SINTOMA'25

8 A 10 DE MAIO

HOTEL INTERCONTINENTAL | SÃO PAULO

PARCERIA soho society of hematologic oncology

APOIO INSTITUCIONAL bp Educação e Pesquisa

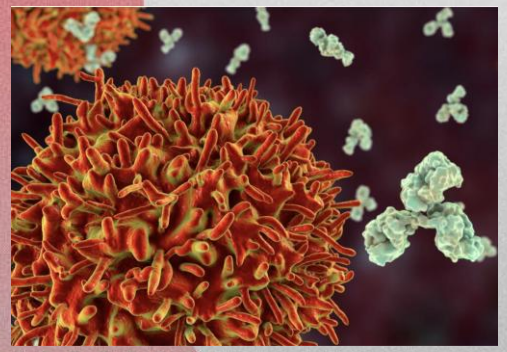
SINTOMA'25

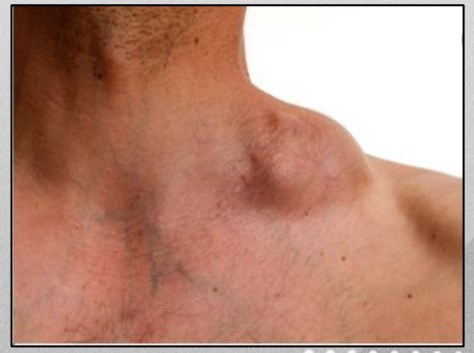
PARCERIA soho society of hematologic oncology

APOIO INSTITUCIONAL bp Educação e Pesquisa

DADOS DE TAFASITAMABE + LENALIDOMIDA

NESSES PACIENTES





DANIELLE LEÃO

Hematologista e Pesquisadora Clínica

BP – A Beneficência Portuguesa de SP

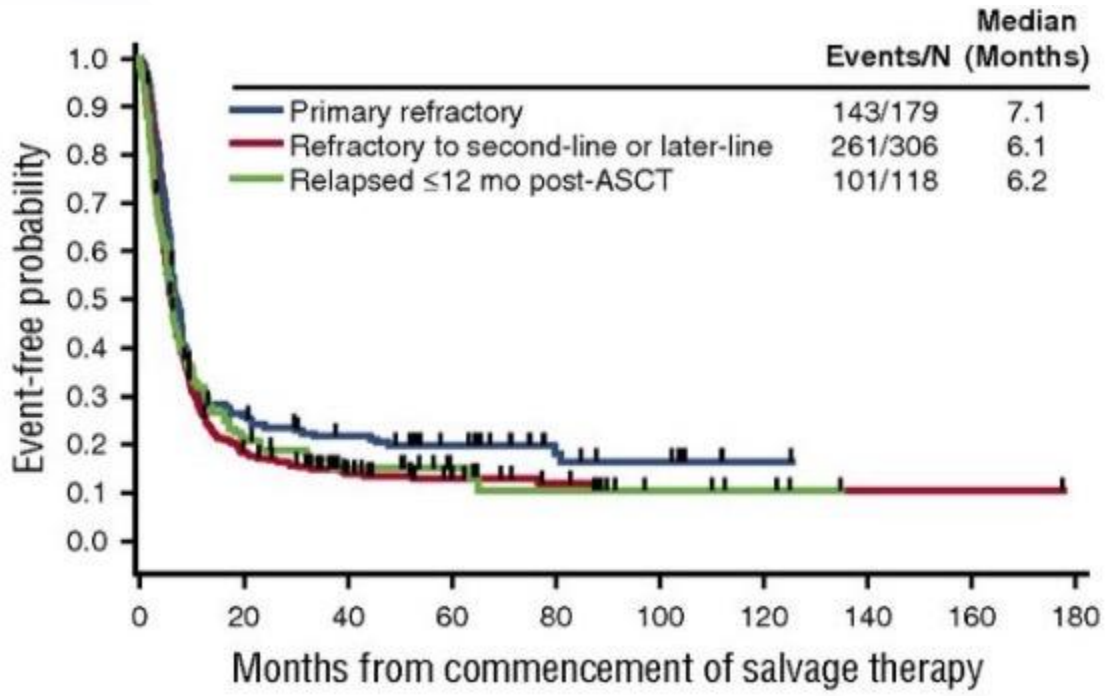
CROMA Oncologia

DISCLOSURES - DECLARAÇÃO DE CONFLITOS DE INTERESSE

Patrocínio para esse evento	Knight Therapeutics
Instituição	BP - Beneficencia Portuguesa de Sao Paulo e CROMA Oncologia
Participação em estudos clínicos (Indústria farmacêutica)	Roche, Novartis, GSK, Janssen, Millenium Takeda, ABBVIE, Daichii Sankyo, Pfizer, Celltrion, BMS, AstraZeneca, Viracta, Sandoz, AGIOS, Astellas, MEDAC, Onconova, MSD, Sanofi, Regeneron, Lilly, ADC Therapeutics, Libbs, Beigene
Participação em estudos clínicos (ITT, RWE ou registros)	T-Cell Project, HOLA registry, MMyBrave registry, REALITY WW, , Brazilian Group of CLL, Brazilian Group of Multiple myeloma, AML-Brazil, Coalizão COVID Brazil,
Palestrante	Janssen, AstraZeneca, Zodiac, Roche, Novartis, Takeda, AMGEN, Roche, Libbs, BMS, Celgene, Pfizer, ABBVIE, Sanofi, Pintfarma, Knight Therapeutics/United Medical
Membro de Advisory Board	Kite/Gilead, Knight Therapeutics/United Medical, Janssen, Novartis, AMGEM, Takeda, Roche, BMS, ABBVIE, Libbs, Celgene, Eurofarma,
Membro de Steering Committee	Janssen
Membro de Independent Data Monitoring Committee	Libbs /Mabxcience
Afiliação	ASH, EHA, ESO, IMS, CDCN (Castleman disease), ABHH (Associaçao Brasileira de Hematologia), Coordinator of Clinical Research Committee at ABHH, Myeloma Committee (ABHH), CLL Committee (ABHH), Lymphoma Committee (ABHH)

Realidade dos pacientes com LDGCB refratário: SCHOLAR-1

SCHOLAR-1 é um estudo retrospectivo que analisou dados de 636 pacientes com LDGCB refratário de 2 grandes estudos randomizados e 2 bancos de dados acadêmicos.



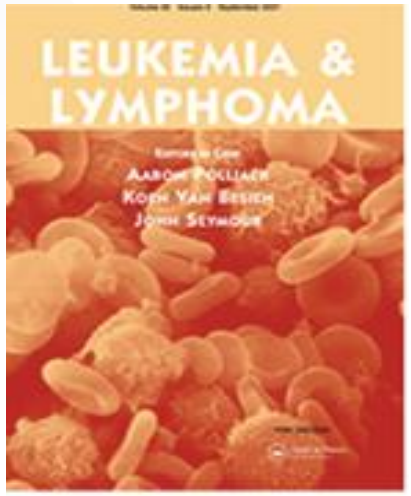
- Idade mediana 55 anos (19-81)
- Estádio III/IV: 72%
- RG 20% a 30% (26%)
- RC 2% a 15% (7%)
- Pior resposta: refratário primário/Alto risco

A Mediana de Sobrevida Global em pacientes com pelo menos 2 linhas de terapia foi 6,3 meses (95%CI, 5,9-7 meses)

Crump M, et al. Blood. 2017 Oct 19;130(16):1800-1808.

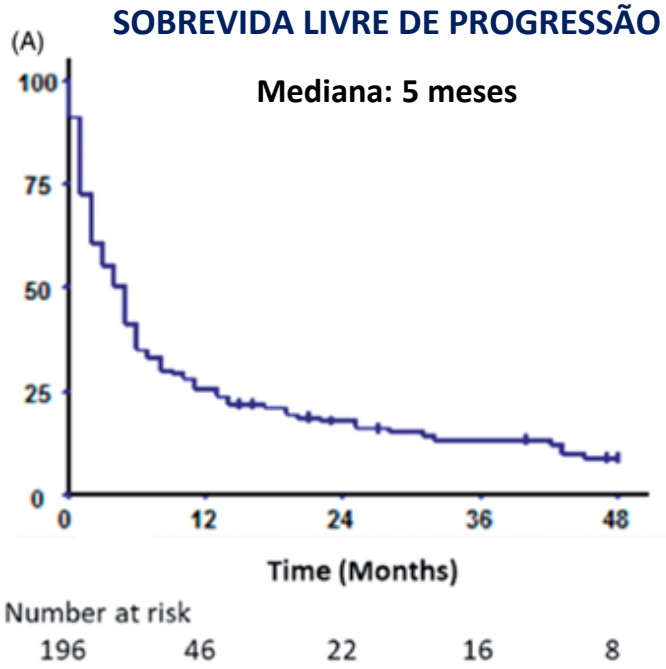
R-GEMOX EM 2ª LINHA

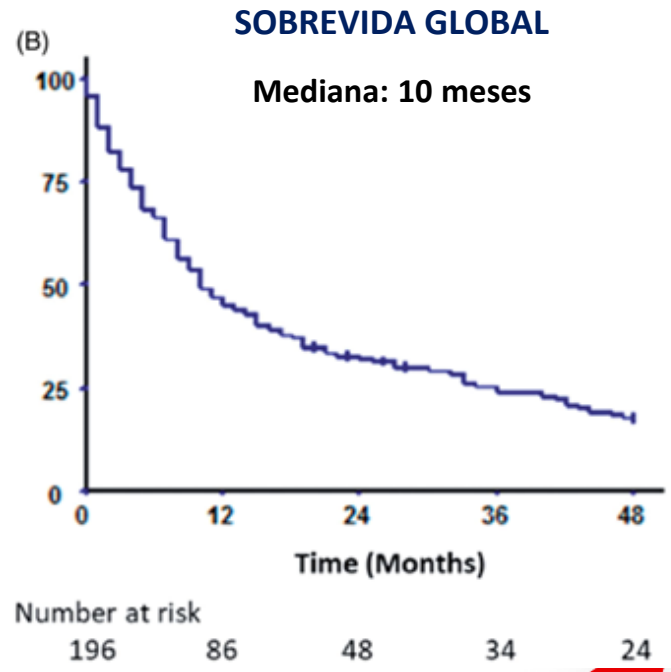
DADOS DE VIDA REAL



Rituximab plus gemcitabine and oxaliplatin (R-GemOx) in refractory / relapsed diffuse large B-cell lymphoma: a real-life study in patients ineligible for autologous stem-cell transplantation

- Mediana de Idade : 72 anos (24 a 89)
- Refratários ao último tratamento: 57%
- Linhas de tratamento prévias:
  - 1: 58%
  - 2 ou mais: 42%
- Taxa de Resposta Completa: 23%



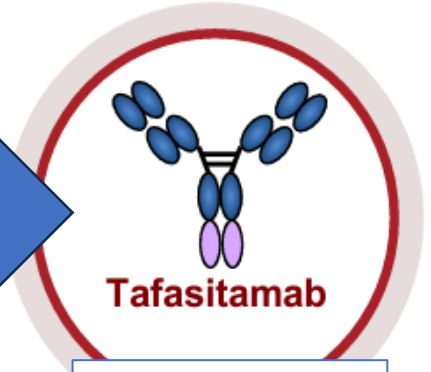


Cazelles C et al. Leuk Lymphoma 2021 Sep;62(9):2161

ANTICORPOS NO TRATAMENTO DOS LNH B

NAKED ANTIBODY

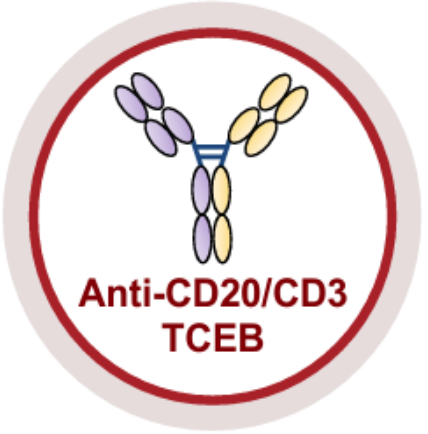
ENGINEERED ANTIBODY



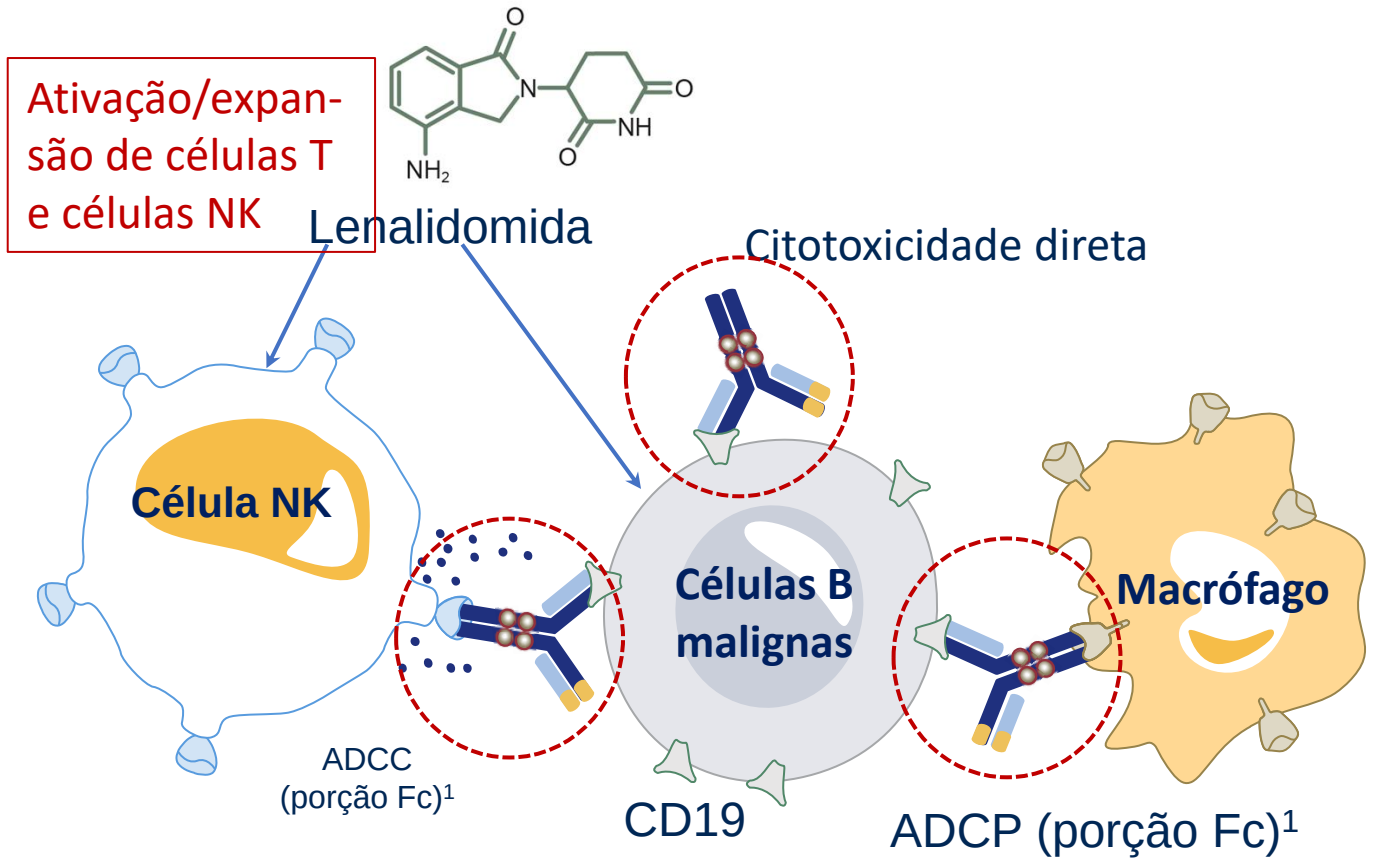
Anti-CD19

ANTIBODY DRUG CONJUGATED

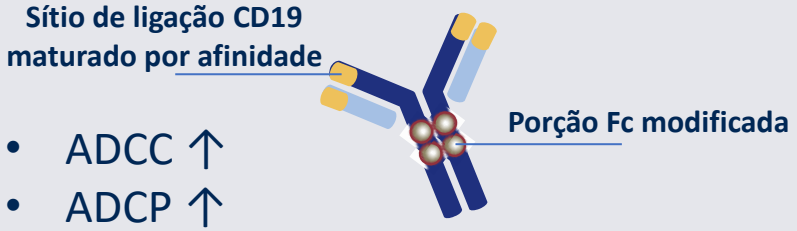
BIESPECIFIC ANTIBODY



Tafasitamabe e lenalidomida: uma nova combinação imunológica



Tafasitamabe-cxix (Fc-modificado, anti-CD19 mAb)[1–4]



