Eppur si muove...

La terapia nel MONDO LINFOMI

Studi RE-MIND e RE-MIND2
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Consulenza ad aziende con interessi commerciali in campo sanitario: **JANSSEN CILAG, GILEAD**

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CLINICAL CANCER RESEARCH | CLINICAL TRIALS: IMMUNOTHERAPY 2021

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

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RE-MIND: PROSPECTIVE-RETROSPECTIVE OBSERVATIONAL STUDY OF LEN MONOTHERAPY AS COMPARATOR TO L-MIND

Aligned Inclusion/Exclusion Criteria

Same histologies, 1–3 prior systemic therapies, not eligible for ASCT

L-MIND: tafasitamab+ LEN, n=80

Of the 81 patients enrolled in L-MIND, five were excluded from the analysis (n = 1 did not receive LEN and n = 4 did not meet the 6-month follow-up criterion).

Matched Comparison Cohort: tafasitamab+LEN vs. LEN monotherapy

Find Matching Patients for

- Age
- Tumor stage
- Response to prior therapies
- Number of prior therapies
- Blood laboratory parameters
- Lenalidomide treatment dose

RE-MIND: LEN monotherapy, n~500 (50%/50% from US/EU)

76 patients

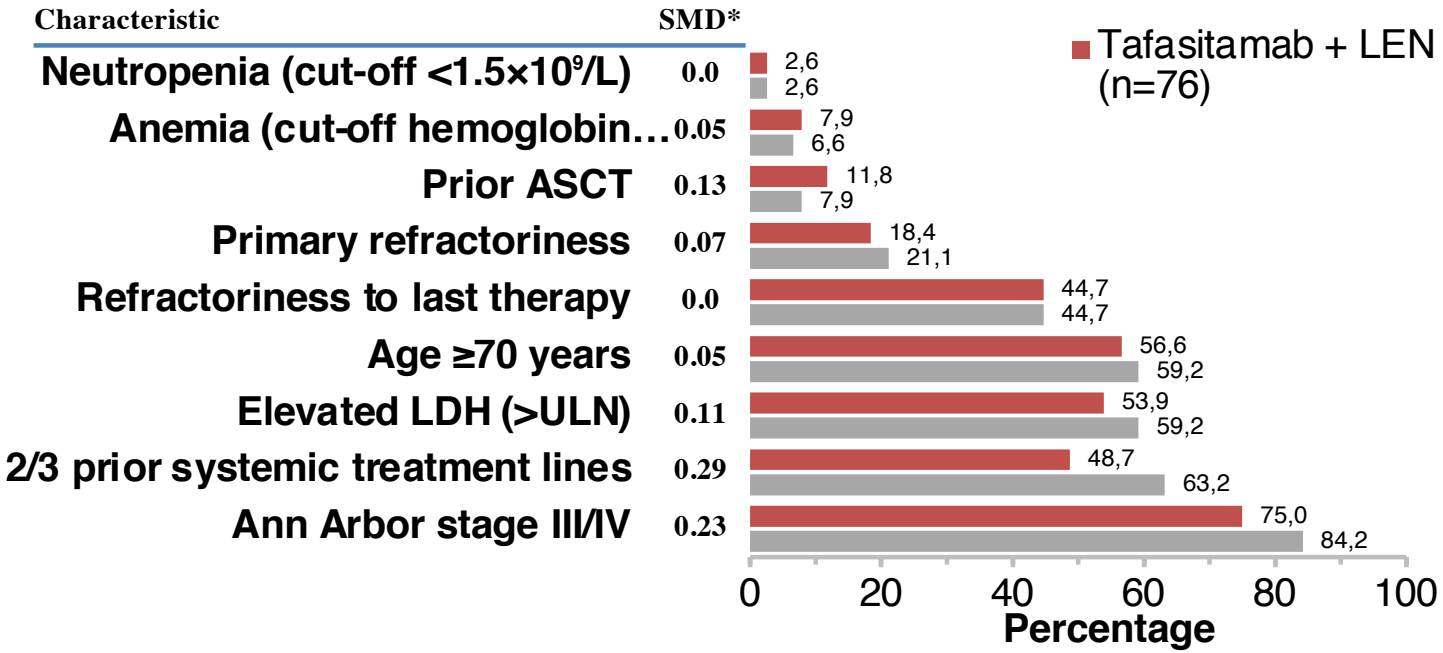
Key Endpoints

- Difference in
  - Best ORR (Primary Endpoint)
  - Complete response rates
  - Duration of Response
  - Progression-free survival
  - Survival

Grzegorz S. Et al; ASCO 2020 Abstract 8020

BASELINE CHARACTERISTICS USED FOR COHORT BALANCING

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

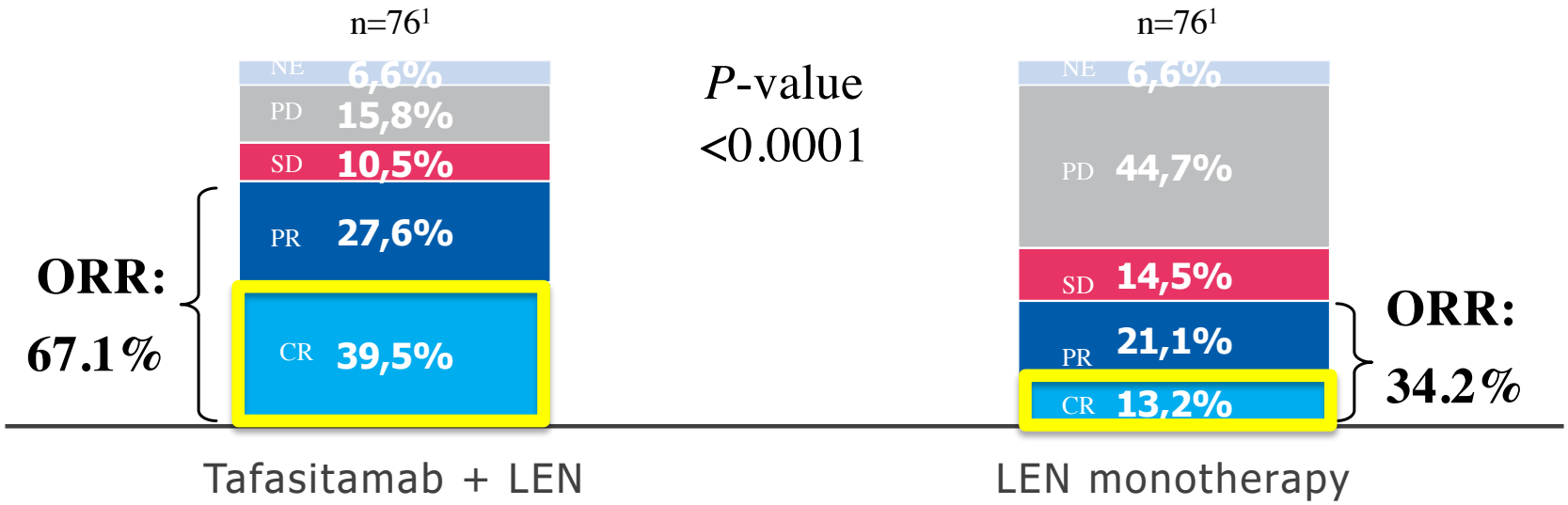


*SMD is defined as the ratio of the difference of proportions of a baseline characteristic to the standard deviation of the pooled difference. This standardisation allows for comparison of the relative balance achieved across different baseline characteristics occurring in a low or high proportion.

ASCT, autologous stem cell transplantation; LDH, lactate dehydrogenase; LEN, lenalidomide; SMD, standardised mean difference; ULN, upper limit of normal.

Nowakowski G, et al. Poster presentation at ASCO 2020; Abstract 8020.

