Overview of the treatment algorithm for R/R patients ineligible for CAR-T and ABMT: current picture and potential new drugs

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Disclosures for Stephen Ansell, MD, PhD

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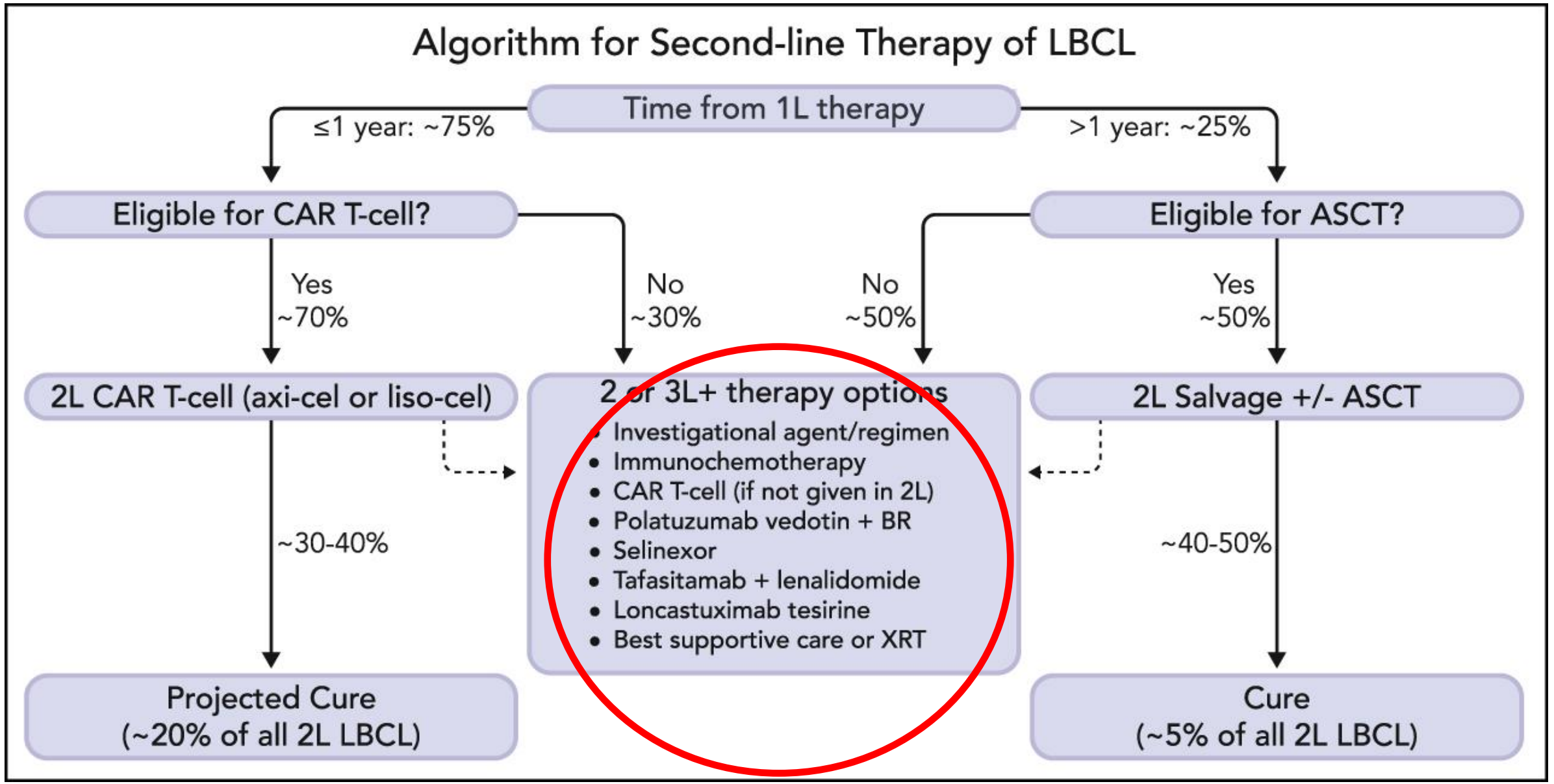
Scientific Advisory Board	N/A

N/A = Not Applicable (no conflicts listed)

Therapy for large B-cell lymphoma

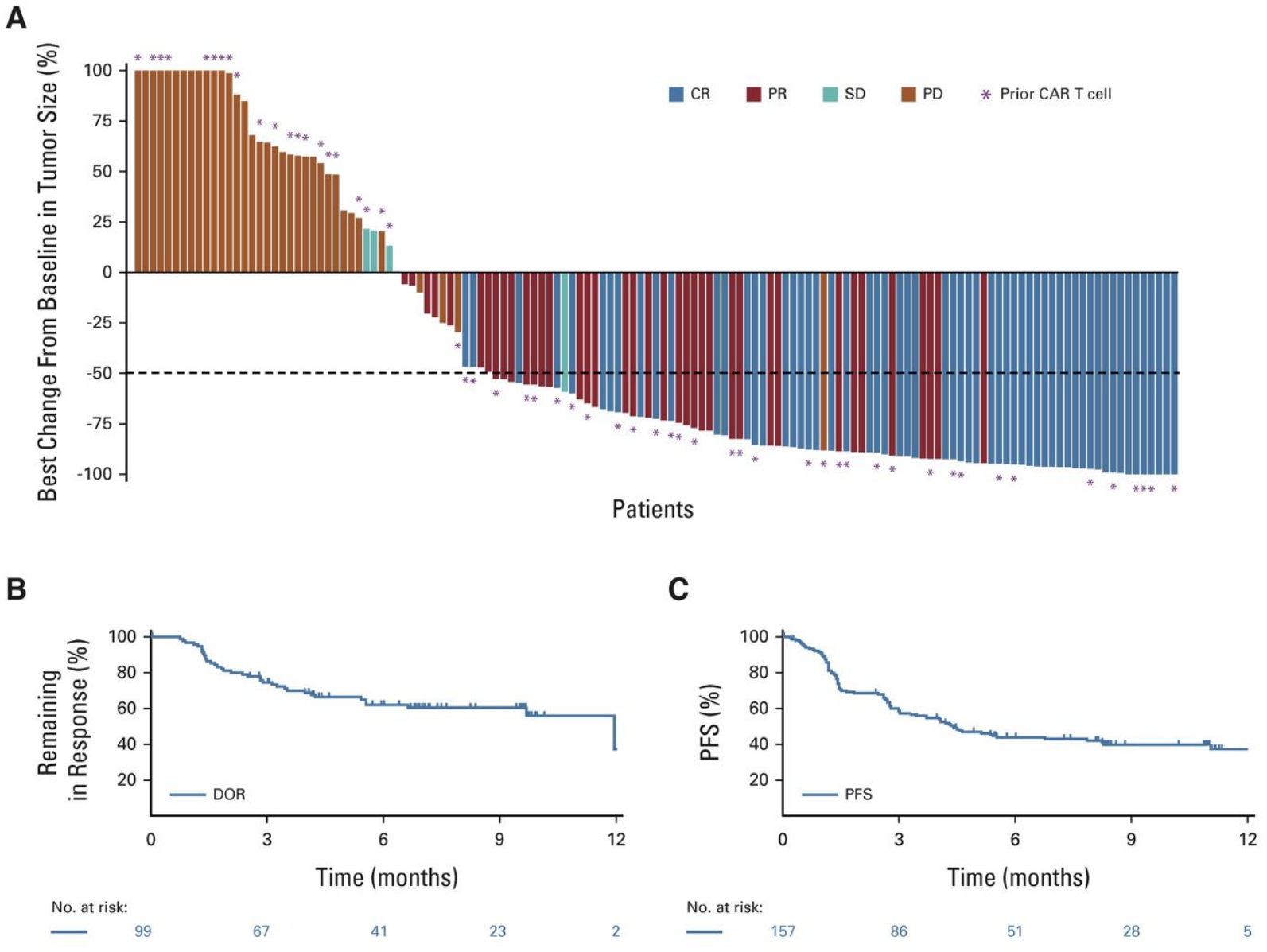


Westin J, Sehn LH. Blood. 2022 May 5;139(18):2737-2746.

