

CORSO EDUCAZIONALE COMMISSIONE ANZIANI

XIII EDIZIONE

Giardini Naxos - Marriott Delta Hotels
17-18 aprile 2026



Debate: bispecifici verso CAR T nella terapia dei linfomi recidivati/refrattari
PRO CART

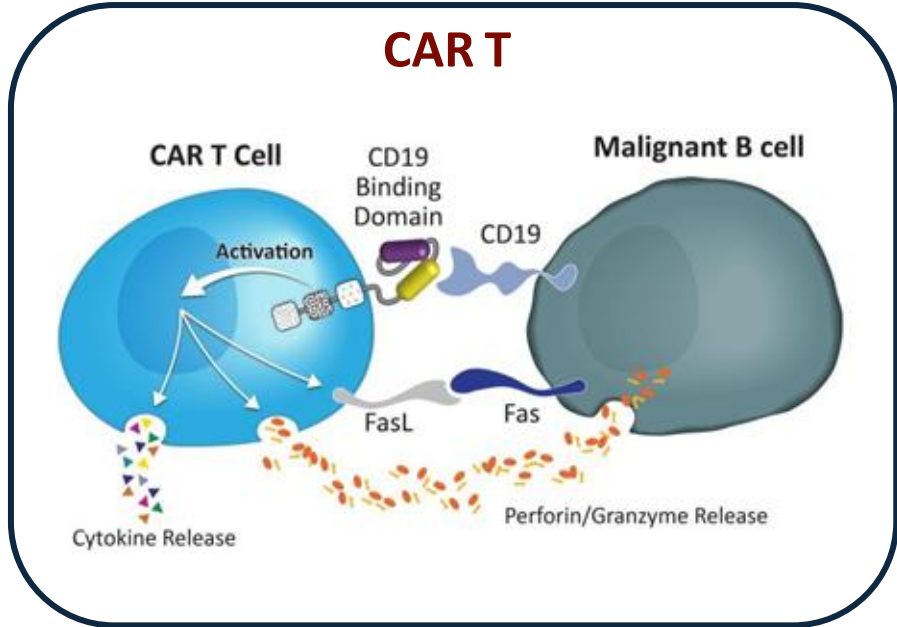
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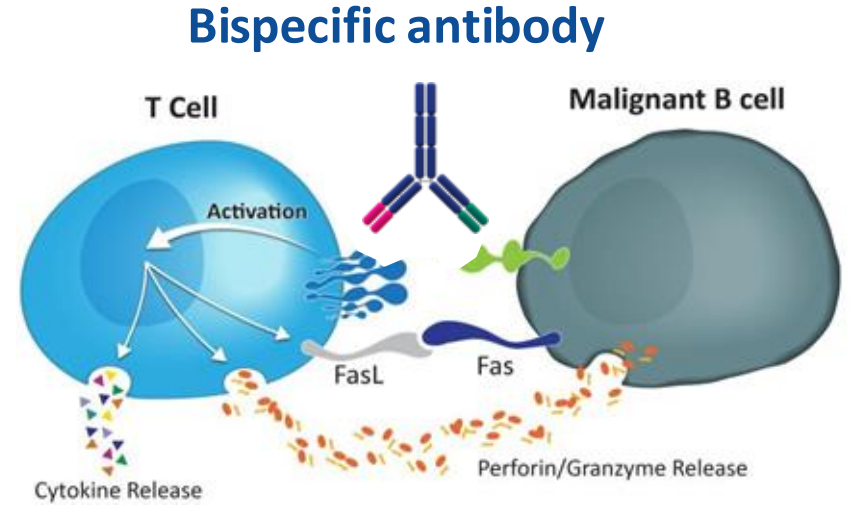
Disclosures of Alice Di Rocco

Company name	Research support	Employee	Consultant	Stockholder	Speaker's bureau	Advisory board	Other
AbbVie			X		X	X	
AstraZeneca					X	X	
Beigene					X		
Eli-Lilly					X		
Incyte			X		X		
Janssen			X		X		
Kite-Gilead					X	X	
Novartis			X		X	X	
BMS			X		X		
Roche			X		X	X	
Recordati-Rare disease					X		
Sobi					X		
Takeda					X	X	

T-cell redirection strategies are changing the scenario



- ### Similarities
- Both CAR Ts and bsAbs bring together T cells and B cells
 - Interaction cause activation of the T cell and release of cytokines, granzyme and perforin
 - Results in T-cell mediated killing of the tumour cell