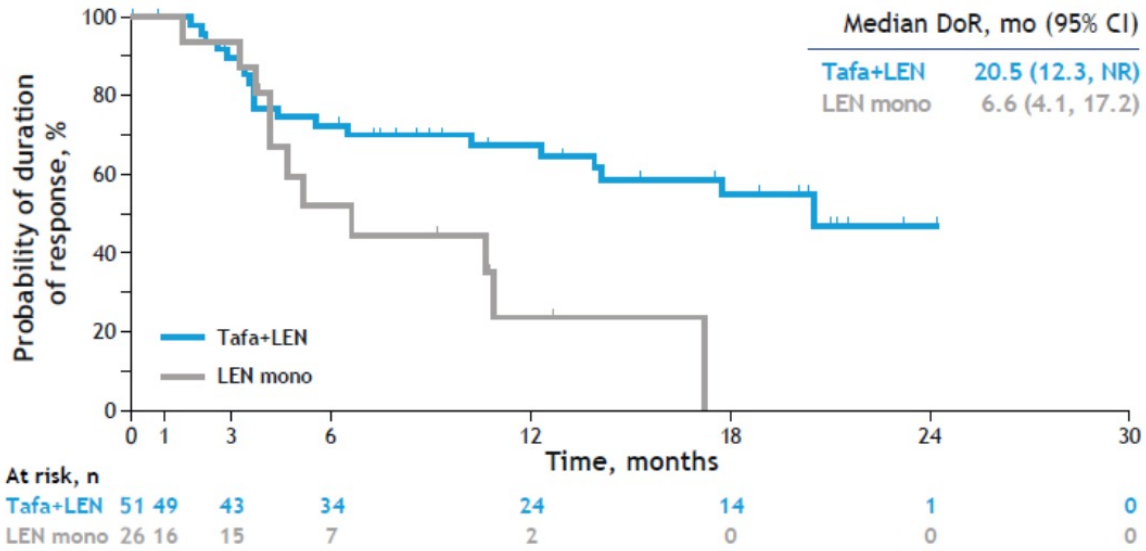
ORR AND CR RATE



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)

Investigator assessed (IRC-assessed ORR for tafasitamab + LEN in L-MIND was 57.5%[2]).
CI, confidence interval; CR, complete response; IRC, independent review committee; LEN, lenalidomide; NE, not evaluated; ORR, overall response rate; PD, progressive disease; PR, partial response; SD, stable disease.
1. Nowakowski G, et al. Poster presentation at ASCO 2020; Abstract 8020; 2. Duell J, et al. Oral presentation at Virtual ICML 2021; Abstract 28.

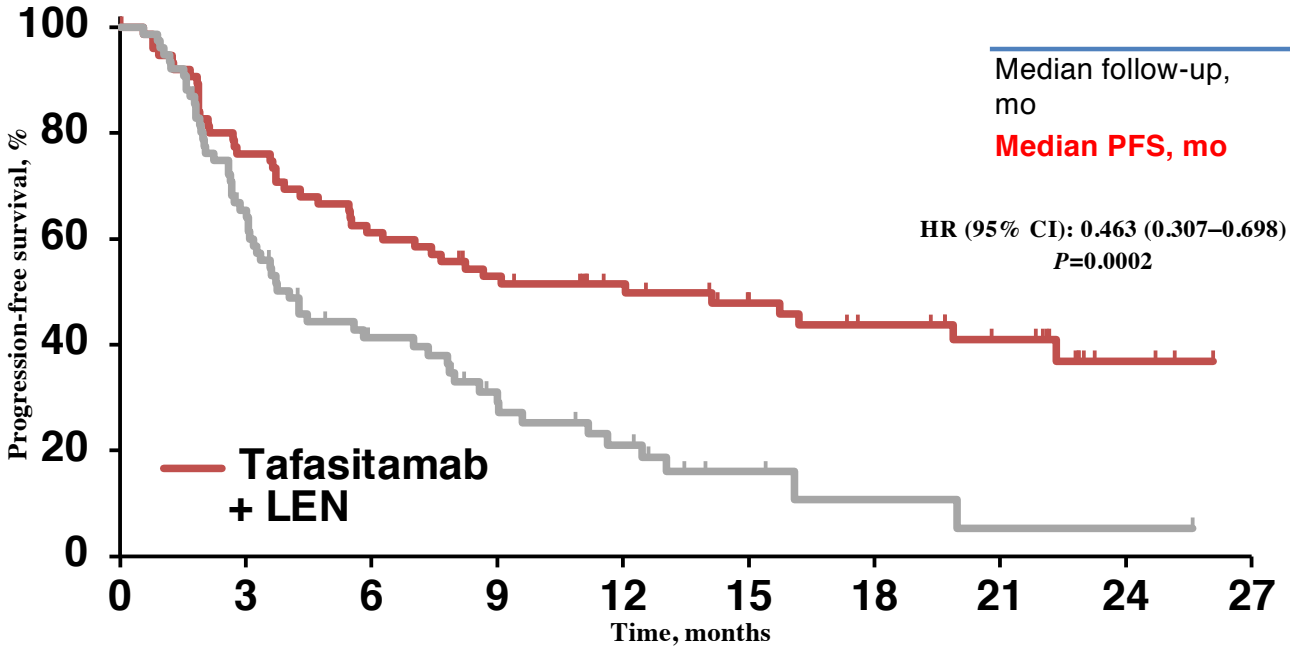
SECONDARY ENDPOINT: DURATION OF RESPONSE



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

Zinzani et al, Journal of Cancer Research and Clinical Oncology 2020

SECONDARY ENDPOINTS: PROGRESSION-FREE SURVIVAL



	Tafa + LEN	LEN mono
Median follow-up, mo	19.7	12.6
Median PFS, mo	**12.1**	**4.0**

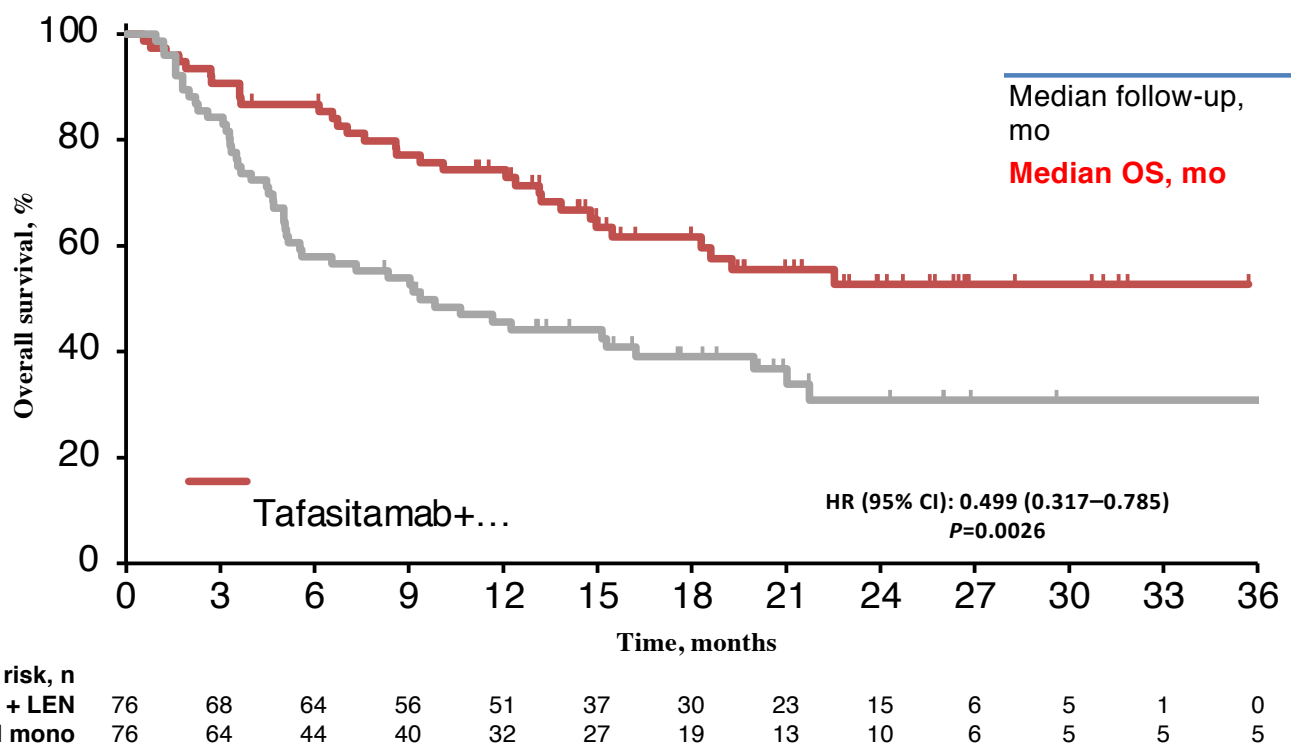
HR (95% CI): 0.463 (0.307–0.698)
P=0.0002

At risk, n										
Tafa + LEN	76	57	45	37	30	24	19	14	3	0
LEN mono	76	48	25	16	10	4	2	1	1	0

CI, confidence interval; HR, hazard ratio; LEN, lenalidomide; mo, month(s); mono, monotherapy; NR, not reached; PFS, progression-free survival.

