con il patrocinio di

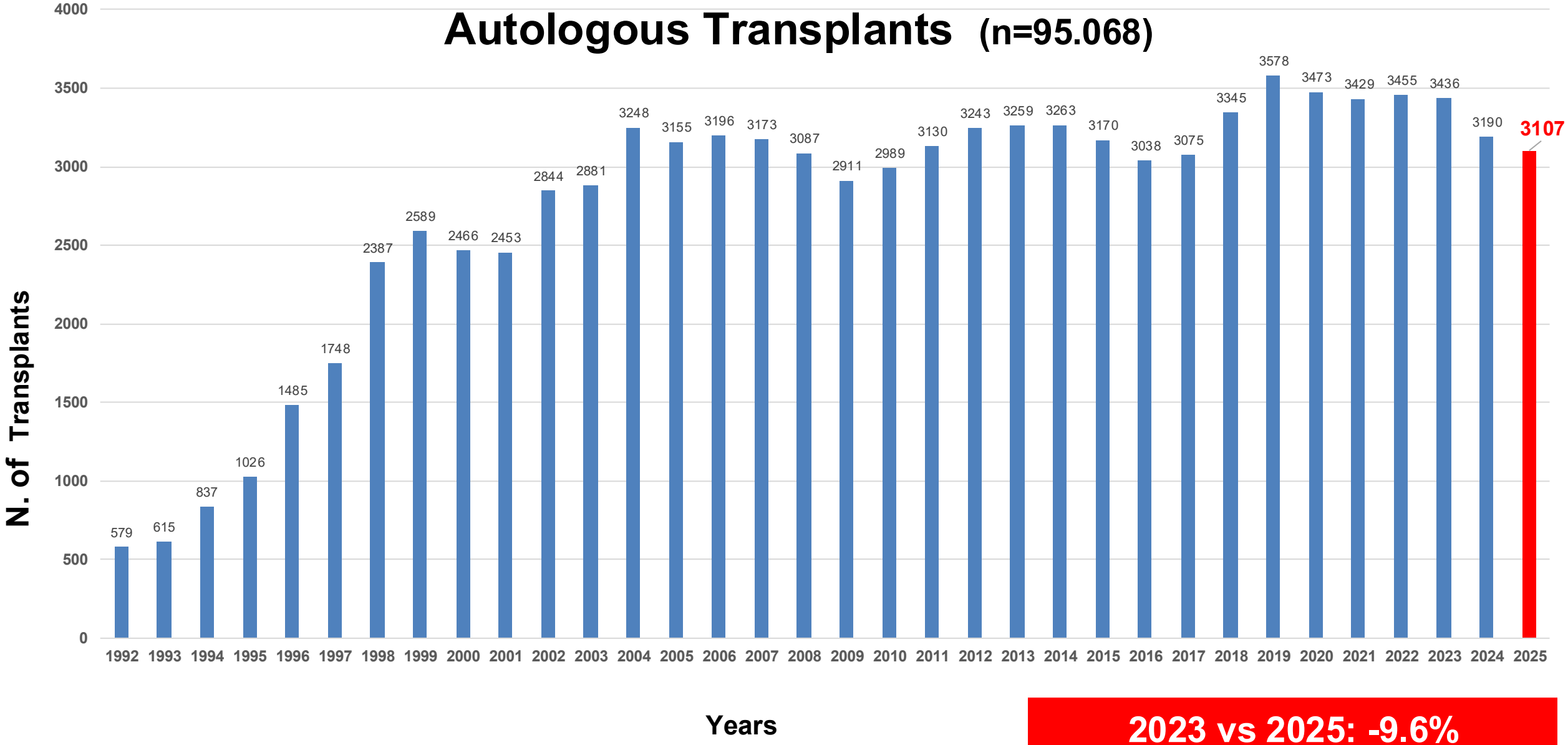
AIL Caserta
Valentina Picazio
ASSOCIAZIONE ITALIANA CONTRO LEUCEMIE - LINFOMI E MIELOMA

SIE
Società Italiana
di Ematologia

La rivoluzione terapeutica nel **linfoma** e nel **mieloma**

Napoli, Hotel Royal Continental • 14–15 Maggio 2026

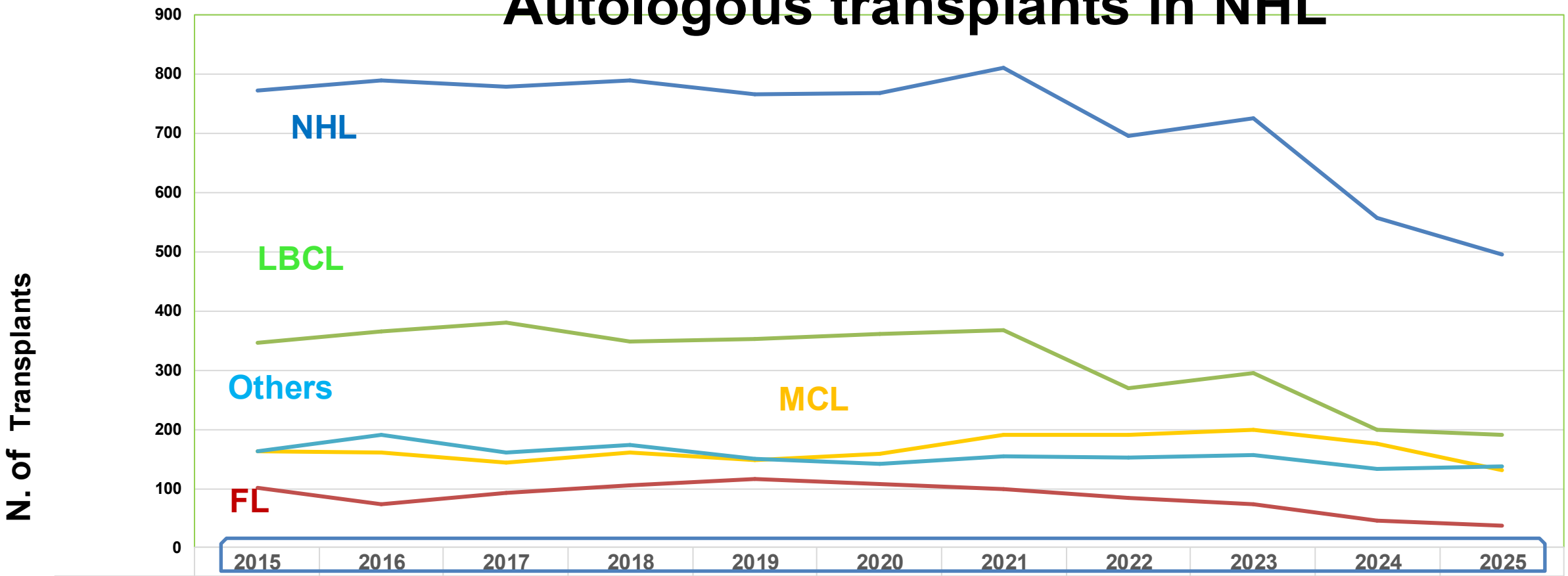
The big debate: CAR-T vs bispecifici nei LNH B cell aggressivi ed indolenti



2023 vs 2025: -9.6%
2024 *vs.* 2025: -2.6 %

Export date 13/04/2026

Autologous transplants in NHL

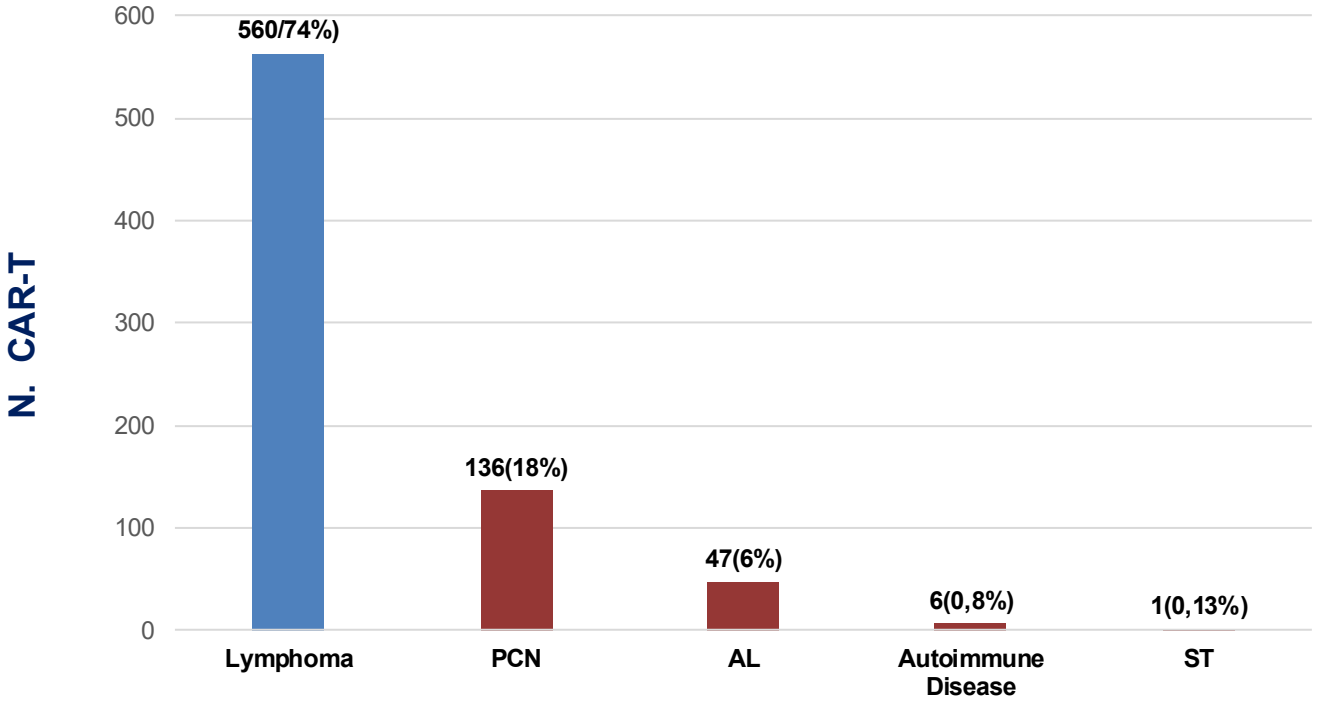


	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025
NHL	773	790	779	789	765	768	811	696	725	556	496
Follicular	102	73	93	105	115	108	99	84	73	46	38
LBCL	347	366	381	349	353	360	368	269	295	200	190
Mantle	162	160	144	161	147	158	190	190	200	176	131
others	162	191	161	174	150	142	154	153	157	134	137

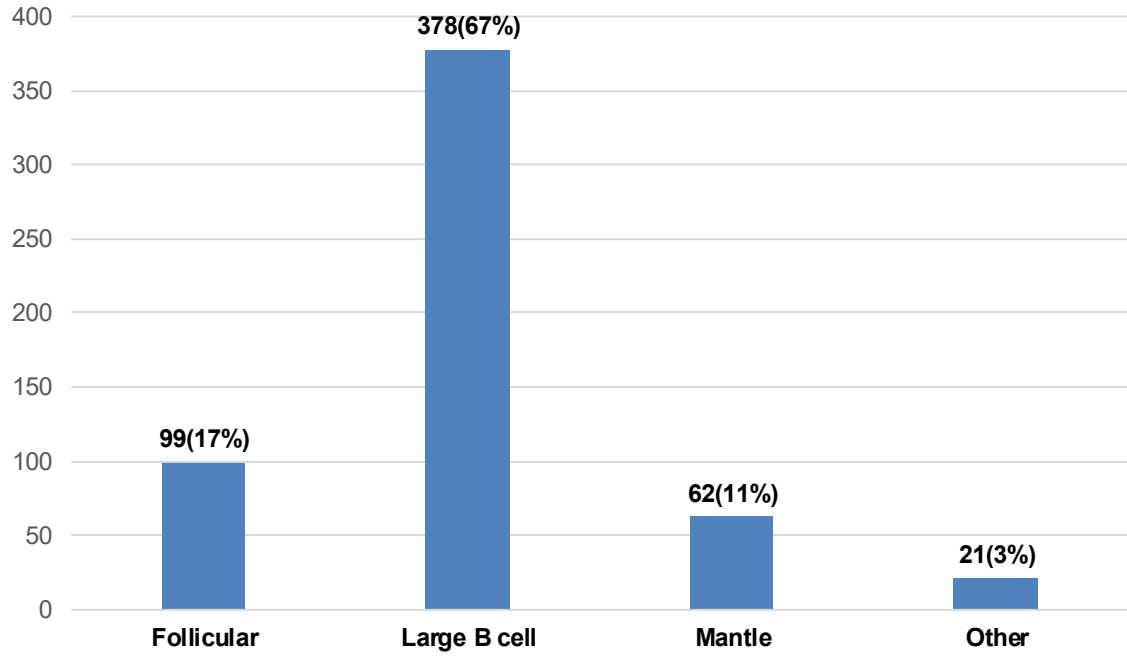
Autologo: variazione percentuale per tipo di linfoma tra il 2020 e il 2025

Tipo	2020	2025	Variazione
NHL (totale)	768	496	**−35,4%**
Follicolare (FL)	108	38	**−64,8%**
LBCL	360	190	**−47,2%**
Mantle (MCL)	158	131	**−17,1%**
Others	142	137	**−3,5%**

2025: CAR-T procedures by disease

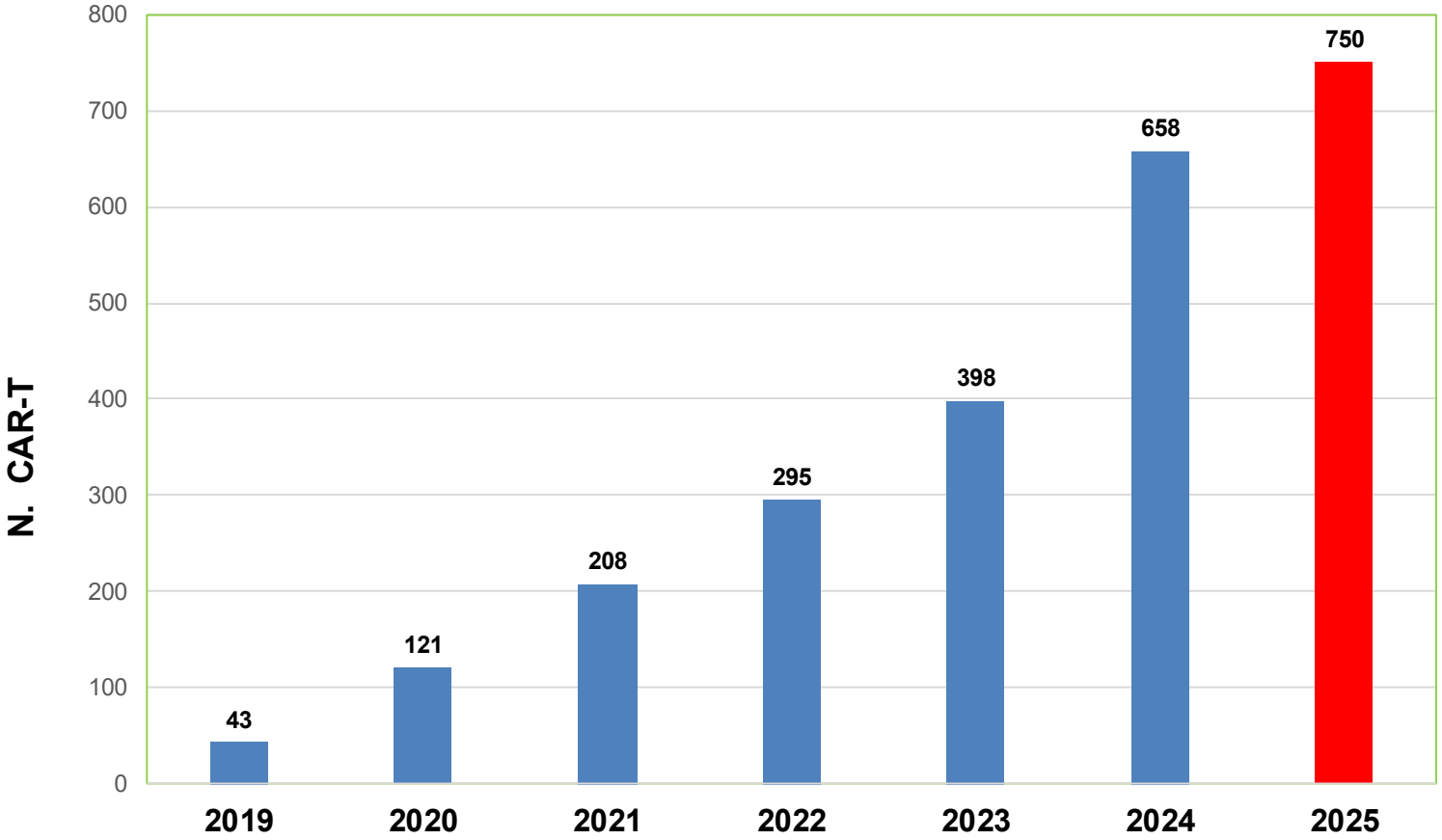


Disease

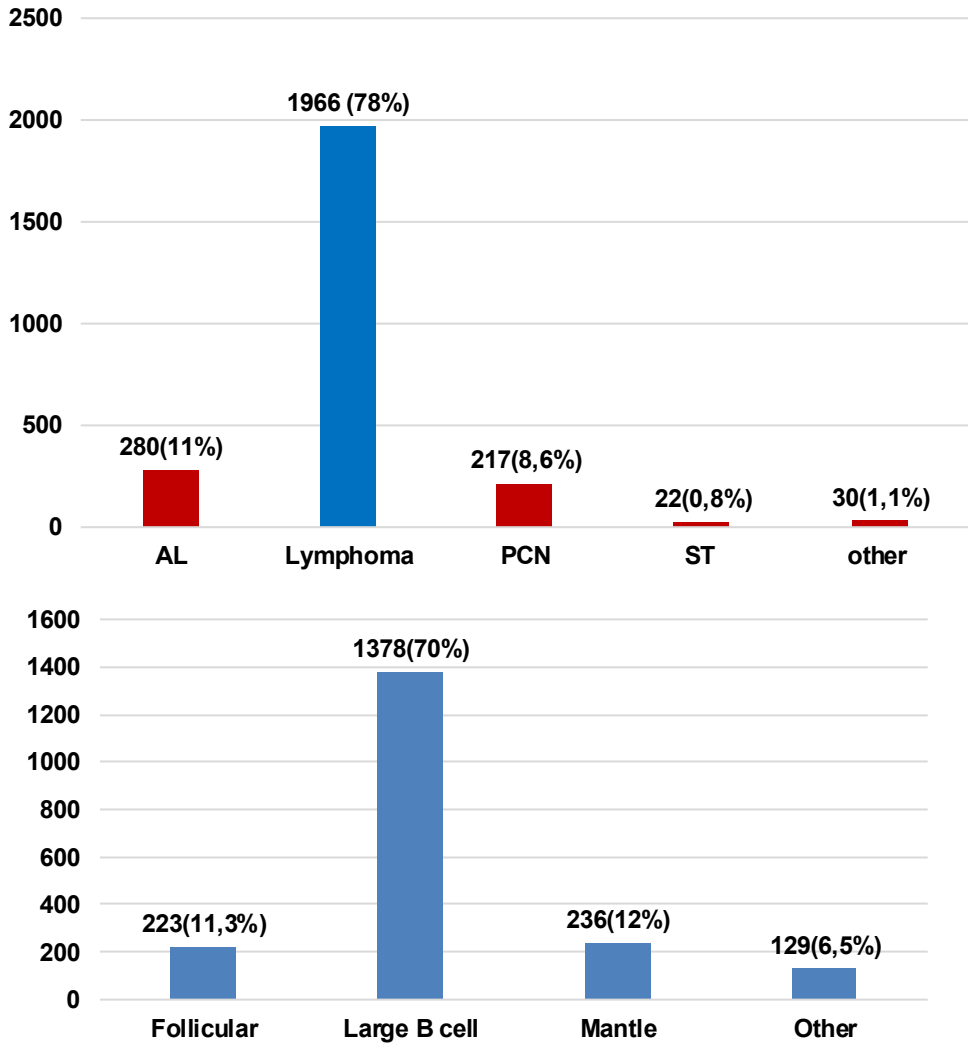


Lymphoma

CAR-T procedures by year (n=2515)

