

CAR-T in follicular and DLBCL lymphoma

Alice Di Rocco

Hematology, Department of Translational and Precision Medicine
Sapienza Università di Roma



ROMA
HEMATOLOGY
CONFERENCE
the lymphomas

Rome

October 15-16, 2026

Hotel nhow Roma

Disclosures: Alice Di Rocco

Company name	Research support	Employee	Consultant	Stockholder	Speakers 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	

Ten-year follow-up: CAR T cells can cure B-cell lymphomas

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

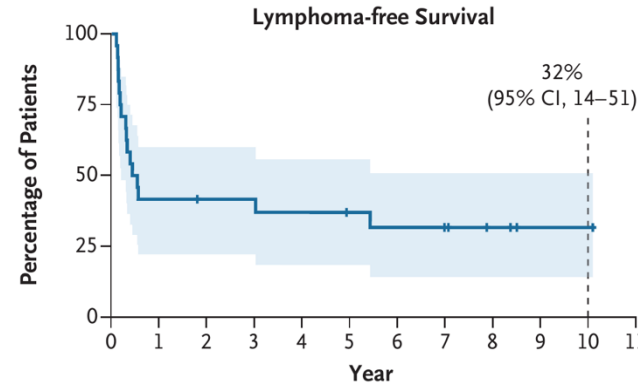
Ten-Year Outcomes after CAR T-Cell Therapy for B-Cell Lymphomas

Marco Ruella, M.D.,^{1,3} Luca Paruzzo, M.D.,^{1,3} Emeline R. Chong, B.A.,¹
 Elise A. Chong, M.D.,^{1,3} Daniel J. Landsburg, M.D.,^{1,3} Sunita D. Nasta, M.D.,^{1,3}
 Pooja Devi, M.D.,⁴ Peter Michener, M.S.,² Federico Stella, M.D.,²
 Alberto Carturan, M.D.,^{1,3} Ellen B. Napier, C.R.N.P.,^{1,3}
 Vivianna M. Van Deerlin, M.D., Ph.D.,⁴ Patrizia Porazzi, Ph.D.,² Bruce L. Levine, Ph.D.,^{2,4}
 Noelle Frey, M.D.,³ David L. Porter, M.D.,^{2,3} Joseph A. Fraietta, Ph.D.,^{2,4,5}
 Jakub Svoboda, M.D.,^{1,3} Carl H. June, M.D.,^{2,4} and Stephen J. Schuster, M.D.^{1,3}

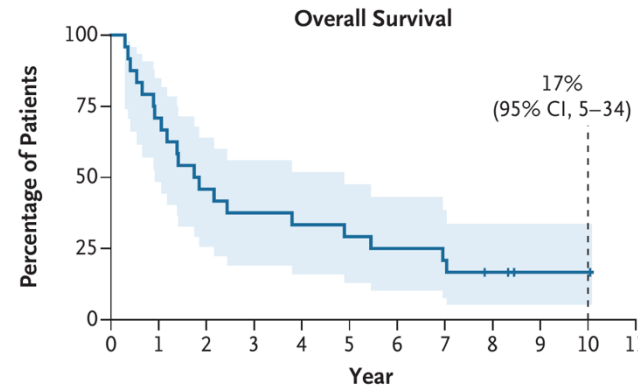
- **Tisa-cel (CTL019)**, UPenn, treated 2014–2019
- **38 patients:** 24 DLBCL, 14 FL; median FU 10.1 yrs
- **No relapses** beyond 5.4 yrs (beyond 2.7 yrs in FL)
- **10-yr PFS:** 17% DLBCL, 29% FL
- **Safety:** no CAR T-cell-derived lymphomas; second cancers 21% at 10 yrs

Ruella M, et al. *N Engl J Med* 2026;394:2440–48

Large B-cell lymphoma n = 24

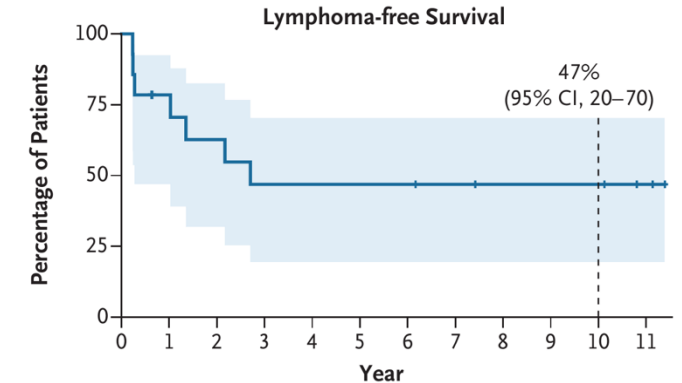


No. at Risk 24 10 9 8 8 7 6 5 3 1 1 0

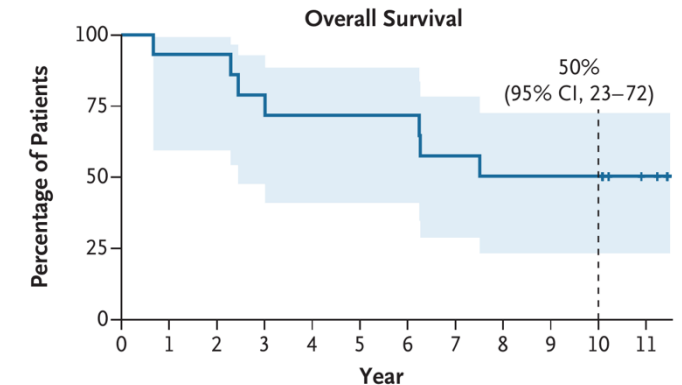


No. at Risk 24 17 11 9 8 7 6 5 3 1 1 0

Follicular lymphoma n = 14



No. at Risk 14 10 8 6 6 6 6 5 4 4 4 2



No. at Risk 14 13 13 10 10 10 10 8 7 7 7 3



ROMA HEMATOLOGY
CONFERENCE

the lymphomas

Rome Hotel nhow Roma
October 15-16, 2026

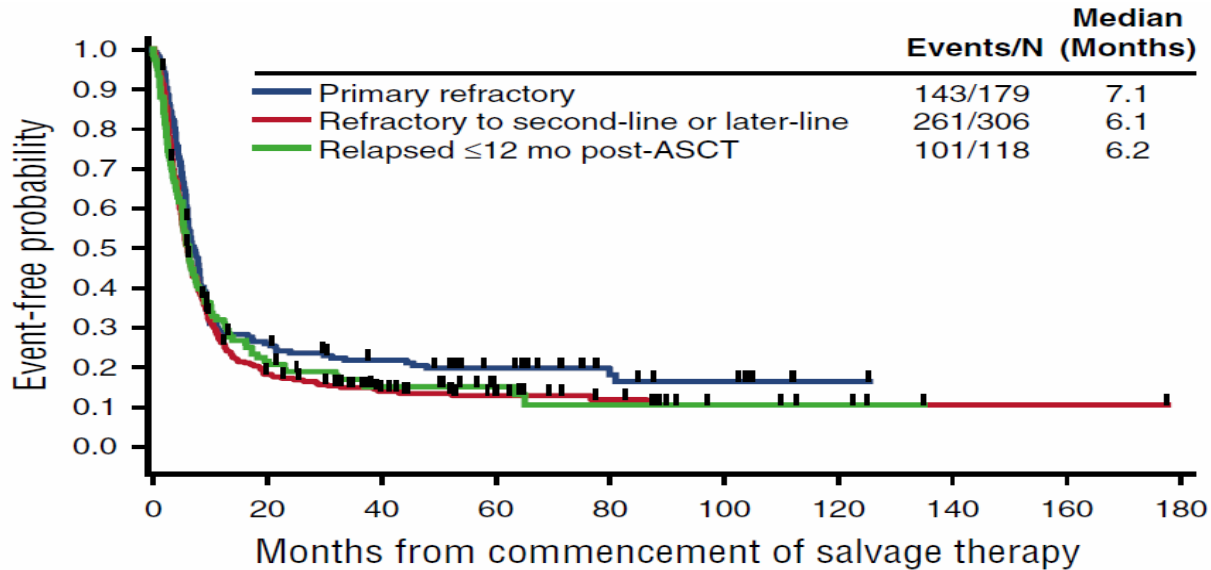
CAR-T in DLBCL and FL: two different scenarios

	Large B-cell lymphoma	Follicular lymphoma
Disease setting	Aggressive; refractory or early relapse carries a poor prognosis	Indolent and relapsing; long survival with many treatment options
Goal of CAR-T	Cure: ~40% long-term survivors after a single infusion	Durable, treatment-free remission: ELARA 5-yr PFS 46%
When	2L if relapse ≤ 12 months or primary refractory (ZUMA-7, TRANSFORM); 3L+ for all others	3L+; best candidates are POD24, double-refractory and high-risk patients
Relapse pattern	Failures mostly within the first year, then a plateau	Late relapses rare: none beyond 2.7 years at 10-year follow-up
Key challenge	Speed: early referral, short vein-to-vein time, effective bridging	Benefit vs toxicity: choice of product, competition with bispecifics, long-term infections

Same cells, different goals: cure in DLBCL, long-lasting disease control in FL

Impact of CAR-T Therapy on Survival in R/R LBCL

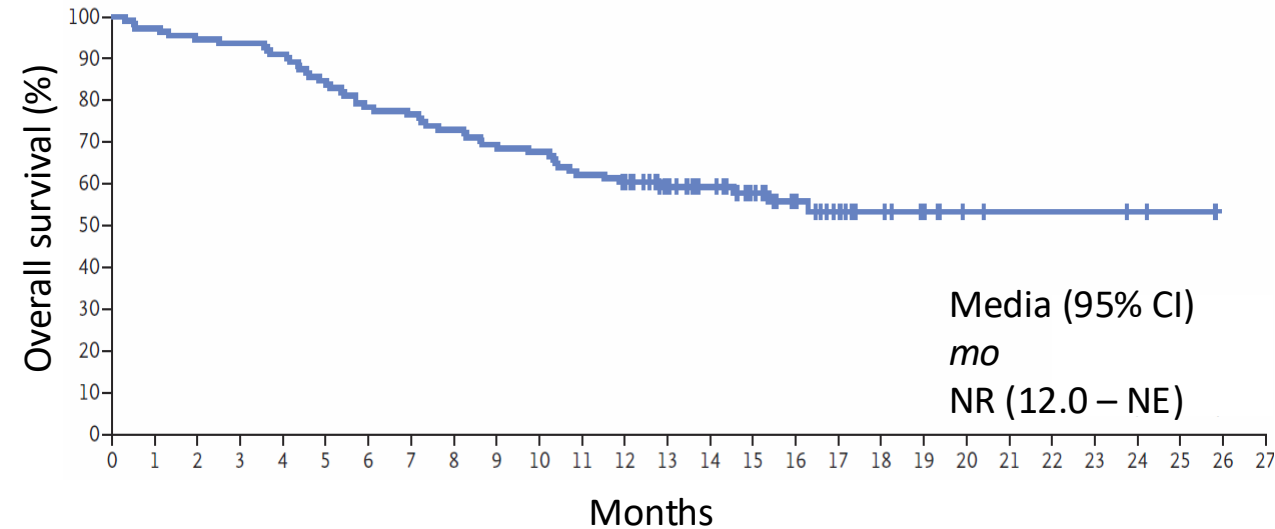
Overall survival: **SCHOLAR-1**



- N = 636
- ORR = 26%; CR rate = 7%
- Median OS = 6.3 months

Crump et al. Blood 2017

Overall survival: **ZUMA1 (Axi-cel)**



- N = 108
- ORR = 82%; CR rate = 54%
- Median OS = >18 months

Neelapu et al. N Eng J Med 2017

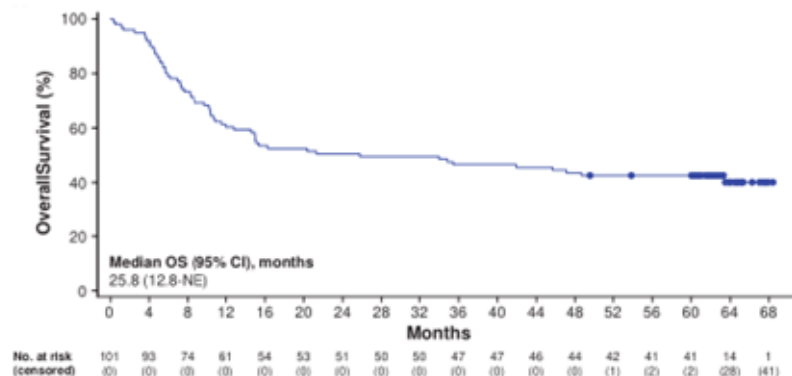
CAR T-cell as 3rd Line or Later Therapy: JULIET, ZUMA-1 and TRANSCEND

