POST-SAN DIEGO 2024
Novità dal Meeting della Società Americana di Ematologia

Novità dal Meeting della Società Americana di Ematologia

Bologna
Palazzo Re Enzo
13-15 Febbraio 2025

COORDINATORI
Angelo Michele Carella
Pier Luigi Zinzani

BOARD SCIENTIFICO
Paolo Corradini
Mauro Krampera
Fabrizio Pane
Adriano Venditti

Enrico Derenzini

CAR-T nel linfoma diffuso a grandi cellule

Divisione di Oncoematologia, Istituto Europeo di Oncologia, Milano
Dipartimento di Scienze della Salute, Università di Milano

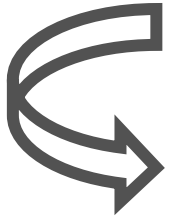
Disclosures of Enrico Derenzini

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Takeda	X					X	
Roche					X	X	
Incyte	X				X		
ADC-Therapeutics	X						
Beigene							X
AbbVie					X	X	
Astra Zeneca						X	
Lilly						X	
Sobi					X	X	
Gilead						X	

GENERAL OVERVIEW

Open issues with CAR-T cell Therapy

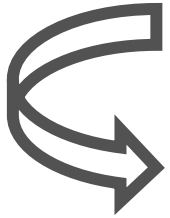
Deliverability in the real world



Efficacy and safety of commercially available products in the real world

- Lisocel 2L
  (Abstr #470, Oral, Dec 8 2024)
- Axicel 2L
  (Abstr #526, Oral, Dec 8 2024
  Abstr #527, Oral, Dec 8 2024)

Brain to Vein time

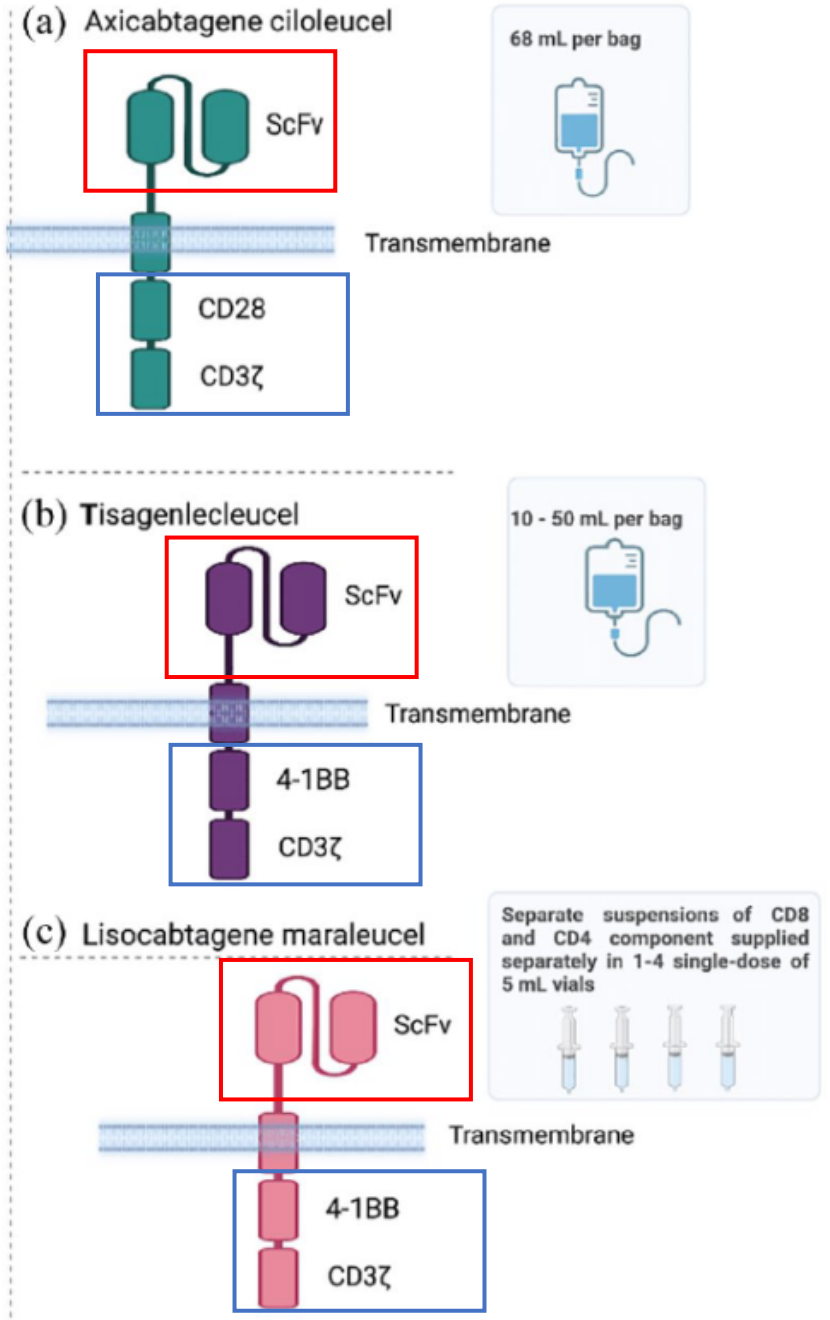


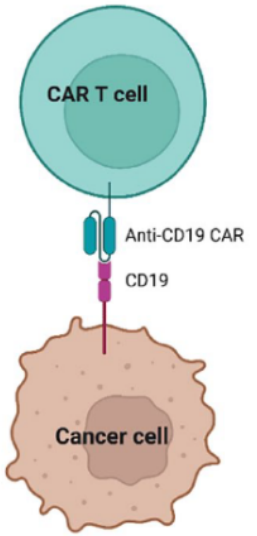
Improving CAR-T manufacturing turnaround time

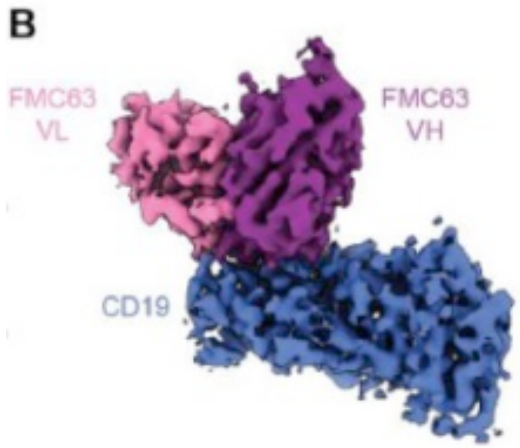
- Rapcabtagene Autoleucel
  (Abstr #67, Oral, Dec 7 2024)
- GLPG5101
  (Abstr #93, Oral, Dec 7 2024)

