«Real World in 2L »

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CAR-T:
e la storia continua...
migliorando

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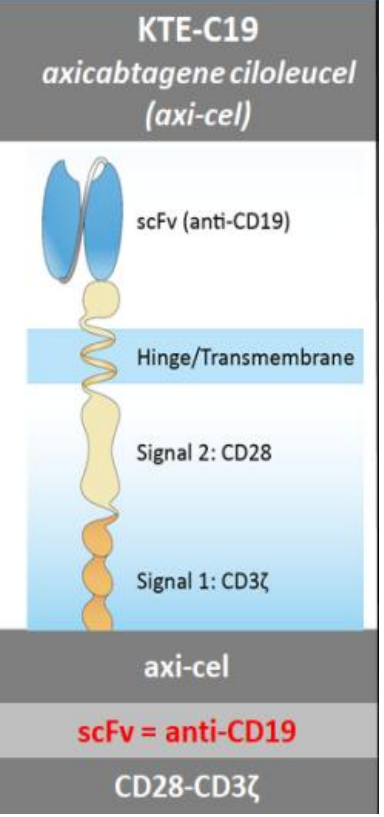
Starhotels E.C.HO.

Disclosures of Stefania Bramanti

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
NOVARTIS			x		x	x	x
KITE					x	x	x
BMS					x	x	
ROCHE						x	

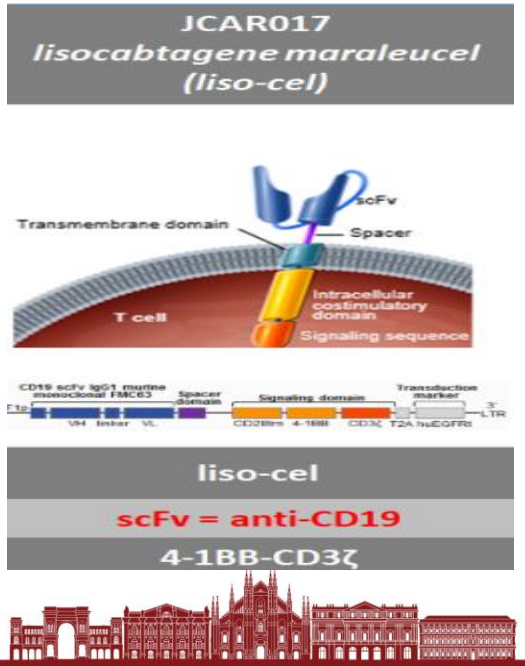


Dasom (Caroline) Lee

Real-World Early Outcomes of Second-Line Axicabtagene Ciloleucel (Axi-Cel) Therapy in Patients (Pts) With Relapsed or Refractory (R/R) Large B-Cell Lymphoma (LBCL) ASH2024

Christopher Sun Strouse

Predictors of Early Safety Outcomes with Axicabtagene Ciloleucel (axi-cel) in Patients with Relapsed or Refractory (R/R) Large B-Cell Lymphoma (LBCL) ASH 2024



Odstrcil Bobillo

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

Real-World Early Outcomes of Second-Line Axicabtagene Ciloleucel Therapy in Patients With Relapsed or Refractory Large B-Cell Lymphoma. Data from CIBMTR between April 2022 and July 2023

