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THE CASE FOR BISPECIFIC ANTIBODIES IN LYMPHOMA

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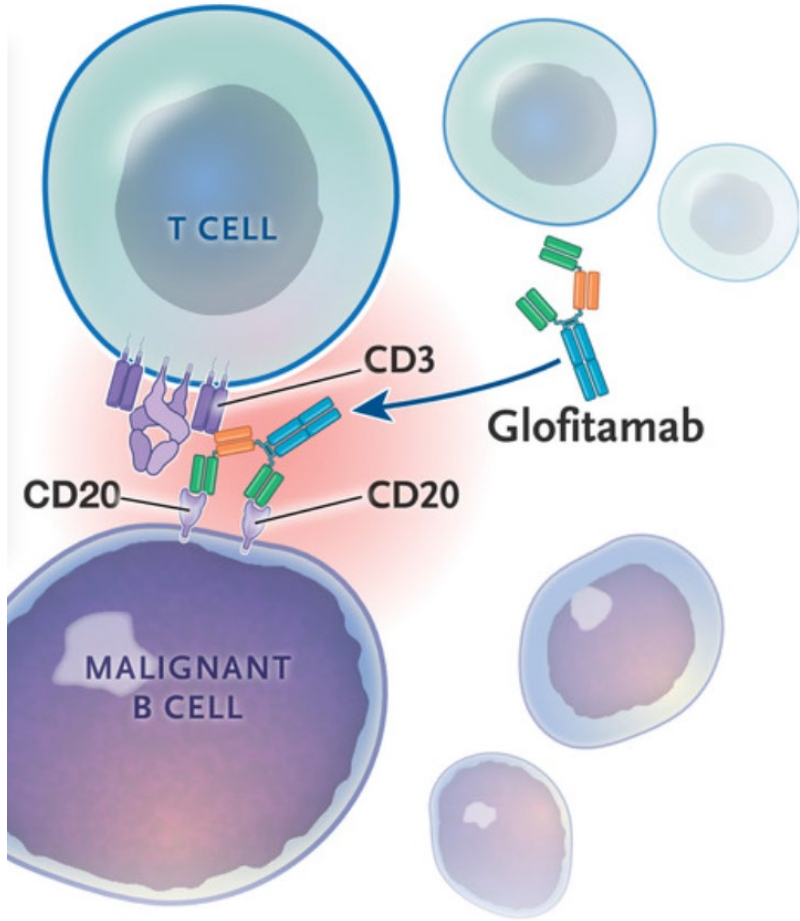
Bispecific antibodies

- Agents that simultaneously bind tumor-associated antigens and endogenous T-cells
- Given IV or SubQ with various dosing strategies
  - Step-up dosing with cycle 1 to mitigate toxicity
- Major AEs: CRS, ICANS, infection
- Durable responses seen in multiple subtypes of B-cell NHL
- “Off-the-shelf”



Dickinson MJ, NEJM 2022; 387:2220-2231

The case for bispecifics

- CAR-T is established as a curative treatment modality in a **subset** of patients with relapsed lymphoma

- Less experience and shorter follow-up with bispecifics in NHL, but very promising early results

- Bispecifics have several advantages:
  - Favorable toxicity profile
  - Ease of administration
  - Greater potential to combine with chemo or targeted agents

