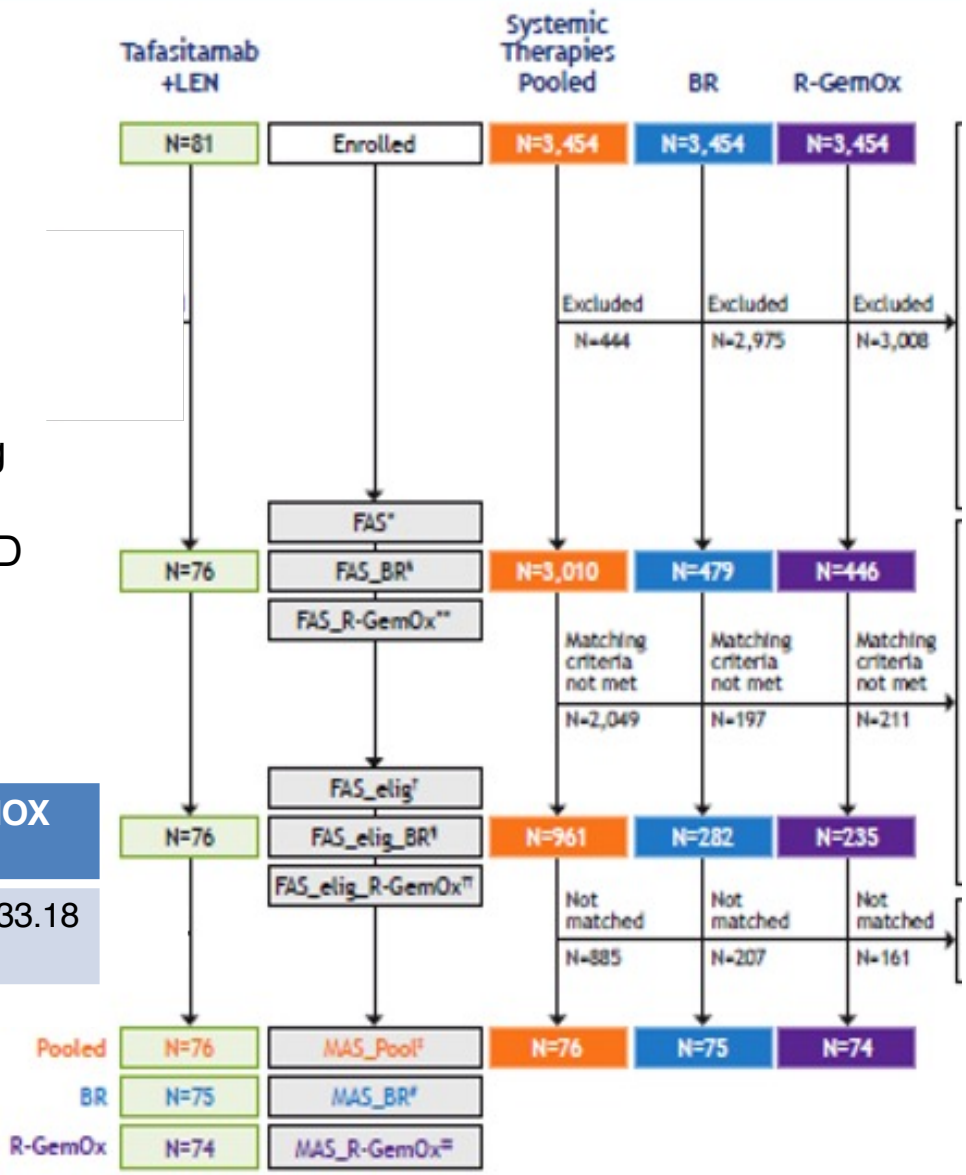
FAS population:
patients with L-mind and RE-MIND2 eligible/non-eligible criteria & minimum 6 months follow-up