Nowakowski G, et al. Poster presentation at ASCO 2020; Abstract 8020.

SECONDARY ENDPOINTS: OVERALL SURVIVAL



	Tafa + LEN	LEN mono
Median follow-up, mo	21.5	20.9
Median OS, mo	**NR**	**9.4**

At risk, n													
Tafa + LEN	76	68	64	56	51	37	30	23	15	6	5	1	0
LEN mono	76	64	44	40	32	27	19	13	10	6	5	5	5

CI, confidence interval; HR, hazard ratio; LEN, lenalidomide; mo, month(s); mono, monotherapy; NR, not reached; OS, overall survival.
Nowakowski G, et al. Poster presentation at ASCO 2020; Abstract 8020.

SUMMARY

Historical patient's level cohort study

Observational national studies

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

	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

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

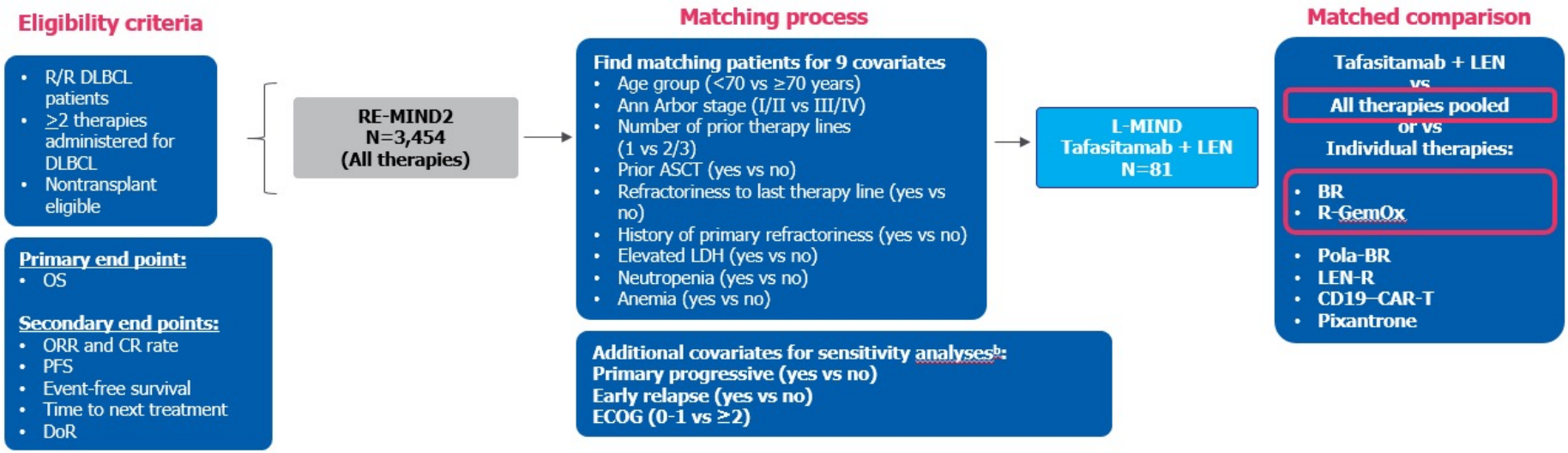
CONCLUSIONS

- Significantly better ORR, CR and OS outcomes indicate substantial additional activity for the novel combination of tafasitamab + LEN versus LEN monotherapy in transplant-ineligible R/R DLBCL patients
- 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
- RE-MIND outcomes are comparable to those published for LEN monotherapy in clinical trials

CR, complete response; DLBCL, diffuse large B-cell lymphoma; ePS, estimated propensity score; LEN, lenalidomide; ORR, overall response rate; OS, overall survival; R/R, relapsed/refractory.
Nowakowski G, et al. Poster presentation at ASCO 2020; Abstract 8020.

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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REMIND2: 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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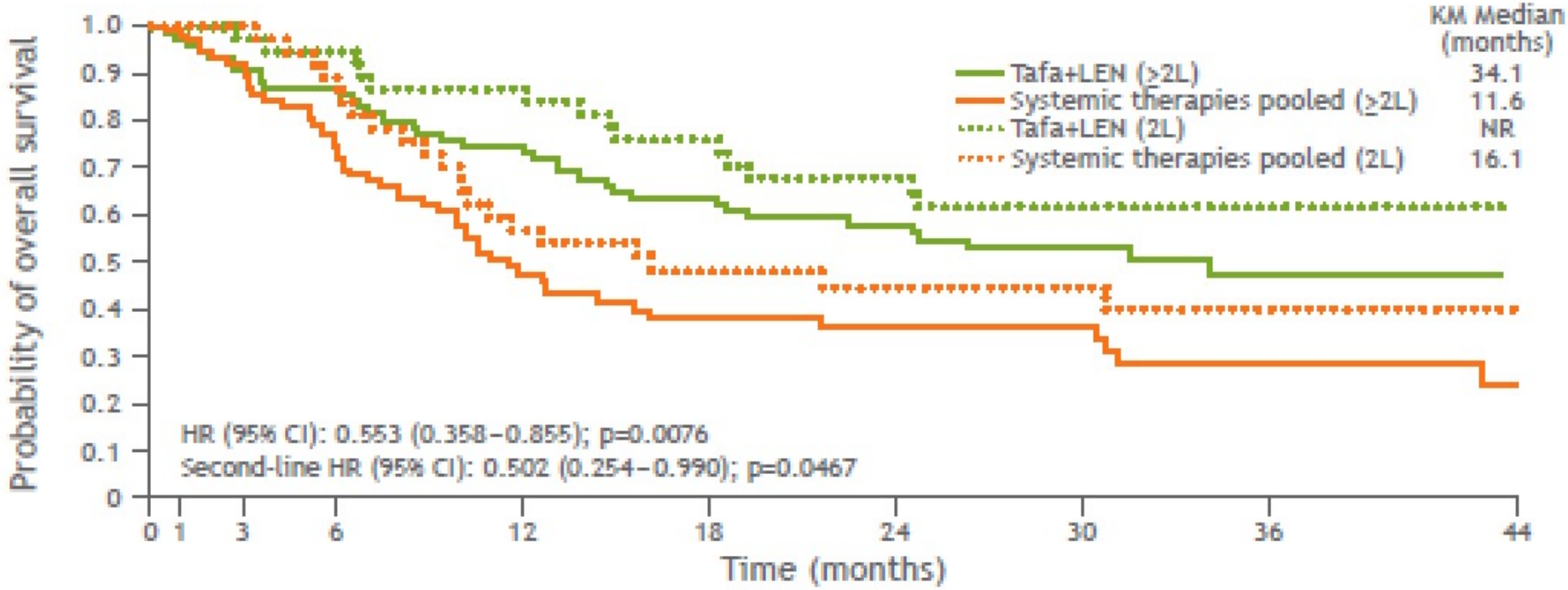
RE-MIND2: OVERALL SURVIVAL VS POOLED THERAPIES