Questions that may influence treatment decisions

- Which agents were given before – would you give brentuximab vedotin if the patient received polatuzumab vedotin in first-line?
- Do you want to use a similar treatment strategy versus a different one – is an immunotherapeutic approach with a bispecific antibody the best choice if a patient just progressed on CAR T cell treatment?
- Should you direct therapy at the same target as before – should you target CD19 with tafasitamab as the next line after CD19 CAR T cell therapy?
- Should you give treatment that has similar side effects – should you give a bispecific if very immunosuppressed, or cytotoxic therapy if neutropenic?
- How long do you plan to treat (tolerability over time) – is this treatment a bridge to another therapy or do you plan to treat to progression?

Bispecific Antibody - Efficacy of Epcoritamab in R/R DLBCL

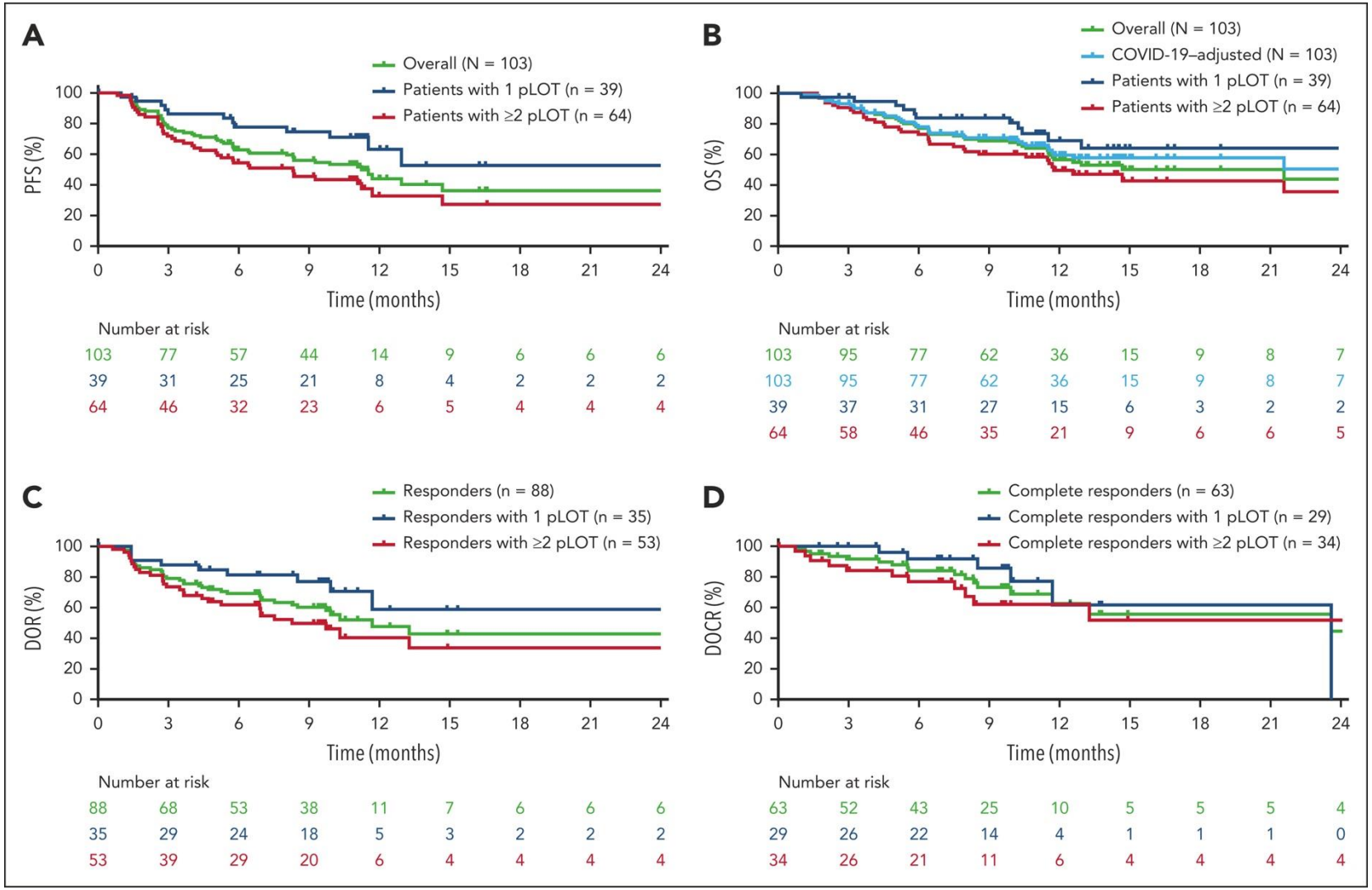


157 DLBCL patients
ORR 63% CR 39%
DOR 12 months

In patients who received prior CAR T-cell therapy (n = 61), the ORR was 54.1% and the CR rate was 34.4%, with a mDOR of 9.7 months

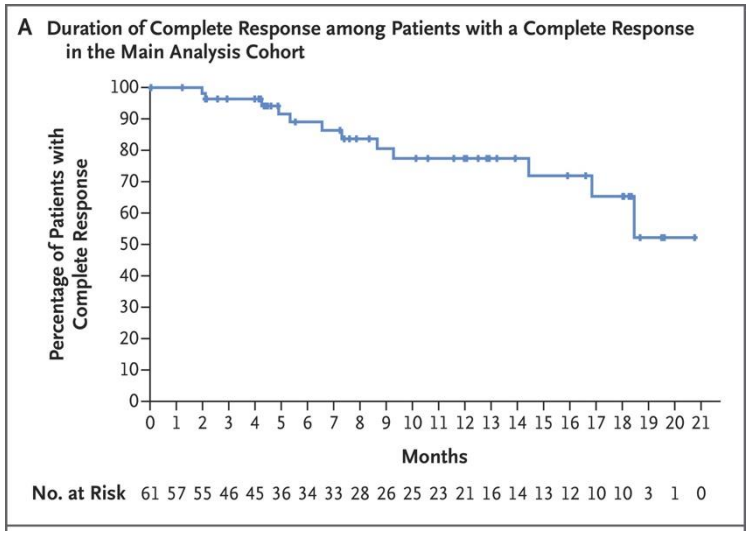
Thieblemont et al. J Clin Oncol. 2023 Apr 20;41(12):2238-2247.

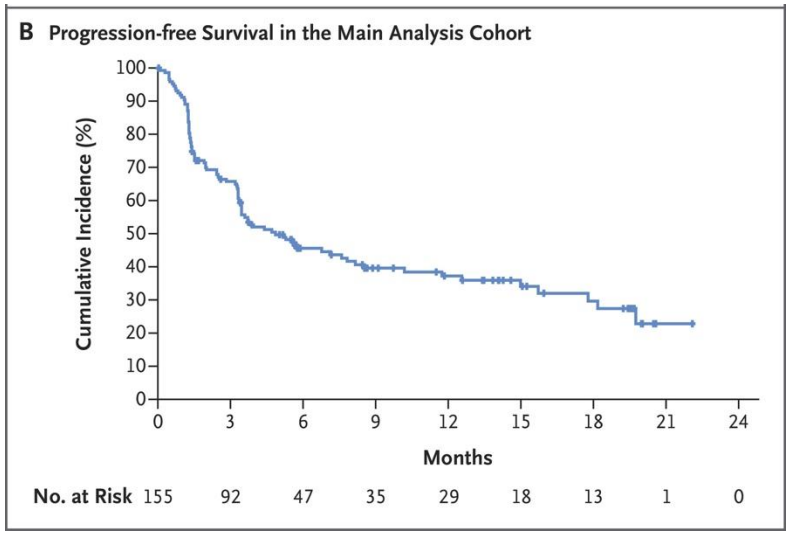
Epcoritamab plus GemOx in transplant-ineligible relapsed/refractory DLBCL: EPCORE NHL-2 trial

