4th MEETING ON
INNOVATIVE IMMUNOTHERAPIES
FOR LYMPHOID MALIGNANCIES

Società Italiana di Ematologia

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Is There a Role for Allogeneic Transplant after Bispecifics and CAR-T in NHL? No

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Disclosures of Stephen J. Schuster

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
AbbVie						X	
ADC Therapeutics						X	
AstraZeneca	X		X			X	
BeiGene						X	
BioNTech			X				
BMS	X					X	
Caribou Bio			X			X	
Genentech/Roche	X					X	
Genmab	X		X			X	
Incyte			X				
Janssen						X	
Novartis	X		X			X	
Vittoria Bio						X	

Framing the Question: “Allogeneic Transplant after Bispecifics and CAR-T ?”

- 2 Possible Interpretations of This Question

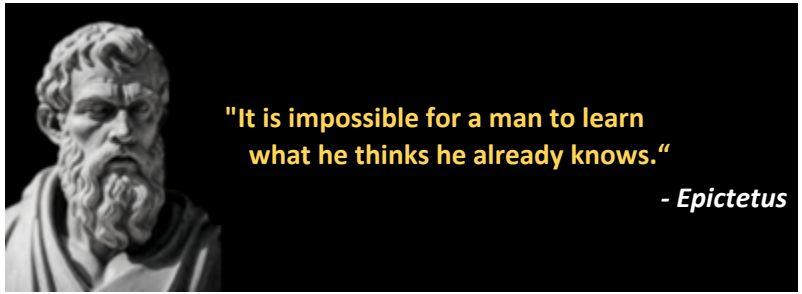
1) Does allotransplant have a therapeutic role in LBCL after prior failure of ***both*** CD19-directed CAR-T *and* CD20-directed bispecific antibody (BsAb) therapies?

2) Should CD20/CD3 BsAb therapies be a ***bridge*** or an ***alternative*** to allotransplant after CD19-CAR-T failure in LBCL?
(or vice versa, i.e., CAR-T as a bridge or an alternative to allotransplant after BsAb failure?)

My Answers to These Questions

1) No *(or almost never, since adequate disease control can rarely be achieved in this setting , i.e., ≥ 2 (or 3) prior lines of therapy, then CAR-T + BsAb failure)*

2) An alternative ℞ *(or possibly a bridge for a very select group of patients)*



BsAb, bispecific antibody; LBCL, large B-cell lymphomas

“Allogeneic Transplant after Bispecifics and CAR-T ?”

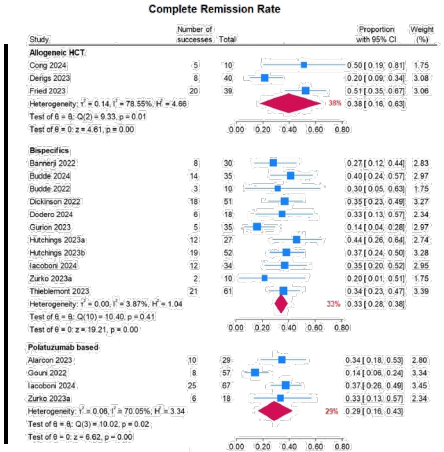
1) Does allotransplant have a therapeutic role in LBCL after ***prior failure* of *both*** CD19-directed CAR-T *and* CD20-directed bispecific antibody (BsAb) therapies? My Answer: No *(or almost never)*

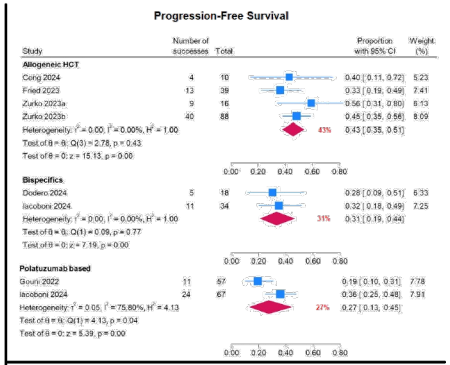
Treatment Outcomes of Patients with LBCL Progressing/Relapsing after CAR-T[1]