CAR-T BACKGROUND

	BINDER	VECTOR
AXICEL	FMC63	RETROVIRAL
TISACEL		LENTIVIRAL
LISOCEL		LENTIVIRAL







Albanyan O, et al. Ther Adv Hem 2022

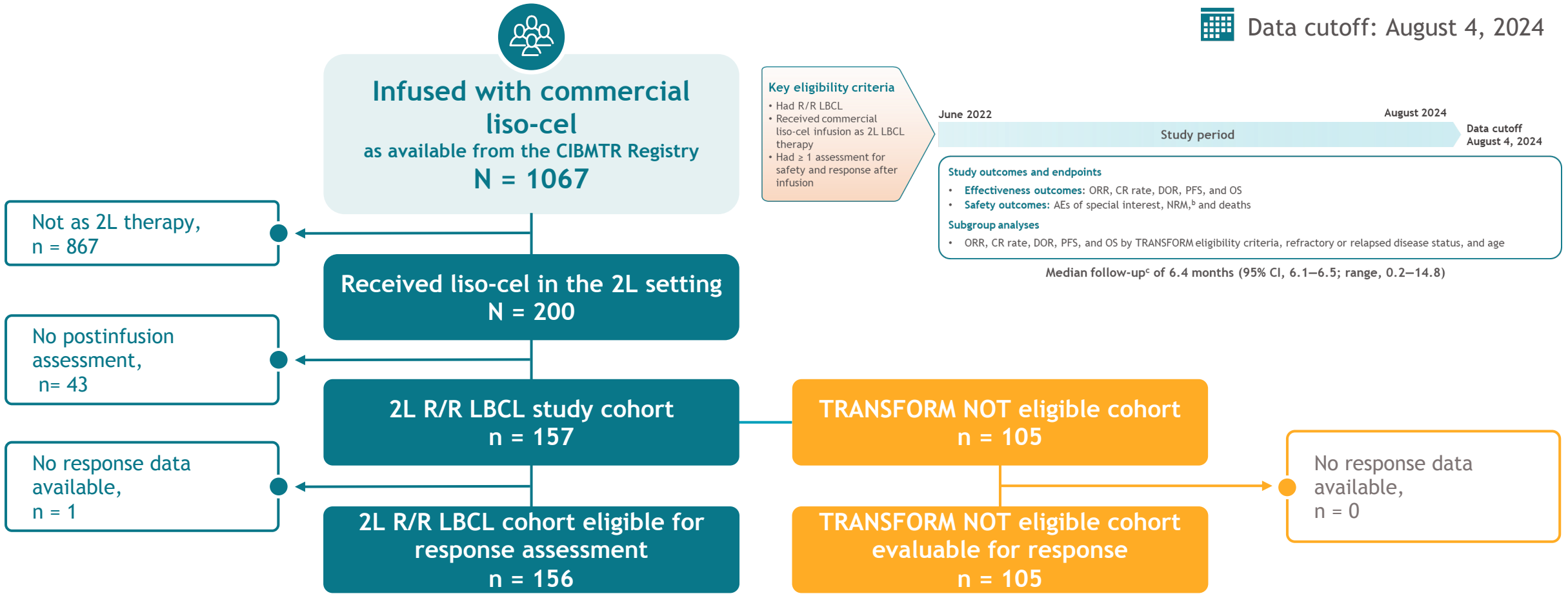
He C, et al. Science Immun 2023

2L CAR-T Results	AXICEL Zuma-7	LISOCEL Transform
TREATED/ ENROLLED	170/180 PTS	89/92 PTS
Median FUP	47m	17m
Bridging R-CHT	No (Dex)	Yes 63% (1 cycle)
Time from Apheresis to infusion	29d	36d
CR RATE	65%	74%
PFS rate	46% at 24m	58% at 18m
Median OS	NR	NR
G3 CRS/ICANS	6%/21%	1%/4%
	Westin et al NEJM 2023	Abramson et al Blood 2023

REAL WORLD OUTCOMES
2L

Real-World Outcomes of Lisocabtagene Maraleucel as Second-Line Therapy in Patients with Relapsed or Refractory Large B-Cell Lymphoma: First Results from the Center for International Blood and Marrow Transplant Research Registry

LISOCEL 2L



Odstrcil Bobillo MS, et al. ASH 2024 [Abstract 470]

Baseline demographics and disease characteristics

LISOCEL 2L

	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)

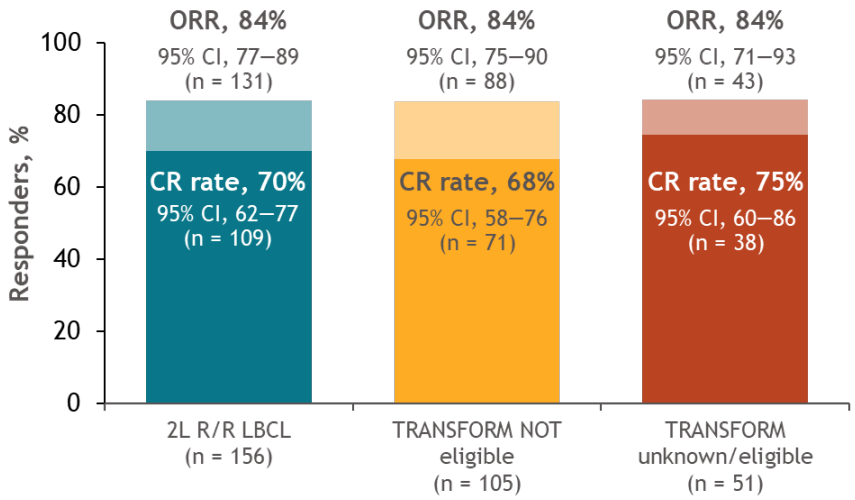
	2L R/R LBCL (n = 157)
ECOG PS, n/N (%)	
0—1	128/135 (95)
2 / 3—4	7/135 (5) / 0
Patients with ≥ 1 comorbidity, n/N (%)	76/126 (60)
Cardiac[d]	34/126 (27)
Pulmonary[d]	22/126 (17)
Obesity[d]	15/126 (12)
Elevated LDH at infusion, n/N (%)	62/151 (41)
Prior therapeutic exposure, n (%)	
Received R-CHOP	137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

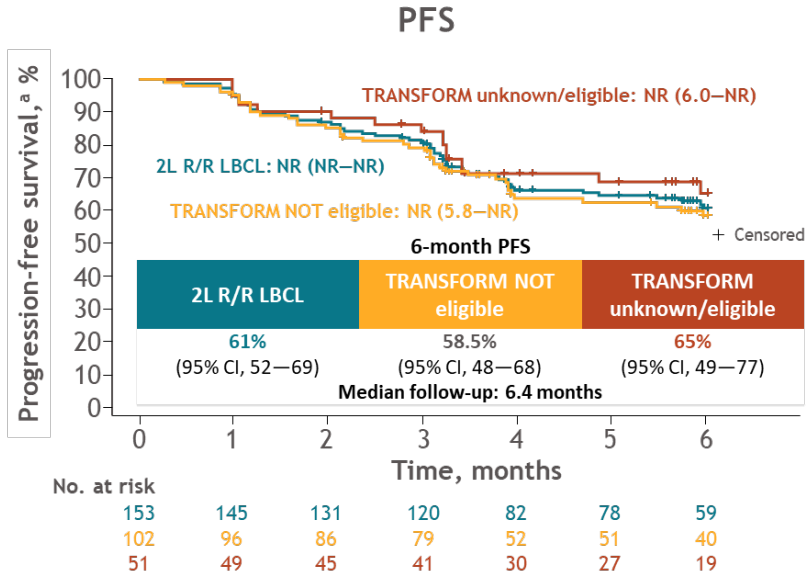
- A total 105 (67%) patients would have been ineligible for TRANSFORM, primarily due to age and/or severity of comorbidities