- ADCC ↑
- ADCP ↑
- Morte celular direta

Lenalidomida[5,6]

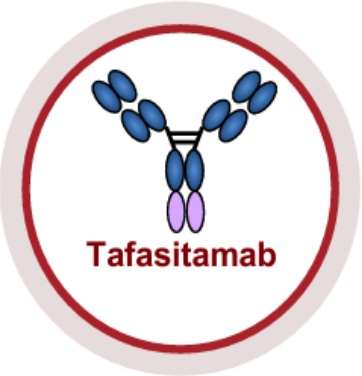
- Ativação/expansão de células T e células NK
- Morte celular direta
- Agente anti-linfoma, sozinho ou em combinação

ADCC, citotoxicidade celular dependente de anticorpos; ADCP, fagocitose celular dependente de anticorpos.

1. Horton HM, et al. *Cancer Res* 2008;68(19):8049–57. 2. Woyach JA, et al. *Blood* 2014;124(24):3553–60. 3. Jurczak W, et al. *Ann Oncol* 2018;29(5):1266–72. 4. Awan FT, et al. *Blood.* 2010;115(6):1204-1213. 5. Witzig TE, et al. *Ann Oncol* 2015; 26(8):1667–77. 6. Czuczman MS, et al. *Clin Cancer Res* 2017;23(15):4127–37.

TAFASITAMABE (MINJUVI®)

INDICAÇÃO



- **Tafasitamabe** com **lenalidomida** (12 ciclos) seguida de monoterapia com **tafasitamabe até progressão**
- A**dultos** com LDGCB **recidivado** ou **refratário não elegíveis para transplante autólogo de células-tronco**

→ Aprovado também para **linfoma de baixo grau transformado para LDGCB**!

Bula de Minjuvi® ANVISA

L-MIND

*Idade, comorbidades, refratariedade QT, recaída pós TACTH, falha de mobilização.

35 centros – Europa e EUA

Fase 2, estudo de braço único, aberto, multicêntrico (NCT02399085)

LDGCB R/R

- 1-3 regimes prévios
- Não elegível p/TACTH*
- Os Refratários primários excluídos *(Mas DP de 3 a 6 meses entrou)

Ciclo 1-3

Tafasitamabe
12 mg/kg IV
q4w; d 1, 8, 15, 22 [b]

+

Lenalidomida
25 mg/d po[d1-21]

Ciclo 4-12

Tafasitamabe-
12 mg/kg IV
q4w; d 1, 15

+

DE
RP
RC

Ciclo 12+

Tafasitamabe-cxix
12 mg/kg
d 1, 15

ATÉ PROGRESSÃO

DESFECHO PRIMÁRIO
Taxa de Resposta Objetiva (avaliação central)

Tamanho da amostra adequado para detectar ≥15% de aumento absoluto da ORR para a combinação Tafasitamabe-cxix/LEN versus monoterapia com LEN a 85% de potência, alfa de 2 lados de 5%.

Dados maduros: análise de desfecho primário com ponto de corte de dados de 30 de novembro de 2018; seguimento mínimo para o desfecho primário 12 meses, mediana de acompanhamento de 13,2 meses

DESFECHOS SECUNDÁRIOS

- SLP
- Duração de Resposta Objetiva
- SG
- Segurança da combinação Tafasitamabe + LEN
- Análises exploratórias e baseadas em biomarcadores

[a] ASCT, transplante autólogo de células-tronco; CR, resposta completa; DOR, Duração da resposta; HDC, quimioterapia em altas doses; IV, intravenoso; LEN, Lenalidomida; ORR, taxa de resposta global; OS, sobrevida global; PFS, sobrevida livre de progressão; po, oralmente; PR, resposta parcial; SD, doença estável.
Salles G, et al. *Lancet Oncol.* 2020;21(7):978-988.

Esquema terapêutico

Tafasitamabe 12mg/kg IV + 25 mg Lenalidomida VO, ciclos de 28 dias

MINJUVI e lenalidomida – Esquema de administração

Ciclo 1

Days	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
MINJUVI IV 12 mg/kg	■			■				■							■							■						
Lenalidomide PO 25 mg daily	●	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	●							

Ciclos 2 e 3

Days	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
MINJUVI IV 12 mg/kg	■							■							■							■						
Lenalidomide PO 25 mg daily	●	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	●							

Ciclos 4 a 12

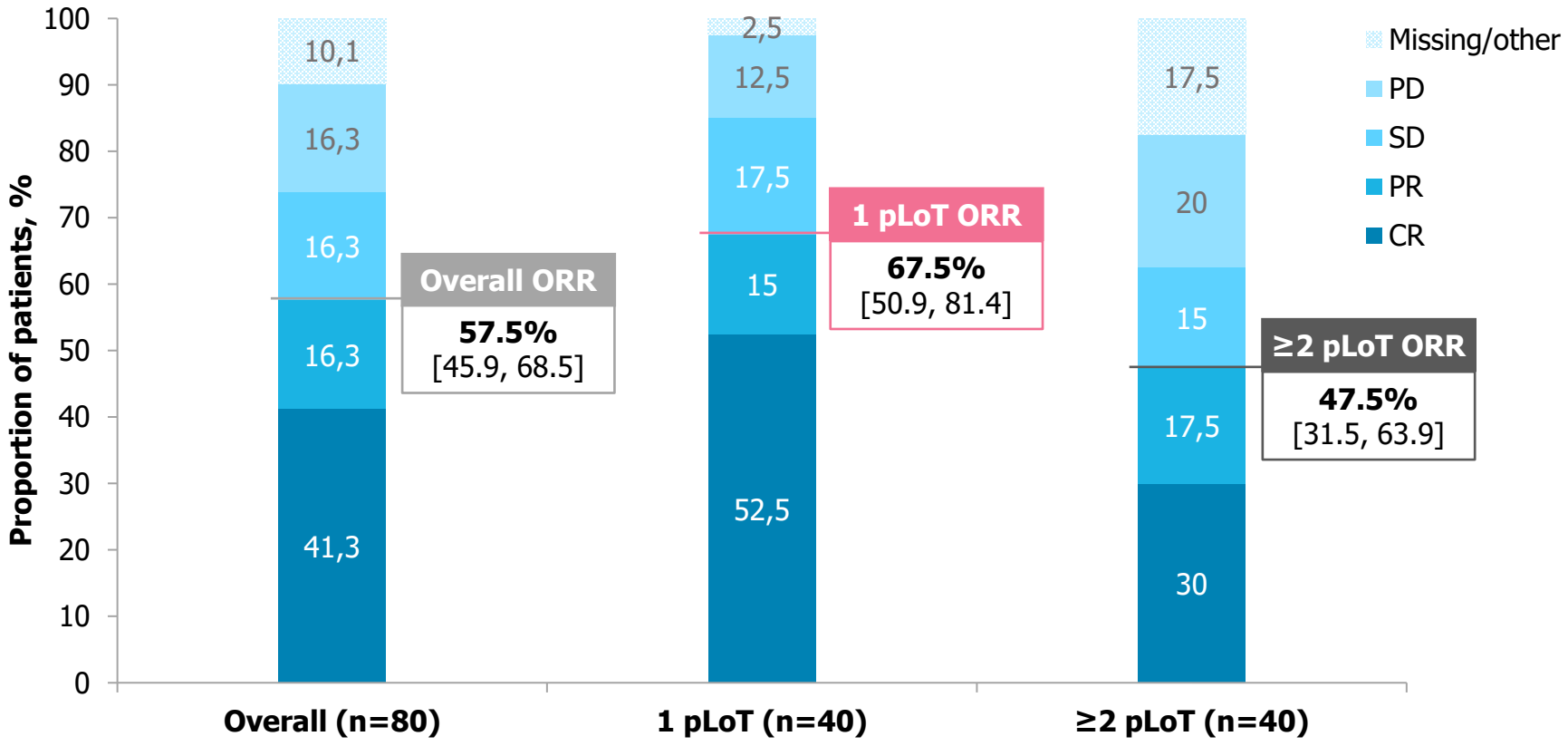
Days	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
MINJUVI IV 12 mg/kg	■														■													
Lenalidomide PO 25 mg daily	●	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	●							

Após 12 ciclos - MINJUVI monoterapia até progressão doença ou toxicidade inaceitável

Days	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
MINJUVI IV 12 mg/kg	■														■													

- **12 ciclos Tafasitamabe + lenalidomida**
- **Tafasitamabe até a progressão ou outro critério de suspensão**

L-MIND: ORR at 5-year Follow-up[1,2]



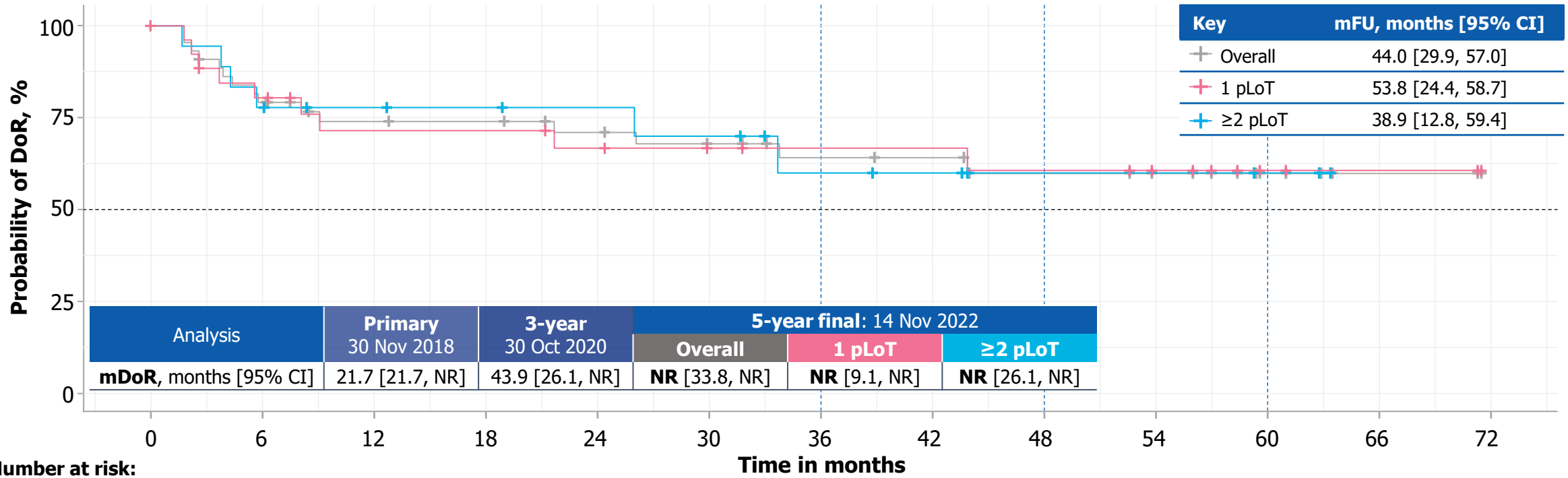
- ORR (FAS) was generally consistent with the primary and 3-year analyses
- Patients with 1 pLoT had higher ORR compared with patients with ≥2 pLoT

Data Cut-off Date: 14 November 2022.

CR, complete response; FAS, full analysis set; ORR, objective response rate; PD, progressive disease; pLoT, prior line of therapy; PR, partial response; SD, stable disease.

1. Kalakonda N (Presenter): Duell J, et al. Oral presented at AACR annual meeting; 14-16 April 2023: Orlando, Florida [Abstract #9810]; 2. Duell J, et al. *Haematologica*. 2024;109(2):553-566.

