New algorithm for relapsed/refractory DLBCL patients: is there a role and if so which one for each actor in this orchestra?

Stephen M. Ansell, MD, PhD

Dorotha W. and Grant L. Sundquist Professor in Hematologic Malignancies Research

Chair, Division of Hematology

Mayo Clinic

Disclosures for Stephen Ansell, MD, PhD

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Research Support/P.I.	PI – BMS, Takeda, Affimed, Regeneron, AI Therapeutics, Pfizer, AstraZeneca, ADC Therapeutics for clinical trials
Employee	N/A
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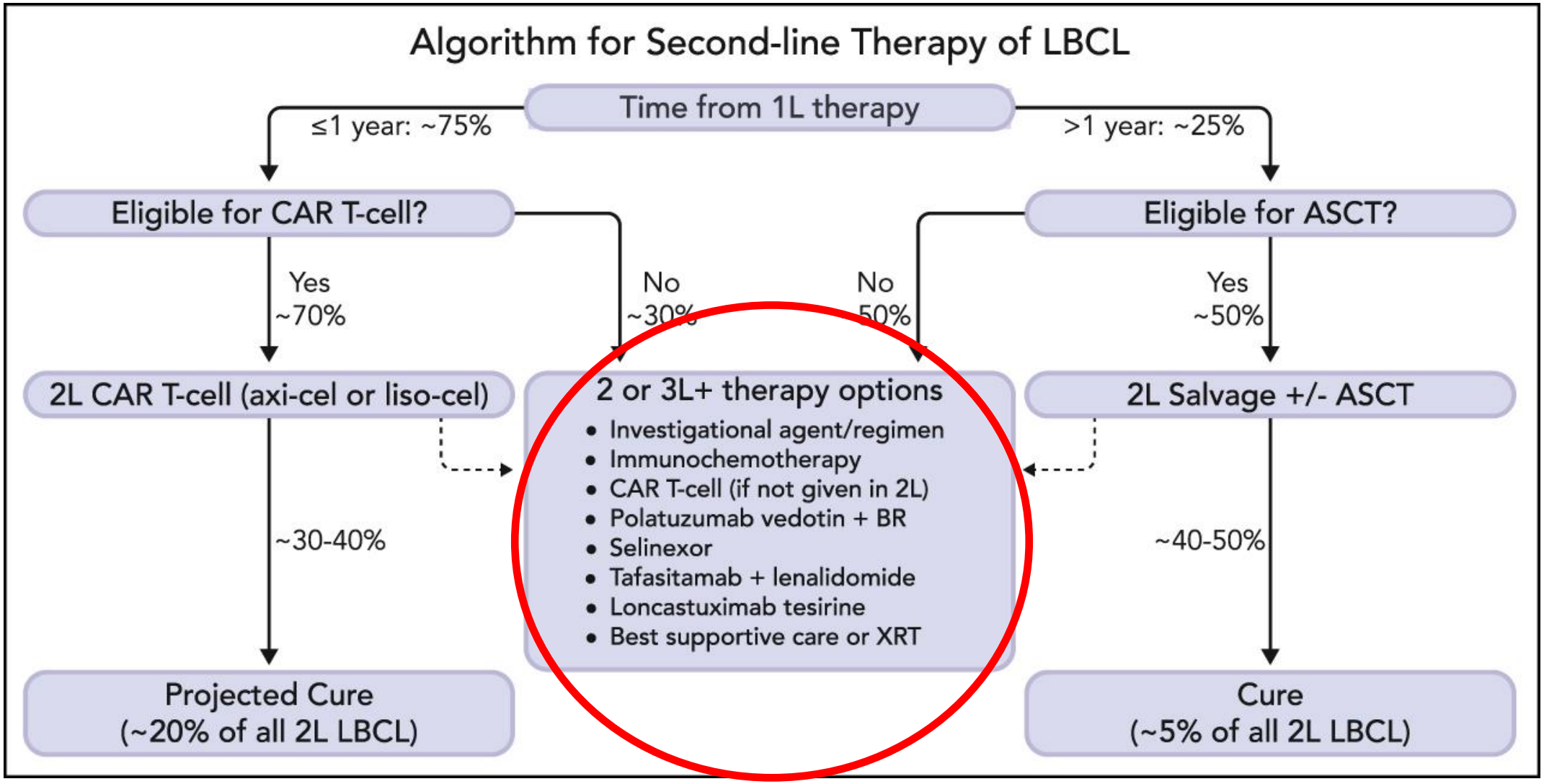
Major Stockholder	N/A
Speakers' Bureau	N/A
Scientific Advisory Board	N/A

N/A = Not Applicable (no conflicts listed)

CAR T cells as a second-line therapy for large B-cell lymphoma: a paradigm shift?



