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Bispecifics in DLBCL

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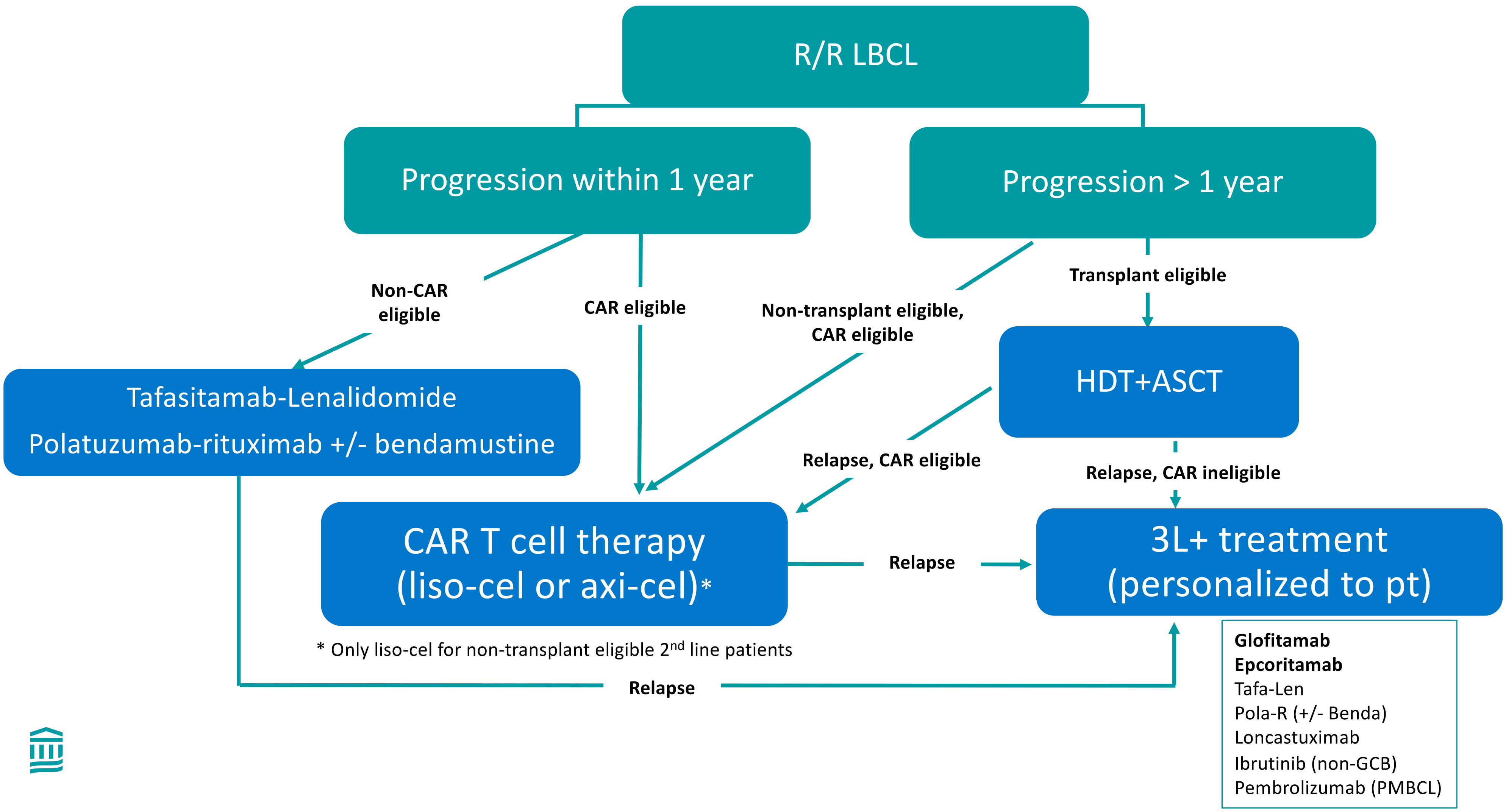
Disclosures for Jeremy Abramson

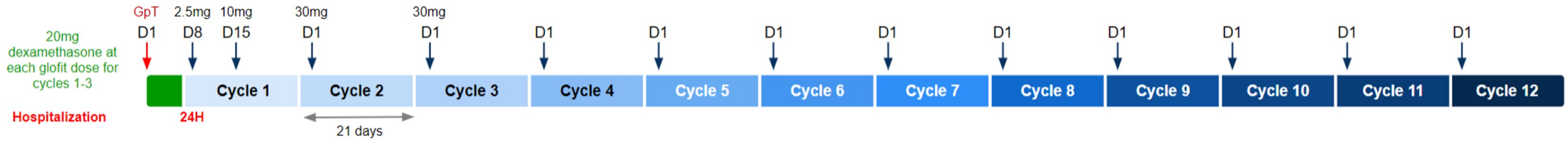
Consulting for AbbVie, Astra-Zeneca, BeiGene, Bristol Myers Squibb, Caribou Biosciences, Cellectar, Genentech, Gilead, Incyte, Interius, Janssen, Lilly, Novartis, Roche, Takeda