L-MIND: DoR at 5-year Follow-up



Analysis	Primary 30 Nov 2018	3-year 30 Oct 2020	5-year final: 14 Nov 2022		
			Overall	1 pLoT	≥2 pLoT
mDoR, months [95% CI]	21.7 [21.7, NR]	43.9 [26.1, NR]	**NR** [33.8, NR]	**NR** [9.1, NR]	**NR** [26.1, NR]

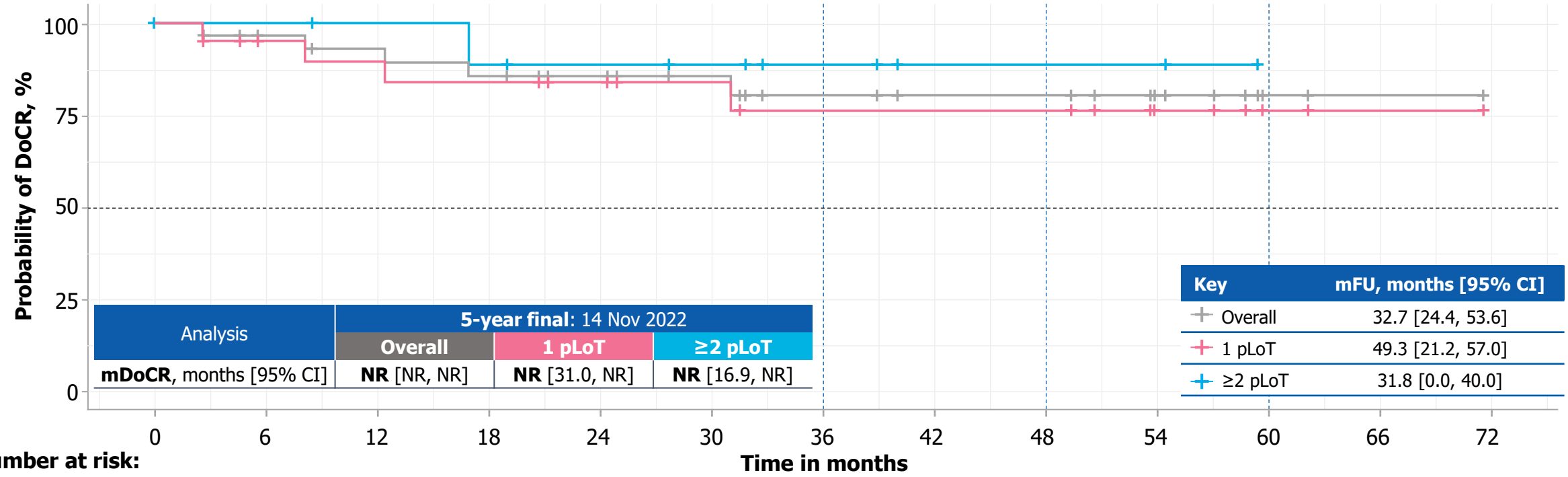
Number at risk:

Overall	46	34	28	27	24	21	17	16	13	11	5	2	0
1 pLoT	27	20	16	16	14	12	11	11	10	8	3	2	0
≥2 pLoT	19	14	12	11	10	9	6	5	3	3	2	0	0

After a median follow-up of 44.0 months, mDoR was not reached

Data Cut-off Date: 14 November 2022.
Data are from the FAS (n=80) and exploratory subgroups by pLoT (1 pLoT, n=40; ≥2 pLoT, n=40).
CI, confidence interval; DoR, duration of response; mDoR, median DoR; mFU, median follow-up; NR, not reached; pLoT, prior line of therapy.
Duell J, et al. *Haematologica*. 2024;109(2):553-566.

L-MIND: DoCR at 5-year Follow-up



Analysis	5-year final: 14 Nov 2022		
	Overall	1 pLoT	≥2 pLoT
mDoCR, months [95% CI]	**NR** [NR, NR]	**NR** [31.0, NR]	**NR** [16.9, NR]

Key	mFU, months [95% CI]
Overall	32.7 [24.4, 53.6]
1 pLoT	49.3 [21.2, 57.0]
≥2 pLoT	31.8 [0.0, 40.0]

Number at risk:

Overall	33	27	25	23	20	17	13	11	11	7	2	1	0
1 pLoT	21	17	16	15	13	11	9	9	9	5	2	1	0
≥2 pLoT	12	10	9	8	7	6	4	2	2	2	0	0	0

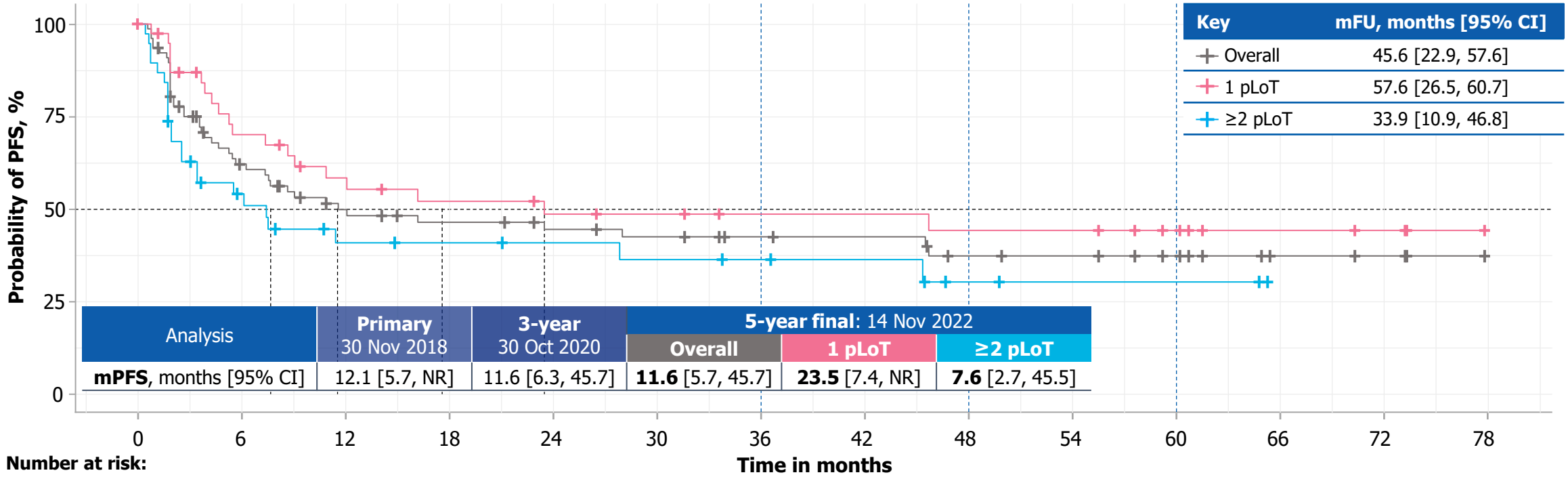
The 5-year DoCR estimate was 80.7% (95% CI: 59.1, 91.6)

Data Cut-off Date: 14 November 2022.

CI, confidence interval; DoCR, duration of complete response; mDoCR, median duration of complete response; mFU, median follow-up; NR, not reached; pLoT, prior line of therapy.

Duell J, et al. *Haematologica*. 2024;109(2):553-566.

L-MIND: PFS at 5-Year Follow-up



Number at risk:

Overall	80	42	30	26	23	21	18	17	13	12	9	4	3	0
1 pLoT	40	25	19	16	14	13	11	11	10	10	7	4	3	0
≥2 pLoT	40	17	11	10	9	8	7	6	3	2	2	0	0	0

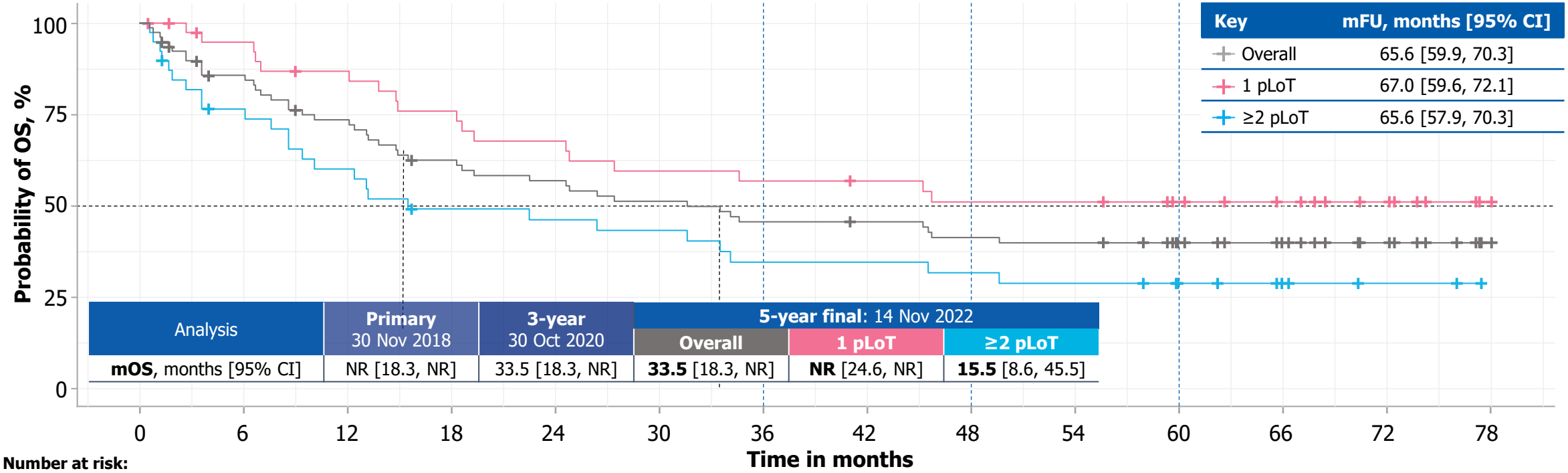
After a median follow-up of 45.6 months, mPFS was 11.6 months

Data Cut-off Date: 14 November 2022.

CI, confidence interval; mFU, median follow-up; mPFS, median PFS; NR, not reached; PFS, progression-free survival; pLoT, prior line of therapy.

Duell J, et al. *Haematologica*. 2024;109(2):553-566.

L-MIND: OS at 5-year Follow-up



Number at risk:

Overall	80	64	54	45	41	37	33	32	29	28	21	15	9	1
1 pLoT	40	36	32	28	25	22	21	20	18	18	14	11	7	1
≥2 pLoT	40	28	22	17	16	15	12	12	11	10	7	4	2	0

After a median follow-up of 65.6 months, mOS was 33.5 months

Data Cut-off Date: 14 November 2022.

CI, confidence interval; mFU, median follow-up; mOS, median OS; NR, not reached; OS, overall survival; pLoT, prior line of therapy.

Duell J, et al. *Haematologica*. 2024;109(2):553-566.

L-MIND – SEGURANÇA – 5 ANOS

Evento	All grades (≥10%) All patients (N=81)	Grade ≥3 (>1 patient) All patients (N=81)
Incidência de EAET não-hematológicos , n (% of patients)		
Redução de appetite	18 (22.2)	0
Hipocalemia	15 (18.5)	5 (6.2)
Tosse	24 (29.6)	1 (1.2)
Dispneia	11 (13.6)	2 (2.5)
Dor nas costas	16 (19.8)	3 (3.7)
Espasmos musculares	12 (14.8)	0
Aumento da proteina C reativa	9 (11.1)	0

- Interrupções temporárias de tafasitamabe: n= 65,
- Interrupção de Lenalidomida N= 28
- Descontinuação de tafasitamabe por EA: 19,8% (n= 16)
- Descontinuação de Lenalidomida por EA: 22,2% (N= 18)
- 7,4% (n=6) óbitos por eventos adversos
- Nenhum óbito por EA relacionado ao tratamento

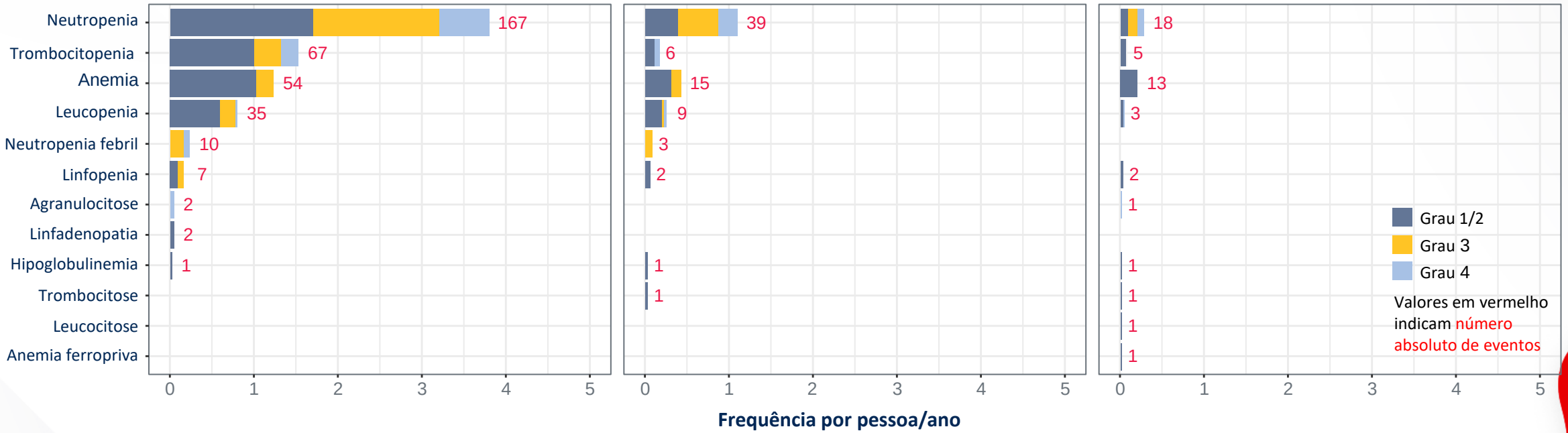
Data Cut-off Date: 14 November 2022.
aMost frequent treatment-emergent SAEs were pneumonia (8.6%), febrile neutropenia (6.2%), neoplasms (4.9%), pulmonary embolism and COVID-19 infections (3.7% each), bronchitis, lower respiratory tract infection, dyspnea, atrial fibrillation, and congestive cardiac failure (2.5% each).
LEN, lenalidomide; SAEs, serious adverse events; TEAE, treatment-emergent adverse event.
Duell J, et al. Haematologica. 2023. doi: 10.3324/haematol.2023.283480.