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

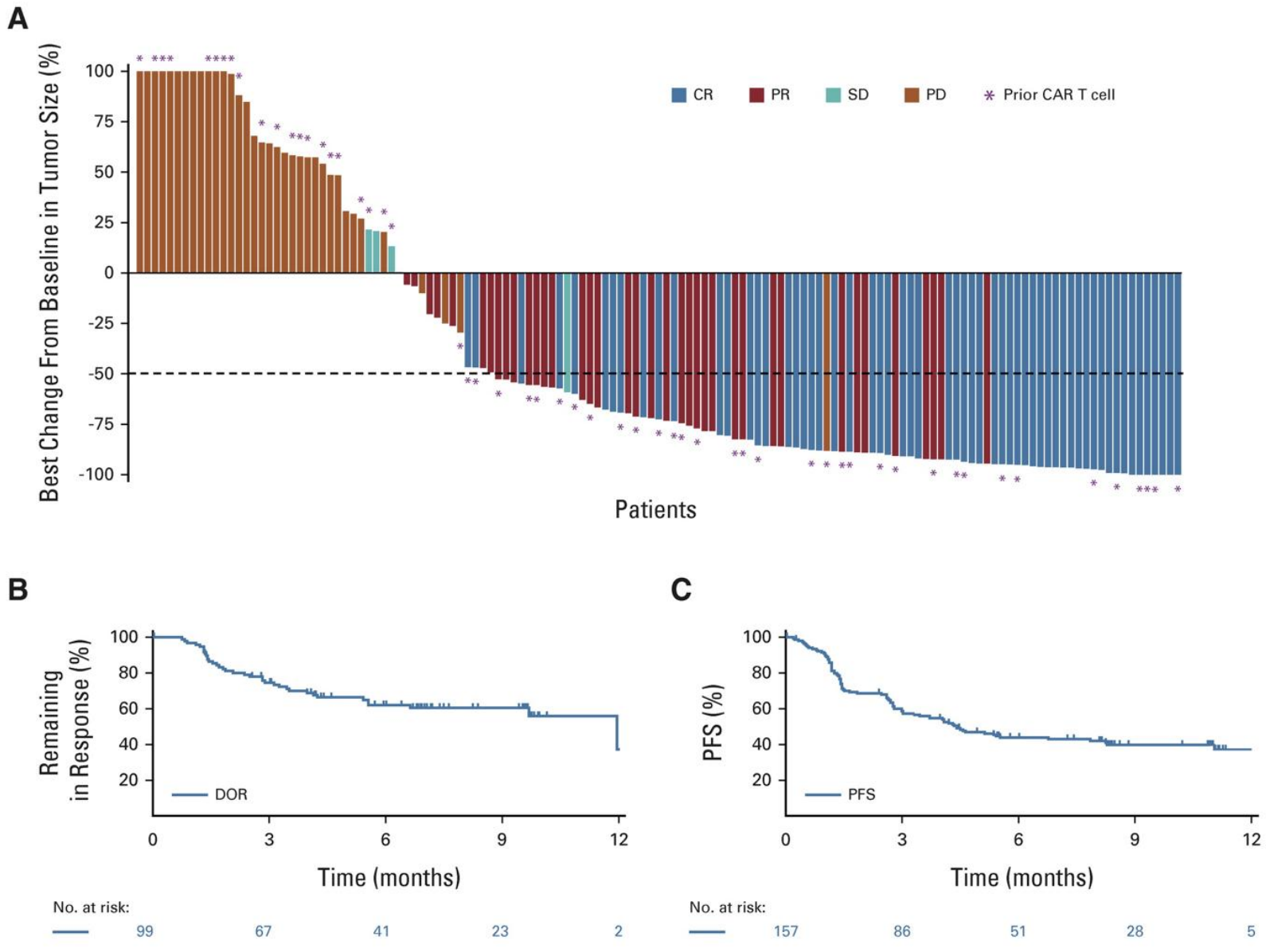
Who are the Actors, Musicians or Players?

- Bispecifics – epcoritamab, glofitamab, (odronextamab)
- Antibody drug conjugates – polatuzumab vedotin, loncastuxtimab, brentuximab vedotin.
- Others – tafasitamab, lenalidomide, bendamustine, selinexor

