Eppur si muove...

La terapia nel MONDO LINFOMI

Re-MIND e Re-MIND2

Caterina Patti

CATANIA, 11 LUGLIO 2022

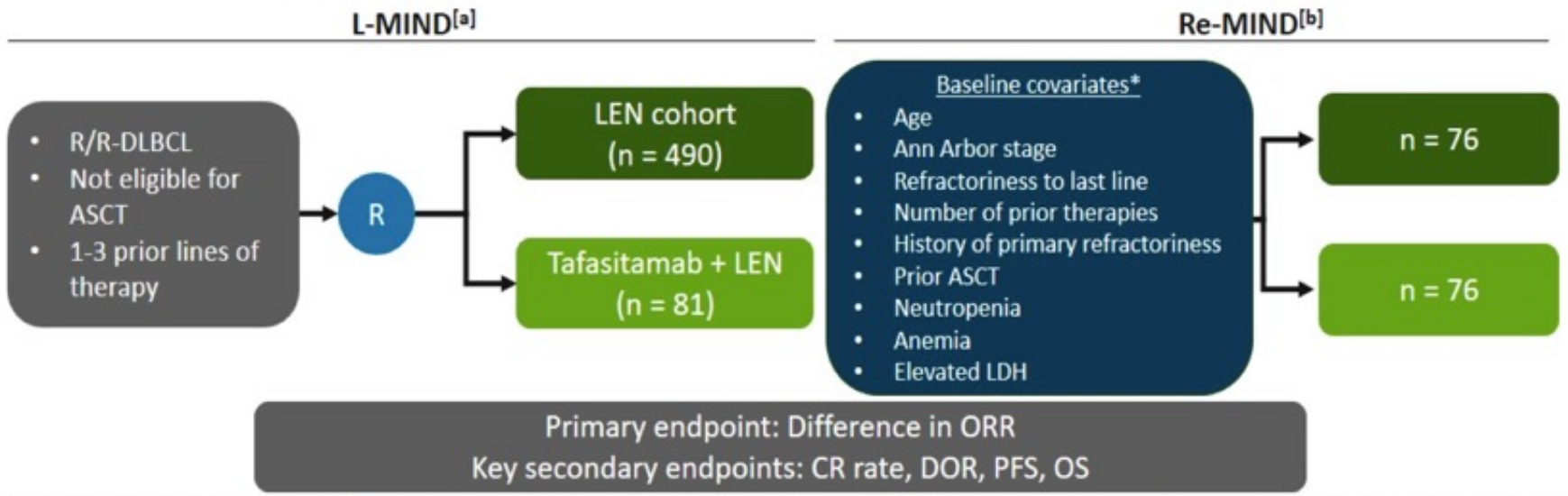
CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY

RE-MIND: Comparing Tafasitamab + Lenalidomide (L-MIND) with a Real-world Lenalidomide Monotherapy Cohort in Relapsed or Refractory Diffuse Large B-cell Lymphoma

Pier Luigi Zinzani[1], Thomas Rodgers[2], Dario Marino[3], Maurizio Frezzato[4], Anna Maria Barbui[5], Claudia Castellino[6], Erika Meli[7], Nathan H. Fowler[8], Gilles Salles[9], Bruce Feinberg[10], Nuwan C. Kurukulasuriya[11], Sascha Tillmanns[12], Stephan Parche[11], Debarshi Dey[11], Günter Fingerle-Rowson[11], Sumeet Ambarkhane[11], Mark Winderlich[11], and Grzegorz S. Nowakowski[12]

Retrospective observational study generated a historic control for L-MIND to disentangle the contribution of tafasitamab to the efficacy of the combination

Re-Mind Study Design

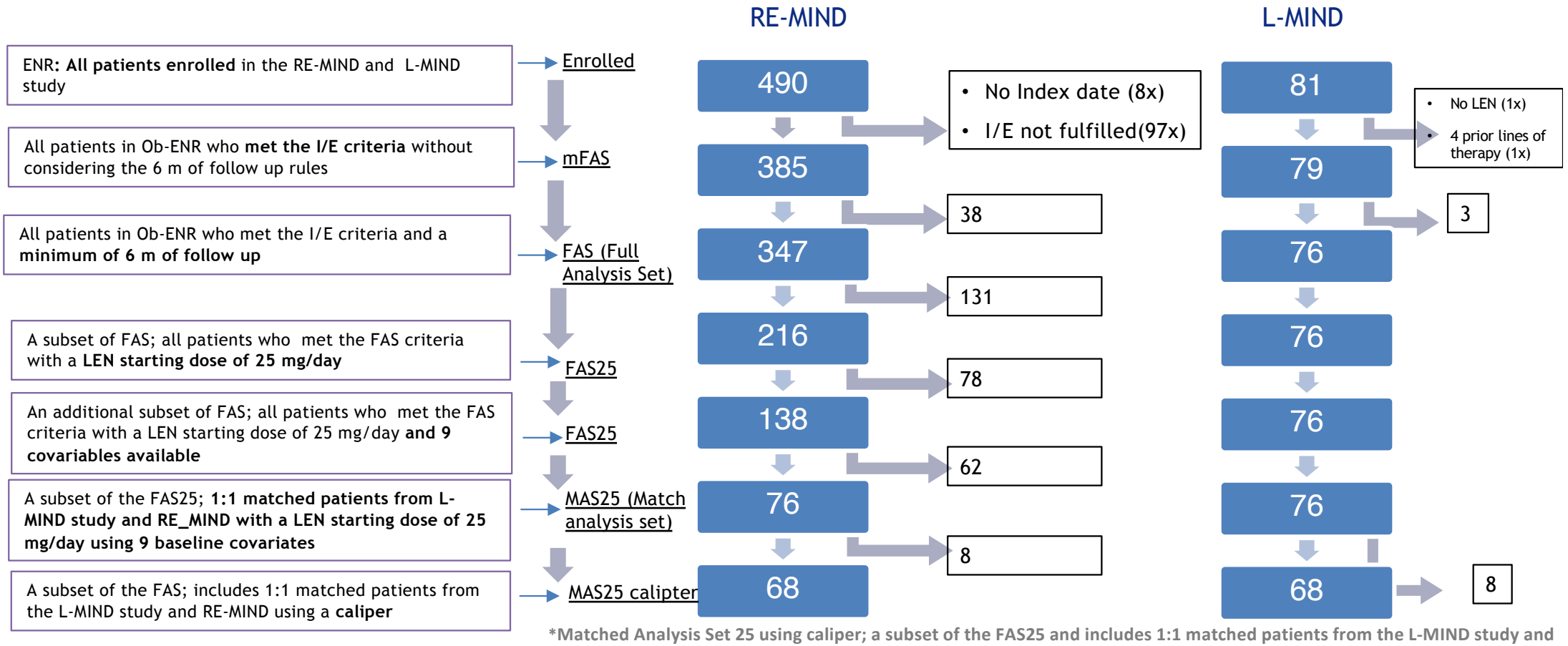


*Age (< 70 vs ≥ 70 years); Ann Arbor stage (I/II vs III/IV); refractoriness to last therapy line (yes vs no); number of prior lines of therapy (1 vs 2 or 3); history of primary refractoriness (yes vs no); prior ASCT (yes vs no); elevated LDH (LDH > ULN vs LDH ≤ ULN); neutropenia (ANC < 1.5 x 10^9/L vs ANC ≥ 1.5 x 10^9/L); anemia (Hb < 10 g/dL vs Hb ≥ 10 g/dL).