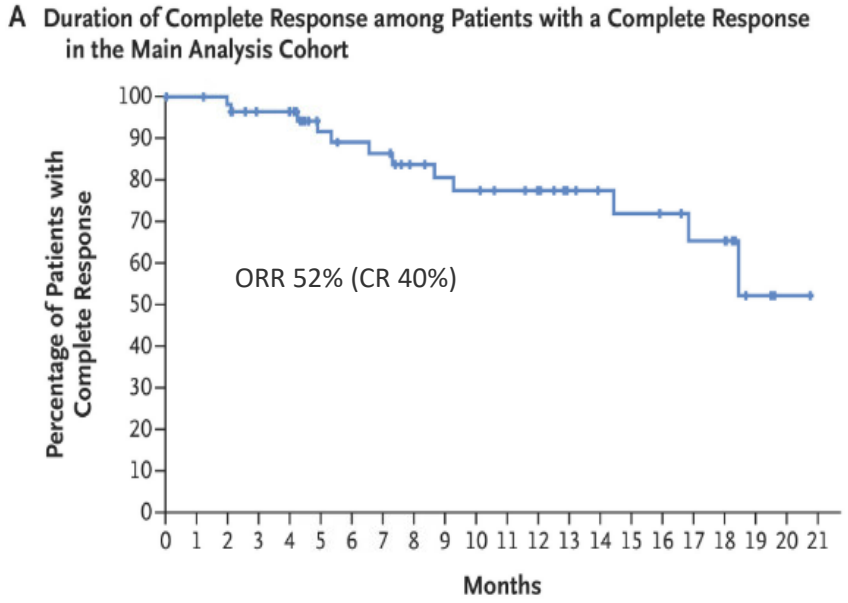
Efficacy comparison in LBCL

Pivotal phase 2 monotherapy trials

	Glofitamab	Epcoritamab	Odronextamab	Axi-cel ZUMA-1	Tisa-cel JULIET	Liso-cel TRANSCEND
Median Age	66 (21-90)	64 (20-83)	66 (24-88)	58 (23-76)	56 (22-76)	63 (54-70)
Prior therapy	3 (2-7)	3 (2-11)	2 (2-8)	3 (1-10)	3 (1-6)	3 (2-4)
ORR (CR)	52 (39)	63 (39)	49 (31)	82 (54)	52 (40)	73 (53)
Median PFS, mo	4.9	4.4	4.4	5.9	2.9	6.8
Median OS, mo	11.5	18.5	-	26	11.1	27.3

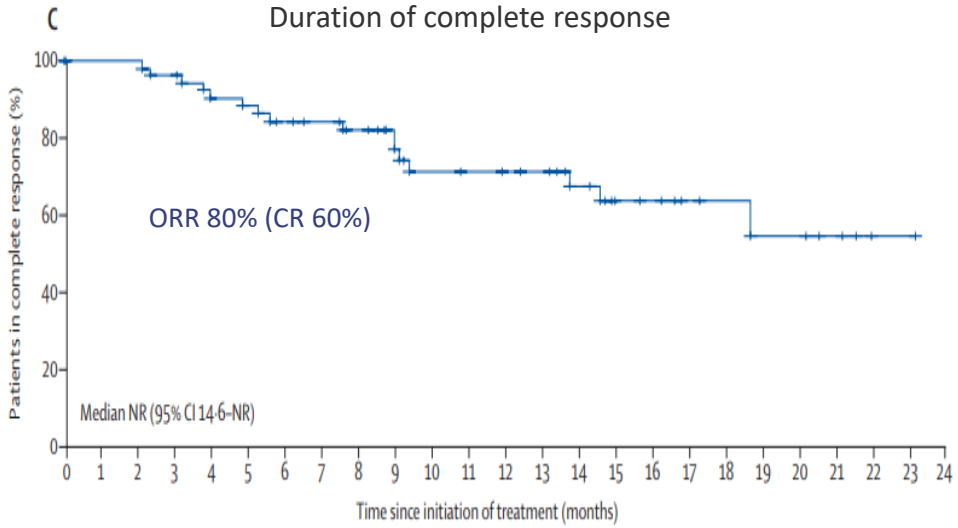
- Older patients participated in bispecific trials
- Bispecific response rates comparable to CAR-T, but limited follow-up for survival and DOR

Glofitamab (DLBCL)