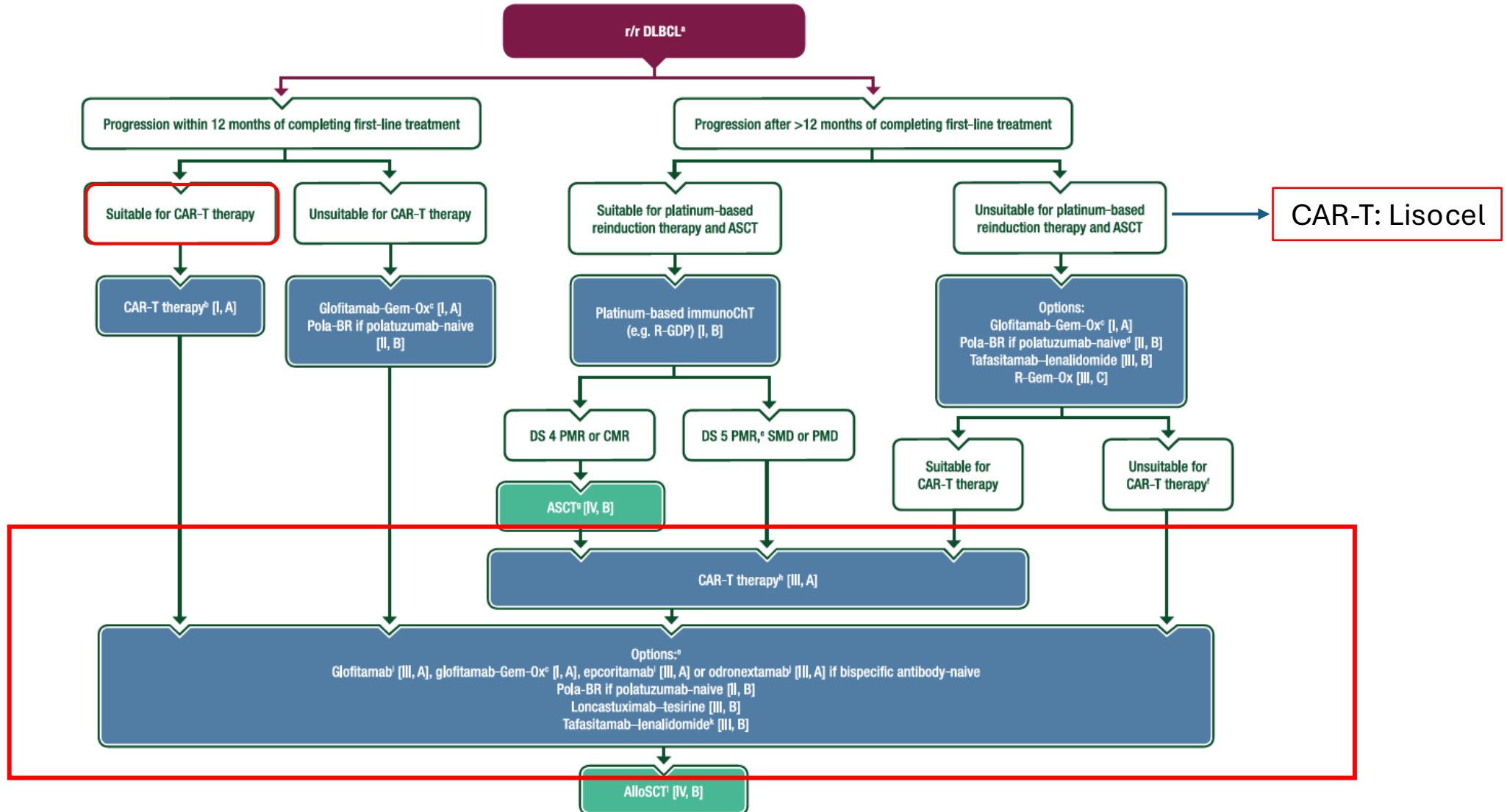


Differences

CAR T therapy modifies the extracellular antigen-binding domain on T cells	Binding	Bispecific antibodies induce effector T-cell binding to the tumour cell
CAR T therapies rely on ex vivo activated and expanded T cells	T cell	Bispecific antibodies use the patient's endogenous T cells
Yes	2nd signal	No (...not yet...)

bsAb, bispecific antibody.

CAR and Bispecifics should not be competing in most patients



Key points of discussion

- **Efficacy**

CRR

Survival

QoL

- **Toxicity**

CRS & ICANS

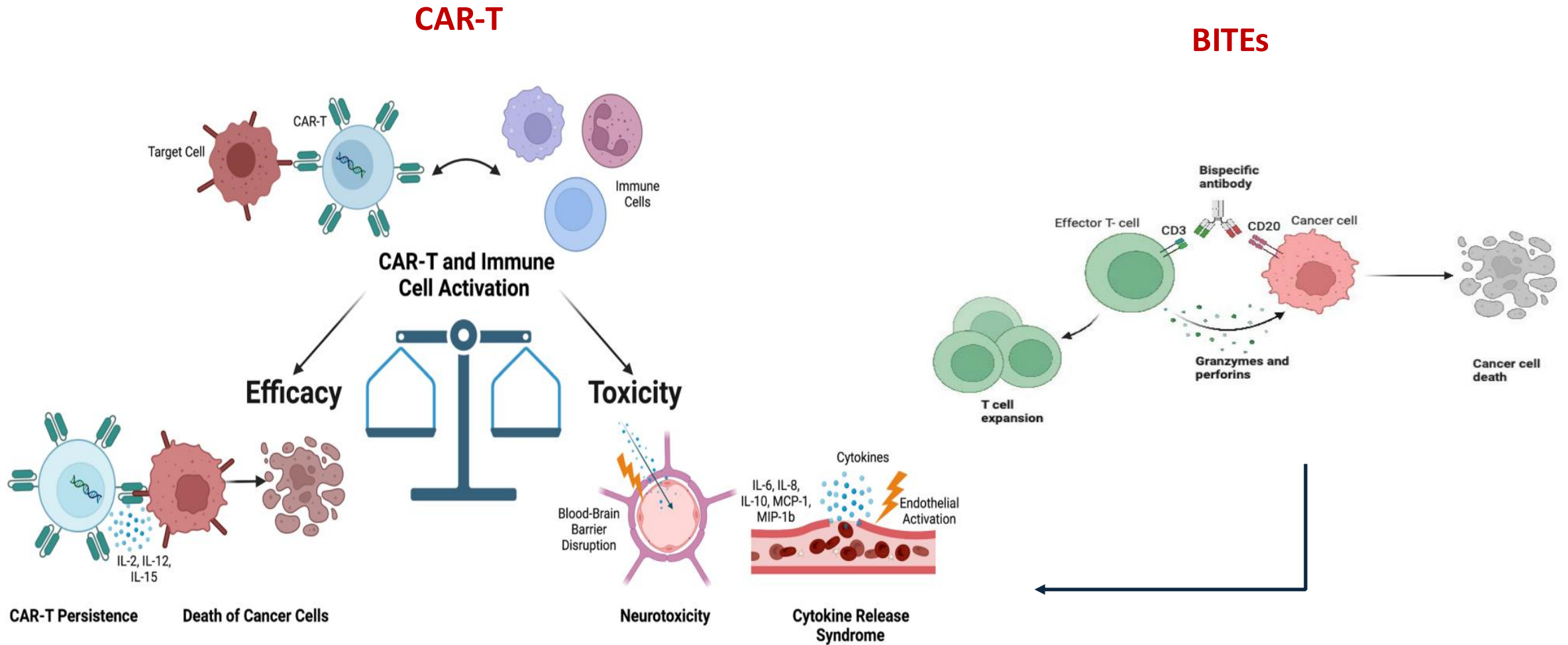
Infections!!!