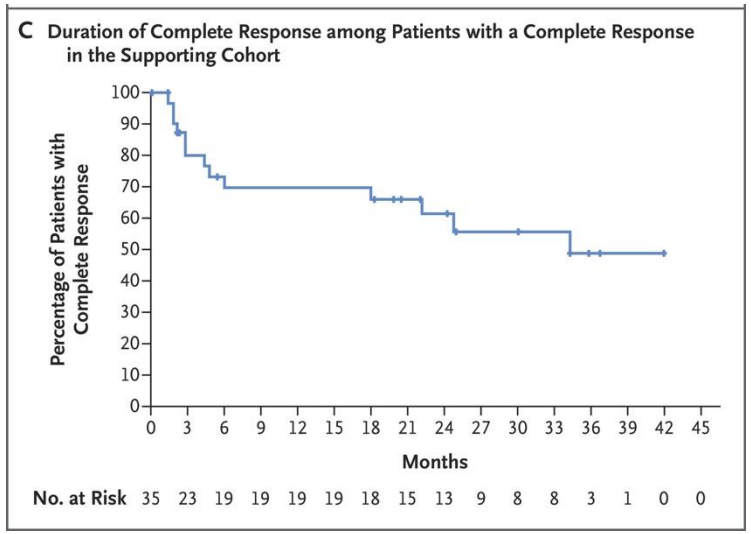


Brody et al. Blood. 2025 Apr 10;145(15):1621-1631.

Bispecific Antibody - Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma





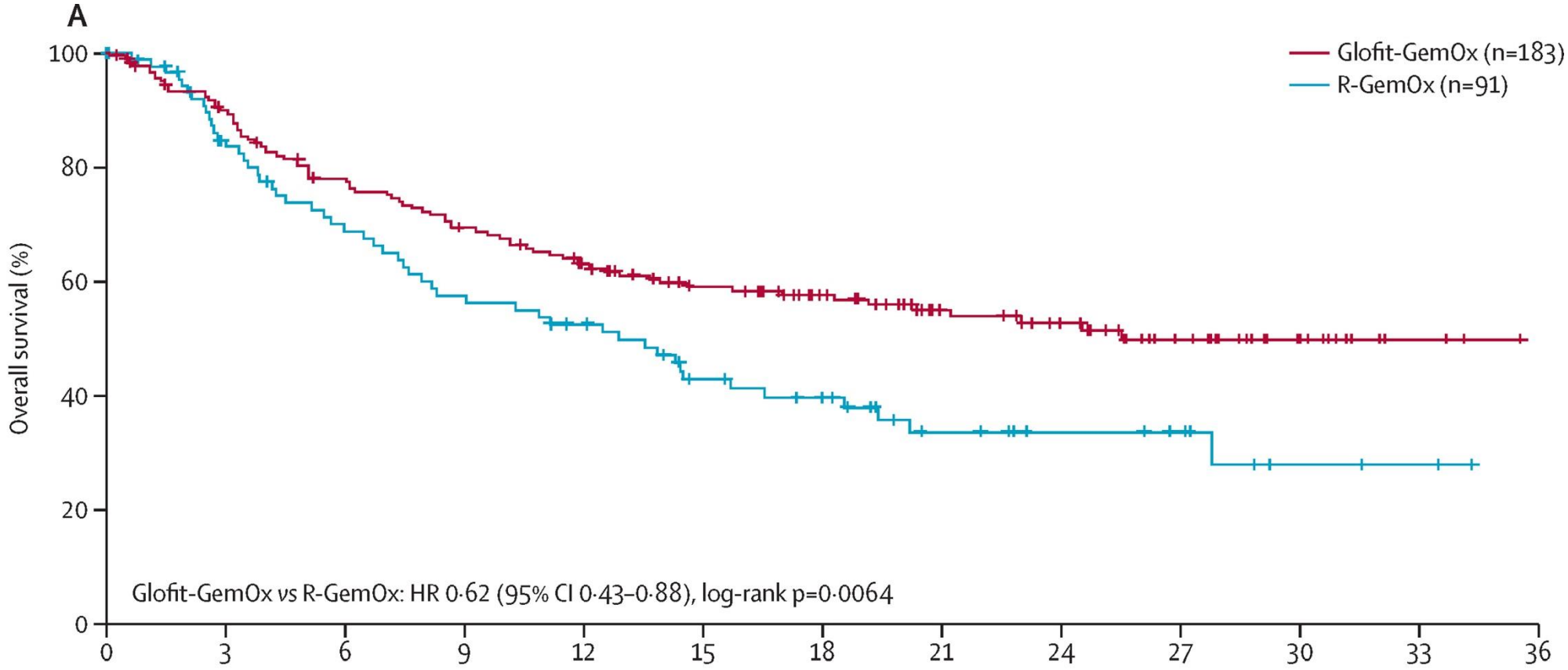


155 patients. Median follow-up of 12.6 months, 39% had a CR.

Results were consistent among the 52 patients who previously received CAR T-cell therapy (35% of whom had a CR).

Dickinson et al. N Engl J Med. 2022 Dec 15;387(24):2220-2231.

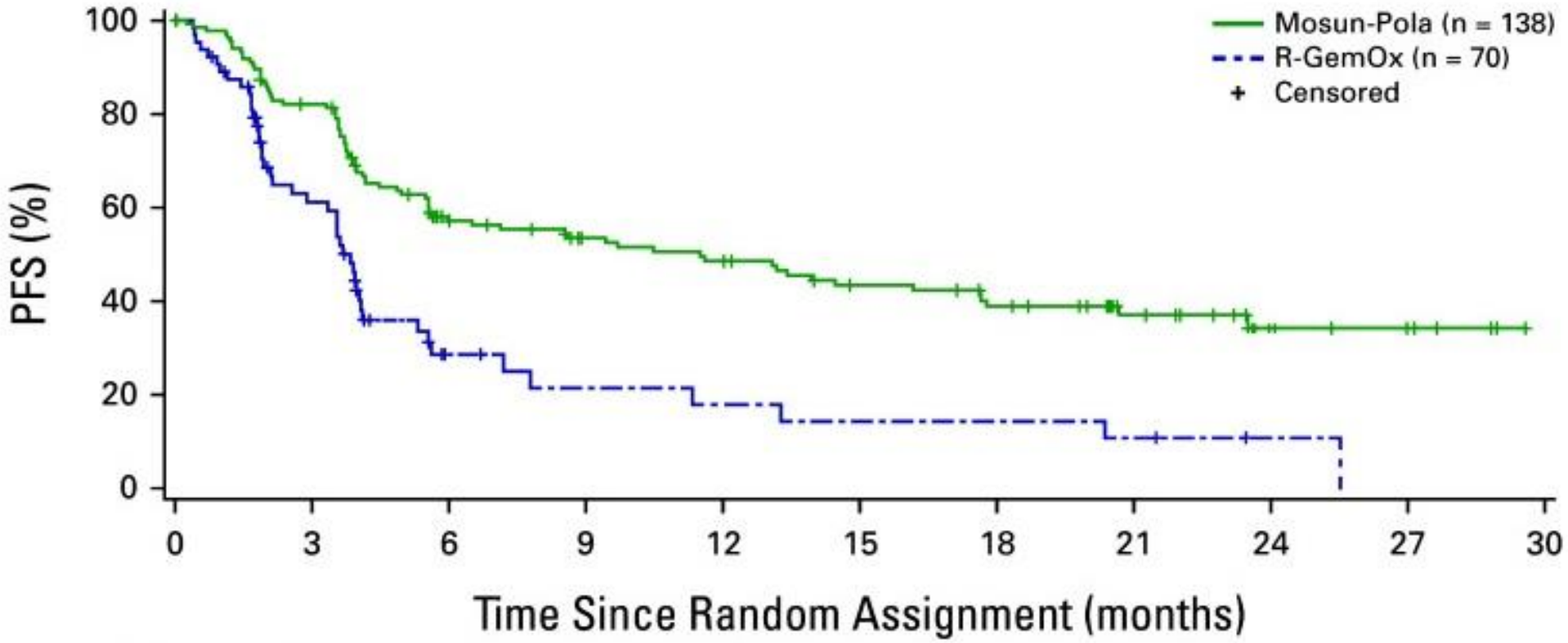
Glofitamab plus GemOx versus rituximab-GemOx for relapsed or refractory DLBCL (STARGLO)