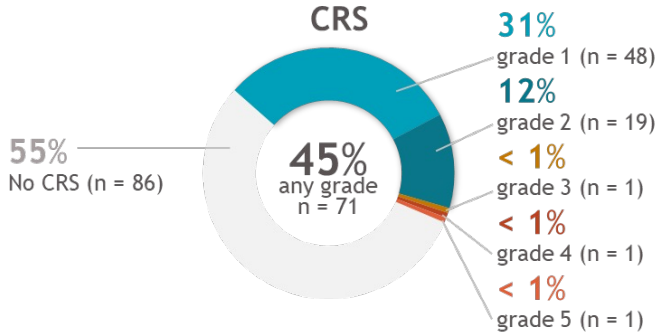
Odstrcil Bobillo MS, et al. ASH 2024 [Abstract 470]

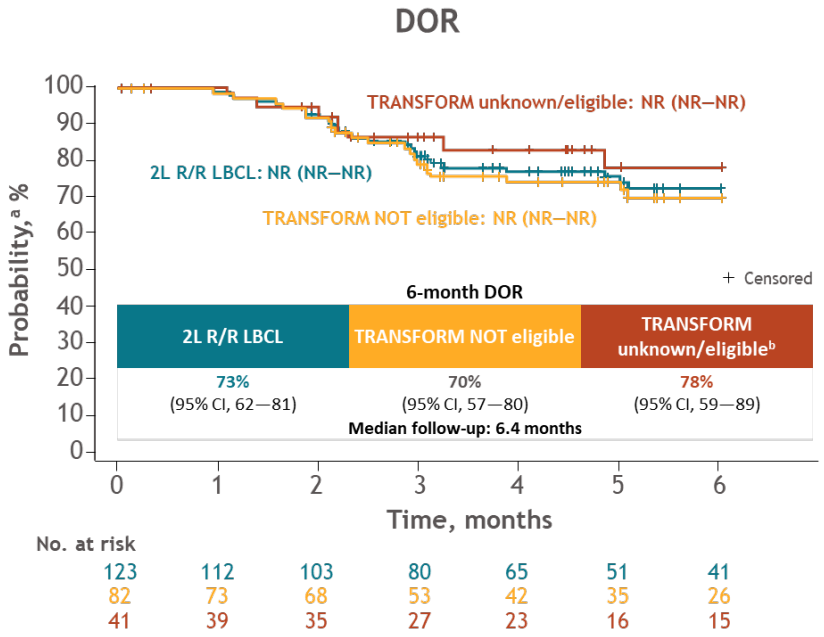
Response rates, duration of response and toxicities

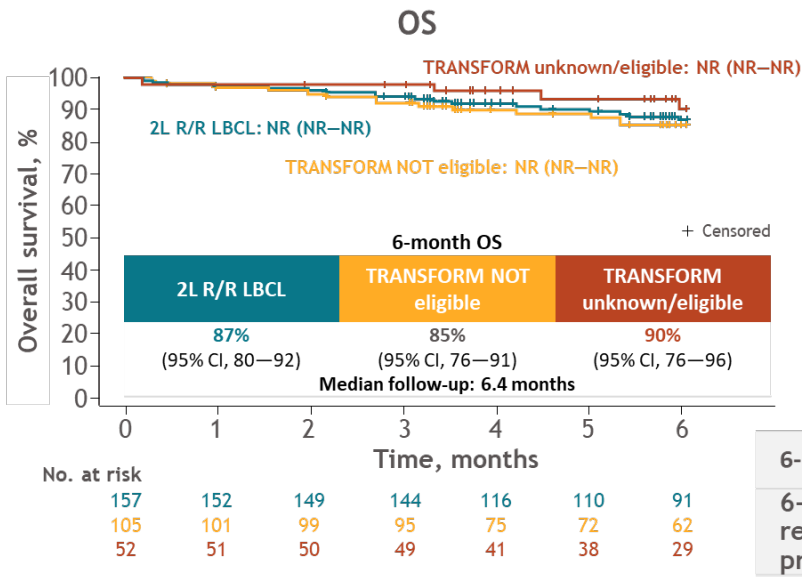
LISOCEL 2L

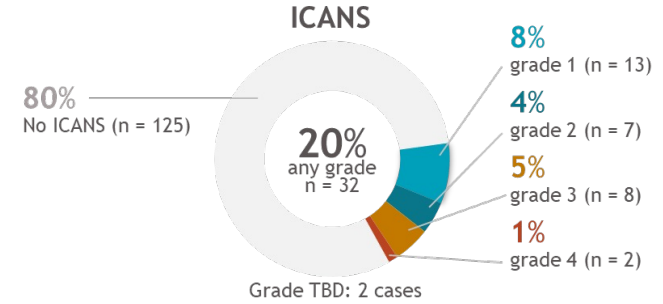












	2L R/R LBCL (n = 157)
6-mo cumulative incidence of NRM (95% CI)	1.3 (0.3—4.3)
6-mo cumulative incidence of relapse/progression or death due to primary disease (95% CI)	37.9 (29.6—46.0)

Odstrcil Bobillo MS, et al. ASH 2024 [Abstract 470]

Real-World Early Outcomes of Second-Line Axicabtagene Ciloleucel Therapy in Patients With Relapsed or Refractory Large B-Cell Lymphoma

AXICEL 2L

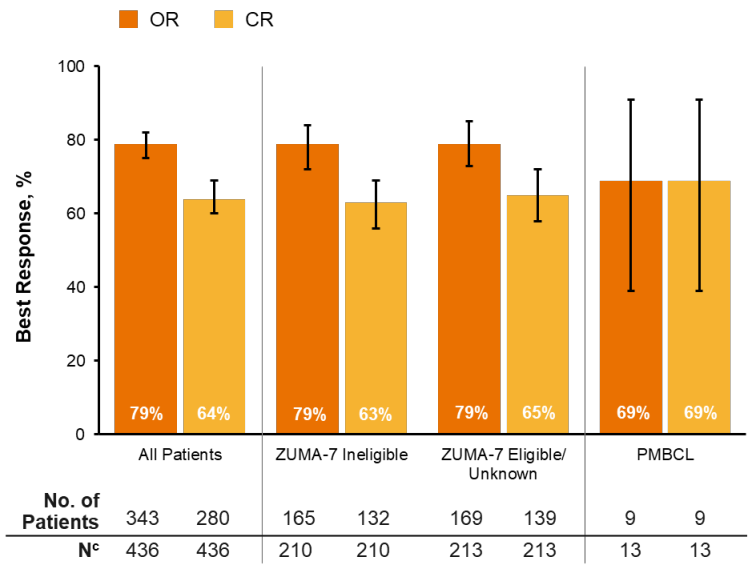
Characteristic	All Patients N=446
ZUMA-7 eligibility,[a] n (%)	
Eligible	214 (48)
Not eligible[b]	219 (49)
Organ impairment	150 (34)
Pulmonary (moderate/severe)	81 (18)
Cardiac	49 (11)
Bone marrow (platelets, ANC, and/or ALC)	37 (8)
Arrhythmia	26 (6)
Cerebrovascular disease	14 (3)
Renal (moderate/severe)	5 (1)
Heart valve disease	4 (<1)
Hepatic (moderate/severe)	1 (<1)
Prior malignancy	70 (16)
Other causes for ineligibility[c]	48 (11)
PMBCL	13 (3)
Transplant ineligible,[d] n (%)	226 (52)