L-MIND – SEGURANÇA – 5 ANOS

TEAEs hematológicos

Exposição ao tratamento, pessoas/ano

Terapia combinada ou Lenalidomida (N=80)	Monoterapia com Tafasitamabe-cxix até 2 anos (N=52)	Monoterapia com Tafasitamabe-cxix além de 2 anos (N=27)
44.06	35.67	64.01



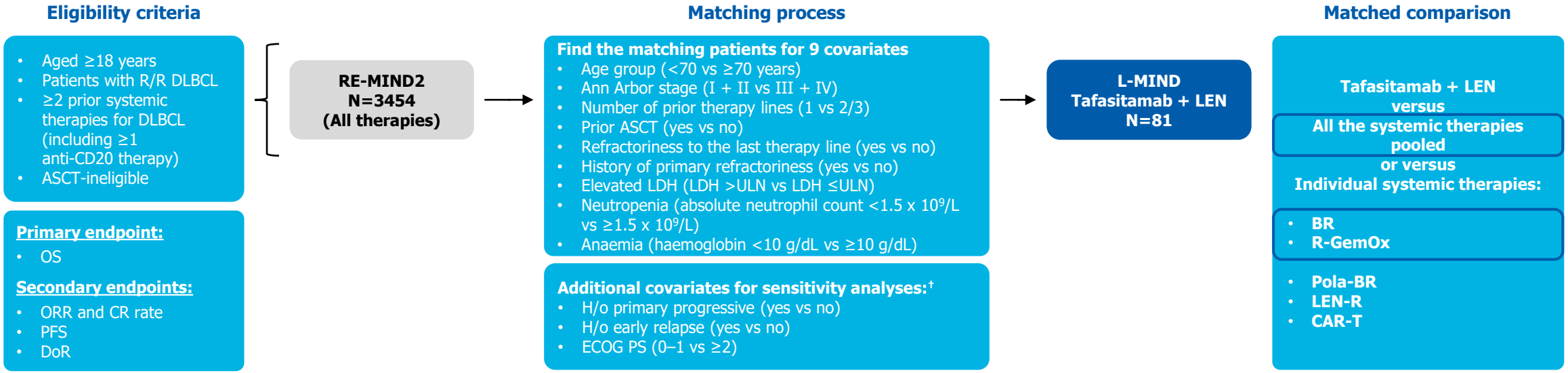
Os TEAEs hematológicos foram menos frequentes durante a monoterapia com Tafasitamabe-cxix em comparação com a terapia combinada com Tafasitamabe-cxix + Lenalidomida

A baixa incidência de TEAEs com Tafasitamabe-cxix em monoterapia até 2 anos foi mantida ou reduzida a partir de 2 anos

RE-MIND2: Tafasitamab + LEN vs Systemic Therapies Pooled or BR or R-GEmOx (Primary Analysis)

A retrospective, observational, cohort study to characterise the effectiveness of tafasitamab + LEN, in a real-world setting, relative to commonly administered systemic therapies for ASCT-ineligible patients with R/R DLBCL

Routinely administered the R/R DLBCL treatments as matched control for L-MIND*

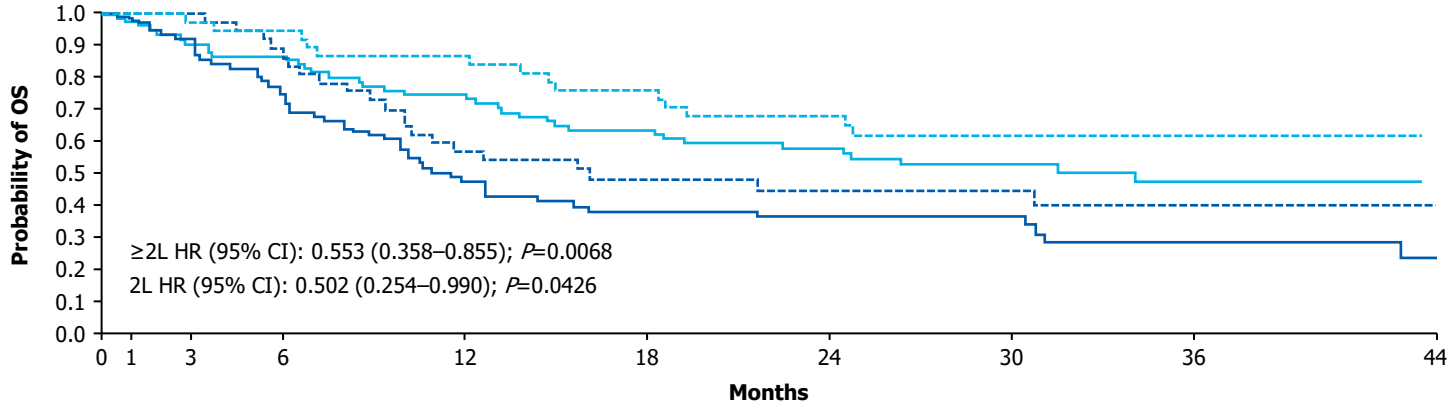


*The assessment time frame for tafasitamab + LEN was March 2016 to November 2017. †The covariate 'history of primary refractoriness' is represented by 'primary progressive' and 'early relapse' in the sensitivity analyses.
ASCT, autologous stem cell transplantation; BR, bendamustine + rituximab; CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; H/o, history of; LDH, lactate dehydrogenase; LEN, lenalidomide; LEN-R, LEN plus rituximab; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Pola-BR, polatuzumab vedotin + bendamustine + rituximab; R-GemOx, rituximab + gemcitabine + oxaliplatin; R/R, relapsed/refractory; ULN, upper limit of normal.

Nowakowski G, et al. *Clin Cancer Res*. 2022;28:4003-4017.

Primary Endpoint: OS (1/3)

Tafasitamab + LEN was associated with statistically significant improvements in OS versus systemic pooled therapies



	KM median (months)
Tafasitamab + LEN (n=76), ≥2L	34.1
Systemic therapies pooled (n=76), ≥2L	11.6
Tafasitamab + LEN (n=39), 2L	NR
Systemic therapies pooled (n=39), 2L	16.1

Tafasitamab + LEN (n=76), ≥2L

At risk	76	74	68	64	54	45	37	24	14	0
Event(s)	0	2	7	10	19	27	31	34	36	36
Censored	0	0	1	2	3	4	8	18	26	40

Systemic therapies pooled (n=76), ≥2L

At risk	76	75	68	54	33	23	18	14	8	0
Event(s)	0	1	7	19	38	44	45	45	48	49
Censored	0	0	1	3	5	9	13	17	20	27

Tafasitamab + LEN (n=39), 2L

At risk	39	39	37	36	32	28	22	14	10	0
Event(s)	0	0	1	2	5	9	12	14	14	14
Censored	0	0	1	1	2	2	5	11	15	25

Systemic therapies pooled (n=39), 2L

At risk	39	39	38	32	21	16	12	10	6	0
Event(s)	0	0	0	5	16	19	20	20	21	21
Censored	0	0	1	2	2	4	7	9	12	18

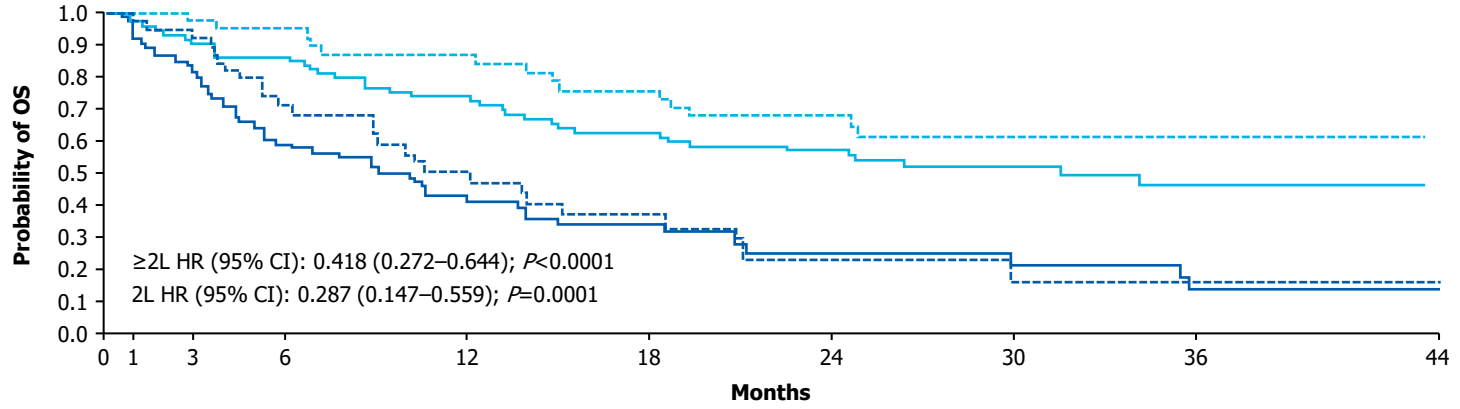
COMPARATORS HAD SAME EFFICACY AS LITERATURE

2L, second-line; CI, confidence interval; HR, hazard ratio; KM, Kaplan–Meier; LEN, lenalidomide; NR, not reached; OS, overall survival.

Nowakowski G, et al. *Clin Cancer Res*. 2022;28:4003-4017.

Primary Endpoint: OS (2/3)

Tafasitamab + LEN was associated with statistically significant improvements in OS versus BR



	KM median (months)
Tafasitamab + LEN (n=75), ≥2L	31.6
BR (n=75), ≥2L	9.9
Tafasitamab + LEN (n=39), 2L	NR
BR (n=39), 2L	12.0

Tafasitamab + LEN (n=75), ≥2L

At risk	75	73	67	63	53	44	36	23	14	0
Event(s)	0	2	7	10	19	27	31	34	36	36
Censored	0	0	1	2	3	4	8	18	25	39

BR (n=75), ≥2L

At risk	75	69	60	42	25	17	10	6	4	0
Event(s)	0	6	15	30	42	46	50	51	53	53
Censored	0	0	0	3	8	12	15	18	18	22

Tafasitamab + LEN (n=39), 2L

At risk	39	39	37	36	32	28	22	14	10	0
Event(s)	0	0	1	2	5	9	12	14	14	14
Censored	0	0	1	1	2	2	5	11	15	25

BR (n=39), 2L

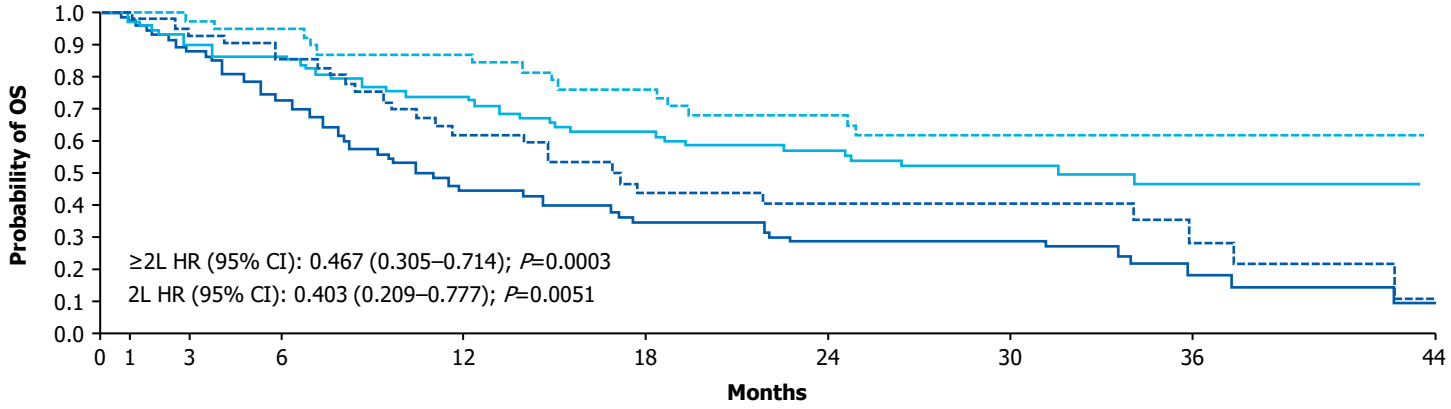
At risk	39	38	36	26	15	9	5	2	2	0
Event(s)	0	1	3	11	19	22	25	26	26	26
Censored	0	0	0	2	5	8	9	11	11	13

2L, second-line; BR, bendamustine + rituximab; CI, confidence interval; HR, hazard ratio; KM, Kaplan–Meier; LEN, lenalidomide; NR, not reached; OS, overall survival.

Nowakowski G, et al. *Clin Cancer Res*. 2022;28:4003-4017.

Primary Endpoint: OS (3/3)

Tafasitamab + LEN was associated with statistically significant improvements in OS versus R-GemOx



	KM median (months)
Tafasitamab + LEN (n=74), ≥2L	31.6
R-GemOx (n=74), ≥2L	11.0
Tafasitamab + LEN (n=39), 2L	NR
R-GemOx (n=41), 2L	16.8

Tafasitamab + LEN (n=74), ≥2L

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), ≥2L

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

Tafasitamab + LEN (n=39), 2L

At risk	39	39	37	36	32	28	22	14	10	0
Event(s)	0	0	1	2	5	9	12	14	14	14
Censored	0	0	1	1	2	2	5	11	15	25

R-GemOx (n=41), 2L

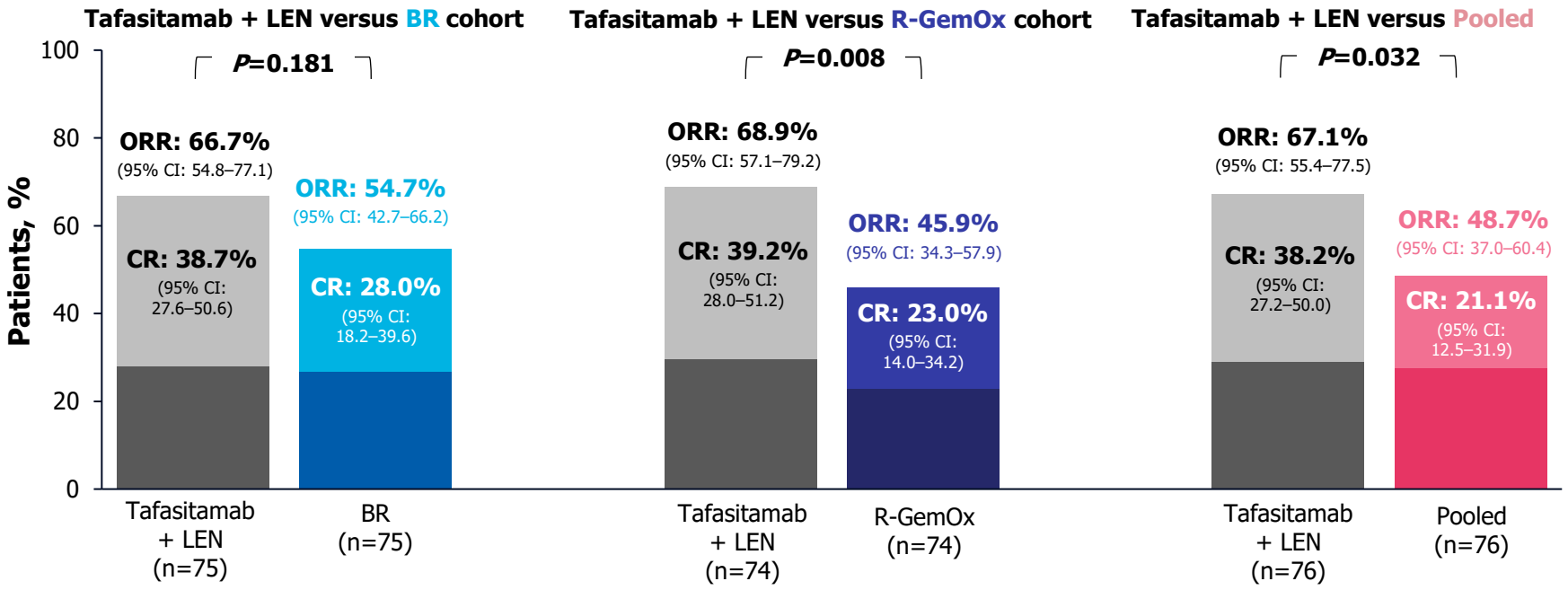
At risk	41	40	38	34	22	14	10	8	4	0
Event(s)	0	1	3	6	15	21	22	22	24	26
Censored	0	0	0	1	4	6	9	11	13	15

2L, second-line; CI, confidence interval; HR, hazard ratio; KM, Kaplan–Meier; LEN, lenalidomide; NR, not reached; OS, overall survival; R-GemOx, rituximab + gemcitabine + oxaliplatin.