	Tisa-cel (Juliet) ¹	Axi-cel (Zuma-1) ²	Liso-cel (Transcend) ³
Source →	Cryopreserved unsorted PBMCs	Fresh unsorted PBMCs	Fresh sorted PBMCs CD4:CD8 = 1:1
Pts infused, n	115 (167 enrolled)	101 (111 enrolled)	269 (344 enrolled)
BT	Allowed →	Not allowed	Allowed
→ LD	FC (25 mg/m ² ; 250 mg/m ²) or Bendamustine (90 mg/m ²)	FC (30 mg/m ² ; 500 mg/m ²)	FC (30 mg/m ² ; 300 mg/m ²)
CAR T-cells dose	Median: 3.0 × 10 ⁸ (range: 0.1 × 10 ⁸ to 6.0 × 10 ⁸ ; target: 5 × 10 ⁸)	2 × 10 ⁶ cells/Kg or fixed 2 × 10 ⁸ cells for pts weighed ≥ 100 kg	DL1 50 × 10 ⁶ ; <u>DL2: 100 × 10⁶</u> , DL3: 150 × 10 ⁶ CAR T-cells
→ CRS grading	UPenn scale	Lee 2014	Lee 2014
NE grading	CTCAE vers 4.03	CTCAE vers 4.03	CTCAE vers 4.03
1st endpoint³	ORR by IRC	ORR by IRC	ORR by IRC, AEs, DLT
2nd endpoints	DOR; time to response; OS; PFS; EFS, cell kinetics, safety	DOR; OS; PFS; EFS, time to progression, TTNT, disease specific survival, cell kinetics, safety	CRR, DOR, PFS, OS, cellular kinetics
Response evaluation	CT at 1 mo and PET at 3 mo from infusion	PET at 1 mo from infusion	PET at 1 mo from infusion

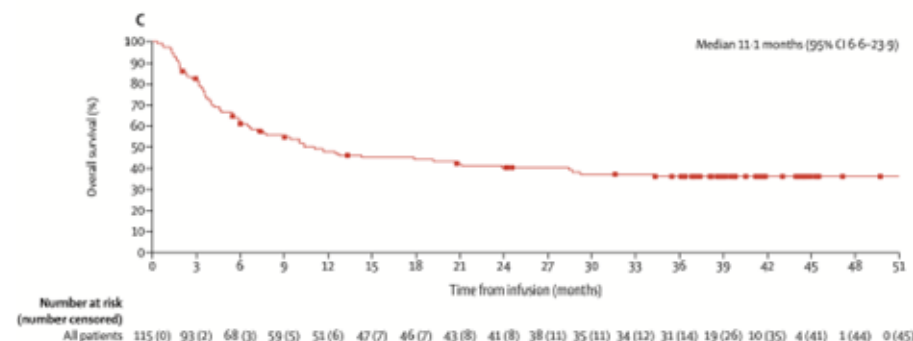
1. Schuster SJ, et al. *Lancet Oncol* 2021;22(10):1403–15; 2. Neelapu SS, et al. *Blood* 2022; 3. Abramson JS, et al. *Lancet*. 2020;396(10254):839-852

CD19 CAR T-cell therapy in ≥ 3 L LBCL

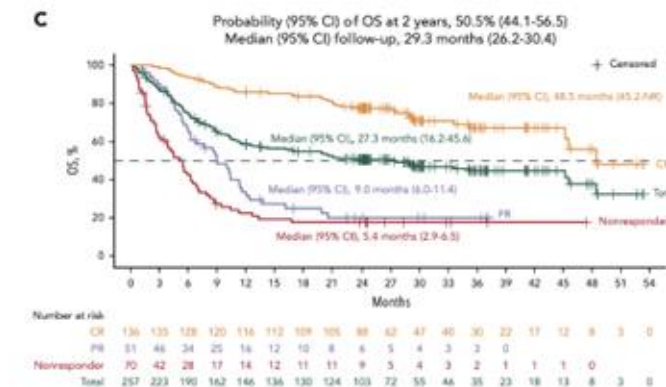
OS Axi-cel¹



OS Tisa-cel²



OS Liso-cel³

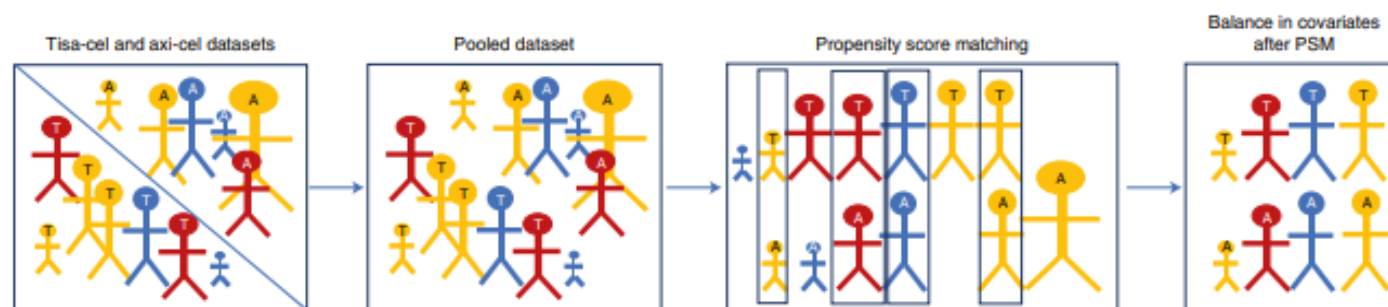


	Axi-cel (N=101)	Tisa-cel (N=115)	Liso-cel (N=257)
Median follow-up, mo	63.1 (range: 58.9–68.4)	40.3 (IQR: 37.8–43.8)	19.9 (range: 0.2–55.6)
ORR (CR), %	83 (58)	53 (39)	73 (53)
Median DoCR, mo (95% CI)	62.2 (12.9–NE)	NR	26.1 (23.1–NR)
Median PFS, mo (95% CI)	5.9 (3.3–15)	2.9 (2.3–5.2)	6.8 (3.3–12.7)
Median EFS, mo (95% CI)	5.7 (3.1–13.9)	NA	NA

~40% of all LBCLs treated with CAR T are potentially cured!

1. Neelapu SS, et al. Blood 2023;141:2307–15;
2. Schuster SJ, et al. Lancet Oncol 2021;22:1403–15;
3. Abramson JS, et al. Blood 2024;143:404–16.

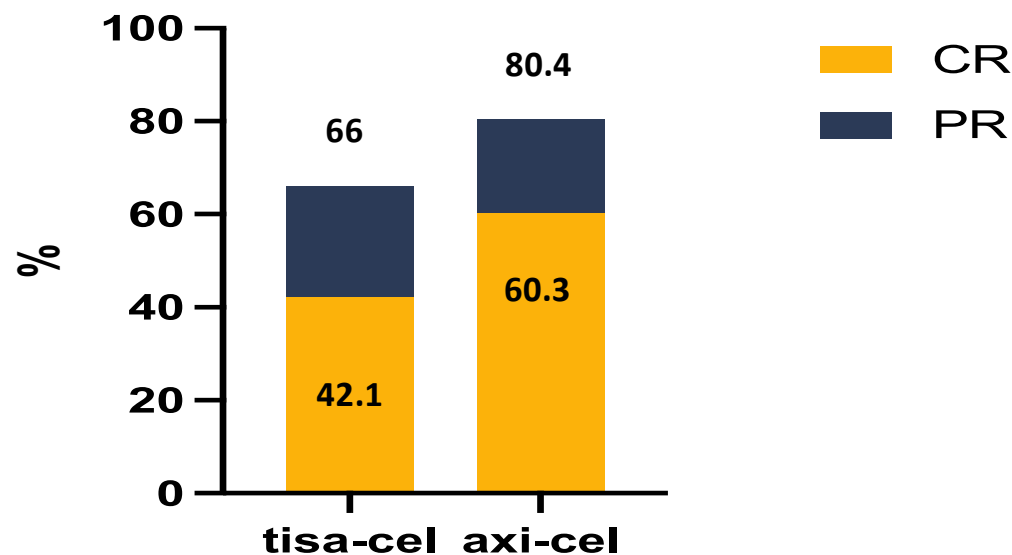
French real-world outcomes according CAR-T products after PSM



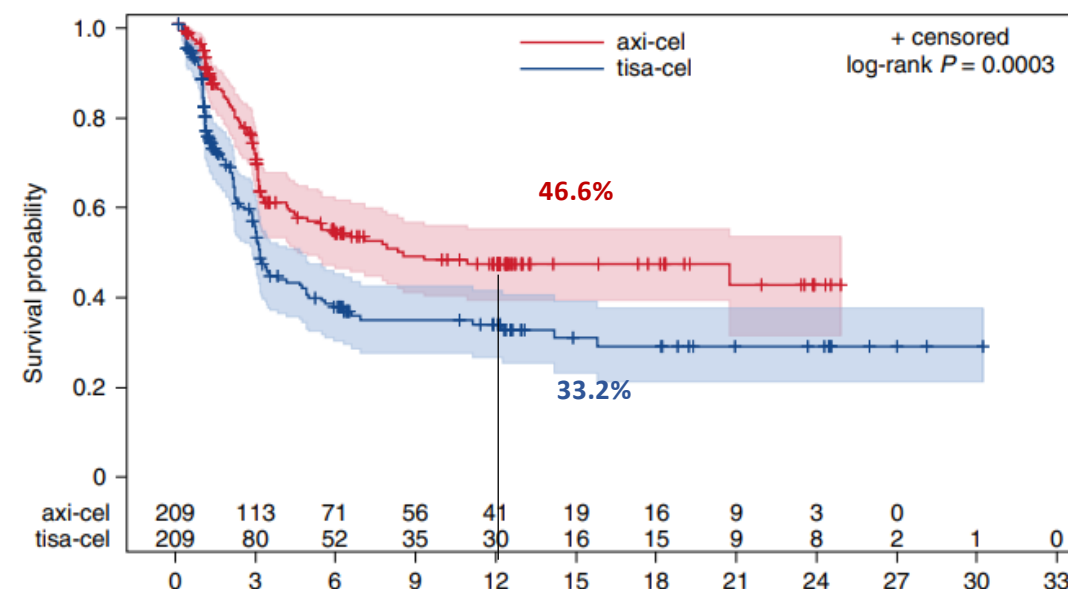
TOXICITY:

- There was **no significant difference** in incidence of CRS
- **Axi-cel** was associated with significantly **more frequent and higher-grade ICANS** (30.6% v 18.1% for grade 1-2 and 10.4% v 2.1% for grade ≥ 3 for axi-cel compared with tisa-cel, respectively, $P < 0.001$)

ORR



PFS



There was no OS difference between axi-cel and tisa-cel

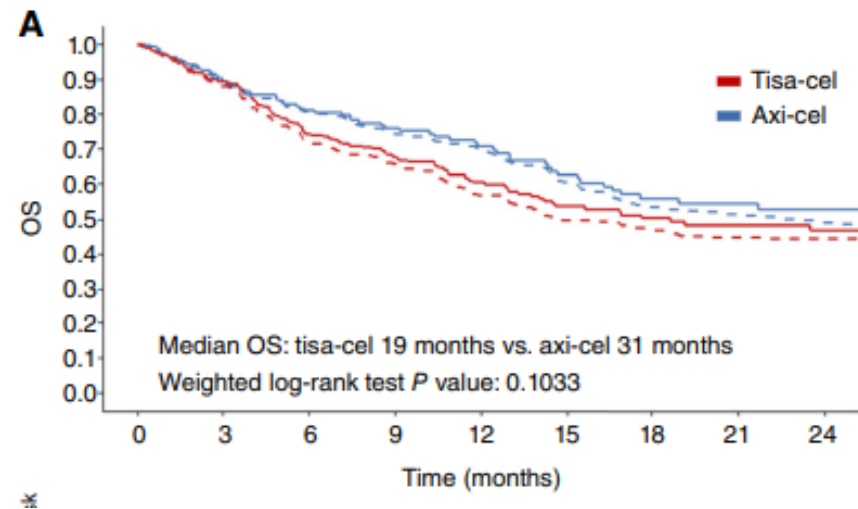
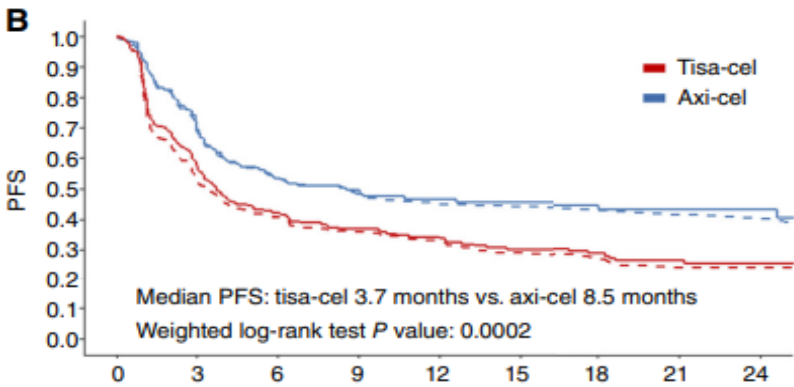
Italian real-world multicenter CAR-T study: Axi-cel vs Tisa-cel