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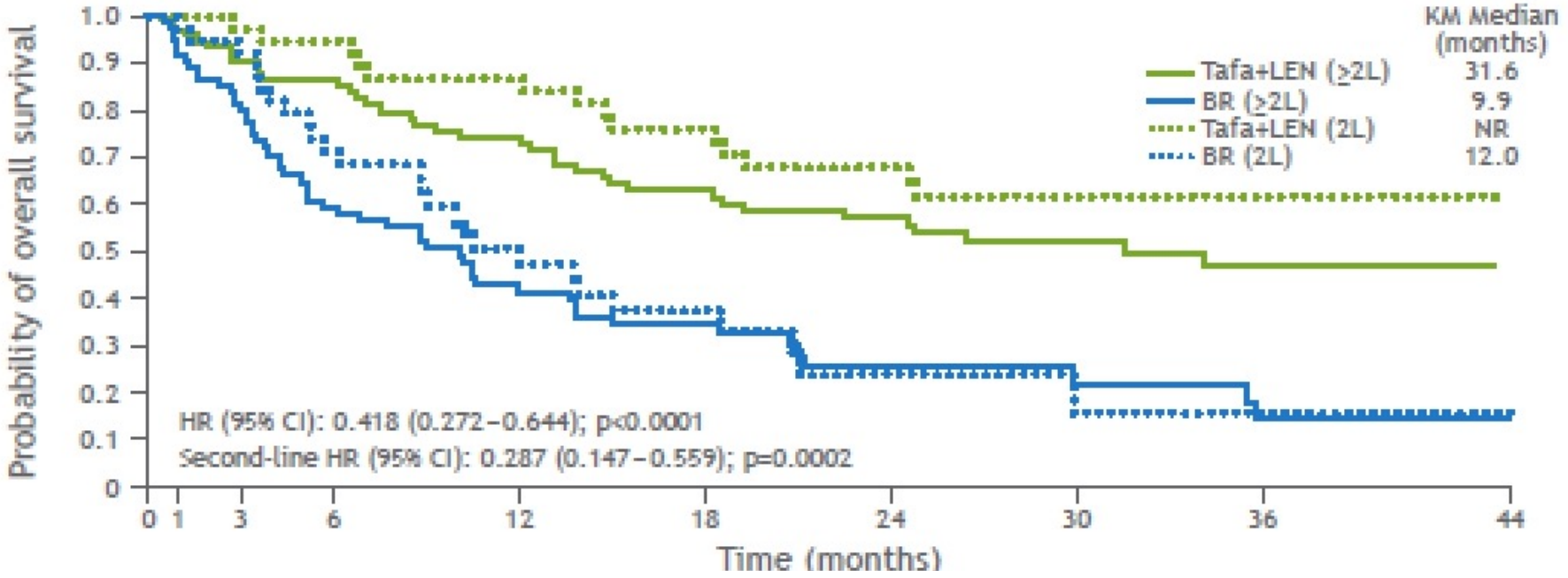
RE-MIND2: OVERALL SURVIVAL VS BR



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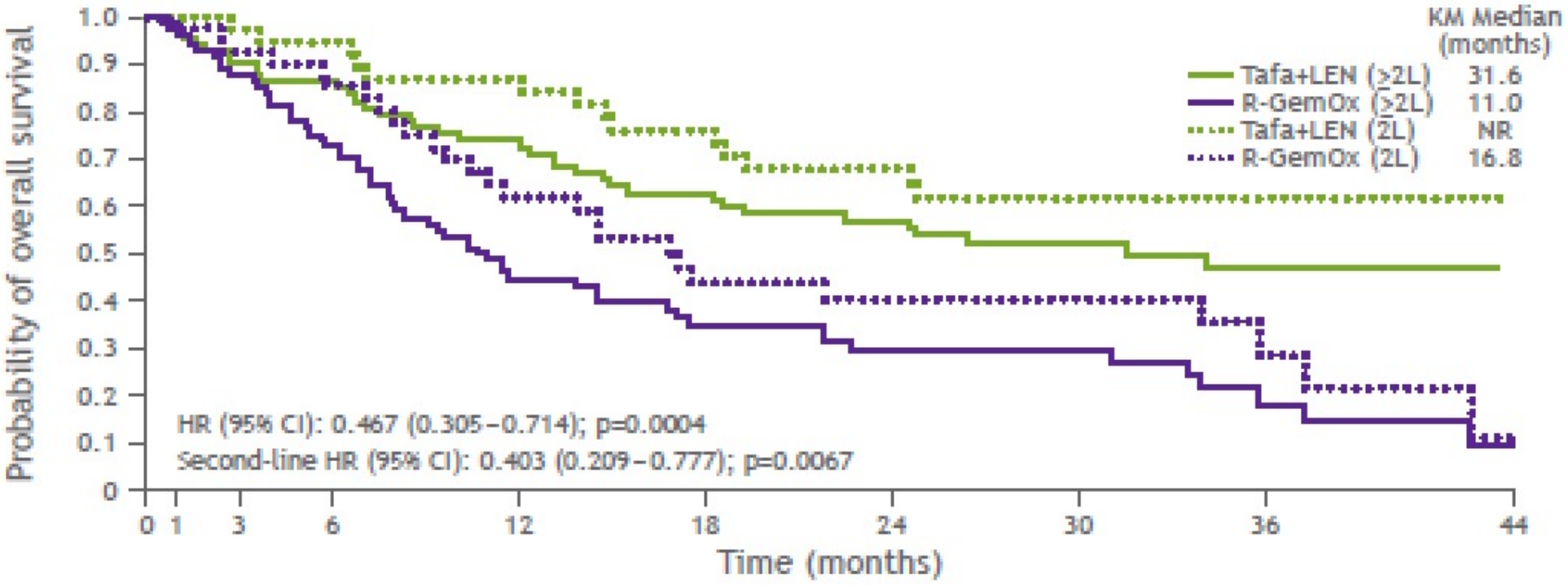
RE-MIND2: OVERALL SURVIVAL VS R-GEMOX



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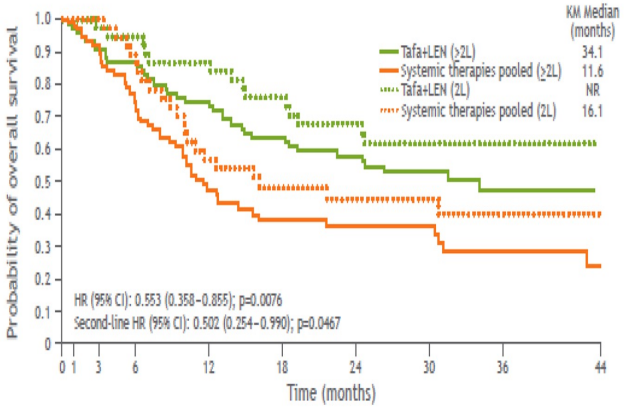
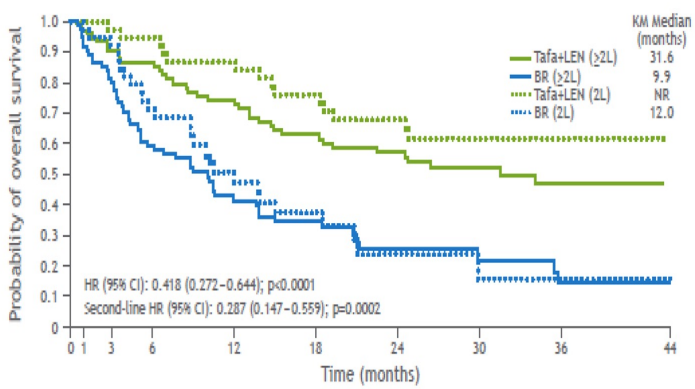
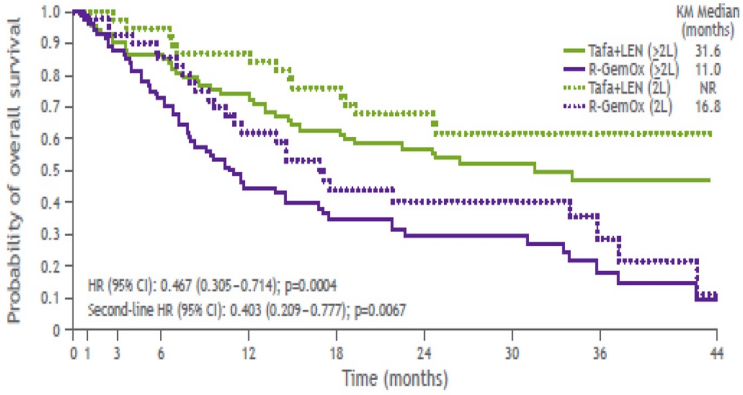
RE-MIND2: OVERALL SURVIVAL

	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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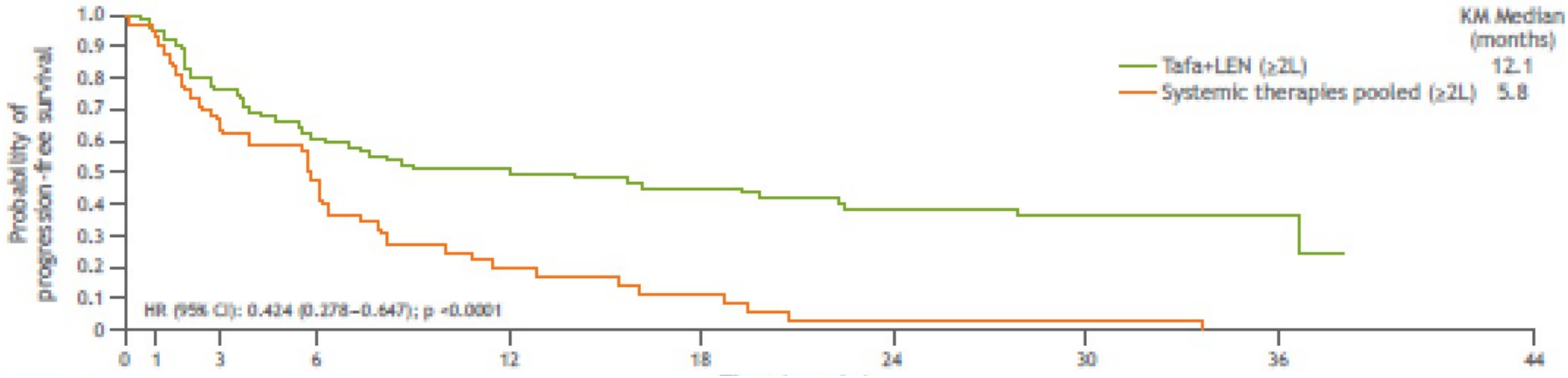
RE-MIND2: PROGRESSION FREE SURVIVAL VS POOLED THERAPIES