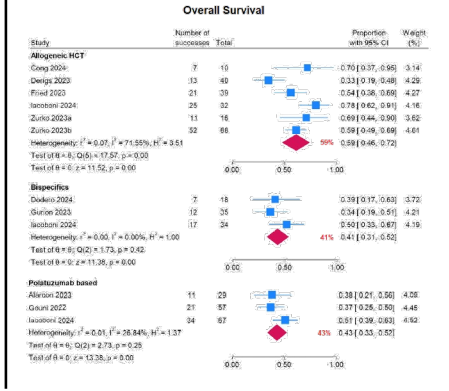
- *systematic review and meta-analysis performed August 2024*
- *of 951 references, 24 studies met inclusion criteria*
- efficacy post CAR-T failure: *allo-HCT > BsAb > polatuzumab-based*
- ***pooled data: allo-HCT, n= 89; BsAb, n=260; pola.-based, n=171***

Pooled Outcomes	Allo-HCT (95% CI) [I^2]	Polatuzumab-Based (95% CI) [I^2]	Bispecifics (95% CI) [I^2]
ORR	59% (48%-69%) [0]	57% (43%-71%) [67.6%]	51% (41%-61%) [57.6%]
CR	38% (16%-63%) [78.6%]	29% (16%-43%) [70.1%]	33% (28%-38%) [3.9%]
PFS	43% (35%-51%) [0]	27% (13%-45%) [75.8%]	31% (19%-44%) [0]
OS	59% (46%-72%) [71.6%]	43% (33%-52%) [26.8%]	41% (31%-52%) [0]
TRM	20% (12%-29%) [27.1%]	NR	17% (6%-32%) [N/A
Relapse	27% (15%-42%) [60.7%]	NR	43% (27%-60%) [N/A]

Allo-HCT indicates allogeneic hematopoietic cell transplantation; ORR, overall response rate; CR, complete remission; PFS, progression-free survival; OS, overall survival; TRM, treatment-related mortality; N/A, not applicable; NR, not reported.







Limitations of this study for cross treatment comparisons

1) can’t ascertain reason(s) leading physicians to choose a specific treatment,
   e.g., older/frail patients not offered allo-HCT ?
2) without individual patient data, can’t establish the impact of therapy prior to described intervention,
   e.g., only responding patients offered allo-HCT ?
3) can’t determine proportion of patients intended for a treatment who didn’t receive it

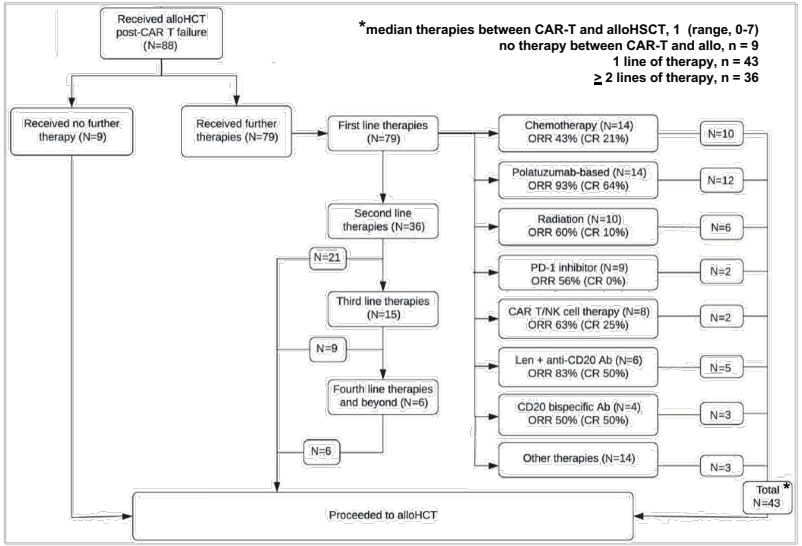
[1]Kharfan-Dabaja M A, Transplant. Cell. Ther. 2025; 31(11):898.e1-898.e12.