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

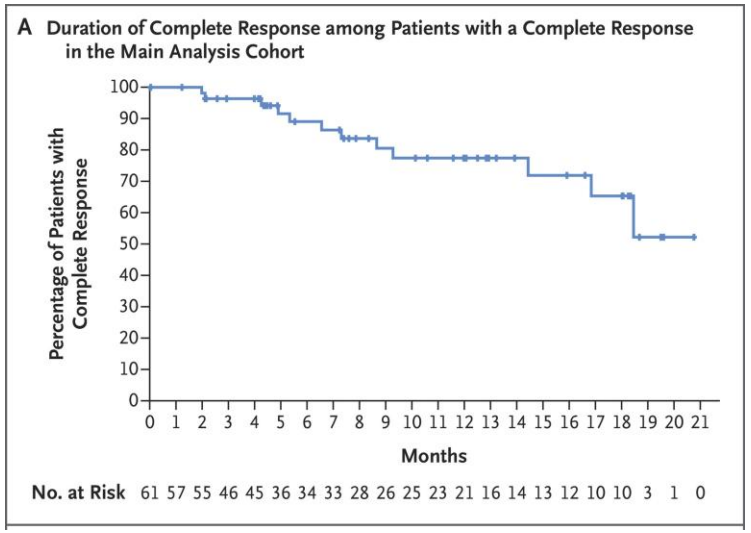


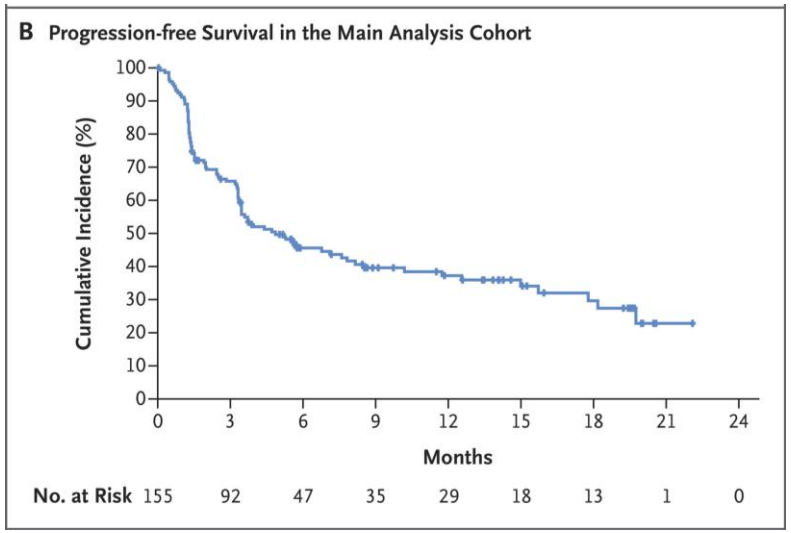
157 DLBCL patients
ORR 63% CR 39%
DOR 12 months

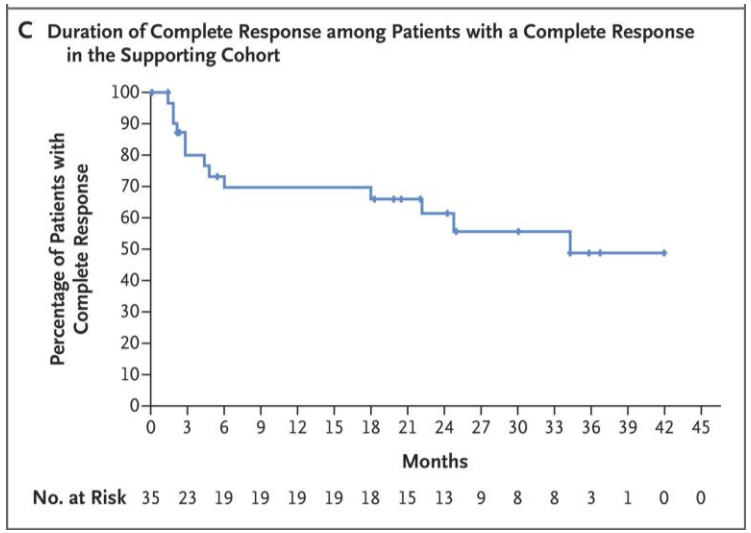
In patients who received prior CAR T-cell therapy (n = 61), the ORR was 54.1% and the CR rate was 34.4%, with a mDOR of 9.7 months

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

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







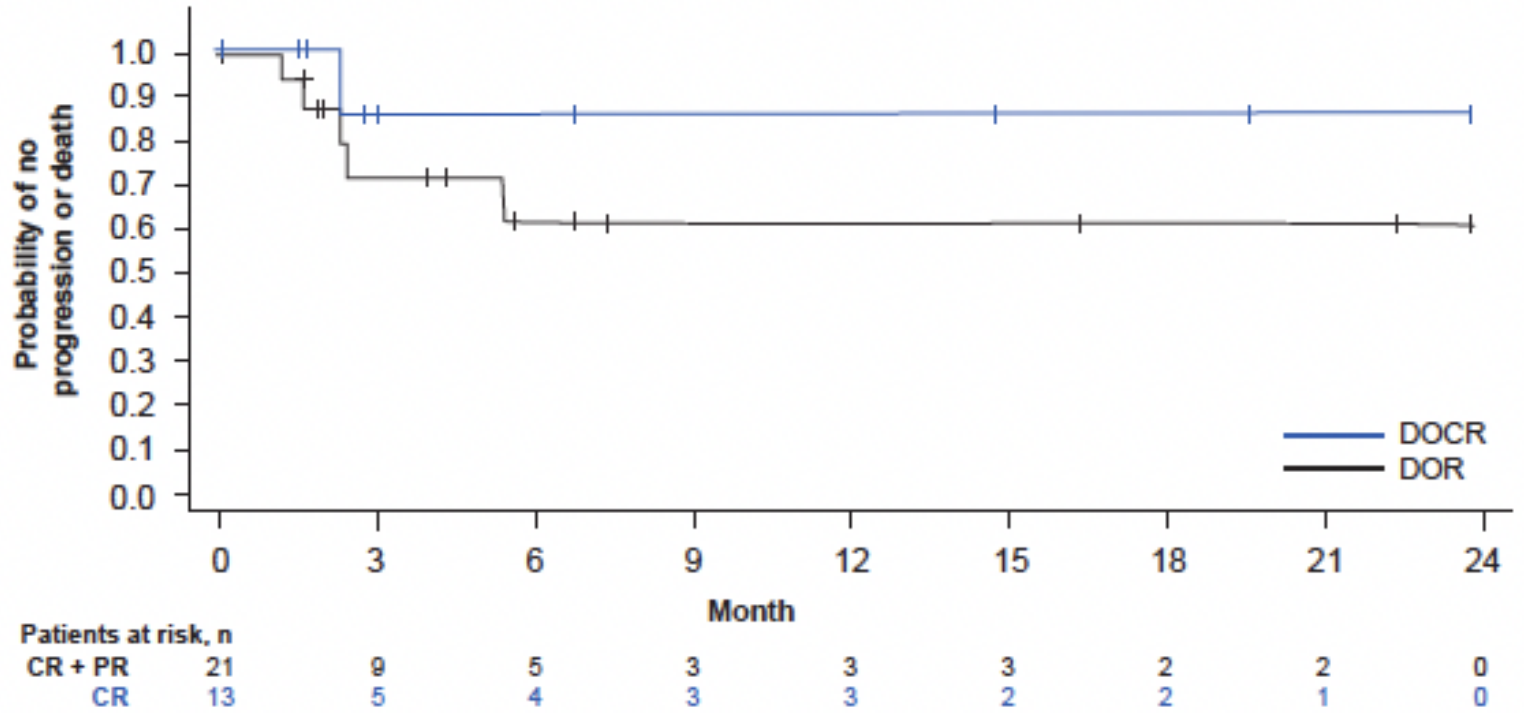
155 patients. Median follow-up of 12.6 months, 39% had a CR.