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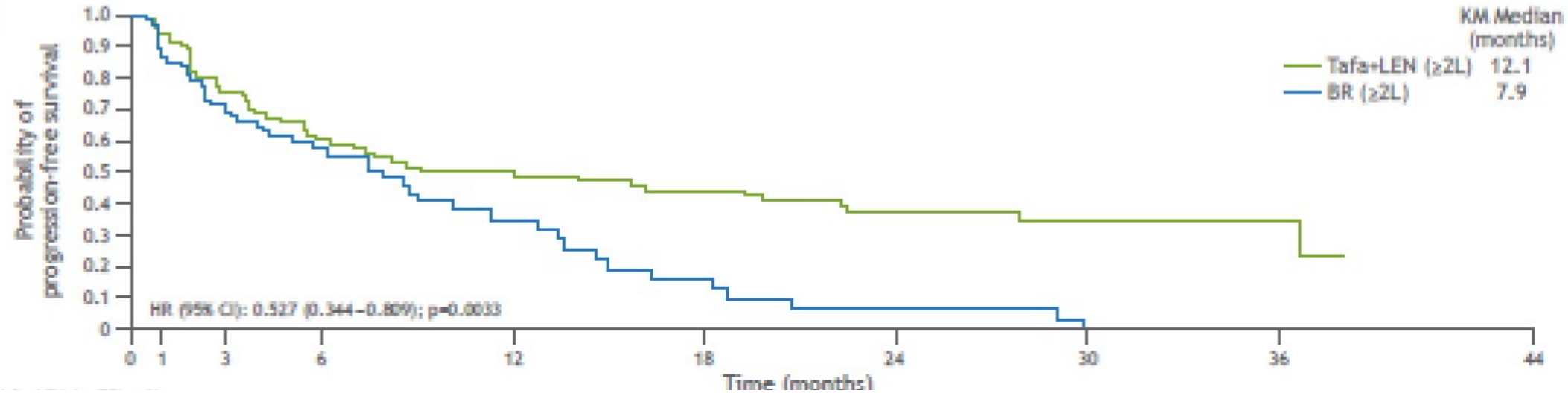
RE-MIND2: PROGRESSION FREE SURVIVAL VS BR



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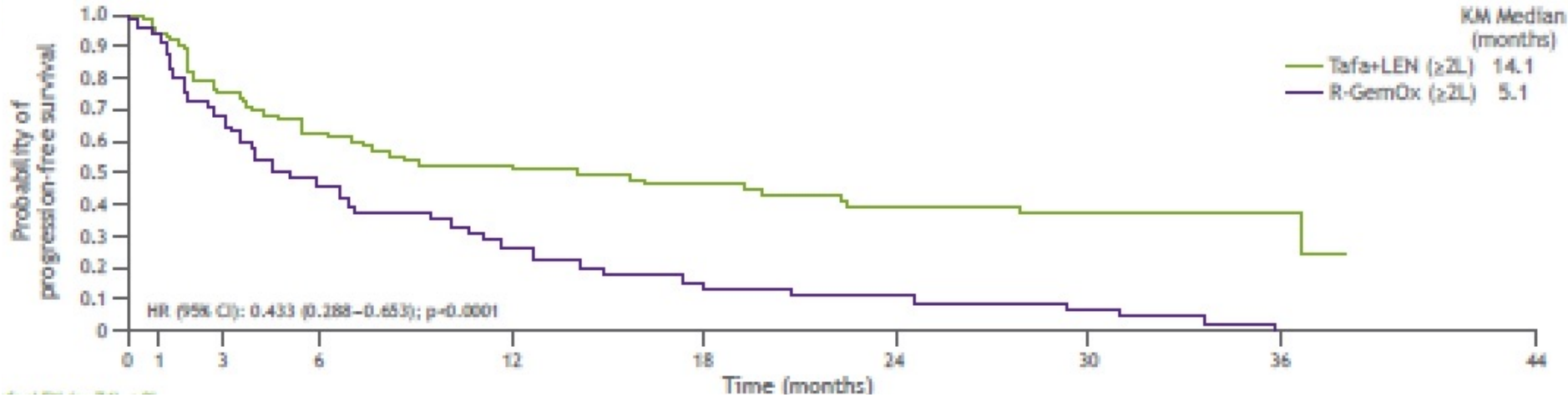
RE-MIND2: PROGRESSION FREE SURVIVAL VS R-GEMOX



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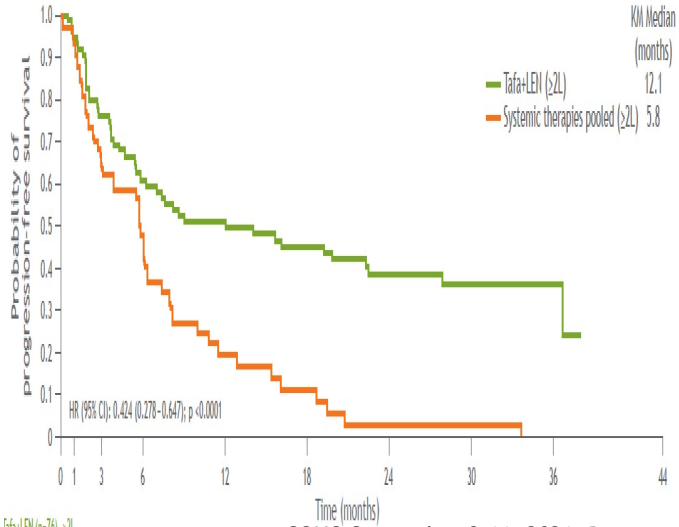
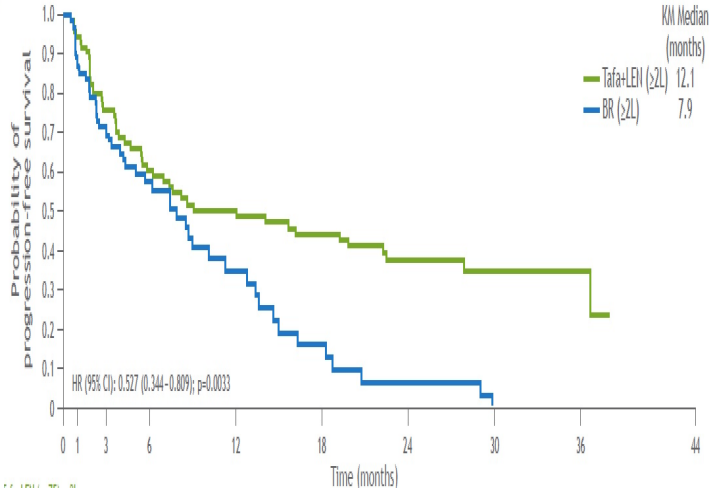
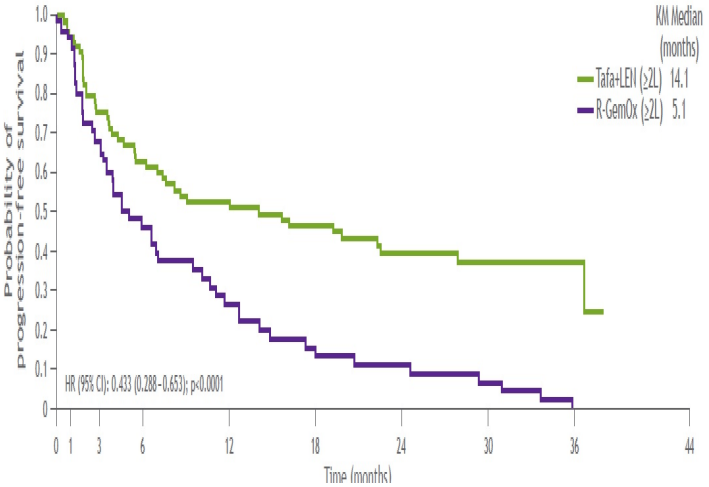
RE-MIND2: PROGRESSION FREE SURVIVAL