"Allogeneic Transplant after Bispecifics and CAR-T ?"

1) Does allotransplant have a therapeutic role in LBCL after ***prior failure* of *both*** CD19-directed CAR-T *and* CD20-directed bispecific antibody (BsAb) therapies? My Answer: No *(or almost never)*

Outcomes after AlloHSCT in Patients with LBCL after CAR-T Failure[1]

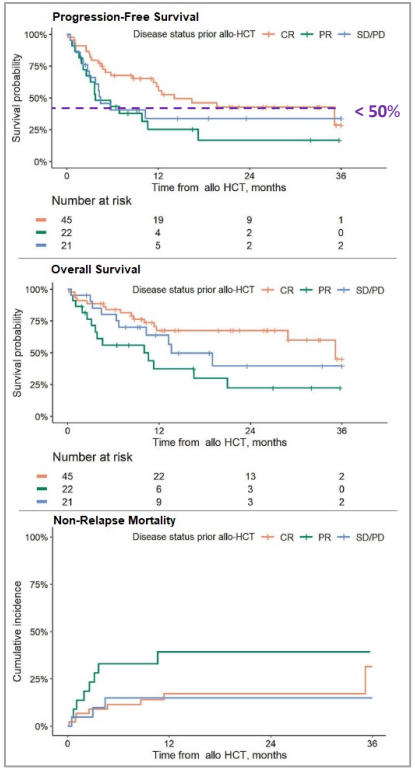
- *multicenter, retrospective study from U.S. centers*
- ***88 patients** with r/r LBCL who received an alloHSCT after anti-CD19 CAR-T failure*
- ***median follow-up was 15 months** (range, 1-72)*



	Outcomes	
	all patients n = 88	CR at allo n = 45
1-year **PFS**	45%	59%
1-year **OS**	59%	67%
1-year **NRM**	22%	9%

PFS, progression-free survival; OS, overall survival; NRM, non-relapse mortality

Overall survival	HR	95% CI	P
Disease status prior to alloHCT			0.01
CR	-	-	
PR	4.32	1.61–11.6	
SD/PD	1.85	0.73–4.70	
Progression-free survival			
Disease status prior to alloHCT			0.03
CR	-	-	
PR	2.61	1.27–5.37	
SD/PD	2.05	0.99–4.26	
Non-relapse mortality			
Disease status prior to alloHCT			0.008
CR	-	-	
PR	4.02	1.63–9.89	
SD/PD	0.87	0.22–3.45	



Limitation: no data on patients who failed CAR-T and were intended for, but did not undergo, alloHSCT

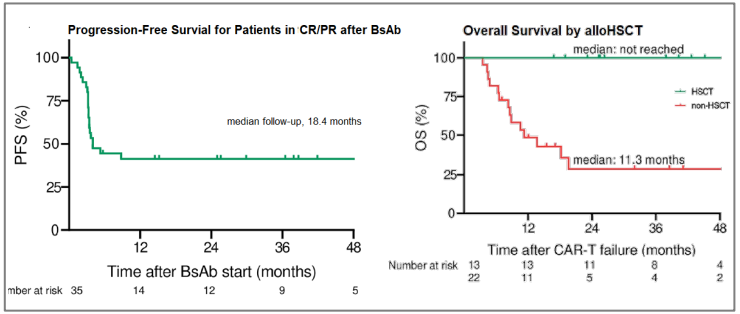
r/r LBCL, relapsed/refractory large B-cell lymphomas; alloHSCT, allogeneic stem cell transplant