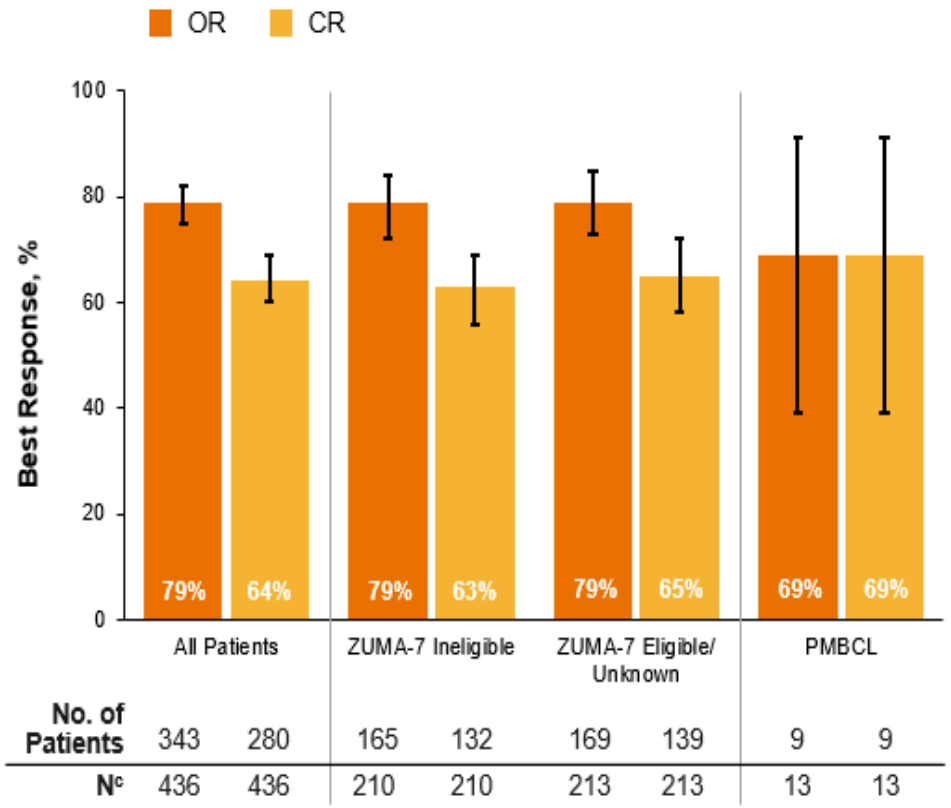
Characteristic	All Patients N=446
Median age, years (range)	63.9 (19.5-86.0)
≥65 to <70, n (%)	74 (17)
≥70, n (%)	137 (31)
Male sex, n (%)	285 (64)
ECOG performance status 0-1,[a] n (%)	401 (97)
Disease type, n (%)	
DLBCL	349 (78)
PMBCL	13 (3)
HGBCL	79 (18)
FL Grade 3B	5 (1)
Elevated lactate dehydrogenase levels pre-infusion,[a] n (%)	199 (48)
Response to last line of therapy pre-leukapheresis,[a,b] n (%)	228 (51)
Median vein-to-vein time, days,[c] (IQR)	29.0 (27.0-35.0)
Bridging therapy,[a,d] n (%)	286 (66)

Median follow-up was 12.0 months

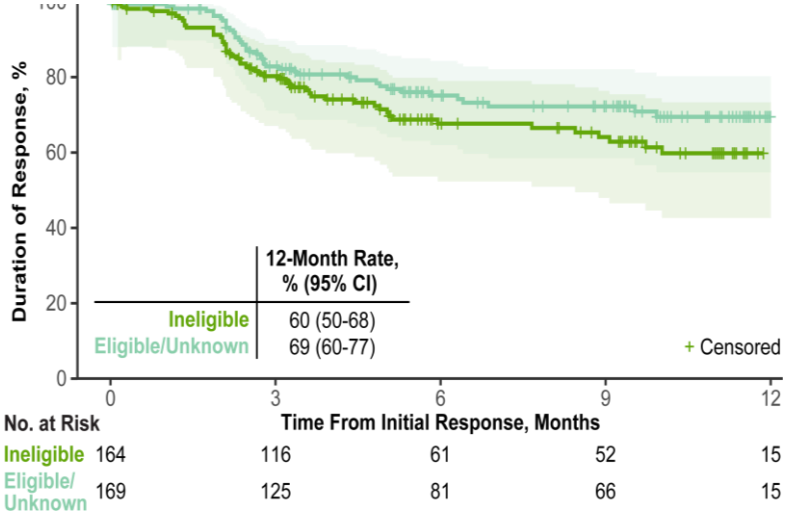
Lee *et al.* ASH 2024 (Abstract 526; oral presentation)