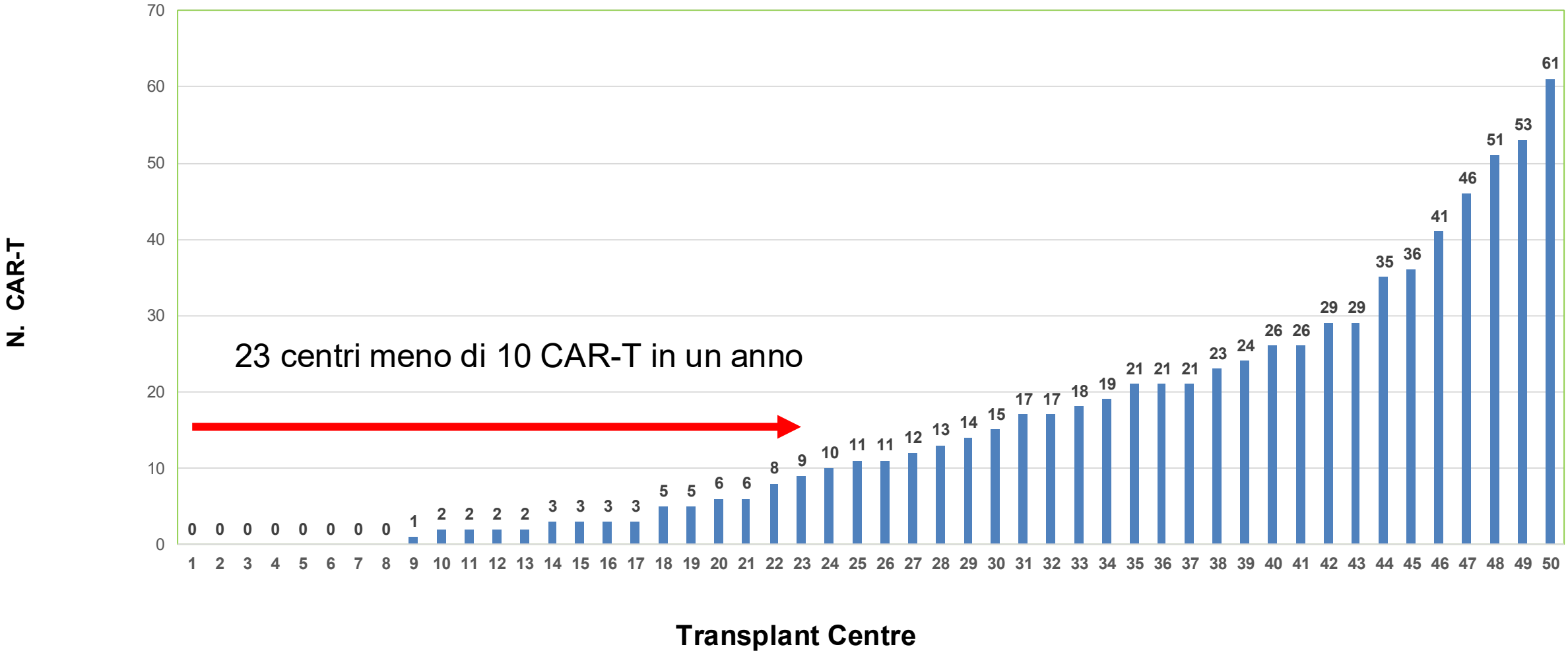


2024 vs 2025: + 14%



Lymphoma

2025 CAR-T procedures by Transplant Centre



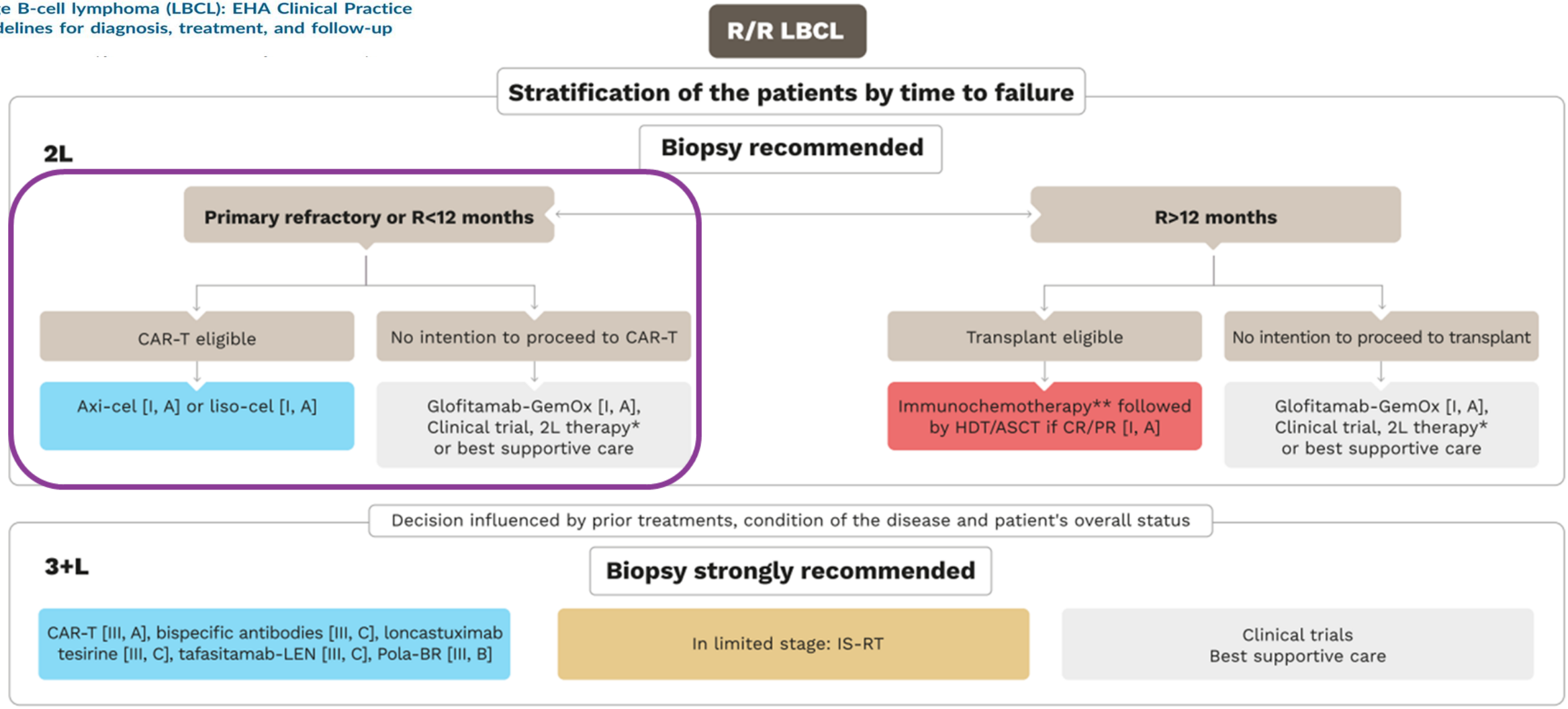
CD19-Targeted CAR T-Cell as SoC 2L Therapy of LBCL

DOI: 10.1002/hem3.70207

GUIDELINES - EXPERT OPINION

HemaSphere eha

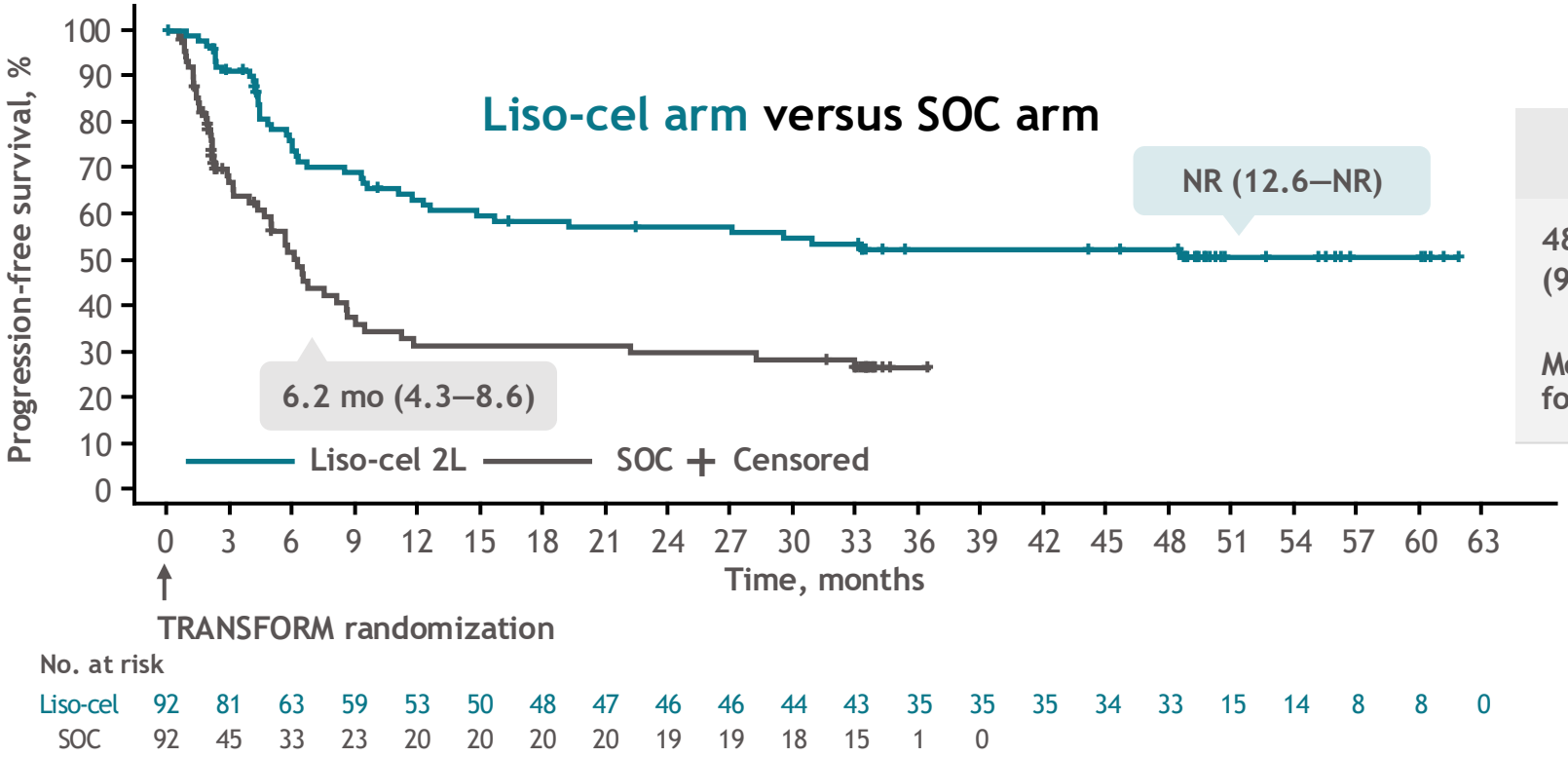
Large B-cell lymphoma (LBCL): EHA Clinical Practice Guidelines for diagnosis, treatment, and follow-up



Thieblemont et al. Haemasphere; September 2025e70207

Liso-cel continued to demonstrate high PFS rates over SOC in 2L, with median PFS not reached in the liso-cel arm

3-year follow-up results from TRANSFORM



	Liso-cel 2L (n = 92)	SOC (n = 92)
48-month rate (95% CI)	**52.2%** (41.5—62.8)	**NA** (NA—NA)
Median (95% CI) follow-up	49.4 months (48.7—50.3)	33.2 months (32.9—33.6)

Kamdar M, et al. ASH 2025. Poster number 3710

NA, not available.

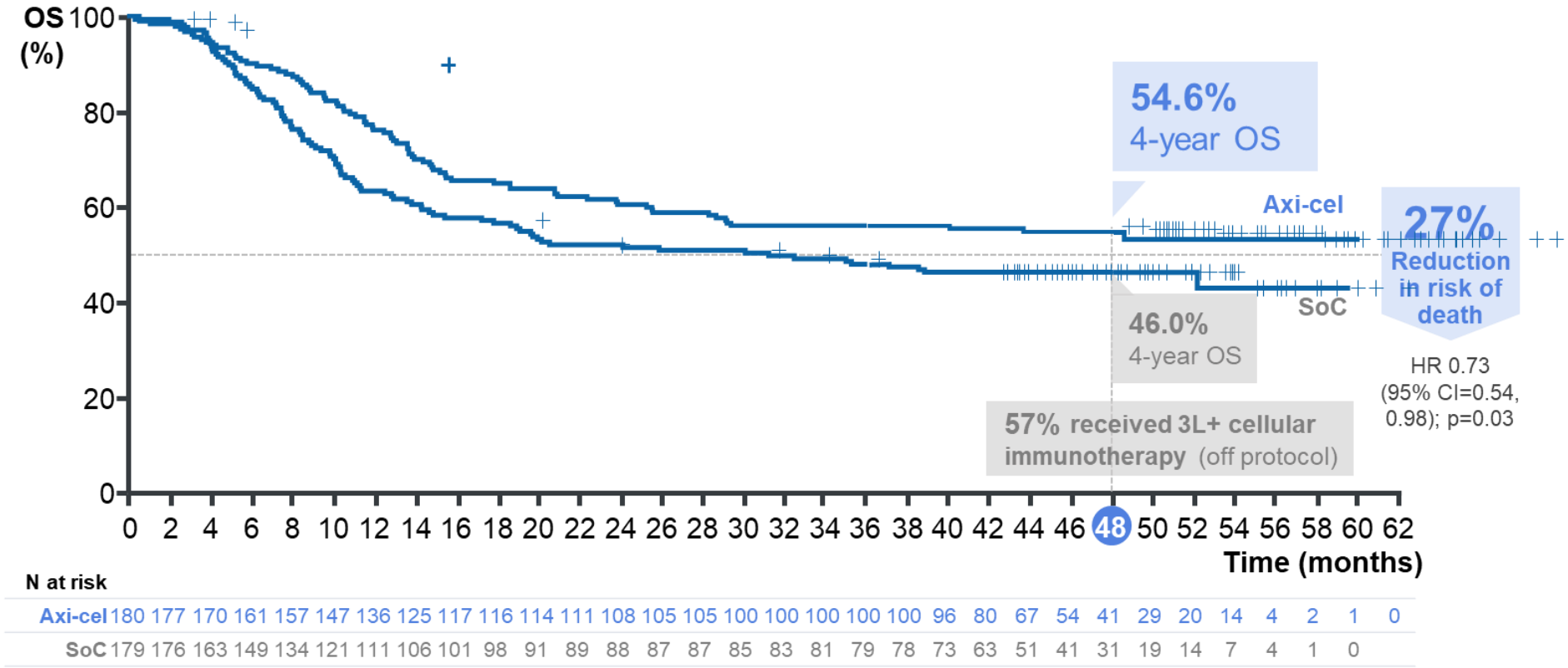
ZUMA-7 - Curative Potential in 2L - Axi-Cel is the first CART product with a statistically significant OS benefit

ZUMA-7

mFU: 47.2 months

OS: axi-cel (n=180) vs. SoC (n=179)

p=0.03



Axi-cel significantly improved overall survival vs. SoC, and median OS was not reached at 47.2 months' median follow-up

- NR: not reached

Westin JR, *et al*. *N Engl J Med* 2023; 389: 148–157.

Axi-cel efficacy in transplant eligible an ineligible pts: combined results from ZUMA 7 and ALYCANTE

CAR-T efficacy is confirmed also in 2L DLBCL inelegible patients

Endpoint	Pooled (%)	ZUMA-7 (%)	ALYCANTE (%)
CMR, mese 3	55,6	51,2	67,7
ORR, mese 12	46,0	46,5	46,0
DOR, mese 12	61,6	60,8	62,1
EFS, mese 24	45,2	45,2	44,6
PFS, mese 24	47,6	46,7	46,8
OS, mese 24	64,9	62,8	70,8

- Efficacy analysis included 178 and 69 leukapheresed patients from ZUMA7 and ALYCANTE of which 170 (on 178) and 62 (on 69) received axi-cel
- Axi-cel delivers similar outcomes regardless of ASCT-eligibility in second line R/R LBCL

Adapted from Houot et al. presented at ASH 2025, abs#7583

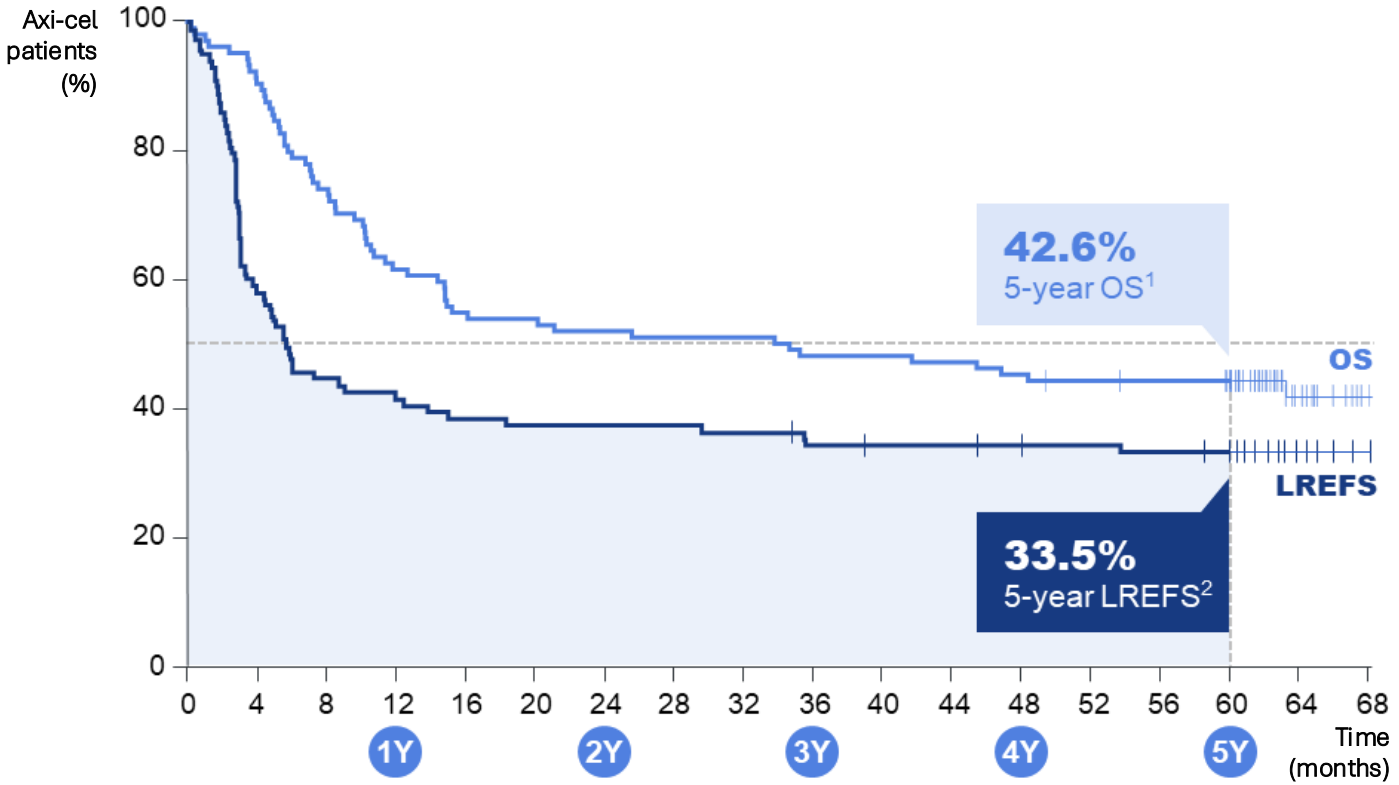
ZUMA-1: curative potential with axi-cel in 3L+ R/R DLBCL

ZUMA-1 3L+

mFU: 63.1 months

Exploratory, long-term survival assessment of axi-cel in patients with R/R DLBCL (N=101)[1,2]

Primary endpoint:
ORR = 83%[1]



Approx. **4/5** patients who responded and are alive at 5 years after axi-cel are potentially cured.