FAS elig population: patients who were eligible for matching

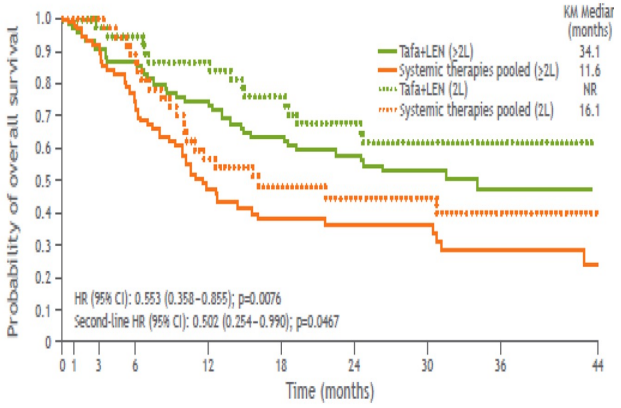
MAS Pool population: 1:1 matched patients from the L-MIND study and the observational cohort using baseline covariates

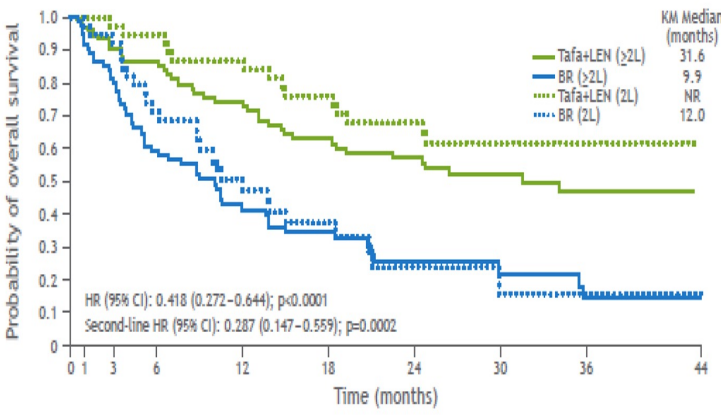
	T-L vs pooled therapies	T-L vs BR	T-L vs R-GEMOX
m follow up in matched cohorts	31.84 vs 33.25	32.92 vs 25.00	32.92 vs 33.18

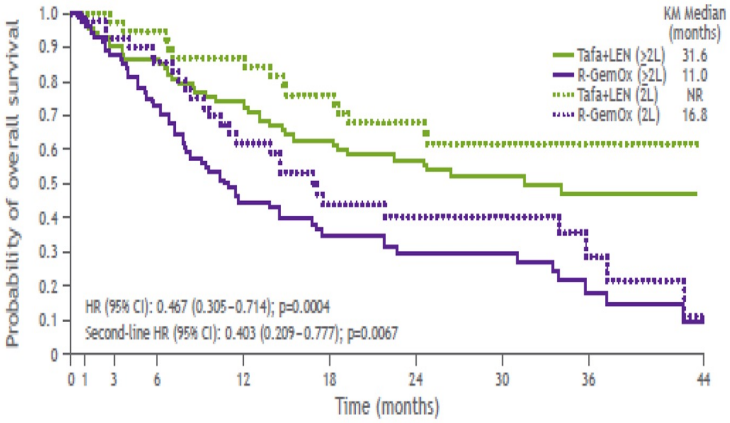


RE-MIND2 study: OVERALL SURVIVAL

	Pooled therapies ≥2L (m)	Tafa-Lena ≥2L (m)	BR ≥2L (m)	Tafa-Lena ≥2L (m)	R-GEMOX ≥2L (m)	Tafa-Lena ≥2L (m)	Pooled therapies 2L (m)	Tafa-Lena 2L (m)	BR 2L (m)	Tafa-Lena 2L (m)	R-GEMOX 2L (m)	Tafa-Lena 2L (m)
mOS	11.6	34.1	9.9	31.6	11.0	31.6	16.1	NR	12.0	NR	16.8	NR
HR (95% CI)	0.553 (0.358-0.855)		0.418 (0.272-0.644)		0.467 (0.305-0.714)		0.502 (0.254-0.990)		0.287 (0.147-0.559)		0.403 (0.209-0.777)	
p value	0.0076		<0.0001		0.0004		0.0467		0.0002		0.0067	