About half the patients would have been ineligible for ZUMA-7

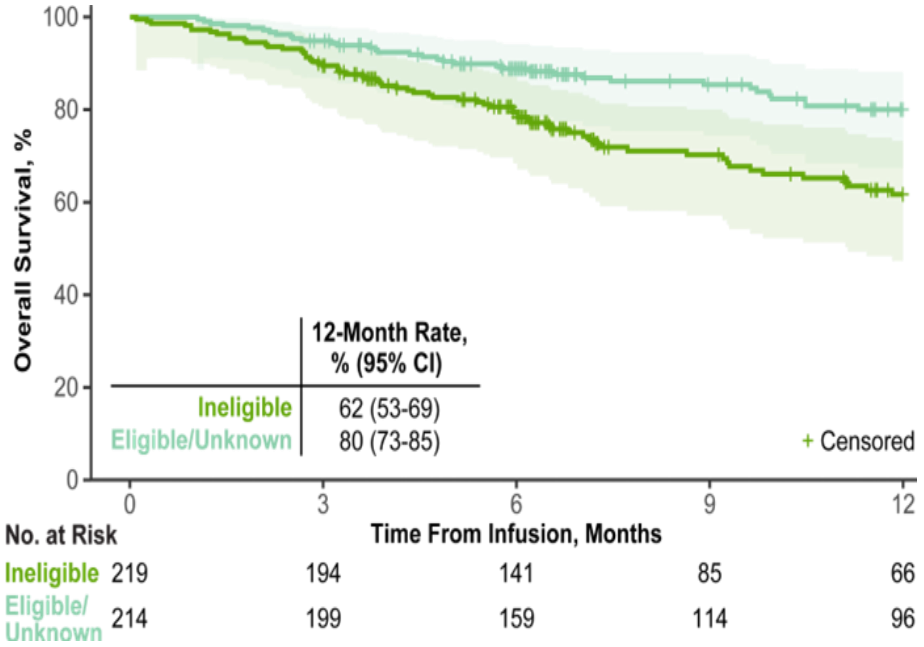
Characteristic	All Patients N=446
ZUMA-7 eligibility,[a] n (%)	
Eligible	**214 (48)**
Not eligible[b]	**219 (49)**
Organ impairment	150 (34)
Pulmonary (moderate/severe)	81 (18)
Cardiac	49 (11)
Bone marrow (platelets, ANC, and/or ALC)	37 (8)
Arrhythmia	26 (6)
Cerebrovascular disease	14 (3)
Renal (moderate/severe)	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)



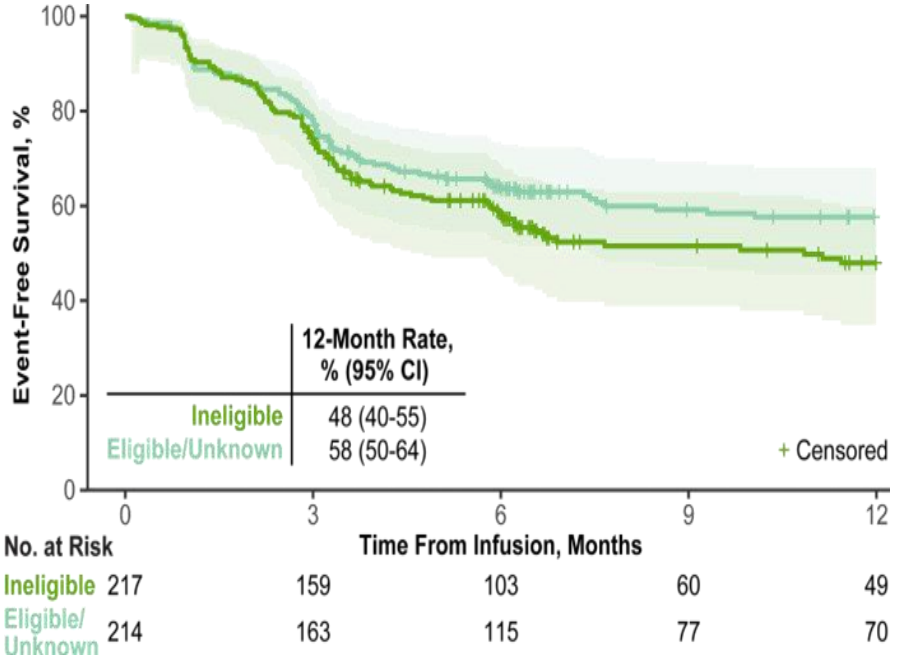
DOR by ZUMA-7 Eligibility[a]



OS by ZUMA-7 Eligibility[a]



EFS by ZUMA-7 Eligibility[a]