Estimated propensity score -based Nearest Neighbour 1:1 matching methodology was used to balance the two cohorts for 9 baseline covariates on advise of regulatory authorities

Zinzani,Clinical Cancer Research 2021

ANALYSIS POPULATIONS



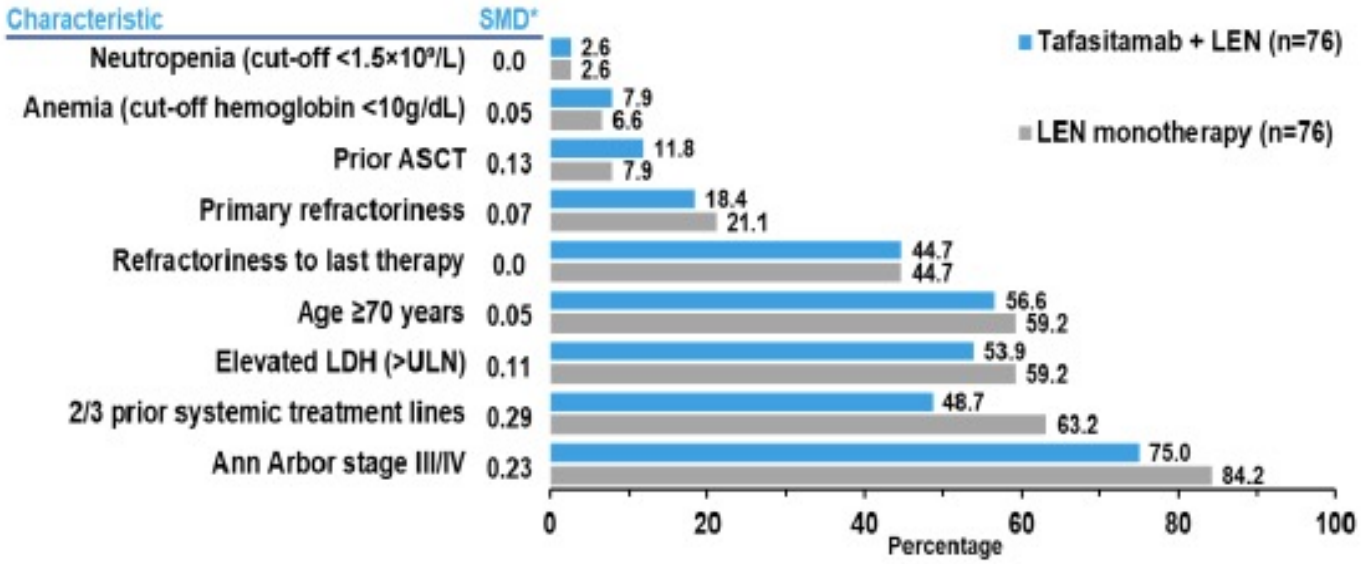
*Matched Analysis Set 25 using caliper; a subset of the FAS25 and includes 1:1 matched patients from the L-MIND study and the observational cohort with a LEN starting dose of 25 mg/day using a caliper, standardized mean difference (SMD) <0.20

Fas, full analysis set; MAS, matched analysis set, Cal, caliper

Zinzani et al, Journal of Cancer Research Clinical Oncology 2021

BASELINE CHARACTERISTICS USED FOR COHORT BALANCING

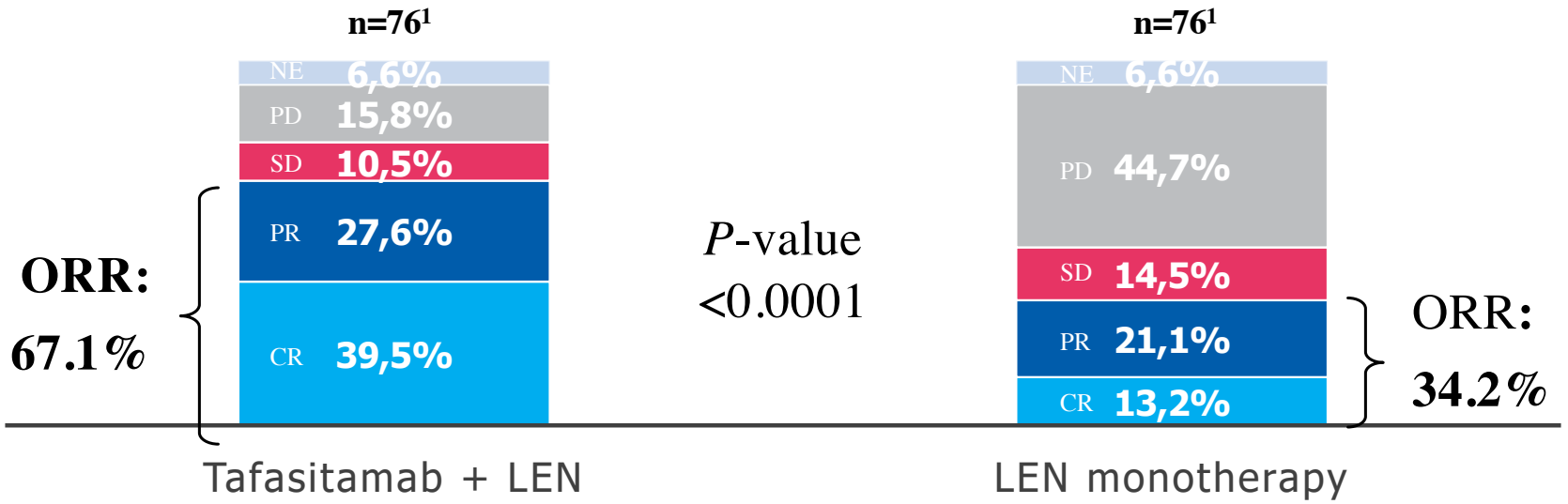
- Baseline characteristics were well balanced across the two cohorts after the matching procedure



*SMD is defined as the ratio of the difference of proportions of a baseline characteristic to the standard deviation of the pooled difference. This standardisation allows for comparison of the relative balance achieved across different baseline characteristics occurring in a low or high proportion.

Zinzani et al, 2021

PRIMARY ENDPOINT: BEST OVERALL RESPONSE RATE



Endpoint/cohort	Tafasitamab + LEN (L-MIND cohort) (n=76[1])	LEN monotherapy (observational cohort) (n=76[1])
ORR (%, 95% CI)	67.1 (55.4–77.5)	34.2 (23.7–46.0)
Odds ratio (95% CI)	3.9 (1.9–8.1); *P*<0.0001	
CR (%, 95% CI)	39.5 (28.4–51.4)	13.2 (6.5–22.9)

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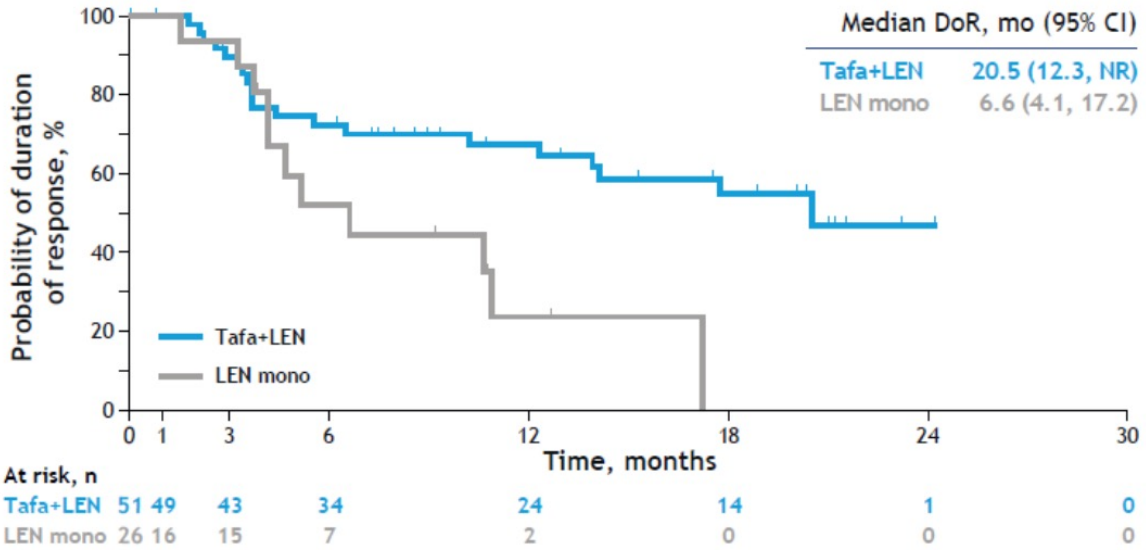
SECONDARY ENDPOINTS: DURATION OF RESPONSE