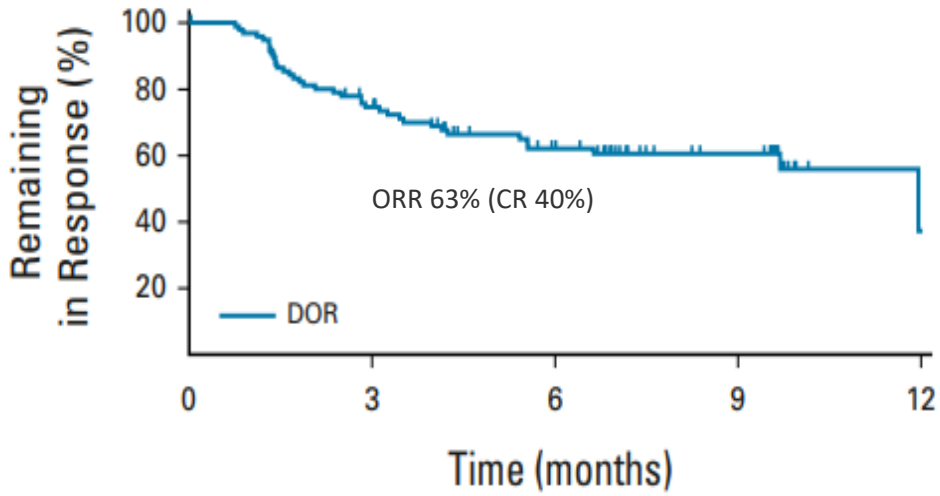
Dickinson MJ, NEJM 2022; 387:2220-2231

Mosunetuzumab (FL)



Budde LE, Lancet Oncol 2022; 23(8):1055-1065

Epcoritamab (DLBCL)



Thieblemont C, J Clin Oncol 2023; 41(12):2238-2247

Bispecifics can be used before or after CAR-T

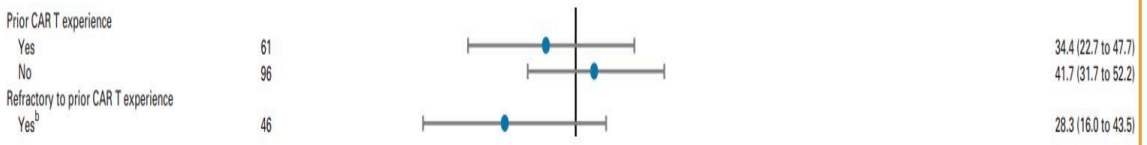
24-39% of participants in phase 2 bispecific studies for LBCL received prior CAR-T

Glofitamab

Subgroup	No. of Patients	Complete Response (95% CI)
Previous CAR T-cell therapy		
Yes	52	35 (22–49)
No	103	42 (32–52)