- 485 patients analysed
- Median Age 60.0 [52.0, 66.0]
- V2V time 2.04 months (1.44)

	OVERALL (485)	Tisa-cel (252)	Axi-cel (233)	P-value
BEST ORR	67.6%	61.1%	74.7%	0.0009
BEST CRR	53.2%	47.6%	59.2%	0.0105
ORR at +90	44.5%	40.9%	48.5%	0.0284
CRR at +90	37.7%	34.1%	41.6%	0.0338
CRS any grade	83.7%	78.6%	89.3%	0.0017
ICANS any grade	20.6%	9.9%	32.2%	<0.00001
CRS g>2	7.8%	7.1%	8.6%	0.8573
ICANS G>2	6.4%	3.2%	9.9%	0.8064

Axicel has better ORR, CRR and PFS than Tisacel



F. Stella et al, Blood Cancer Discov 2024;5:318–30

Lisocabtagene maraleucel for relapsed/refractory large B-cell lymphoma: a cell therapy consortium real-world analysis



- Retrospective data analysis from 7 US academic centers (N= 101)
- 101 adults treated with commercial liso-cel between Feb 2021 and Jun 2023

Baseline characteristics	N = 101
Median age at apheresis, years (range)	71 (30-85)
< 65, %	28
65-74, %	38
≥ 75, %	35
Male, %	60
ECOG PS of 0 / 1, ^b %	84
Charlson Comorbidity Index 0-1 / 2 / ≥ 3, %	7 / 25 / 68
Ineligible for TRANSCEND due to comorbidities, ^c %	30
Diagnosis, %	
DLBCL	86
HGBL	7
TFL	5
PMBCL	2
Disease stage III/IV, ^d %	80
Bulky disease (≥ 10 cm), ^e %	18
Baseline comorbidities, %	
Diabetes	18
Stage IV chronic kidney disease	5
Cerebrovascular disease	5
Impaired cardiac EF	2
Pulmonary dysfunction	2
Impaired hepatic function	2
Active infection	3

Baseline characteristics	N = 101
Active secondary CNS involvement, %	11
Pre-lymphodepletion LDH > institutional ULN, ^a %	44
Prior autologous SCT, %	16
Median number of prior therapies, n (range)	3 (1-8)
1, %	16
2, %	31
3, %	26
> 4, %	28
Bridging therapy, %	62
Polatuzumab-based	41
Chemotherapy	24
Radiation therapy	21
Targeted therapy	13
Steroids	1
Disease status at time of lymphodepletion, ^f %	
Active disease	82
Complete response	18
Lymphodepleting chemotherapy, %	
Fludarabine and cyclophosphamide	74
Bendamustine	26
Median time from leukapheresis to infusion, days (IQR)	39 (34-43)
Out of specification, %	7

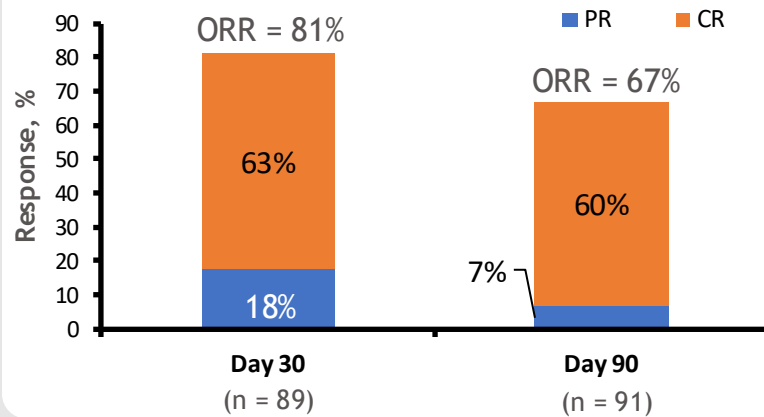
Median age: 71 years
(35% ≥75 years)

High-risk cohort:
68% had high
comorbidity scores;
33% would have been
ineligible for the
TRANSCEND trial.

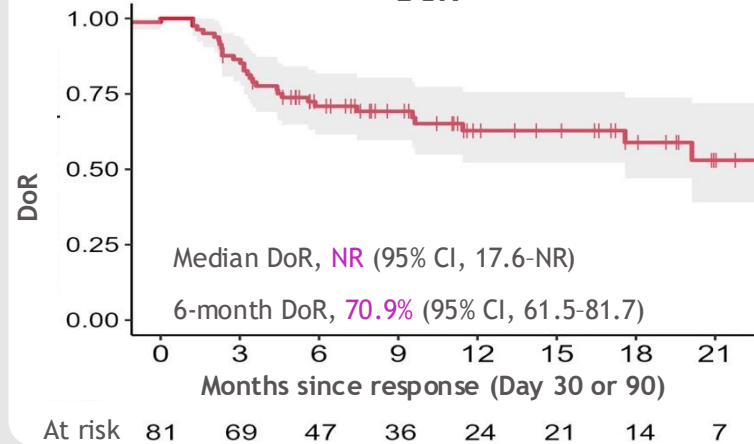
Vein to vein time : 39 days (34-43)

Real-world liso-cel: efficacy, DoR, PFS and OS

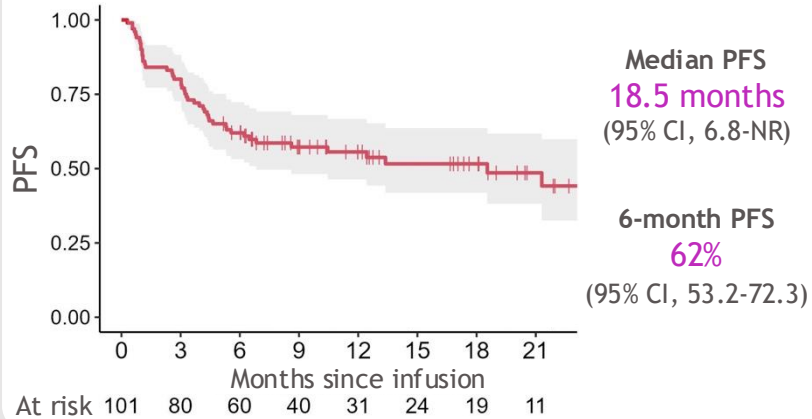
ORR at Days 30 and 90 post-infusion



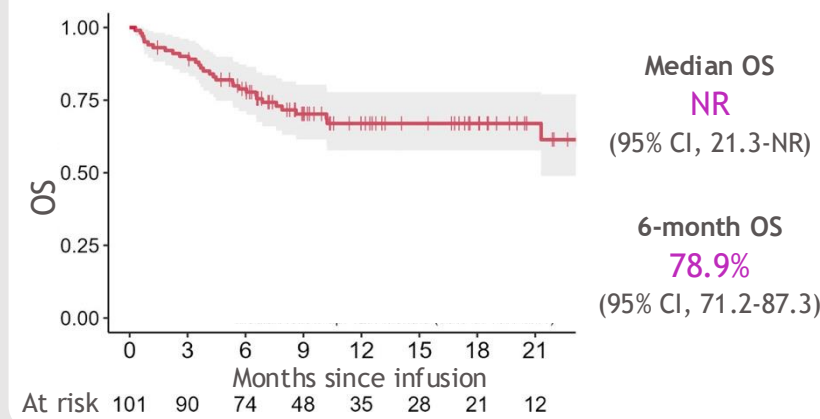
DoR



PFS



OS



Key points

- **Median follow-up:** 12.4 months (0.3–25.1)
- **Bridging therapy:** 60% of patients, mostly polatuzumab-based
- **Normal LDH** before lymphodepletion strongly associated with better PFS and OS
- **Response to bridging** (CR or PR) associated with improved PFS

Liso-cel in secondary CNS involvement: real-world data

11

patients with secondary CNS lymphoma

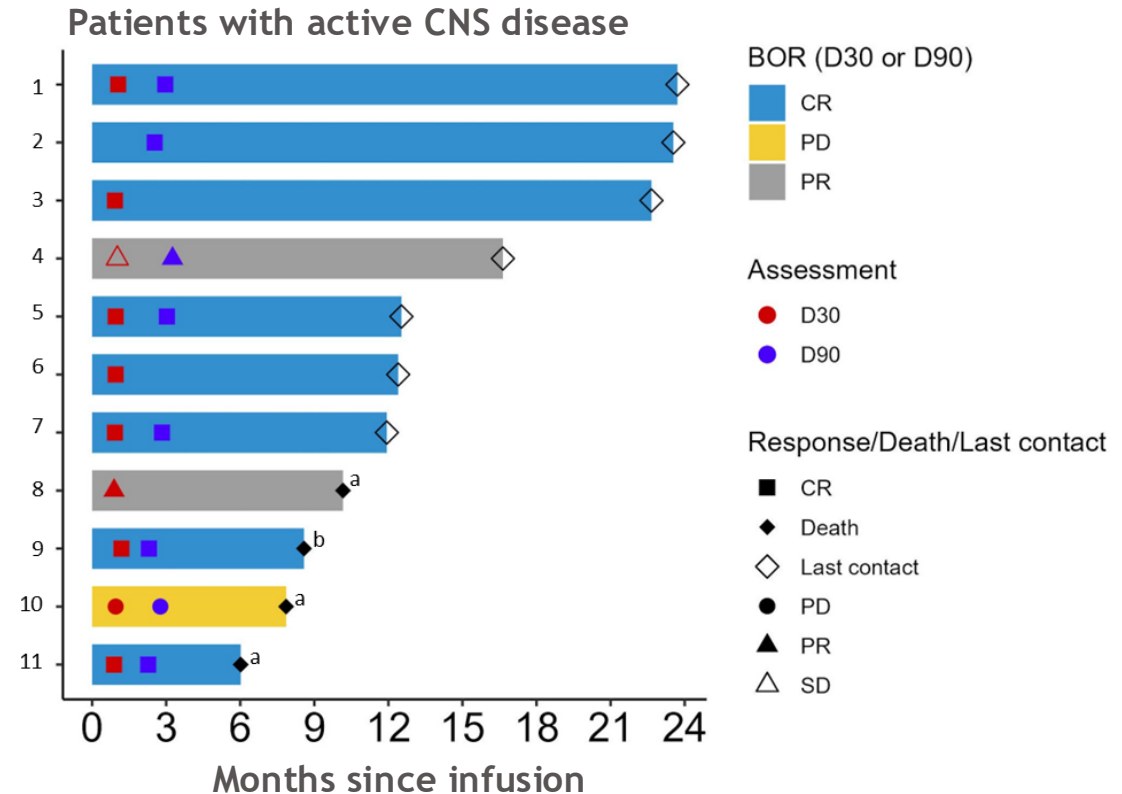
8 / 11

achieved CR (best response, day 30 or 90)

72.7%

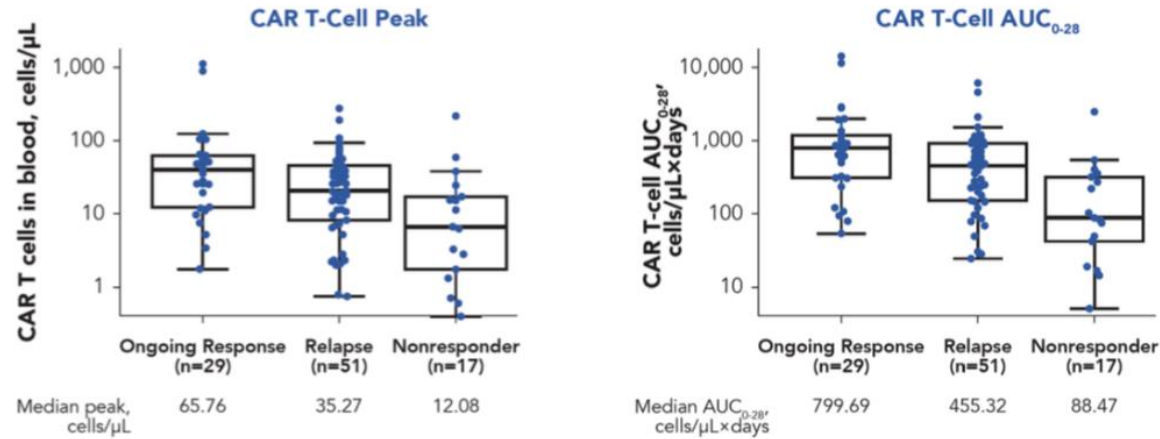
6-month PFS (95% CI, 50.6–100)