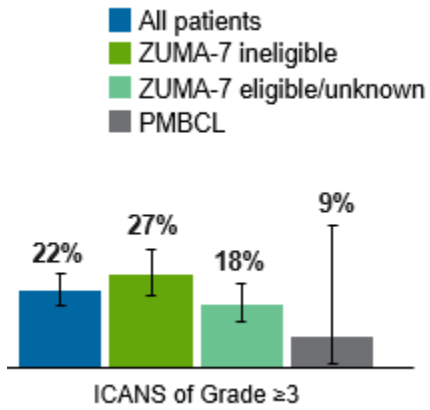


SAFETY

Characteristic	All Patients N=446	ZUMA-7 Eligibility[a]		Patients With PMBCL n=13
		Ineligible n=219	Eligible/ Unknown n=214	
Any-grade CRS, n (%)	390 (87)	193 (88)	186 (87)	11 (85)
Median time from infusion to CRS onset, days (IQR)	4 (2-6)	4 (2-5)	4 (2-6)	4 (2-6)
Median time from CRS onset to resolution, days (IQR)	5 (4-7)	5 (4-7)	5 (4-7)	7 (4-8)
Cumulative incidence of CRS resolution at 3 weeks since onset, % (95% CI)	98 (96-99)	-	-	-

Grade ≥3 CRS occurred in 5%

Characteristic	All Patients N=446	ZUMA-7 Eligibility[a]		Patients With PMBCL n=13
		Ineligible n=219	Eligible/ Unknown n=214	
Any-grade ICANS, n (%)	221 (50)	118 (54)	96 (45)	7 (54)
Median time from infusion to ICANS onset, days (IQR)	7 (5-9)	7 (5-9)	7 (5-8)	10.5 (8-11)
Median time from ICANS onset to resolution, days (IQR)	6 (3-10)	5 (3-10)	6 (3-10)	3.5 (2-6)
Cumulative incidence of ICANS resolution at 3 weeks since onset, % (95% CI)	88 (83-92)	-	-	-



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)

- Incidence of prolonged cytopenia and infections were similar across patient groups[a,b]
- Prolonged neutropenia and thrombocytopenia occurred in 7% and 11% of all patients, respectively
- Almost half the patients (44%) had clinically significant infections

Predictors of Early Safety Outcomes With Axicabtagene Ciloleucel (Axi-Cel) in Patients With Relapsed or Refractory Large B-Cell Lymphoma

Adult patients with R/R LBCL treated with axi-cel with ≥1 prior line of therapy between Jan 2021–Oct 2023
N=928
106 treatment centers

↓

Analysis Set
N=888
105 treatment centers

Endpoints

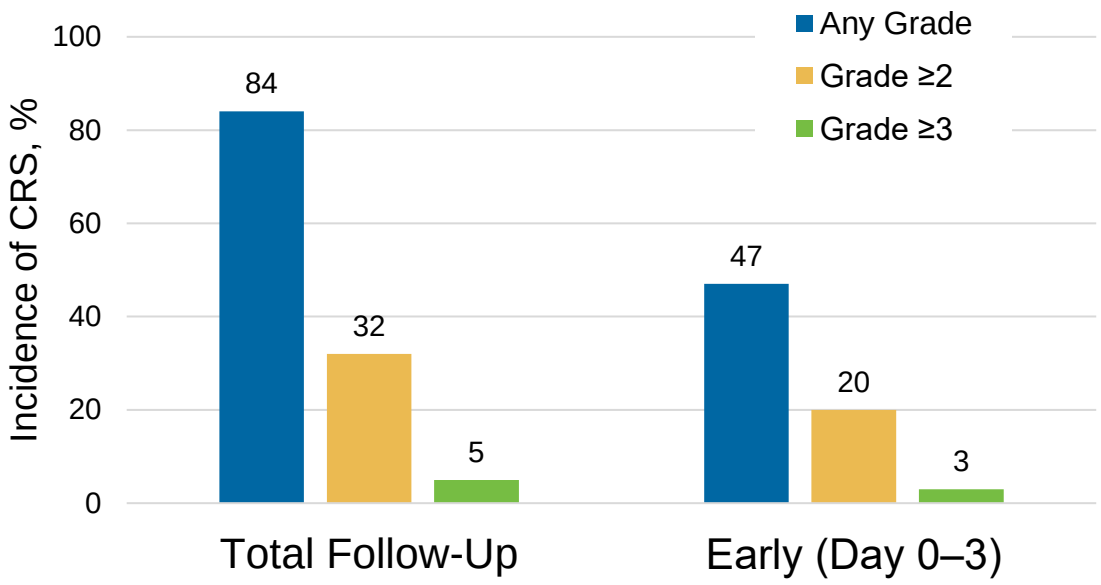
- **Primary:** incidence of early CRS and early ICANS of any grade occurring from infusion (Day 0) through end of Day 3
- **Secondary:** Early Grade ≥2 CRS, early Grade ≥3 CRS, and early Grade ≥3 ICANS[1]