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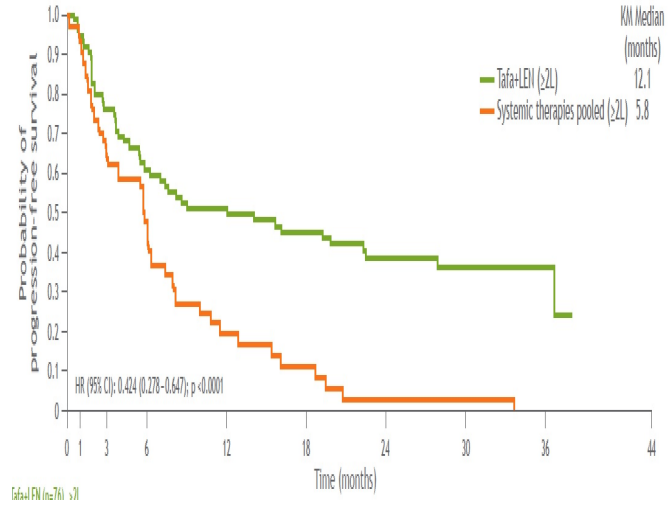
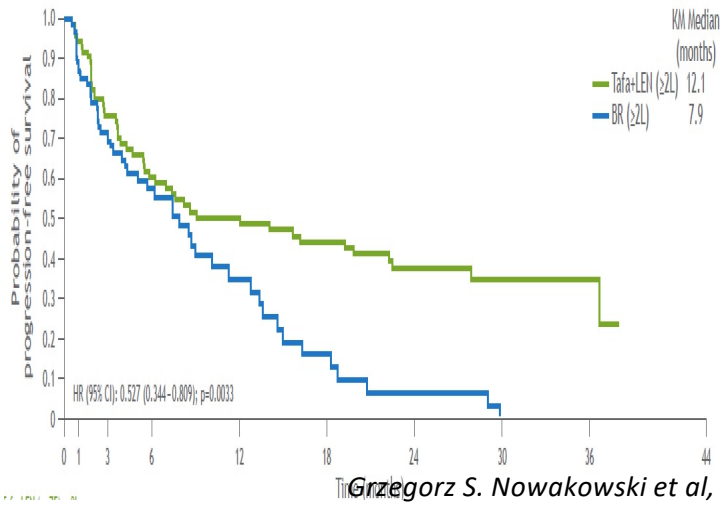
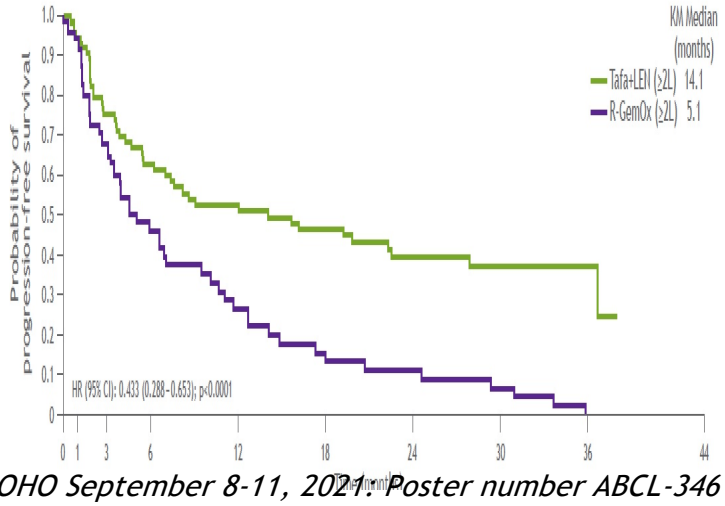
RE-MIND2 study: PROGRESSION-FREE SURVIVAL

	Pooled therapies ≥2L (m)	Tafa-Lena ≥2L (m)	BR ≥2L (m)	Tafa-Lena ≥2L (m)	R-GEMOX ≥2L (m)	Tafa-Lena ≥2L (m)	Pooled therapies 2L (m)	Tafa-Lena 2L (m)	BR 2L (m)	Tafa-Lena 2L (m)	R-GEMOX 2L (m)	Tafa-Lena 2L (m)
mPFS	5.8	12.1	7.9	12.1	5.1	14.1	8.0	16.2	8.8	16.2	7.1	16.2
HR (95% CI)	0.424 (0.278-0.647)		0.527 (0.344-0.809)		0.433 (0.288-0.653)		0.452 (Not reported)		0.475 (Not reported)		0.466 (Not reported)	
p value	<0.0001		0.0033		0.0001		0.0081		0.0155		0.0096	