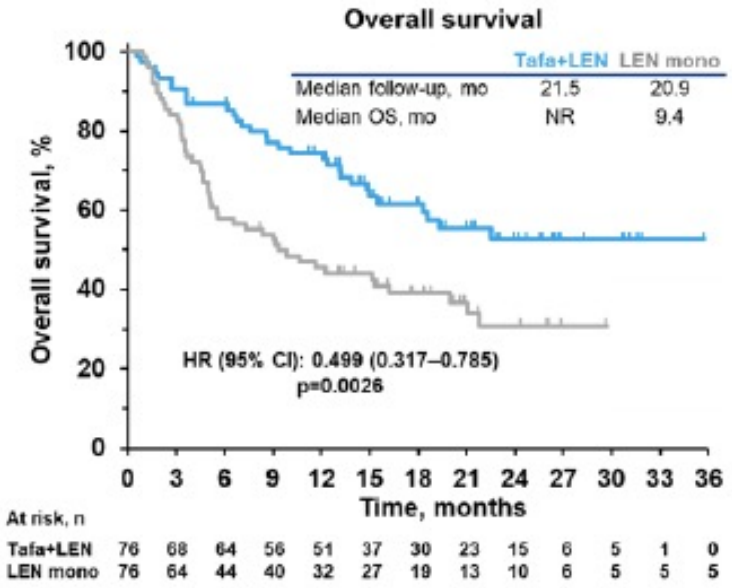


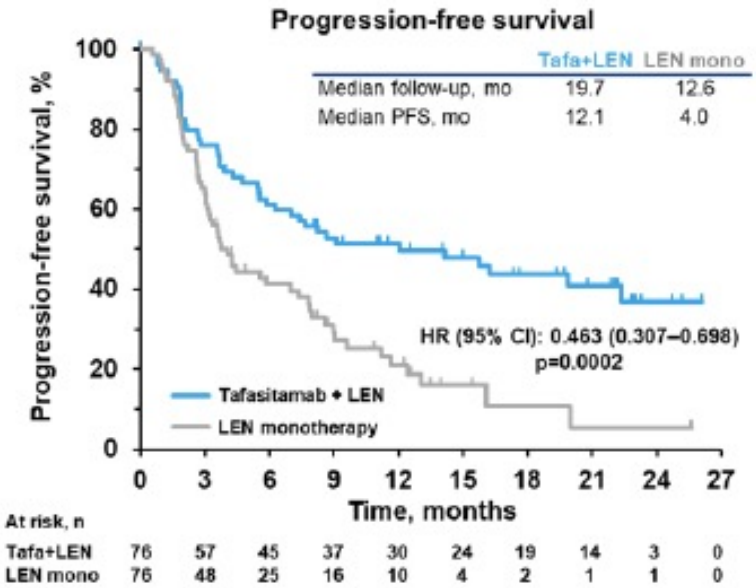
Median DoR was 20.5 (95% CI: 12.3, NE) months in the tafasitamab+LEN cohort and 6.6 (95% CI: 4.1, 17.2) months in the LEN-mono cohort.

CI, confidence interval; DoR, duration of response; LEN, lenalidomide; MAS25, matched analysis set 25; mo, month; NR, not reached

Zinzani et al, 2021

SECONDARY ENDPOINTS: OVERALL SURVIVAL AND PROGRESSION-FREE





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SUMMARY

	L-MIND (n 81)	RE-MIND (n 76)	Broccoli et al (n 153)	Mondello et al (n 123)	SCHOLAR trial (n 636)
	Tafa + Lena	Tafa+lena vs Lena	Lena	Lena	r/r therapies
ORR	**59%**	**67% vs 34%**	**29%**	**37%**	**26%**
CR	41%	39% vs 12%	23%	21%	7%
PR	17%	27% vs 22%	6%	16%	18%
mOS	31.6m	NR vs 9.4m	12m	Not reported	6.3m

Historical patient's level cohort study

Observational national studies

Historical pooled analysis from 2 Phase III CT and 3 observational studies

Salles et al, Lancet Onc 2020
Salles G et al. EHA. 2020; Abstract EP1201
Crump et al, Blood 2017
Broccoli et al, The Oncologist 2019
Mondello et al, The Honcologist 2016

RE-MIND
CONCLUSIONS

- **Significantly better ORR, CR, OS and PS outcomes indicate substantial clinical benefit of adding tafasitamab to lenalidomide treatment in transplant-ineligible R/R DLBCL patients**
- **Tafasitamab plus lenalidomide is an additional treatment option for a historically poor prognosis population**
- **Within the limitations of non-randomised trials, estimated propensity score -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**
- **RE-MIND outcomes are comparable to those published for LEN monotherapy in clinical trials**

Transplant ineligible?

Chemotherapy[1]

R-GemOx

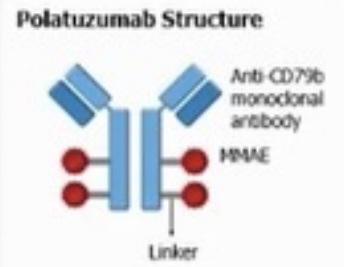
R-GDP

R-DHAP

Polatuzumab[4]

+ bendamustine

+ rituximab

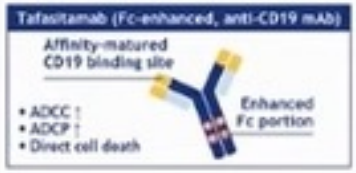


CAR-T cells[2,3]

+ FC conditioning

Tafasitamab[5]

+ lenalidomide



1.Tilly H et al, 2015; 2.Schuster et al, 2019;3.Locke et al, 2019; 4. Sehn et al,2020; Salles et al, 2020

RE-MIND2: STUDY DESIGN AND METHODS

RE-MIND2 is a **retrospective**, **observational cohort study** designed to generate a real-world control for outcomes from the L-MIND study, to characterize the effectiveness of tafasitamab + LEN, in a real-world setting, relative to commonly administered systemic therapies for ASCT ineligible patients with R/R DLBCL

Data were collected between April and November 2020 in North America, Europe, and the Asia Pacific region