	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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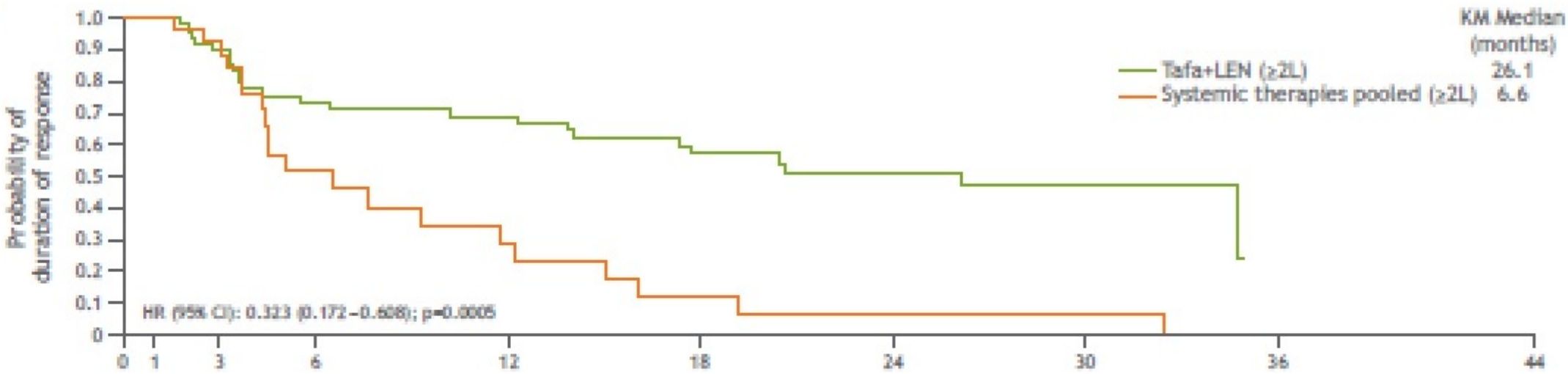
RE-MIND2: DURATION FO RESPONSE VS POOLED THERAPIES



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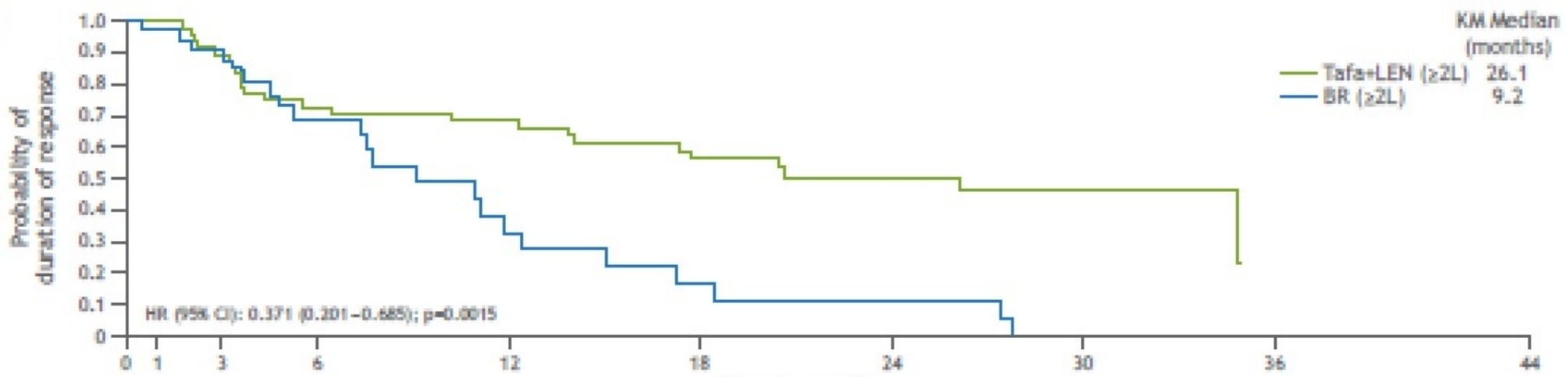
RE-MIND2: DURATION OF RESPONSE VS BR



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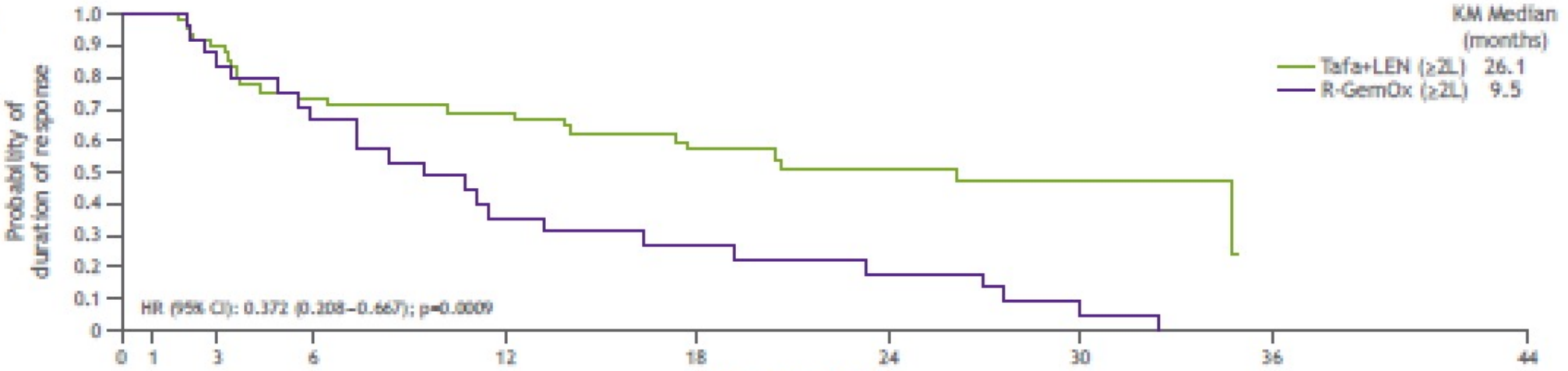
RE-MIND2: DURATION OF RESPONSE VS R-GEMOX



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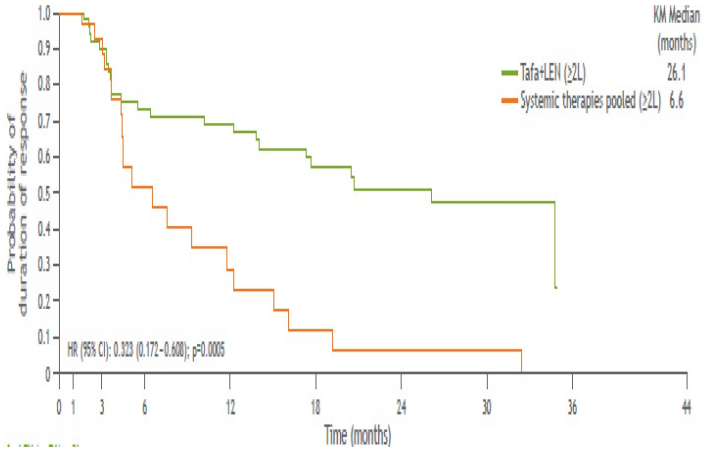
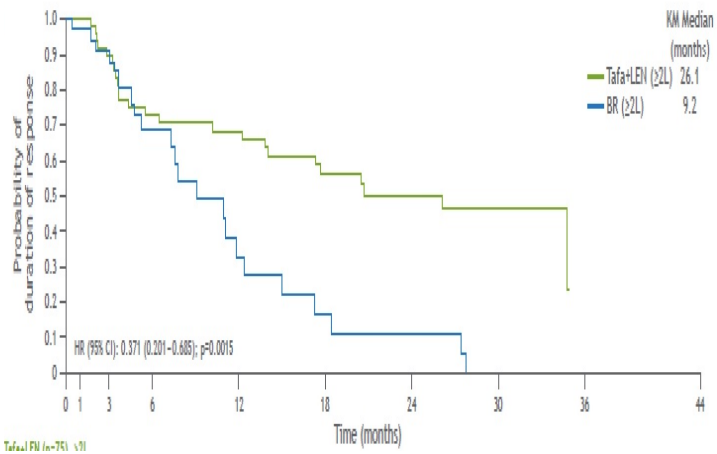
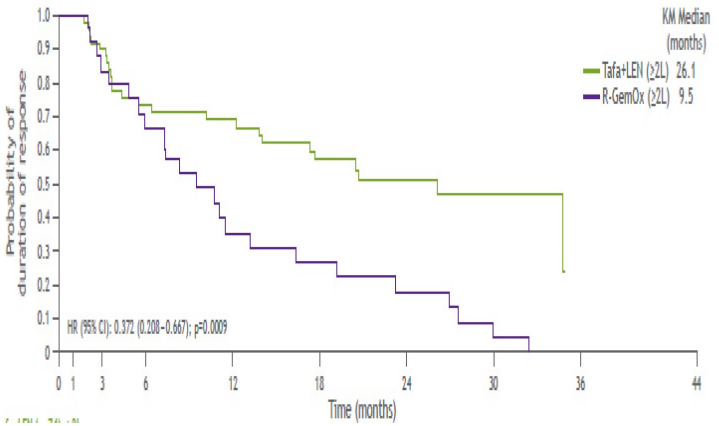
RE-MIND2: DURATION OF RESPONSE