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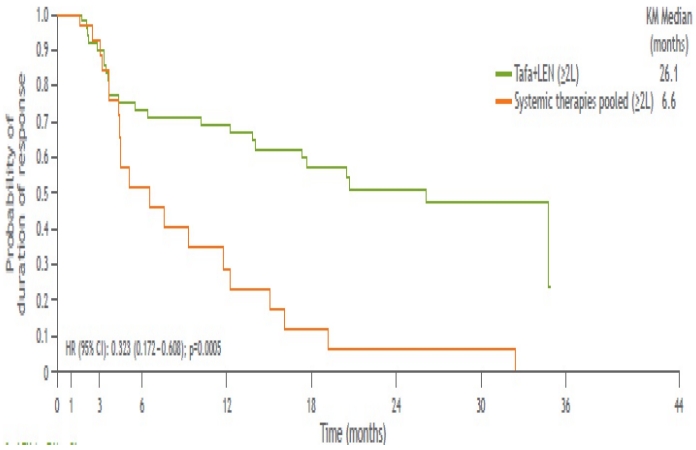
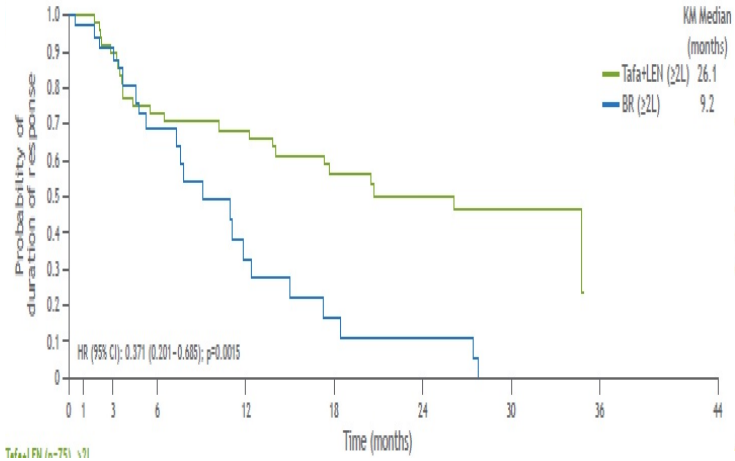
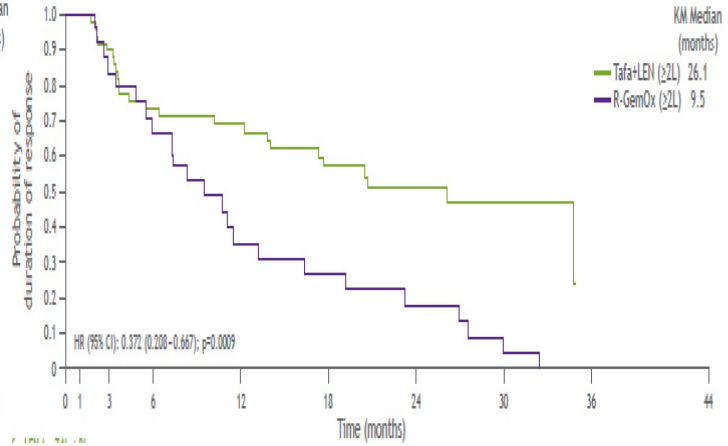
RE-MIND2 study: DURATION OF RESPONSE

	Pooled therapies ≥2L (m)	Tafa-Lena ≥2L (m)	BR ≥2L (m)	Tafa-Lena ≥2L (m)	R-GEMOX ≥2L (m)	Tafa-Lena ≥2L (m)
mDoR	6.6	26.1	9.2	26.1	9.5	26.1
HR	0.323		0.371		0.372	
p value	0.005		0.0015		0.0009	