- **Logistics**

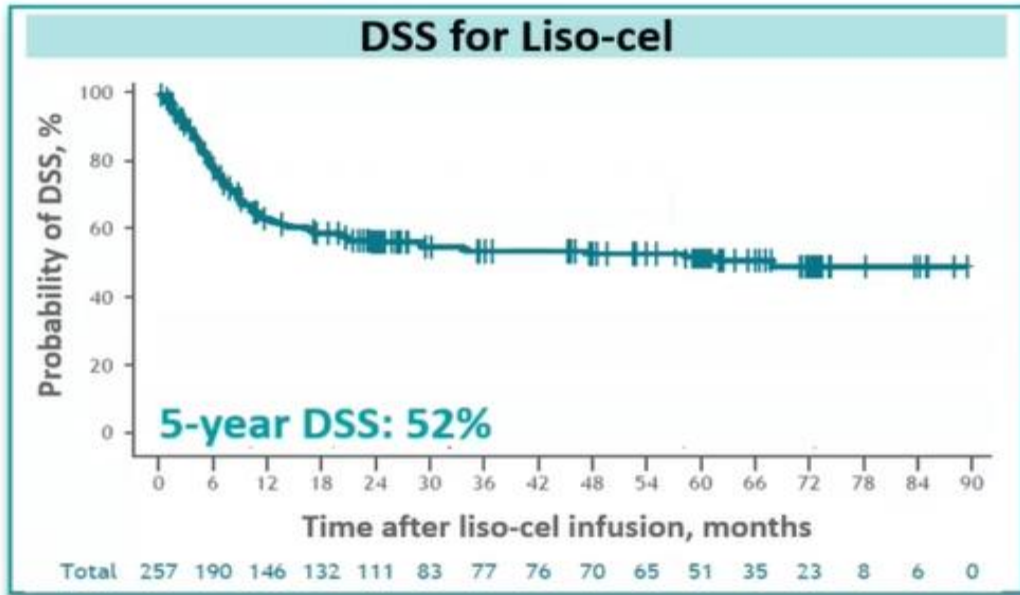
hospitalization

caregiver

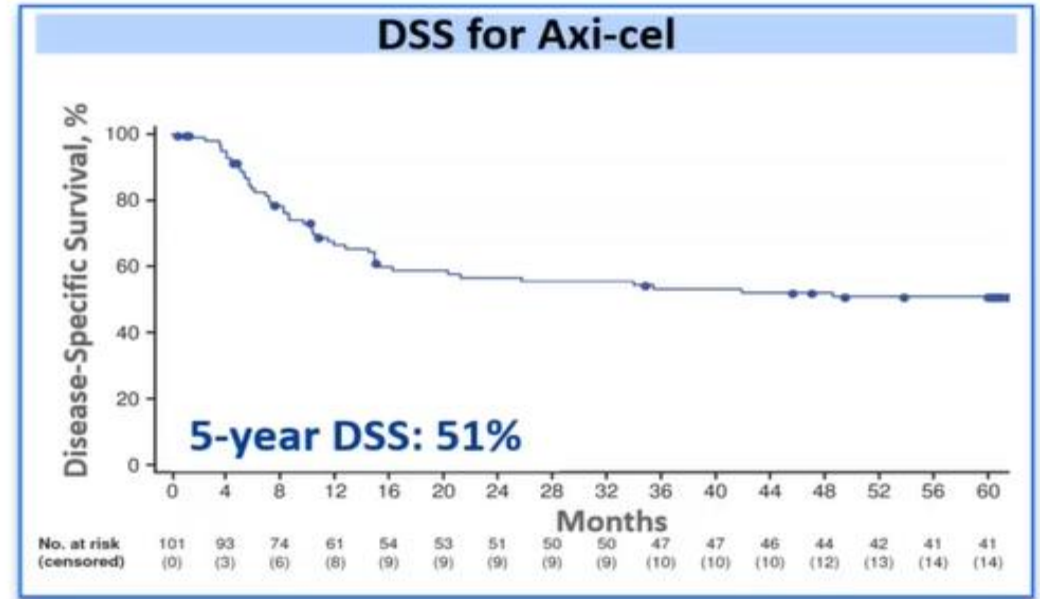
Immunotherapy: the Efficacy and Toxicity Balance



EFFICACY: The curative potential of CAR-T cells as 3L or later



Liso-cel durable efficacy	
Overall response	73%
Complete response	53%
Median PFS	6.8 m
Median DOCR	NR at 5y



Axi-cel durable efficacy	
Overall response	74%
Complete response	54%
Median PFS	5.9 m
Median DOCR	62 m