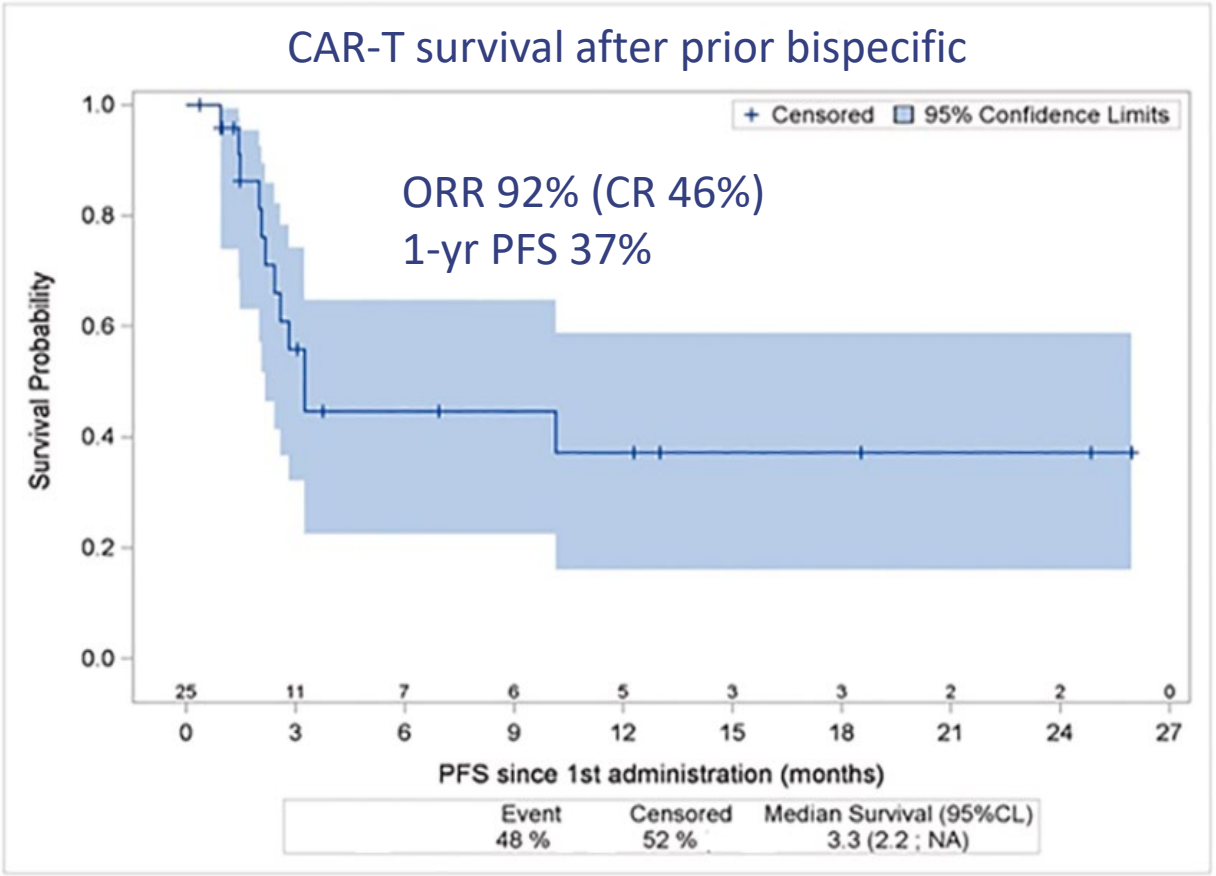
Dickenson, NEJM, 2022

Epcoritamab



Thieblemont, JCO, 2023

CAR-T survival after prior bispecific



Crochet G, et al, ASH 2022

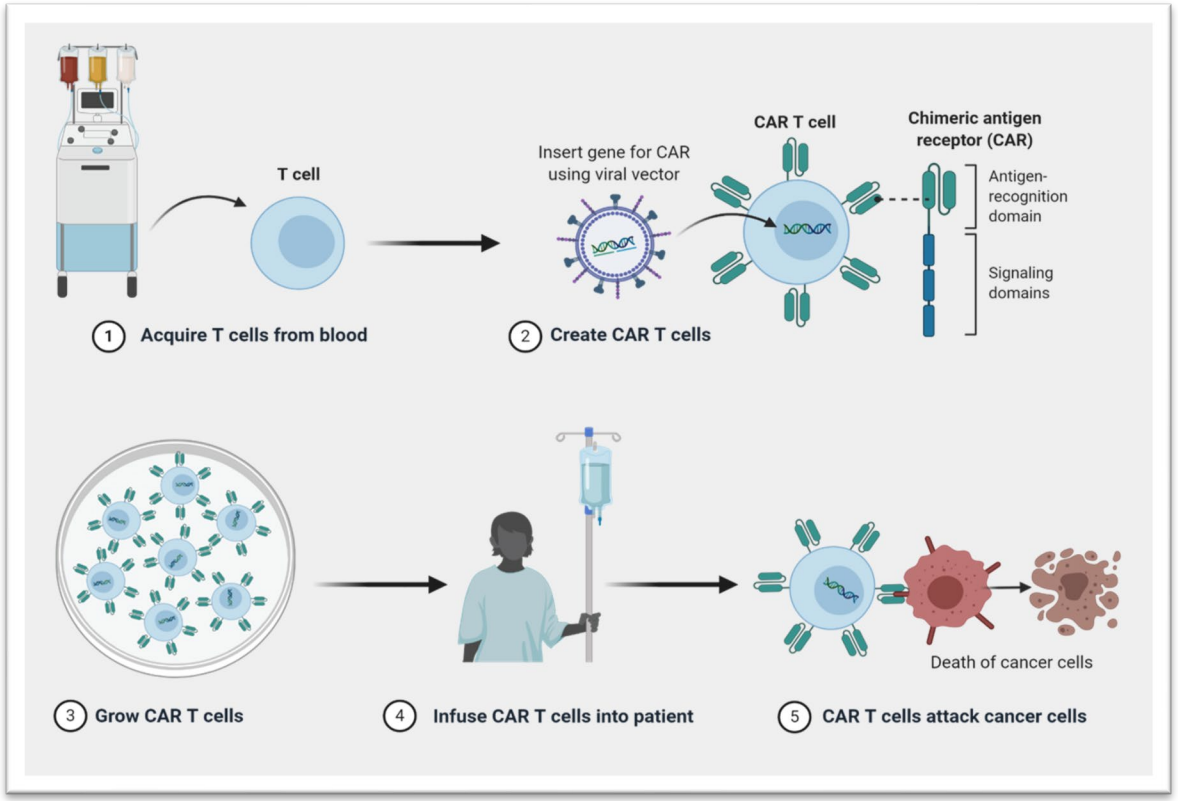
Bispecifics have lower rates of CRS/ICANS