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.

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.

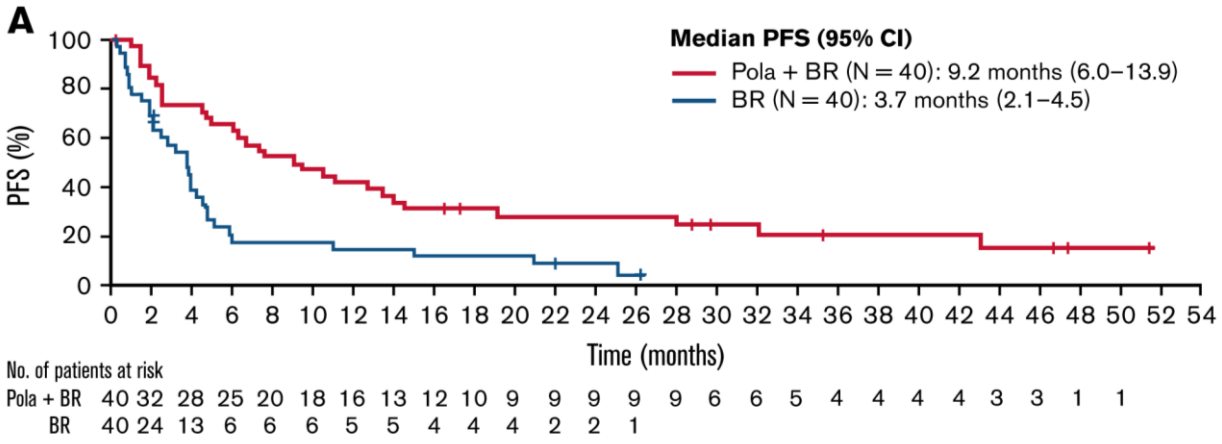
In patients with DLBCL who had previous CAR T-cell therapy and received doses of 80 mg or higher, the objective response rate was 33% (10 of 30) and CR rate was 27% (8 of 30).

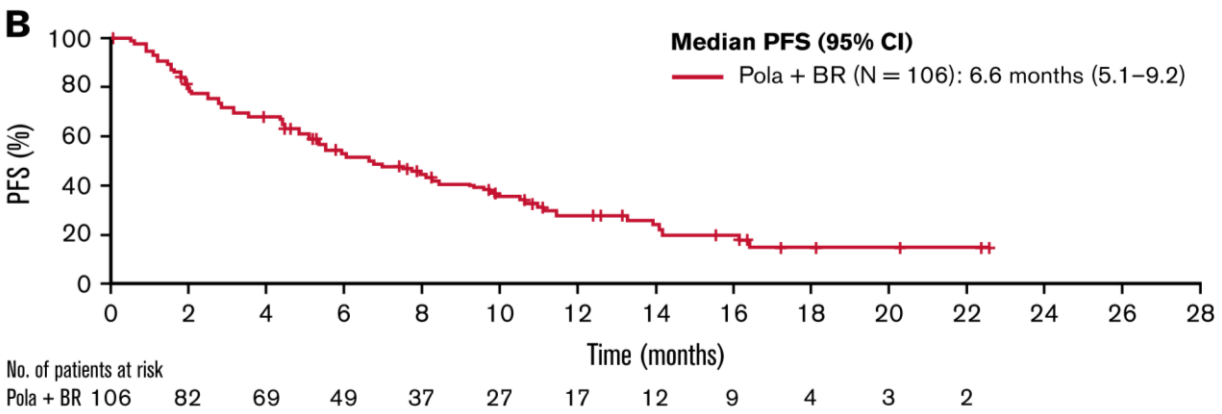
- 12-month PFS rate in all patients: 32.9% (95% CI 16.4–50.6)
- 12-month OS rate in all patients: 49.6% (95% CI 30.4–66.2)