Number at risk (number censored)													
Glofit-GemOx	183 (0)	159 (6)	135 (9)	119 (10)	104 (14)	86 (26)	71 (39)	51 (56)	40 (65)	26 (77)	11 (92)	3 (100)	0 (0)
R-GemOx	91 (0)	68 (9)	55 (10)	46 (10)	40 (12)	29 (16)	23 (20)	14 (26)	10 (30)	8 (32)	3 (36)	2 (37)	0 (0)

Abramson et al. Lancet. 2024 Nov 16;404(10466):1940-1954.

Mosunetuzumab Plus Polatuzumab Vedotin in Transplant-Ineligible Refractory/Relapsed DLBCL: Phase III SUNMO Trial



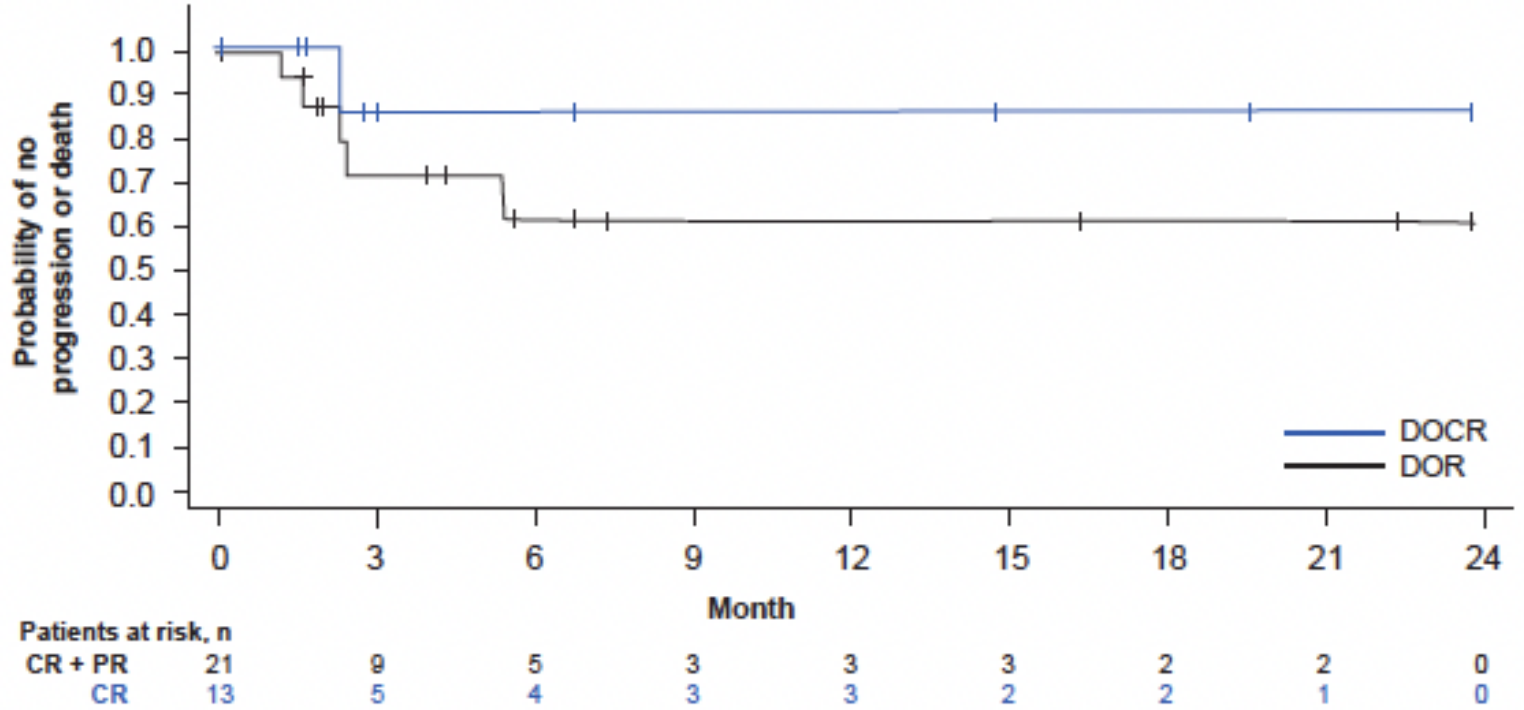
Number at risk (censored)

Mosun-Pola	138 (0)	108 (6)	65 (17)	54 (24)	49 (24)	40 (28)	34 (30)	20 (43)	8 (54)	5 (57)	NE
R-GemOx	70 (0)	33 (14)	9 (22)	6 (23)	5 (23)	4 (23)	4 (23)	3 (23)	1 (25)	NE	NE

Budde et al. J Clin Oncol. 2025 Dec 20;43(36):3799-3811.

Odronextamab demonstrates durable CRs in patients with DLBCL progressing after CAR-T therapy: ELM-1 study

Figure 2. DOR and DOCR by independent central review



CR, complete response; DOCR, duration of complete response; DOR, duration of response; PR, partial response.

In patients with DLBCL who had previous CAR T-cell therapy and received doses of 80 mg or higher, the objective response rate was 33% (10 of 30) and CR rate was 27% (8 of 30).

- 12-month PFS rate in all patients: 32.9% (95% CI 16.4–50.6)
- 12-month OS rate in all patients: 49.6% (95% CI 30.4–66.2)

Bannerji R, et al. Lancet Haematol. 2022 May;9(5):e327-e339.
Michot et al. EHA 2024, June 2024. Poster P1162.

Surovatamig (AZD0486), a CD19xCD3 T-cell engager, in relapsed or refractory diffuse large B-cell lymphoma

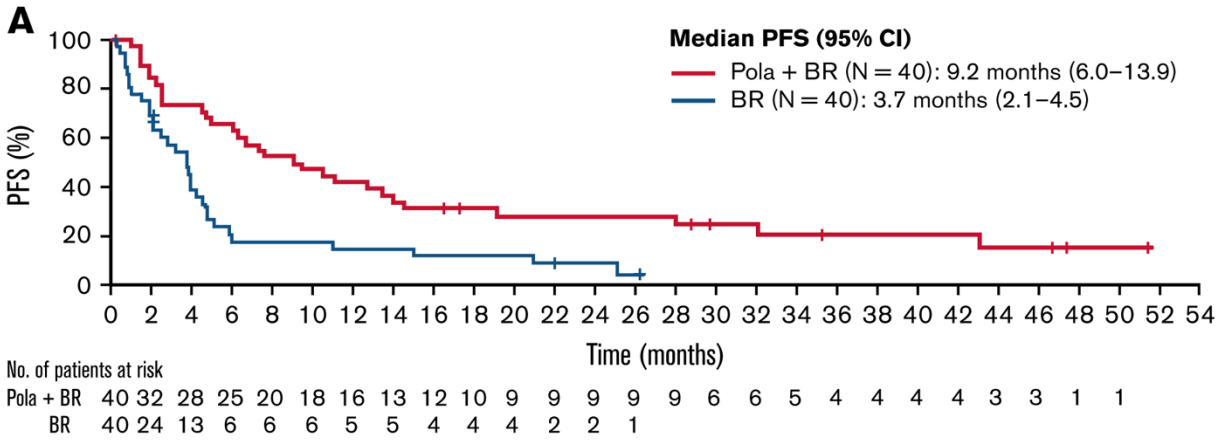
- AZD0486 showed clinical activity in patients who were heavily pretreated, including those with DLBCL and exposed to CAR-T and CD20 TCE treatments[1]