My current algorithm for relapsed/refractory DLBCL

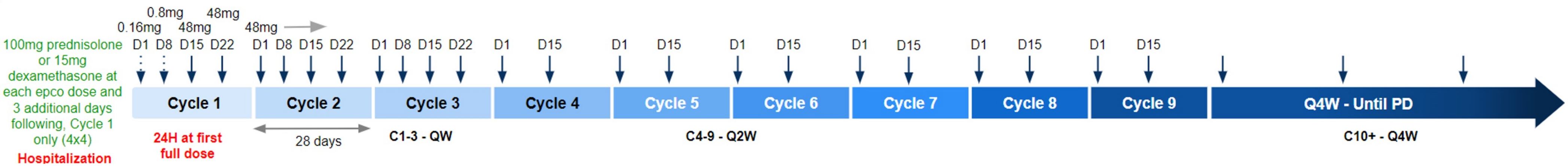


Glofitamab and Epcoritamab Schedules

Glofitamab IV



Epcoritamab SC



Glofitamab in Relapsed/Refractory LBCL

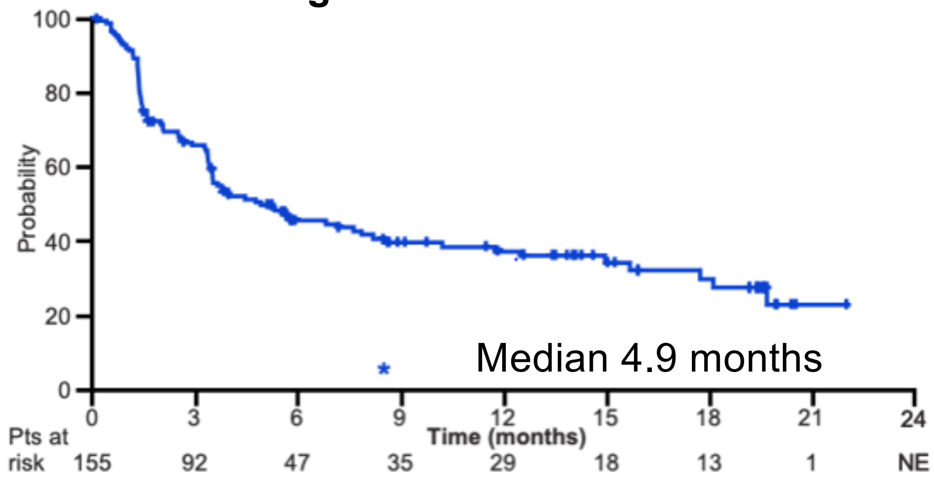
Fixed duration therapy

- Glofitamab IV administration fixed dose with step-up dosing during C1 (target dose: 16mg or 30mg) q21 days
- Obinutuzumab pretreatment (1 x 1000mg) to mitigate CRS
- Fixed duration treatment maximum 12 cycles (8.3 months)

Baseline Characteristics	N=154
Median age (range)	66 (21-90)
Median prior tx (range)	3 (2-7)
Prior ASCT	28 (18%)
Prior CAR	51 (33%)
Refractory to last tx	132 (86%)