Characteristic	Patients (N=888)
Median age (IQR), years	63 (54–71)
≥65 years, n (%)	399 (45)
Male sex, n (%)	583 (66)
ECOG PS ≥2 prior to infusion, n (%)	40 (5)
Clinically significant comorbidity, n (%)[a]	625 (70)
Disease stage III-IV at diagnosis, n (%)[b]	606 (68)
Extranodal involvement prior to infusion, n (%)	17 (2)
Bulky disease prior to infusion, n (%)[c]	57 (6)
Elevated LDH prior to infusion, n (%)[d]	387 (44)
1 line of prior therapy, n (%)	448 (50)
Prior autologous HCT, n (%)	92 (10)
Chemoresistance prior to infusion, n (%)[e]	540 (61)
Bridging therapy (any type), n (%)	522 (59)
Median time from leukapheresis to infusion (IQR), days	30 (27–34)
Bendamustine lymphodepletion regimen, n (%)	130 (15)

Patients With Any Grade CRS	
Total Follow-Up (N=748)	Early (N=421)

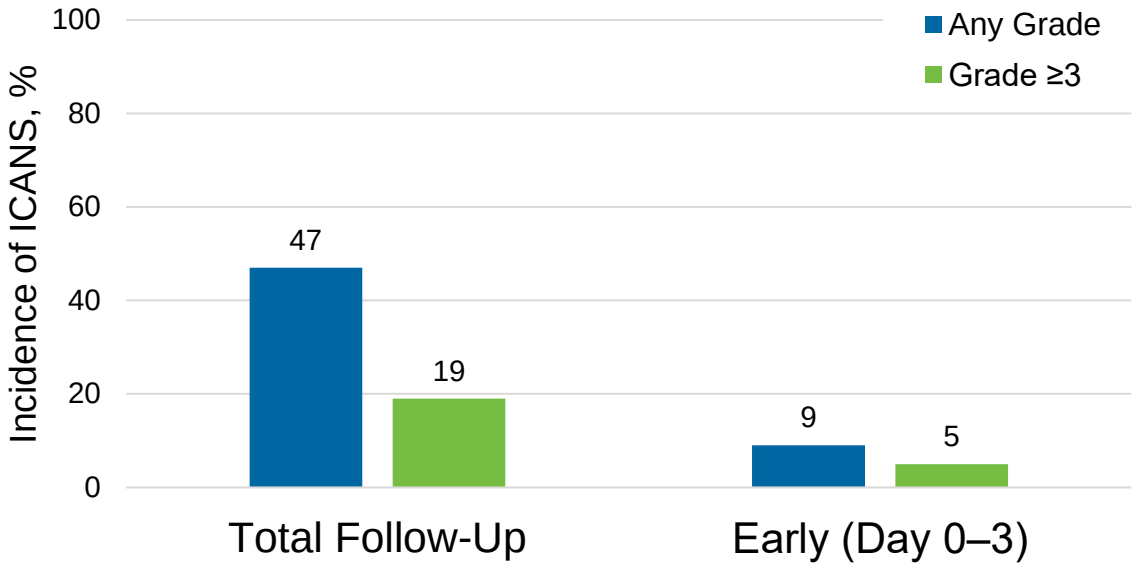
Patients With Any Grade ICANS	
Total Follow-Up (N=405)	Early (N=76)

CRS



CRS Characteristic	Patients With Any Grade CRS	
	Total Follow-Up (N=748)	Early (N=421)
Median time to onset (IQR), days	4 (2–6)	2 (2–3)
Median duration (IQR), days	4 (3–6)	5 (4–7)
Resolution by day 21 (95% CI), %	99 (98–100)	99 (98–100)

ICANS



ICANS Characteristic	Patients With Any Grade ICANS	
	Total Follow-Up (N=405)	Early (N=76)
Median time to onset (IQR), days	7 (5–9)	3 (2–4)
Median duration (IQR), days	5 (2–9)	10 (5–18)
Resolution by day 21 (95% CI), %	93 (90–95)	84 (71–91)