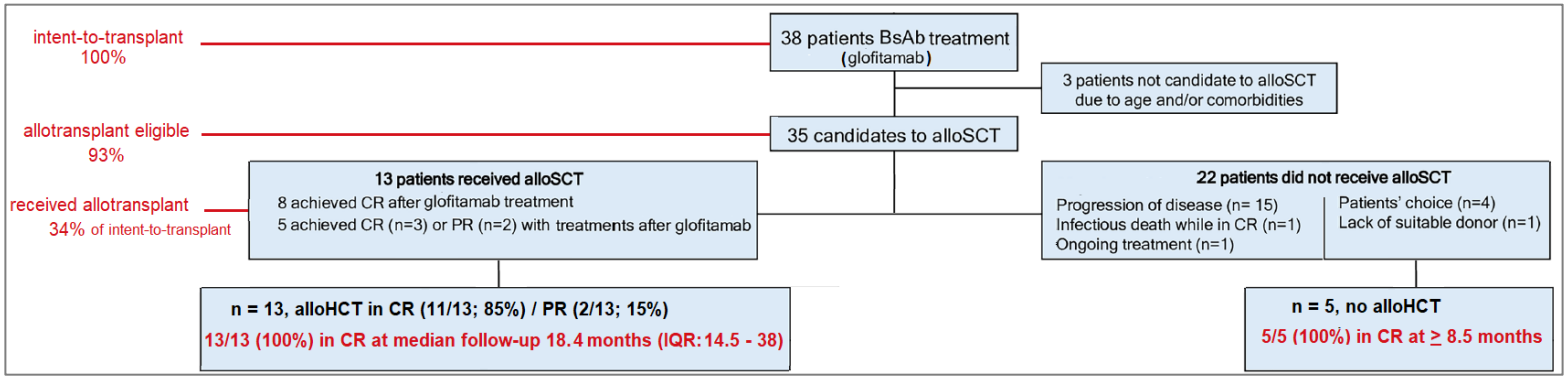
[1] Zurko J., et al. Haematologica. 2023;108(1):98-109.

1) Does allotransplant have a therapeutic role in LBCL after ***prior failure of both*** CD19-directed CAR-T *and* CD20-directed bispecific antibody (BsAb) therapies? My Answer: No *(or almost never)*

Allogeneic Transplantation in CAR-T Failures who Respond to BsAb[1]

- Retrospective study of 83 LBCL patients with relapsed/progressive disease after CAR-T
- Between 2019 and 2025, 69 (83%) pts received salvage treatment, most frequently glofitamab in (**n = 38**; 55%)
- Evaluated the feasibility of alloHSCT after glofitamab as salvage therapy for CAR-T failure
- **median follow-up: 18 months for PFS; 11 months for survival**





LBCL, large B-cell lymphomas; BsAbs, bispecific antibodies

[1]Barone A, et al. Br J Haematol 2025;207:956-964.

2) Should CD20-BsAb therapies be a ***bridge*** or an ***alternative*** to allotransplant after CD19-CAR-T failure in LBCL?
(or vice versa, CAR-T as a bridge or an alternative to allotransplant after BsAb failure?)

My Answer: An alternative ℞ *(possibly a bridge for a very select group of patients)*

Bridge or Alternative Therapy to Allotransplant?

1) **CD20/CD3 bispecific antibody after CAR-T failure: CAR-T ▼ ⟶ BsAb ▲ - - -→ ? allo-HCT**
2) **CD19-CAR-T after CD20/CD3 bispecific antibody failure: BsAb ▼ ⟶ CAR-T ▲ - - -→ ? allo-HCT**

LBCL, large B-cell lymphomas; ▼, failure; ▲, success

BsAb as an Alternative to Allotransplant after CAR-T Failure

- CD20/CD3 BsAb (mosunetuzumab) outcomes after CD19-CAR-T failure

Table 1. Patient characteristics

Characteristic	N = 30 (100%)
Age, median (range), y	63 (18-82)
Ann Arbor stage, n (%)	
I-II	6 (20)
III-IV	24 (80)
B-NHL subtype, n (%)	
DLBCL	19 (63)
trFL	7 (23)
PMBCL	1 (3)
FL	3 (10)
Prior lines of therapy, median (range)	4 (3-8)
3 previous lines, n (%)	7 (23)
>3 previous lines, n (%)	23 (77)
Prior lymphoma therapies, n (%)	
Anti-CD20 antibody	30 (100)
Anthracycline	30 (100)
CAR-T	30 (100)
Prior ASCT	4 (13)
Response to prior therapies, n (%)	
Refractory† to last therapy	25 (83)
Relapsed after last therapy	5 (17)
Refractory to any prior anti-CD20	27 (90)
Refractory to CAR-T	24 (80)