Best response
ORR: 52%
CRR: 40%
Median DoR: 18 mo
Median DoCR: 27 mo

Progression-free survival



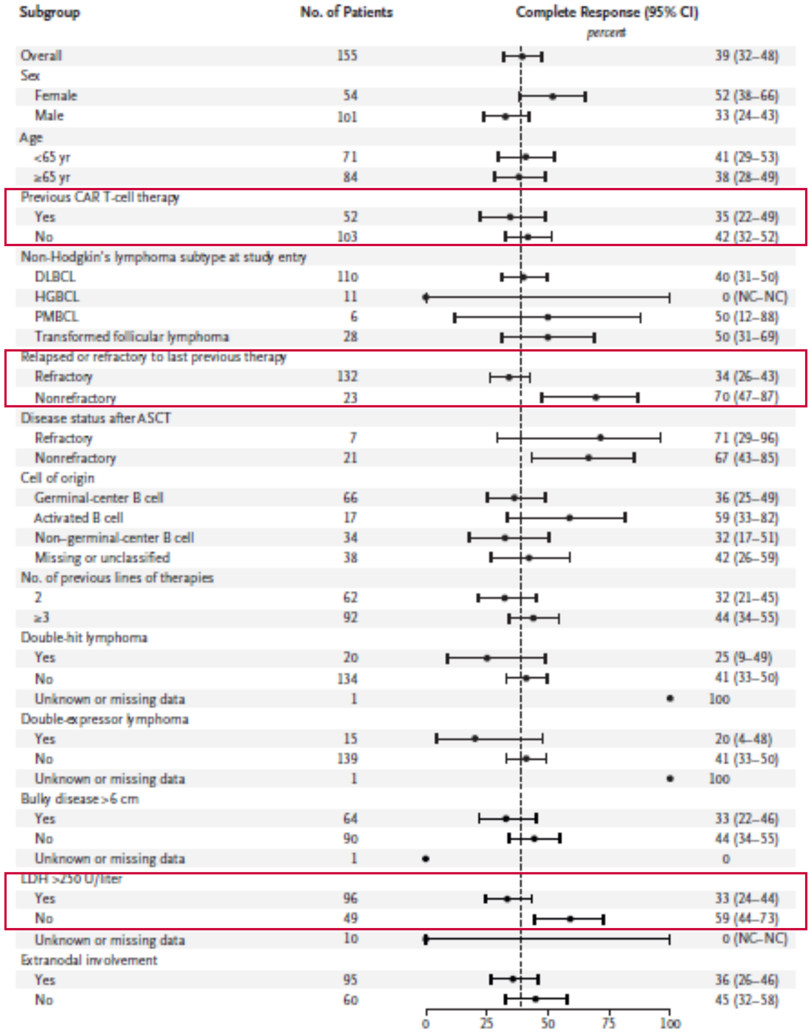
median follow-up of 12.6 months

Notable Adverse Events

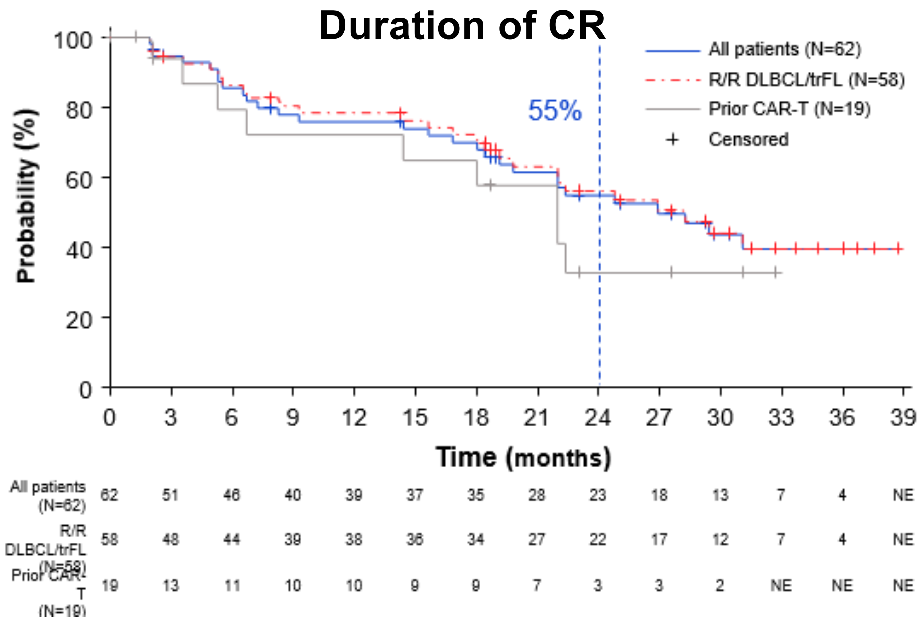
- CRS: 63% (grade 3-4: 4%)
- ICANS: 8% (grade 3-4: 3%)
- Neutropenia: 38%

Dickinson, et al. NEJM 2022, Dickinson, et al. ICML 2023; Hutchings, et al. ASH 2022 Hutchings, et al.; ASH 2023

Glofitamab Complete Responders



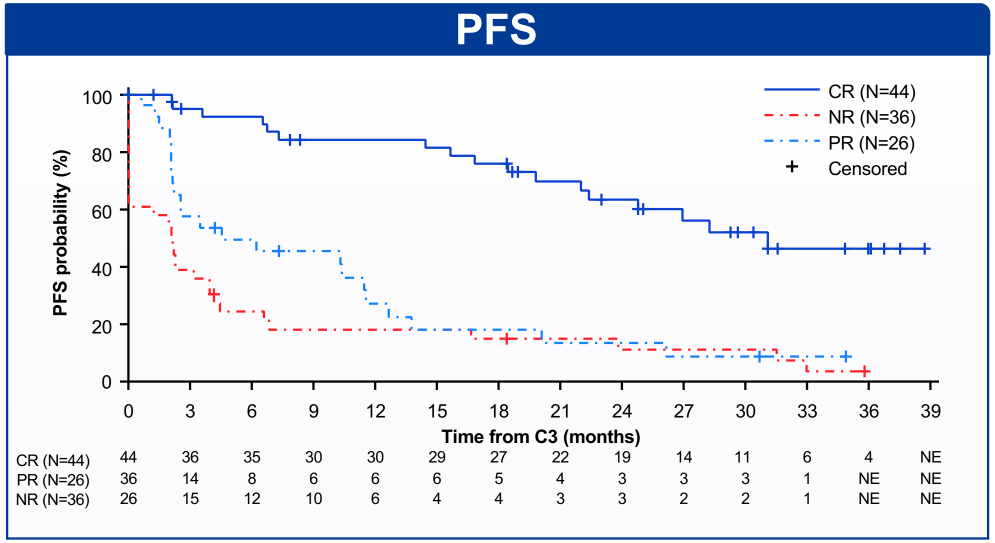
	All patients (N=155)	R/R DLBCL/ trFL (N=132)	Prior CAR-T (N=52)
ORR, n (%)	80 (52)	74 (56)	26 (50)
CR rate, n (%)	62 (40)	58 (44)	19 (37)
Median DOCR, mo	27	28	22
24-month DOCR, %	55	56	33