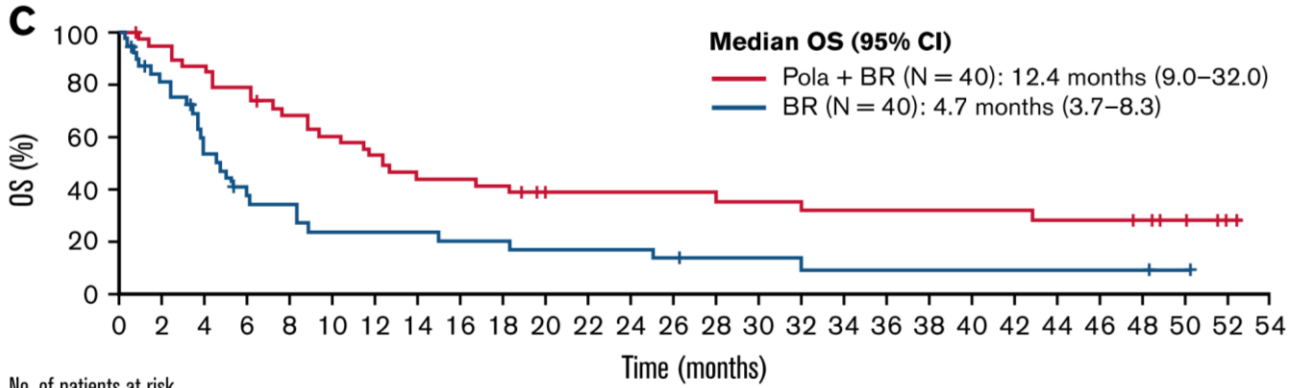
Bannerji R, et al. Lancet Haematol. 2022 May;9(5):e327-e339.

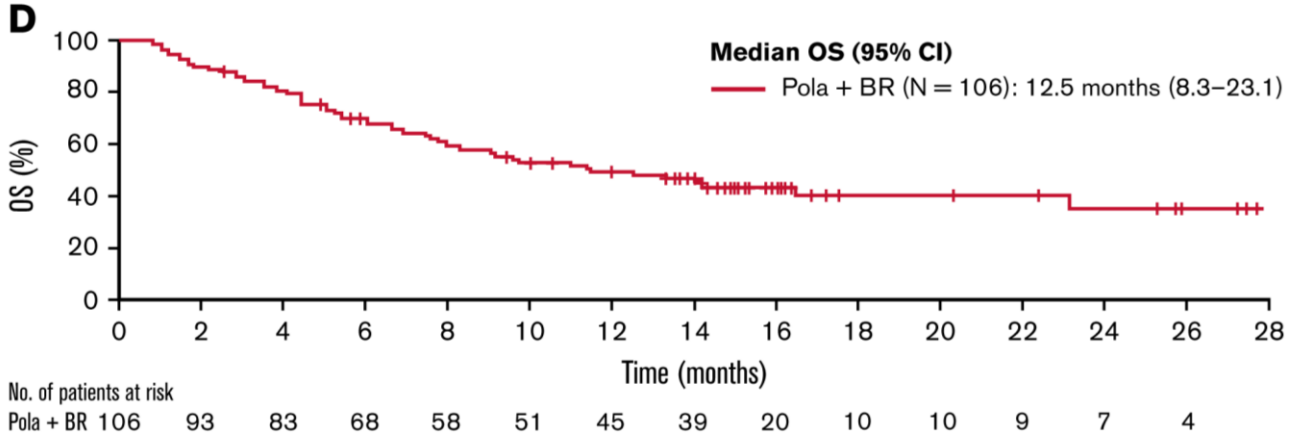
Michot et al. EHA 2024, June 2024. Poster P1162.

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

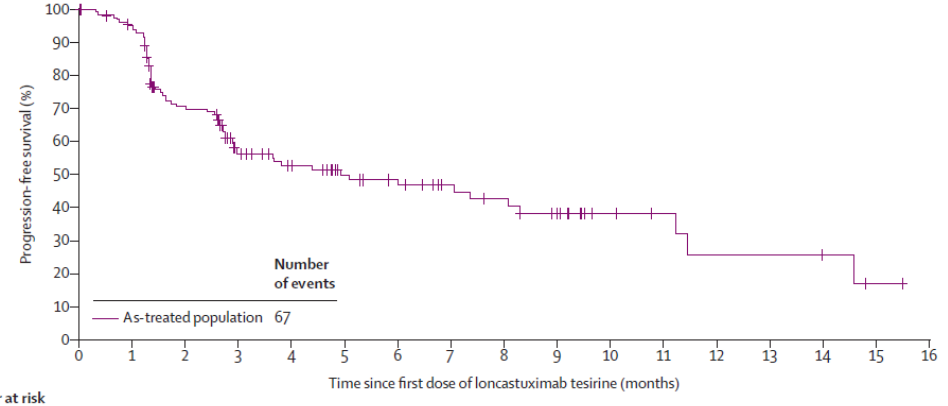
Sehn et al. Blood Adv. 2022 Jan 25;6(2):533-543.