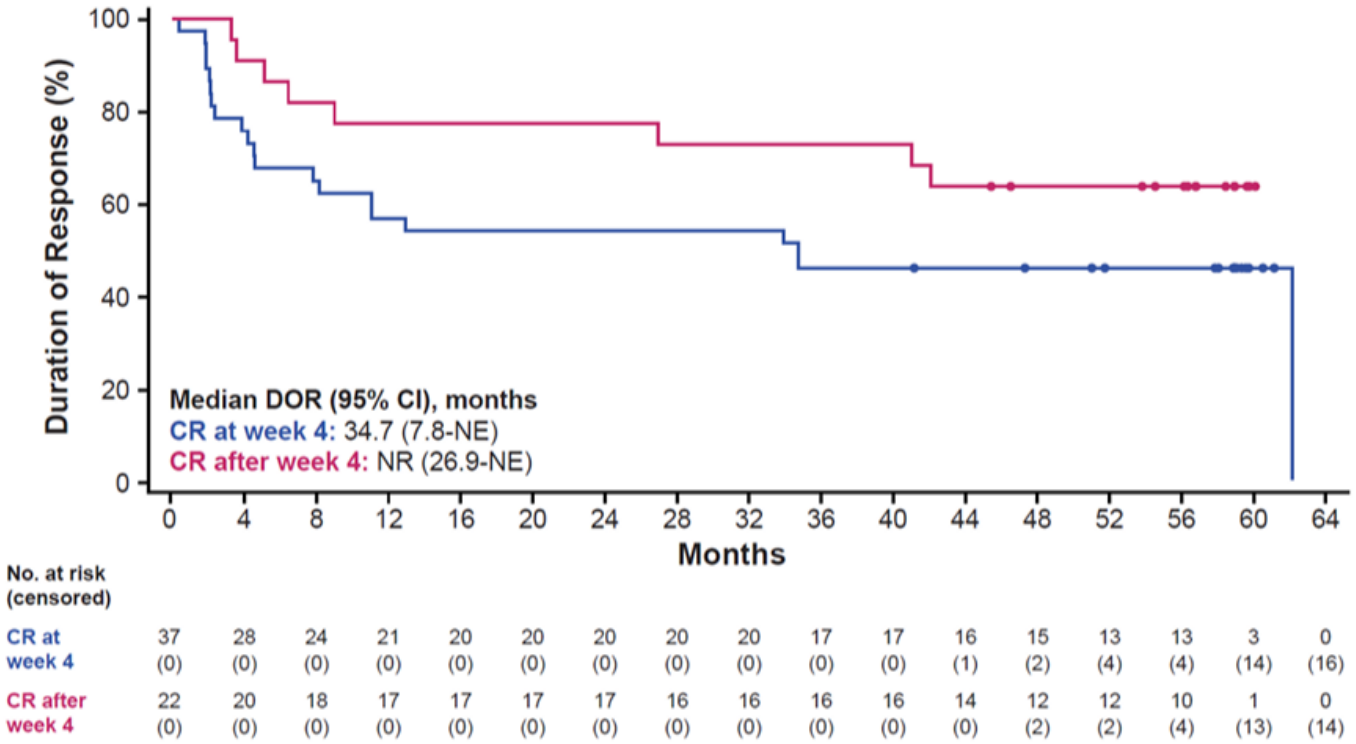
Axi-cel has demonstrated **curative potential in 3L+ R/R DLBCL**[1,2]

2L: second line; 3L+: third line or later; DLBCL: diffuse large B-cell lymphoma; LREFS: lymphoma-related event-free survival; mFU: median follow-up; ORR: objective response rate; OS: overall survival; R/R: relapsed/refractory; Y: year.

1. Neelapu SS, *et al*. *Blood*. 2023;141:2307–2315; 2. Neelapu SS, *et al*. ASH 2023 (Abstract 4864; poster).

ZUMA1: Duration of Complete Response (DoCR)

Duration of Response by Complete Response at or After Week 4 Postinfusion



This figure shows Kaplan-Meier estimates of DOR in treated patients with LBCL (n=101) in Cohorts 1 and 2 of phase 2 who had a complete response to axi-cel, either at the week 4 disease assessment or afterward. Axi-cel, axicabtagene ciloleucel; CR, complete response; DOR, duration of response; LBCL, large B-cell lymphoma; NE, not estimable.

Table 2. Investigator-assessed response

	N = 101
Best response, n (%, 95% CI)	
Objective response	84 (83, 74-90)
CR	59 (58, 48-68)
PR	25 (25, 17-34)
SD	10 (10, 5-17)
PD	5 (5, 2-11)
Not done	2 (2, 0-7)
Ongoing response, n (%)	31 (31)
CR	30 (30)
PR	1 (1)
DOR (95% CI)	
Median DOR, mos	11.1 (4.2-51.3)
Median duration of CR, mos	62.2 (12.9-NE)
Median duration of PR, mos	1.9 (1.3-2.1)

- Adapted Neelapu et al. Blood 2023 and Suppl Mat.

QoL recovery was faster for patients receiving axi-cel vs. SoC treatment

ZUMA-7 2L

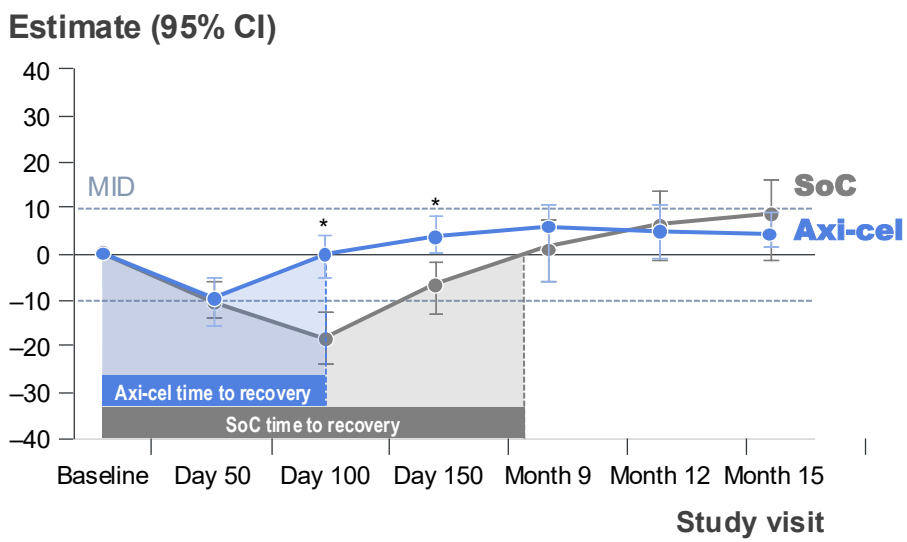
mFU: 24.9 months

Phase 3, randomised, multicentre trial of **axi-cel** vs. **SoC** (chemo + HDCT ± ASCT) as 2L treatment in patients with R/R LBCL (N=359)

EORTC QLQ-C30 (prespecified secondary outcome):
Axi-cel vs. **SoC (N=296)**

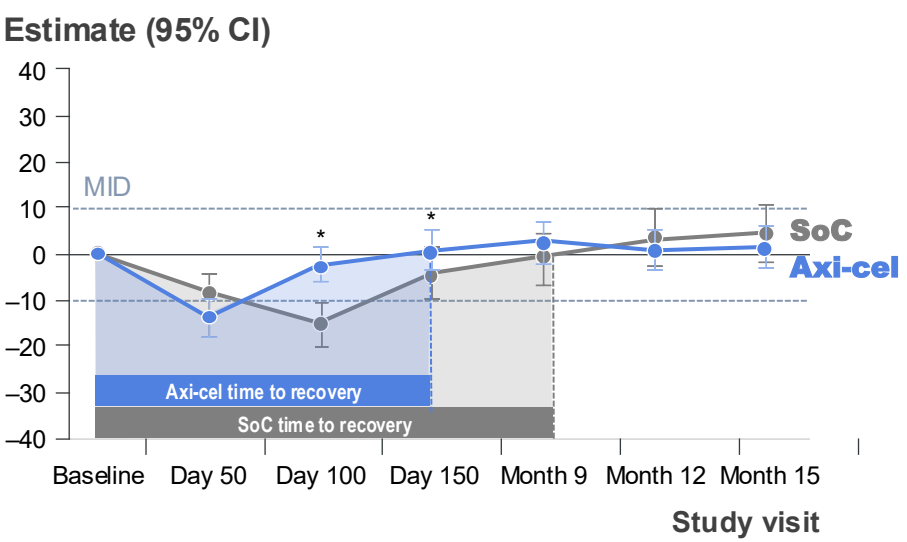
*p<0.05

EORTC QLQ-C30
Global health status/QoL



Axi-cel	165	163	146	110	88	79	67
SoC	130	125	62	56	40	33	26

EORTC QLQ-C30
Physical functioning



	164	163	146	109	88	79	67
	131	126	64	56	40	33	26

Prespecified MMRM analysis including variables for treatment, time, and treatment by time interaction (primary analysis) and controlled for response to 1L therapy (primary refractory, relapse ≤6 months vs. >6 and ≤12 months of 1L therapy) and age-adjusted IPI (0–1 vs. 2–3)

1L: first-line; 2L: second-line; ASCT: autologous system cell transplantation; EORTC QLQ-C30: European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30; HDCT: high-dose chemotherapy; IPI: International Prognostic Index; mFU: median follow-up; MID: minimally important difference; MMRM: mixed model for repeated measures; QoL: quality of life; R/R LBCL: relapsed or refractory large B-cell lymphoma; SoC: standard of care.

Elsawy M, *et al. Blood* 2022; 140:2248–2260.

Real World Data confirm pivotal outcomes for CAR-T in 2L

CIBMTR US

US CIBMTR RW

N = 446 pts

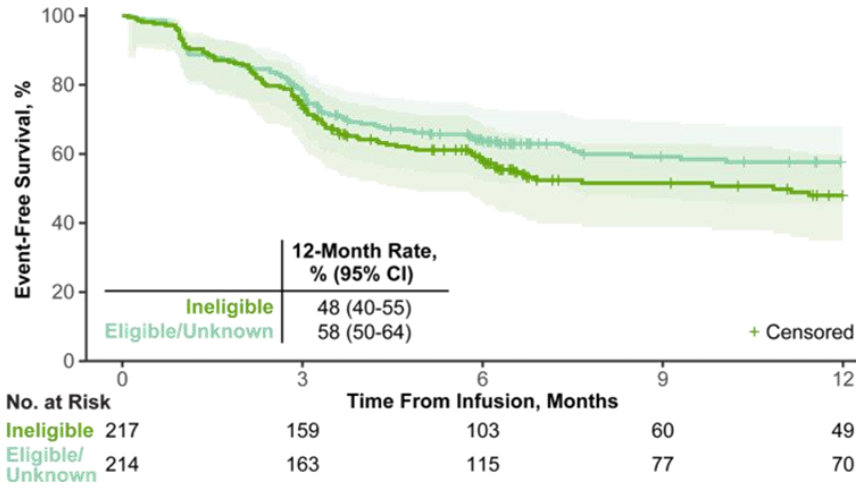
48% ZUMA7-eligible

49% ZUMA7-inelegible

mFU: 12.0 mo

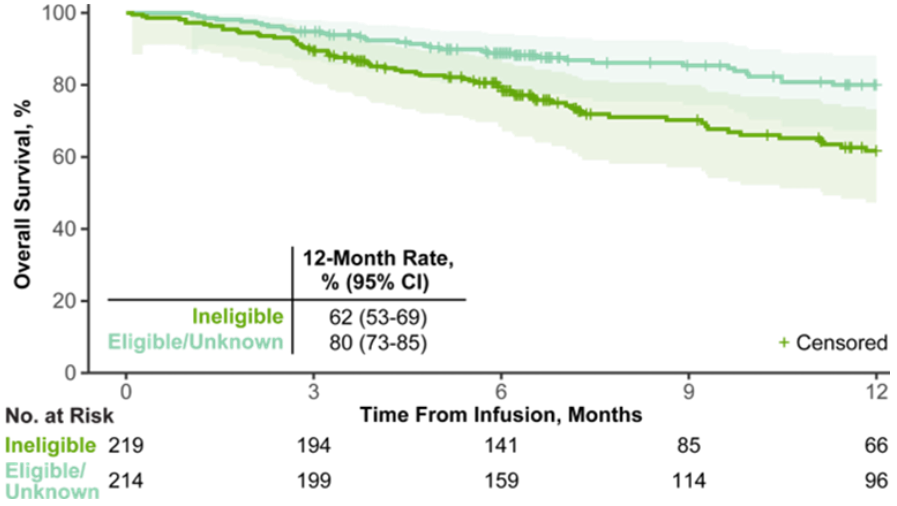
April 2022 - July 2023

EFS by ZUMA-7 elegibility



- Among all patients, the 12-month EFS rate was 53%
- 12-month EFS: 48% in ZUMA-7 ineligible patients
- 12-month EFS : 58% in ZUMA-7 eligible patients

OS by ZUMA-7 eligibility



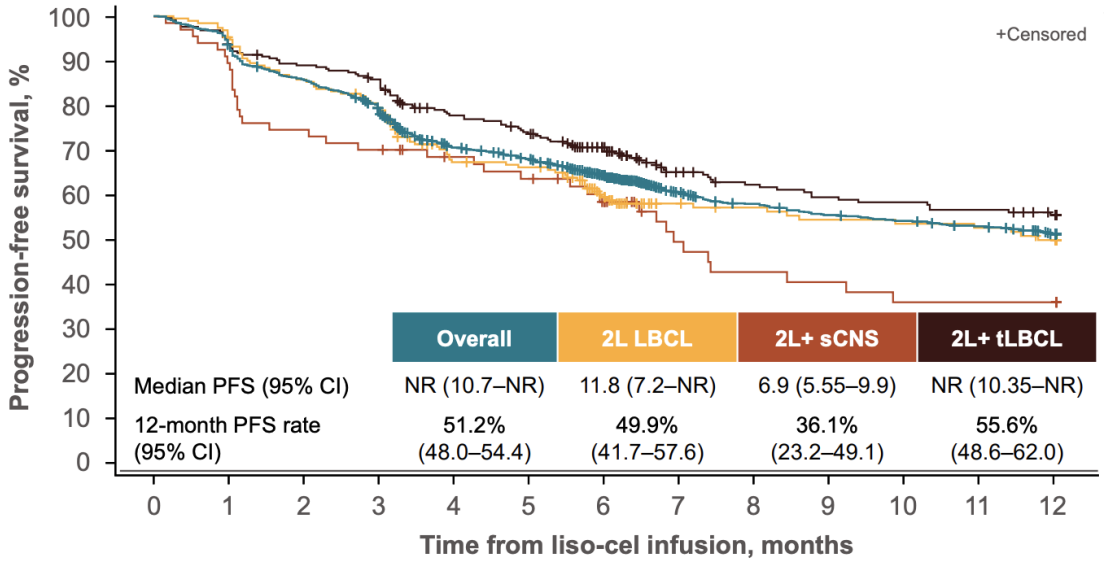
- Among all patients, the 12-month EFS rate was 53%
- 12-month OS: 62% in ZUMA-7 ineligible patients
- 12-month OS : 80% in ZUMA-7 eligible patients

In this large real world study where 446 pts had been treated with axi-cel as 2L, about half of patients (52%) would have been ineligible for ZUMA-7.
Despite a broader patient population beyond the ZUMA-7 trial, effectiveness and safety outcomes at median follow-up of 12 months were consistent with those observed in ZUMA-7

Lee et al. ASH2024

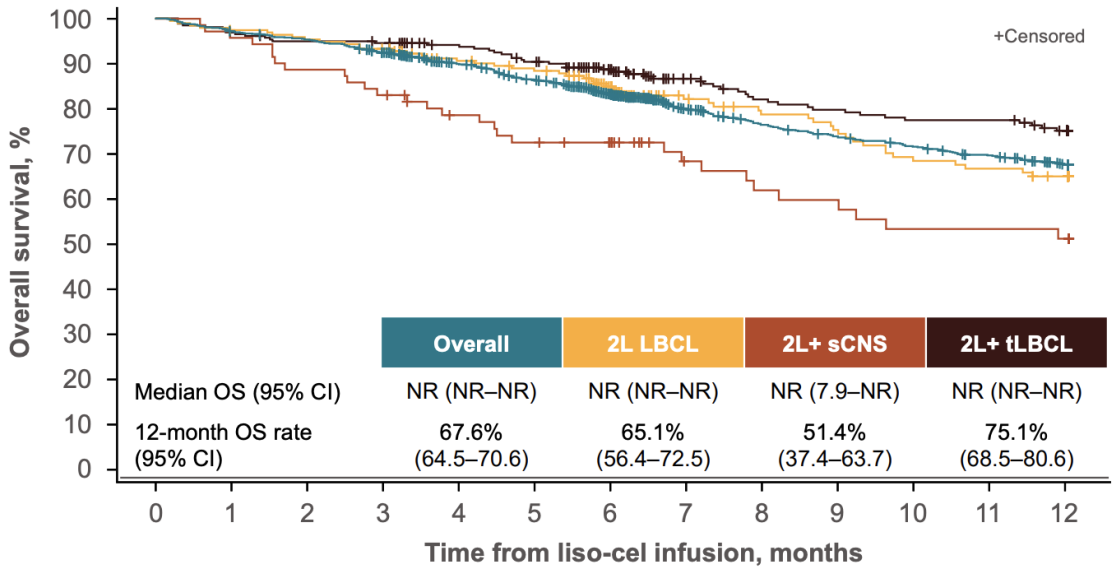
Real-world outcomes for lisocabtagene maraleucel in patients with relapsed or refractory large B-cell lymphoma