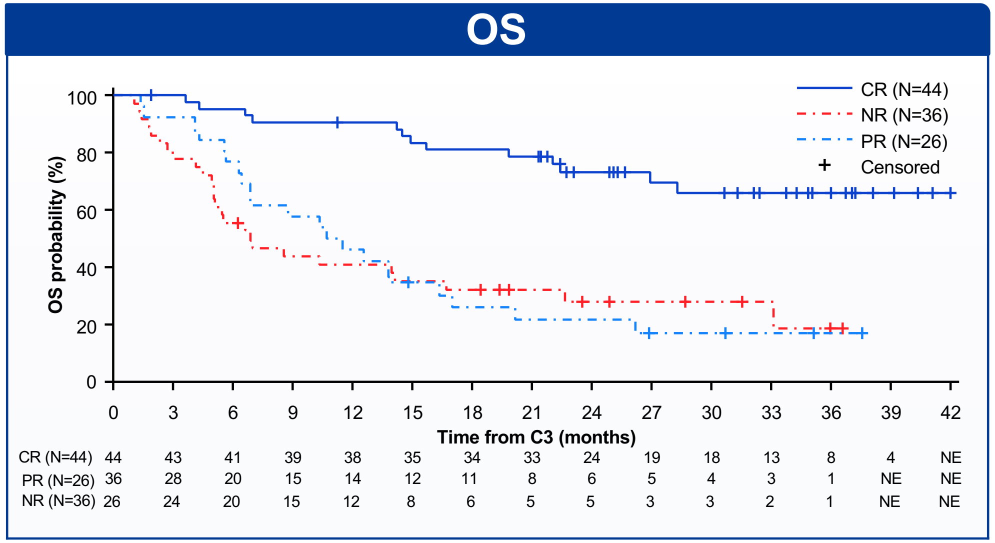


32 months median follow-up

Dickinson, et al. NEJM 2022; Hutchings, et al. Proc ASH 2023

Glofitamab Landmark Analysis at 3 months



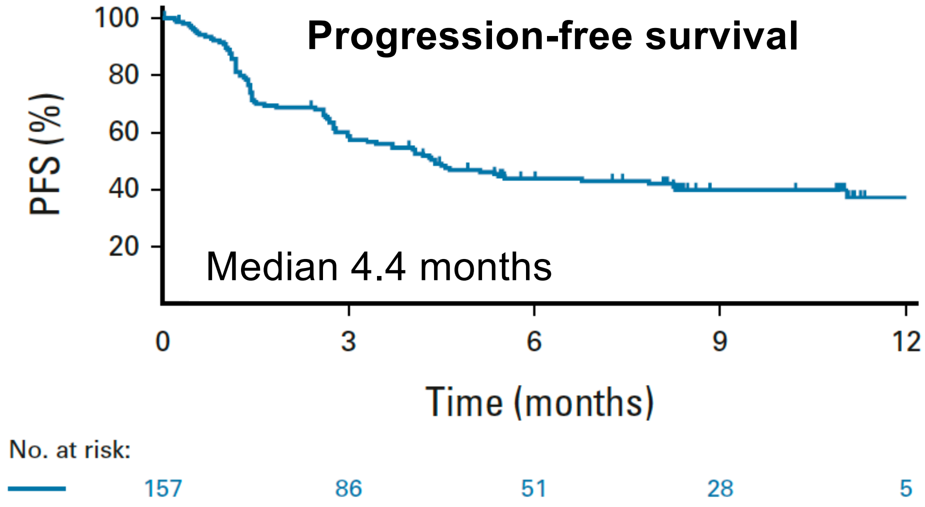


Hutchings, et al. Proc ASH 2023

Epcoritamab in Relapsed/Refractory DLBCL

Treatment until progression or intolerance
Median 9 cycles, 23% continued at data cutoff

Baseline Characteristics	N=157
Median age (range)	64 (20-83)
Median prior tx (range)	3 (2-11)
Prior ASCT	31 (20%)
Prior CAR	61 (39%)
Refractory to last tx	130 (83%)



Best IRC-assessed overall response
ORR: 63%
CRR: 39%
Median DoR: 12.0 mo
Median DoCR: 21 mo (68% at 15 mo)

Notable Adverse Events

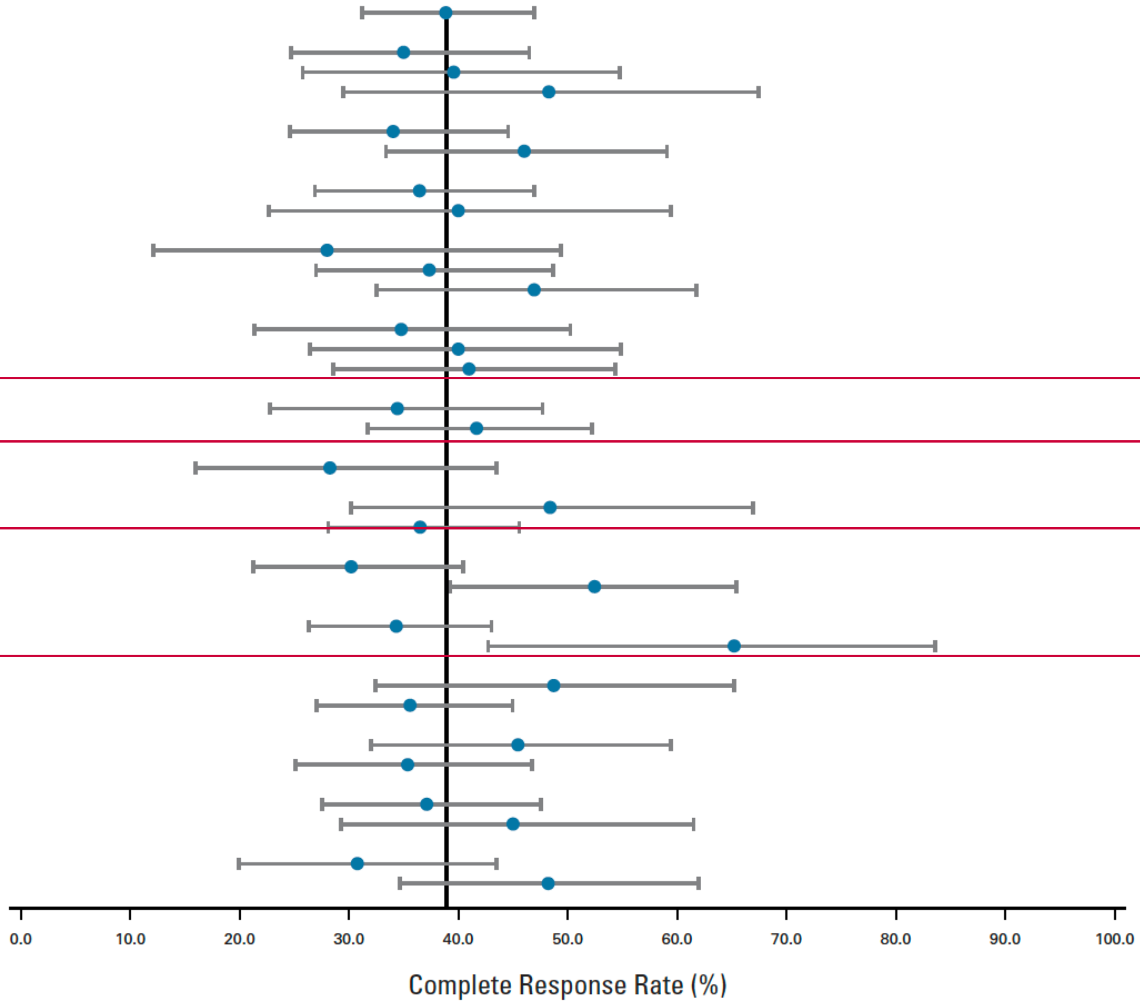
- CRS: 50% (grade 3-4: 2.5%)
- ICANS: 6% (grade 3-4: 0.6%)
- Neutropenia: 22% (grade 3-4: 15%)
- Injection site reactions 20%