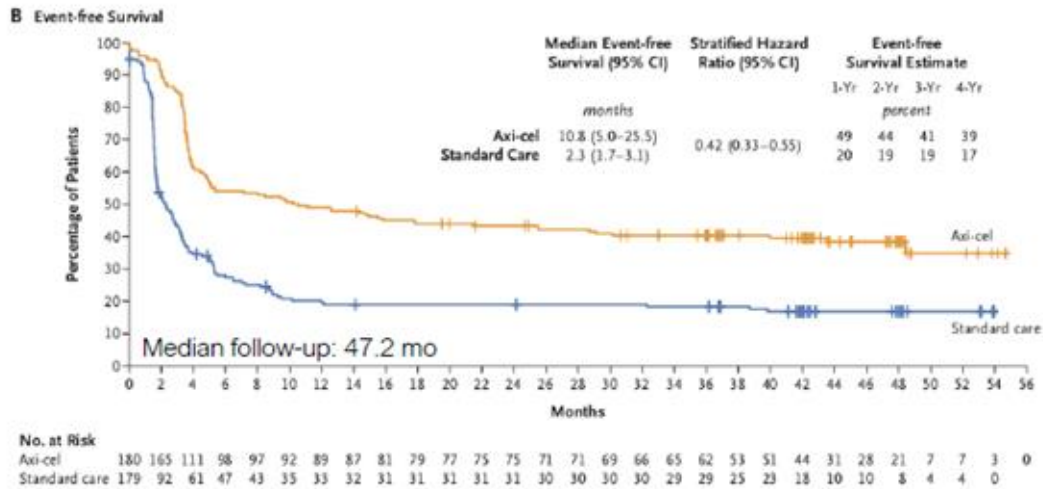
EFFICACY in RWE by patients age group

Data source	US lymphoma CAR-T consortium ⁴⁷		DLBCL CAR-T surveillance database ³⁷		Medicare claims database ⁵⁰			DRST registry ^{51 55}	
CAR-T cell therapy	Axicabtagene ciloleucel		Tisagenlecleucel and axicabtagene ciloleucel		CAR-T cell therapy*			Tisagenlecleucel and axicabtagene ciloleucel	
Indication	≥3L r/r LBCL		≥3L r/r DLBCL		r/r DLBCL			LBCL†	
Median follow-up, months	12.9		7		11.9			11	
Age group, years	<60	≥60	<70‡	≥70	65–69	70–74	≥75	<65	≥65
Efficacy set, n	–	–	41	41	202	176	173	216	140
ORR, %	–	–	78	63	–	–	–	58	69
CR, %	55§	72§	59	46	–	–	–	31	43
Median PFS, months	–	–	NR	3.6	–	–	–	–	–
12-month PFS, %	42	51	54	32	–	–	–	26	36
Median OS, months	–	–	NR	NR	17.2	20.1	13.4	–	–
12-month OS, %	66	70	53	69	57	64	54	51	55
Median EFS, months	–	–	–	–	6.5	12.6	5.3	–	–
12-month EFS, %	–	–	–	–	43	52	34	–	–
Safety set, n	–	–	41	41	–	–	–	–	–
CRS, %	–	–	69.3	69.3	–	–	–	–	–
Grade ≥3, %	6	8	7.3	9.8	–	–	–	13	10
ICANS, %	–	–	17.1	27.5	–	–	–	–	–
Grade ≥3, %	30	32	4.9	2.5	–	–	–	9	16



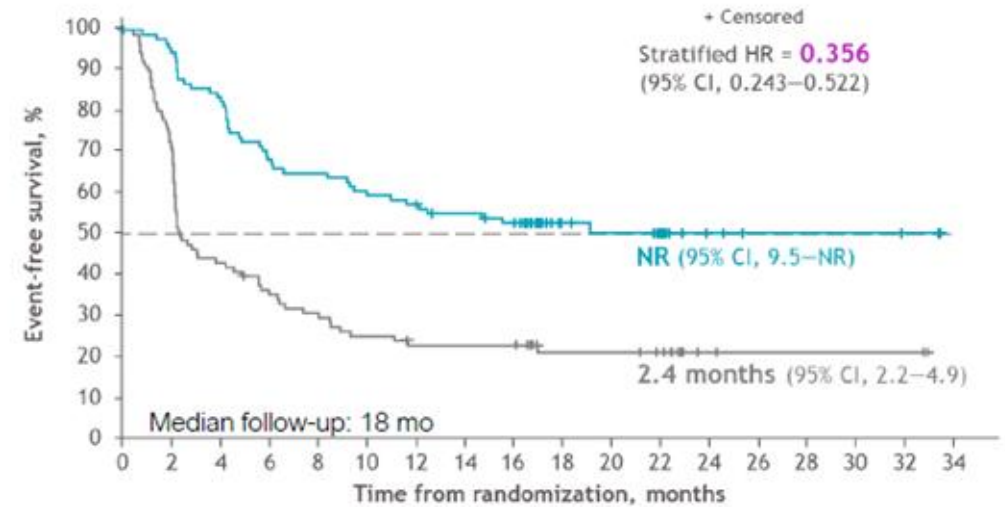
CD19 CAR T vs SoC in 2L LBCL

EFS: Axi-cel vs SoC (ZUMA-7)^{1,2}



Response n (%)	Axi-cel (n=180)	SoC (n=179)	P
ORR	150 (83)	90 (50)	<0.0001
CR	117 (65)	58 (32)	
Survival, mo			HR
Median PFS	14.7	3.7	0.49
Median OS	NR	31.1	0.73