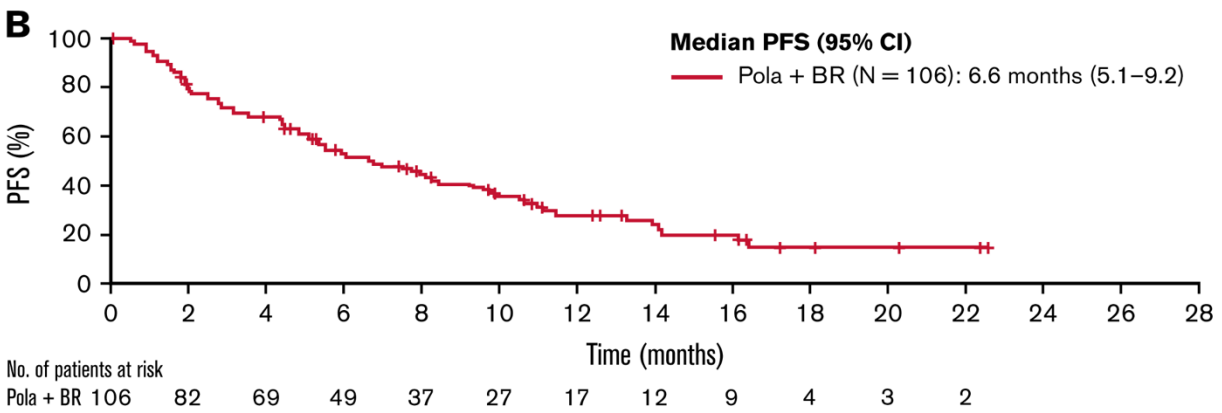
		Overall (N = 58)			CAR-T Naïve (n = 31)			CAR-T Exposed (n = 27)	
Dose	n	ORR, %	CR, %	n	ORR, %	CR, %	n	ORR, %	CR, %
7.2 mg	24	46	33	9	67	44	15	33	27
15 mg	26	62	39	16	75	38	10	40	40
25 mg	8	75	63	6	83	67	2	50	50

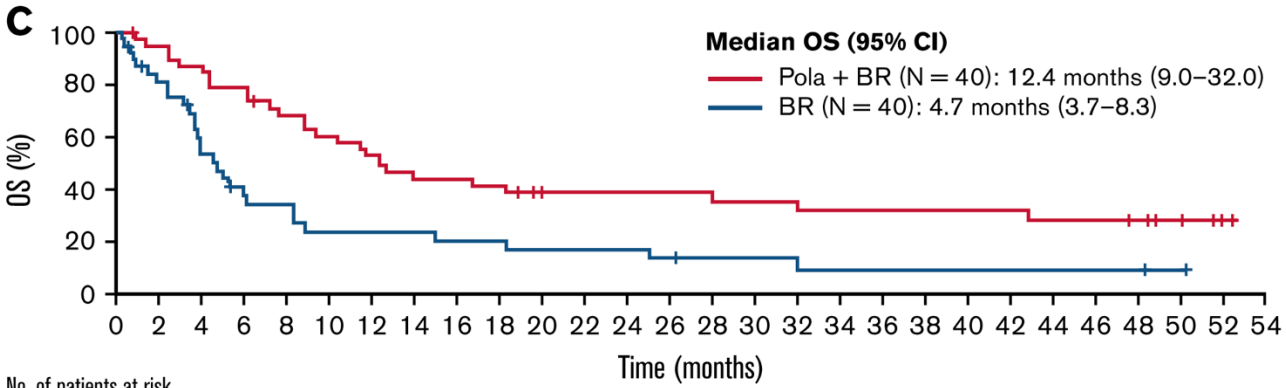
- Median study follow up: 5 mo (range, 0.4 29.3)
- No patients who achieved CR progressed

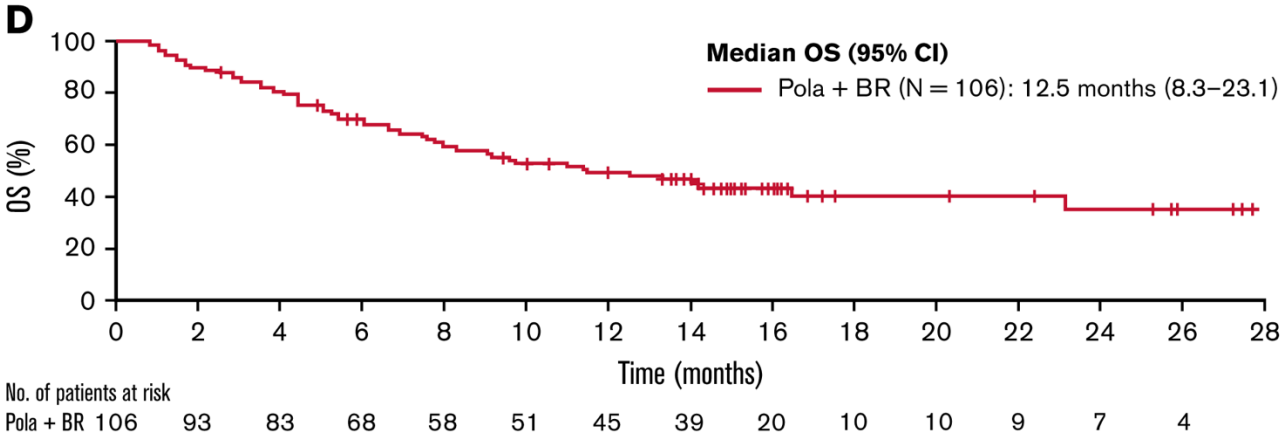
Kim et al. J Clin Oncol 43, 7046 (2025)

ADCs - Polatuzumab vedotin plus bendamustine and rituximab in relapsed/refractory DLBCL: survival update and new extension cohort data