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Overview of BR and R-GemOx results reported in literature vs RE-MIND2 study

	Key studies with BR				Key studies with R-GemOx				
	Literature-reported outcomes			RE-MIND2 outcomes	Literature-reported outcomes				RE-MIND2 outcomes
Reference:	12	13	8		14	9	15	16	
N	59	59	40	75	49	196	32	46	74
ORR, %	62.7	45.8	25	54.7	61	38	78	83	45.9
CR, %	37.3	15.3	22.5	28.0	44	33	50	50	23.0
mPFS, months	6.7	3.6	3.7	7.9	5	5	NA	NA	5.1
mOS, months	NA	NA	4.7	9.9	11	10	NA	NA	11.0

8. Sehn LH, et al. J Clin Oncol 2019;38(2):155-65; 9. Cazelles C, et al. Leuk Lymphoma 2021;25; 12. Ohmachi K, et al. J Clin Oncol 2013;312103-9; 13. Vacirca JL, et al. Ann Hematol 2014;93(3):403-9; 14. Mounier N, et al. Haematologica 2013;98(11):1726-31; 15. Corazzelli G, et al. Cancer Chemother Pharmacol 2009;64(5):907-16;: 16. El Gnaoui T, et al. Ann Oncol 2007;18(8):1363-8

RE-MIND2 study: CONCLUSIONS

Tafasitamab + LEN was associated with longer OS

vs systemic therapies pooled	- HR = 0.553
vs BR	- HR = 0.418
vs R-GemOx	- HR = 0.467

This immunomodulatory regimen may improve outcomes compared with NCCN/ESMO-recommended therapies used in routine clinical care for the treatment of R/R DLBCL

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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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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 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)

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

Matched comparison

Tafasitamab + LEN vs

- Pola-BR
- R2
- CAR-T

Primary endpoint:

- OS

Key secondary endpoints:

- ORR and CR rate
- DoR
- PFS

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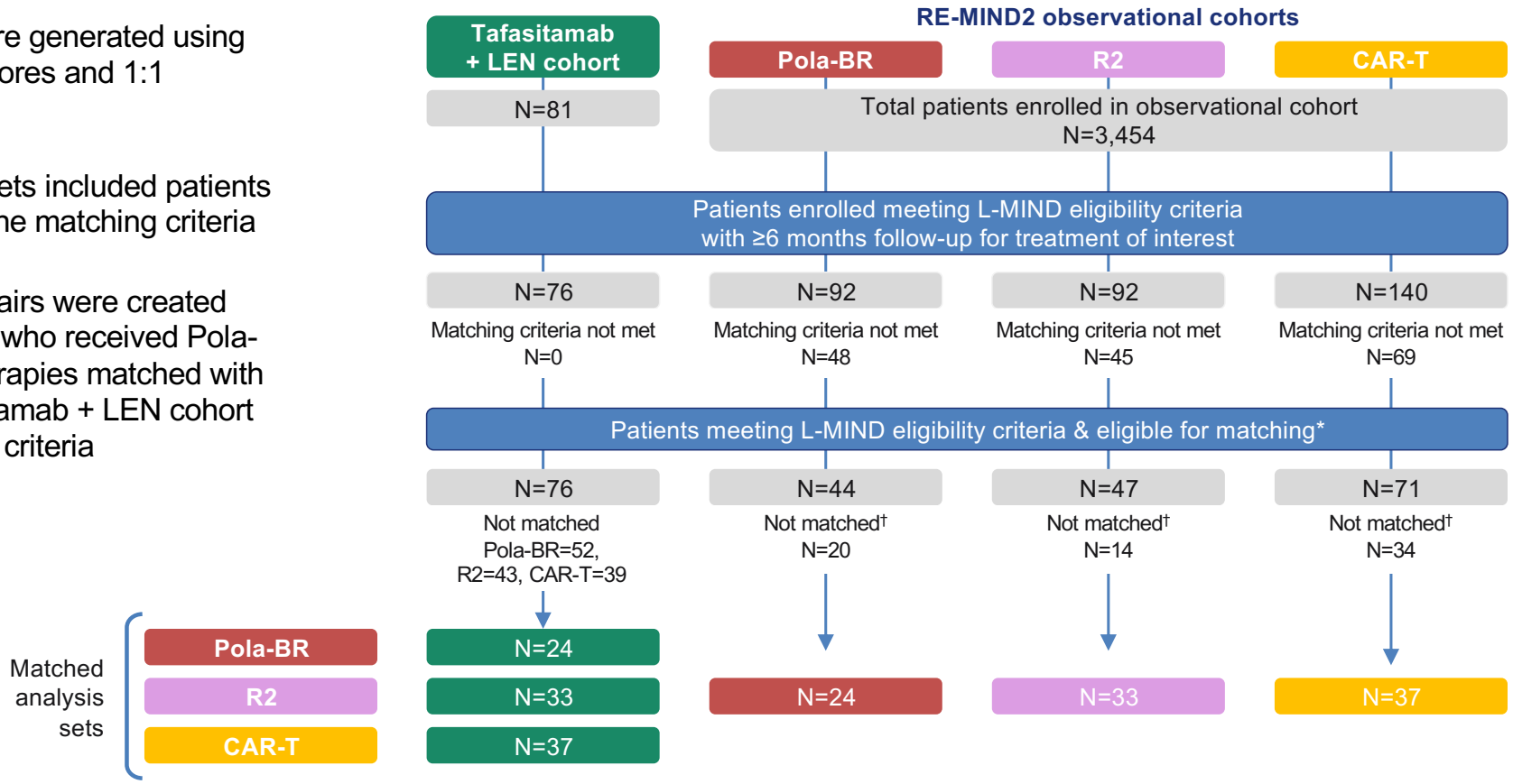
RE-MIND2 study: analysis population