EFS: Liso-cel vs SoC (TRANSFORM)^{3,4}



Response n (%)	Axi-cel (n=180)	SoC (n=179)	P
ORR	80 (87)	45 (49)	<0.0001
CR	68 (74)	40 (43)	
Survival, mo			HR
Median PFS	NR	6.2 mo	0.40
Median OS	NR	29.9 mo	0.72

CAR T-cell as Second Line Treatment: The Real World Evidence



Baseline demographics and disease characteristics

Characteristics	2L R/R LBCL (n = 157)
Median (range) age, ^a y	72 (27—85)
Male, n (%)	90 (57)
Histology, n (%)	
DLBCL ^b	132 (84)
Activated B-cell type	57 (36)
Germinal center B-cell type	61 (39)
NOS	13 (8)
THRBCL	1 (1)
High-grade B-cell lymphoma	18 (11)
Other, including PMBCL	7 (4)
Disease status at time of infusion, n (%)	
Active disease	137/156 (88)
Primary refractory	79 (50)
Early relapse ^c	76 (48)
CNS involvement, n (%)	5 (3)

Characteristics	2L R/R LBCL (n = 157)
ECOG PS, n/N (%)	
0—1	128/135 (95)
2 / 3—4	7/135 (5) / 0
Patients with ≥ 1 comorbidity, n/N (%)	76/126 (60)
Cardiac ^d	34/126 (27)
Pulmonary ^d	22/126 (17)
Obesity ^d	15/126 (12)
Elevated LDH at infusion, n/N (%)	62/151 (41)
Prior therapeutic exposure, n (%)	
Received R-CHOP	137 (87)
Single regimen	89 (65)
Intrathecal therapy	23 (15)
Radiation therapy	35 (22)
Bridging therapy, n (%)	113 (72)

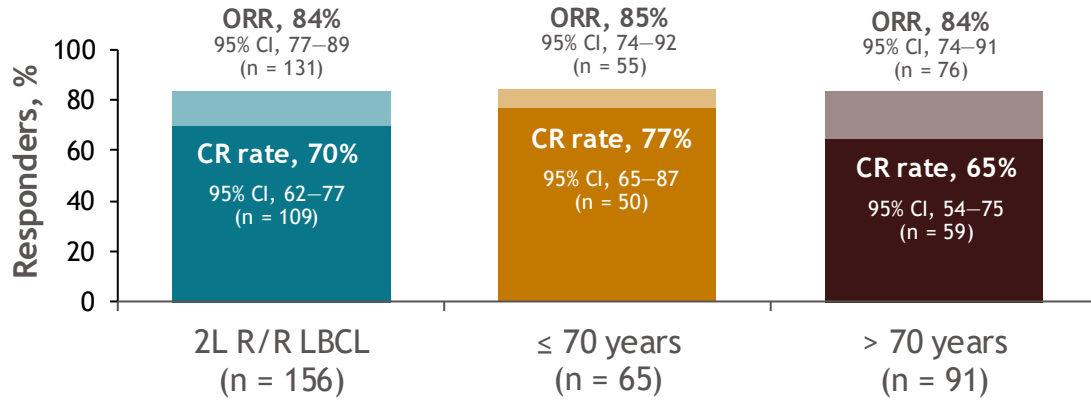
- A total 105 (67%) patients would have been ineligible for TRANSFORM, primarily due to age and/or severity of comorbidities

There were 66 (42%) patients who were ≥ 75 years of age

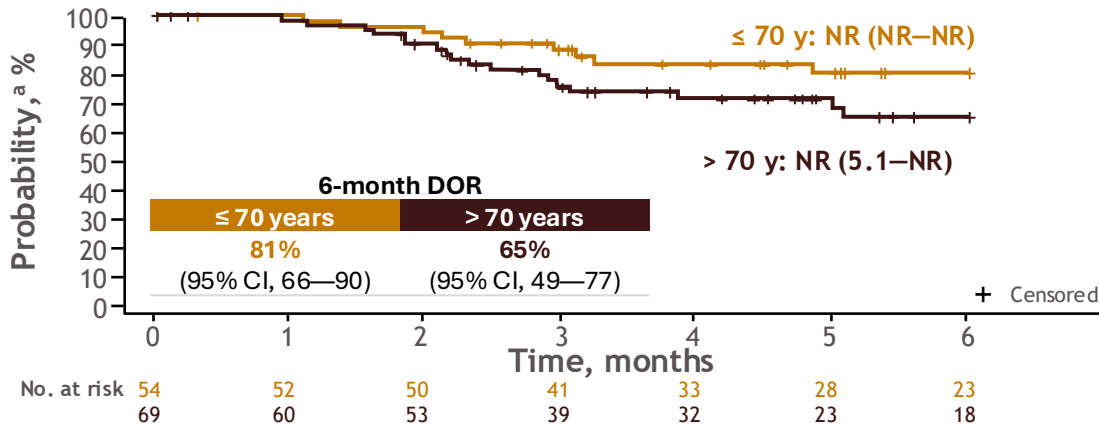
CAR T-cell as Second Line Treatment: The Real World Evidence