A



Overall	1096	1025	939	860	733	698	617	473	443	423	412	399	373
2L LBCL	191	181	163	149	118	115	91	66	63	60	59	58	54
2L+ sCNS	67	60	50	47	42	39	33	22	19	18	16	16	16
2L+ tLBCL	256	239	226	217	188	177	153	119	111	106	104	101	95

B



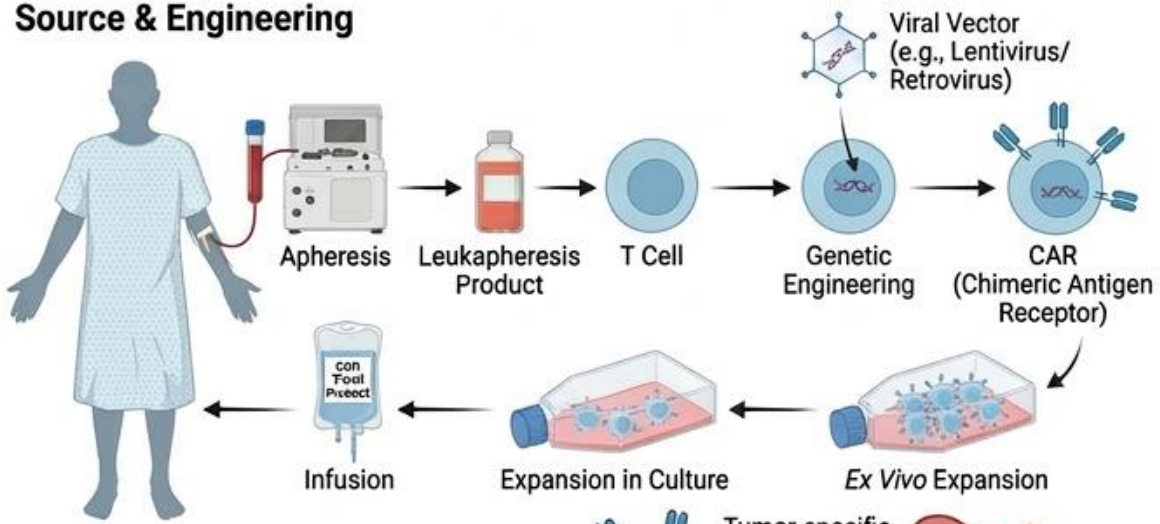
Overall	1116	1084	1062	1021	951	904	813	645	603	581	561	541	507
2L LBCL	195	189	185	179	166	160	137	99	92	88	80	78	73
2L+ sCNS	71	68	63	59	52	48	44	32	29	28	25	25	24
2L+ tLBCL	257	248	242	240	227	217	190	155	143	139	135	135	126

Crombie JL,.et al Blood. 2026 Mar 3

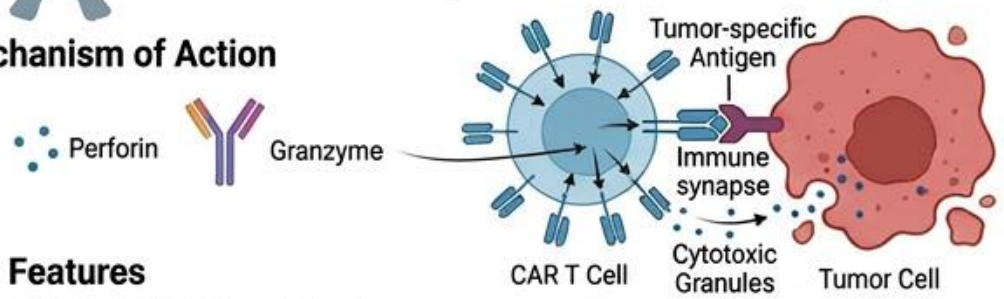
CAR T-Cell Therapy vs. Bispecific Antibodies: Simplified Mechanism & Features

CAR T-Cell Therapy

Source & Engineering



Mechanism of Action

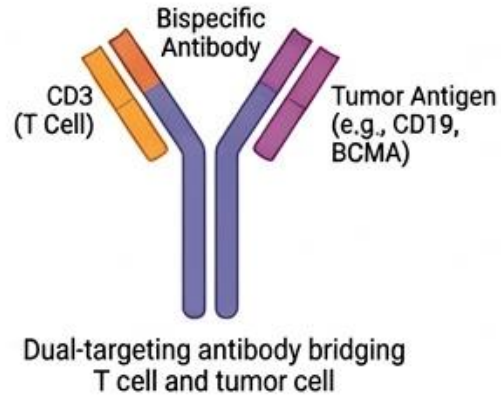


Key Features

- **Efficacy:** High (e.g., blood cancers)
- **Safety:** CRS, Neurotoxicity Risks
- **Manufacture:** Personalized, Complex, Long

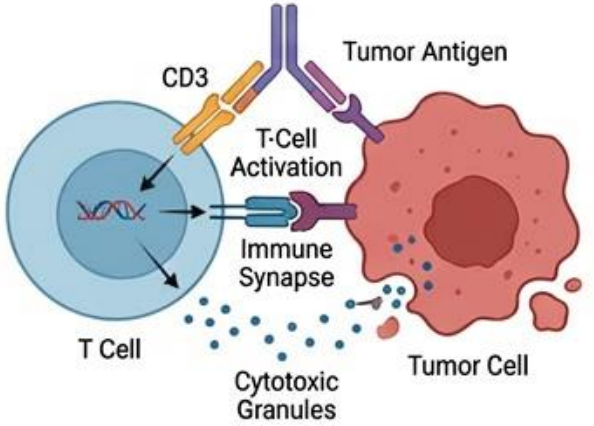
Bispecific Antibody

Design of Antibody



Dual-targeting antibody bridging T cell and tumor cell

Mechanism of Action



Key Features

- **Efficacy:** Effective in certain tumors
- **Safety:** CRS, lower neurotoxicity risk
- **Manufacture:** "Off-the-shelf", Standardized, Quick
- **Access:** More viely available, less personalized

Direct Comparison

	Manufacturing	Administration	Time	Accessibility	Safety
CAR T-Cell	Personalized	Single Infusion	Long	Limited	High Risk
Bispecific Antibody	Off-the-shelf	Repeat Dosing	Short	Widespread	Lower Risk

Oluwole OO, et al.. *Blood Cancer J*. 2024 (Adapted)

Efficacy of CAR-T Cell Therapies vs Bispecific Antibodies in Aggressive B-cell Lymphomas (DLBCL, ≥2L)

CAR-T Cell Therapies	axi-cel (Axicabtagene ciloleucel)	tisa-cel (Tisagenlecleucel)	liso-cel (Lisocabtagene maraleucel)	Bispecific Antibodies	Bispecifics (EPCORE NHL-1, NP30179)
ORR% (Overall Response Rate)	52–83%			ORR% (Overall Response Rate)	38–63%
CR Rate (Complete Response Rate)	40–65%			CR Rate (Complete Response Rate)	24–40%
PFS at 12 months	~40–44%			PFS at 12 months	~30–35%
Durable Response at 2 yrs	~30–40%			Durable Response at 2 yrs	~20–30%
Key Clinical Trials	ZUMA-1, JULIET, TRANSFORM			Key Clinical Trials	EPCORE NHL-1, NP30179
Approved Setting	2L+ ≥2L DLBCL			Approved Setting	3L+ ≥3L DLBCL

CAR-T Advantages
- Superior CR & durable response
- Potential for long-term remission

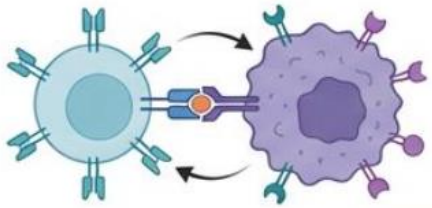
Bispecific Highlights
- Immediate availability
- Simpler administration in some settings

Oluwole OO, et al.. *Blood Cancer J*. 2024 (Adapted)

No Prospective RCT: CAR-T vs Bispecifics in DLBCL – Structural Barriers

① Current Indications (Side-by-side comparison)

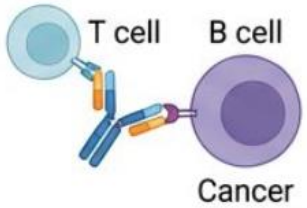
CAR-T Cell Therapy



Indicated for **≥2nd-line** (≥2L) DLBCL

Requires JACIE-accredited center

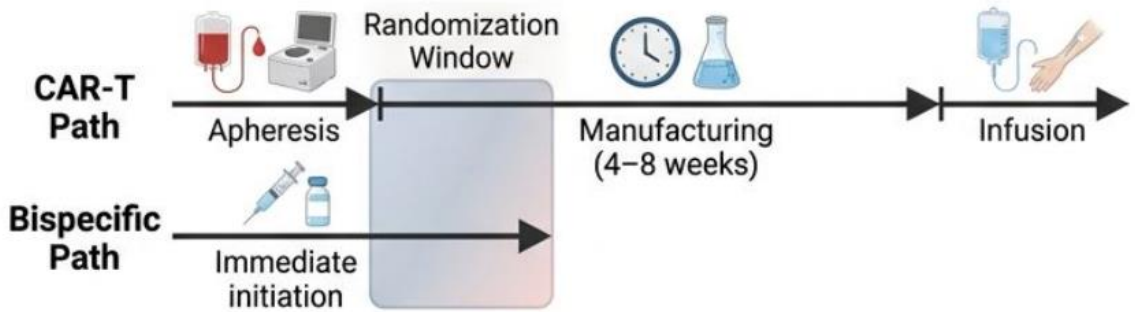
Bispecific Antibodies



Indicated for **≥3rd-line** (≥3L) DLBCL

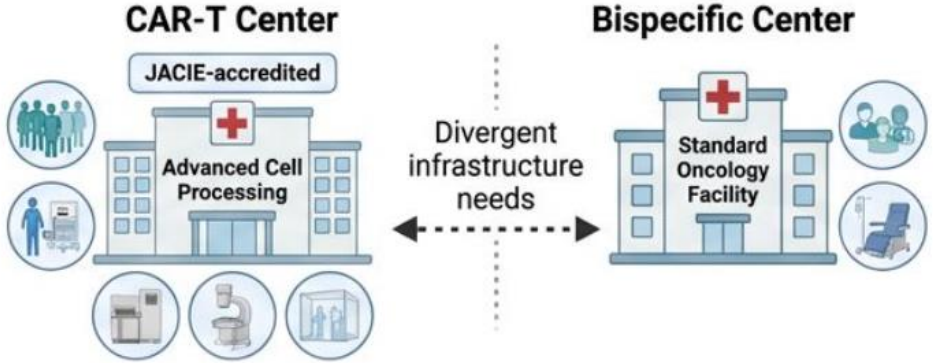
Broader accessibility

② Lead-time Incompatibility

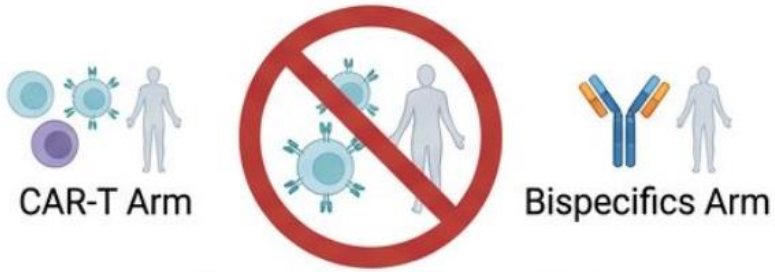


Unmatched logistics hinder a unified randomization window

③ Divergent Infrastructure Requirements

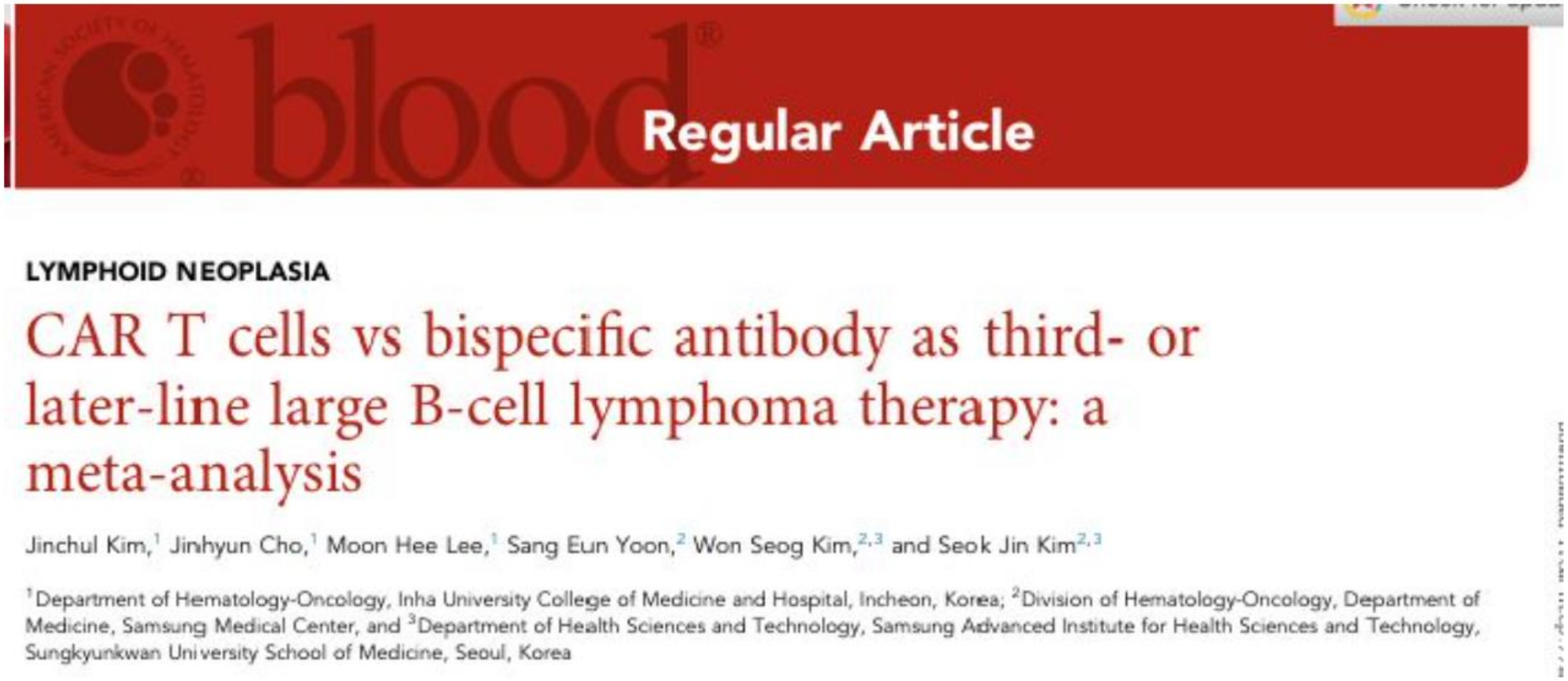


④ Central 'No RCT' Summary



No prospective, head-to-head RCT exists — and unlikely to ever exist in classical form.

Take-home Box: Direct head-to-head comparison of CAR-T versus bispecifics in DLBCL is structurally precluded by differing indications, incompatible timelines, and divergent infrastructure.



blood

Regular Article

LYMPHOID NEOPLASIA

CAR T cells vs bispecific antibody as third- or later-line large B-cell lymphoma therapy: a meta-analysis

Jinchul Kim,[1] Jinhyun Cho,[1] Moon Hee Lee,[1] Sang Eun Yoon,[2] Won Seog Kim,[2,3] and Seok Jin Kim[2,3]

[1]Department of Hematology-Oncology, Inha University College of Medicine and Hospital, Incheon, Korea; [2]Division of Hematology-Oncology, Department of Medicine, Samsung Medical Center, and [3]Department of Health Sciences and Technology, Samsung Advanced Institute for Health Sciences and Technology, Sungkyunkwan University School of Medicine, Seoul, Korea

16 trial con 1347 pazienti con DLBCL r/r trattati in ≥3L

Kim et al. (*Blood* 2024; 144:629-638),

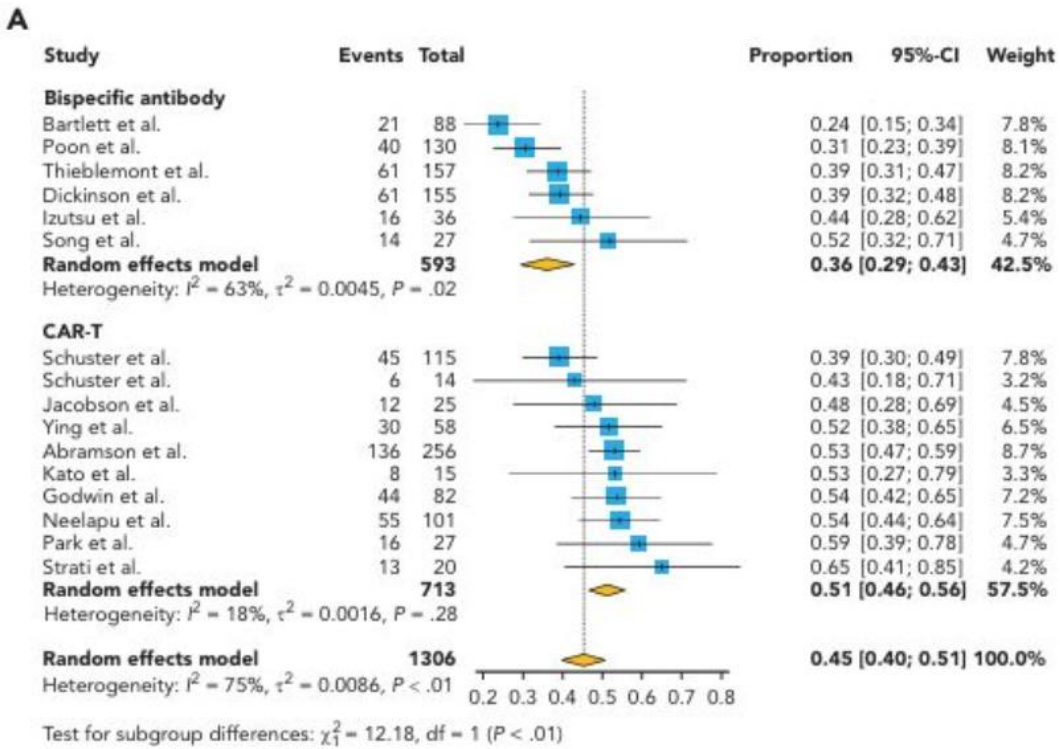
Table 1. Baseline characteristics of included studies