- 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



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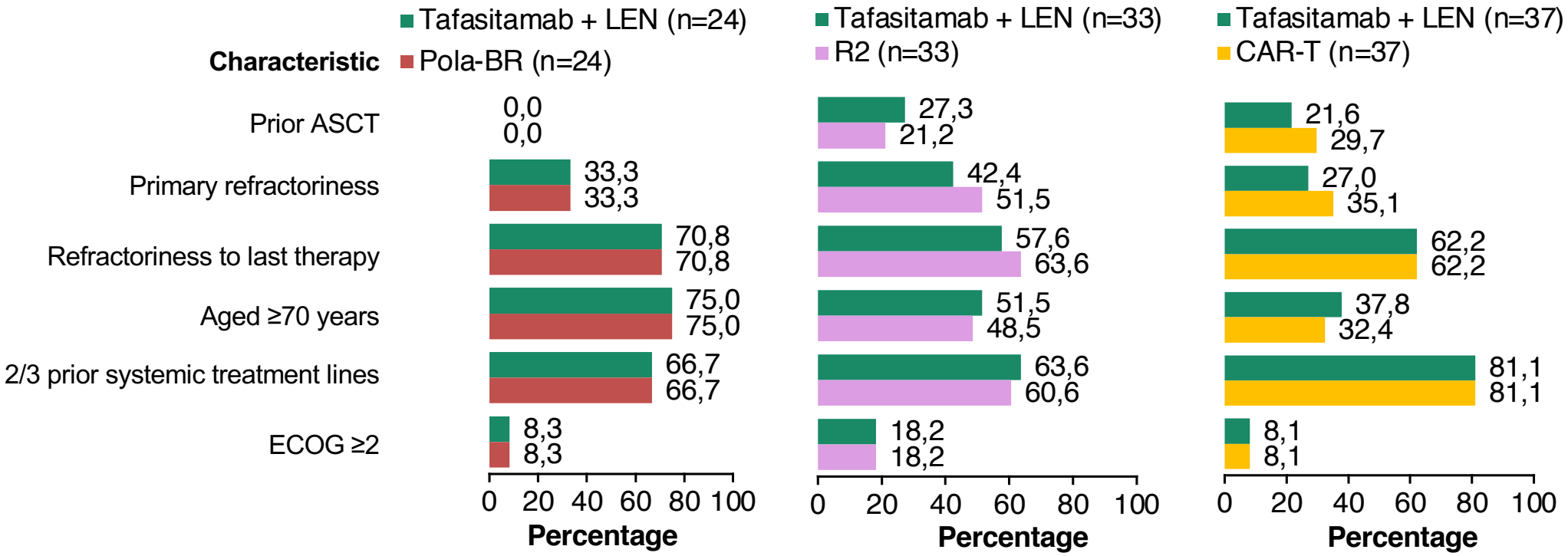
RE-MIND2