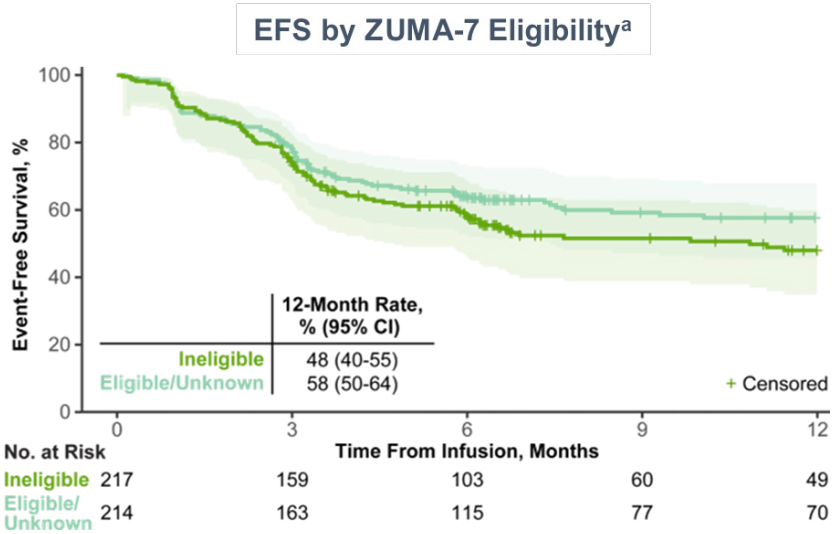
About half the patients would have been ineligible for ZUMA-7, mainly due to organ impairment (34%) and prior malignancy (16%)

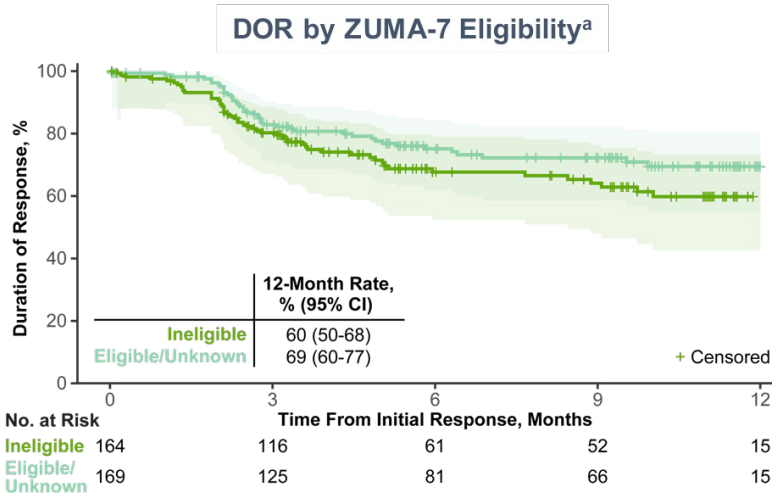
Lee DC, et al. ASH 2024 [Abstract 526]

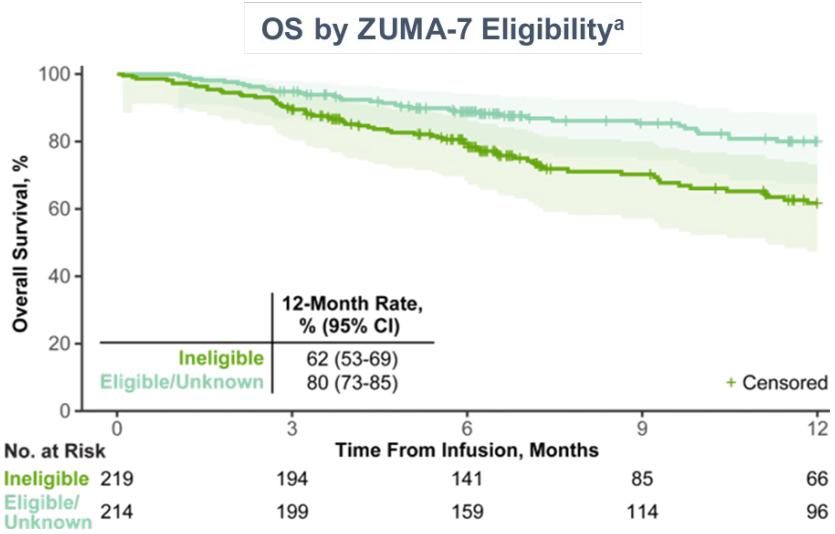
Response rates, duration of response and toxicities

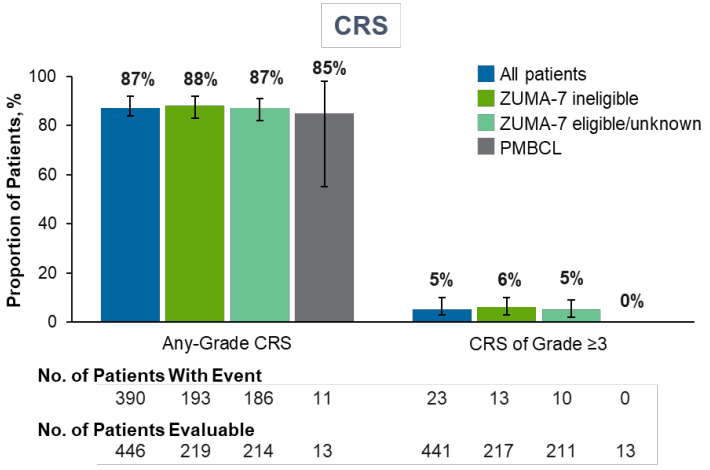
AXICEL 2L

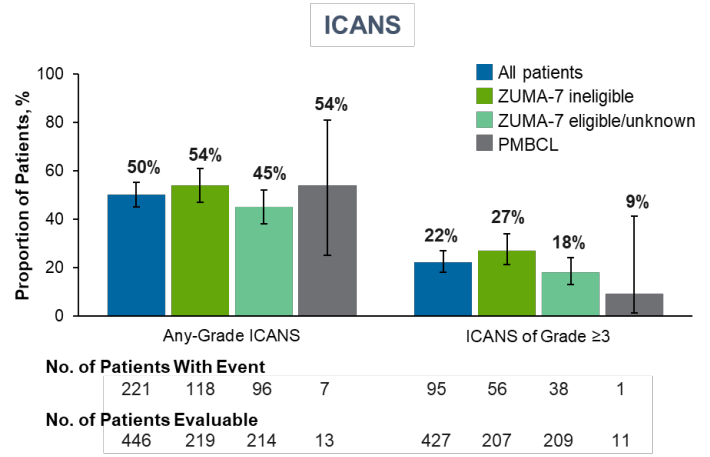












- Prolonged neutropenia and thrombocytopenia occurred in 7% and 11% of all patients, respectively
- Almost half the patients (44%) had clinically significant infections