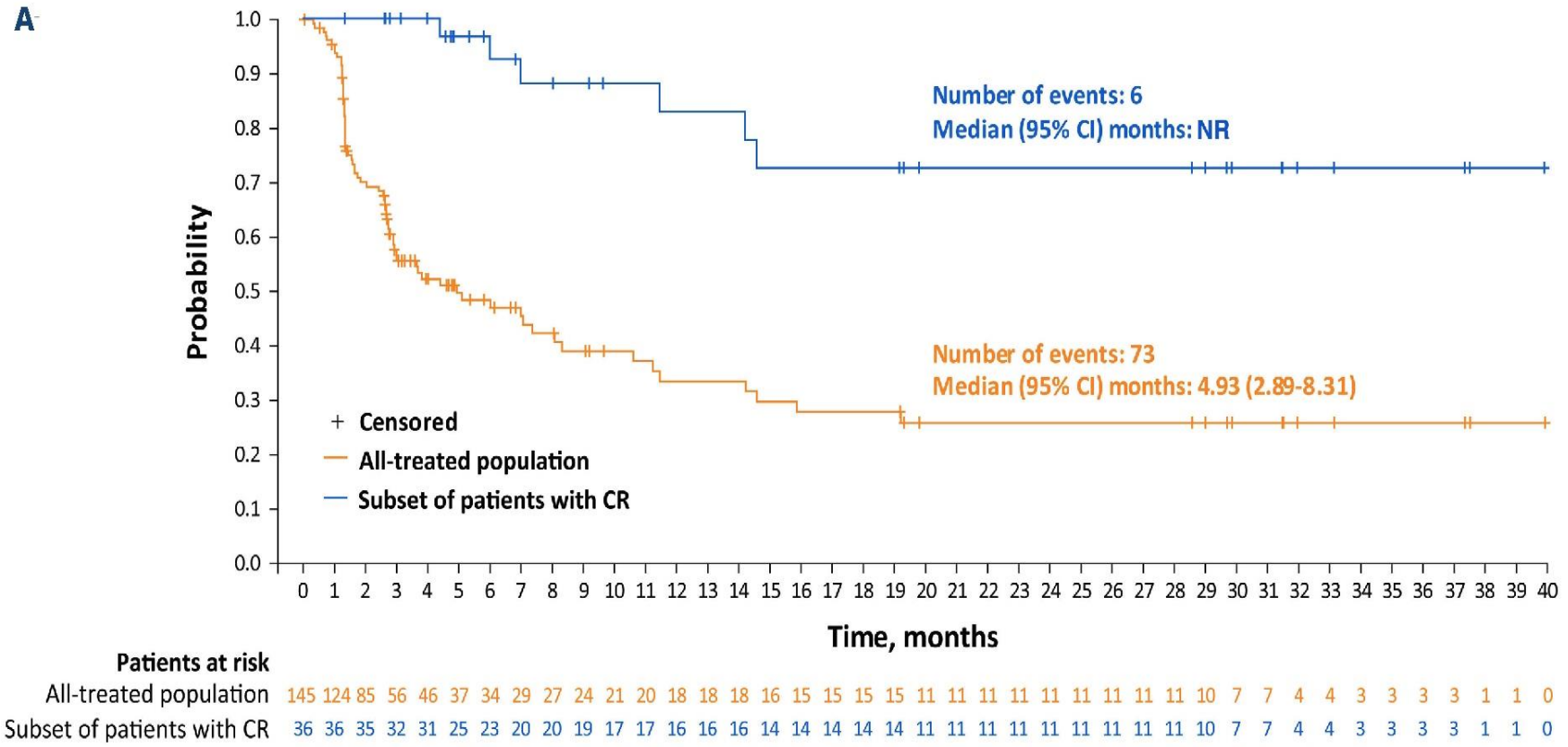




Only 1 patient had prior CART therapy

Sehn et al. Blood Adv. 2022 Jan 25;6(2):533-543.

ADCs - Loncastuximab tesirine in relapsed/refractory diffuse large B-cell lymphoma: long-term efficacy

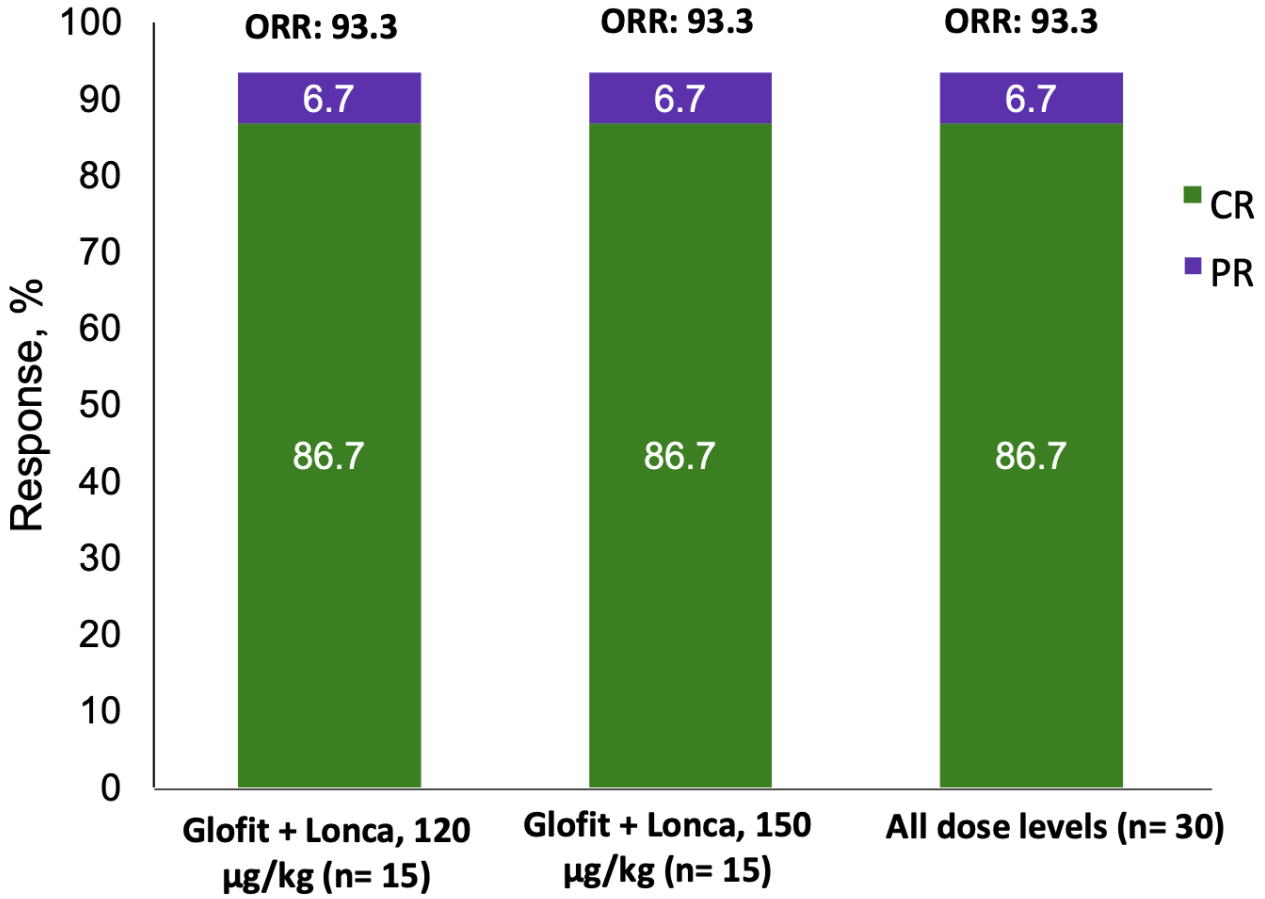


- 145 patients enrolled.
- ORR 48.3%.
- Thirty-six (24.8%) achieved CR, of which 16 (44%) and 11 (31%) were event-free for ≥1 year and ≥2 years, respectively.
- Median OS 9.5 months
- Median PFS 4.9 months.

Caimi PF, et al. Haematologica. 2024 Apr 1;109(4):1184-1193.

Loncastuximab Tesirine plus Glofitamab in Relapsed/ Refractory DLBCL (LOTIS-7)