median follow-up of 20 months

Thieblemont, et al. JCO 2022. Thieblemont, et al. ICML 2023

Epcoritamab in Relapsed/Refractory DLBCL

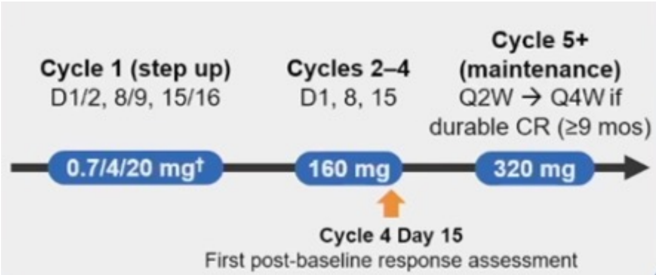
Subgroup	Patients, No.	CRR, % (95% CI)
All patients	157	38.9 (31.2 to 46.9)
Age, years		
< 65	80	35.0 (24.7 to 46.5)
65 to < 75	48	39.6 (25.8 to 54.7)
≥ 75	29	48.3 (29.4 to 67.5)
Sex		
Male	94	34.0 (24.6 to 44.5)
Female	63	46.0 (33.4 to 59.1)
Race		
White	96	36.5 (26.9 to 46.9)
Asian	30	40.0 (22.7 to 59.4)
Region		
North America[a]	25	28.0 (12.1 to 49.4)
Europe	83	37.3 (27.0 to 48.7)
Other	49	46.9 (32.5 to 61.7)
Prior lines of treatment, No.		
2	46	34.8 (21.4 to 50.2)
3	50	40.0 (26.4 to 54.8)
4+	61	41.0 (28.6 to 54.3)
Prior CAR T experience		
Yes	61	34.4 (22.7 to 47.7)
No	96	41.7 (31.7 to 52.2)
Refractory to prior CAR T experience		
Yes[b]	46	28.3 (16.0 to 43.5)
Prior ASCT		
Yes	31	48.4 (30.2 to 66.9)
No	126	36.5 (28.1 to 45.6)
Primary refractory		
Yes	96	30.2 (21.3 to 40.4)
No	61	52.5 (39.3 to 65.4)
Most recent prior anti-CD20–containing therapy		
Refractory	134	34.3 (26.3 to 43.0)
Relapse	23	65.2 (42.7 to 83.6)
Ann Arbor staging		
I/II	39	48.7 (32.4 to 65.2)
III/IV	118	35.6 (27.0 to 44.9)
IPI		
0–2	55	45.5 (32.0 to 59.4)
≥ 3	82	35.4 (25.1 to 46.7)
DLBCL disease state		
De novo	97	37.1 (27.5 to 47.5)
Transformed	40	45.0 (29.3 to 61.5)
Molecular cell of origin (local)		
GCB	65	30.8 (19.9 to 43.4)
ABC/non-GCB	56	48.2 (34.7 to 62.0)



Thieblemont, et al. JCO 2022

Odronextamab in Relapsed/Refractory DLBCL

Treatment until progression or intolerance



Baseline Characteristics	N=127
Median age (range)	67 (24-88)
Median prior tx (range)	2 (2-8)
Prior ASCT	16%
Double/triple hit	20%
Refractory to last tx	86%

Best IRC-assessed response (n=27)