Small cohort, short follow-up

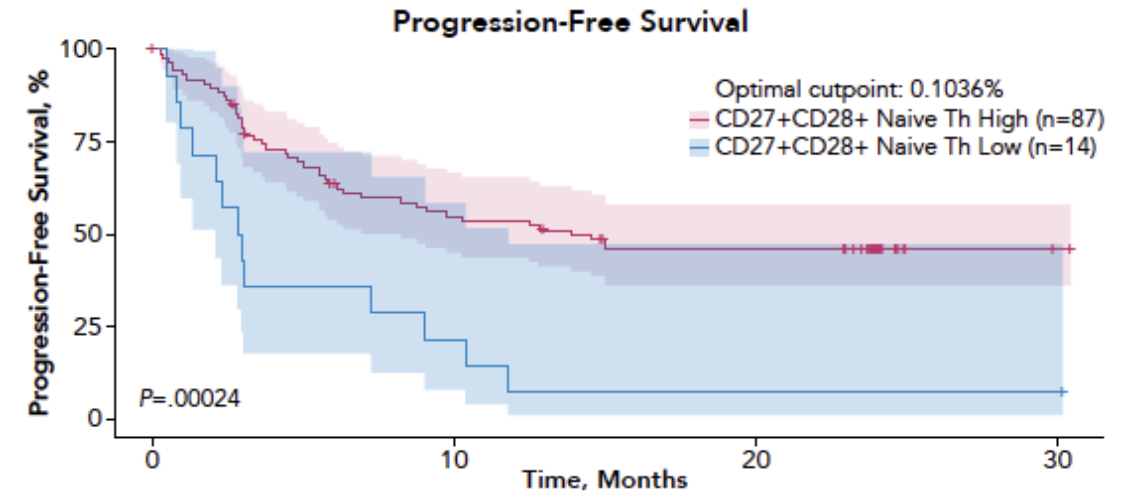


Potential factors correlating with CAR T cell treatment efficacy

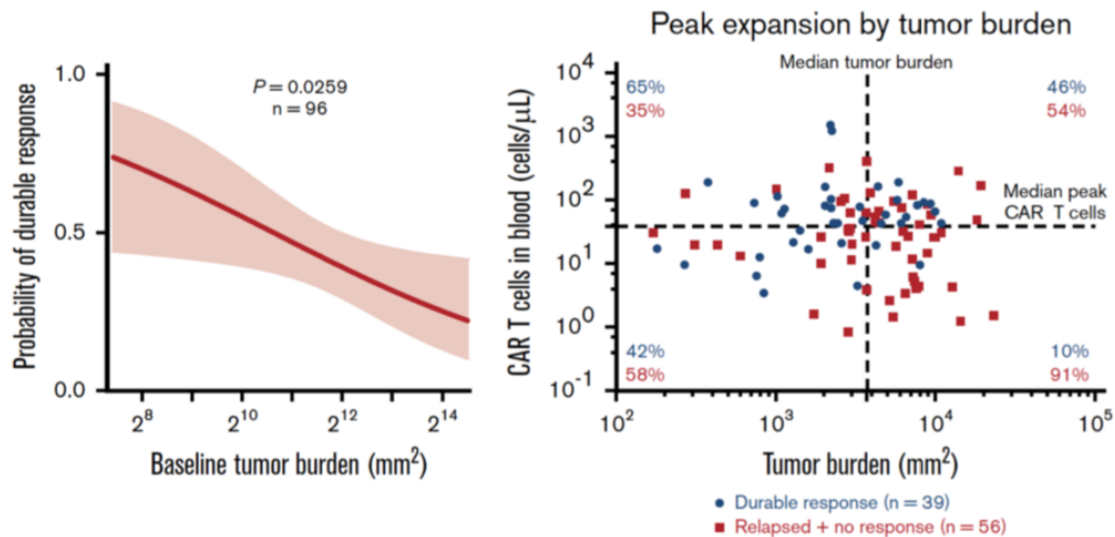
Early CART cell expansion associated with ongoing response at 5 years¹



CD27+CD28+ naïve T cells in apheresis associated with CART cell product fitness and better efficacy



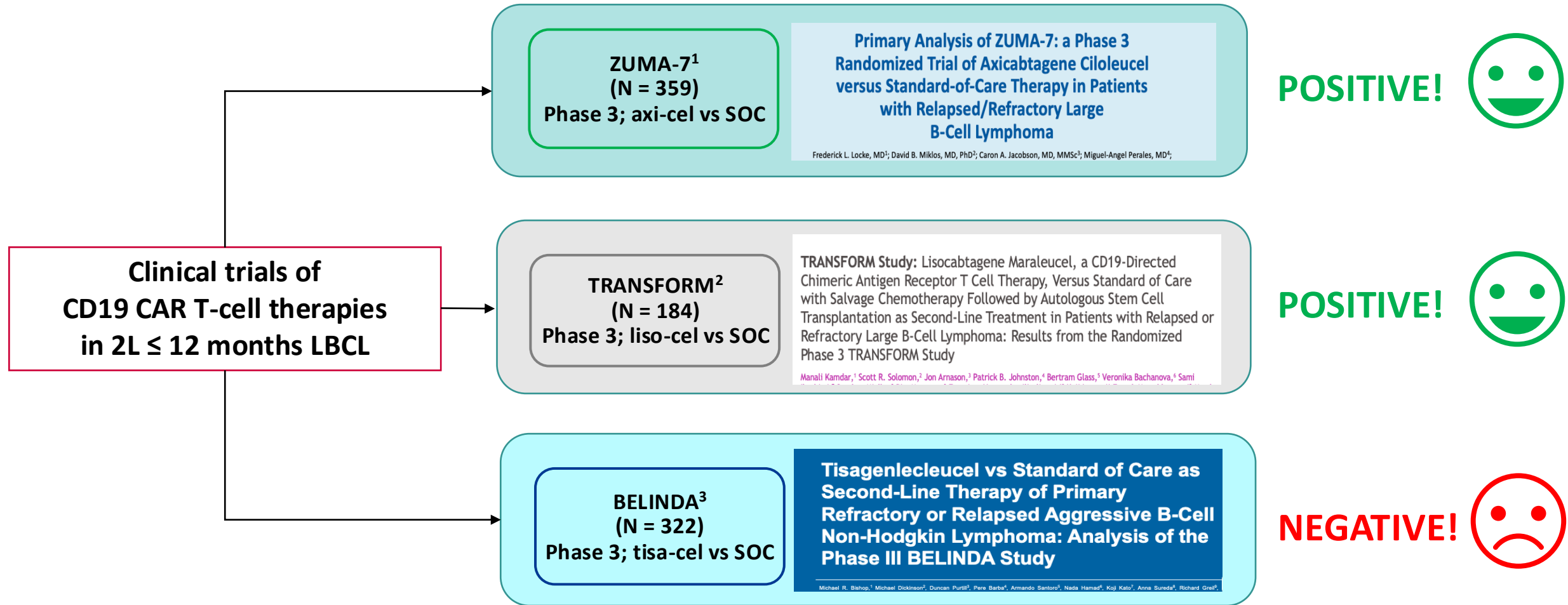
Patients with high tumor burden have lower CART cell expansion³



CART cell fitness is inversely proportional to the number of previous line of therapy → Early referral!

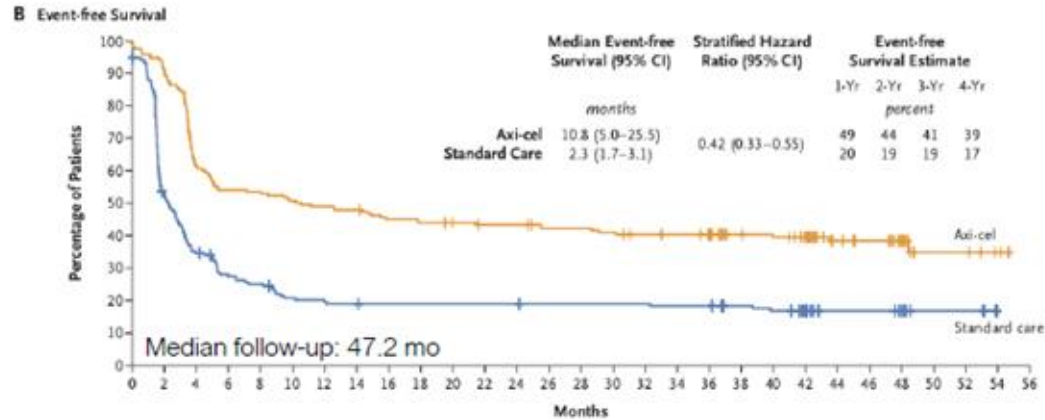
# Prior Lines	Quartile (# Subjects)	Doubling Time	Median CAR AUC _{Dy0-28}	%ORR (n, %)	%Ongoing @12Mth (n, %)
Healthy Donor	n=152	1.34	-	-	
≤2 Lines	Q1 (n=31)	1.42	469.3	28 (90%)	12 (39%)
3 Lines	Q2 (n=29)	1.51	476.6	28 (97%)	10 (34%)
4 Lines	Q3 (n=28)	1.7	491.4	23 (82%)	13 (46%)
≥5 Lines	Q4 (n=12)	1.68	211.0	5 (42%)	3 (25%)

Randomized trials of Chimeric Antigen Receptor (CAR) T-cell therapy versus SOC in transplant-eligible DLBCL with early relapse or primary refractory disease



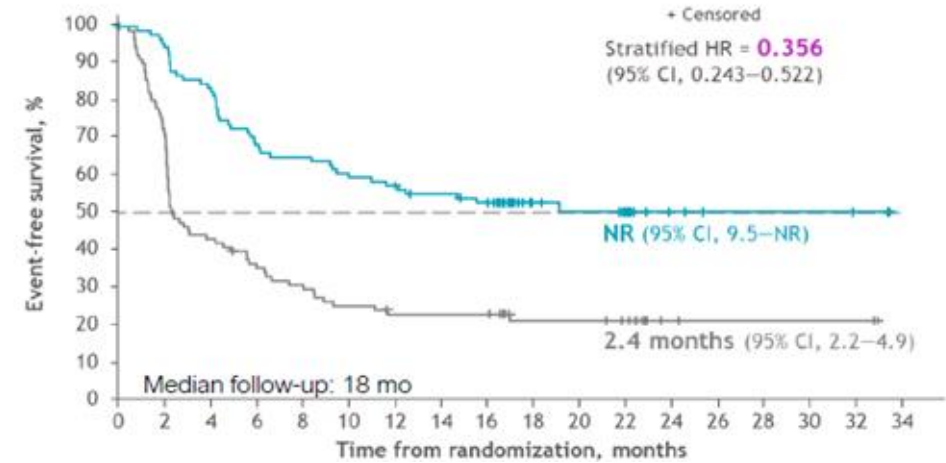
CD19 CAR T vs SoC in 2L LBCL

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 (%)	Liso-cel (n=92)	SoC (n=92)	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

1. Westin JR, et al. New Engl J Med 2023;389:148–57; 2. Locke FL, et al. New Engl J Med 2022;386:640–54; 3. Abramson JS, et al. Blood 2023;141:1675–84; 4. Kamdar M, et al. J Clin Oncol 2025;43:2671–78.

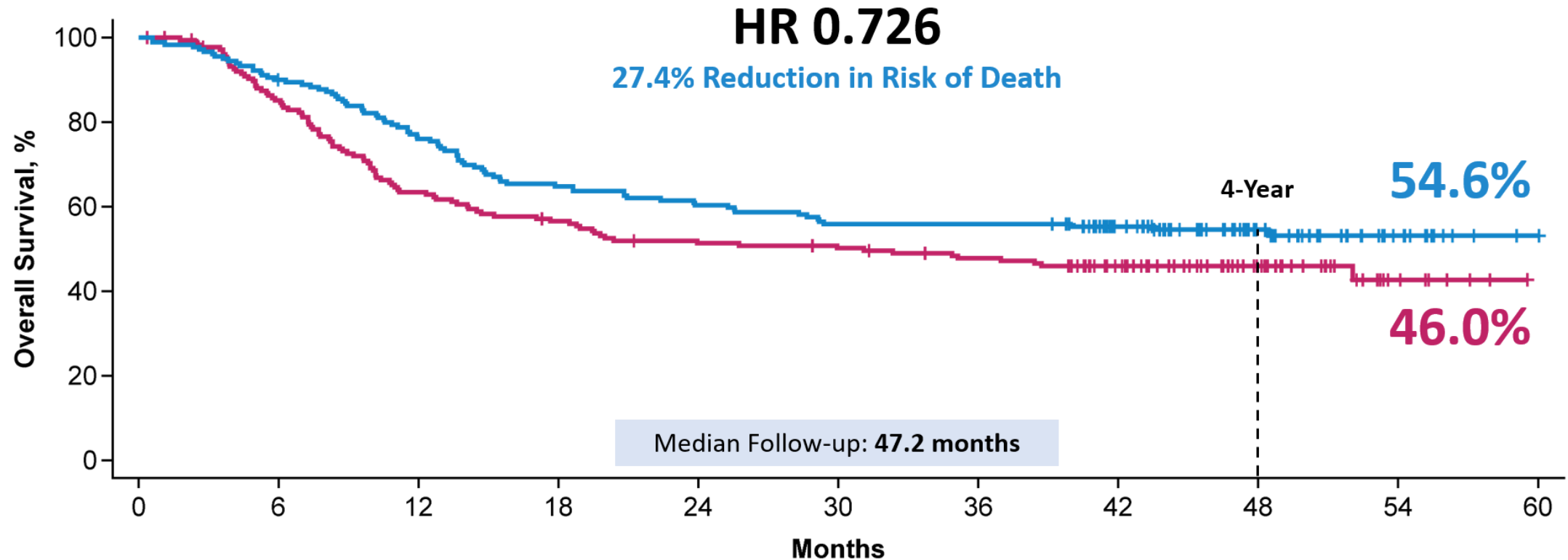


ROMA HEMATOLOGY
CONFERENCE

the lymphomas

Rome Hotel nhow Roma
October 15-16, 2026

Axi-Cel Improved Overall Survival Versus Standard of Care



- 57% (n=102/179) of SOC patients received subsequent cellular immunotherapy (off protocol)
- Despite the increased survival in the SOC arm versus historical studies, axi-cel increased survival over SOC