Nowakowski G, et al. *Clin Cancer Res*. 2022;28:4003-4017.

Secondary Endpoints: ORR and CR Rate

- ORR and CR rate were significantly higher for tafasitamab + LEN versus systemic therapies pooled and R-GemOx
- Numerical improvement was observed for tafasitamab + LEN versus BR

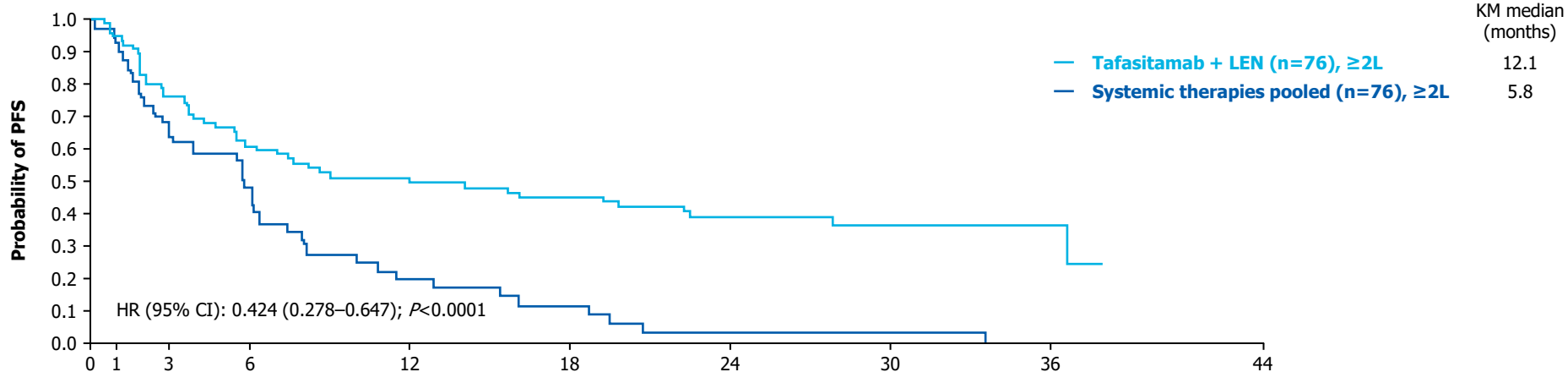


BR, bendamustine + rituximab; CI, confidence interval; CR, complete response; LEN, lenalidomide; ORR, overall response rate; R-GemOx, rituximab + gemcitabine + oxaliplatin.

Nowakowski G, et al. *Clin Cancer Res*. 2022;28:4003-4017.

Secondary Endpoints: PFS (1/3)

PFS was significantly improved for tafasitamab + LEN versus systemic therapies pooled (12.1 months vs 5.8 months; HR: 0.424; *P*<0.0001)



Tafasitamab + LEN (n=76), ≥2L

At risk	76	71	57	43	34	30	17	12	4	0
Event(s)	0	4	18	29	36	40	44	45	45	46
Censored	0	1	1	4	6	6	15	19	27	30

Systemic therapies pooled (n=76), ≥2L

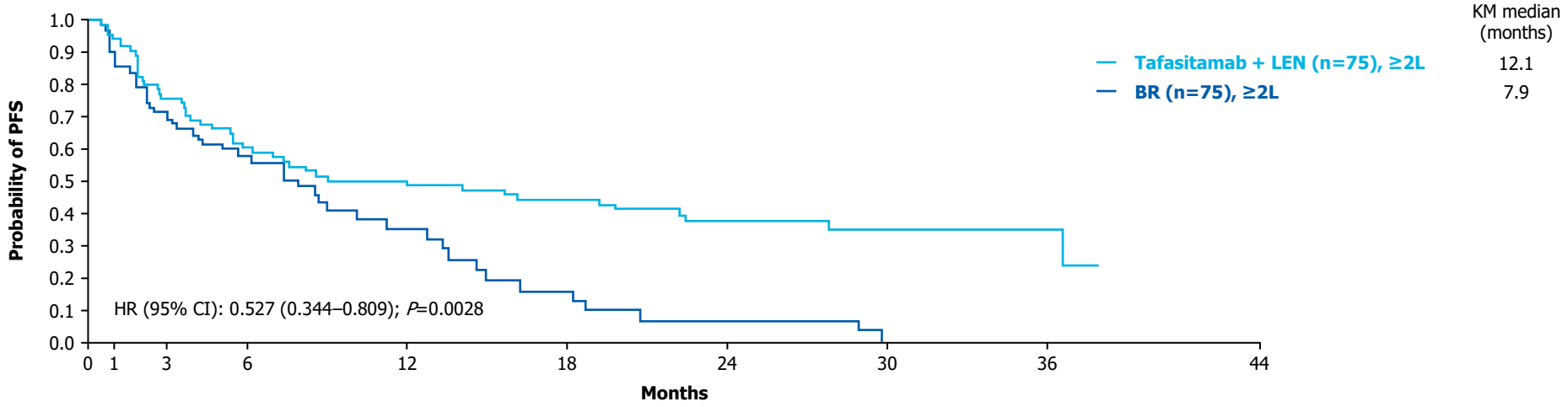
At risk	76	68	41	21	8	4	1	1	0	0
Event(s)	0	5	24	34	45	48	51	51	52	52
Censored	0	3	11	21	23	24	24	24	24	24

2L, second-line; CI, confidence interval; HR, hazard ratio; KM, Kaplan–Meier; LEN, lenalidomide; PFS, progression-free survival.

Nowakowski G, et al. *Clin Cancer Res*. 2022;28:4003-4017.

Secondary Endpoints: PFS (2/3)

PFS was significantly improved for tafasitamab + LEN versus BR (12.1 months vs 7.9 months; HR: 0.527; *P*=0.0028)



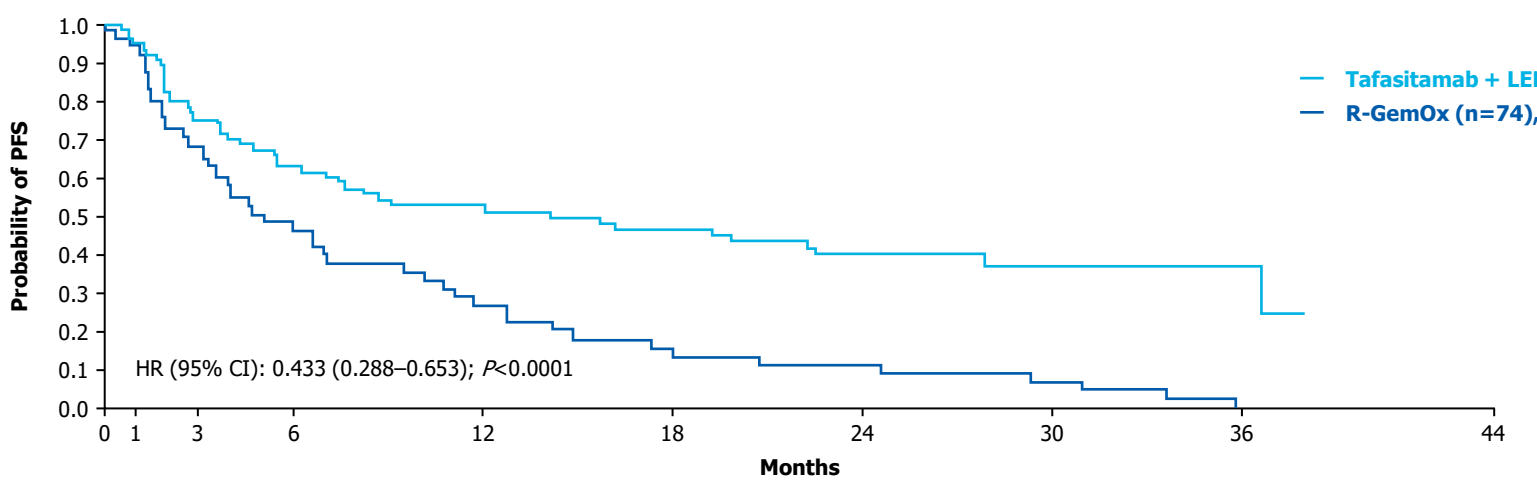
Tafasitamab + LEN (n=75), ≥2L										
At risk	75	70	56	42	33	29	17	12	4	0
Event(s)	0	4	18	29	36	40	44	45	45	46
Censored	0	1	1	4	6	6	14	18	26	29
BR (n=75), ≥2L										
At risk	75	60	45	29	11	5	2	0	0	0
Event(s)	0	7	19	27	36	42	45	47	47	47
Censored	0	8	11	19	28	28	28	28	28	28

2L, second-line; BR, bendamustine + rituximab; CI, confidence interval; HR, hazard ratio; KM, Kaplan–Meier; LEN, lenalidomide; PFS, progression-free survival.

Nowakowski G, et al. *Clin Cancer Res*. 2022;28:4003-4017.

Secondary Endpoints: PFS (3/3)

PFS was significantly improved for tafasitamab + LEN versus R-GemOx (14.1 months vs 5.1 months; HR: 0.433; *P*<0.0001)



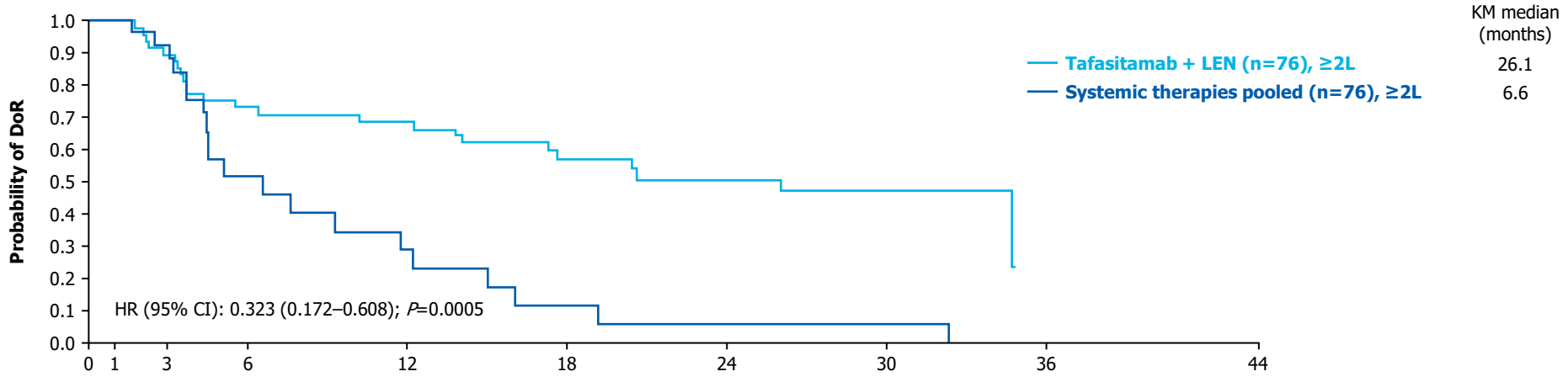
Tafasitamab + LEN (n=74), ≥2L									
At risk	74	69	55	43	34	30	17	12	4	0
Event(s)	0	4	18	27	34	38	42	43	43	44
Censored	0	1	1	4	6	6	15	19	27	30
R-GemOx (n=74), ≥2L									
At risk	74	66	44	21	12	7	5	3	0	0
Event(s)	0	4	22	34	43	48	50	52	55	55
Censored	0	4	8	19	19	19	19	19	19	19

2L, second-line; CI, confidence interval; HR, hazard ratio; KM, Kaplan–Meier; LEN, lenalidomide; PFS, progression-free survival; R-GemOx, rituximab + gemcitabine + oxaliplatin.

Nowakowski G, et al. *Clin Cancer Res*. 2022;28:4003-4017.

Secondary Endpoints: DoR (1/3)

DoR was significantly improved in the tafasitamab + LEN cohort versus systemic therapies pooled (26.1 months vs 6.6 months; HR: 0.323; *P*=0.0005)[1,2]



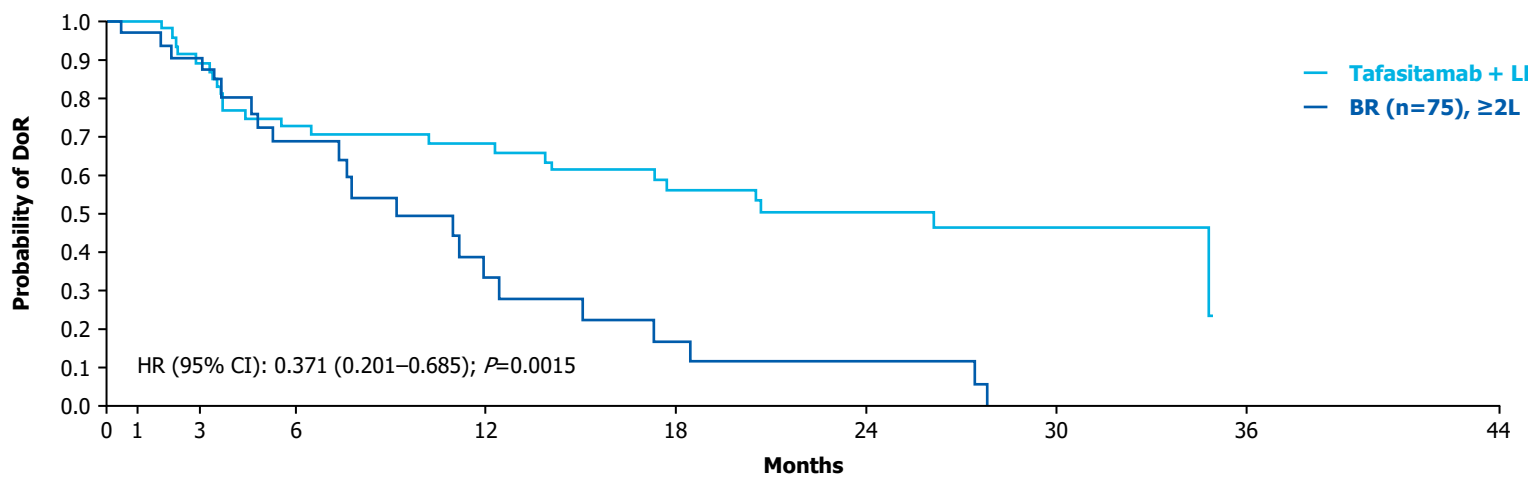
Tafasitamab + LEN (n=76), ≥2L										
At risk	51	50	44	35	30	23	15	10	0	0
Event(s)	0	0	5	13	15	20	22	23	24	24
Censored	0	1	2	3	6	8	14	18	27	27
Systemic therapies pooled (n=76), ≥2L										
At risk	37	32	22	10	5	2	1	1	0	0
Event(s)	0	0	2	11	15	18	19	19	20	20
Censored	0	5	13	16	17	17	17	17	17	17

2L, second-line; CI, confidence interval; DoR, duration of response; HR, hazard ratio; KM, Kaplan–Meier; LEN, lenalidomide.