Baseline characteristics for tafa + 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

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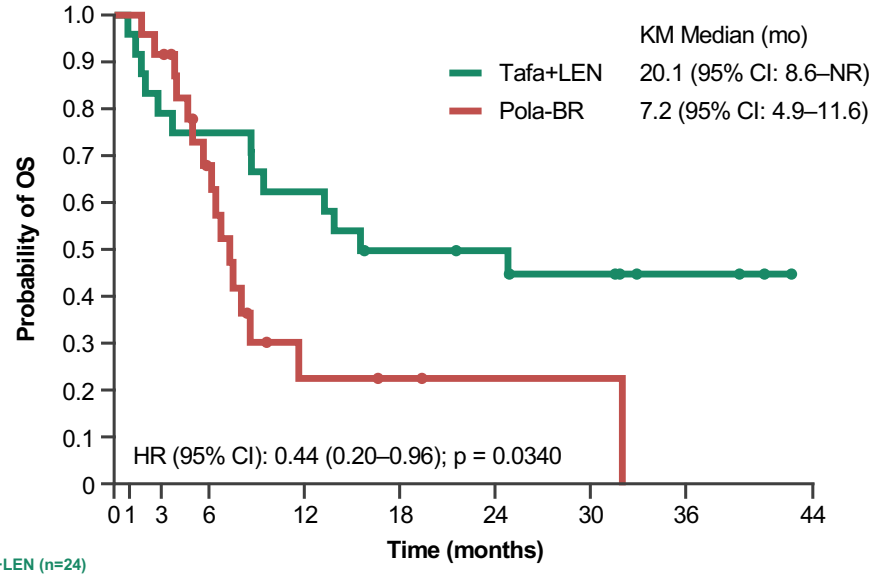
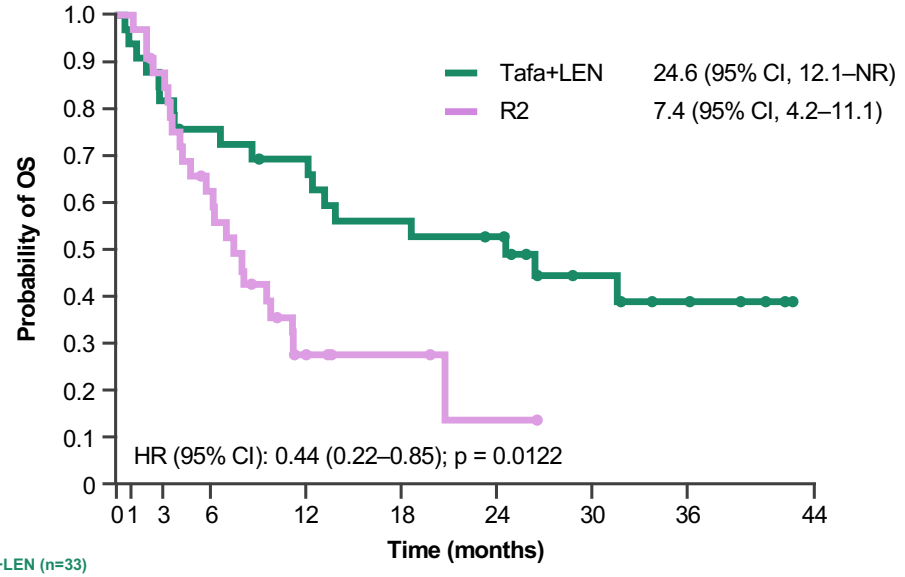
RE-MIND2 study: primary endpoint - OS