Lee DC, et al. ASH 2024 [Abstract 526]

Causes of Death and Non-Relapse Mortality

AXICEL 2L

Characteristic	All Patients N=446	ZUMA-7 Eligibility[a]		Patients With PMBCL n=13
		Ineligible n=219	Eligible/ Unknown n=214	
Deaths, n (%)	110 (25)	71 (32)	38 (18)	1 (8)
Primary cause of death among those who died during follow-up,[b] n (%)				
Primary disease	81 (18)	48 (22)	32 (15)	1 (8)
CRS	1 (<1)	1 (<1)	0	0
Neurotoxicity	3 (1)	3 (1)	0	0
Infection	7 (2)	6 (3)	1 (<1)	0
Pulmonary	2 (<1)	1 (<1)	1 (<1)	0
Organ failure	8 (2)	6 (3)	2 (1)	0
Secondary malignancy	2 (<1)	1 (<1)	1 (<1)	0
Other	5 (1)	5 (2)	0	0
Cumulative incidence of non-relapse mortality at 6 months,[c] % (95% CI)	4 (2-6)	7 (4-10)	1 (<1-4)	0 (NE-NE)

- Across all patient populations (median follow-up, 12 months), the primary cause of death was primary disease

Lee DC, et al. ASH 2024 [Abstract 526]

REAL WORLD OUTCOMES
SAFETY

Real-World Trends of Cytokine Release Syndrome and Neurologic Events, and Pattern of Their Management Among Patients Receiving Axicabtagene Ciloleucel for Relapsed or Refractory Large B-Cell Lymphoma in the US: A CIBMTR Report

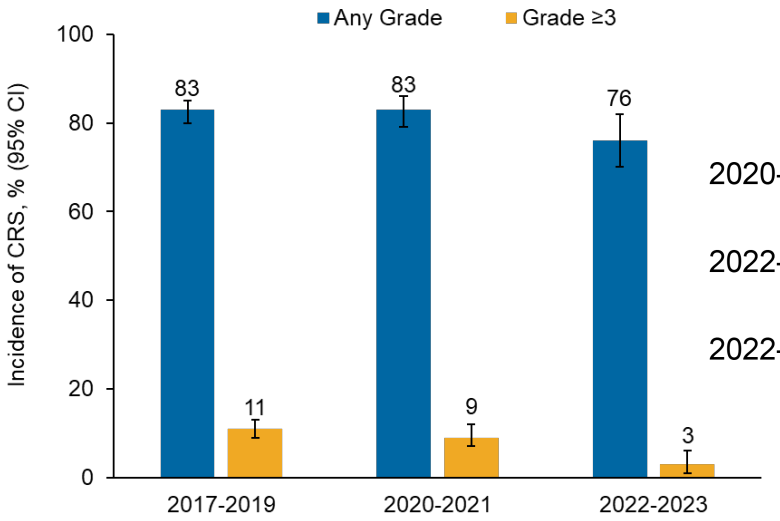
AXICEL

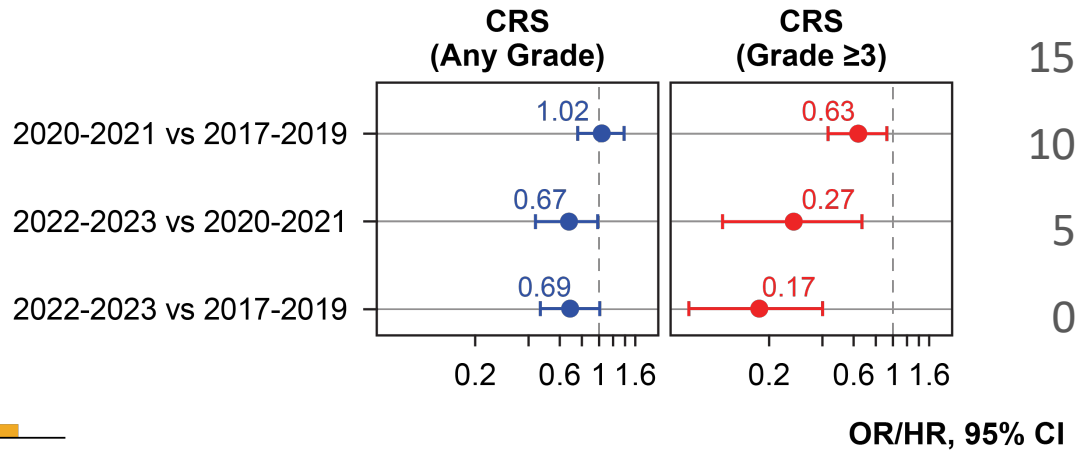
Characteristic	2017-2019 n=923	2020-2021 n=486	2022-2023 n=206
Median age (IQR), years	61.6 (52.9-67.7)	63.1 (55.2-69.6)	63.2 (54.8-70.9)
≥65 years, n (%)	**322 (35)**	**210 (43)**	**91 (44)**
≥70 years, n (%)	163 (18)	116 (24)	59 (29)
ECOG performance status 0-1, n (%)	881 (95)	455 (94)	192 (93)
Clinically significant comorbidity,[a] n/N (%)	684/910 (75)	365/485 (75)	165/206 (80)
Secondary CNS lymphoma, n/N (%)	25/836 (3)	9/456 (2)	9/194 (5)
Number of lines of prior therapies (excluding prior HCT), n (%)			
2 lines	284 (31)	159 (33)	63 (31)
3 lines	311 (34)	155 (32)	70 (34)
4 or more lines	328 (36)	172 (35)	73 (35)
Prior HCT,[b] n (%)	**274 (30)**	**103 (21)**	**40 (19)**
Response to last line of therapy prior to leukapheresis			
Relapse, n/N reported (%)	125/809 (15)	63/401 (16)	32/153 (21)
Refractory, n/N reported (%)	684/809 (85)	338/401 (84)	121/153 (79)
Received bridging therapy, n (%)	**310 (34)**	**203 (42)**	**119 (58)**
Received single-agent bendamustine for lymphodepletion, n (%)	1 (<1)	0 (0)	33 (16)