1. Nowakowski G, et al. *Clin Cancer Res*. 2022;28:4003-4017; 2. Nowakowski G, et al. Poster Presentation. SOHO 2021; ABCL-346.

Secondary Endpoints: DoR (2/3)

DoR was significantly improved in the tafasitamab + LEN cohort versus BR (26.1 months vs 9.2 months; HR: 0.371; *P*=0.0015)[1,2]



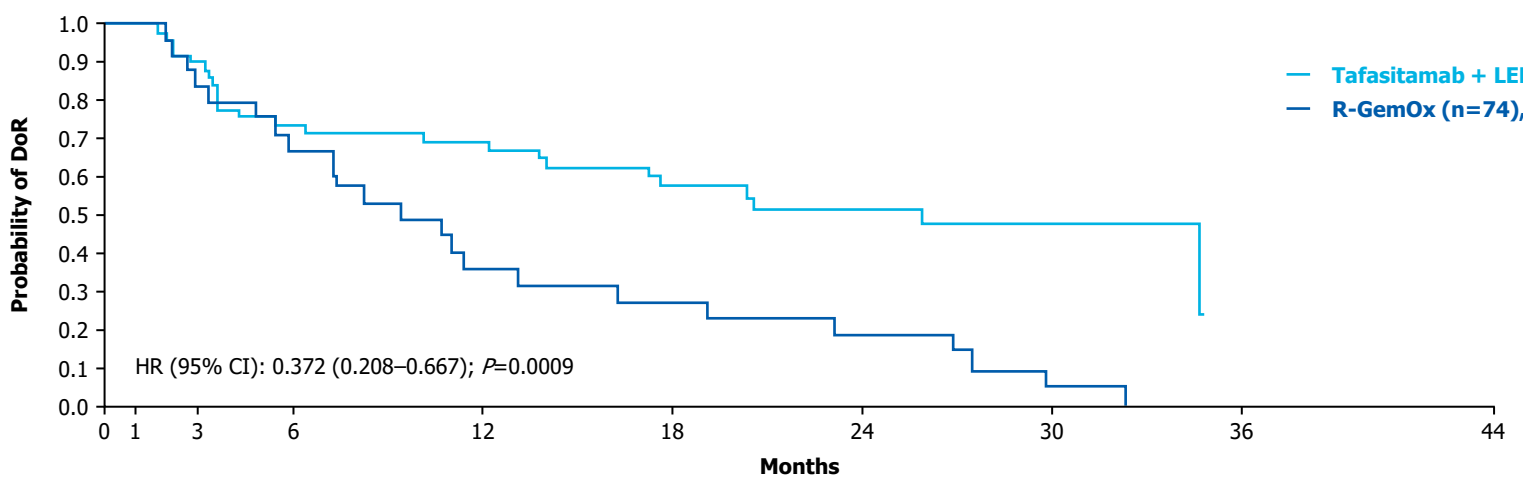
Tafasitamab + LEN (n=75), ≥2L										
At risk	50	49	43	34	29	23	15	10	0	0
Event(s)	0	0	5	13	15	20	22	23	24	24
Censored	0	1	2	3	6	7	13	17	26	26
BR (n=75), ≥2L										
At risk	41	35	26	17	6	3	2	0	0	0
Event(s)	0	1	3	9	16	19	20	22	22	22
Censored	0	5	12	15	19	19	19	19	19	19

2L, second-line; BR, bendamustine + rituximab; CI, confidence interval; DoR, duration of response; HR, hazard ratio; KM, Kaplan–Meier; LEN, lenalidomide.

1. Nowakowski G, et al. *Clin Cancer Res*. 2022;28:4003-4017.; 2. Nowakowski G, et al. Poster Presentation. SOHO 2021; ABCL-346.

Secondary Endpoints: DoR (3/3)

DoR was significantly improved in the tafasitamab + LEN cohort versus R-GemOx (26.1 months vs 9.5 months; HR: 0.372; *P*=0.0009)[1,2]



Tafasitamab + LEN (n=74), ≥2L										
At risk	51	50	44	35	30	23	15	10	0	0
Event(s)	0	0	5	13	15	20	22	23	24	24
Censored	0	1	2	3	6	8	14	18	27	27
R-GemOx (n=74), ≥2L										
At risk	34	26	20	15	8	6	4	1	0	0
Event(s)	0	0	4	8	15	17	19	22	23	23
Censored	0	8	10	11	11	11	11	11	11	11

2L, second-line; CI, confidence interval; CR, complete response; DoR, duration of response; HR, hazard ratio; KM, Kaplan–Meier; LEN, lenalidomide; R-GemOx, rituximab + gemcitabine + oxaliplatin.

1. Nowakowski G, et al. *Clin Cancer Res*. 2022;28:4003-4017.; 2. Nowakowski G, et al. Poster Presentation. SOHO 2021; ABCL-346.

RE-MIND2: Tafasitamab + LEN Versus Pola-BR, CAR-T Therapies and R2

Study design

Routinely administered R/R DLBCL treatments as matched control for L-MIND

Eligibility criteria

- Aged ≥18 years
- R/R DLBCL patients
- ≥2 systemic therapies administered for DLBCL (including ≥1 anti-CD20 therapy)
- Non-transplant-eligible

RE-MIND2
N=3454
(All therapies)

Primary end point:
- OS

Secondary end points:
- ORR and CR rate
- PFS
- DoR

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)
- Refractoriness to the last therapy line (yes vs no)
- History of primary refractoriness (yes vs no)
- ECOG PS (0–1 vs ≥2)‡

Additional covariates for sensitivity analyses:†
- Ann Arbor stage (I + II vs III + IV)
- Elevated LDH (LDH >ULN vs LDH ≤ULN)
- Neutropenia (absolute neutrophil count <1.5 x10^9/L vs ≥1.5 x 10^9/L)
- Anaemia (haemoglobin <10 g/dL vs ≥10 g/dL)

L-MIND
Tafasitamab + LEN
N=81

Matched comparison

Tafasitamab + LEN
versus
All systemic therapies pooled
or versus
Individual systemic therapies:
- **Pola-BR**
- **R²**
- **CAR-T**
- **BR**
- **R-GemOx**

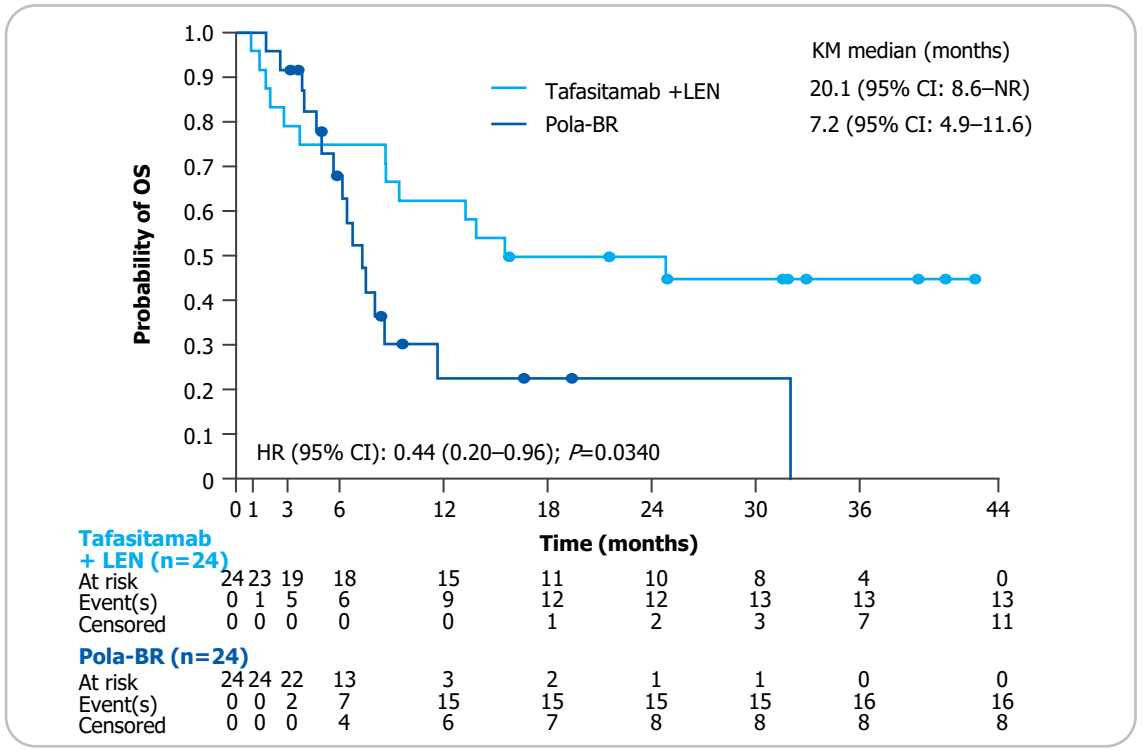
*Nine covariates were used for the primary analysis; †Two separate sensitivity analyses were performed: one with inverse probability of treatment weights method and another with 1:1 NN matching with multiple imputation (MI) of missing propensity scores caused by incomplete baseline characteristics, to counteract the effects of potential bias arising from missing data; ‡Not included in the sensitivity analyses.

ASCT, autologous stem cell transplantation; BR, bendamustine + rituximab; CAR-T, chimeric antigen receptor T-cell therapy; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DoR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; LEN, lenalidomide; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; Pola-BR, polatuzumab vedotin + bendamustine + rituximab; R², rituximab + lenalidomide; R-GemOx, rituximab + gemcitabine + oxaliplatin; R/R, relapsed/refractory; ULN, upper limit of normal.

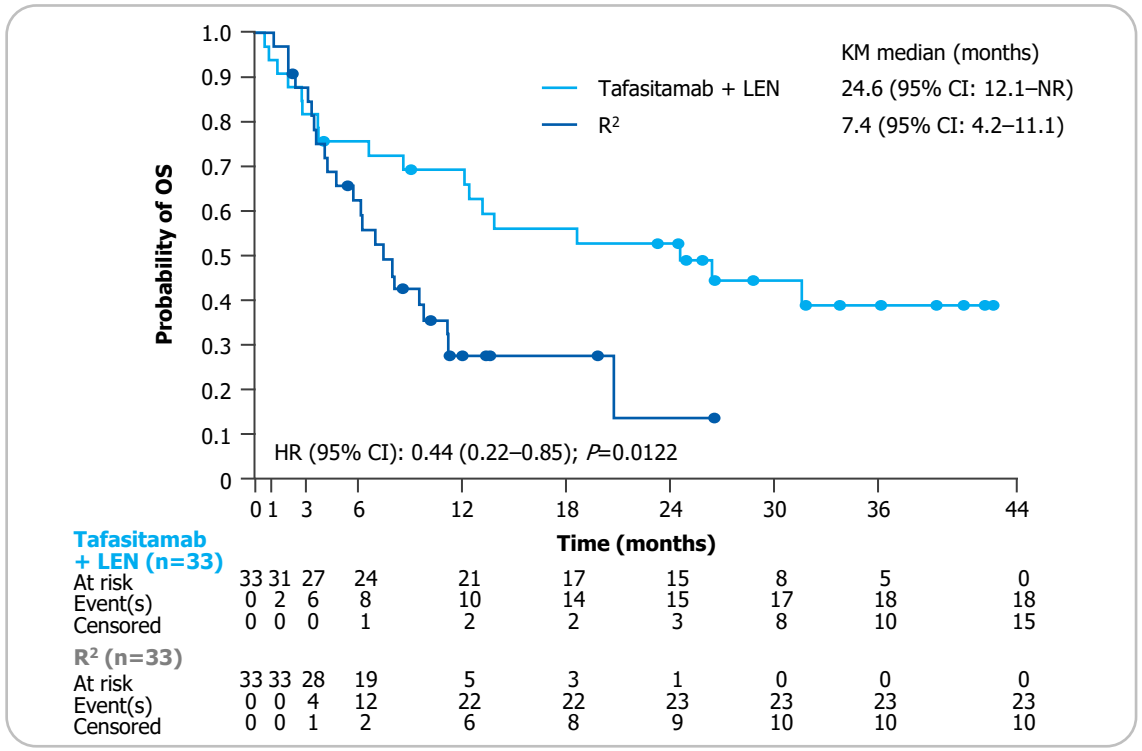
Nowakowski G, et al. *Ann Hematol*. 2023;102(7):1773-1787.