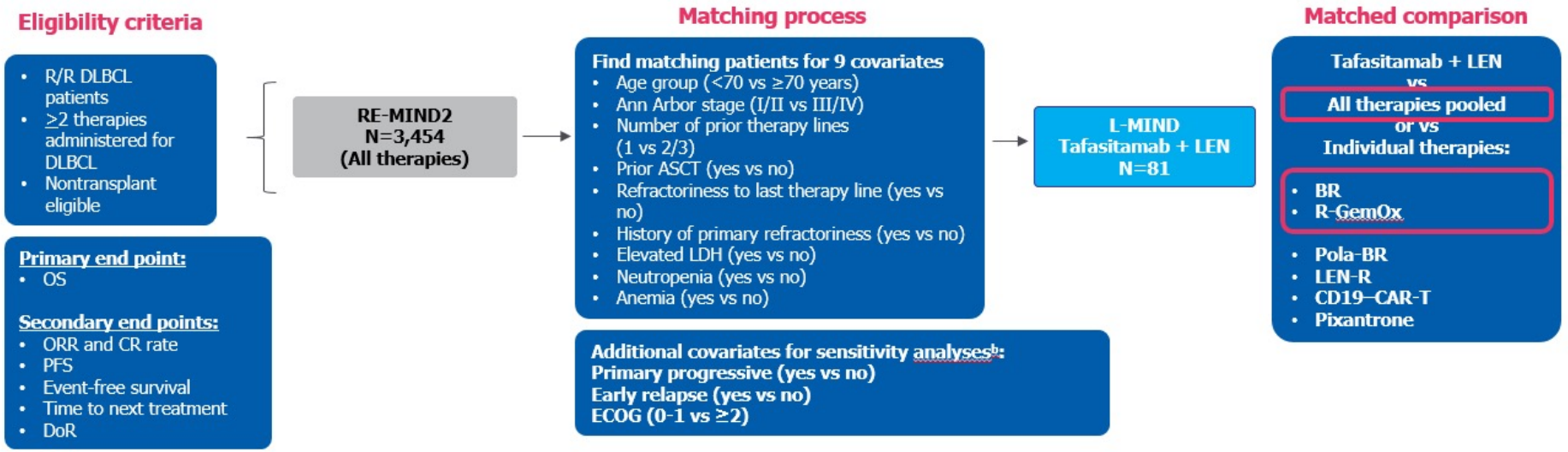
Eligibility criteria were based on the L-MIND study: patients aged ≥18 years with histologically confirmed DLBCL and who had received ≥2 prior systemic therapies for R/R DLBCL (including ≥1 anti-CD20 therapy)

The primary endpoint was OS and secondary endpoints included ORR, CR rate, progression-free survival (PFS), and DoR

***Grzegorz S. Nowakowski et al,* ,Clinical Cancer Research 2022**

RE-MIND2: STUDY DESIGN AND METHODS

Matching criteria and estimated propensity score (ePS)-based method were applied and efficacy outcomes from the L-MIND cohort were compared with those treated with the observational cohort of patients enrolled in RE-MIND2 database



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RE-MIND2: STUDY DESIGN AND METHODS

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

The cohorts in each MAS were matched using ePS-based 1:1 nearest neighbor (NN) matching, balanced for nine baseline prognostic covariates. To achieve high quality of balance between cohorts, the standard mean difference of each covariate post-matching was pre-defined as ≤0.2

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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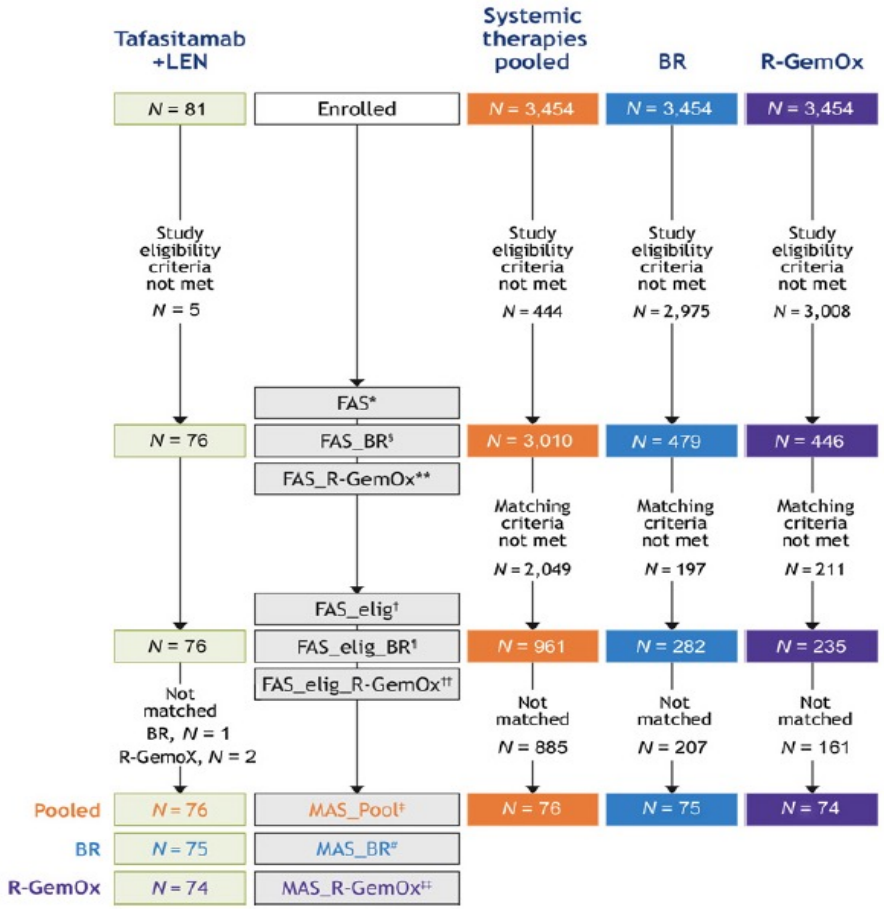
RE-MIND2: POPULATION



FAS population: patients who met the eligible/non-eligible criteria of RE-MIND2 and L-MIND study with a minimum of 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	31.84m vs 33.25m	32.92 vs 25.00	32.92 vs 33.18

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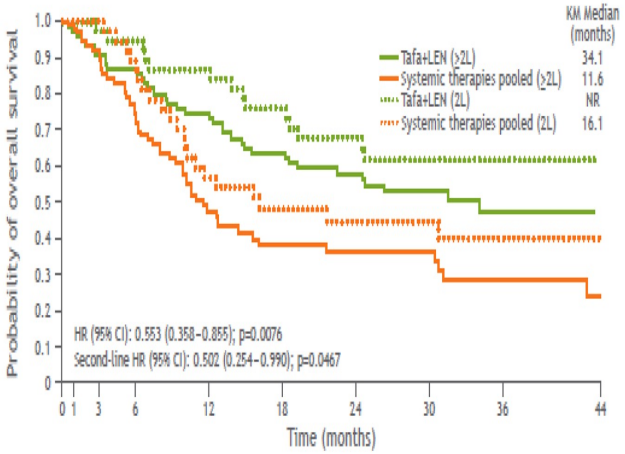
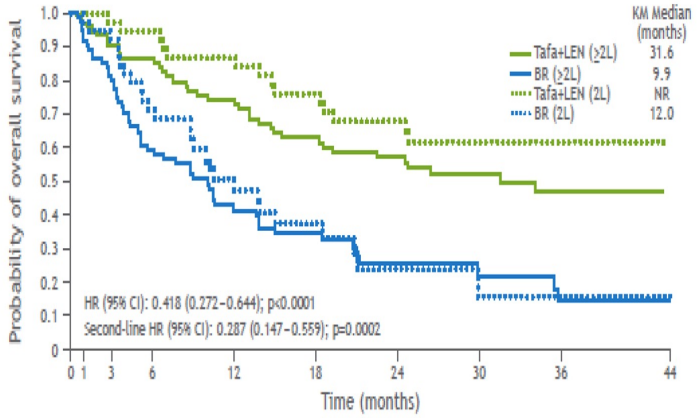
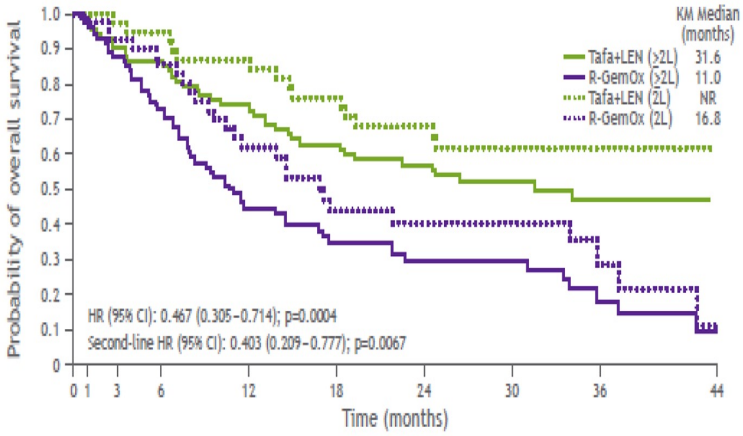
PRIMARY ENDPOINT: OVERALL SURVIVAL