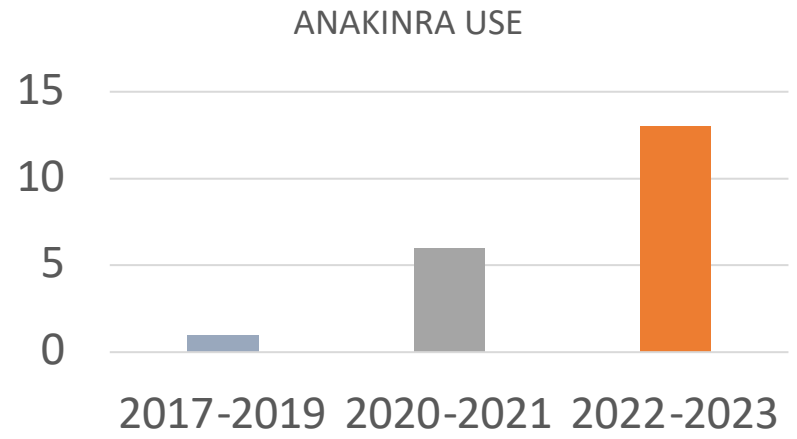
Wang J, et al. ASH 2024 [Abstract 527]

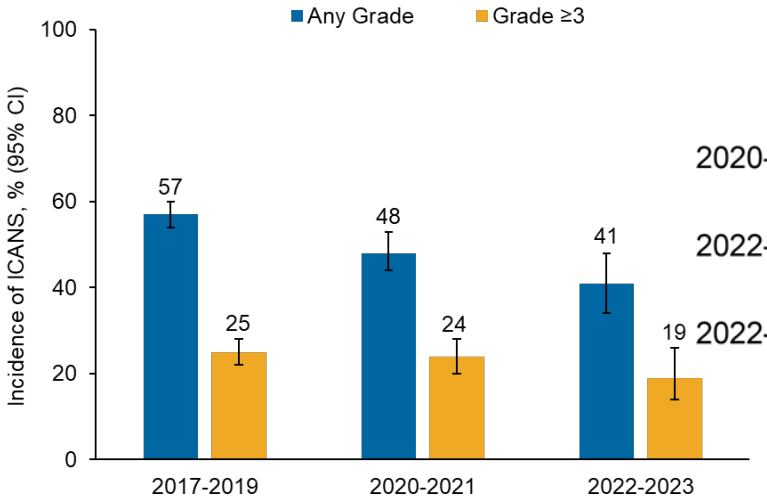
Real-World Trends of Cytokine Release Syndrome and Neurologic Events, and Pattern of Their Management Among Patients Receiving Axicabtagene Ciloleucel for Relapsed or Refractory Large B-Cell Lymphoma in the US: A CIBMTR Report

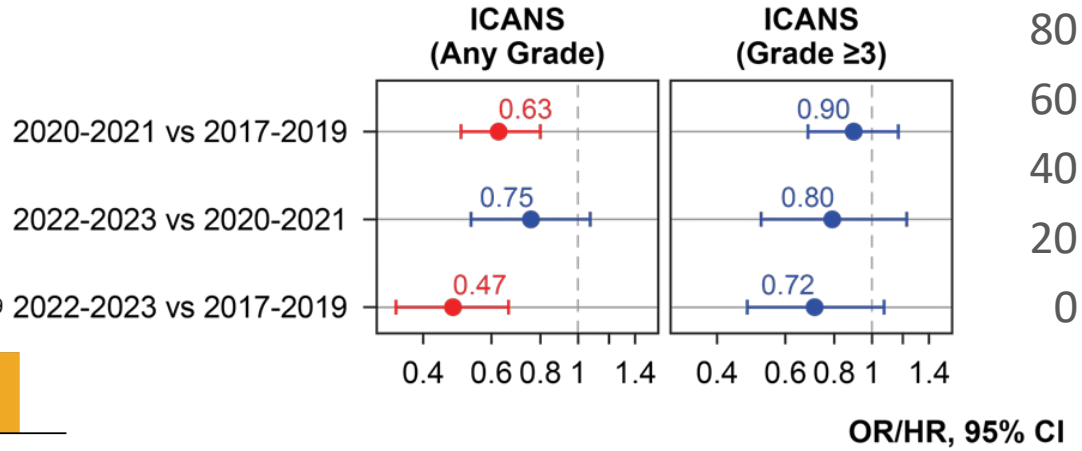
AXICEL

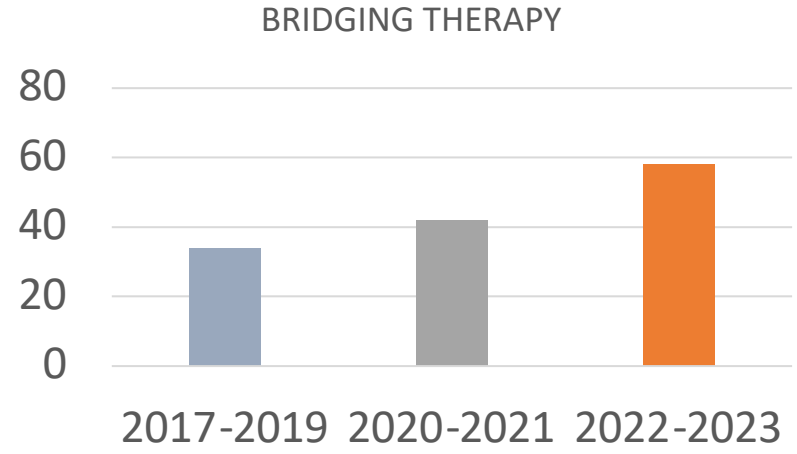










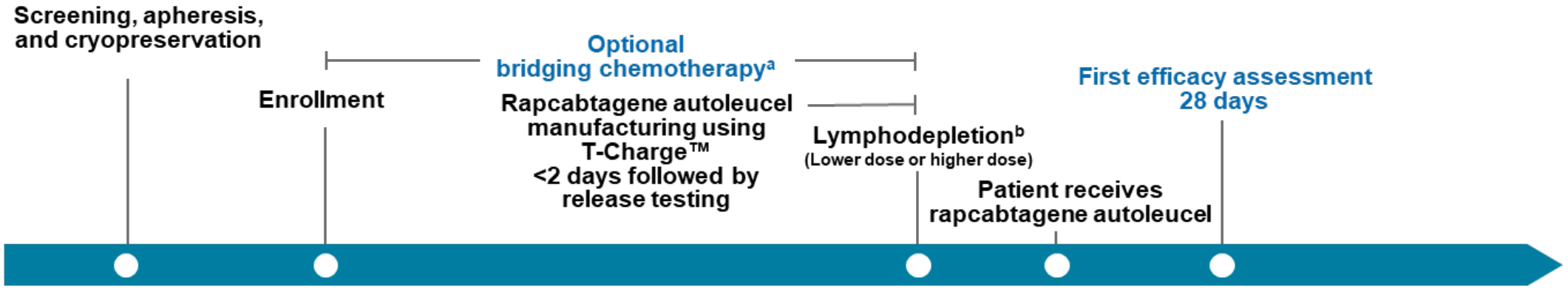


Wang J, et al. ASH 2024 [Abstract 527]