	Glofitamab	Epcoritamab	Odronextamab	Axi-cel	Tisa-cel	Liso-cel
CRS (All), %	63	50	53	93	58	42
CRS (≥ Gr 3), %	4	3	1	13	22	2
ICANS (All), %	8	6	3	64	21	30
ICANS (≥ Gr 3), %	3	1	1	28	12	10
Infection (≥ Gr 3), %	15	15	23	-	19	12

Other long-term toxicities with CAR-T

- Prolonged cytopenias
- B-cell aplasia/hypogammaglobulinemia
- Late TRM (~5%)

Bispecifics are easier to administer



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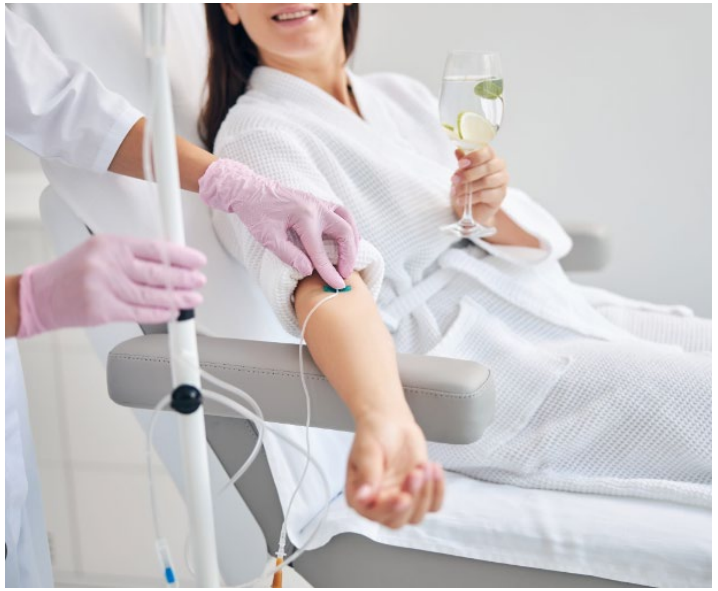

More combination potential with bispecifics

- 1st line DLBCL: Phase 3 Epcoritamab + R-CHOP vs. R-CHOP (NCT05578976)
- Consolidation after CAR-T: Phase 2 Mosunetuzumab, polatuzumab, or combo if not in CR at day +30 (SWOG 2114; NCT05633615)
- 2nd line FL: Phase 3 mosunetuzumab + len vs. rituximab + len (CELESTIMO; NCT04712097)
- 1st line low tumor burden FL: mosunetuzumab vs rituximab

Cost comparison

- No formal cost effectiveness analyses conducted
- CAR-T is one-time treatment (full cost incurred), whereas bispecific monotherapy can be discontinued if not working
- Time-limited bispecific regimens in earlier lines of therapy may be advantageous

Conclusions

CAR-T is an incredible technology that provides benefit to many lymphoma patients

HOWEVER

Bispecifics have many potential advantages:

- Less toxic
- Easier to administer
- More accessible
- Easier to combine with other therapies

The bottom line

Bispecifics antibodies have arrived

Anyone who treats lymphoma should learn how to use these medications

THANK YOU!