	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	







Second line median OS for Tafa+Lena: not reached, indicating >50% patients were alive by end of follow-up time

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SECONDARY ENDPOINT: ORR

Table 2. ORR and CR rate for tafasitamab + LEN vs systemic therapies pooled, BR, and R-GemOx

	MAS for systemic therapies pooled		MAS for BR		MAS for R-GemOx	
	Tafasitamab + LEN (n=76)	Systemic therapies pooled (n=76)	Tafasitamab + LEN (n=75)	BR (n=75)	Tafasitamab + LEN (n=74)	R-GemOx (n=74)
ORR, n (%) (95% CI)	51 (67.1) (55.4–77.5)	37 (48.7) (37.0–60.4)	50 (66.7) (54.8–77.1)	41 (54.7) (42.7–66.2)	51 (68.9) (57.1–79.2)	34 (45.9) (34.3–57.9)
Fisher's exact test p-value of ORR	0.032		0.181		0.007	
CR rate as best response, n (%) (95% CI)	29 (38.2) (27.2–50.0)	16 (21.1) (12.5–31.9)	29 (38.7) (27.6–50.6)	21 (28.0) (18.2–39.6)	29 (39.2) (28.0–51.2)	17 (23.0) (14.0–34.2)
Fisher's exact p-value of CR rate	0.032		0.225		0.050	

BR, bendamustine + rituximab; CI, confidence interval; CR, complete response; LEN, lenalidomide; MAS, matched analysis set; ORR, overall response rate; R-GemOx, rituximab + gemcitabine + oxaliplatin.

Tafasitamab + LEN vs therapies pooled and R-GemOx: ORR and CR significantly higher

A numerical improvement was observed for tafasitamab + LEN vs BR but no statistically significant

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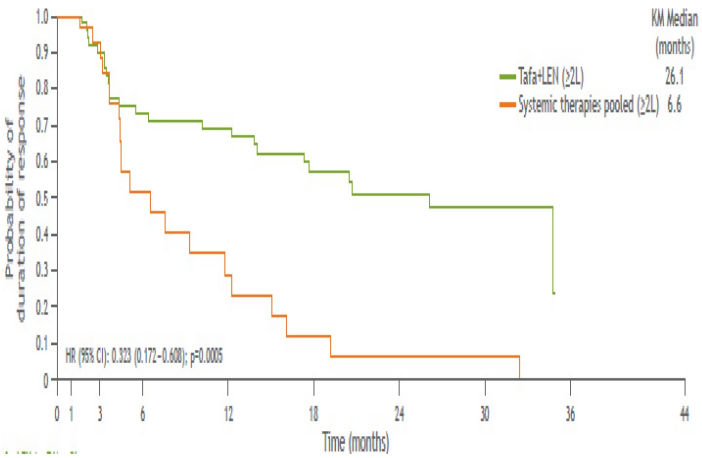
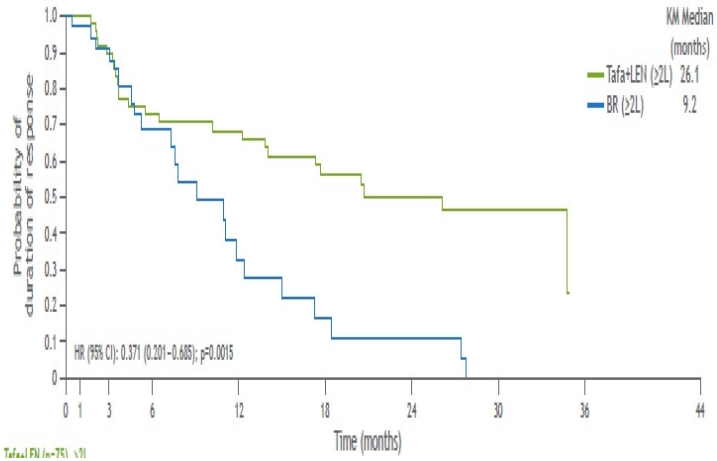
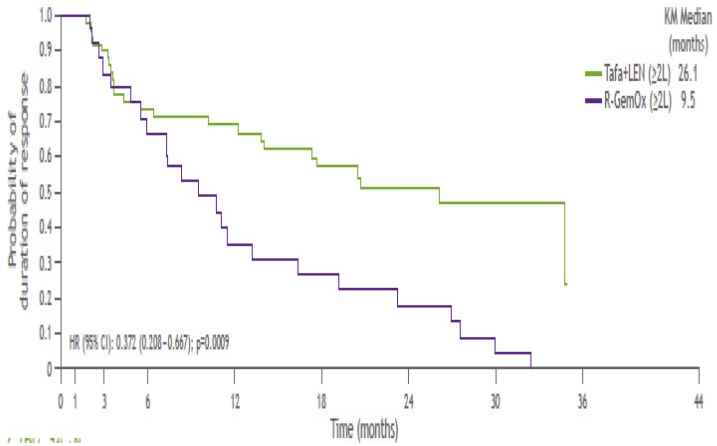
SECONDARY ENDPOINT: DURATION OF RESPONSE

	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	

DoR was significantly improved in the tafasitamab + LEN cohort compared with systemic therapies pooled, with BR and with R-GemOx