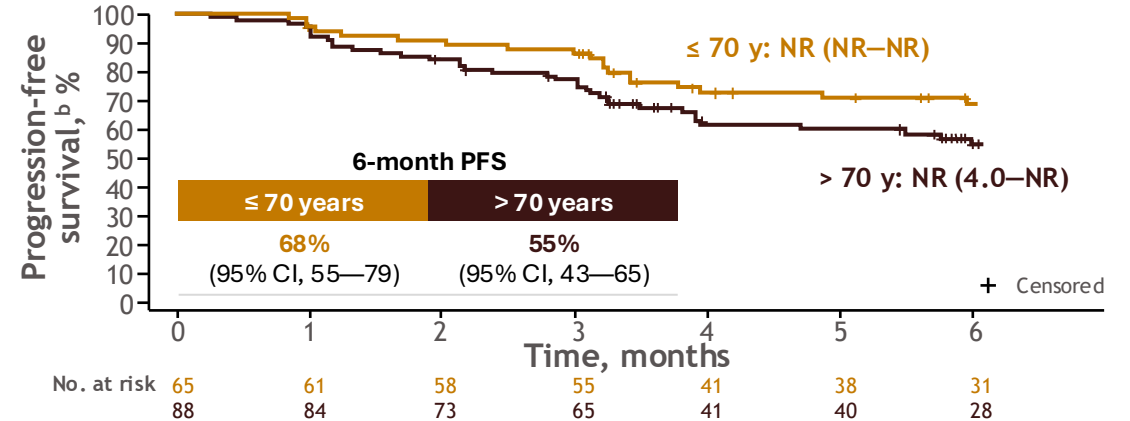
Response rates



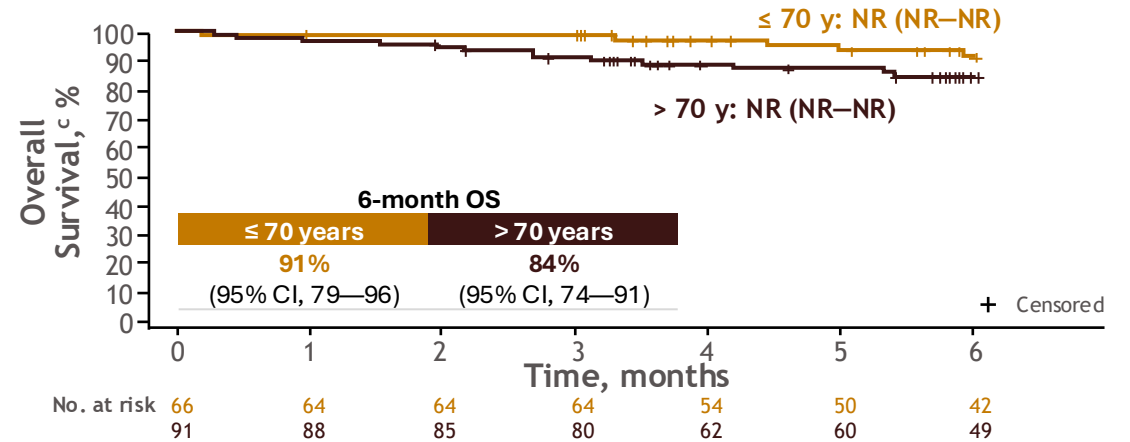
DOR



PFS



OS

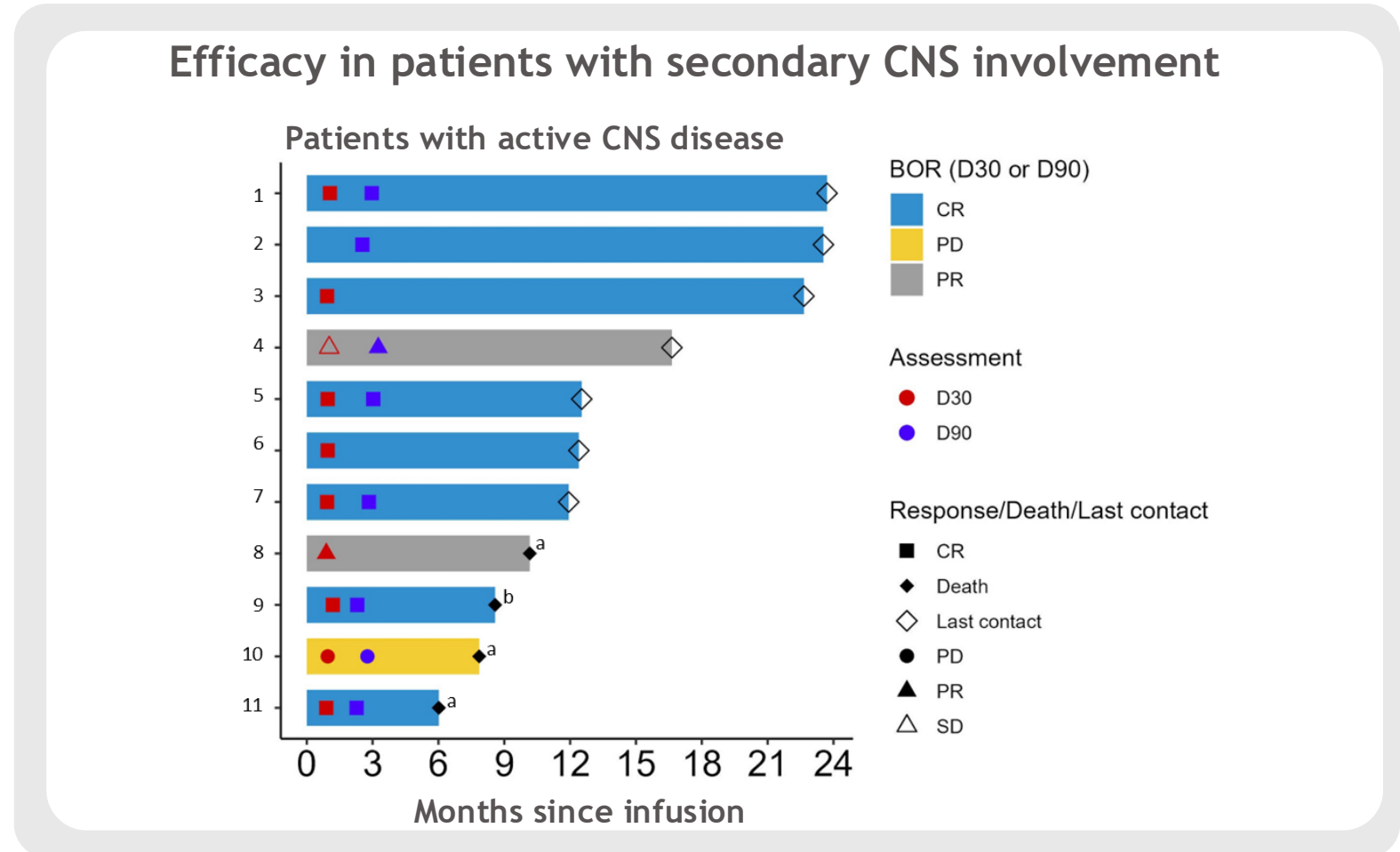


- Liso-cel was effective across both age subgroups

Efficacy in patients with secondary CNS involvement

- Eleven patients treated with liso-cel had secondary CNS involvement
- The majority of patients with active CNS disease achieved a CR

PFS at 6 months in patients with secondary CNS lymphoma
72.7% (95% CI, 50.6-100)



Liso-cel safety profile and resource utilization

- In this real-world study, safety was similar or superior to that observed in patients enrolled in prospective clinical trials of liso-cel in R/R LBCL