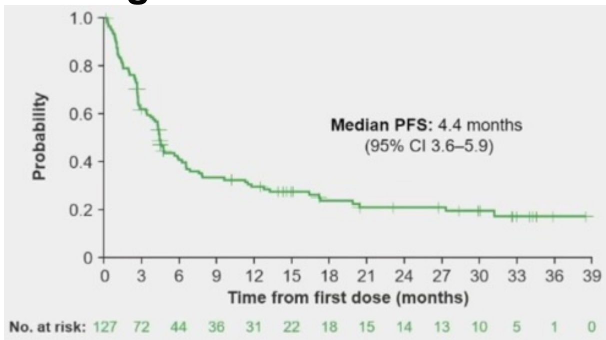
ORR: 52%

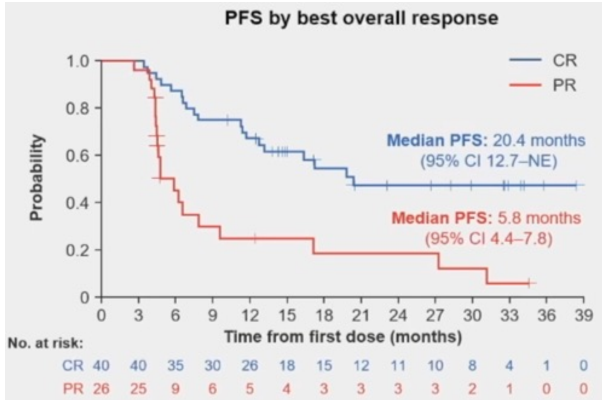
CRR: 32%

Median DoR: 10 mo

Median DoCR: 18 mo

Progression-free survival





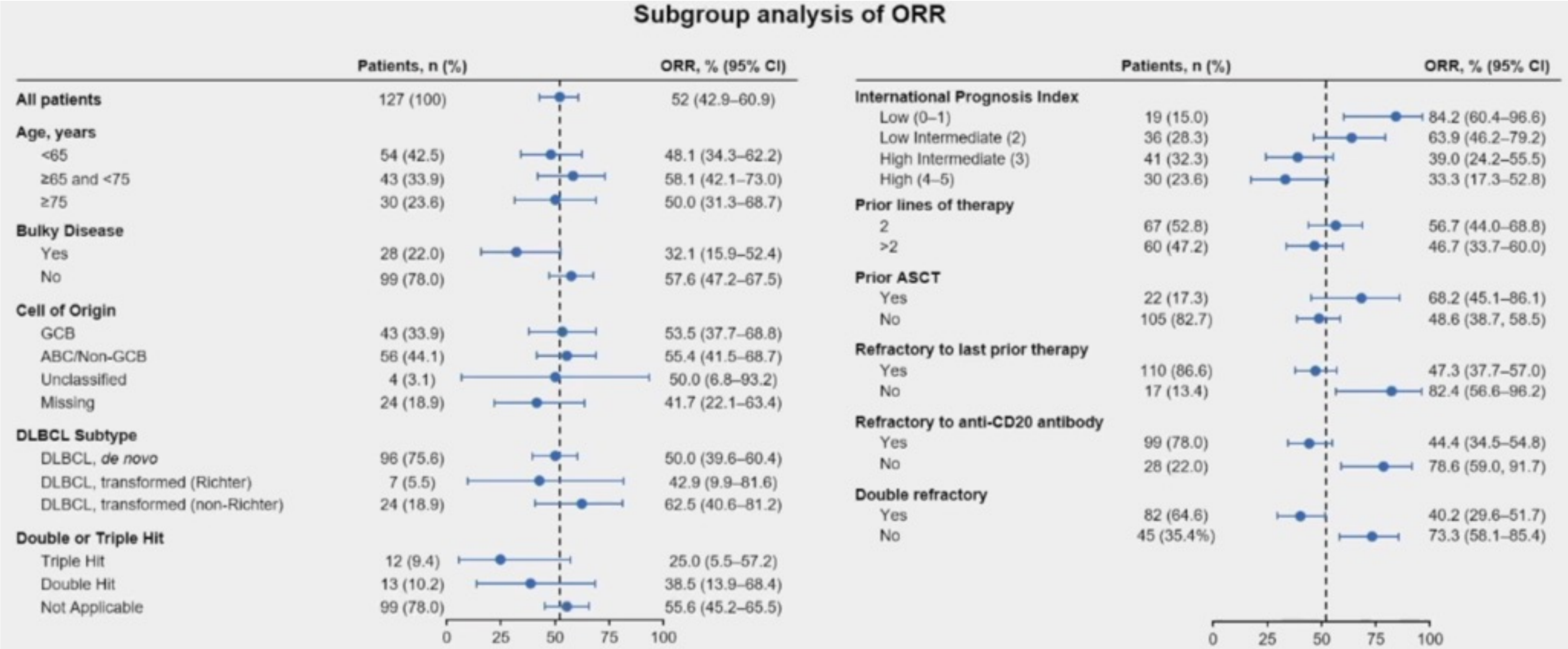
Notable Adverse Events

- CRS: 55% (grade 3: 4%)
- ICANS: 3% (grade 3: 1%)
- Neutropenia: 31%

Median follow-up 33 months

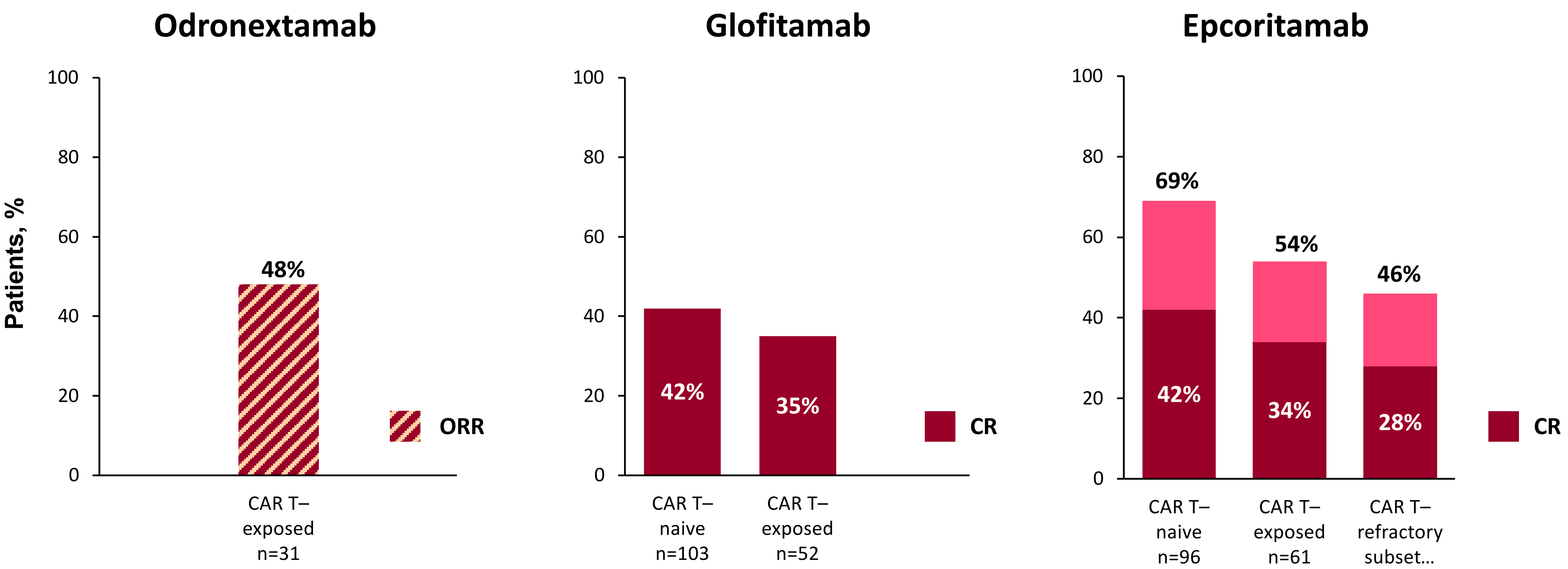
Ayyappan, et al. Proc ASH 2023

Odronextamab Forest Plot for ORR



Ayyappan, et al. Proc ASH 2023

Bispecific antibodies remain effective in CAR T exposed patients



Adapted from: 1. Kim SW, et al. Oral 444. ASH. Dec 10-13, 2022.