Trial name	Authors (trial identifier)	Phase	Regimen	No.	Median age (range), y	DH/TH lymphoma, %	Stage III/IV, %	Median no. of previous therapy (range)	Prior ASCT, %	Refractory to last prior treatment, %
Bispecific antibody										
EPCORE NHL-1	Thieblemont et al[15] (NCT03625037)	2	Epcoritamab	157	64 (20-83)	0.131	0.752	3 (2-11)	0.197	0.828
NR	Dickinson et al[14] (NCT03075696)	2	Glofitamab	154	66 (21-90)	0.129	0.753	3 (2-7)	0.182	0.857
NR	Bartlett et al[18] (NCT02500407)	2	Mosunetuzumab	88	66.5 (24-96)	0.193	0.841	3 (2-13)	0.17	0.795
ELM-2	Poon et al[17] (NCT03888105)	2	Odronextamab	140	66 (24-88)	0.193	0.80	2 (2-8)	0.157	0.864
NR	Song et al[20] (NCT04657302)	2	Glofitamab	30	57.5 (20-82)	NR	0.90	2 (2-6)	0.10	0.90
EPCORE NHL-3	Izutsu et al[21] (NCT04542824)	2	Epcoritamab	36	68.5 (44-89)	0.0	0.778	3 (2-8)	0.194	0.806
CAR T cell										
NR	Schuster et al[11] (NCT02030834)	2	Tisa-cel	14	58 (25-77)	0.214	0.643	3 (1-8)	0.5	0.86
ZUMA-1	Neelapu et al[10] (NCT02348216)	2	Axi-cel	111	58 (51-64 [IQR])	0.095	0.775	3 (2-4)	0.189	0.604
JULIET	Schuster et al[12] (NCT02445248)	2	Tisa-cel	115	56 (46-84)	0.27	0.765	3 (2-6)	0.487	0.548
TRANSCEND NHL 001	Abramson et al[13] (NCT02631044)	Seamless	Liso-cel	269	63 (54-70)	0.134	NR	3 (2-4)	0.335	0.673
RELIANCE	Ying et al[19] (NCT04089215)	2	Relmacabtagene	59	56 (18-75)	0.051	NR	2 (2-7)	0.102	0.814
NR	Kato et al[20] (JapicCTI-183914)	2	Axi-cel	16	58 (44-70)	0.067	0.5	3 (NR)	0.375	0.625
NR	Park et al[21] (NCT04148430)	2	Axi-cel/tisa-cel	27	62 (25-77)	NR	0.61	3 (2-5)	0.19	0.71
NR	Jacobson et al[26] (NCT03954106)	2	Axi-cel	25	68 (31-78)	NR	NR	2 (1-6)	0.20	0.84
NR	Strati et al[27] (NCT04432506)	1	Axi-cel	20	58 (26-81)	NR	0.95	3 (2-8)	0.05	1.00
OUTREACH	Godwin et al[25] (NCT03744676)	2	Liso-cel	82	66 (28-86)	0.18	NR	2 (2-6)	0.16	0.91

DH, double-hit; IQR, interquartile range; TH, triple-hit.

Kim et al. (*Blood* 2024; 144:629-638),

- **CAR T-cell therapy demonstrates superior efficacy to bispecific antibody in DLBCL treatment, with higher CR rates.**



The overall pooled proportion of CR was 0.45 (95% CI, 0.40 0.51). There was significant difference in CR rate between the bispecific antibody and CAR T-cell therapy (P < .01); 0.36 (95% CI, 0.29-0.43) in the bispecific antibody group and 0.51 (95% CI, 0.46-0.56) in the CAR T-cell group

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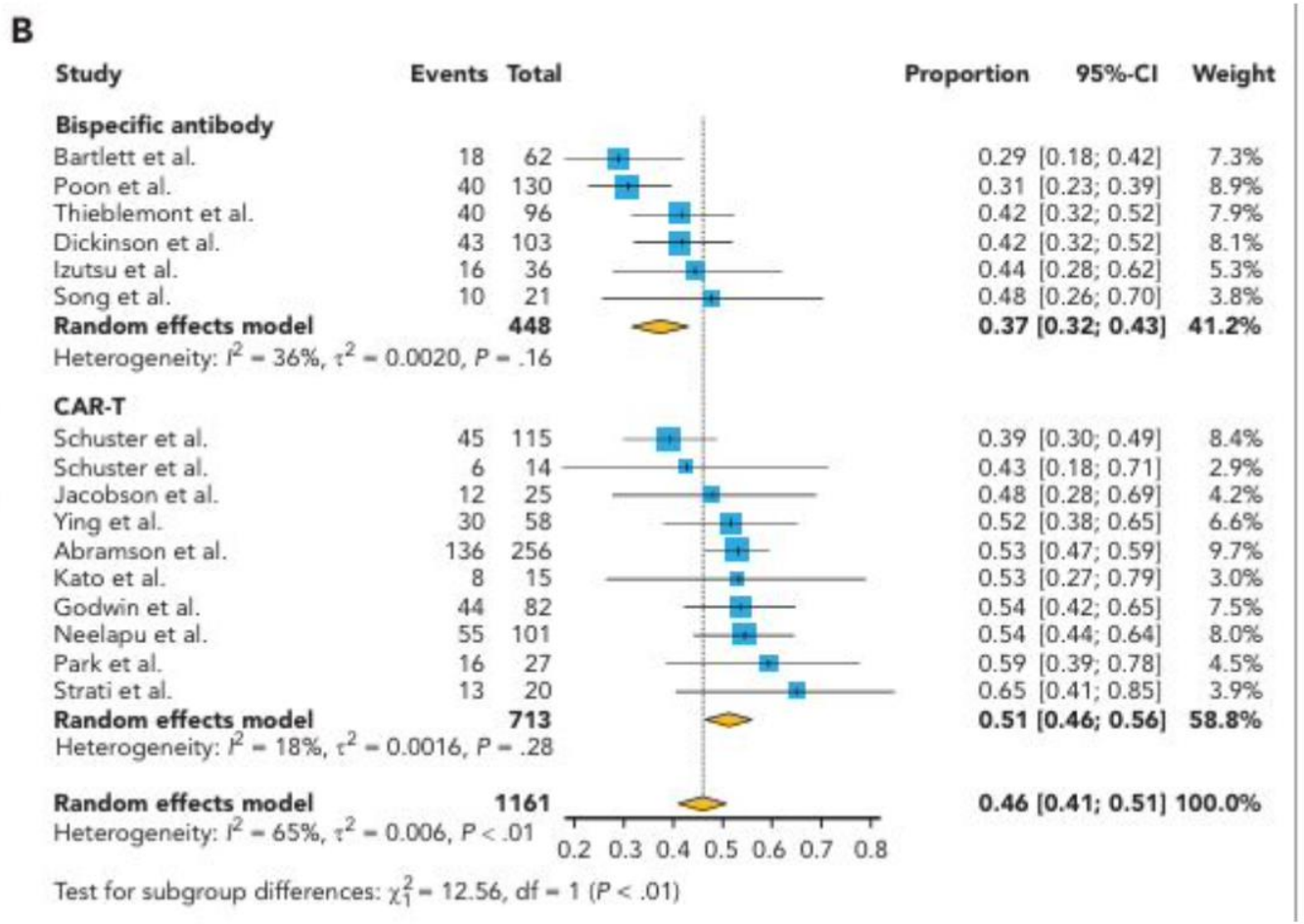
Kim et al. (*Blood* 2024; 144:629-638)

- **CAR T-cell therapy demonstrates superior efficacy to bispecific antibody in DLBCL treatment, with higher CR rates.**



Even when limiting the bispecific antibody group to patients who had not previously undergone CAR T-cell treatment, there was a significant difference between the 2 groups

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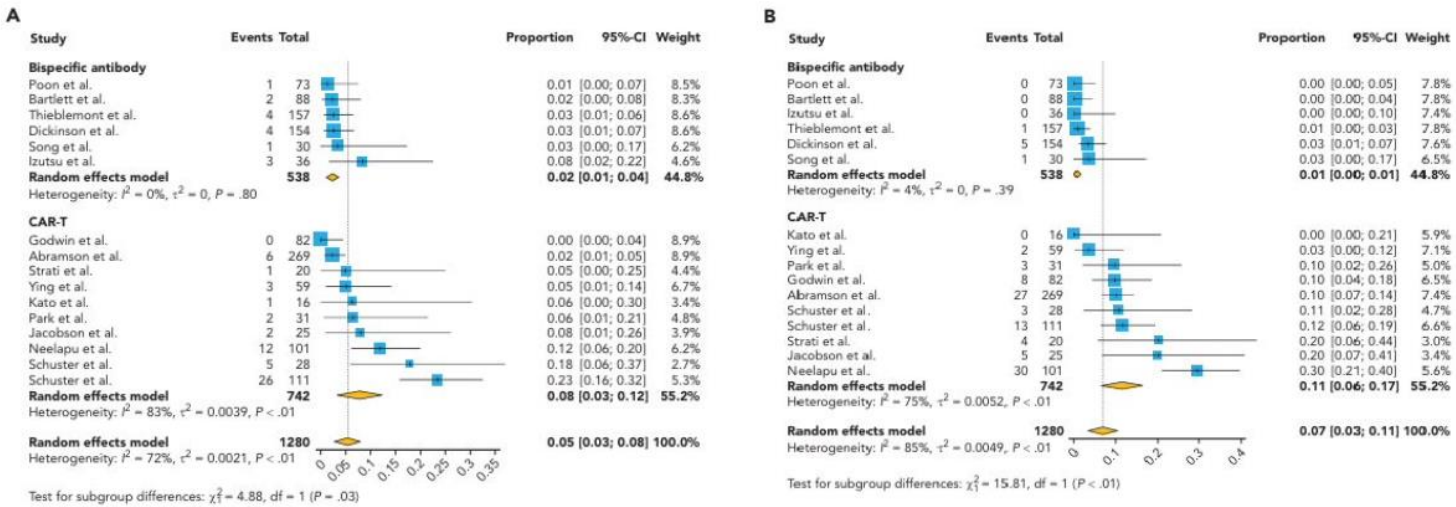
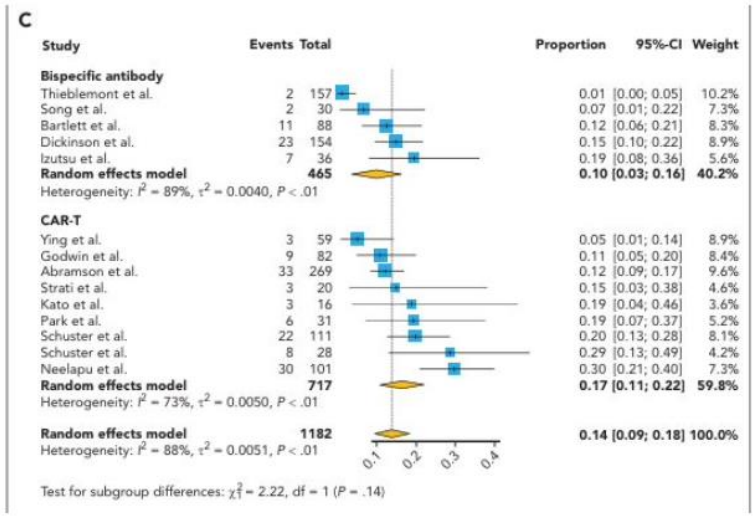
Kim et al. (*Blood* 2024; 144:629-638)

Pooled grade ≥3 adverse events rate by the treatment category. (A) CRS, (B) neurotoxicity,and(C) infection



- **CAR T-cell therapy exhibits higher incidence of grade ≥3 adverse events than bispecific antibody.**



blood 8 AUGUST 2024 | VOLUME 144, NUMBER 6

Kim et al. (*Blood* 2024; 144:629-638)

Cosa abbiamo: la meta-analisi Kim et al., *Blood* 2024

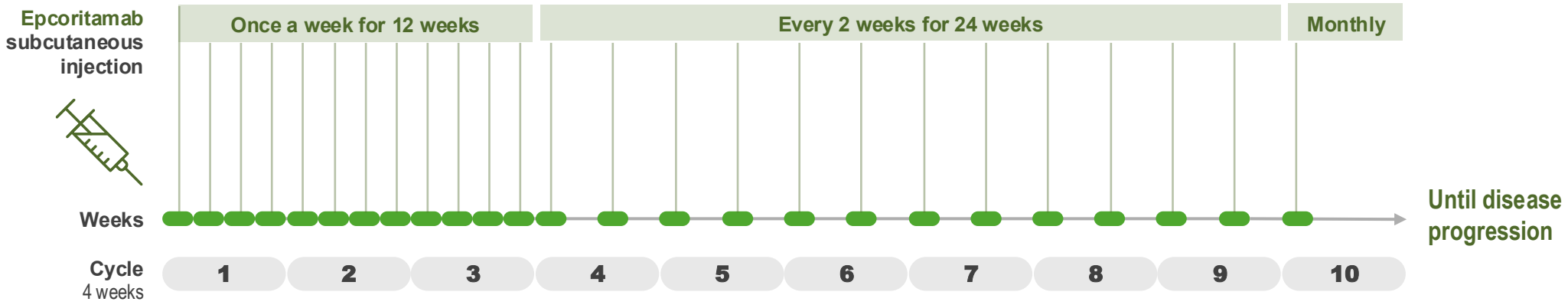
- CR rate poolato: 0.51 (95% CI 0.46-0.56) per CAR-T vs 0.36 (0.29-0.43) per bispecifici ($p<0.01$)
- PFS a 1 anno: 0.45 per CAR-T vs 0.37 per bispecifici ($p=0.02$)
- CRS G≥3 e ICANS G≥3 significativamente più frequenti nel braccio CAR-T.

Limiti metodologici

- eterogeneità delle popolazioni (diverso numero di linee pregresse, proporzione di double-hit, bridging diversity)
- follow-up diverso tra i trial dei due gruppi,
- la maggioranza dei pazienti nei bracci bispecifici erano già stati esposti a CAR-T
- La multivariata ha confermato la superiorità del CAR-T con aggiustamento per proporzione di DHL, e la superiorità persisteva anche nel sottogruppo CAR-T naïve nel braccio bispecifici (CR 0.37, 0.32-0.43).

How many patients completed epcoritamab monotherapy in the 3L clinical trial?

- **Dose expansion cohort of EPCORE NHL-1:[1]**
- **mFU: 30.6 months[2]**
- Phase 1/2, single-arm, open-label trial of **epcoritamab** in patients with R/R LBCL and ≥2 prior therapies (N=157)[1]



d15 Time to full dose

d40 Time to response

85%
Patients discontinued[2]

Reasons for discontinuation[2]

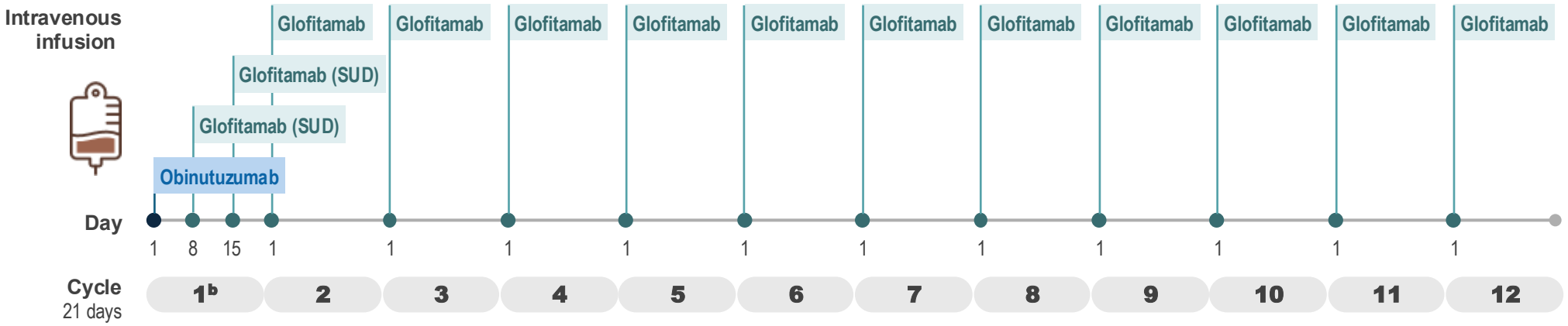
- **PD:** n=90
- **AE:** n=23
- **Allo-transplantation:** n=7
- **Subject withdrawal:** n=6
- **Maximum clinical benefit:**[a] n=1
- **Other:** n=6

- **Epcoritamab treatment continues until disease progression,**
- at 30.6 months mFU, 85% of patients had discontinued

[a]Decision due to investigator assessment that maximum clinical benefit was obtained.
3L: third-line; AE: adverse event; mFU: median follow-up; PD: progressive disease; PR: partial response; R/R LBCL: relapsed/refractory large B-cell lymphoma.
1. Thieblemont C, *et al*. *J Clin Oncol*. 2023;41:2238–2247; 2. Karimi Y, *et al*. ASCO 2024; Abstract 7039 (poster presentation).