Westin JR , et al. *N Engl J Med.* 2023;



ROMA HEMATOLOGY
CONFERENCE

2L, second line; HR, hazard ratio; SoC, standard of care.

the lymphomas

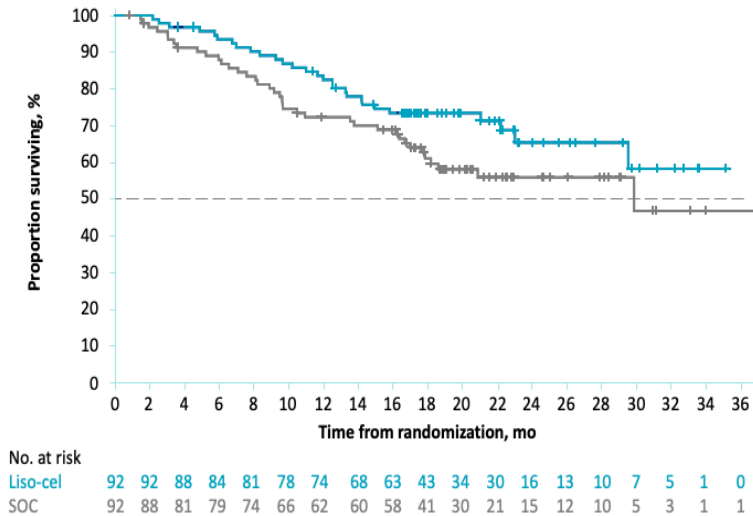
Rome Hotel nhow Roma

October 15-16, 2026

Liso-cel vs. SOC as 2nd line therapy: OS and Crossover

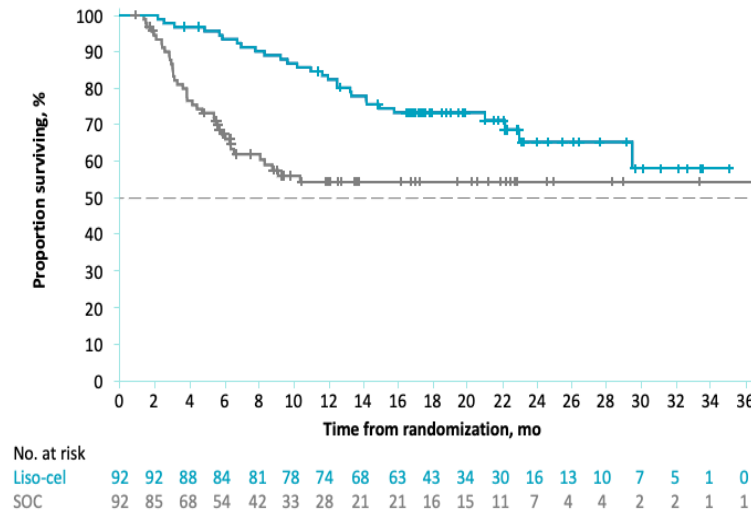
OS

Median NR vs. 29.9 mos
HR 0.724 (0.443—1.183)



OS adjusted for crossover

Median NR vs. NR
HR 0.415 (0.251—0.686)



Crossover subgroup

N=61 (66% of SOC)

	Crossover subgroup (n = 57 treated)
Median f/u	12.0 m (1.4—28.1)
ORR / CRR	61% / 53%
Median EFS	5.9 m (3.1—15.1)
Median PFS	5.9 m (3.2—26.5)
Median OS	15.8 m (11.8—NR)

Median Follow-up: 17.5 mo

Liso-cel associated with improved QOL by PRO

Abramson, et al. Blood 2023



ROMA HEMATOLOGY
CONFERENCE

2L, second line; HR, hazard ratio; SoC, standard of care.

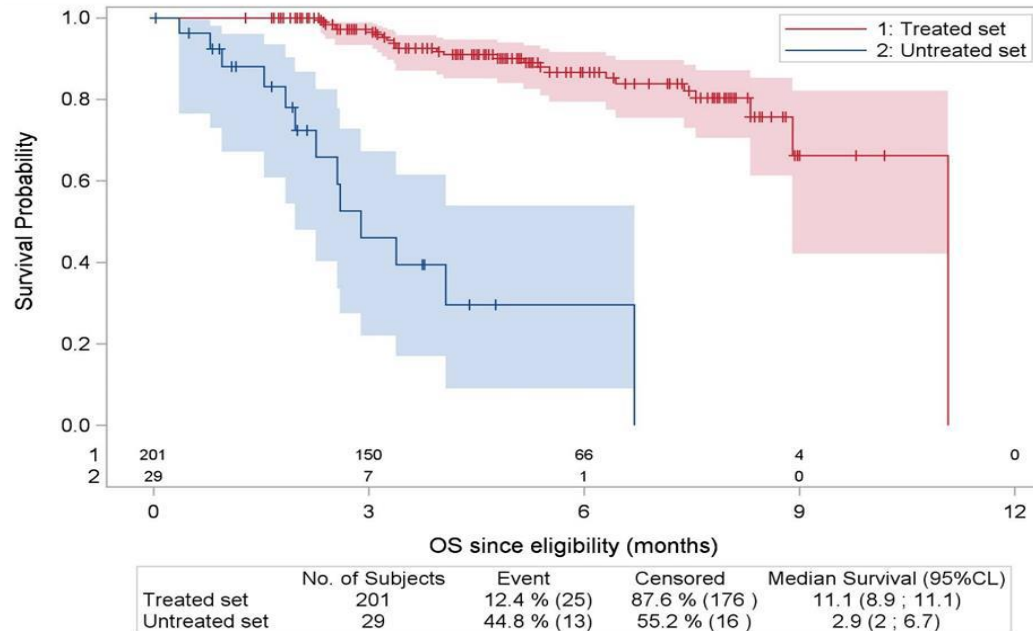
the lymphomas

Rome Hotel nhow Roma

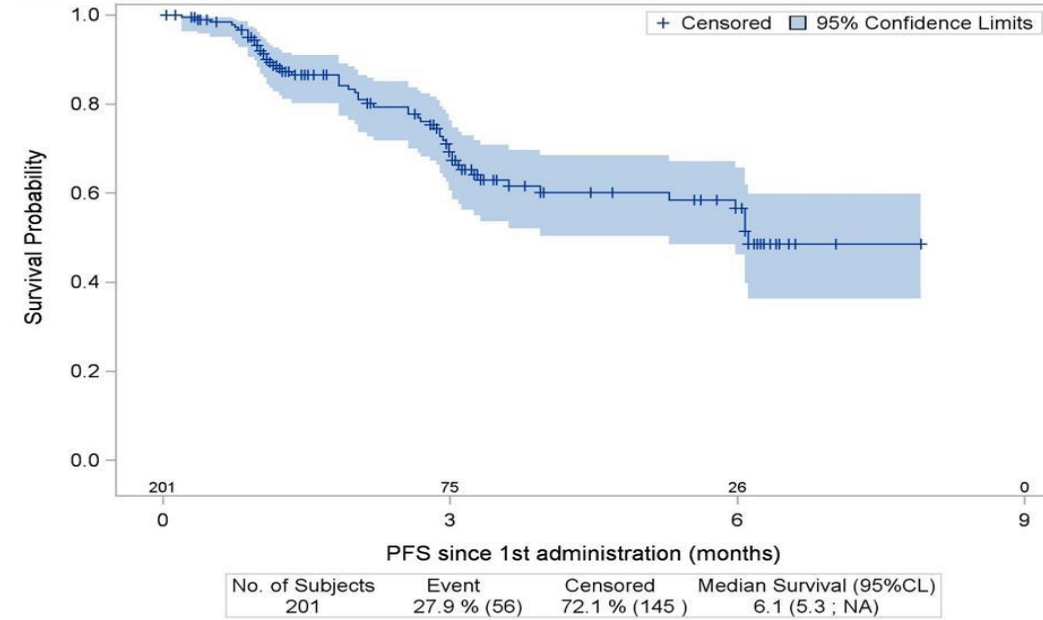
October 15-16, 2026

Second-line axi-cel in LBCL: real-world outcomes

Overall survival according to treatment set
Since treatment decision



PFS since CAR-T infusion



- 201 of 230 patients (87%) received axi-cel after the treatment decision
- Patients who did not reach infusion had poor outcomes, with a median OS of 2.9 months
- Timely referral and an efficient pathway to infusion are key priorities for second-line CAR-T therapy

Brisou et al ASH 2023



ROMA HEMATOLOGY
CONFERENCE

the lymphomas

Rome Hotel nhow Roma
October 15-16, 2026

After CAR-T failure in LBCL: dismal outcome (DESCAR-T)

43%

238 of 550 patients progressed or relapsed

2.7 mo

median time to failure; 23% within day 30

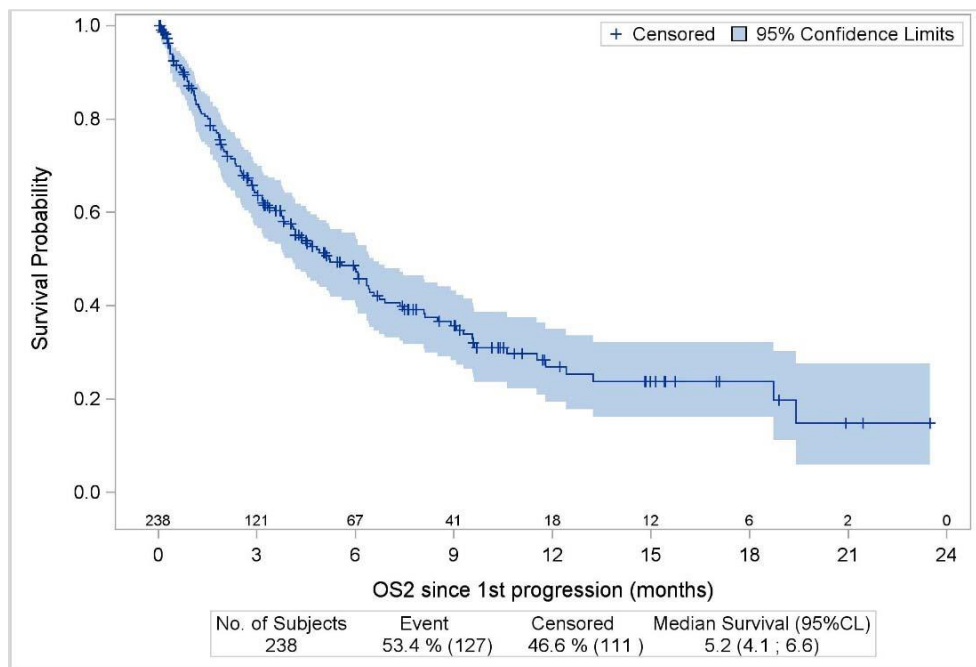
5.2 mo

median OS from failure; 27% alive at 1 year

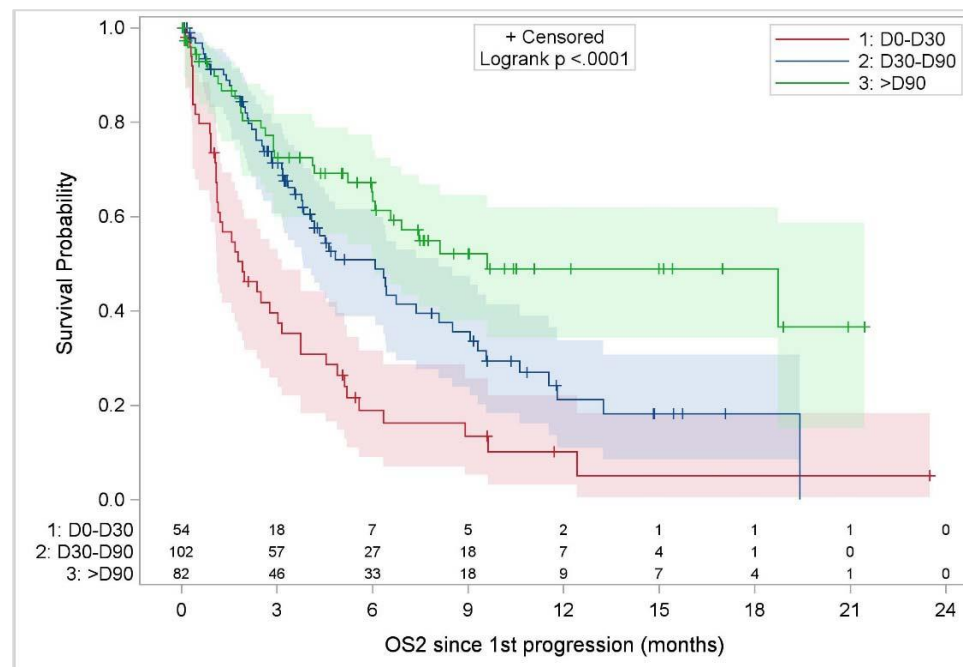
14%

ORR to salvage therapy (CR 6.6%)