Strouse *et al.* ASH 2024

Multivariate analyses

- After adjustment for other factors, age ≥65 years was associated with a greater risk of early ICANS (any grade and Grade ≥3), and ECOG PS ≥2 was associated with a greater risk of early Grade ≥3 CRS and early Grade ≥3 ICANS
  - There was no association between any comorbidity and early CRS nor early ICANS

Real World Data of Axicabtagene Ciloleucel As Second Line Therapy for Patients with Large B Cell Lymphoma: First Results of a Lysa Study from the French Descar-T Registry

	Treated patients, n = 78	
Sex Male	48	(61.5%)
Age (years)		
Median (min; max)	60.0 (23; 79)	
Age ≥ 65 years	27	(34.6%)
ECOG		
0-1	62	(79.5%)
≥ 2	7	(9.0%)
Missing	9	(11.5%)
LDH > Normal		
No	29	(37.2%)
Yes	48	(61.5%)
Missing	1	(1.3%)
Ann Arbor Stage		
Unknown	11	(14.1%)
I-II	8	(10.3%)
III-IV	59	(75.6%)
At least one HCT-CI Comorbidity	35	(44.9%)
Bulky disease (>5cm)		
No	58	(75.3%)
Yes	13	(16.9%)
Missing	6	(7.8%)
Histology		
DLBCL	61	(78.2%)
Transformed FL	5	(6.4%)
PMBL	3	(3.8%)
HGBL	1	(1.3%)
Other#	6	(7.7%)
Missing	2	(2.6%)
Prior autologous transplant	2	(2.6%)
Primary refractory disease		
Yes	58	(74.3%)
No	17	(21.8%)
Missing	3	(3.8%)
Bridging therapy	65	(83.3%)
Disease status before CAR-T infusion		
Complete Response	6	(9.2%)
Partial Response	17	(26.2%)
Stable Disease	6	(9.2%)
Progressive Disease	35	(53.8%)
Not Evaluated	1	(1.5%)

Table 1. Characteristics of treated patients at enrollment in the axi-cel 2nd line LBCL early access program. HCT-CI: Hematopoietic Cell Transplantation-specific Comorbidity Index, DLBCL: diffuse large B cell lymphoma, FL: follicular lymphoma, PMBL: primary mediastinal B cell lymphoma, HGBL: high grade B cell lymphoma.

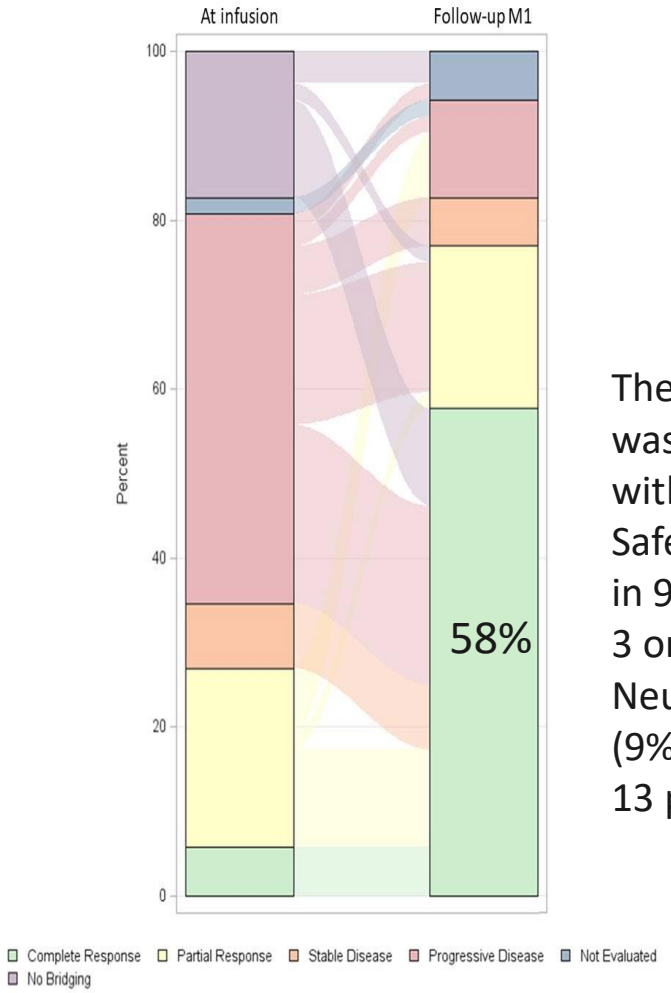


Figure 1. Sankey plot of evaluable patients 1 month (M1) after CAR-T cells infusion.