ADC - Loncastuximab tesirine: PFS, OS, and Subsequent Treatment (LOTIS-2)

Median PFS:

Apr 6 2020 Cut Off: 4.9 mo (95% CI, 2.9-8.3)[1]

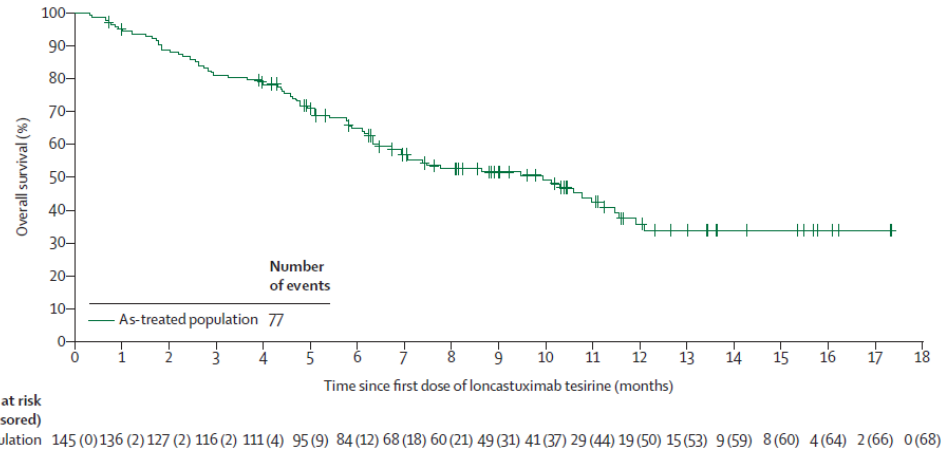
Aug 6 2020 Cut Off: 5.1 mo (95% CI, 2.9-8.3)[2]



Median OS:

Apr 6 2020 Cut Off: 9.9 mo (95% CI, 6.7-11.5)[1]

Aug 6 2020 Cut Off: 9.5 mo (95% CI, 6.9-11.3)[2]



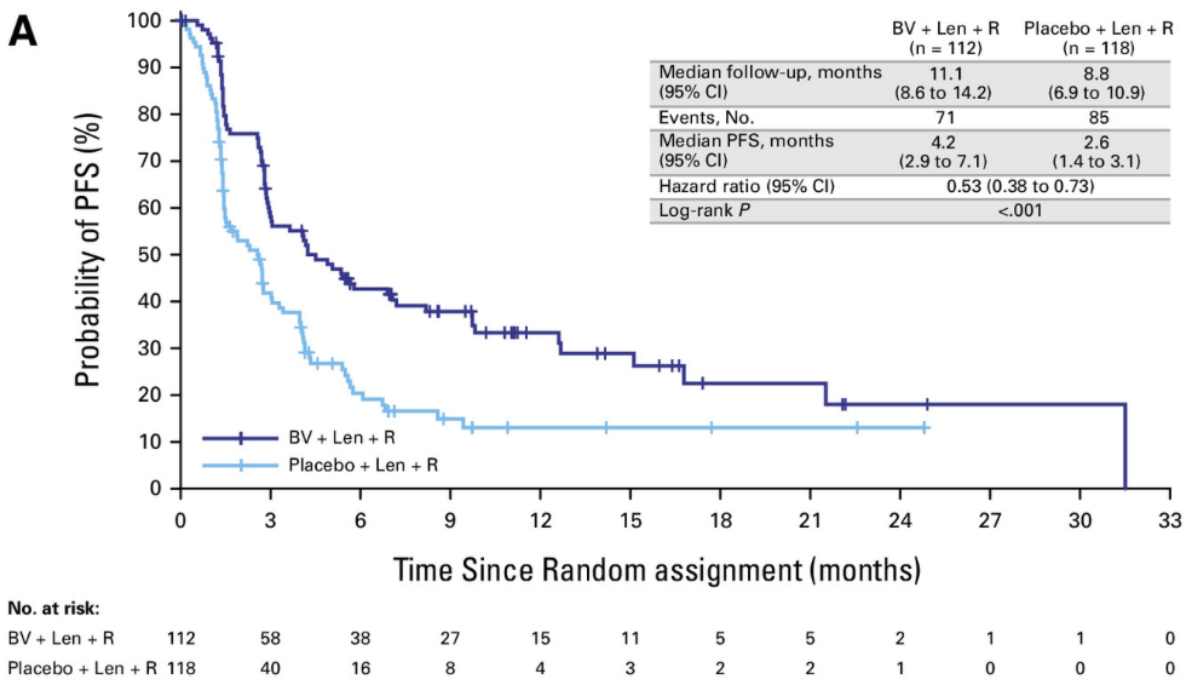
Subsequent Treatment[2]

- **15 patients** received CD19-directed CAR-T therapy with an investigator-assessed ORR of 46.7% (6 CR; 1 PR)
- **9 patients** proceeded to SCT as consolidation after response to lonca