	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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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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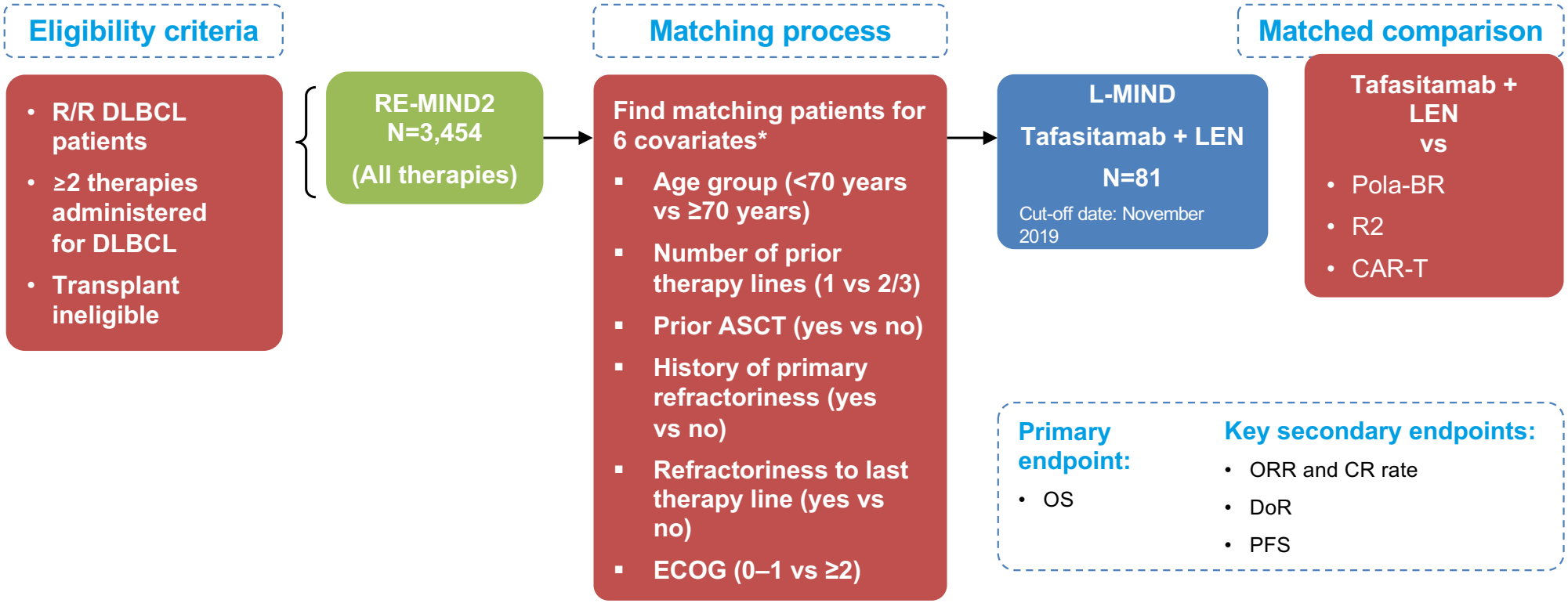
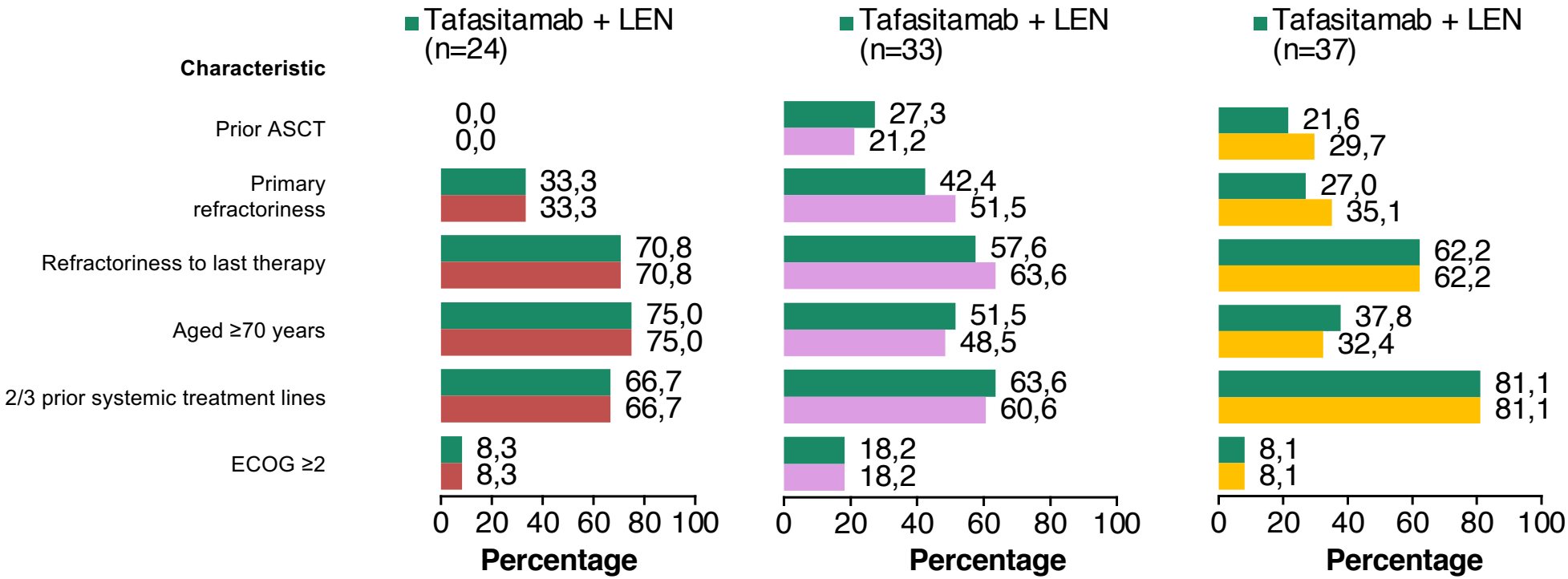
RE-MIND2 expanded analysis study design



G. S. Nowakowski, Saturday, ASH December 11, 2021

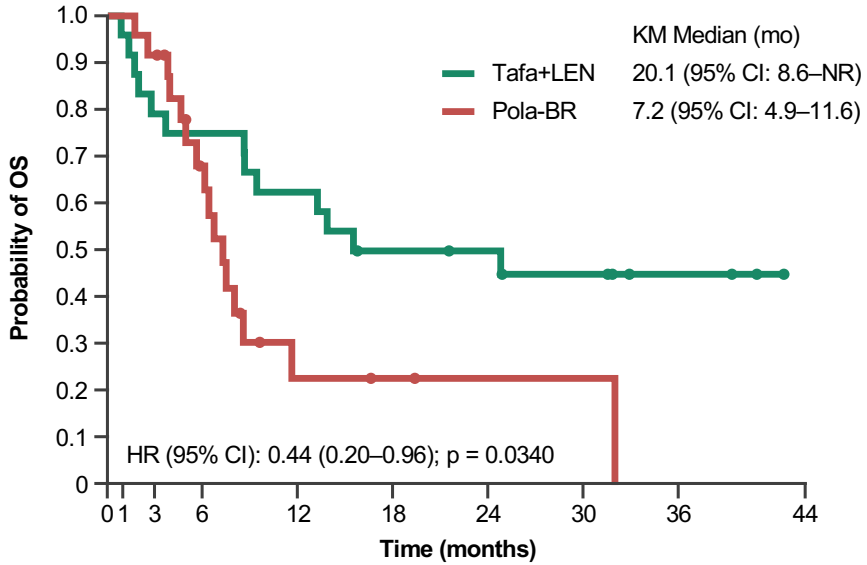
Results: Baseline characteristics for tafasitamab + LEN versus Pola-BR, R2, and CAR-T