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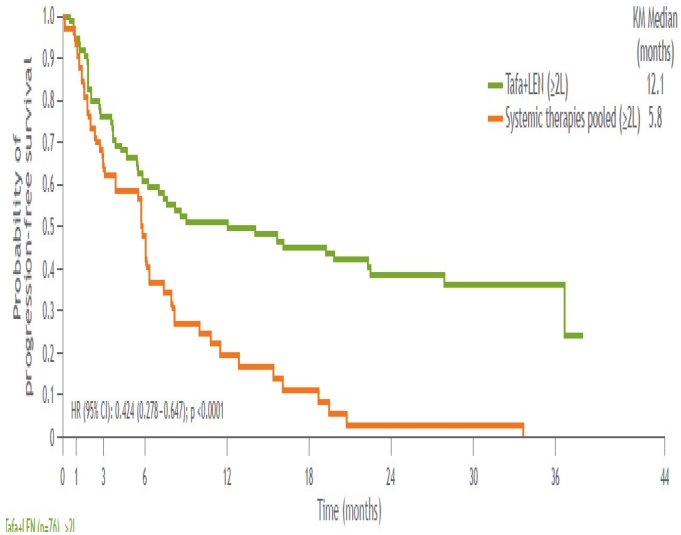
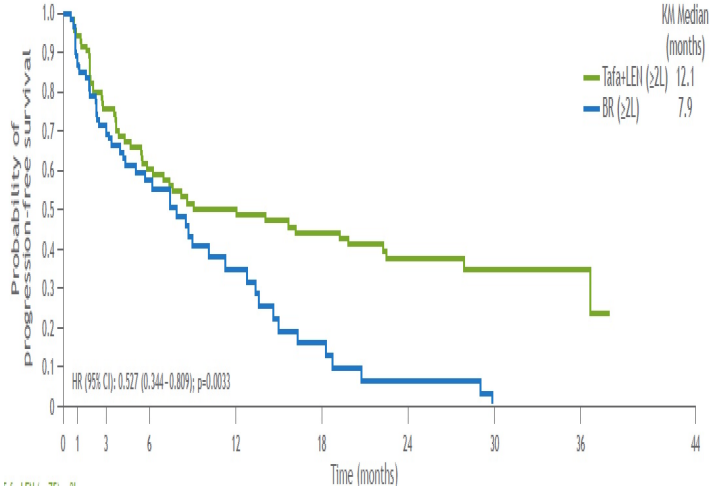
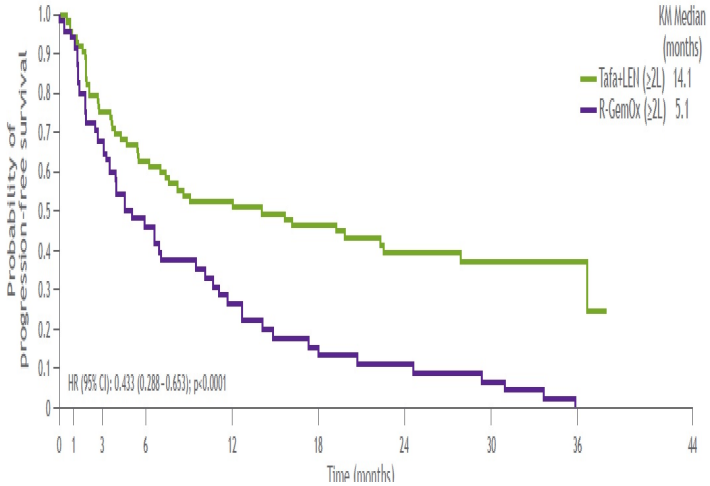
SECONDARY ENDPOINT: PROGRESSION FREE SURVIVAL

	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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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

Grzegorz S. Nowakowski,[1*] Dok Hyun Yoon,[2] Patrizia Mondello,[3] Erel Joffe,[3] Anthea Peters,[4] Isabelle Fleury,[5] Richard Greil,[6] Matthew Ku,[7] Reinhard Marks,[8] Kibum Kim,[9] Pier Luigi Zinzani,[10] Judith Trotman,[11] Lorenzo Sabatelli,[12] Dan Huang,[13] Eva E. Waltl,[13] Mark Winderlich,[13] Sumeet Ambarkhane,[13†] Nuwan C. Kurukulasuriya,[14] Raul Cordoba,[15] Georg Hess,[16] Gilles Salles[3]

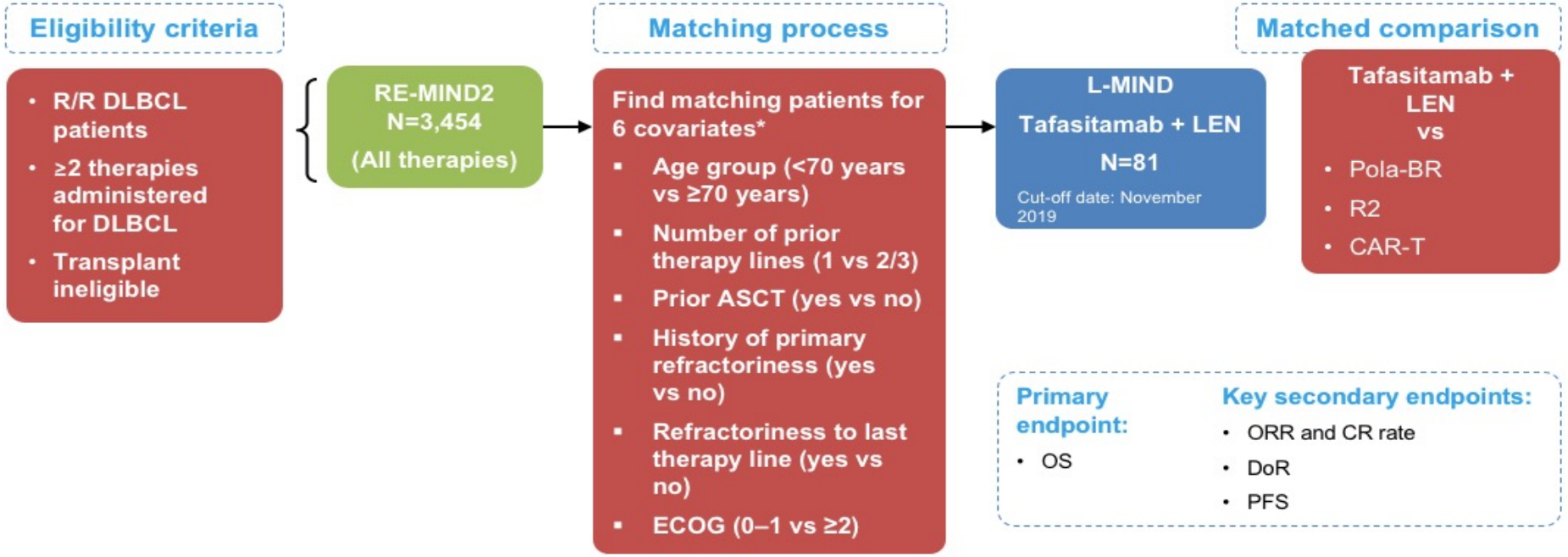
[1]Division of Hematology, Mayo Clinic, Rochester, MN, USA, [2]Department of Oncology, Asan Medical Center, Songpa-gu, Seoul, South Korea, [3]Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA, [4]Department of Oncology, University of Alberta, Edmonton, Alberta, Canada,[5]Maisonneuve-Rosemont Hospital, Institute of Hematology, Oncology and Cell Therapy, Montreal University, Montreal, Canada, [6]Paracelsus Medical University Salzburg, Salzburg Cancer Research Institute-CCCIT, and Cancer Cluster Salzburg, Austria, [7]Department of Haematology, St Vincent's Hospital and University of Melbourne, Melbourne, Victoria, Australia, [8]University Hospital Freiburg Internal Medicine I, Freiburg im Breisgau, Germany, [9]University of Utah, Salt Lake City, UT & University of Illinois at Chicago, Chicago, IL USA; [10]IRCCS Azienda Ospedaliero-Universitaria di Bologna, Istituto di Ematologia "Seràgnoli" & Dipartimento di Medicina Specialistica, Diagnostica e Sperimentale Università di Bologna, Bologna, Italy; [11]Haematology Department, Concord Repatriation General Hospital, University of Sydney, Concord, NSW, Australia, [12]Incyte Biosciences International Sàrl, Morges, Switzerland, [13]MorphoSys AG, Planegg, Germany, [14]MorphoSys AG, Boston, MA, USA, [15]Department of Hematology, Fundacion Jimenez Diaz University Hospital, Health Research Institute IIS-FJD, Madrid, Spain, [16]Department of Hematology, Oncology and Pneumology, University Medical Center, Johannes Gutenberg-University Mainz, Germany.

Meeting Abstract | 2022 ASCO Annual Meeting I

HEMATOLOGIC MALIGNANCIES—LYMPHOMA AND CHRONIC LYMPHOCYTIC LEUKEMIA

RE-MIND2 expanded analysis

Subgroup analysis in RE-MIND2, an observational, retrospective cohort study of tafasitamab plus lenalidomide versus systemic therapies in patients with relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL).