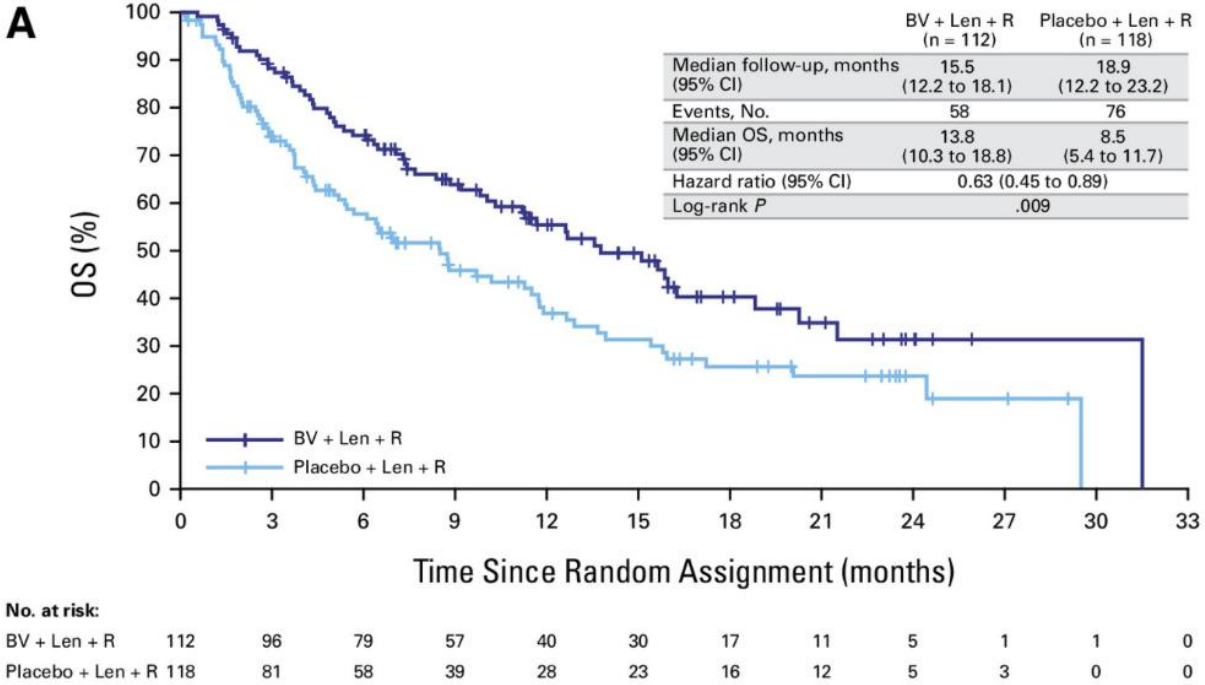
145 patients enrolled. 14 patients had prior CART therapy – 3 (21%) of these had a CR.

1. Caimi PF, et al. Lancet Oncol. 2021 Jun;22(6):790-800.
2. Caimi PF, et al. Haematologica. 2024 Apr 1;109(4):1184-1193.

ADC - Brentuximab Vedotin in Combination with R² 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	

30% of patients had received prior CAR T therapy

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

Antibody - Long-term outcome of tafasitamab plus lenalidomide in patients with relapsed or refractory DLBCL