Primary Endpoint: OS

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



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



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

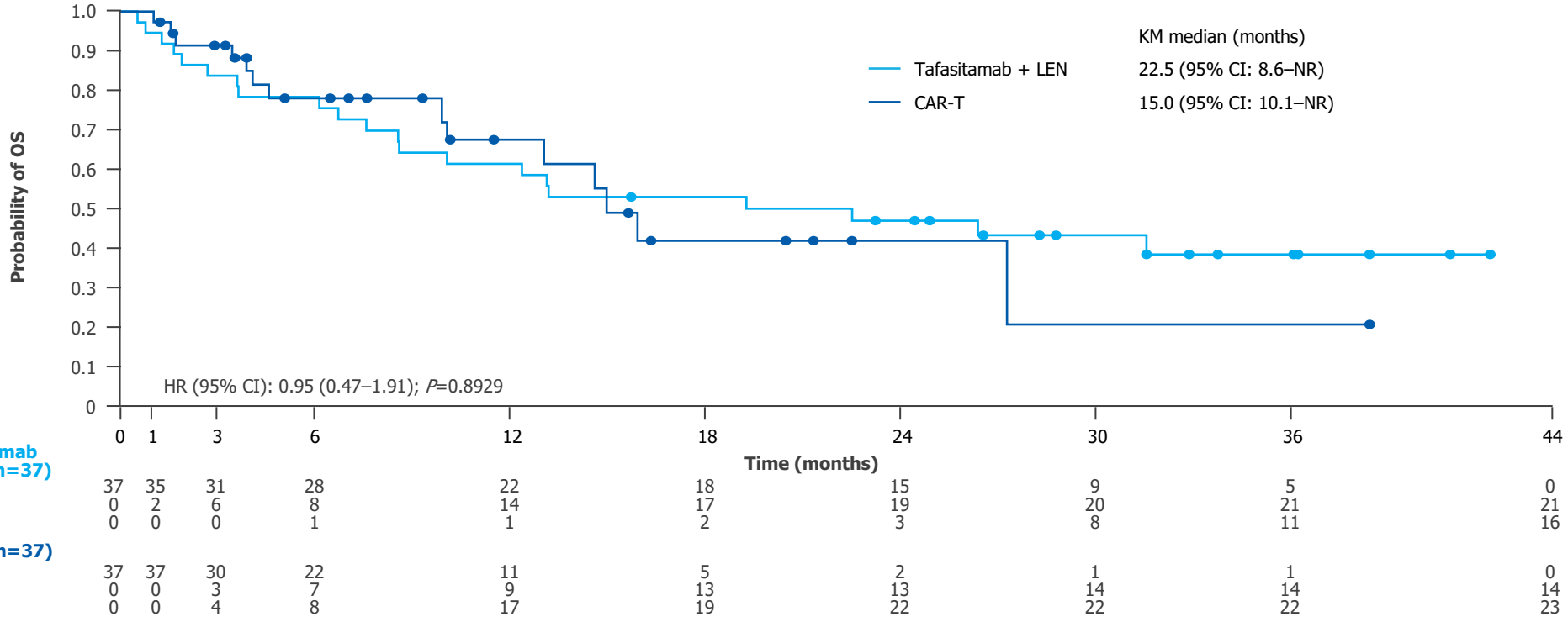
P-values were calculated using log-rank test.

CI, confidence interval; HR, hazard ratio; KM, Kaplan–Meier; LEN, lenalidomide; NR, not reached; OS, overall survival; Pola-BR, polatuzumab vedotin + bendamustine + rituximab; R², rituximab + lenalidomide.

Nowakowski G, et al. *Ann Hematol*. 2023;102(7):1773-1787.

Primary Endpoint: OS

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



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

CAR-T, chimeric antigen receptor T-cell therapy; CI, confidence interval; HR, hazard ratio; KM, Kaplan–Meier; LEN, lenalidomide; NR, not reached; OS, overall survival.

Nowakowski G, et al. *Ann Hematol*. 2023;102(7):1773-1787.

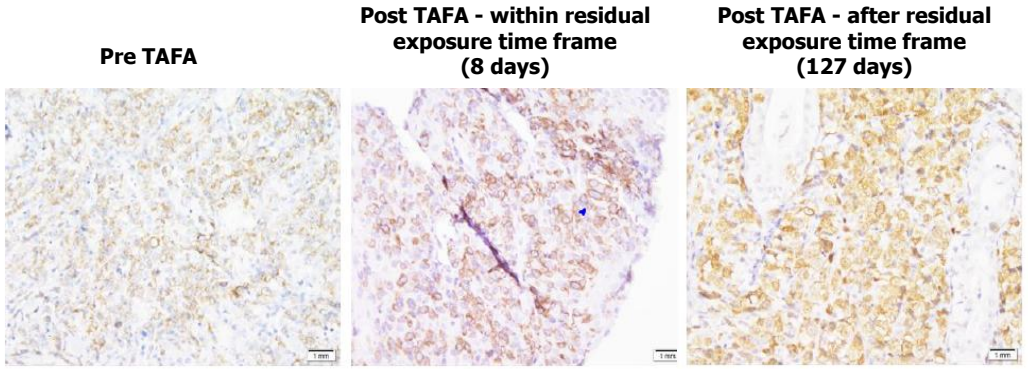
Sustained CD19 Expression After Tafasitamab Treatment

- **L-MIND PATIENTS - = 6**
- 100% CD19 expression was positive even before the washout period (85 days) after the final treatment

DLBCL, diffuse large B-cell lymphoma; IHC, immunohistochemistry; LEN, lenalidomide; mRNA, messenger ribonucleic acid; TAFA, tafasitamab; R/R, relapsed/refractory.

Duell J, et al, *Leuk Lymphoma*. 2022;63:468–472.

Longitudinal IHC (CD19 staining) of representative patient from L-MIND



Subgroup Analysis of Additional Follow-Up: Real-World Sequential Use of CD19-Directed Therapies for R/R DLBCL - Tafasitamab Preceding Chimeric Antigen Receptor T-Cell Therapy

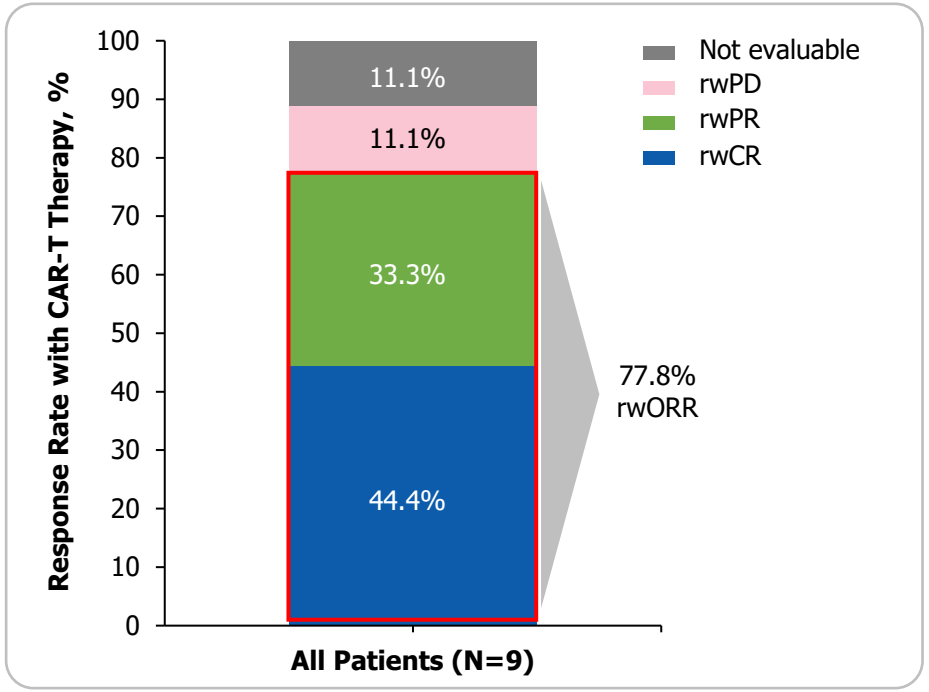
N=9

OPEN, Oncology Provider Extended Network; R/R, relapsed/refractory.

Epperla N, et al. Poster HEMO 2024;

Real-World Best Response to CAR-T Therapy Following Tafasitamab

Real-World Best Response to CAR-T Therapy Following Tafasitamab Treatment for R/R DLBCL

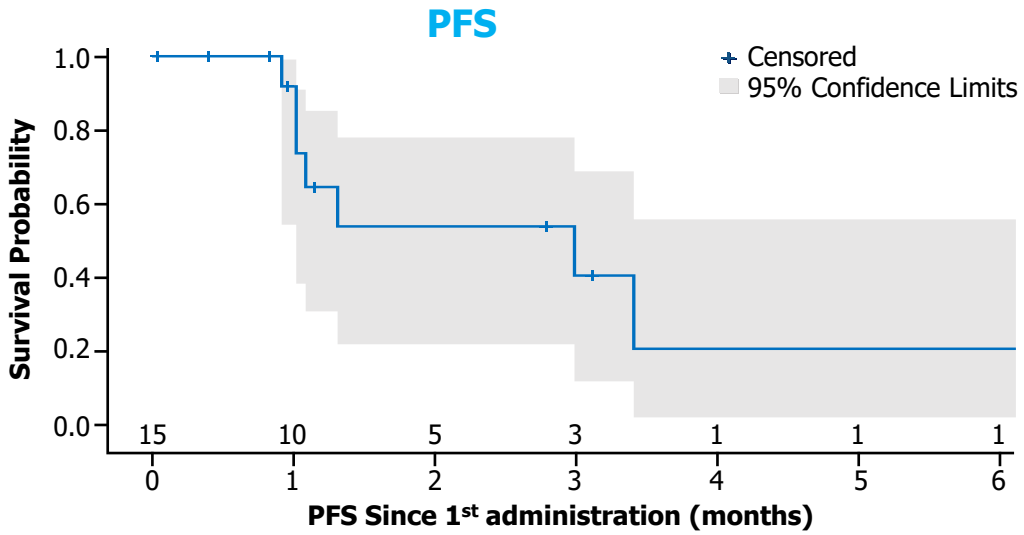


Among the 9 patients, rwORR after CAR-T therapy was 77.8% (n=7/9)

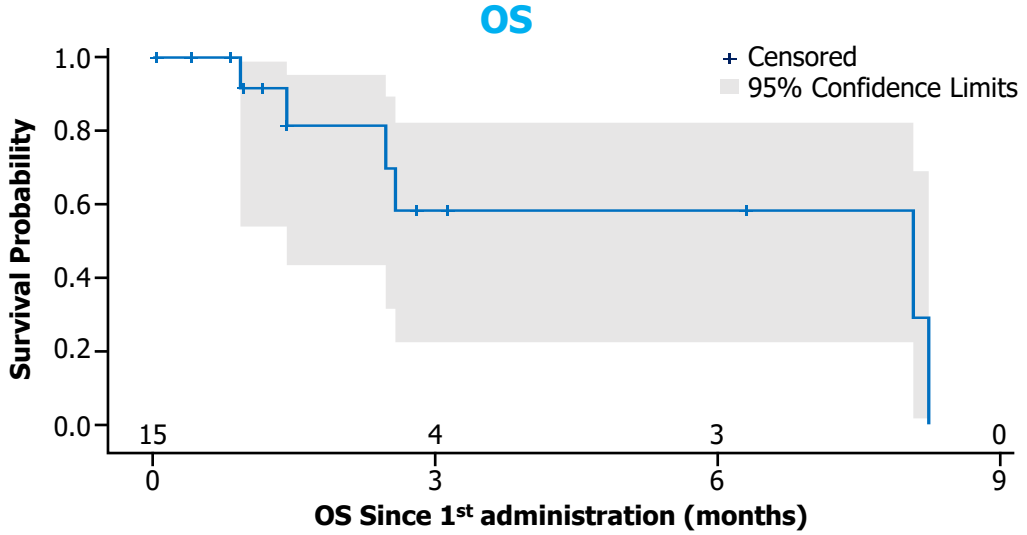
CAR-T, chimeric antigen receptor T-cell; DLBCL, diffuse large B-cell lymphoma; R/R, relapsed/refractory; rwCR, real-world complete response; rwORR, real-world overall response rate; rwPR, real-world partial response; rwPD, real-world progressive disease; tafa+LEN, tafasitamab plus lenalidomide.

Epperla N, et al. Poster presented at: Brazilian Congress of Hematology, Hemotherapy, and Cellular Therapy (HEMO); October 23-26, 2024; Sao Paulo, Brazil.

TL-pre-CAR-T Set: PFS and OS After CAR T-Cell Infusion



No. of subjects	Event	Censored	Median survival (95% CI)
15	46.7% (7)	53.3% (8)	3.0 (1.0 ; NA)



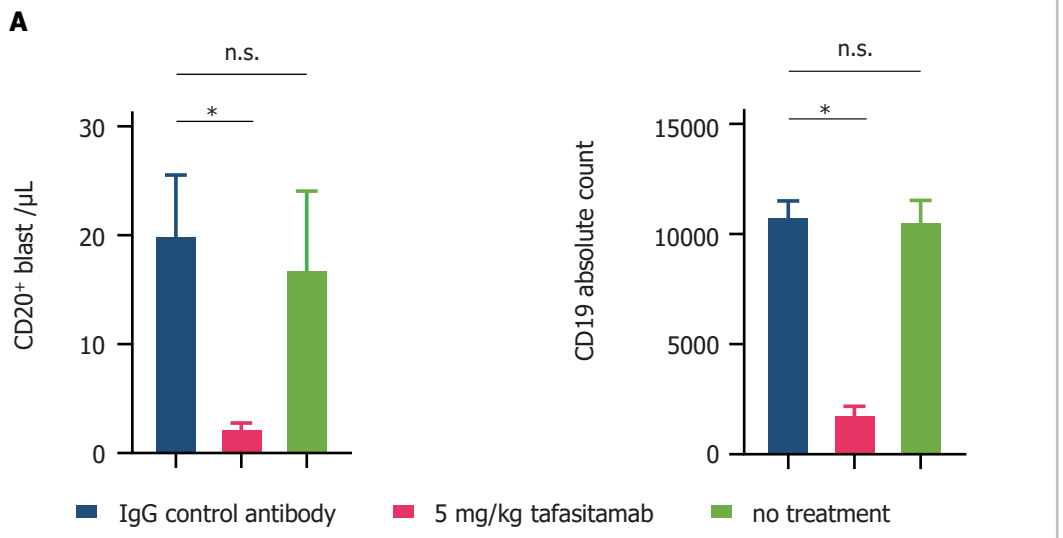
No. of subjects	Event	Censored	Median survival (95% CI)
15	40% (6)	60% (9)	8.1 (1.4 ; NA)

- With a median follow-up duration of 2.8 (1; 6.3) months, the bORR, bCRR, 6-month PFS rate, and OS rate after CAR T-cell infusion were 45.5%, 36.4%, 20.1%, and 58.2%, respectively
- The median washout time between the last tafasitamab + lenalidomide and CAR T-cell infusion was 2.7 (2.1; 3.4) months for patients receiving tafasitamab + lenalidomide before treatment and 20 (3; 31) days for patients receiving tafasitamab + lenalidomide as BT

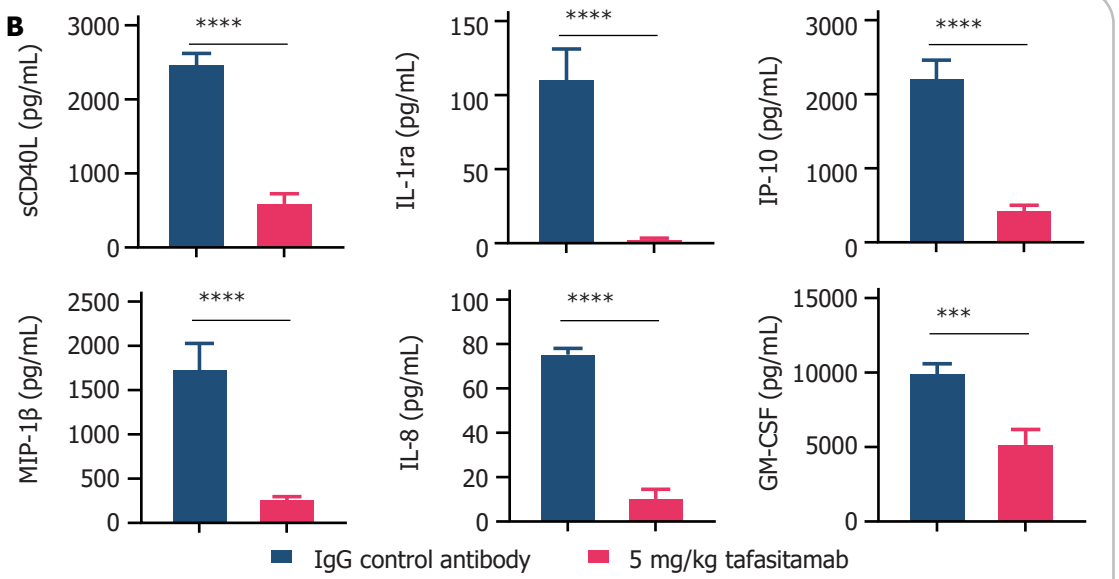
BT, bridge therapy; bCCR, best complete response rate; bORR, best overall response rate; CAR-T, chimeric antigen receptor T-cell; CI, confidence interval; NA, not available; OS, overall survival; PFS, progression-free survival; TL, tafasitamab plus lenalidomide.