Best overall response

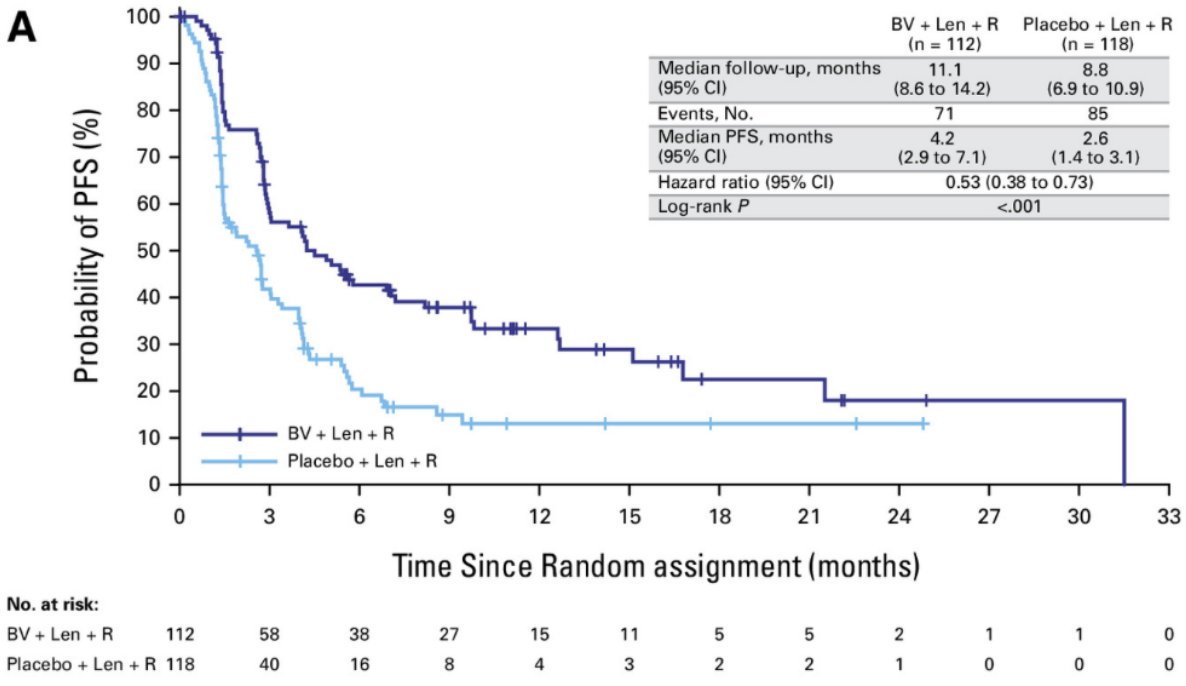


Duration of response

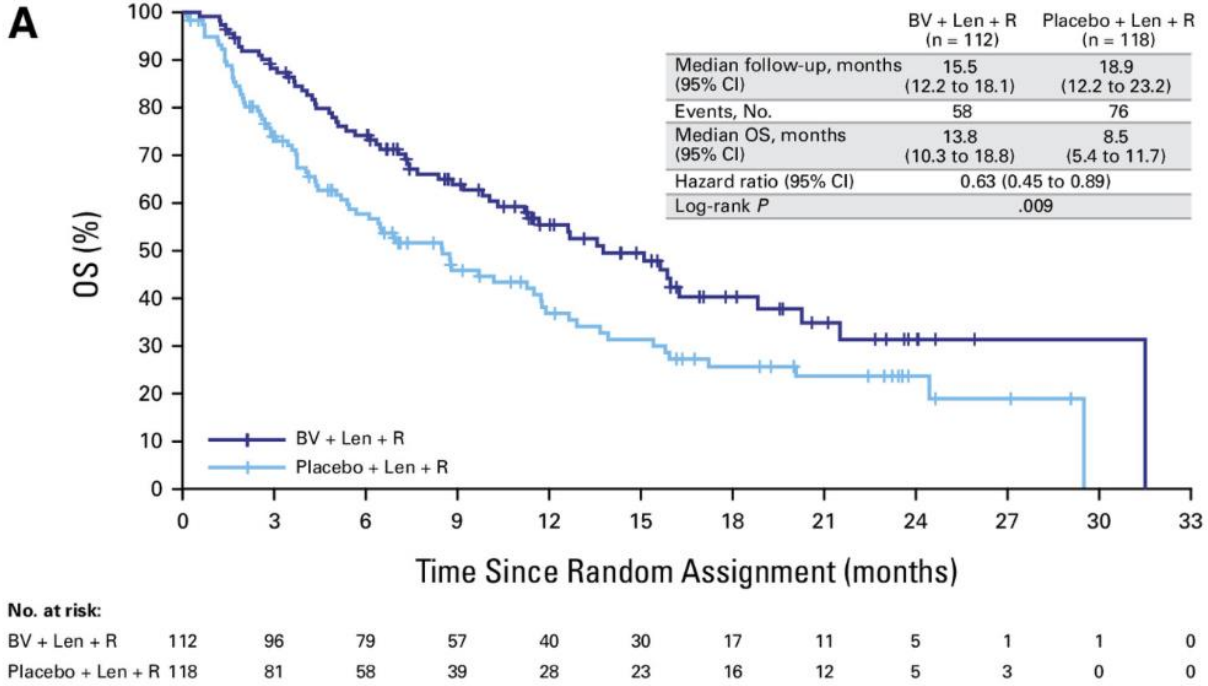
Characteristic, n (%)	Glofit + Lonca, 120 µg/kg (n=15)	Glofit + Lonca, 150 µg/kg (n=15)	All dose levels (N=30)
DOR Median	(n=14) NE	(n=14) NE	(n=28) NE
Time to first response (CR or PR) Median, days	(n=14) 42.0	(n=14) 42.0	(n=28) 42.0
Time to first CR Median, days	(n=13) 80.0	(n=13) 42.0	(n=26) 70.5

Alderuccio JP. *Hematol Oncol (18-ICML meeting abstracts)*, 2025; 43 (S3): 78

ADCs - Brentuximab Vedotin in Combination with R^2 for Relapsed Diffuse Large B-Cell Lymphoma (ECHELON-3)



	BV + Len + R (n = 112)	Placebo + Len + R (n = 118)
Median follow-up, months (95% CI)	11.1 (8.6 to 14.2)	8.8 (6.9 to 10.9)
Events, No.	71	85
Median PFS, months (95% CI)	4.2 (2.9 to 7.1)	2.6 (1.4 to 3.1)
Hazard ratio (95% CI)	0.53 (0.38 to 0.73)	
Log-rank *P*	<.001	