Resource utilization:

Inpatient/outpatient administration

85%/15%

Unplanned hospitalization^{b,c}

33%

Intensive care unit transfer

10%

Safety summary:

	N = 101
CRS	
Any grade, %	49
Grade ≥ 3, %	3
Median time to onset, days (IQR)	4 (3–5)
Median duration, days (IQR)	4 (2–5)
ICANS	
Any grade, %	26
Grade ≥ 3, %	10
Median time to onset, days (IQR)	6 (3–9)
Median duration, days (IQR)	4 (1–13)
Toxicity management	
Tocilizumab, %	31
Median doses, n (IQR)	1 (1–2)
Steroids, %	31
Standard-dose ^d	77
High-dose ^e	23

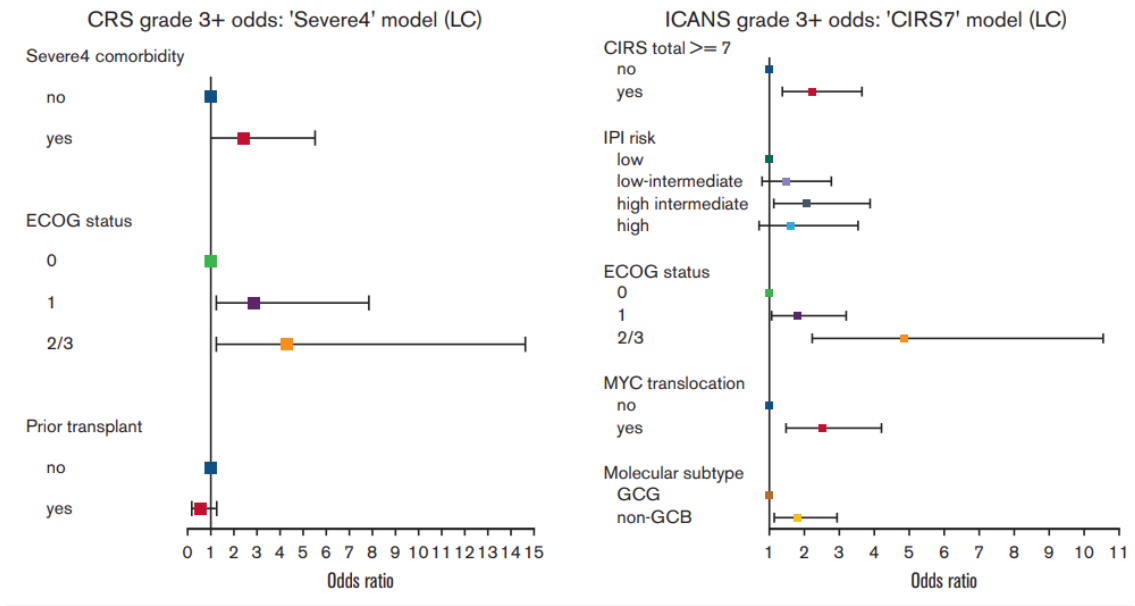
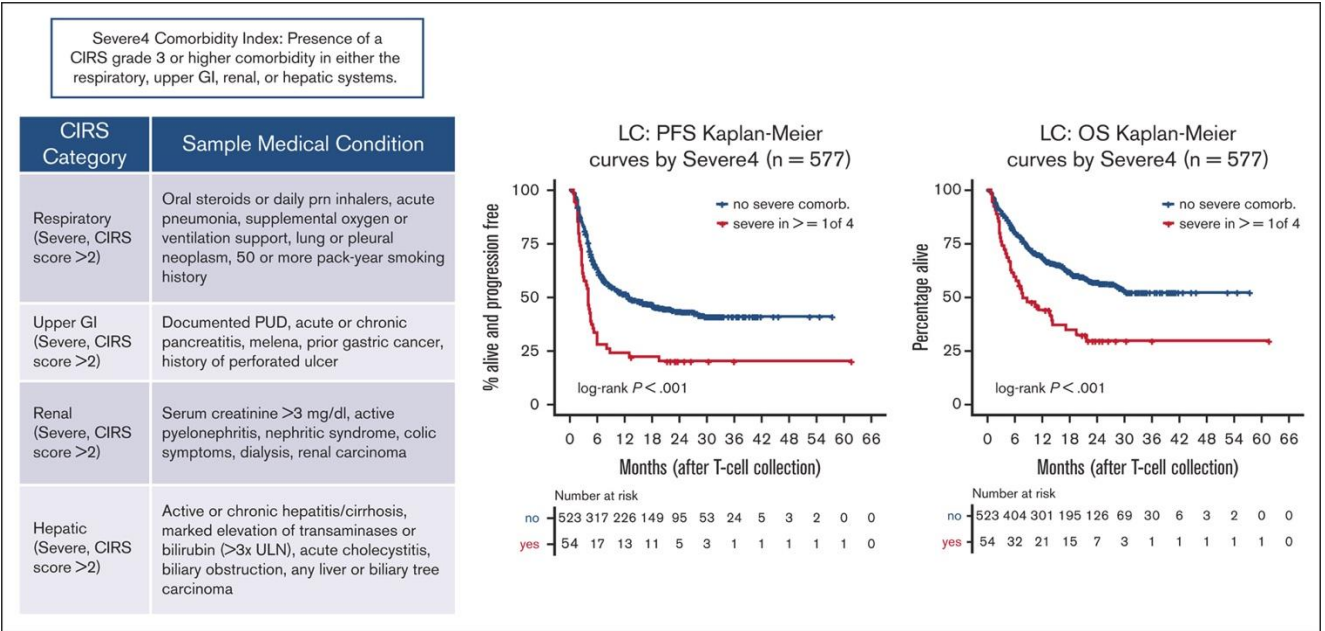
Grade 5 AEs:

	N = 101
Death <i>within</i> 28 days, n	3
Infectious complications	1
Concurrent Grade 5 NT and Grade 5 CRS	1
Grade 5 NT	1
Death <i>beyond</i> 28 days, n	7
Other malignancy	2
Accidental death	1
Infectious complications	1
Unknown	3

The 12-month incidence of non-relapse mortality was 7% (95% CI, 3.1–13.1)

A validated composite comorbidity index predicts outcomes of CAR T-cell therapy in patients with diffuse large B-cell lymphoma

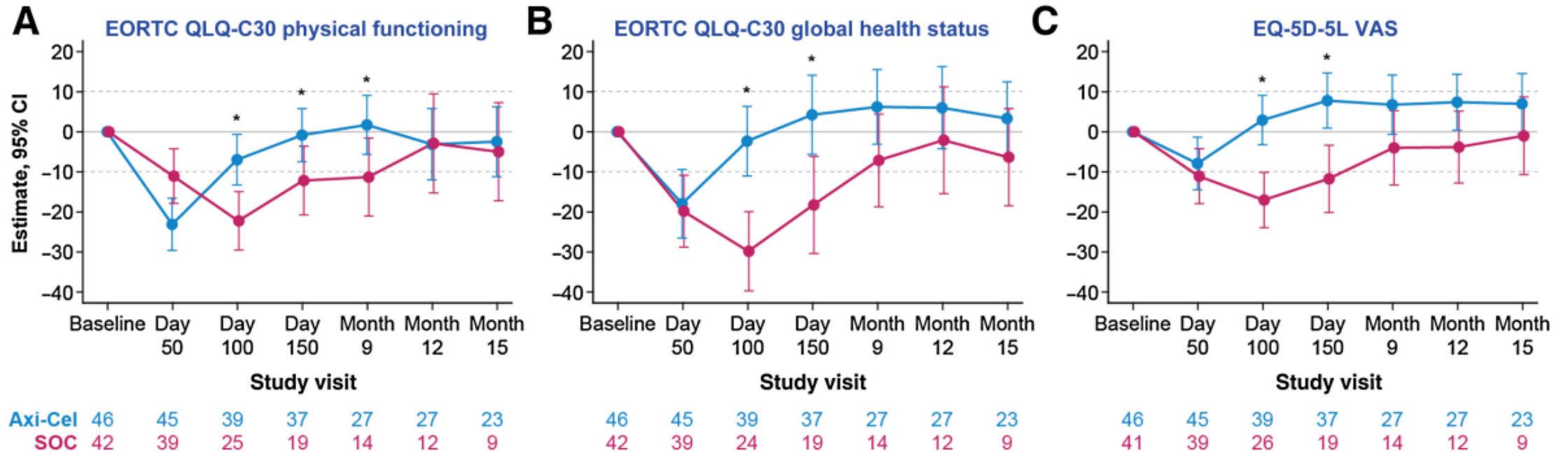
- 9 academic medical centers in the United States
- 550 patients infused with CART, 71% (n = 393) received axi-cel, 22% (n = 120) tisa-cel, and 7% (n = 37) liso-cel.



✓ Severe comorbidity in the **cardiac system** was **not predictive** of survival or toxicity in our large data set.

✓ ECOG performance status scores of ≥ 2 were independently associated with worse OS and

Patient-reported outcome endpoints in patients ≥ 65 years



Differences between CAR-T therapy and BsAb

CAR-T Therapy	Bispecific antibody therapy
Curative potential confirmed at 5 yr FU (plateau)	Excellent efficacy
Single infusion- One shot!	Repeated infusion (12 cycles vs indefinite)
Established CNS efficacy	Unknown CNS efficacy
Prospective trials: Efficacy of BITE after CAR-T	Retrospective efficacy of CAR-T after BsAb
Inpatient and Outpatient	Inpatient and Outpatient
Need of Lymphodepleting Chemotherapy	No Lymphodepleting Chemo but more steroids
Accredited centers	Community setting
Manufacturing Time 3-4w	Off-the shelf therapy
Increased risk of CRS/ICANS (not with all CAR-T)	Lower risk of CRS/ICANS



Grazie



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