Camus V, et al. *Blood Adv*. 2024;8(20):5371-5381.

Tafasitamab and CAR-T19 Sequential Therapy Decreases CRS Severity and Increases Antitumour Activity



- Flow cytometric analysis showed significant tumour cell regression (*P<0.05) and masking of CD19 on CD20+ leukaemic cells (*P<0.05) in the mice that underwent tafasitamab pretreatment versus those pretreated with IgG control (Figure A).

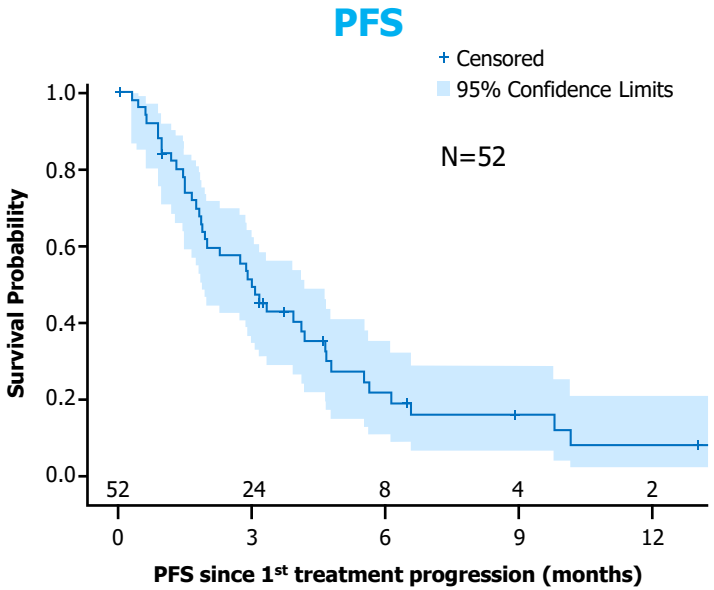


- Cytokine analysis on day 4 showed significantly higher levels of CRS-associated cytokines (e.g., sCD40L, IL-1 receptor antagonist, IP-10, IL-8, MIP-1β and GM-CSF) in mice pretreated with IgG control versus those pretreated with tafasitamab (***P<0.001, ****P<0.0001, t-test) (Figure B)

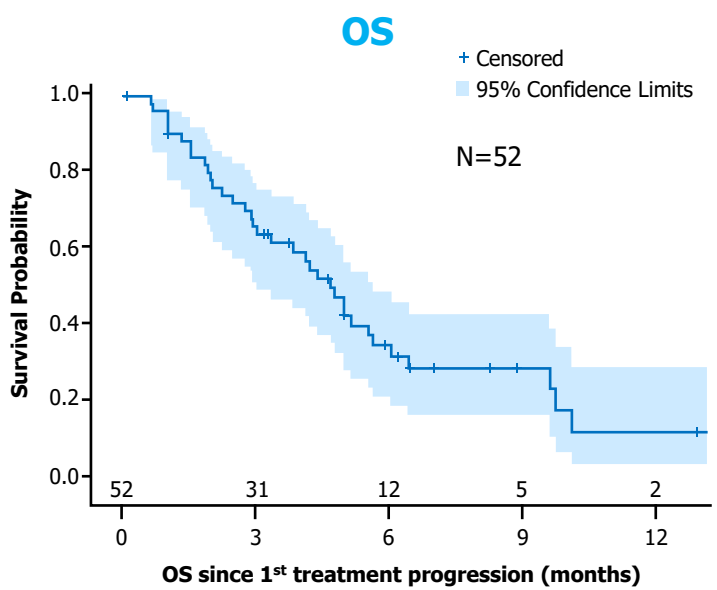
CAR-T19, CD19 chimeric antigen receptor T-cell; CD, cluster differentiation; CRS, cytokine release syndrome; GM-CSF, granulocyte-macrophage colony-stimulating factor; IgG, immunoglobulin G; IL, interleukin; IL-1ra; interleukin 1 receptor antagonist; IP-10, interferon gamma-inducible protein 10; MIP, macrophage inflammatory protein; n.s, not significant.

Sakemura RL, et al. *Blood.* 2024;143(3):258-271.

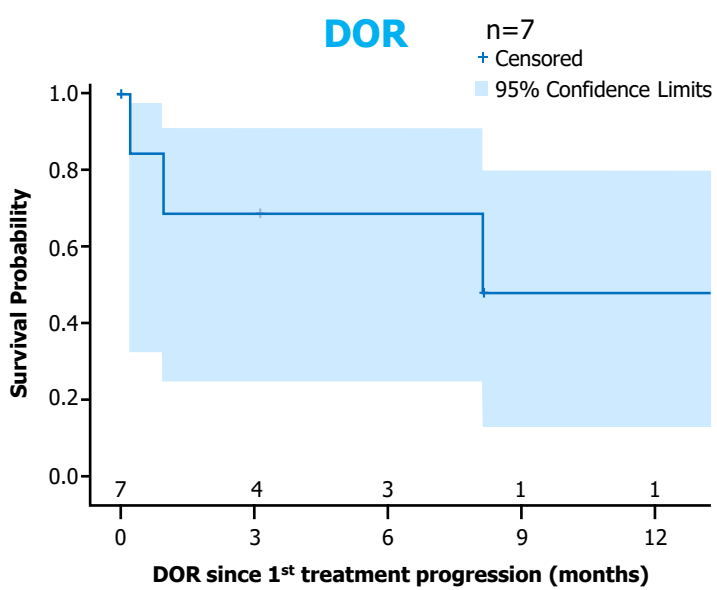
TL-post-CAR-T Set: PFS, OS and DOR Since Treatment for the First Progression After CAR T-Cell Therapy



Events	Censored	Median survival (95% CI)
76.9% (40)	23.1% (12)	3.0 (1.9; 4.2)



Events	Censored	Median survival (95% CI)
67.3% (35)	32.7% (17)	4.7% (3.0; 5.6)



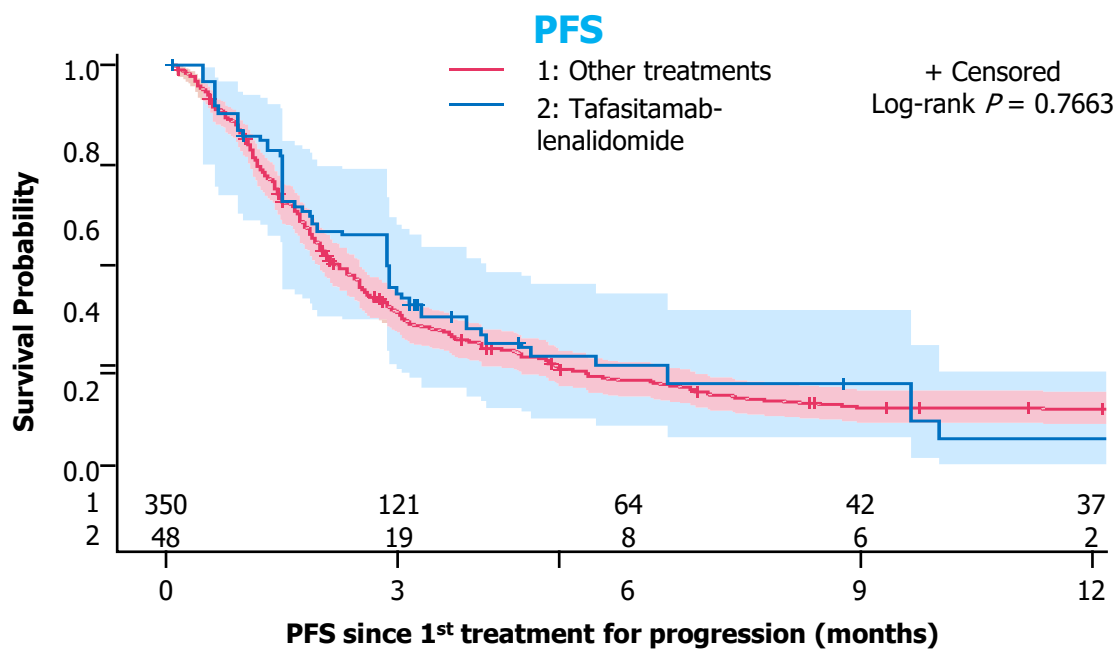
Events	Censored	Median survival (95% CI)
42.9% (3)	57.1% (4)	8.1 (0.2; NA)

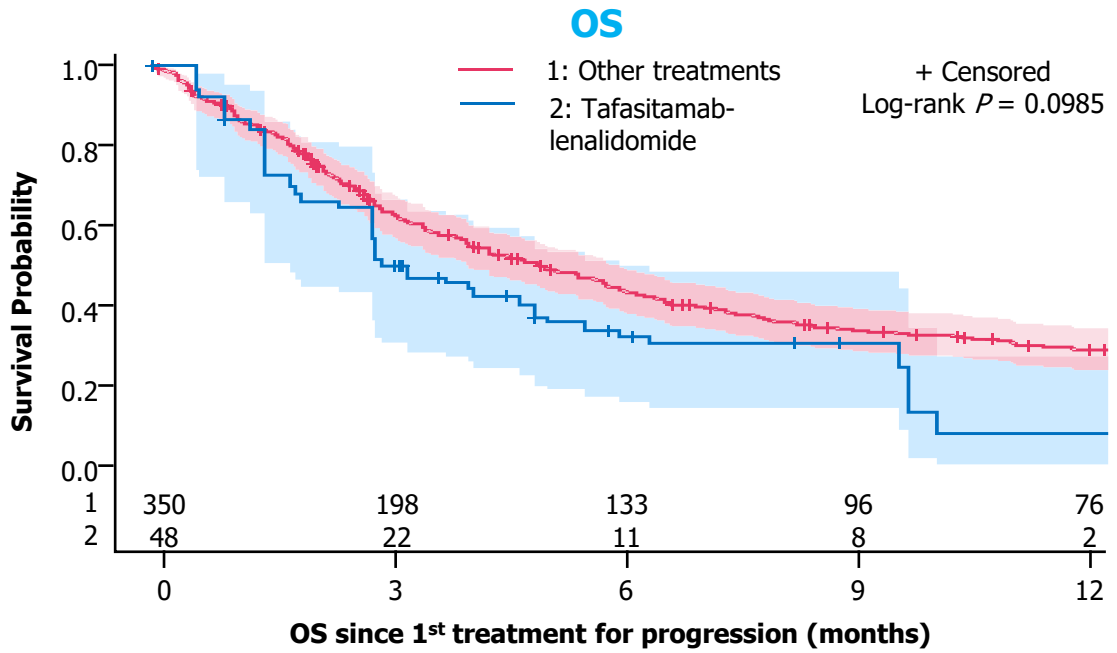
- After a median follow-up duration of 7 (5.9-13) months, the median PFS and OS since the first treatment for progression were 3 (95% CI, 1.9-4.2) and 4.7 (3-5.6) months, respectively. The median DOR2 was 8.1 (0.2; NA) months
- The mPFS after treatment for the first progression post CAR T-cell therapy increased when tafasitmab + LEN was initiated >6 months after CAR T-cell infusion: 5.6 (3.2-NA) v. 2 (1.6-3.1), *P*=0.0138
- The mOS2 after treatment for the first progression post CAR T-cell therapy was not reached (5.6-NA) when tafasitmab + LEN was introduced later than the 6-month cutoff (v. 3.8 [2.2-5] months) for patients in the ≤6-month subset (*P*=0.0034)

CAR-T, chimeric antigen receptor T-cell; CI, confidence interval; DOR, duration of response; LEN, lenalidomide; NA, not available; OS, overall survival; PFS, progression-free survival; TL, tafasitamab plus lenalidomide.
Camus V, et al. *Blood Adv*. 2024;8(20):5371-5381.

TL-post-CAR-T Set: PFS and OS Since Treatment for the First Progression After CAR T-Cell Therapy According to IPW Using SW Method Between Tafasitamab-Lenalidomide and Other Treatments

PFS and OS were not significantly different between two groups





	No. of subjects	Event	Censored	Median survival (95% CI)
Other treatments	354	81.9% (290)	18.1% (64)	2.2 (2.0; 2.5)
Tafasitamab-lenalidomide	43	74.4% (32)	25.6% (11)	2.9 (1.5; 4.2)

	No. of subjects	Event	Censored	Median survival (95% CI)
Other treatments	354	68.6% (243)	31.4% (111)	5.1 (4.1; 6.0)
Tafasitamab-lenalidomide	43	65.1% (28)	34.9% (15)	3.3 (1.8; 6.4)

CAR-T, chimeric antigen receptor T-cell; CI, confidence interval; IPW, inverse probability weighting; OS, overall survival; PFS, progression-free survival; SW, stabilized weight; TL, tafasitamab plus lenalidomide.

Camus V, et al. *Blood Adv*. 2024;8(20):5371-5381.

DISCUSSÃO