How many patients completed glofitamab monotherapy in the 3L clinical trial?‡

- **Dose expansion cohort of NP30179:**
- Phase 2, open-label, interventional trial of **glofitamab** monotherapy in patients with R/R LBCL and ≥2 prior therapies (N=155)[a]



d21 Time to full dose

d42 Time to best response

70%
Patients discontinued[c]

Reasons for discontinuation[b]

- **PD:** n=63
- **Death:** n=10
- **AE:** n=11
- **Physician decision:** n=9
- **Subject withdrawal:** n=5
- **Other:** n=9
- **Protocol deviation:** n=1

- **Treatment with glofitamab** continues for **up to ~8.5 months**, in the clinical trial **only one in four patients completed treatment**

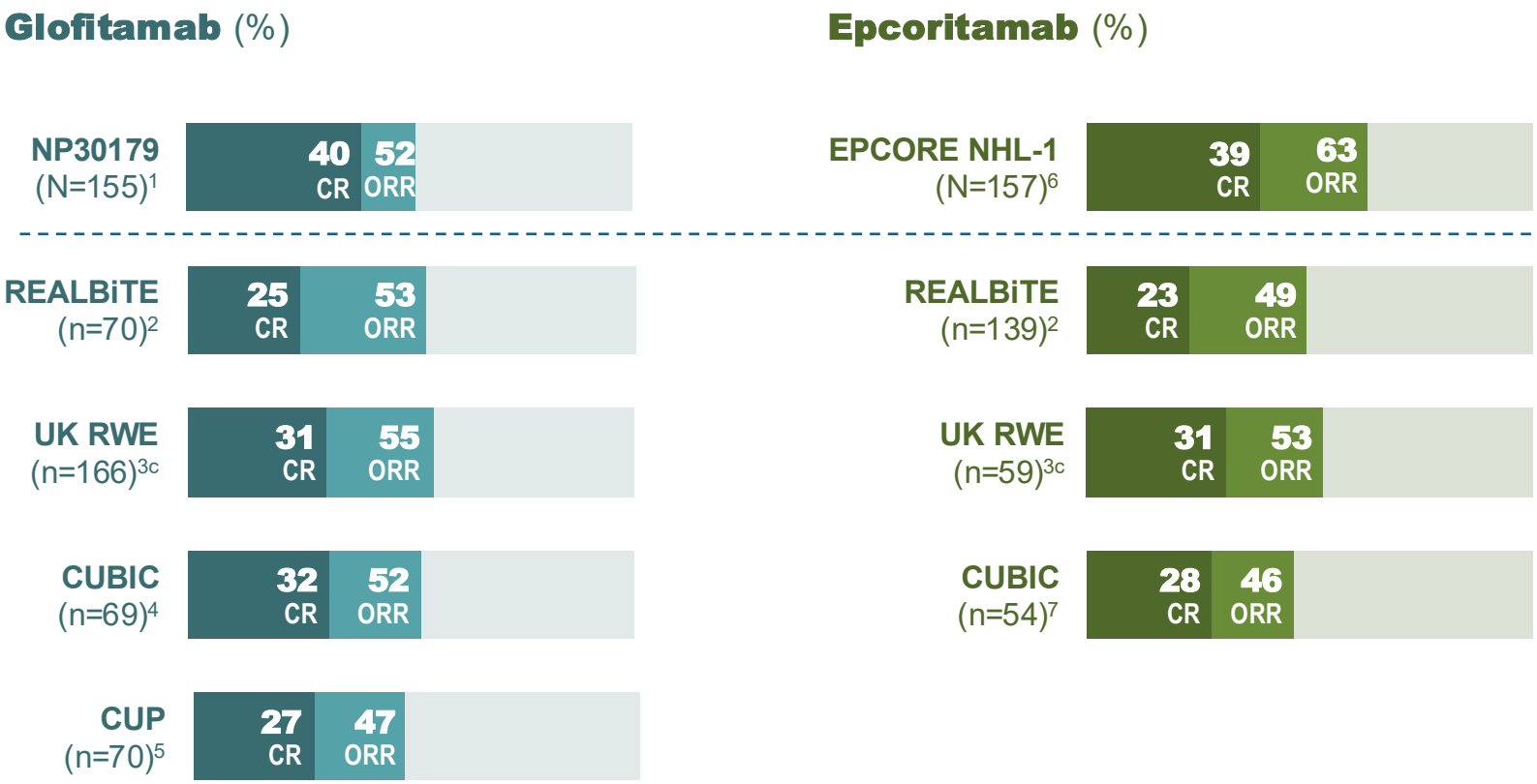
- [a]One patient was enrolled in error (was not screened) and did not receive study treatment. [b]Inpatient infusion occurs once every 7 days in Cycle 1. [c]Combined treatment group including patients who had received either corticosteroid or dexamethasone pretreatment.
- 3L, third-line; AE: adverse event; mFU: median follow-up; PD: progressive disease; R/R LBCL: relapsed/refractory large B-cell lymphoma; SUD, step-up dosing.
- 1. Dickinson MJ, *et al. N Engl J Med.* 2022; 387:2220–2231 (incl. suppl. appendix).

Dati RW in 3L+
(Epcoritamab – Glofitamab)

How do the real-world BsAbs effectiveness compare vs clinical trials?

BsAbs trials + RW 3L+

- **NP30179 mFU: 32 months**[a]
- Phase 2 trial of **glofitamab** monotherapy (N=155)[1,b]
- **REALBiTE RWE mFU: 5 months**
- Retrospective multicentre study of **epcoritamab** (n=139) and **glofitamab** (n=70)[2]
- **UK RWE mFU: 9.9 months**
- Retrospective analysis of **glofitamab** (n=217) and **epcoritamab** (n=113); (N=330)[3]
- **CUBIC mFU: 5.6 months**
- Retrospective analysis of **glofitamab** (N=69)[4]
- **CUP Germany, Austria, Switzerland mFU: 5 months**
- Retrospective analysis of **glofitamab** (N=70)[5]
- **EPCORE NHL-1 mFU: 20 months**[a]
- Phase 1/2 trial of **epcoritamab** (N=157)[6]
- **CUBIC mFU 12.9 months**
- Retrospective analysis of **epcoritamab** (N=54)[7]



- **With a broader patient population, real world data suggests lower CR rates with glofitamab and epcoritamab in R/R LBCL compared with clinical trials**

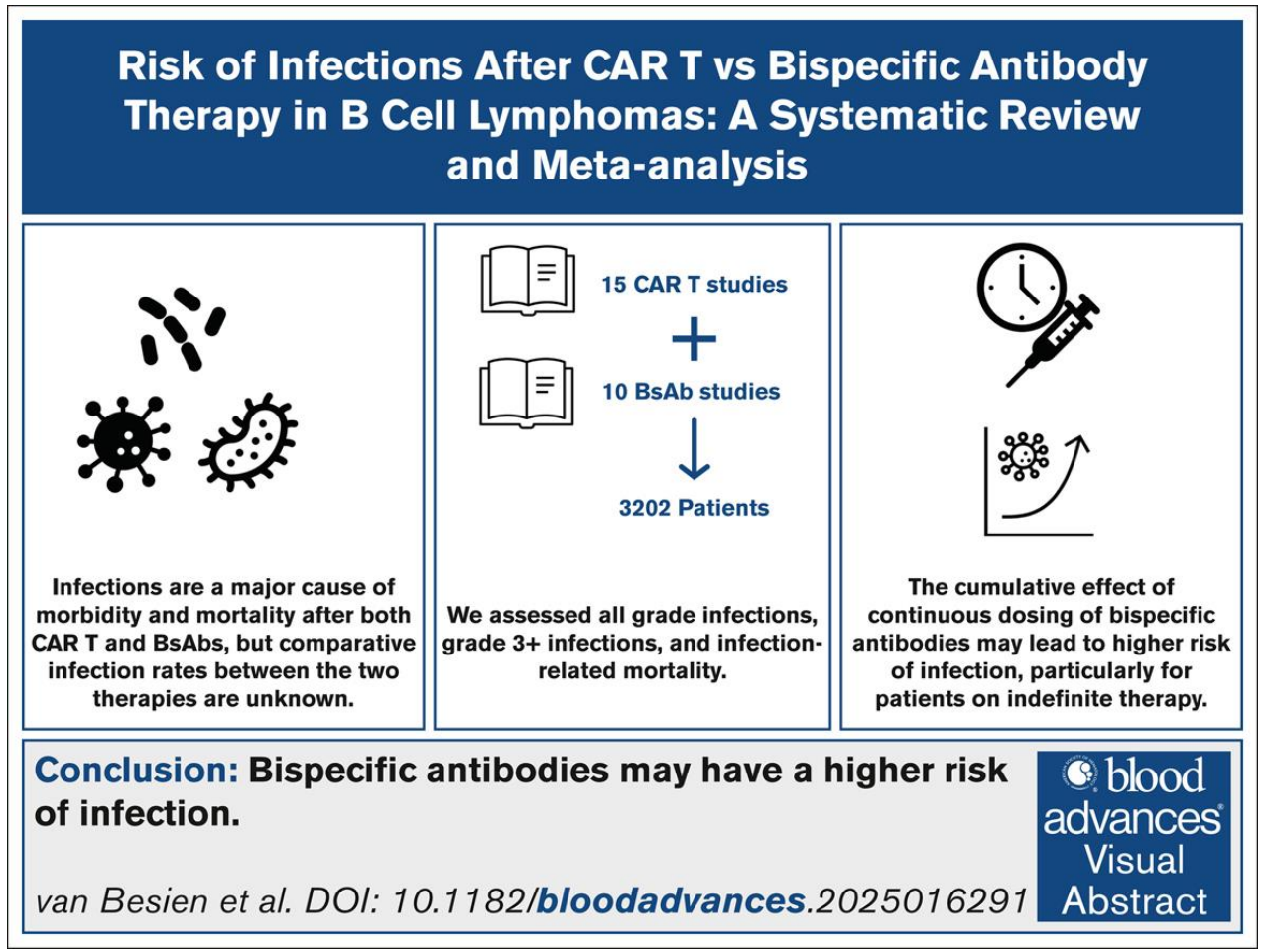
Response cannot be directly compared across clinical trials due to differences in study design and patient population.
[a]Dose expansion cohort. [b]One patient was enrolled in error (was not screened) and did not receive study treatment.
[c]≥2 cycles of glofitamab or epcoritamab.
2L: ≥ second-line; 3L: third-line; BsAb: bispecific antibody; CR: complete response; CUP: compassionate use patient programme; mFU: median follow-up; ORR: overall response rate; R-GemOx: rituximab-gemcitabine-oxaliplatin; R/R LBCL: relapsed/refractory large B-cell lymphoma.
1. Hutchings M, *et al.* ASH 2023; (Abstract 433, oral); 2. Brooks TR, *et al.* ASH 2024; (Abstract 1111); 3. Haynes E, *et al.* ICML 2025; (Abstract 1326, poster); 4. Shouse G, *et al.* ICML 2025; (Abstract 1671); 5. Shumilov E, *et al. Blood Adv.* 2025; 9:3885–3877; 6. Karimi Y, *et al.* ASCO 2023; (Abstract 7525, poster); 7. Bock AM, *et al.* ICML 2025; (Abstract 1667).

Comparative infection risk in CAR T vs bispecific antibodies in B-cell lymphoma: a systematic review and meta-analysis

Blood Adv (2025) 9 (23): 6063–6075.

Herman van Besien,[1,*] Neela Easwar,[1,*] Michelle Demetres,[2] Michelle Pasciolla,[3] Tsiporah Shore,[1] John Leonard,[1] Juliet Barker,[1] Peter Martin,[1] and Samuel Yamshon[1]

[1]Division of Hematology/Oncology, Department of Medicine, Weill Cornell Medicine, Cornell University, New York, NY; [2]Samuel J. Wood Library & C.V. Starr Biomedical Information Center, New York, NY; and [3]Department of Pharmacy, New York Presbyterian Hospital/Weill Cornell Medical Center, New York, NY



Key Points

- A meta-analysis of trials of approved BsAbs and CAR T in B-cell lymphomas was performed to assess infection risk.
- Standardizing infection rates per patient-month reveals a significantly greater infection risk for BsAbs, particularly grade 3+ infections.

DLBCL — Quando CAR-T, Quando Bispecifici: Guida Clinica

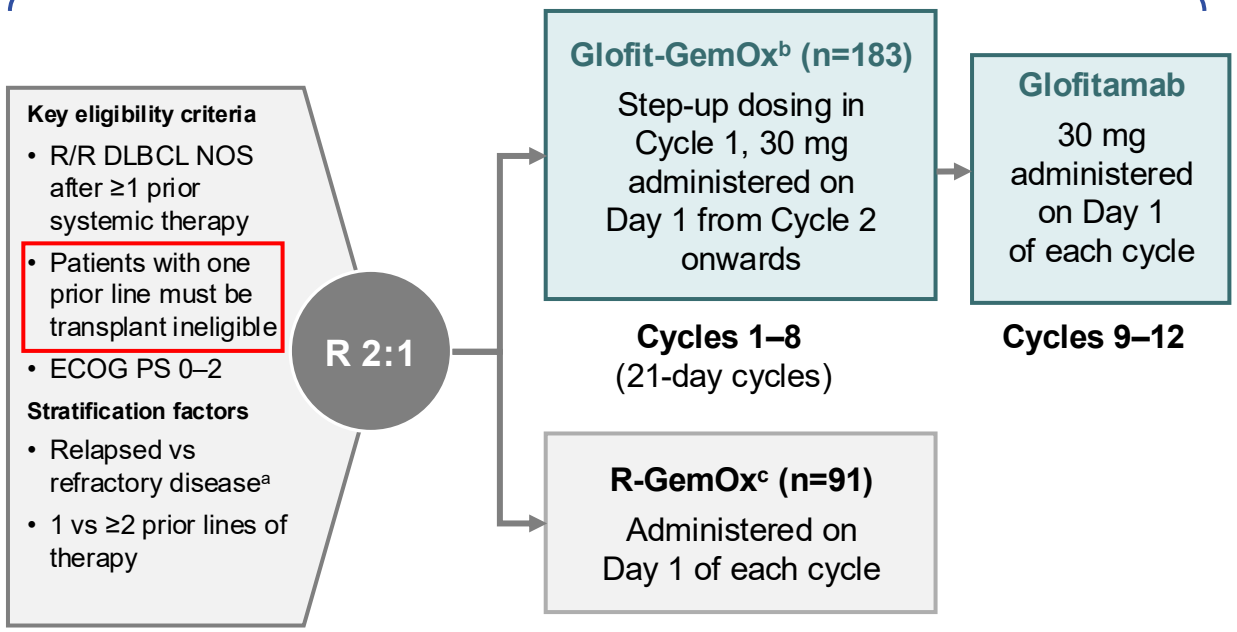
Scenario / Paziente	→ CAR-T	→ Bispecifici	Nota
Fit, ≥2L, centro JACIE, malattia stabile	✓ **PRIMA SCELTA** **axi-cel o liso-cel**	Alternativa se non eligibile	CR+OS superiore. Plateau documentato. Bridging accettabile.
High-risk early relapse (< 12m da 1L) o refrattario a R-CHOP	✓ **PREFERITO** **liso-cel/axi-cel in 2L**	Solo se non eleggibile CAR-T	TRANSFORM: EFS 1yr 44% vs 24% SoC. liso-cel approvato in 2L.
Malattia rapidly progressive non permette bridging 4-8 sett.	Non praticabile (lead-time troppo lungo)	✓ **PRIMA SCELTA** **Risposta rapida C1-2**	Epcoritamab/glofitamab: risposta in 4-6 settimane. Ponte verso CAR-T.
Anziano ≥70aa o comorbidità (cardiaca, neurologica, cognitiva)	ICANS 10-32% rischio inaccettabile	✓ **PRIMA SCELTA** **ICAN <2%, ambulat.**	Profilo tossicità favorevole. No requisito caregiver. Setting spoke.
PS ECOG ≥2 o fragilità non candidabile a ricovero	Non eleggibile standard	✓ **PRIMA SCELTA**	Trial registrativi bispec includono PS2. Step-up ambulatoriale.
≥3L post-2 linee compreso CAR-T failure	Già eseguito o non ripetibile	✓ **PRIMA SCELTA** **ORR ~30-40%**	Nessuna cross-resistenza completa. Attività preservata post-CD19 CAR-T
Bridging verso CAR-T durante attesa manifattura	In attesa	✓ **OPZIONE** **come bridge**	Dati rassicuranti su CD19 downregulation (<5% impatto clinico).
Double-hit/triple-hit lymphoma (MYC + BCL2/BCL6)	✓ **PREFERITO** **CR rate documentato**	Attivo ma dati limitati in DHL	Meta-regressione Kim 2024: vantaggio CAR-T persiste in DHL.
No accesso a centro JACIE o in area geograficamente remota	Non disponibile praticamente	✓ **UNICA OPZIONE** **praticabile**	Bispec erogabili in centri spoke. Riduzione gap di accesso.

NCCN v2.2024: axi-cel/liso-cel raccomandati in 2L DLBCL HR; epcoritamab/glofitamab in ≥3L · No head-to-head RCT disponibile

STARGLO trial in 2L+
e sottopopolazioni

STARGLO: Glofitamab plus gemcitabine and oxaliplatin (Glofit-GemOx) in patients with R/R DLBCL

Study design



Baseline patient characteristics

Characteristic, n (%) unless otherwise stated		R-GemOx n=91	Glofit-GemOx n=183
Median age (range)		69 (20–84)	68 (22–88)
Age ≥65 years		57 (62.6)	116 (63.4)
Race	Asian	51 (56)	86 (47.0)
	White	33 (36.3)	82 (44.8)
	Black or African American	1 (1.1)	2 (1.1)
	Unknown	6 (6.6)	13 (7.1)
Number of prior lines of therapy: 1 / ≥2		57 (62.6) / 34 (37.4)	115 (62.8) / 68 (37.2)
R/R status to last therapy: relapsed / refractory		37 (40.7) / 54 (59.3)	71 (38.8) / 112 (61.2)
Primary refractory		47 (51.6)	106 (57.9)
ECOG PS: 0 or 1 / 2		(n=88) 80 (90.9) / 8 (9.1)	(n=180) 160 (88.9) / 20 (11.1)
Bulky disease (≥10 cm)		(n=90) 14 (15.6)	(n=183) 23 (12.6)
Prior CAR T-cell therapy		8 (8.8)	14 (7.7)

Some high-risk patients, such as those with HGBCL, DH and TH LBCL, were excluded from the study
PRIMARY REFRACTORY disease was defined as disease that did not respond to, or that progressed within 6 months after completing therapy

- [a]Relapsed disease: recurrence following a response that lasted ≥6 months after completion of the last line of therapy; refractory disease: disease that did not respond to, or that progressed <6 months after completion of the last line of therapy. [b]Gemcitabine 1000 mg/m² and oxaliplatin 100 mg/m². In Cycle 1, obinutuzumab pre-treatment was administered on Day 1, GemOx on Day 2, followed by Glofit 2.5 mg on Day 8 and Glofit 10 mg on Day 15. In Cycles 2-8, Glofit 30 mg and GemOx were administered on Day 1. [c]Rituximab 375 mg/m².

Abramson J, *et al.* ASCO 2025 (Abstract 7015; poster presentation)

Estratto criteri di inclusione STARGLO trial

- Patients who had failed only one prior line of therapy and were not a candidate for high-dose chemotherapy followed by autologous stem cell transplant by meeting at least one of the following criteria:
  - Left ventricular ejection fraction ≤40%
  - Creatinine clearance or glomerular filtration rate ≤45 mL/min
  - Eastern Cooperative Oncology Group performance status of ≥2
  - Age ≥70 years
  - Patient refused high-dose chemotherapy and/or transplant
  - Patient had insufficient response to pre-transplant chemotherapy to be able to proceed to transplant
  - Other comorbidities or criteria that precluded the use of transplant based on local practice standards or in the investigator's opinion

Supplement to: Abramson JS, Ku M, Hertzberg M, et al. Glofitamab plus gemcitabine and oxaliplatin (GemOx) versus rituximab-GemOx for relapsed or refractory diffuse large B-cell lymphoma (STARGLO): a global phase 3, randomised, open-label trial. *Lancet* 2024; **404:** 1940–54.