* 9 covariates were used for the primary analysis;

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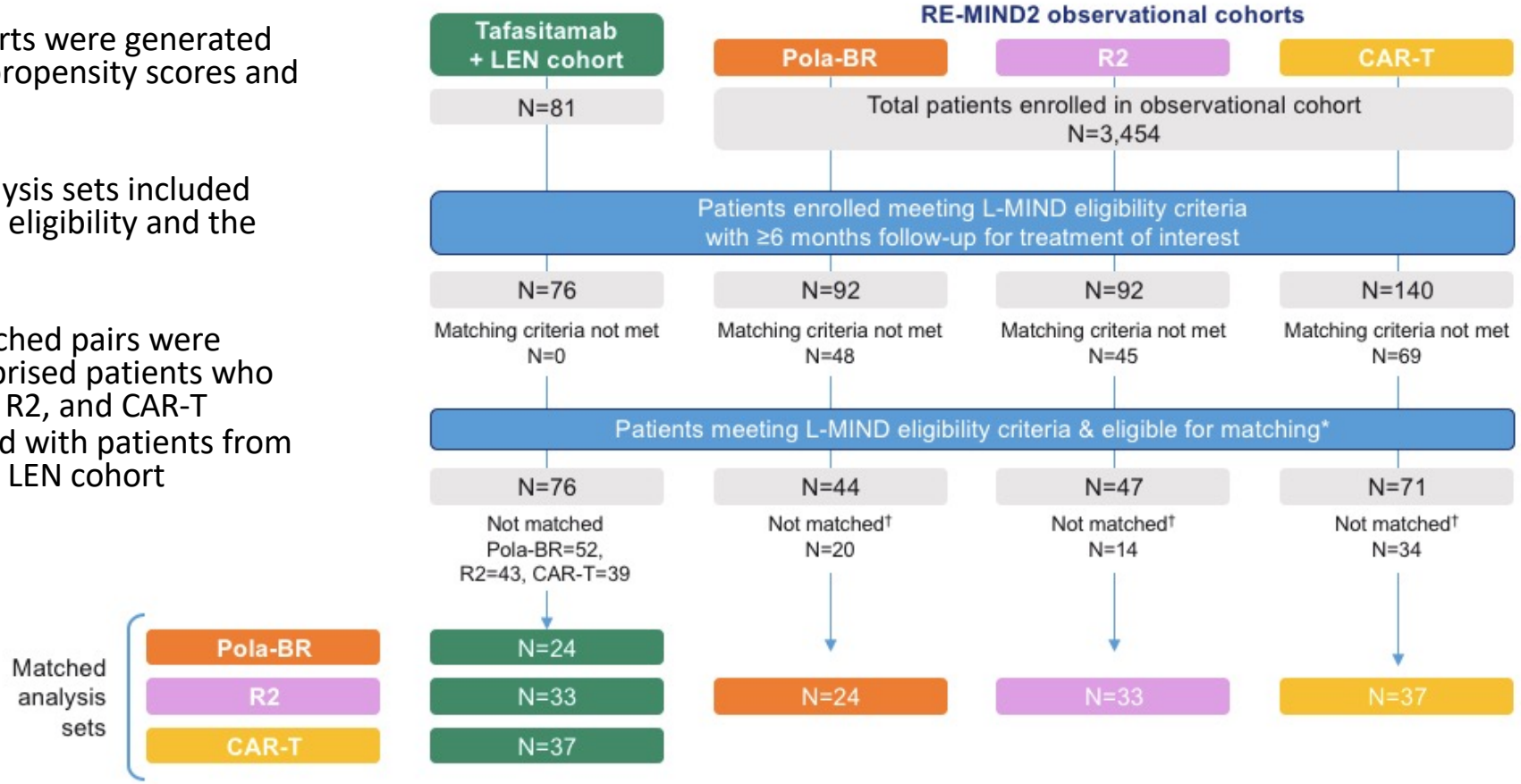
Analysis Population

- 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



- *With complete data for six matching covariates, Based on 1:1 nearest neighbor propensity score.

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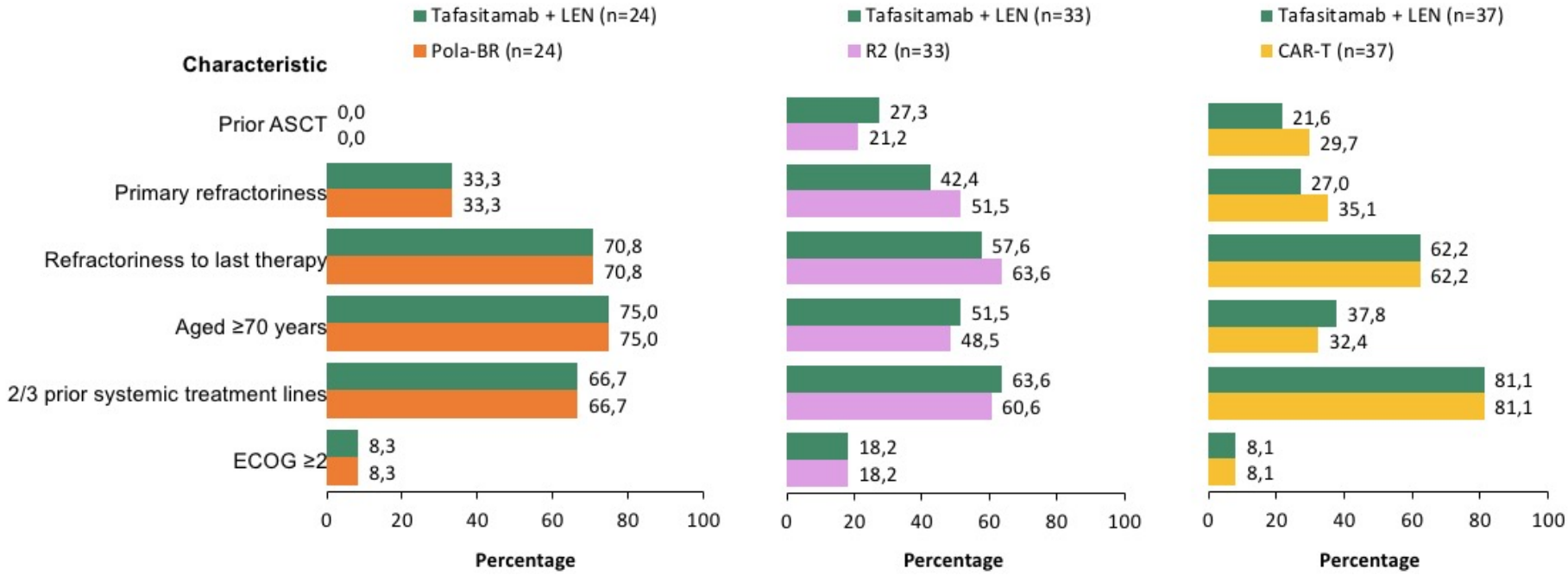
Baseline characteristics for tafasitamab + LEN versus Pola-BR, R2, and CAR-T