Dickinson MJ, et al. N Engl J Med. 2022;387(24):2220-2231.
Thieblemont C, et al. J Clin Oncol. 2023;41(12):2238-2247.

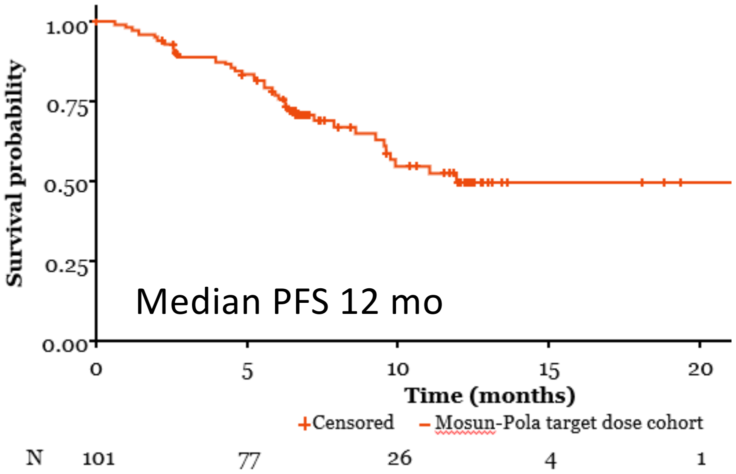
Bispecific combinations in DLBCL

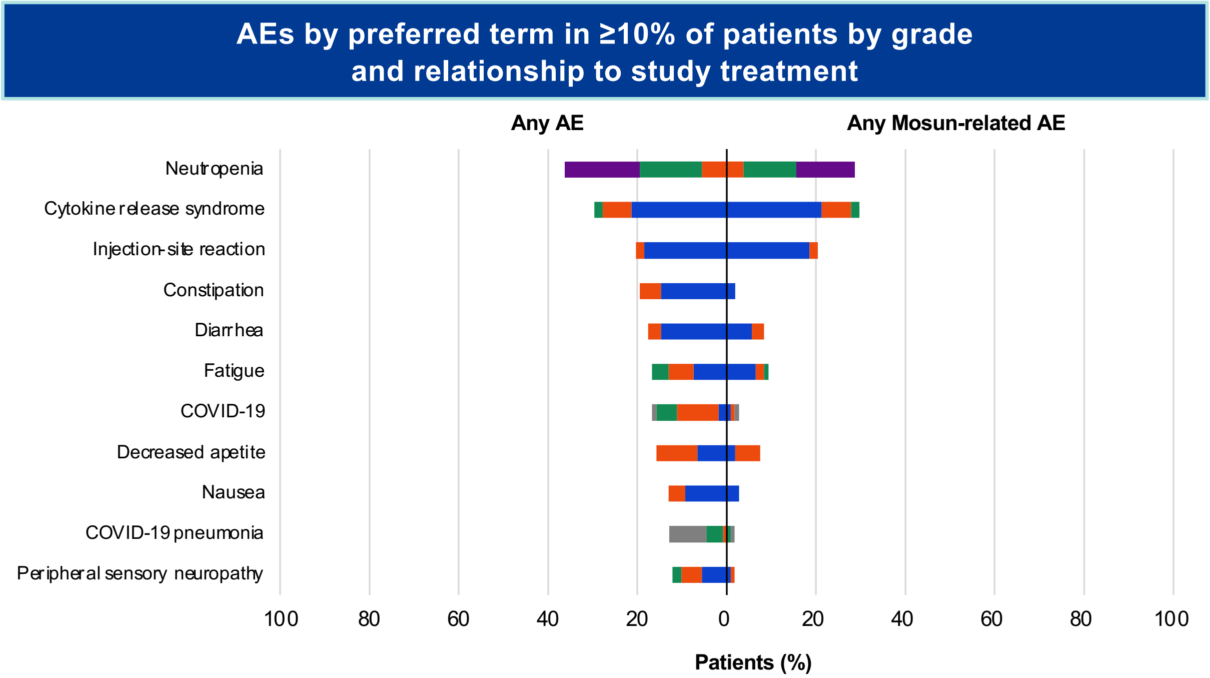
Upfront Chemo Combinations

- Epcoritamab + R-CHOP (n=47): ORR 100%, CR 76% Falchi, et al. Proc ASCO 2023
- Epcoritamab + R-mini-CHOP (n=28): ORR 100%, CR 85% Vermaat, et al. Proc ASH 2023
- Glofitamab + R-CHOP (n=29): ORR 95%, CR 85% Falchi, et al. Proc ASH 2023
- Glofitamab + R-CHOP (n=56): ORR 93%, CR 84% Topp, et al. Proc ASH 2023
- Glofitamab + Pola-R-CHOP (n=24): ORR 100%, CR 92% Topp, et al. Proc ASH 2023