n = 27/30 (90%) LBCL

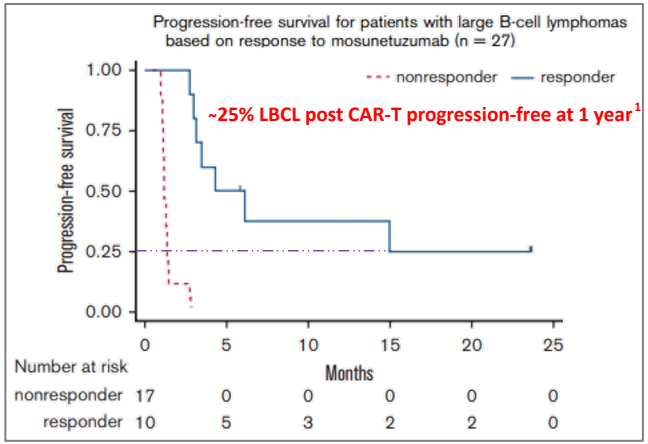
DLBCL, diffuse large B-cell lymphoma; trFL, transformed follicular lymphoma; PMBCL, primary mediastinal B-cell lymphoma; FL, follicular lymphoma

REGULAR ARTICLE

blood advances

Impact of prior CAR T-cell therapy on mosunetuzumab efficacy in patients with relapsed or refractory B-cell lymphomas

Overall response rate, 40%
Complete response rate, 23%



[1]Chong, E. A.,….Schuster, S. J. Blood Adv 2025; 9 (4): 696–703.

BsAbs as an Alternative to Allotransplant after CAR-T Failure

- **CD20/CD3 BsAb outcomes after CD19-CAR-T failure**

Glofitamab[1]

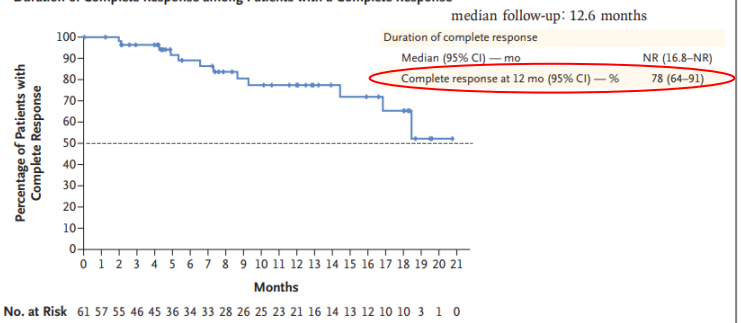
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma

	No. of Patients	Complete Response (95% CI) percent
Previous CAR T-cell therapy		
Yes	52	35 %(22–49)
No	103	42 %(32–52)
Refractory to previous CAR T-cell therapy	46 (88% of CAR-T Patients)	

Duration of Complete Response among Patients with a Complete Response



[1]Dickinson M.J. et al. N Engl J Med. 2022;387(24): 2220-2231.

Epcoritamab[2,3]

Journal of Clinical Oncology
An American Society of Clinical Oncology Journal

OPEN ACCESS | ORIGINAL REPORTS | December 22, 2022

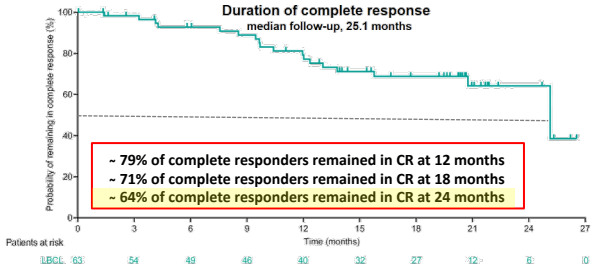
Epcoritamab, a Novel, Subcutaneous CD3xCD20 Bispecific T-Cell–Engaging Antibody, in Relapsed or Refractory Large B-Cell Lymphoma: Dose Expansion in a Phase I/II Trial

J Clin Oncol 41, 2238-2247(2023) • Volume 41, Number 12 • DOI: 10.1200/JCO.22.01725

Table 1. Demographic and clinical characteristics at baseline for patients with LBCL ($N = 157$).