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



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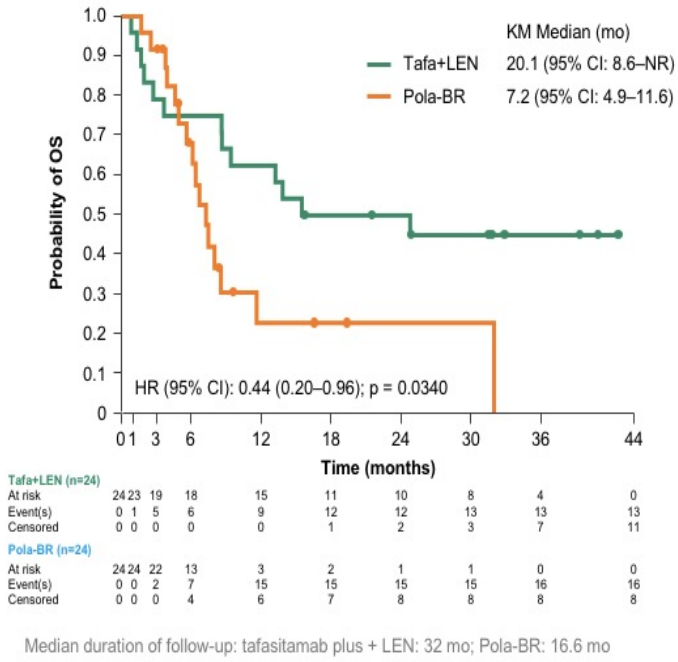
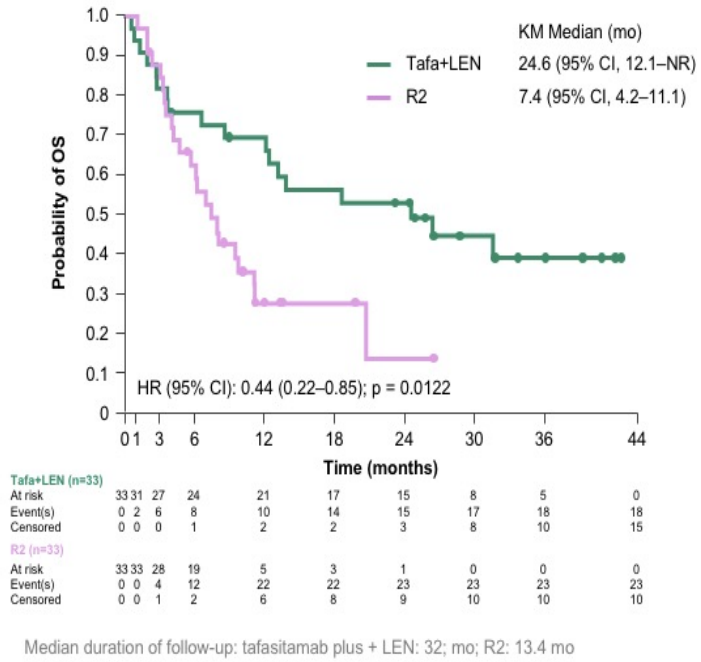
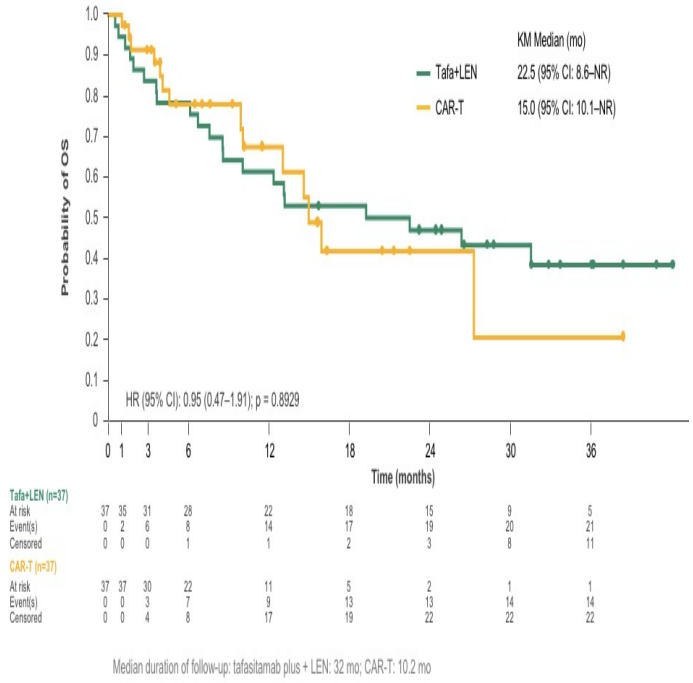
Primary endpoint: OS



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



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



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

Tafasitamab + LEN was associated with statistically significant improvements in OS versus Pola-BR and versus R2. A comparable OS benefit with tafasitamab + LEN versus CAR-T (22 versus 15 months), without statistical significance was observed

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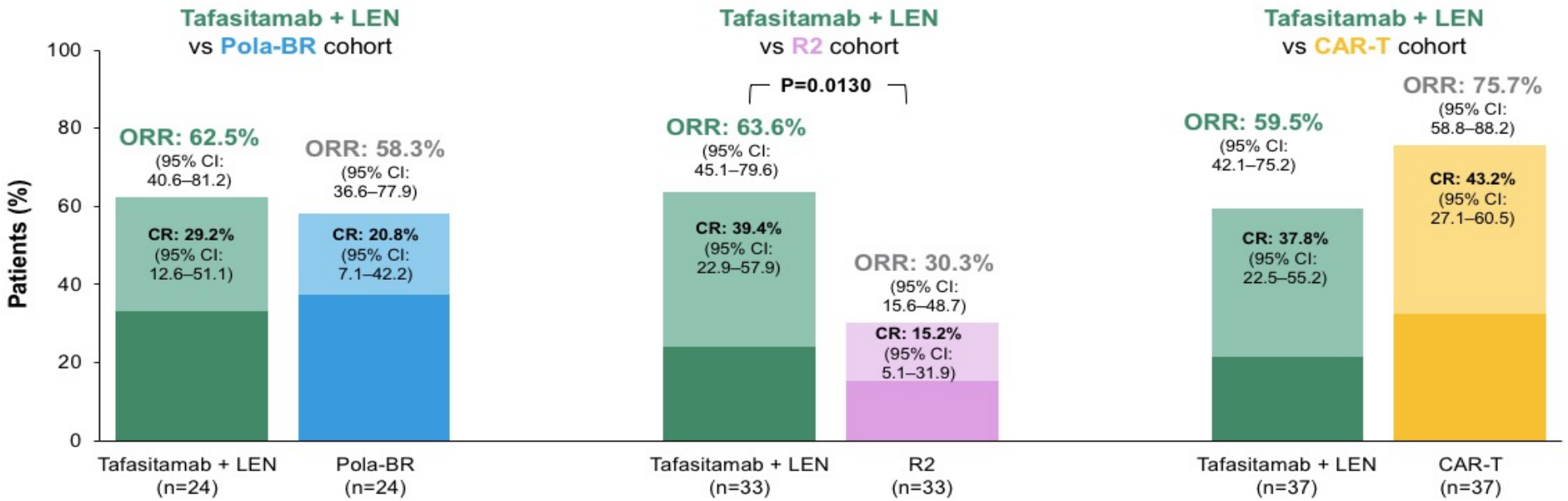
Secondary endpoint: ORR and CR

- 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



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Secondary endpoint: 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)

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Conclusions

- **RE-MIND2 was designed to generate a real-world control for outcomes from the L-MIND study to characterize the effectiveness of tafasitamab + LEN relative to other systemic therapies, currently recommended for the treatment of ASCT ineligible patients with R/R DLBCL, using a 1:1 Nearest-Neighbor estimated Propensity Score-based matching method**
- **Tafasitamab + Lenalidomide was associated with longer OS vs systemic therapies pooled, BR, and R-GemOx, Pola BR and R2 . A comparable OS benefit with tafasitamab + LEN versus CAR-T without statistical significance was observed**
- **Overall, results of this study show that this immunomodulatory regimen may improve outcomes compared with NCCN/ESMO-recommended therapies used in routine clinical care for the treatment of R/R DLBCL**


Grazie per l’attenzione