Overall survival from failure (n = 238; median follow-up 7.9 mo)



By time of failure: median OS 1.9 vs 6.1 vs 9.6 mo



Predictors of worse OS

(multivariate)

- High LDH at infusion
- Elevated CRP at infusion
- Failure within day 30

Lenalidomide-based salvage associated with better OS (HR 0.42)

Di Blasi R, et al. Blood 2022;140:2584–93. Axi-cel and tisa-cel, French DESCAR-T registry

CAR T-cells in R/R Follicular Lymphoma

Agent and trial	Ph	Pts n	POD24 %	Prior tx median	BT %	V2Vt, days	ORR/CR [^] %	Median f-up, mo	PFS, %	OS, %	CRS (any/ gr ≥3) %	ICANS (any/ gr ≥3) %
Tisa-cel (ELARA)^{1,2,3}	II	97	63	4 (2-13)	45	46*	86 / 68	53	48mo: 50.2	48mo: 79.3	48/0	4/1
Axi-cel (ZUMA-5) ^{4,5}	II	124	56	3 (2-4)	4	40	90 / 75	64.6	60mo: 49.8	60mo: 69%	97/8	56/15
Liso-cel^{6,7} (TRANSCEND-FL)	I/II	101 (3L) 23 (2L)	55	3 (2-10)	38	49	97 / 94	24	12mo: 83	12mo: 93	58/1	15/2

*median time from enrollment to infusion. ^consistent response rates were seen also in those patients with high-risk characteristics

1. Dreyling M. et al. Blood 2024. 2. Fowler N.H. et al, Nature Med 2022, 3. Thieblemont C. et al. ICML 2025; 4 Jacobson A.C. et al, Lancet Oncol 2022; 5 Neelapu S. et al. JCO 2025; 6. Morschauer F et al. Nature 2024 . 7. Nastoupil L. et al. ASH 2024



ROMA HEMATOLOGY
CONFERENCE

2L, second line; HR, hazard ratio; SoC, standard of care.

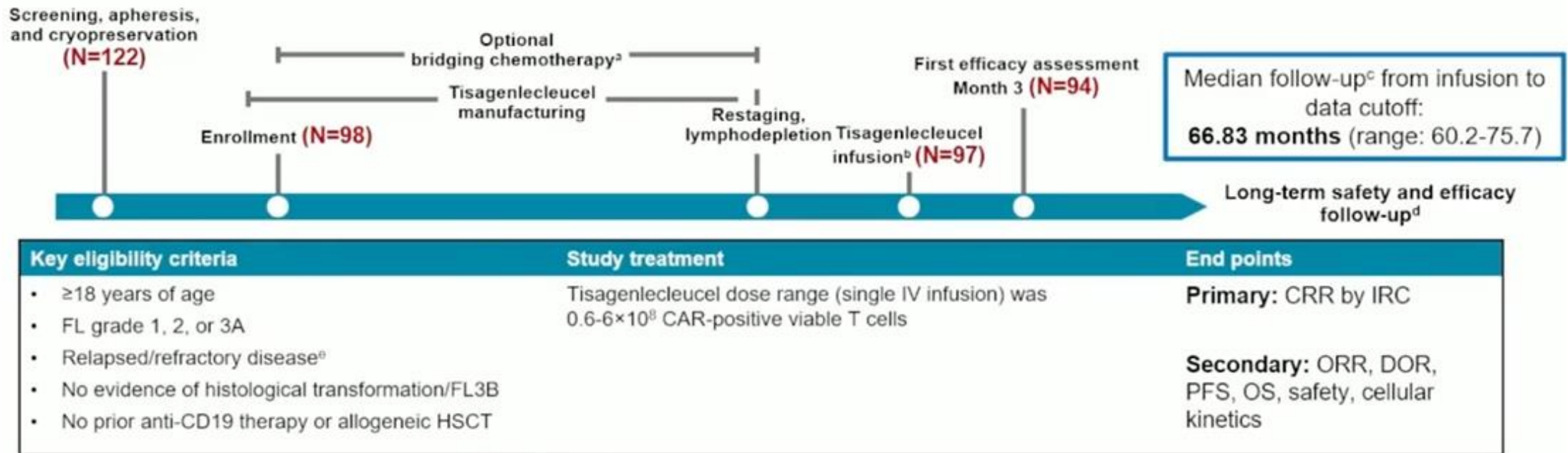
the lymphomas

Rome Hotel nhow Roma

October 15-16, 2026

Clinical Outcomes of Tisagenlecleucel in Patients with Relapsed/Refractory Follicular Lymphoma (r/r FL): Phase 2 ELARA, 5-year update.

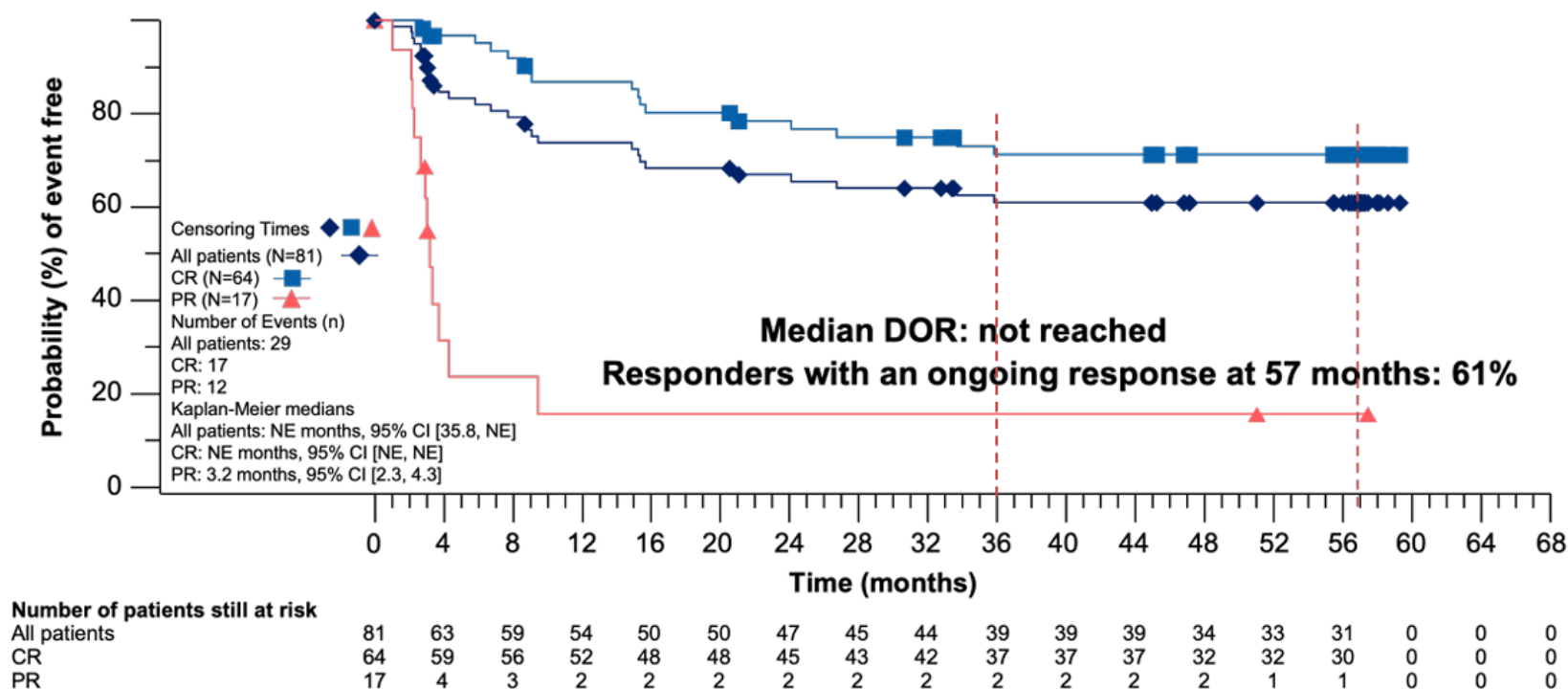
ELARA Study Design



- ✓ 97 patients treated with a single tisa-cel infusion, with a **median follow-up of 66.8 months** to assess long-term efficacy and safety

Schuster S. et al, abs#468

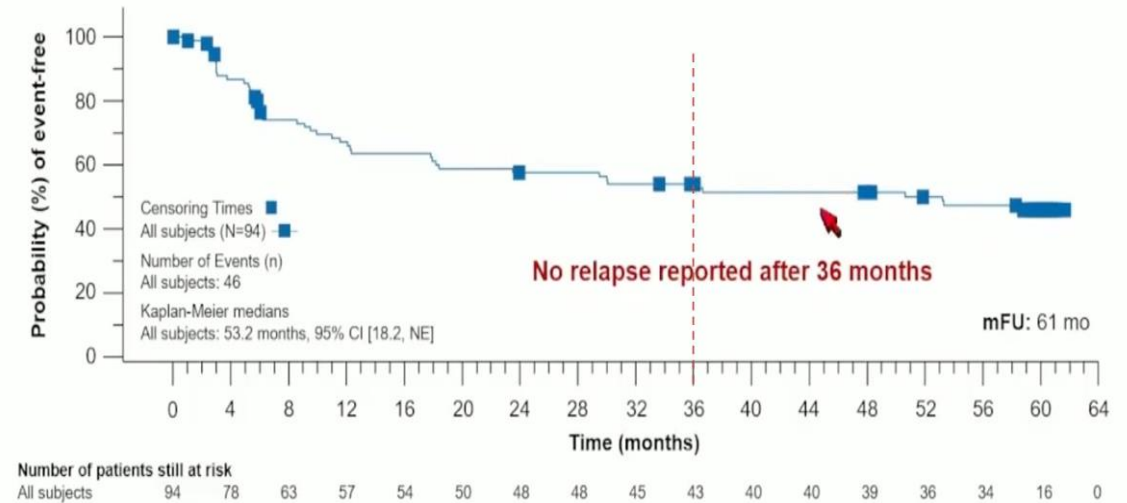
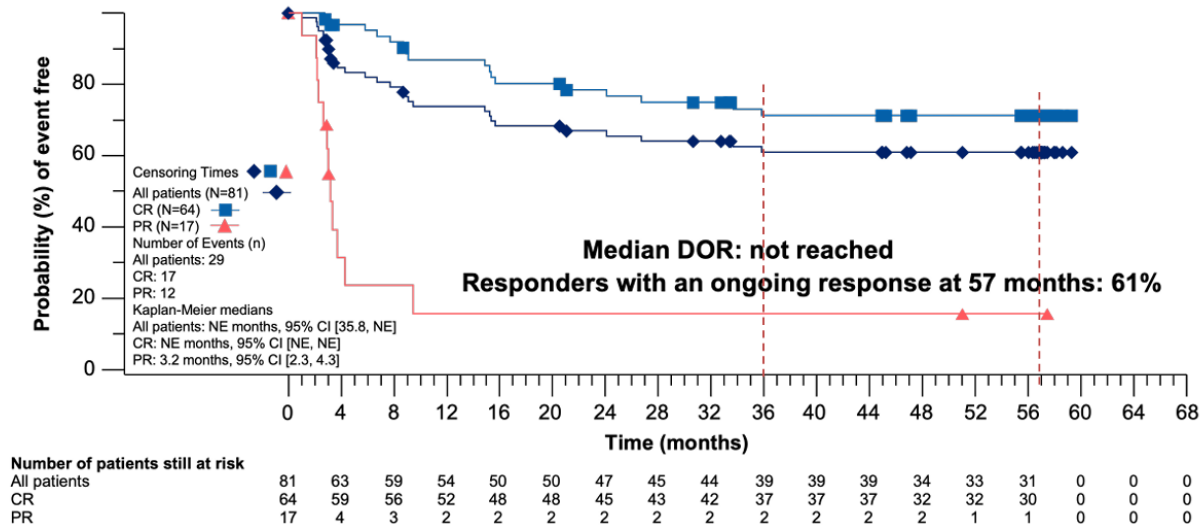
Median Duration of Response was Not Reached