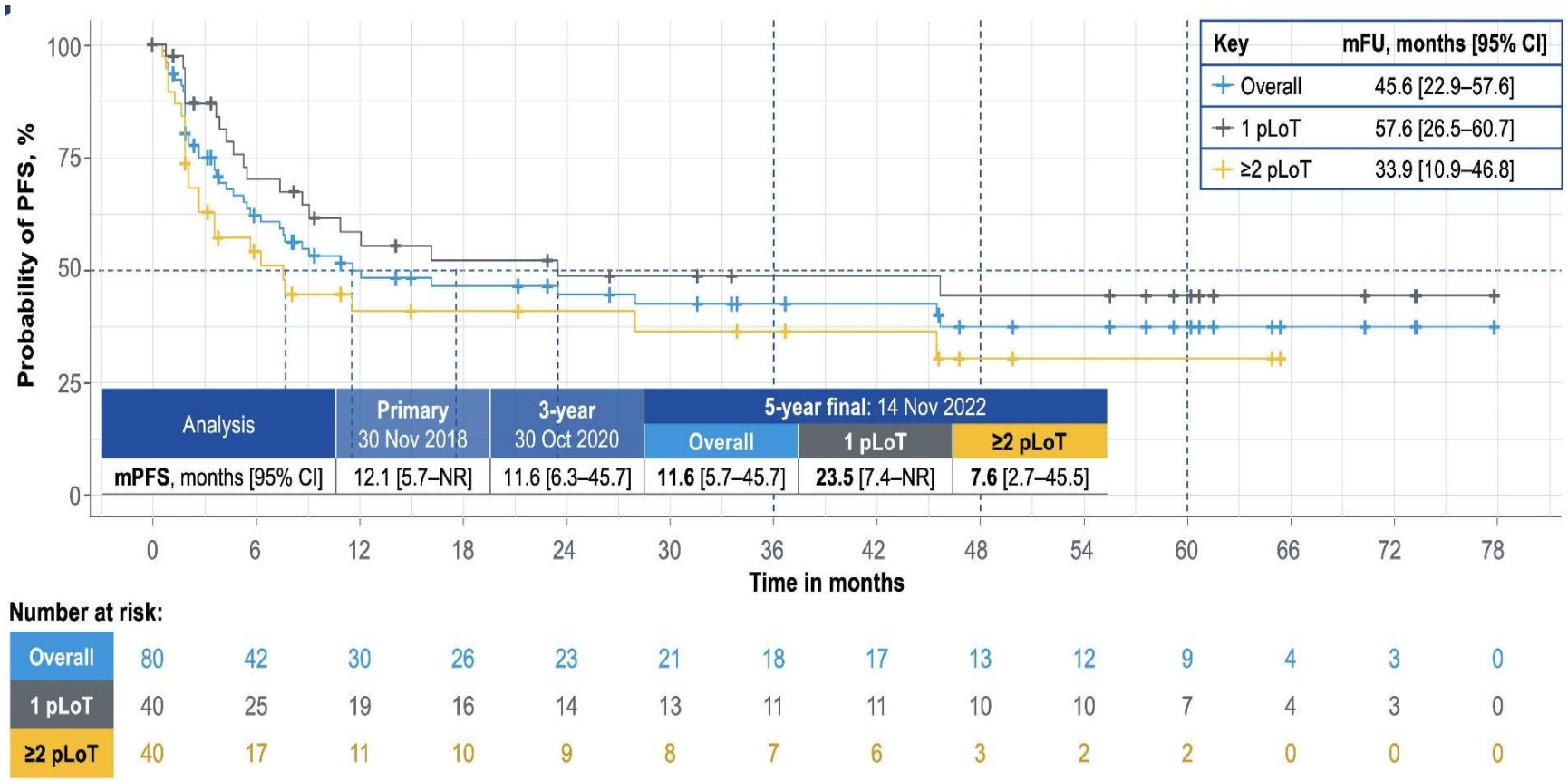


	BV + Len + R (n = 112)	Placebo + Len + R (n = 118)
Median follow-up, months (95% CI)	15.5 (12.2 to 18.1)	18.9 (12.2 to 23.2)
Events, No.	58	76
Median OS, months (95% CI)	13.8 (10.3 to 18.8)	8.5 (5.4 to 11.7)
Hazard ratio (95% CI)	0.63 (0.45 to 0.89)	
Log-rank *P*	.009	

- 230 patients - BV + Len + R (n = 112) or placebo + Len + R (n = 118).
- Median OS was 13.8 months with BV + Len + R versus 8.5 months with placebo + Len + R (*P* = .009).
- Median PFS was 4.2 months with BV + Len + R versus 2.6 months with placebo + Len + R (*P* < .001).
- ORR was 64% with BV + Len + R and 42% with placebo + Len + R
- CR rates were 40% and 19%, respectively.

Bartlett et al. J Clin Oncol. 2025 Jan 7:JCO2402242.

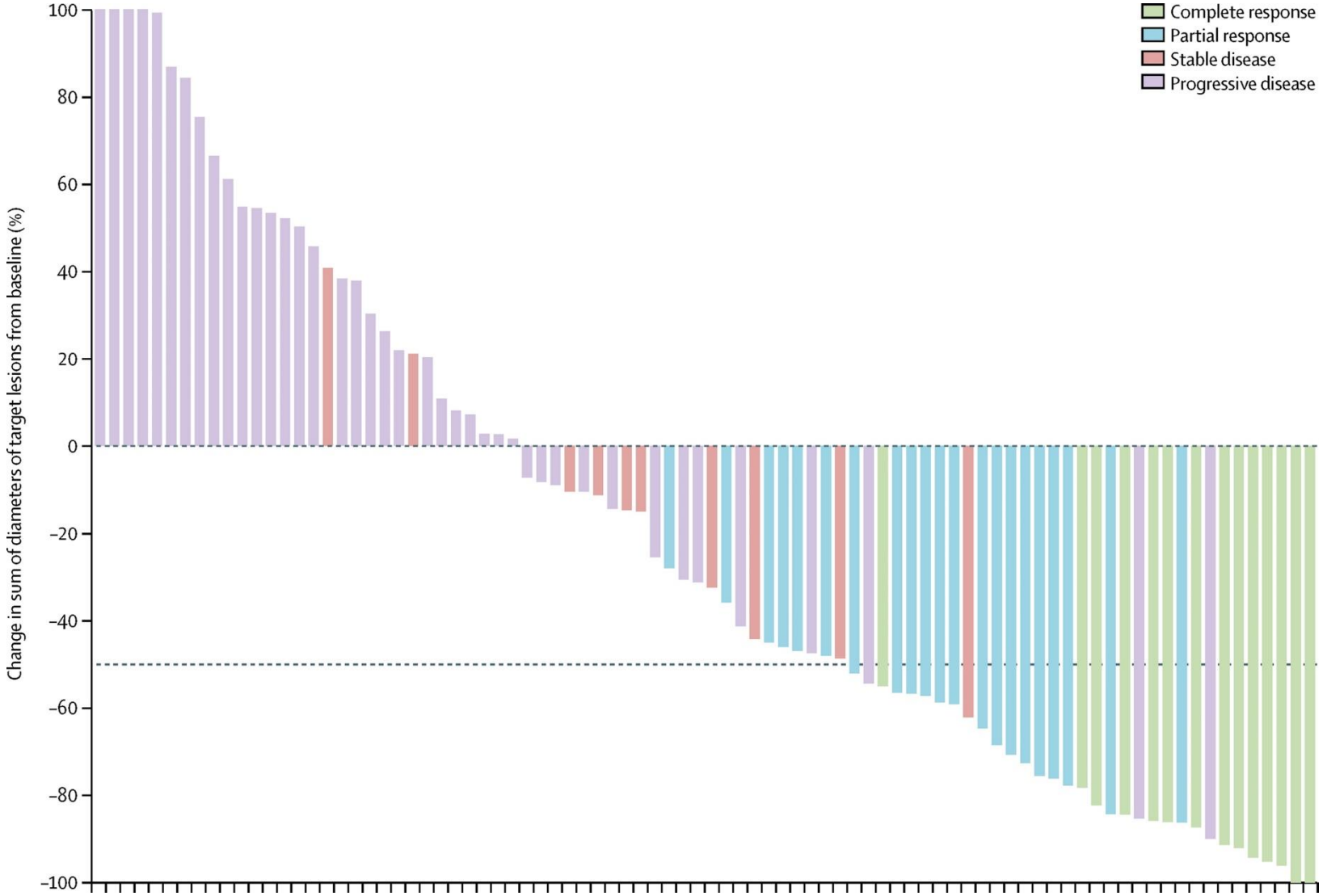
Antibodies - Tafasitamab for relapsed or refractory diffuse large B-cell lymphoma: final 5-year efficacy



- 80 R/R DLBCL patients
- Received up to 12 cycles of co-administered tafasitamab and lenalidomide, followed by tafasitamab monotherapy until progression
- ORR 57.5%, CR rate 41.3% (n=33).
- Median PFS 11.6 months.
- Median OS 33.5 months.

Duell et al. Haematologica. 2024 Feb 1;109(2):553-566.

Selinexor in patients with relapsed or refractory diffuse large B-cell lymphoma (SADAL)



267 patients

175 allocated to the 60 mg selinexor group and 92 to the 100 mg selinexor group.

Overall response rate was 28%

15 (12%) achieved a complete response and 21 (17%) a partial response.

Median overall survival was 9.0 months and median progression free survival was 2.6 months

No patient had received prior CART therapy

Kalakonda et al. Lancet Haematol. 2020 Jul;7(7):e511-e522.

Questions that may influence treatment decisions

- Which agents were given before – would you give brentuximab vedotin if the patient received polatuzumab vedotin in first-line? **Personally - No**
- Do you want to use a similar treatment strategy versus a different one – is an immunotherapeutic approach with a bispecific antibody the best choice if a patient just progressed on CAR T cell treatment? **Yes – bispecifics are effective after CART**
- Should you direct therapy at the same target as before – should you target CD19 with tafasitamab as the next line after CD19 CAR T cell therapy? **You can**
- Should you give treatment that has similar side effects – should you give a bispecific if very immunosuppressed, or cytotoxic therapy if neutropenic? **Depends**
- How long do you plan to treat (tolerability over time) – is this treatment a bridge to another therapy or do you plan to treat to progression? **Tafa/len if long-term**