The median time between leukapheresis and axi-cel infusion was 36 days, and 65 patients (83%) received bridging therapy, with only 23 patients (29%) responding to bridging therapy.
Safety information was reported for 65 patients: CRS occurred in 95% of patients, however only 3 patients (<5%) had a grade 3 or higher CRS.
Neurotoxicity occurred in 43% of the cases, with 6 patients (9%) presenting grade 3 or higher toxicity.
13 patients (21%) were transferred to intensive care unit.

G.Brisou ASH 2023

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

From june 2022 to August 4, 2024

Infused with commercial liso-cel
as available from the CIBMTR Registry
N = 1067

Received liso-cel in the 2L setting
N = 200

Key eligibility criteria
- Had R/R LBCL
- Received commercial liso-cel infusion as 2L LBCL therapy
- Had ≥ 1 assessment for safety and response after infusion

2L R/R LBCL study cohort
n = 157

TRANSFORM NOT eligible cohort
n = 105 (67%)

2L R/R LBCL cohort eligible for response assessment
n = 156

TRANSFORM NOT eligible cohort evaluable for response
n = 105

A collaboration of BMS and CIBMTR

Comparison to PILOT was not feasible due to the lack of granularity around organ function that was used to define the PILOT population.

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

Baseline demographics and disease characteristics

A collaboration of BMS and CIBMTR

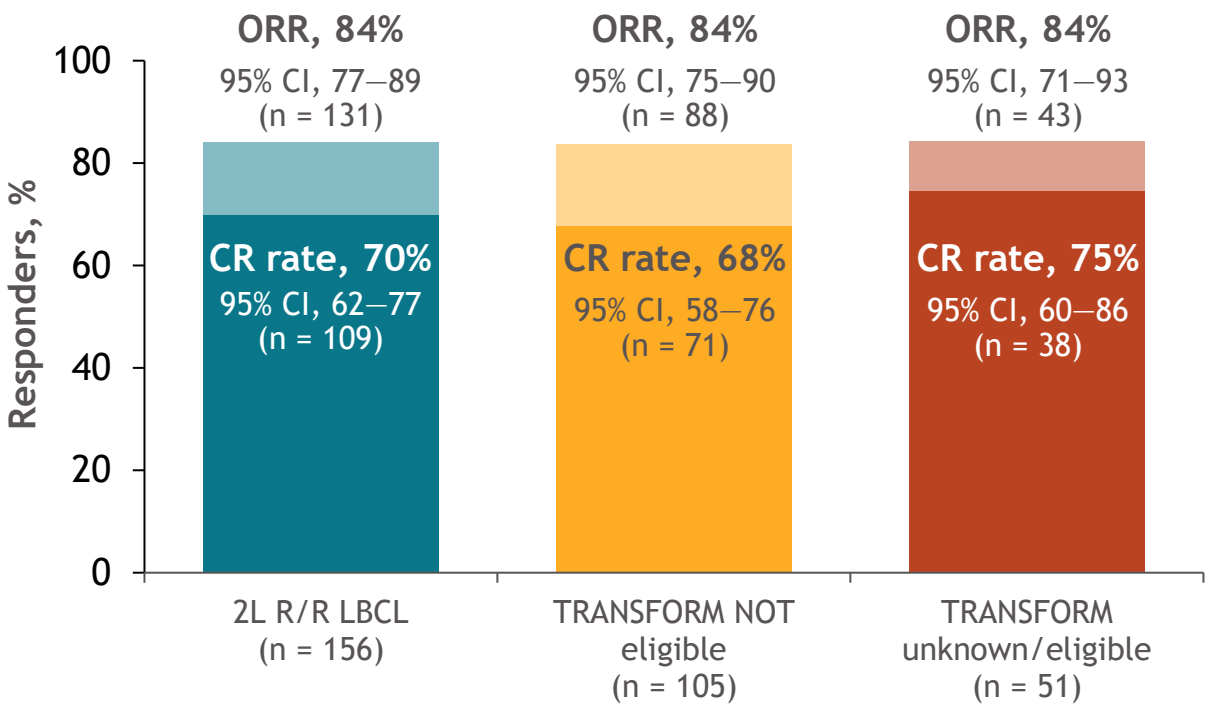
	2L R/R LBCL (n = 157)
Median (range) age,[a] y	72 (27—85)
Male, n (%)	90 (57)
Histology, n (%)	
DLBCL[b]	132 (84)
Activated B-cell type	57 (36)
Germinal center B-cell type	61 (39)
NOS	13 (8)
THRBCL	1 (1)
High-grade B-cell lymphoma	18 (11)
Other, including PMBCL	7 (4)
Disease status at time of infusion, 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)