IMPROVING CAR-T TURNAROUND TIME WITH FAST MANUFACTURING

RAPCABTAGENE AUTOLEUCEL (YTB323) IN PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA: PHASE 2 TRIAL CLINICAL UPDATE

RAPCABTAGENE AUTOLEUCEL

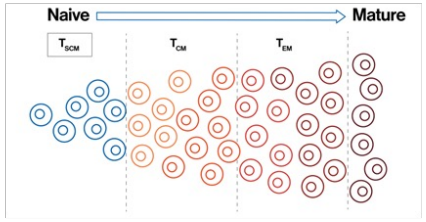


Key eligibility criteria	Study treatment	End points
• ≥18 years of age • Measurable disease at enrollment • ECOG PS 0-1 • Relapsed/refractory disease[c]	• Rapcabtagene autoleucel single IV dose at 12.5×10^6 CAR+ cells	**Primary:** CRR (BOR of CR)

Rapcabtagene autoleucel is a next-generation anti-CD19 CAR-T cell therapy **manufactured on the T-Charge™ platform** that

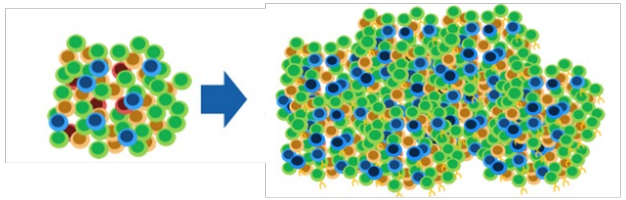
preserves T cell stemness[1-4]

increasing the stem and central memory T cells[3]



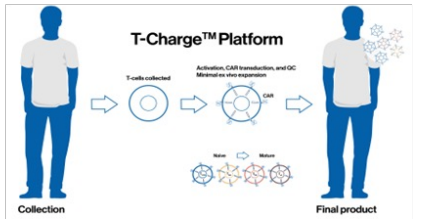
enhances in vivo expansion[4]

with the potential of high response rates that are durable



has < 2 days manufacturing time[4]

and aim for <10 days door-to-door time in the US



Riedell PA, et al. ASH 2024 [Abstract 67]

RAPCABTAGENE AUTOLEUCEL (YTB323) IN PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA: PHASE 2 TRIAL CLINICAL UPDATE

RAPCABTAGENE AUTOLEUCEL

PATIENTS CHARACTERISTICS

Baseline variable	All infused (N = 63)[a]
Median age, years (range)	64.0 (26.0-81.0)
≥65 y, n (%)	29.0 (46.0)
IPI score, n (%)	
<3	34.0 (54.0)
≥3	24.0 (38.1)
Unknown	5.0 (7.9)
Rearrangements in *MYC/BCL2/BCL6* genes, n (%)	
Double/triple hits	16.0 (25.4)
Negative	25.0 (39.7)
Unknown	22.0 (34.9)
Relapsed/refractory disease status, n (%)	
Refractory to last line of therapy	37.0 (58.7)
Refractory to all prior lines	13.0 (20.6)
Relapsed after last line of therapy	26.0 (41.3)
Histology, n (%)	
DLBCL	52.0 (82.5)
Transformed lymphoma	8.0 (12.7)
Elevated LDH (>ULN), n (%)	27.0 (42.9)
Prior HCT, n (%)	19.0 (30.2)
Prior lines of therapy, n (%)	
2	46.0 (73.0)
≥3	17.0 (27.0)
Received bridging therapy, n (%)	38.0 (60.3)

TOXICITIES

	Rapcabtagene autoleucel 12.5×10^6 (N = 63)
CRS[a], n (%)	28.0 (44.4)
Grade 1	17.0 (27.0)
Grade 2	7.0 (11)
Grade 3	**2.0 (3.2)**
Grade 4	**2.0 (3.2)**
ICANS[a], n (%)	
Grade 1	2.0 (3.2)
Grade 2	0.0
Grade 3	**2.0 (3.2)**
Grade 4	**1.0 (1.6)**

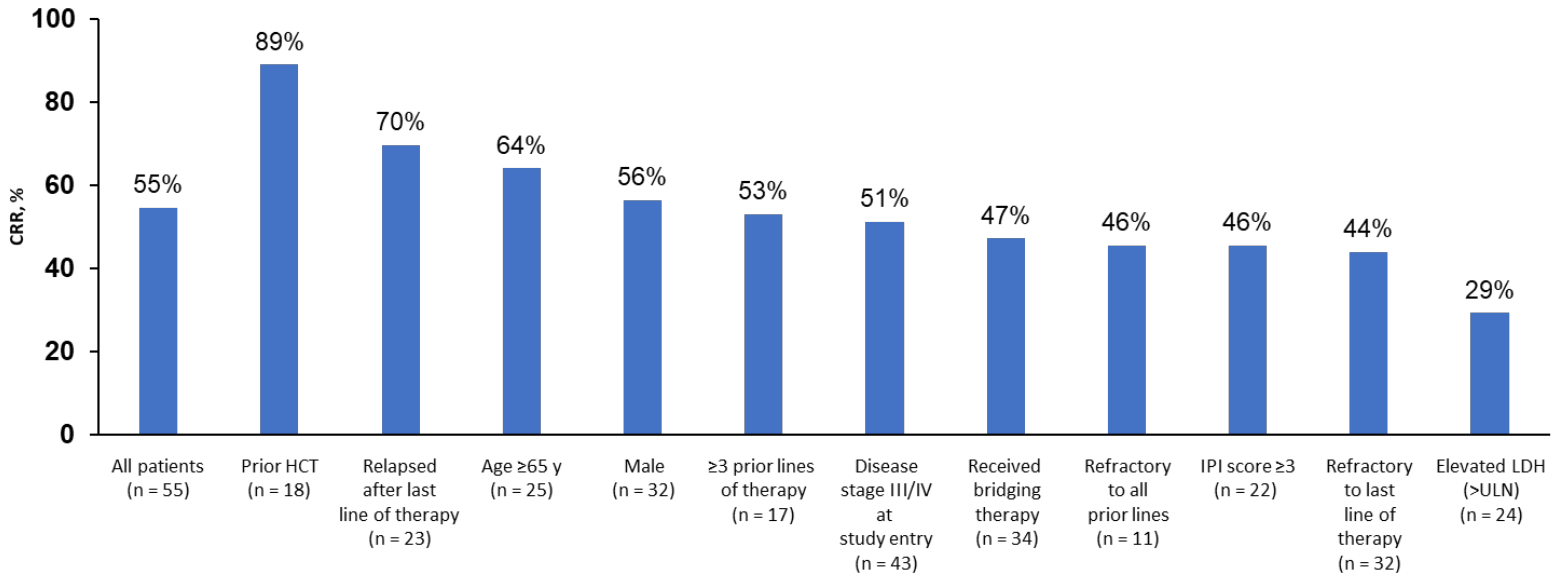
Riedell PA, et al. ASH 2024 [Abstract 67]