- **Median PFS**
  - **At median 33.9 mo follow up: 11.6 mo**

    12-mo PFS, 50%

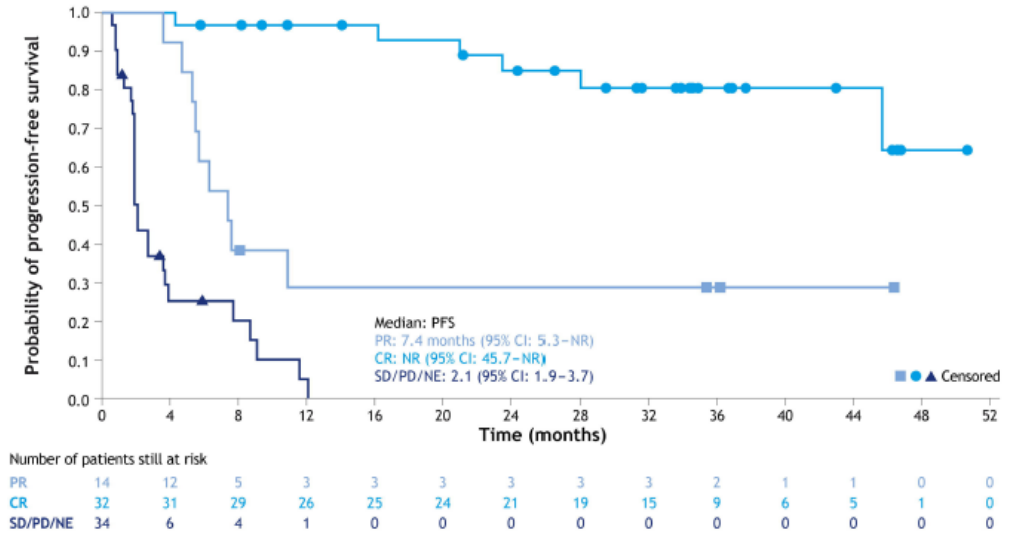
    18-mo PFS: 46%

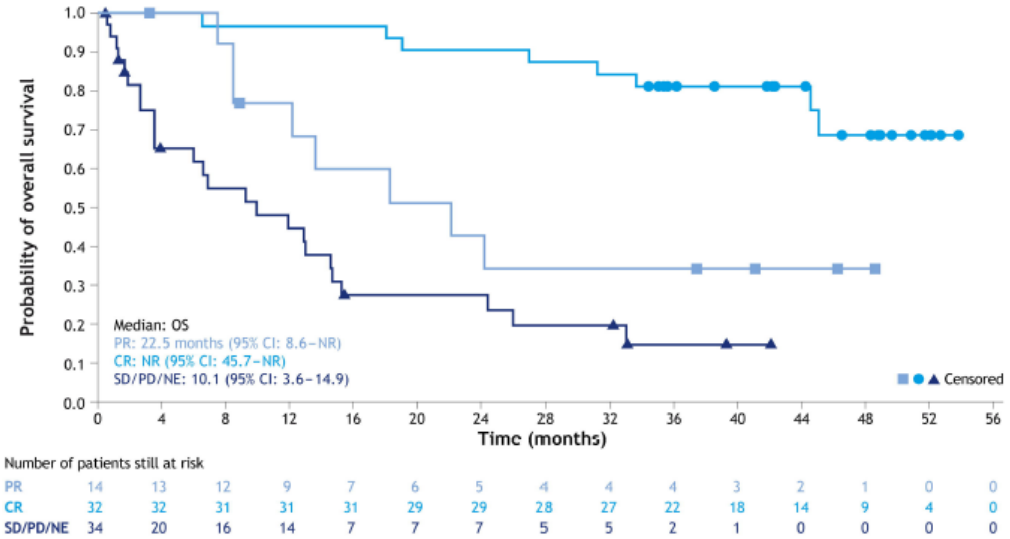
- **Median OS**
  - **At median 42.7 mo follow up: 33.5 mo**

    12-mo OS: 74%

    18-mo OS: 64%

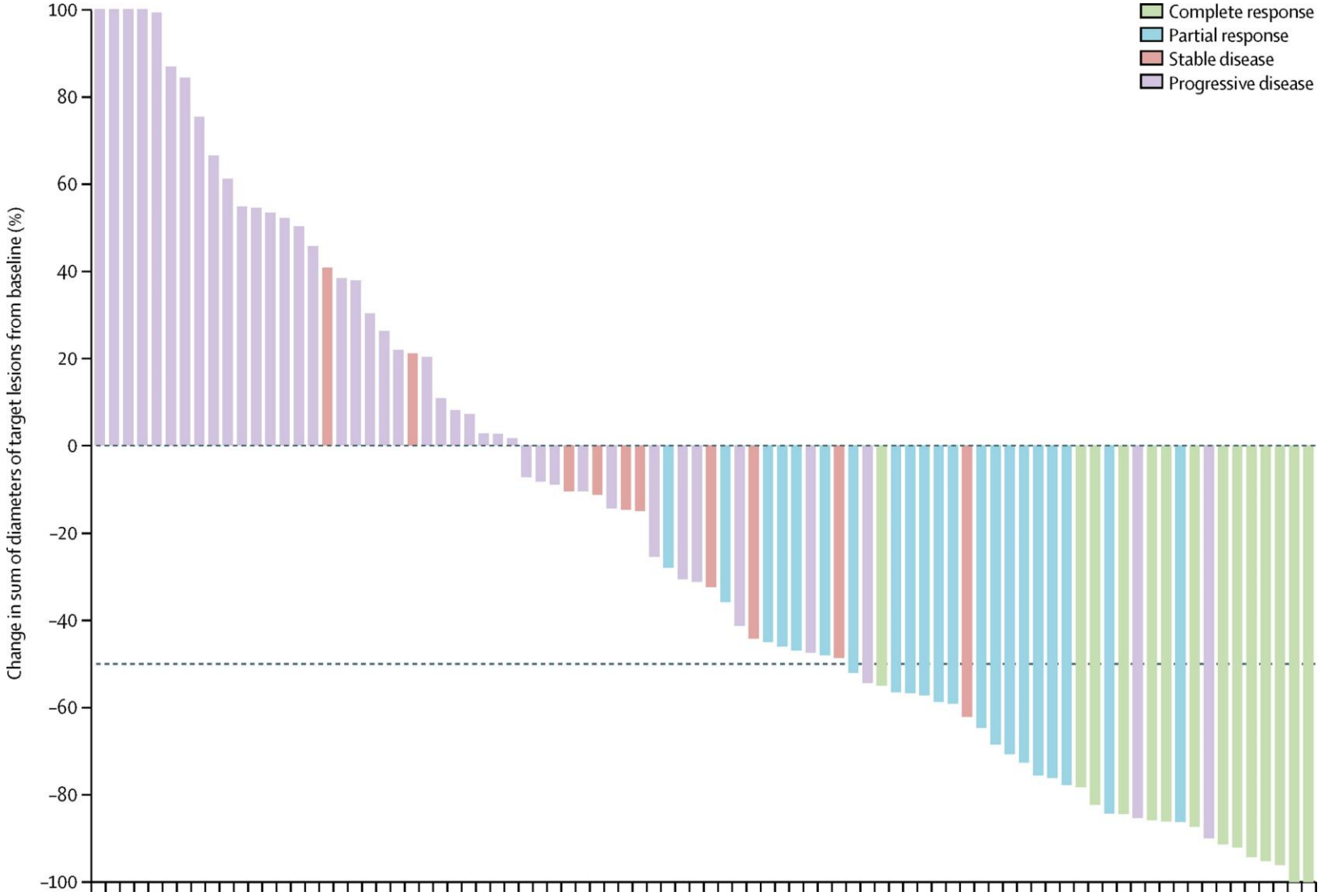
- **No patients had received prior CART therapy**





Duell J, et al. *Haematologica*. 2021;106:2417-2426

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**