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

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

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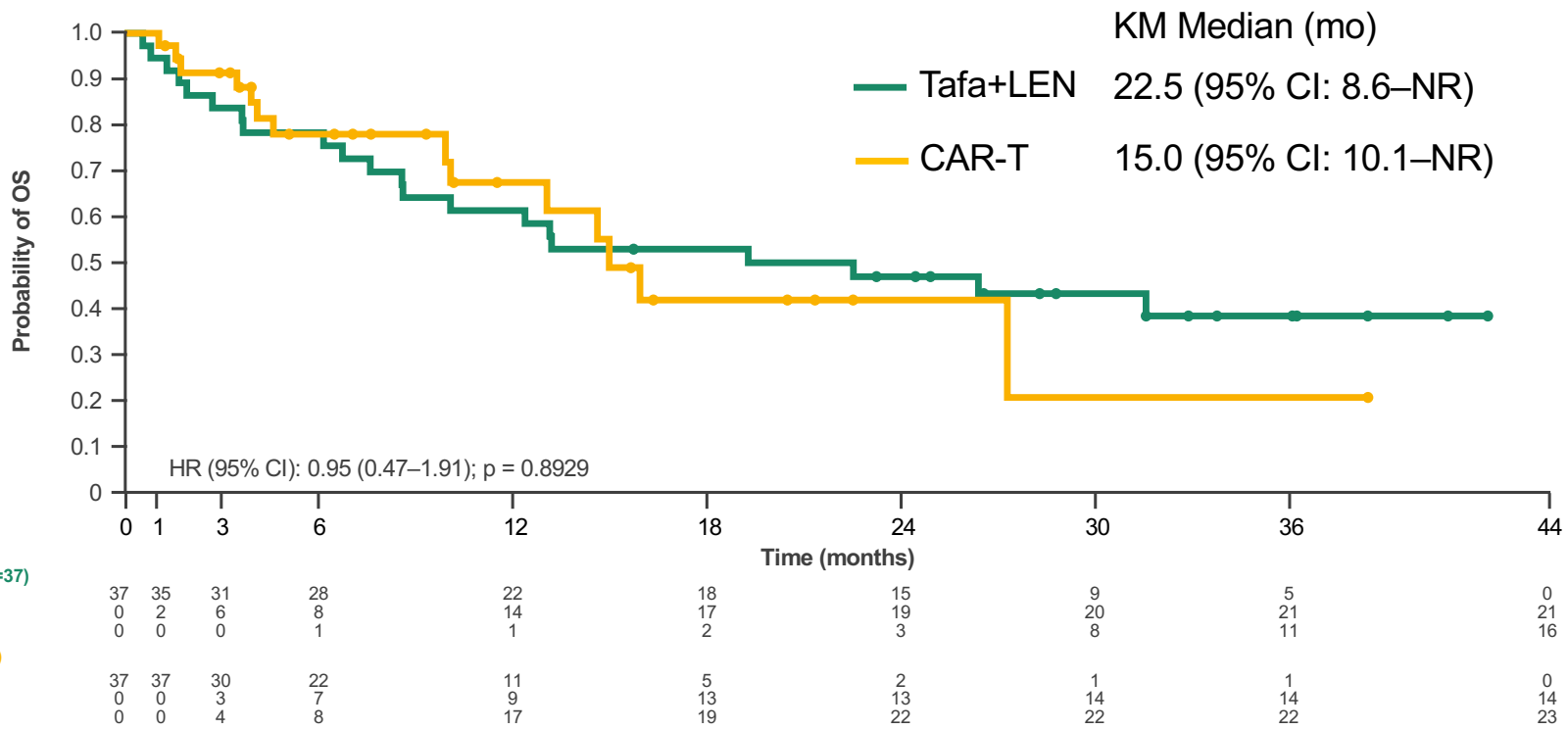
RE-MIND2 study: primary endpoint - OS



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

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

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RE-MIND2 study: secondary endpoints – PFS & 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)

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

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R-MIND2 study: conclusions

- Tafasitamab + LEN improved survival outcomes compared with pola-BR and R2 in closely matched patient populations
- Comparable outcomes were observed for tafasitamab + LEN vs CAR-T
- More rigorous than inter-trial comparison
- 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

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