- The probability of maintaining CR/PR response at 48-mo was 61%
- The probability of maintaining CR at 48-mo was 71.2%

Schuster S. et al, abs#468; Thieblemont C et al. Blood. 2024

ELARA: Sustained Remissions at 5 Years After Tisa-cel

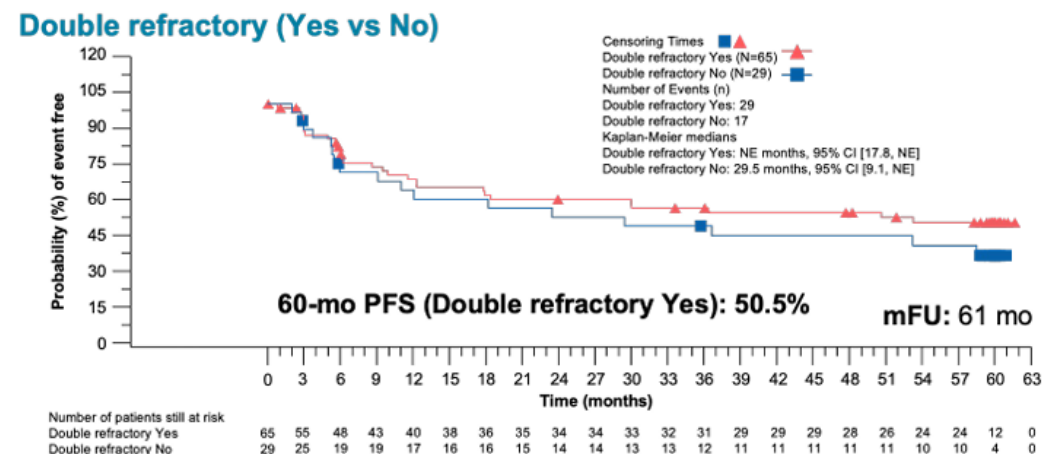
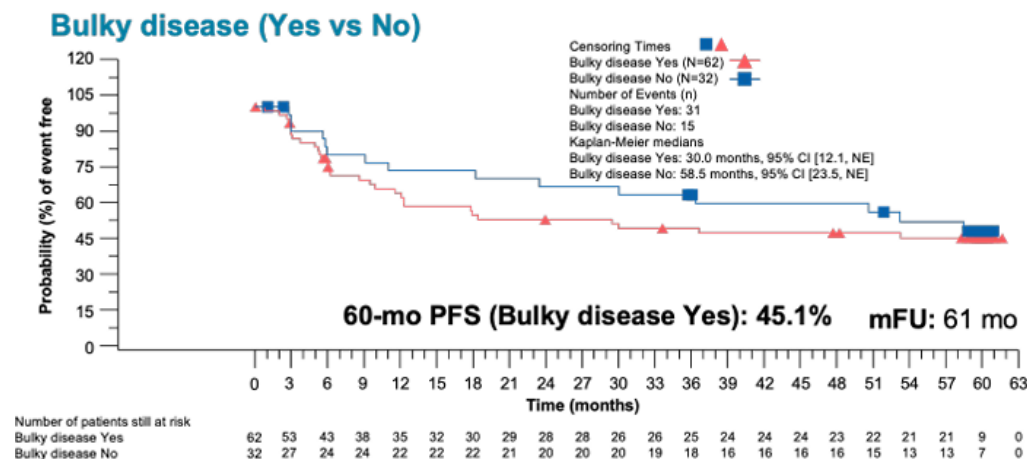
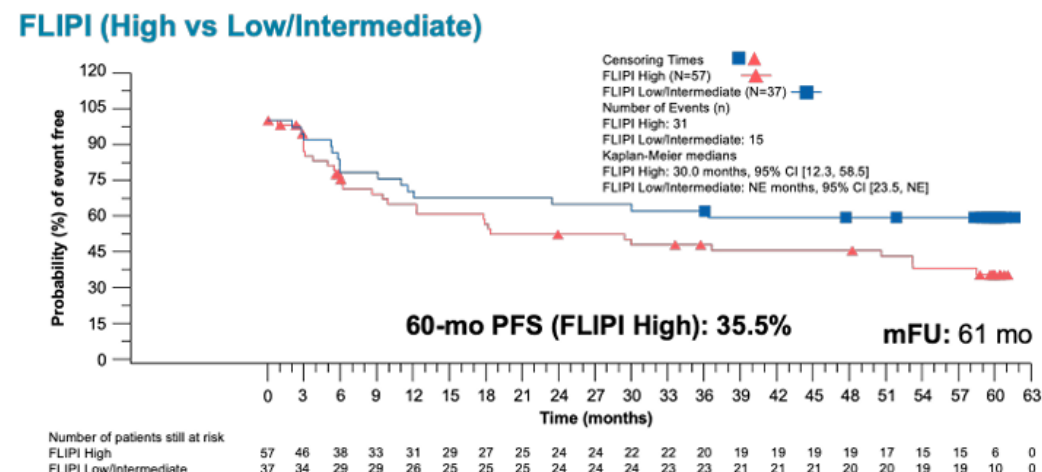
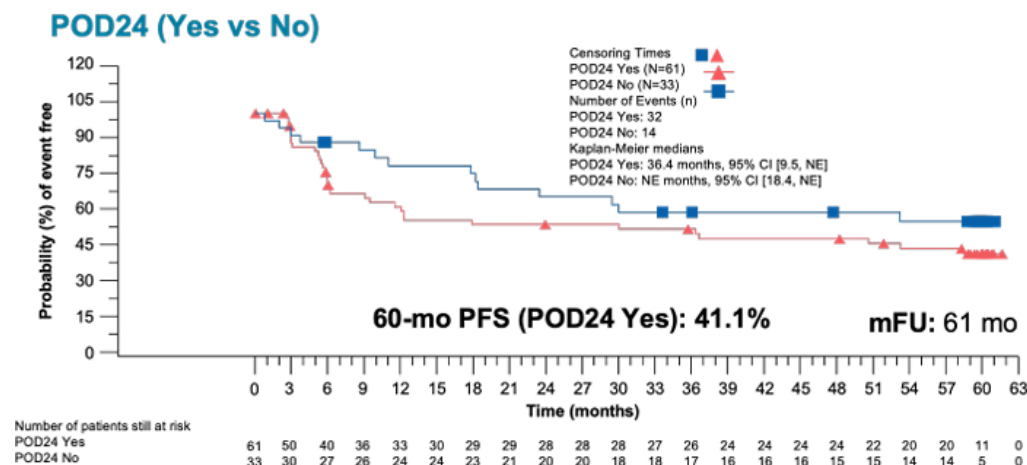


- The probability of maintaining CR/PR response at 48-mo was 61%
- The probability of maintaining CR at 48-mo was 71.2%

- The 60-mo PFS was 46% in all pts, and 59.8% in CR
- The 60-mo OS was 74.1% in all pts, the median OS was NR

Schuster S. et al, abs#468; Thieblemont C et al. Blood. 2024

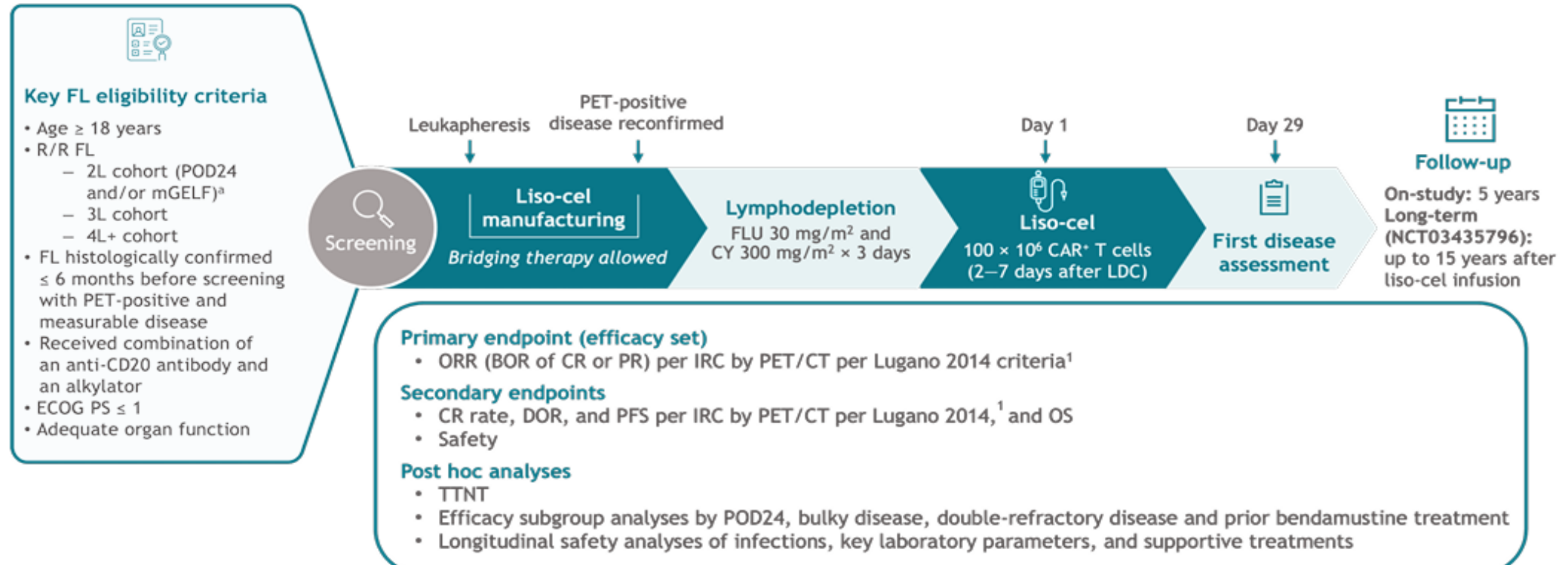
Prolonged and Sustained PFS and OS was Seen Across High-Risk Subgroups



Schuster S. et al, abs#468

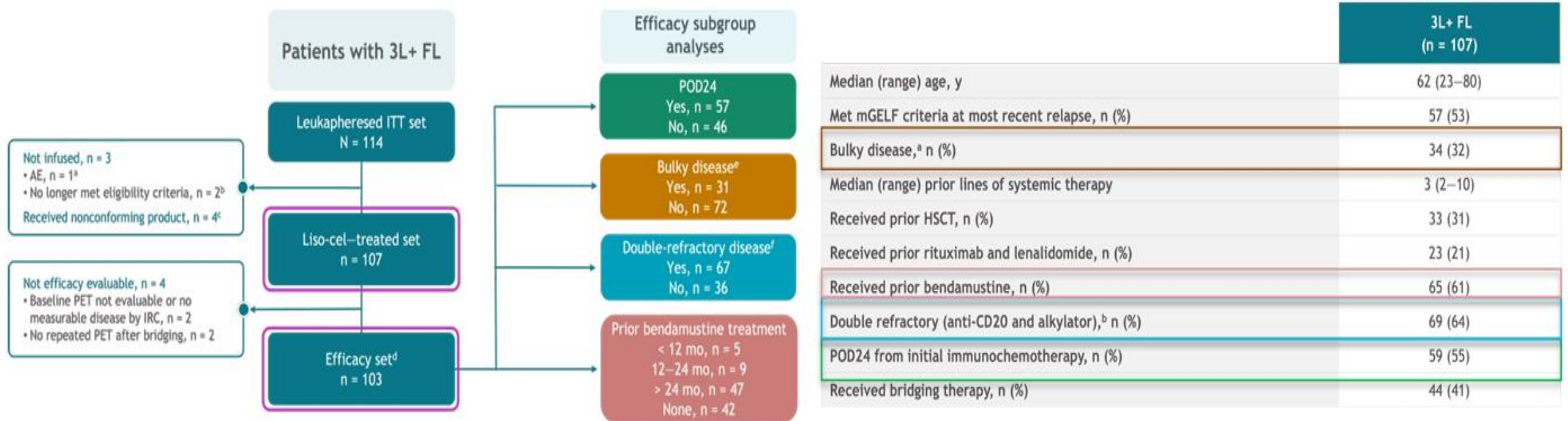
Three-Year Efficacy and Longitudinal Safety of Lisocabtagene Maraleucel in Patients with Third-Line or Later Follicular Lymphoma from TRANSCEND FL