Prior CAR T-cell therapy, No. (%)	61 (38.9)
Progressed within 6 months of CAR T-cell therapy, No. (%)	46 (29.3)

Subgroup	Patients, No.	CRR, % (95% CI)
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 (n = 46; 75% of prior CAR T)	46	28.3 % (16.0 to 43.5)



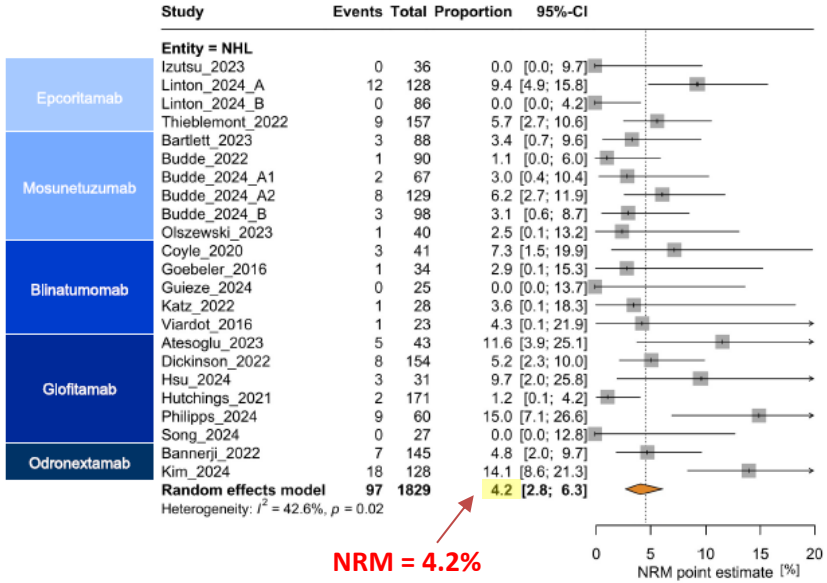
[2]Thieblemont C. et al. J Clin Oncol. 2023;41(12):2238-2247; [3]Thieblemont C. et al. Leukemia 2024;38:2653–2662.

BsAb as an Alternative to Allotransplant after CAR-T Failure

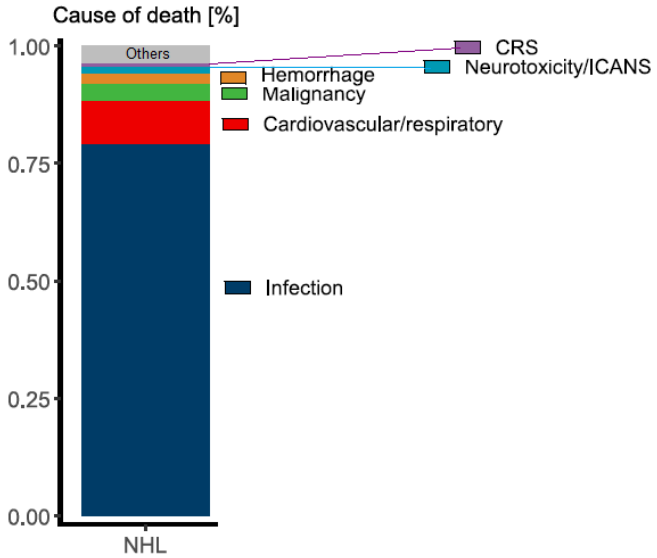
- CD20/CD3 BsAb outcomes after CD19-CAR-T failure

Non-relapse mortality (NRM) with BsAbs: systematic review and meta-analysis[1]

NRM point estimates across 21 studies (1,829 patients)



NRM point estimate: 4.2% (95% CI 2.8% - 6.3%)



[1] Tix T. et al. Molecular Therapy, Volume 33, Issue 7, 3163 – 3176.