Mosunutezumab – Polatuzumab as Initial Therapy (n=108)

- Age ≥80, or ≥65 with and chemo-ineligible
- Median age 81 (66–94)
- 107/108 unfit or frail by simplified geriatric assessment
- 8-17 cycles based on response
- Best ORR 80%, CR 65%

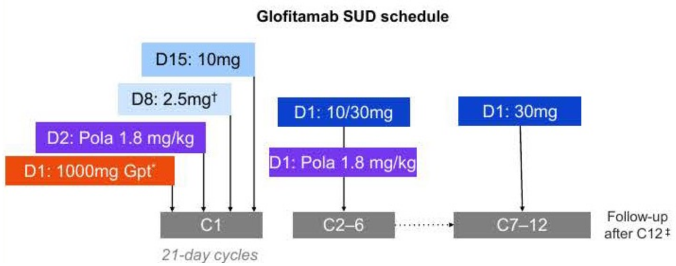




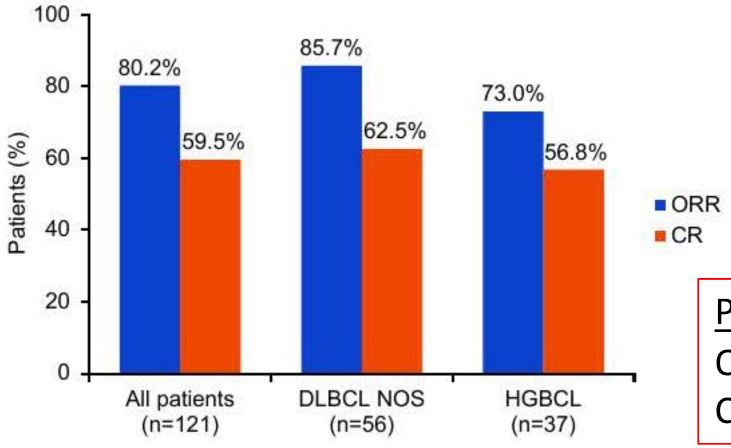
- CRS Any grade 30%, Grade 3 2%
- Fatal adverse events in 17%, COVID most common

Olszewski, et al. Proc ASH 2023

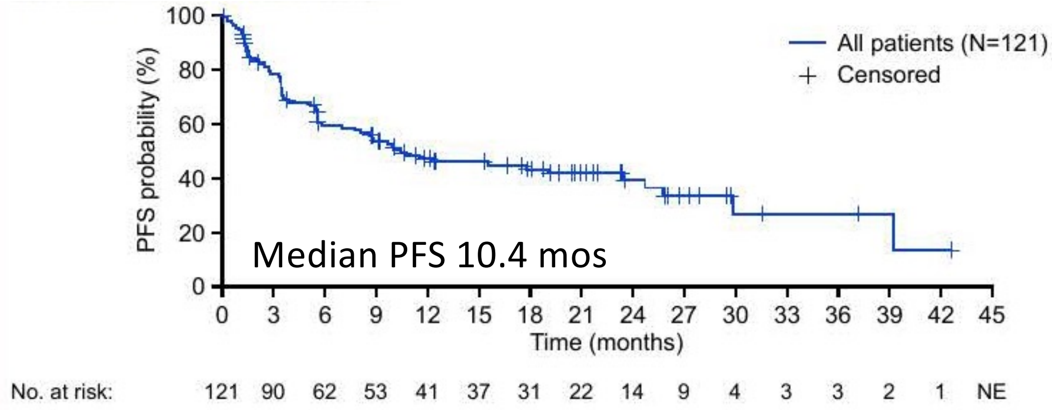
Glofitamab-Polatuzumab in R/R DLBCL (n=125)



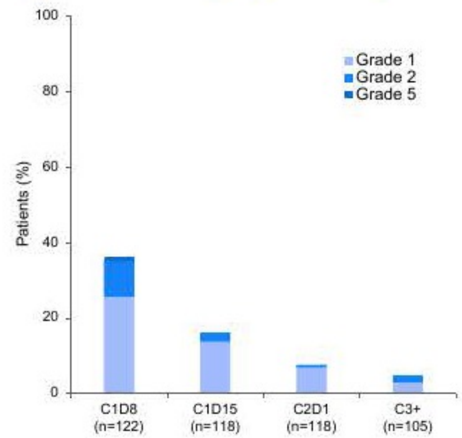
Characteristic	N=125
Median age	67 (23-84)
Median prior lines	2 (1-7)
Refractory to last tx	72%
Prior CAR	22%



Prior CAR
ORR 78%
CRR 48%



	n=122*
CRS, n (%)	
Any grade	56 (45.9)
Grade 1	36 (29.5)
Grade 2	19 (15.6)
Grade 5†	1 (0.8)
Serious AE (any grade)	37 (30.3)
Median time to CRS onset after glofitamab dose, hours (range)	
2.5mg	16.2 (5.4–42.1)
10mg	35.9 (8.9–129.5)
30mg	36.2 (18.5–55.9)



*122/125 patients who received ≥1 dose of glofitamab.
†Patient (aged 73, with advanced HGBCL and multiple CRS risk factors) developed Grade 3 CRS (with a background of urosepsis and herpetic stomatitis) and declined further intensive management for CRS, resulting in fatal outcome.

Hutchings, et al. Proc ASH 2023

Bispecific antibodies in DLBCL

- I currently reserve for relapsed/refractory patients who are post CAR or cannot get to CAR
- Selection of product is personalized to the patient (schedule, continuous vs. time limited, IV vs SC, etc)
- Combination strategies are appealing and warrant ongoing evaluation in relapsed/refractory as well as previously untreated disease

Thank you for your attention!

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