RAPCABTAGENE AUTOLEUCEL (YTB323) IN PATIENTS WITH RELAPSED/REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA: PHASE 2 TRIAL CLINICAL UPDATE

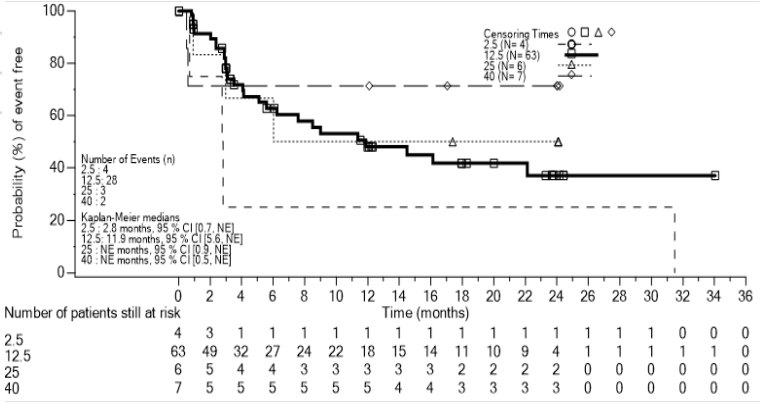
RAPCABTAGENE AUTOLEUCEL

EFFICACY

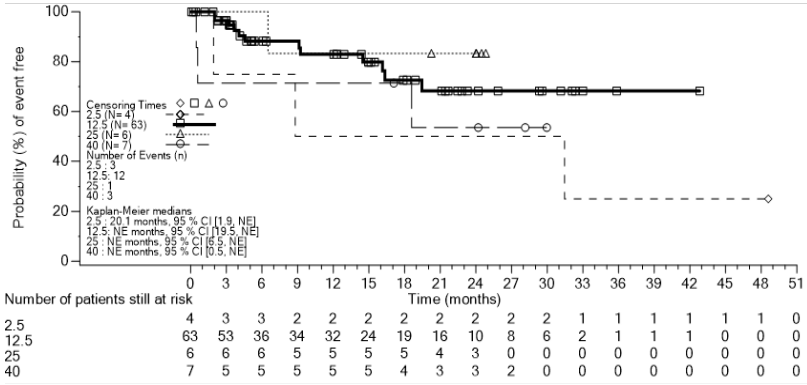
	Rapcabtagene autoleucel 12.5×10^6 (N = 60[a]) n (%)
Median follow-up, mo (range)	16.4 (0.1-44.1)
Overall response rate,[b] n (%) [95% CI][c]	**53.0 (88.3) [77.4-95.2]**
Best overall response	
CR, n (%) [95% CI]	**39.0 (65.0) [51.6-76.9]**
CR excluding patients with CR before infusion, n/N (%)[d]	**35.0/56.0 (62.5)**
PR, n (%)	14.0 (23.3)
Complete response rate, n/N (%)	
Mo 3	30.0/55.0[e] (54.5)
Mo 6	25.0/44.0[e] (56.8)
Mo 12	18.0/38.0[e] (47.4)



PFS



OS



Riedell PA, et al. ASH 2024 [Abstract 67]

Atalanta-1: A Phase 1/2 Trial of GLPG5101, a Fresh, Stem-like, Early Memory CD19 CAR T-Cell Therapy with a 7-Day Vein-to-Vein Time, for the Treatment of Relapsed/Refractory Non-Hodgkin Lymphoma

GLPG5101

Phase 1/2 study of GLPG5101

DLBCL, MCL, FL, MZL, BL, PCNSL
3 dose levels
50x10^6, 110x10^6 and 250x10^6 CAR+ viable T cells

Decentralized manufacturing
Cocoon Platform

53 pts had undergone leukapheresis (≥3L)

49 had received an infusion

47 (96%) receiving a fresh product.

A 7-day vein-to-vein time was achieved in 43/47 (91%) pts.

2 pts received less than prespecified dose (excluded)

45 included in this analysis

42 evaluable for efficacy

Kersten MJ, et al. ASH 2024 [Abstract 93]

Atalanta-1: A Phase 1/2 Trial of GLPG5101, a Fresh, Stem-like, Early Memory CD19 CAR T-Cell Therapy with a 7-Day Vein-to-Vein Time, for the Treatment of Relapsed/Refractory Non-Hodgkin Lymphoma

GLPG5101

Toxicity evaluable population N=45

PTS N=45	Overall	Grade ≤2	Grade 3
CRS	**42% (19/45)**	**40% (18/19)**	2% (1/19)
Phase 1 (n=20)	45% (9/20)	40% (8/9)	5% (1/9)
Phase 2 (n=25)	40% (10/25)	40% (10/10)	-
ICANS	**22% (10/45)**	**20% (9/10 G1)**	2% (1/10)
Phase 1 (n=20)	30% (6/20)	30% (6/6 G1)	-
Phase 2 (n=25)	16% (4/25)	12% (3/4 G1)	4% (1/4)

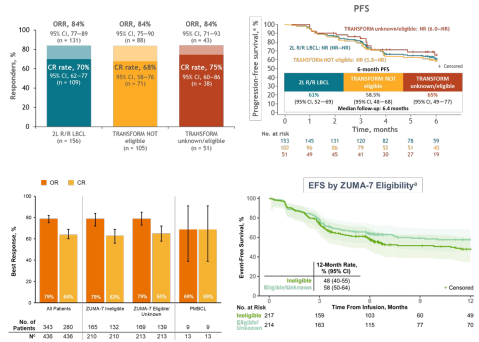
Efficacy evaluable population N=42

Lymphoma Subtype	ORR % (N)	CR % (N)
FL/MZL N=21	95% (20)	**95% (20)**
DLBCL N=13 Higher Dose N=7	69% (9) 86% (7)	**54% (7)** 71% (5)
MCL N=8	100% (8)	**100% (8)**

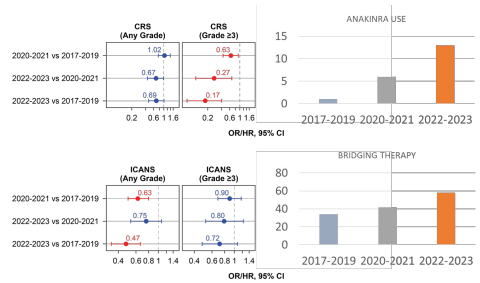
Kersten MJ, et al. ASH 2024 [Abstract 93]

CONCLUSIONS

Real world outcome data are in line with results of registration studies, confirming efficacy and toxicity profiles



The safety and deliverability of CAR-T cell therapy is improving over time, with the optimization of toxicity management (pre-emptive and mitigation strategies)



Fast CAR-T and decentralized manufacturing represent feasible strategies, with promising early efficacy and safety results. These strategies have the potential of increasing the access and deliverability of CAR-T cell therapy in the next future