STARGLO: Glofitamab plus gemcitabine and oxaliplatin (Glofit-GemOx) in patients with R/R DLBCL

	Non-Asian Region N=143	Asian Region N=131
Age		
Median Age, y (range)	**71 (20, 88)**	**62 (22, 82)**
<65y, n (%)	**30 (21)**	**72 (55)**
≥65 to <75y, n (%)	66 (46)	41 (31)
≥75y, n (%)	47 (33)	18 (14)
Race, n (%)		
Asian	**6 (4)**	**131 (100)**
Black	3 (2)	0
White	**115 (80)**	**0**
Unknown	19 (13)	0
Ethnicity, n (%)		
Hispanic	13 (9)	3 (2)

Reason for Transplant Ineligibility	Non-Asian Region N=143 n (%)	Asian Region N=131 n (%)
Age	**86 (60%)**	**30 (23%)**
Performance Status	2 (1%)	0
Comorbidity	11 (8%)	0
Insufficient response to salvage	**19 (13%)**	**8 (6%)**
Failed prior transplant	**9 (6%)**	**3 (2%)**
Lack of access to transplant center	0	2 (2%)
Patient refused transplant	**10 (7%)**	**85 (65%)**
Other*	4 (3%)	2 (2%)
None listed	2 (1%)	1 (0.8%)

*other: non-chemosensitive disease, too chemo refractory, risk of many adverse events, expected insufficient response; not ≥2 prior lines of treatment, insufficient response to pre-transplant chemotherapy

Available from: https://www.fda.gov/media/186557/download

STARGLO: Glofitamab plus gemcitabine and oxaliplatin (Glofit-GemOx) in patients with R/R DLBCL

Prior Therapy Characteristics: Different Prior Treatment Exposures

Prior Therapy	Non-Asian Region N=143 n (%)	Asian Region N=131 n (%)
Median lines (range)	1 (1-5)	1 (1-5)
Component of Prior therapy		
Anthracycline	139 (97)	129 (98)
CD20 (ritux, obinu) or taf [CD19]	142 (99)	128 (98)
Platinum	31 (22)	36 (27)
Lenalidomide	**5 (3)**	**22 (13)**
Polatuzumab (pola-BR)	8 (6)	2 (2)
Radiotherapy	33 (23)	15 (11)
CART	**19 (13)**	**2 (2)**
ASCT	7 (5)	4 (3)
Other (PD1i, BTKi, Selinexor, etc)	**3 (2)**	**19 (15)**

- **Asian-enrolled** patients: higher % exposed to lenalidomide-containing regimens and "other therapy"
- **Non-Asian enrolled** patients: higher % CAR-T

www.fda.gov

Abbreviations: Ritux: Rituximab; Obinu: Obinutuzumab; Taf: Tafasitamab; Pola-BR: polatuzumab+bendamustine+ritixumab; ASCT: autologous or allogeneic stem cell transplantation; BTKi: Bruton Tyrosine Kinase inhibitor; PD1i: Programmed-cell Death inhibitor

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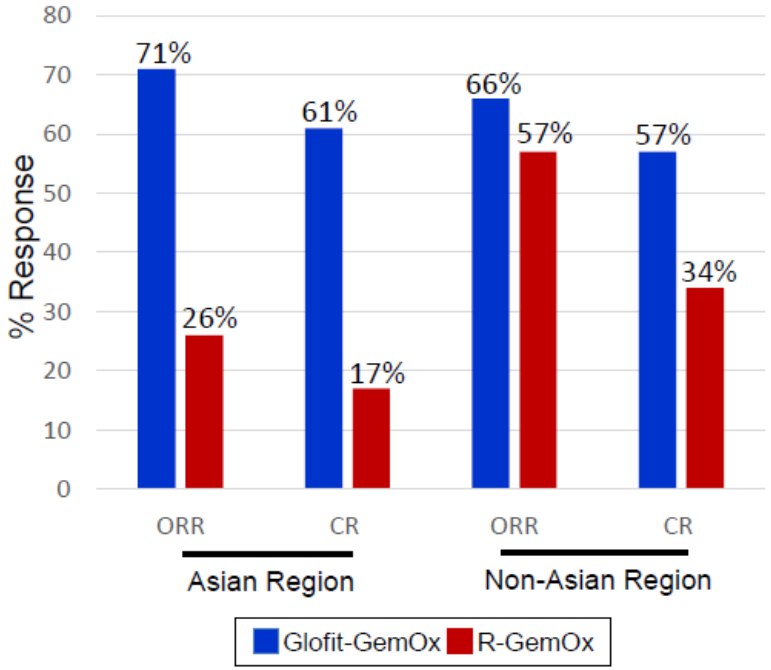
STARGLO: Glofitamab plus gemcitabine and oxaliplatin (Glofit-GemOx) in patients with R/R DLBCL

Differential ORR/CR Rates Across Regions



	Asian Region N=143		Non-Asian Region N=131	
	Glofit-GemOx N=84	R-GemOx N=47	Glofit-GemOx N=99	R-GemOx N=44
CR rate[a], n (%)	51 (61)	8 (17)	56 (57)	15 (34)
[95% CI]	[49,71]	[8,31]	[46,67]	[20,50]
ORR, n (%)	60 (71)	12 (26)	65 (66)	25 (57)
[95% CI]	[61,81]	[14,40]	[55,75]	[41,72]

[a]Key secondary endpoint

Source: FDA Analysis; Data cutoff: Feb 2024

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Abbreviations: ORR: Overall response rate; CR: Complete response; CI: Confidence interval

Available from: https://www.fda.gov/media/186557/download

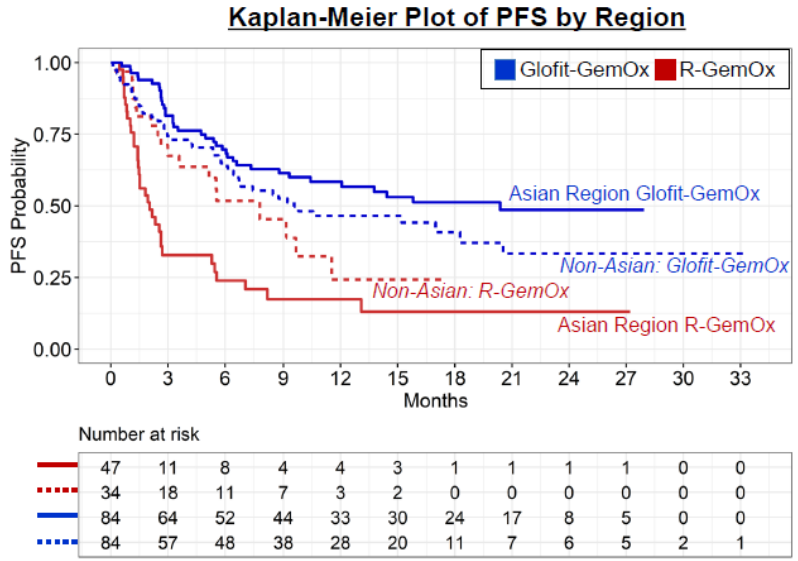
STARGLO: Glofitamab plus gemcitabine and oxaliplatin (Glofit-GemOx) in patients with R/R DLBCL

Differential PFS Effects Across Regions

PFS	Non-Asian Region	
	Glofit-GemOx N=99	R-GemOx N=44
Median PFS	9.2 mo	7.8 mo
HR (95%CI)	0.81 (0.48, 1.35)	

PFS	Asian Region	
	Glofit-GemOx N=84	R-GemOx N=47
Median PFS	20.4 mo	2.0 mo
HR (95%CI)	0.25 (0.15, 0.41)	

Source: FDA analysis; Data Cutoff: Feb 2024



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Abbreviations: PFS: Progression-free survival; mo: Months; HR: Hazard ratio; CI: Confidence interval

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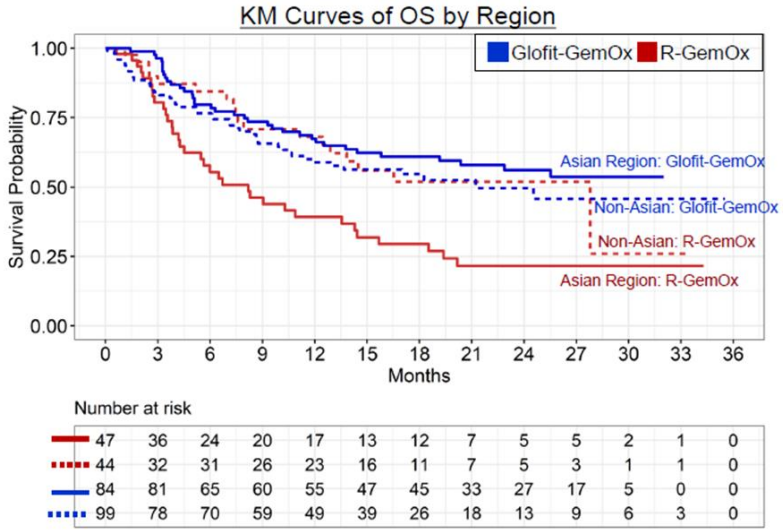
Differential OS Effects Across Regions



OS	Non-Asian Region	
	Glofit-GemOx N=99	R-GemOx N=44
Median OS	21.2 mo	27.8 mo
HR (95%CI)	1.06 (0.61, 1.84)	

U.S. HR 2.62 (0.56, 12.34)

OS	Asian Region	
	Glofit-GemOx N=84	R-GemOx N=47
Median OS	NE	8.2 mo
HR (95%CI)	0.39 (0.25, 0.63)	

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Abbreviations: Glofit-GemOx: Glofitamab, Gemcitabine and Oxaliplatin; R-GemOx: Rituximab, Gemcitabine and Oxaliplatin; HR: Hazard Ratio; CI: Confidence Interval; NE: Not estimable

Source: FDA analysis
Data Cut-off: 2024

7

Available from: https://www.fda.gov/media/186557/download

STARGLO — perché i pazienti asiatici vanno meglio?

Vantaggio asiatici Svantaggio non asiatici Dato neutro / HR

Variabile	Asia (48%)	Non-Asia (52%)	Impatto
CARATTERISTICHE BASELINE			
Età mediana	62 anni	71 anni	Più fit
Motivo ASCT-ineleggibilità: rifiuto paziente	65%	7%	Selezione più fit
Malattia primariamente refrattaria nel braccio sperimentale	Bilanciata	Squilibrata (↑ nel braccio glofit)	Confounding
EFFICACIA (HR OS GLOFITAMAB VS RITUXIMAB)			
Asia + Australia ("resto del mondo")	HR 0.41 (95% CI 0.27–0.64)		Netto beneficio
Europa	HR 1.09 (95% CI 0.54–2.18)		Nessun beneficio
Nord America	HR 2.62 (95% CI 0.56–12.34)		Trend sfavorevole
PFS HR Asia vs non-Asia	0.25	0.81	p = 0.0006
ΔCR rate (glofit vs rit)	+44%	+22%	p = 0.06
IPOTESI ESPLICATIVE			
Braccio di controllo più debole in Asia	Meno accesso a terapie salvage post-progressione	Più opzioni post-progressione disponibili	Confounding OS
Razionale farmacologico	Nessuna differenza PK identificata da Genentech		Non spiegato

I punti chiave sono tre: i pazienti asiatici erano più giovani e più fit (molti erano ASCT-ineleggibili solo perché *rifiutavano* il trapianto, non per comorbidità), il braccio di controllo con rituximab + GemOx era intrinsecamente più debole in Asia per scarsità di terapie salvage alternative, e c'era uno squilibrio prognostico nel braccio glofitamab americano (più malattia primariamente refrattaria). Nessuna spiegazione farmacocinetica è stata identificata.

FDA ODAC votes 8-1 glofitamab trial does not apply to US patients

BY LEAH SHERWOOD MAY 20, 2025 0 COMMENTS 1 MINUTE READ 12 MONTHS AGO

A federal advisory panel voted 8-1 Tuesday that results from the global STARGLO trial, which was intended as the confirmatory trial for full approval of glofitamab-gxbm, were not applicable to the US patient population.

The central concern was the regional variation in the trial's outcomes. While glofitamab showed a significant overall survival benefit in patients with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), nearly half of the 274 participants were enrolled in Asia, where the benefit was most pronounced. In contrast, only 9% were from the US and high hazard ratios in that subgroup raised concerns.

"Are the STARGLO population and trial results applicable to the proposed US patient population?" was the panel's voting question.

"While I'm a strong proponent of drug development, strong proponent of access to therapies, the question that was asked of me is, are the results from the trial applicable to the US general population? I'm not convinced with the data that is provided by the sponsor that it is applicable to the general population," said Ajay Nooka, MD, MPH who voted no.

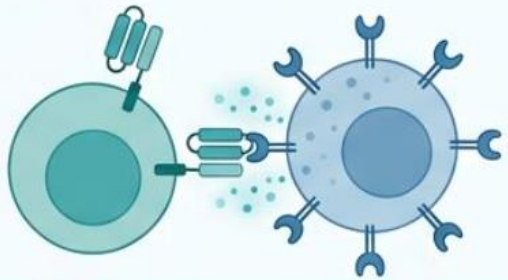
The sole yes came from patient representative Paul Majkowski, Esq, who provided the rationale for his "yes" vote.

"While it is on the sponsor to meet the burden of proof, maybe I was willing to relax that burden of proof for the considerations of the patient perspective," he said.

Efficacia nei Linfomi B Indolenti (FL, MZL): Confronto tra CAR-T e Anticorpi Bispecifici

"Dati principali su efficacia, follow-up, approvazioni e schemi terapeutici."

CAR-T (axi-cel in FL ≥3L)



~92% ORR

~74% CR rate

~57% PFS a 24m

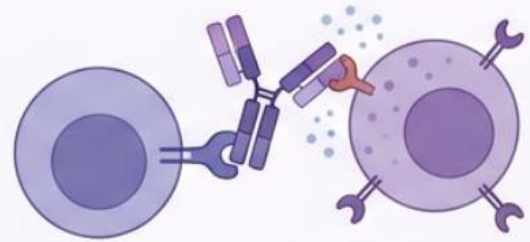
Risposta stabile: **3–4 anni**

ZUMA-5

FDA/EMA approvato FL ≥3L

Follow-up lungo: Risposte stabili a 3–4 anni.

Bispecifici (mosunetuzumab, epcoritamab in FL ≥2L)



~80% ORR

~60% CR rate

~40% PFS a 24m

GO29781 (mosune)

EPCORE FL

FDA approvato (mosune FL ≥2L)

Mosunetuzumab: 8 cicli fissi (schema fisso)

Dati ricavati da studi registrativi; confronti indiretti. Immagine esclusivamente illustrativa.

Efficacia Comparata nel FL r/r — Dati dei Trial Chiave

Dati aggiornati 2024-2025 · Confronto indiretto (nessun RCT head-to-head disponibile)

▶ CAR-T cells — anti-CD19

Trial / Agente	Linee	N	ORR	CR	PFS med.	DOR med.	FU med.	Schema / Setting
Axi-cel ZUMA-5	≥3L	104	**92%**	**74%**	NR (≥38m)	NR	38m	Infusione singola IV · ricovero req.
Tisa-cel ELARA	≥3L	97	86%	69%	NR	NR	24m	Infusione singola IV · ricovero req.

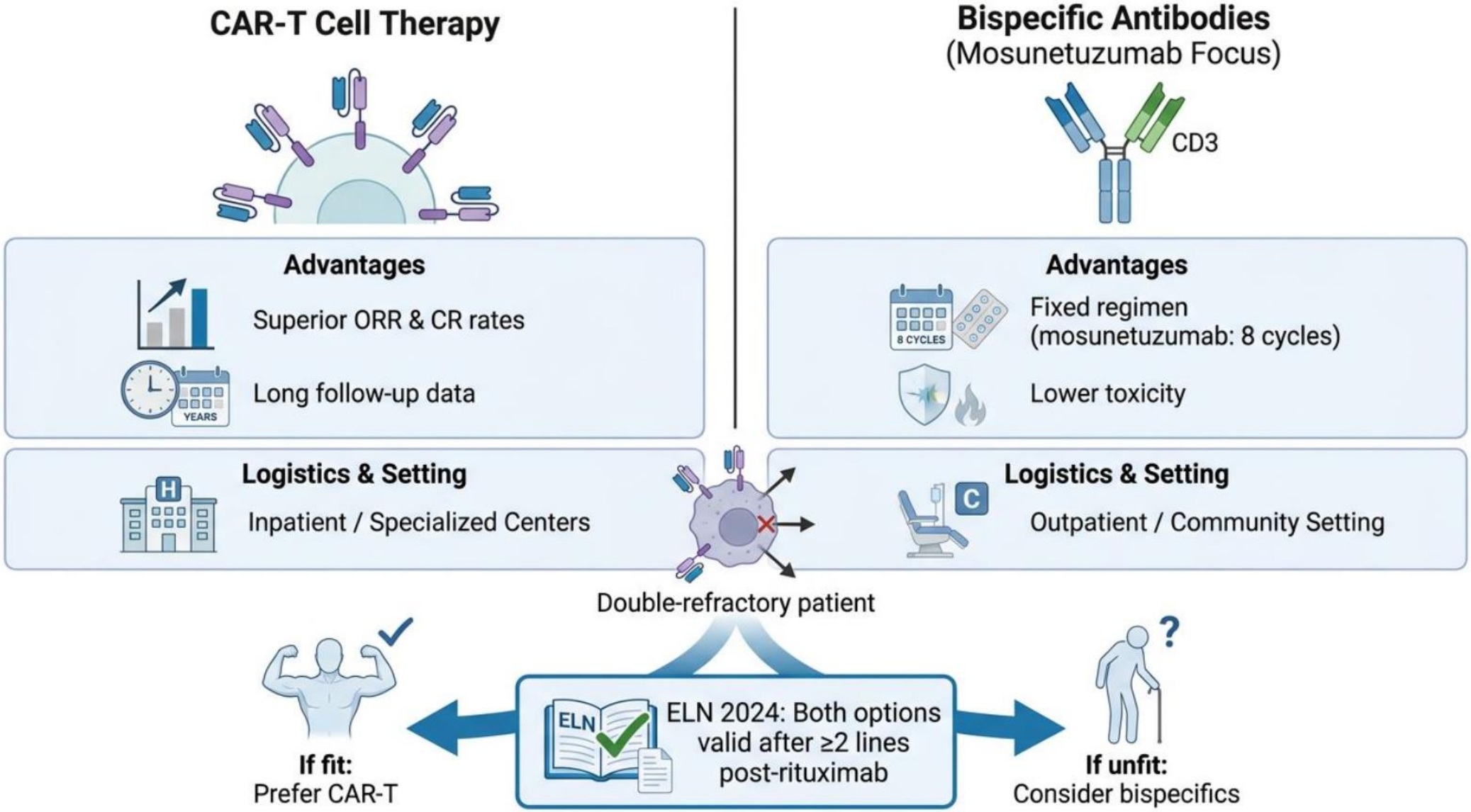
▶ Anticorpi Bispecifici — CD20×CD3

Trial / Agente	Linee	N	ORR	CR	PFS med.	DOR med.	FU med.	Schema / Setting
Mosunetuzumab GO29781	≥2L	90	78%	60%	24.0m	**46.4m**	49m	FISSO 8 cicli IV · ambulatoriale · recovery B-cell a 18m
Epcoritamab EPCORE FL	≥2L	128	82%	63%	17.9m	22.8m	17m	Continuo fino a PD · sottocutaneo · ambulatoriale

▶ PI3K Inibitori — status regolatorio 2025

Trial / Agente	Linee	N	ORR	CR	PFS med.	DOR med.	FU med.	Schema / Setting
Copanlisib CHRONOS-1	≥2L	104	59%	14%	11.2m	12.7m	—	IV day-hosp. 3/4 sett. · unico PI3Ki rimasto (USA)
Idelalisib / Duvelisib / Umbralisib	—	—	—	—	—	—	—	⚠ **RITIRATI — morti da infezioni e colite autoimmune fatale**