TRANSCEND FL: phase 2, open-label, multicenter, multicohort study



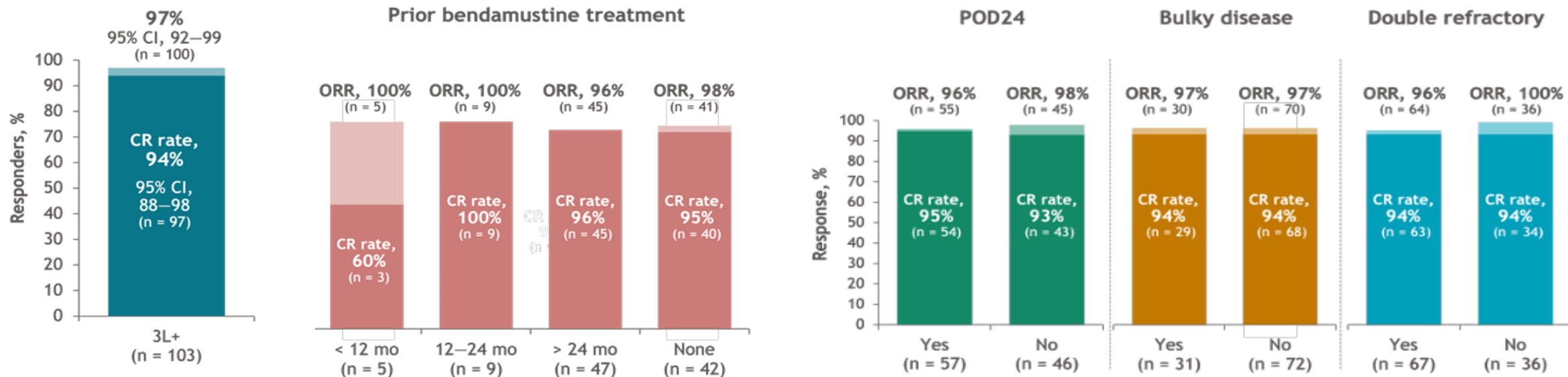
Ahmed S. et al, abs#467

Patients Disposition and Characteristics

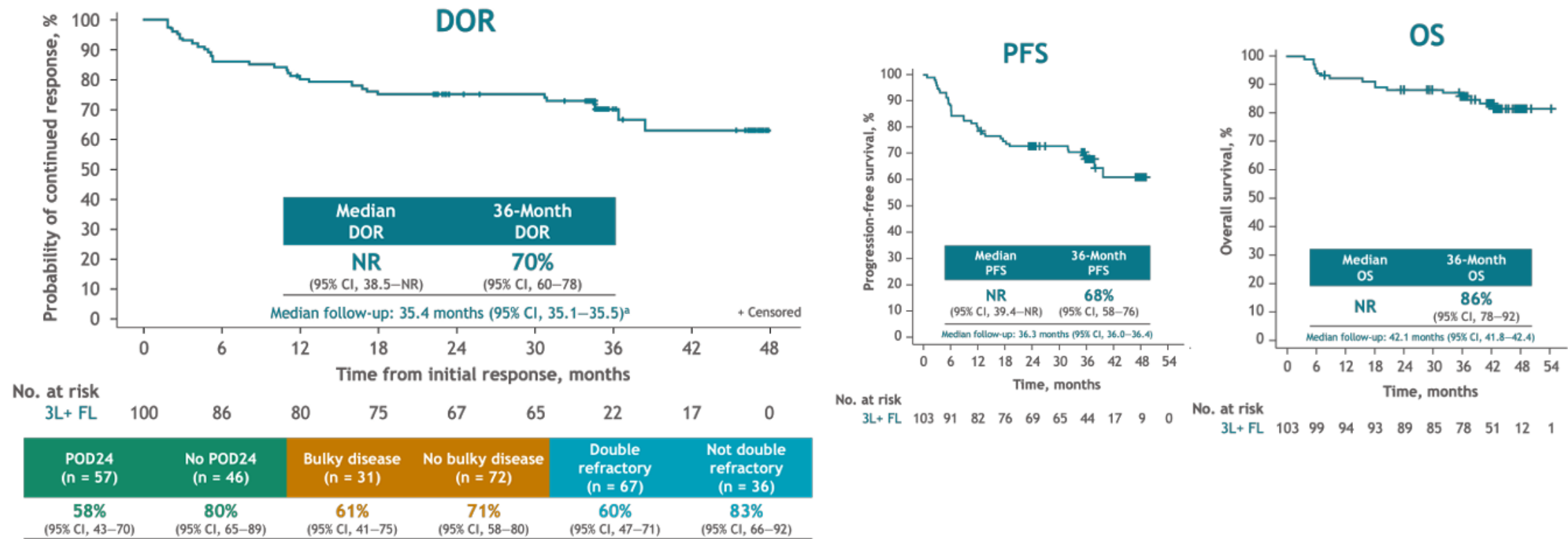


Ahmed S. et al, abs#467

Responses were Deep and Consistent Across Subgroups

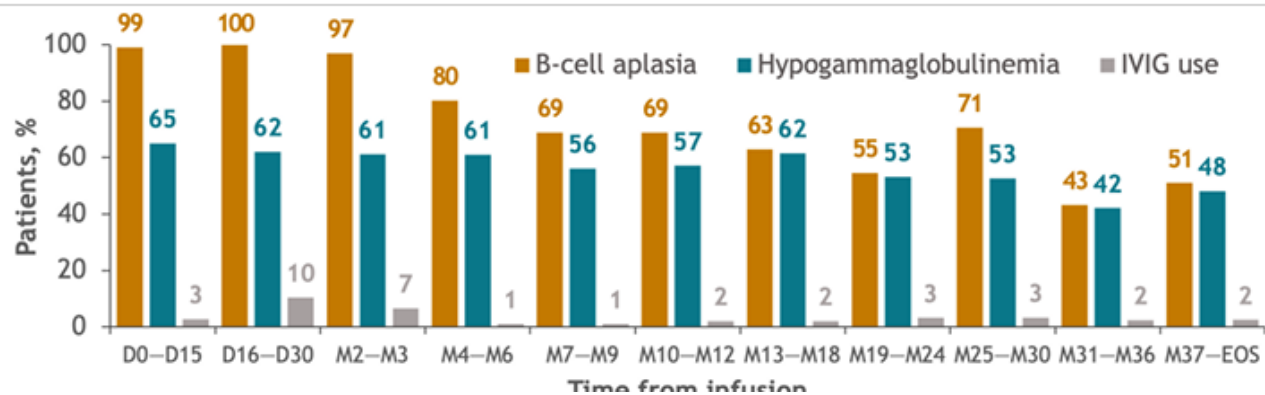
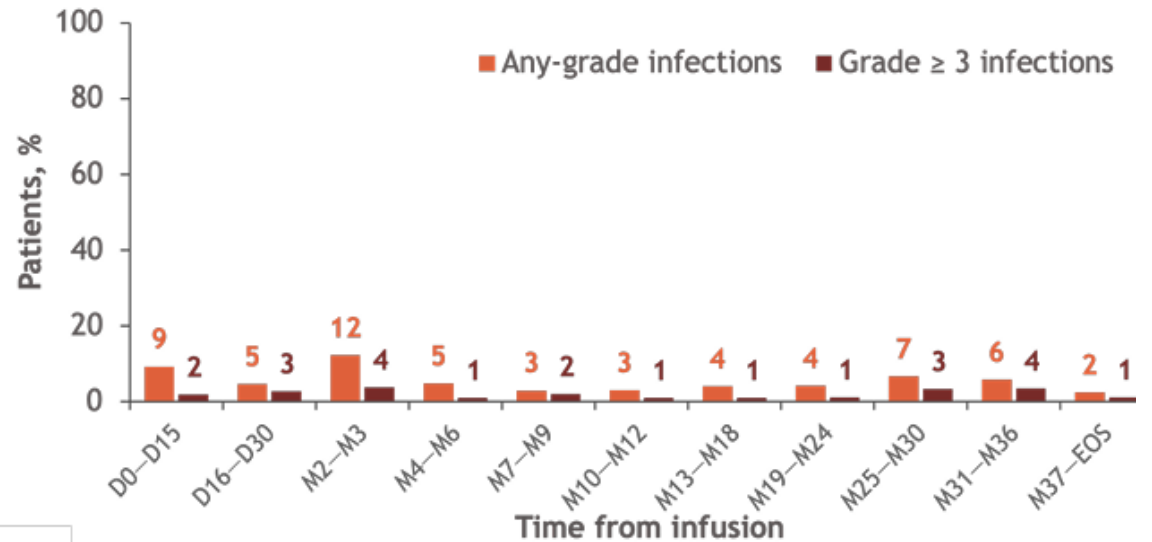
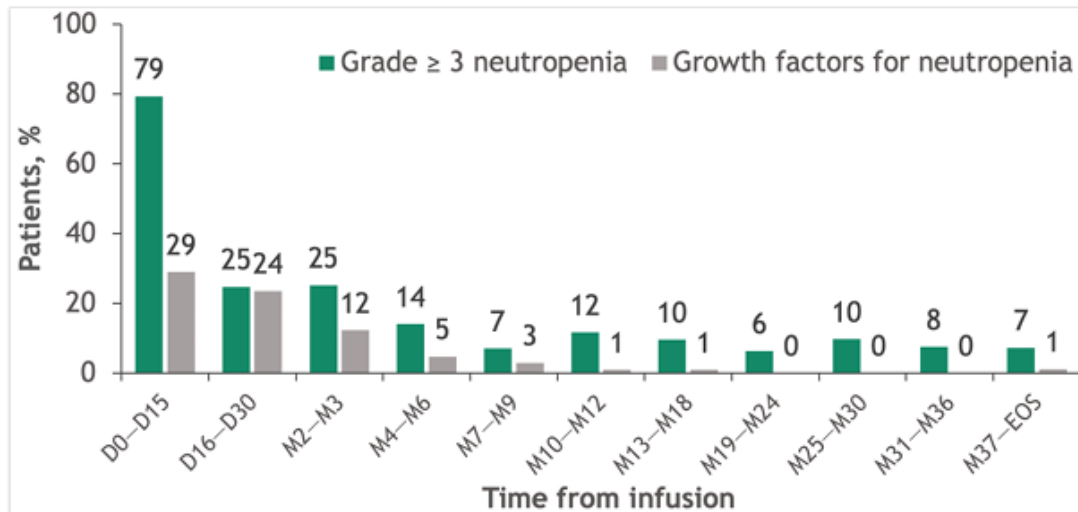


Responses were Durable even in Patients with High-Risk Disease



Ahmed S. et al, abs#467

Liso-cel Showed Favorable Long-term Safety



Use of growth factors, transfusions, and IVIG therapy, n (%)	3L+ FL (n = 107)
Growth factors for neutropenia	54 (50)
Erythropoiesis stimulating agents	5 (5)
RBC transfusions for anemia	24 (22)
Platelet transfusions ^a	16 (15)
IVIG therapy	29 (27)

Ahmed S. et al, abs#467

Conclusions

- CAR T-cell therapy offers curative potential in B-cell lymphomas, with remissions lasting beyond 10 years in a subset of patients.
- In primary refractory or early-relapsing LBCL, axi-cel and liso-cel improve outcomes over conventional salvage therapy, supporting their use in second line.
- Early referral is essential: disease control and timely access to infusion remain major determinants of treatment success.
- In R/R follicular lymphoma, CAR T cells induce deep and durable remissions, including in patients with high-risk disease, with sustained benefit after a single infusion.
- Long-term follow-up remains essential to monitor immune recovery, infections and second primary malignancies.

Grazie



SAPIENZA
UNIVERSITÀ DI ROMA



SISTEMA SANITARIO REGIONALE

AZIENDA OSPEDALIERA UNIVERSITARIA
POLICLINICO UMBERTO I



PROGRAMMA TRAPIANTO REPARTO TERAPIA INNOVATIVE

Anna Paola Iori

Walter Barberi

Sabina Chiaretti

Michela Ansuinelli

Giovanna Palumbo

Luigi Petrucci

Livia Donzelli

Roberto Ricci

*Marta Montanari e tutto il personale
infermieristico*

Gli specializzandi

LABORATORIO :

Maria Stefania De Propriis,

Nadia Peragine, Giulia Radice

UOC IMMUNOEMATOLOGIA E MEDICINA TRASFUSIONALE

Mahnaz Shafii Bafti

Chiara Montagna

Flavia Antonucci

Daniela Carmini

Loredana Piro

Giancarlo Ferrazza

Nadia Cinelli

Serelina Coluzzi

FARMACIA:

Maria Teresa Carretta

Silvia Berlenghini

Giacomo Polito

Enrica Maria Proli

UOD Anestesia e Terapia Intensiva nei Trapianti

Prof. Pugliese e Prof. Ruberto

Sabina Martelli, Paola Celli,

Monica Portieri, Teresa Messina,

Francesco Alessandri

Maria Grazia de Angelis e il

personale infermieristico

Neurologia

Patrizia Pulitano

Cardiologia:

Prof. Vizza

Prof.ssa Chimenti

Dr.ssa Maria Alfarano

Prof. Robin Foà



ROMA HEMATOLOGY
CONFERENCE

the lymphomas

Rome Hotel nhow Roma

October 15-16, 2026

«I have seen further, it is by standing on the shoulders of giants.»

«Se ho visto più lontano, è perché ero sulle spalle di giganti.» ...

Isaac Newton, 1675

Grazie Prof. Martelli