CD19-CAR-T as an Alternative to Allotransplant after BsAb failure

- **CD19-CAR-T is active after CD20/CD3 BsAb exposure/failure; do we need the allo-HSCT?**

Gilles Crochet, et al.[1]
Retrospective multicenter study of efficacy and toxicity of anti-CD19 CAR-T in patients with R/R LBCL previously exposed to BsAbs
N = 47
ORR/CRR after BsAb: 46%/19% ORR/CRR after CAR-T: 85%/43%
1-year PFS: 42% **1-year OS: 55%**
post CAR-T CRS, grade ≥ 3 = 6% post CAR-T ICANS, grade ≥ 3 = 2%

- ***Prior BsAb therapy does not impair subsequent CAR-T outcomes***

CRR, complete response rate, LBCL, large B-cell lymphomas, ORR, overall response rate, OS, overall survival, PFS, progression-free survival DOR Duration of response, CRS cytokine release syndrome, ICANS immune effector cell-associated neurotoxicity syndrome

[1]Crochet G. et al. Blood 2024; 144 (3): 334–338.

BsAbs after CAR-T Failure: Bridge or Alternative Therapy to Allotransplant?

BsAb after CAR-T failure, without alloHSCT: ***CR rate ~ 1/3; ~ 2/3 remain in CR at 2 years[1] (assumes NRM = ~ 4.2%[2])***

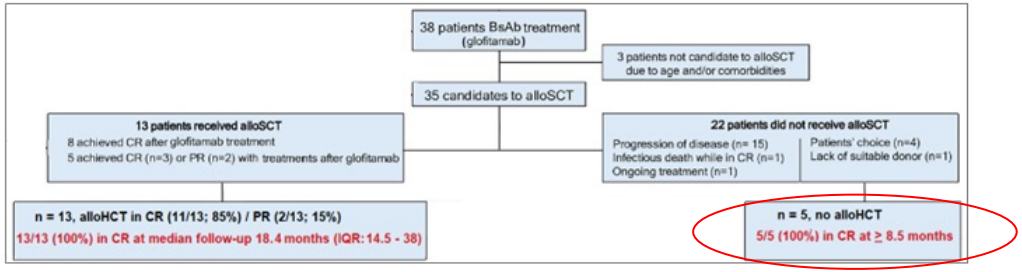
e.g., 100 patients → 33 patients achieve CR with BsAb → 22 patients in CR at 2-years

CAR-T failure with CR after BsAb, f/b alloHSCT: ***~ 1/3 remain in CR at 1.5 years (IQR: 1.2 - 3)[3]; NRM = 0[3] or 20%[4]***

e.g., NRM = 0: 100 patients → 93 patients HSCT-eligible → 34 patients in CR after BsAb + alloHSCT → 34 patients in CR at 1.5-years

e.g., NRM = 20%[5]: 100 patients → 93 patients HSCT-eligible → 27 patients in CR after BsAb + alloHSCT → 27 patients in CR at 1.5-years

Outcome estimates are close; in the absence of a randomized trial, you can decide



but recall

CR, complete response; f/b, followed by; NRM, non-relapse mortality

[1] Thieblemont C., et al. Leukemia 2024;38:2653–2662.
[2] Tix T., et al. Molecular Therapy, Volume 33, Issue 7, 3163 – 3176.
[3] Barone A., et al. Br J Haematol 2025;207:956-964.
[4] Kharfan-Dabaja M. A., Transplant Cell Ther 2025; 31(11):898.e1-898.e12.
[5] Zurko J., et al. Haematologica. 2023;108(1):98-109.

Grazie / Thank You!