NR=Not Reached · FU=follow-up · PD=progressione · DOR=Duration of Response · Fonte: trial registrativi + ASH 2024 update (mosunetuzumab 4yr FU)


CAR-T Cell Therapy
Bispecific Antibodies
(Mosunetuzumab Focus)
CD3
Advantages
Superior ORR & CR rates
Long follow-up data
YEARS
Advantages
8 CYCLES
Fixed regimen
(mosunetuzumab: 8 cycles)
Lower toxicity
Logistics & Setting
Inpatient / Specialized Centers
Logistics & Setting
Outpatient / Community Setting
Double-refractory patient
ELN
ELN 2024: Both options valid after ≥2 lines post-rituximab
If fit:
Prefer CAR-T
If unfit:
Consider bispecifics

ARTICLE OPEN

Systematic review and meta-analysis: CAR-T vs bispecific antibody as third or later-line therapy for follicular lymphoma

Lawrence Cheng Kiat Ng[1,2,6✉], Xiu Hue Lee[1,2,6], Yan Chin Tan[1,2], Kye Ling Wong[1,2], Johnny Chung Yue Chow[1], Victor Wei Teik Ling[3,4], Edwin Wei Sheng Thong[3,4], Esther Hian Li Chan[3,4], Wee Lee Chan[3,5], Miny Samuel[3,4,7] and Michelle Li Mei Poon[3,4,7]

There is currently no clear consensus on the standard of care for relapsed or refractory follicular lymphoma (FL) beyond third-line therapy, where both anti-CD19 CAR-T-cell therapy (CAR-T) and CD3×CD20 bispecific antibodies (BsAbs) have demonstrated efficacy. This study aimed to examine their efficacy and toxicity profiles. Relevant studies published between January 2010 and June 2025 were identified through major databases. Of 3960 records screened, 12 studies met the inclusion criteria—7 involving CAR-T and 5 involving BsAbs. The pooled overall response rate (ORR) and complete response rate (CRR) were 93% and 82% for CAR-T, compared with 82% and 67% for BsAbs ($p = 0.0002$ and $p = 0.005$, respectively). Among patients with POD24, the CRR was 75% for CAR-T and 69% for BsAbs ($p = 0.56$). This translated into improved progression-free survival (PFS) with CAR-T: 6-month, 1-year and 3-year PFS rates were 85%, 74% and 54%, respectively, compared with 74%, 62%, and 42% for BsAbs ($p = 0.006$, $p = 0.002$ and $p = 0.009$, respectively). A trend toward higher 3-year overall survival (OS) was observed with CAR-T (80%) versus BsAbs (73%) ($p = 0.48$). Grade ≥3 immune effector cell-associated neurotoxicity syndrome (ICANS) occurred more frequently with CAR-T (8% vs. 0%, $p = 0.04$), whereas grade ≥3 infections were numerically higher with BsAbs (17% vs. 9%, $p = 0.31$). One-year non-relapse mortality (NRM) was similar between groups at 3%. Overall, CAR-T demonstrated potentially higher efficacy in this non-comparative meta-analysis, while the two therapies exhibited noticeable differences in toxicity profiles.

The pooled overall response rate (ORR) and complete response rate (CRR) were 93% and 82% for CAR-T, compared with 82% and 67% for BsAbs (p = 0.0002 and p = 0.005, respectively).

Among patients with POD24, the CRR was 75% for CAR-T and 69% for BsAbs (p=0.56)

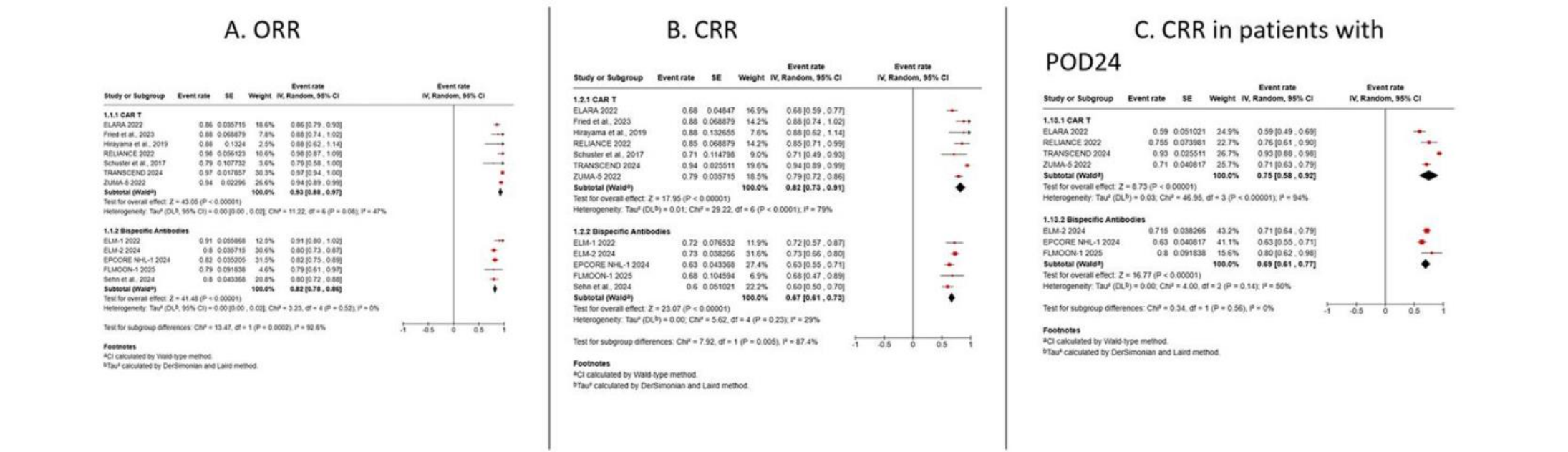


Fig. 2 Meta-analysis of response rate. A Overall response rate (ORR), **B** complete response rate (CRR), **C** CRR in patients with POD24.

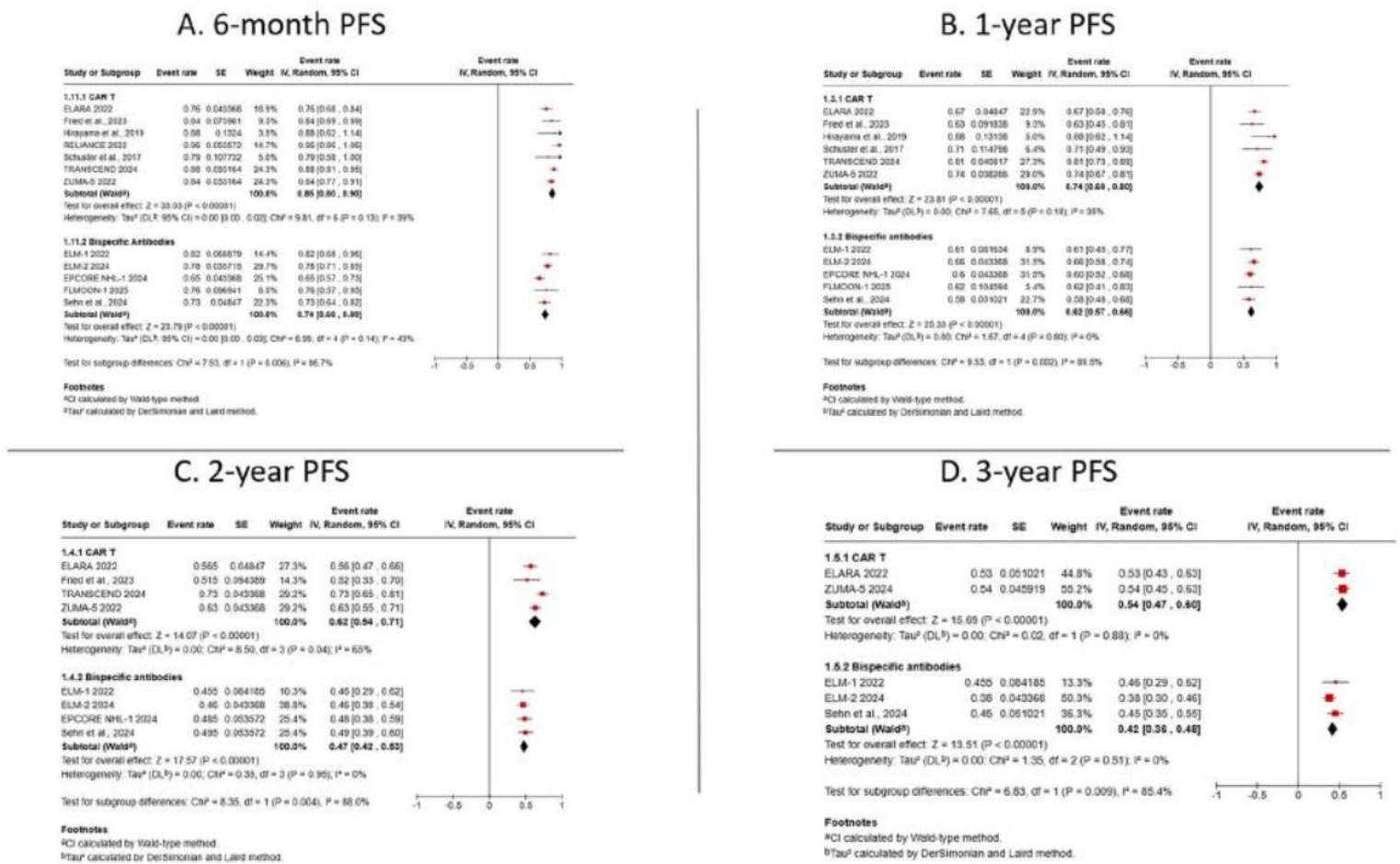


Fig. 3 Meta-analysis of progression-free survival (PFS). A 6-month PFS, **B** 1-year PFS, **C** 2-year PFS, **D** 3-year PFS.

improved progression-free survival (PFS) with CAR-T: 6-month, 1-year and 3-year PFS rates were 85%, 74% and 54%, respectively, compared with 74%, 62%, and 42% for BsAbs (p=0.006, p=0.002 and p=0.009, respectively).

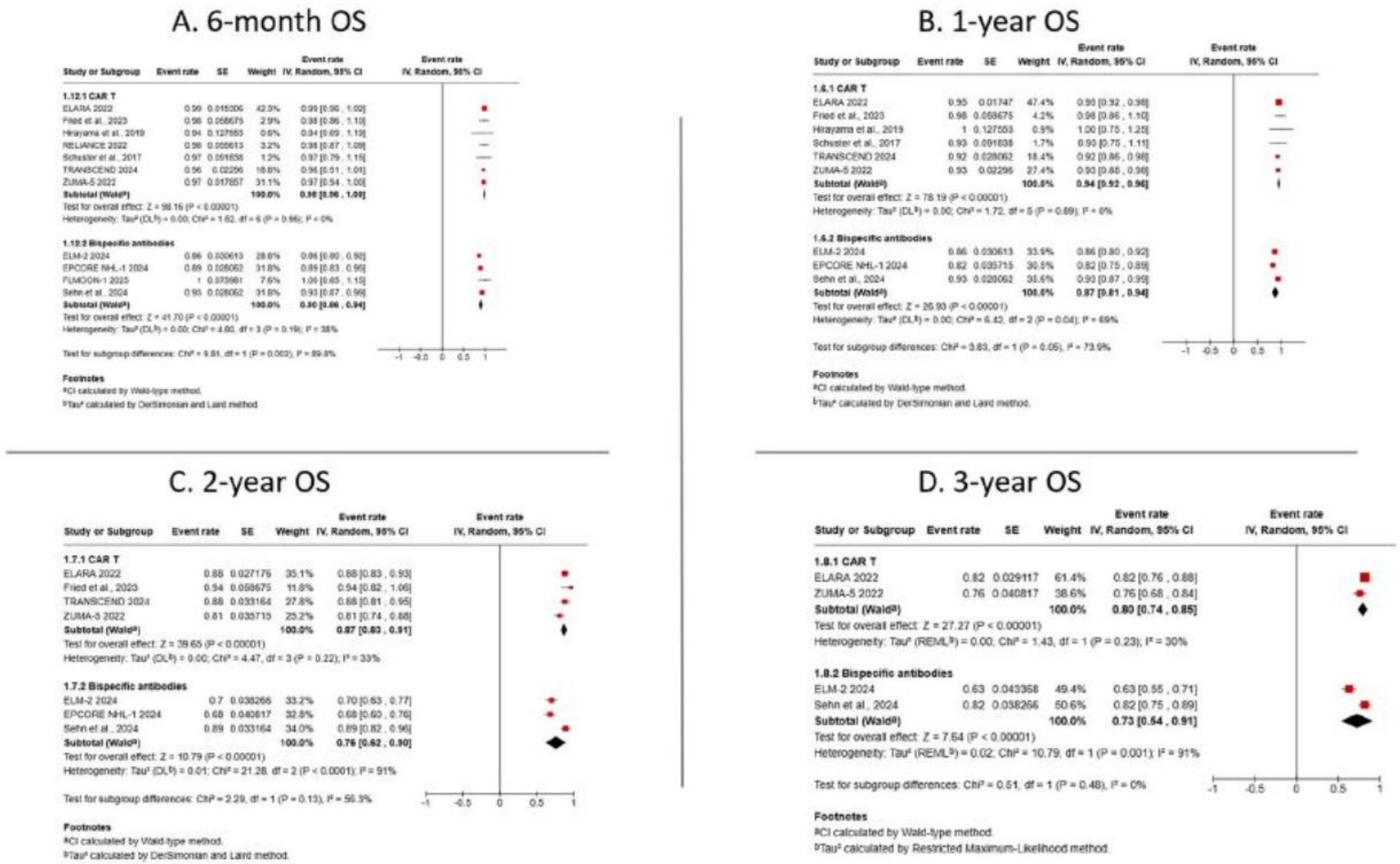


Fig. 4 **Meta-analysis of overall survival (OS). A** 6-month OS, **B** 1-year OS, **C** 2-year OS, **D** 3-year OS.

A trend toward higher 3-year overall survival (OS) was observed with CAR-T (80%) versus BsAbs (73%) (p=0.48)

CAR-T nel FL: il confronto indiretto

- 12 studi (7 CAR-T, 5 BsAb) in FL r/r, fornisce la migliore stima indiretta disponibile
- **ORR 93% e CRR 82% per CAR-T** vs **ORR 82% e CRR 67% per BsAb** (***p=0.0002 e p=0.005***)
- Nei pazienti con POD24, la **CRR era 75% per CAR-T** vs **69% per bispecifici** (p***=0.56 — non significativo***).
- La PFS a 6 mesi, 1 anno e 3 anni era rispettivamente **85%, 74%, 54% per CAR-T** vs **74%, 62%, 42% per bispecifici** (***p=0.006***).

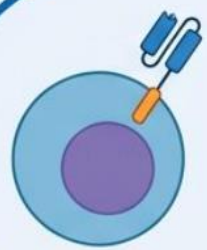
Il dato **sul POD24 è cruciale**: la differenza di CR rate scompare, il che suggerisce che nei pazienti ad alto rischio la scelta tra le due strategie sia molto più sfumata di quanto appaia guardando solo le coorti generali.

2025 Therapeutic Hierarchy in Relapsed/Refractory Follicular Lymphoma

Patient with r/r FL (2025)

Fit, JACIE center access

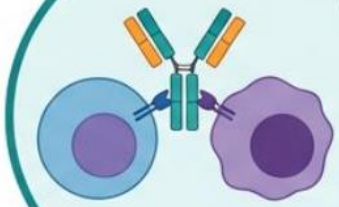
Elderly/Frail
OR urgent need
OR no JACIE access



Consider CAR-T

- Preferred if fit & JACIE access
- CR 82% vs 67% bispec (meta-analysis)
- Plateau PFS at 38 months (ZUMA-5)
- Curative potential
- Indication: ≥3L (axi-cel, tisa-cel), ≥2L POD24 (liso-cel)

Plateau PFS | **Potentially curative**



Consider Bispecific Antibodies

- Preferred in elderly/frail, urgent clinical need, or no JACIE
- Time-limited: mosunetuzumab (8 fixed cycles)
- Longest DOR: median 46.4m at 4yr (mosune, GO29781 FU)
- Indication: ≥2L (more permissive than CAR-T)

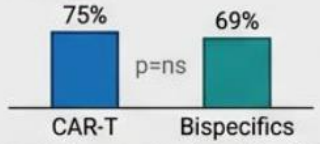
Fixed duration option | **Lower logistics/timing barrier**

PI3K inhibitors: nearly phased out

- Idelalisib, duvelisib, umbralisib withdrawn (toxicity)
- Copanlisib (FDA): ORR 59%, CR 14% — Last resort only

POD24 Subgroup: Subtlety in Choice

CR Rate: CAR-T 75% vs Bispecifics 69%
(p=ns, He et al. 2025 meta-analysis)



CR advantage disappears in POD24 — choice for this high-risk group is nuanced and individualized

FL r/r — Quando CAR-T, Quando Bispecifici: Guida Clinica

Scenario / Paziente	→ CAR-T	→ Bispecifici	Nota
FL ≥3L, fit, JACIE disponibile	✓ **PREFERITO** **axi-cel o tisa-cel**	Alternativa se non eleggibile	CR 82% CAR-T vs 67% bispec. Plateau PFS a 38m.
FL ≥2L, POD24 ad alto rischio	✓ **PREFERITO** **liso-cel (2L)**	Equivalente in POD24 (CR 75% vs 69%, p=ns)	CR non differisce significativamente in POD24 (meta-analisi).
HT (trasformazione istolocica) accertata o sospetta	✓ **PRIMA SCELTA** **potenziale curativo**	Solo se non eleggibile CAR-T	Curabilità nel DLBCL documentata. Dati bispec in HT assenti.
Anziano / comorbidità rischio ICANS elevato	ICANS 11-19% non accettabile	✓ **PRIMA SCELTA** **ICAN <1%, ambulat.**	Profilo tossicità nettamente favorevole. No caregiver 30gg.
Schema time-limited preferito dal paziente	**Sì — singola infusione**	✓ **MOSUNE** **8 cicli fissi IV**	Mosune: unico bispecifico a schema fisso. DOR 46.4m a 4yr FU.
Malattia indolente stabile, nessuna urgenza	✓ **PREFERITO** **efficacia superiore**	Valida alternativa se no JACIE	Decisione condivisa paziente-clinico su logistica vs efficacia.
Refrattario a PI3Ki (idelalisib, copanlisib, etc.)	Attivo ma dati limitati	✓ **PRIMA SCELTA** **ORR 88.9% post-PI3Ki**	Epco post-PI3Ki: sottopop. con risposta più elevata osservata.
Post-CAR-T failure	Già eseguito	✓ **PRIMA SCELTA** **nessuna cross-resistenza**	Mosune post-CAR-T: ORR 100%/CR 50% in piccola serie (n=4).
No accesso JACIE o area remota	Non disponibile praticamente	✓ **UNICA OPZIONE**	Bispec erogabili in spoke. Epco SC: minima infrastruttura.

Basato su Russler-Germain & Bartlett ASH 2024 · GELTAMO 2025 · meta-analisi He et al. Front Immunol 2025