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

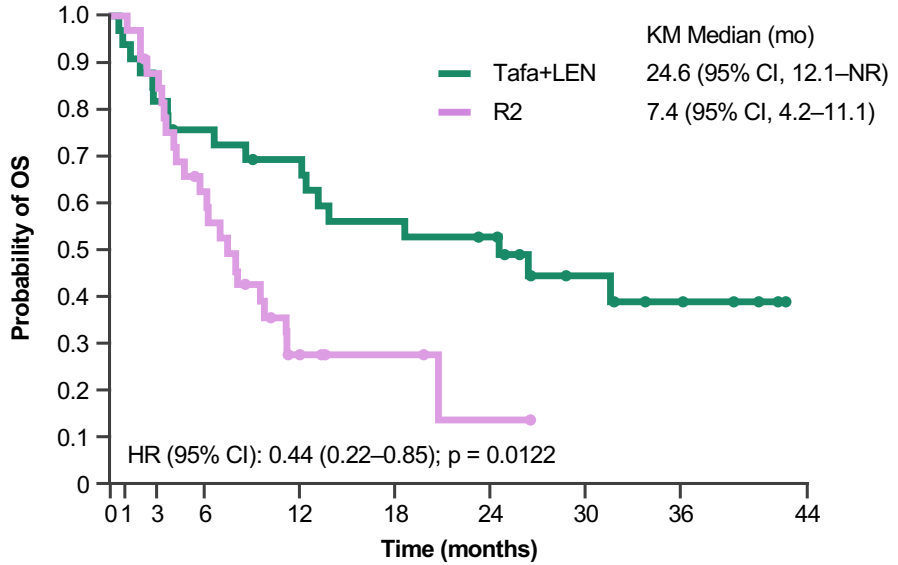


- ASCT, autologous stem-cell transplant; CAR-T, CD19 chimeric antigen receptor T-cell therapies; ECOG, Eastern Cooperative Oncology Group; LEN, lenalidomide; Pola-BR, polatuzumab vedotin plus bendamustine plus rituximab; R2, rituximab plus lenalidomide.

Primary endpoint: OS



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

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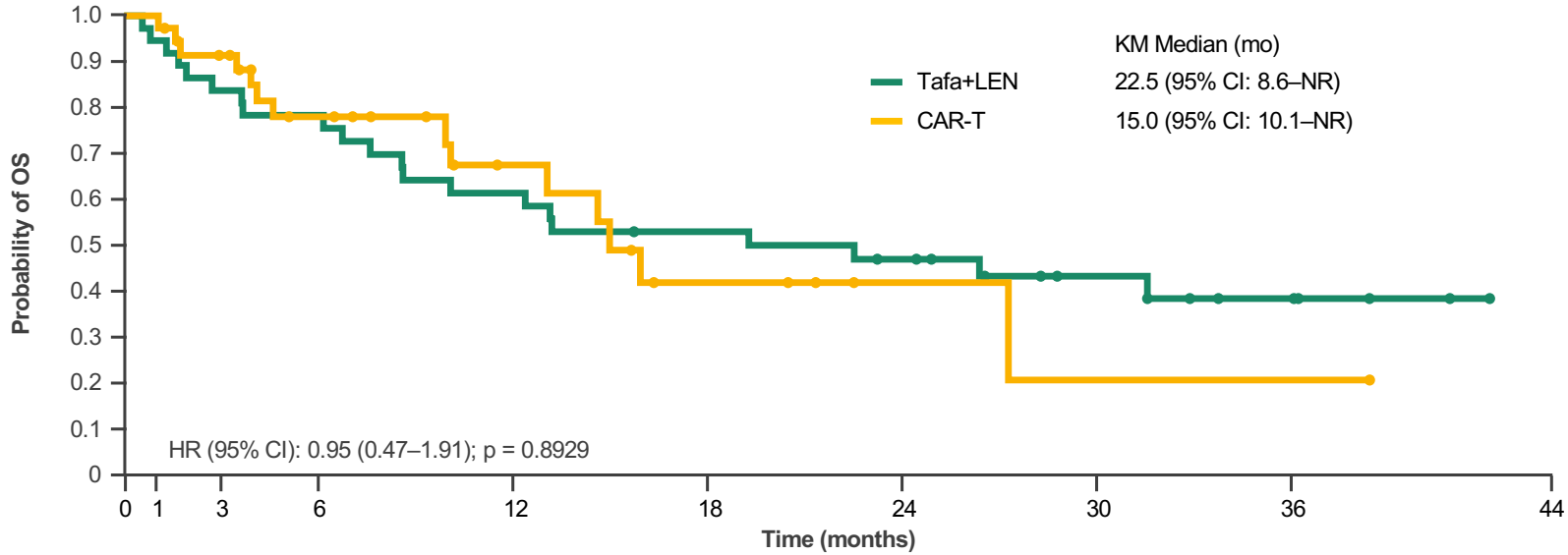
Primary endpoint: OS

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



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

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Secondary endpoints: PFS and DoR

- Tafasitamab + LEN was associated with statistical and clinically meaningful improvements in PFS

	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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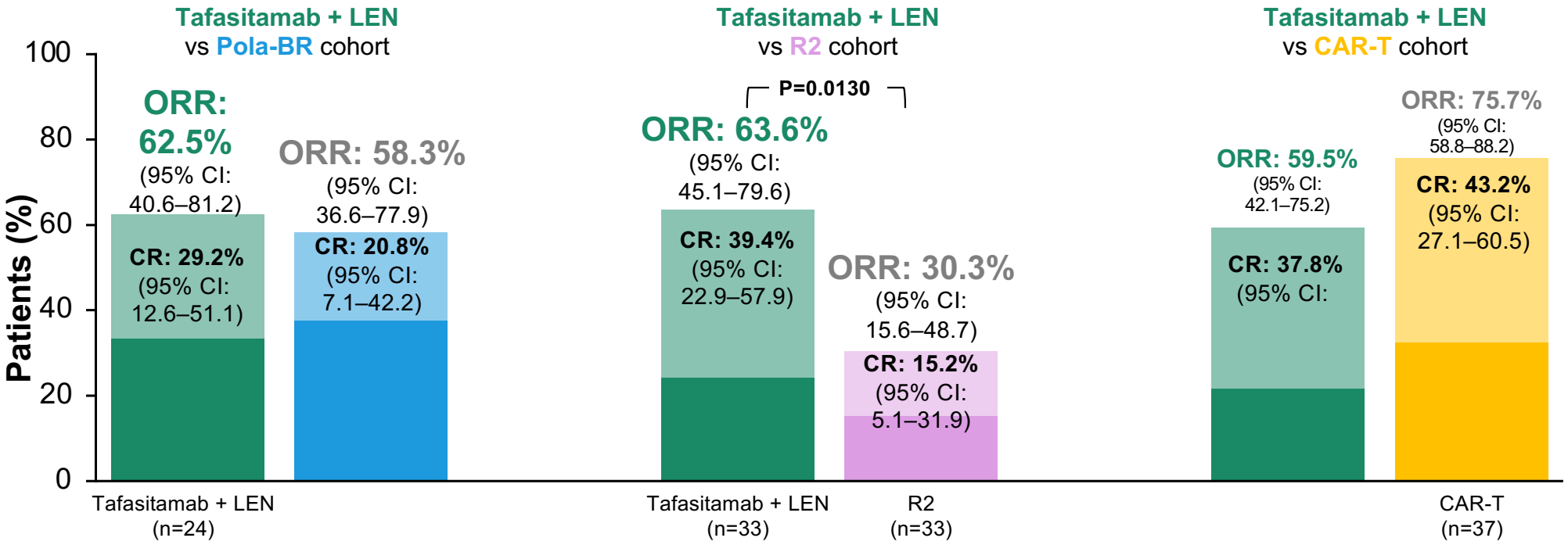
Secondary endpoint: ORR and CR rate

- 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



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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
- 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

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