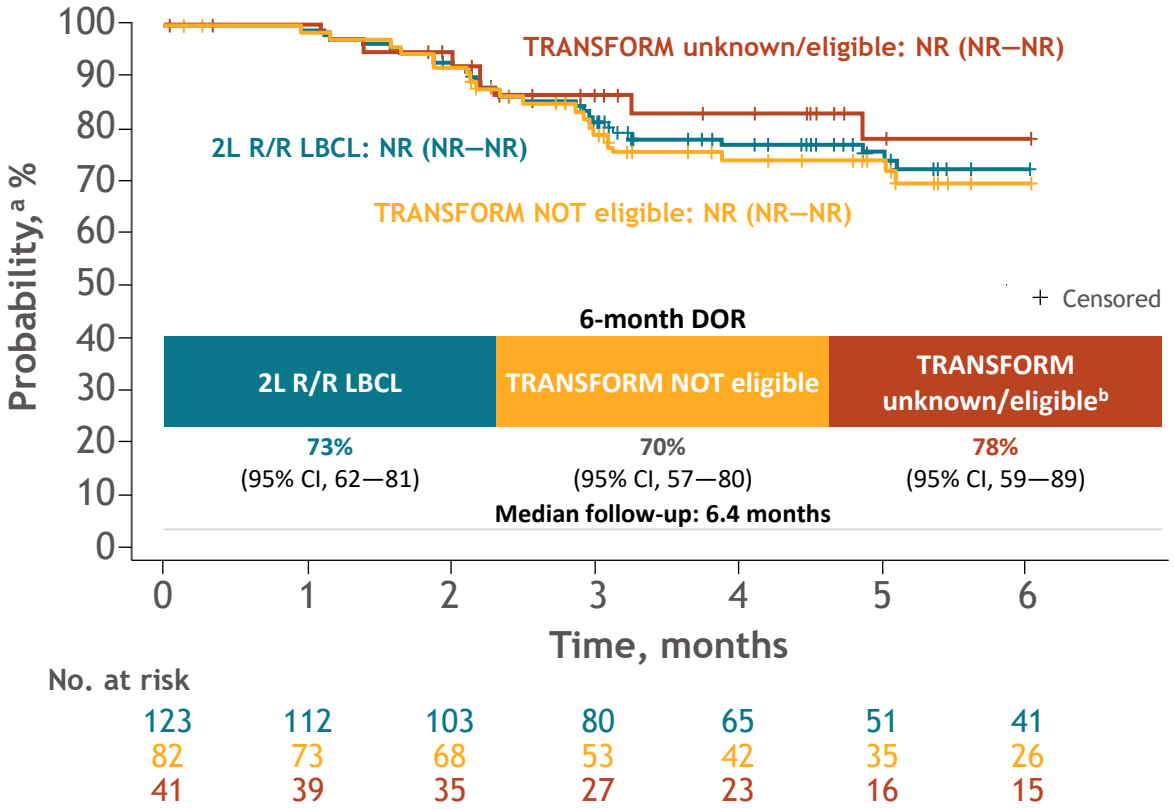
[a]There were 66 (42%) patients who were ≥ 75 years of age; [b]Of 132 patients with DLBCL, 109 had no transformation in their disease, 21 had DLBCL transformed from a different lymphoma histology, and 2 had DLBCL transformed from CLL; [c]Patients whose disease relapsed < 12 months; [d]Most common comorbidities occurring in ≥ 10% of patients.
NOS, not otherwise specified; THRBCL, T-cell/histiocytic rich large B-cell lymphoma.

Response rates and duration of response

Response rates

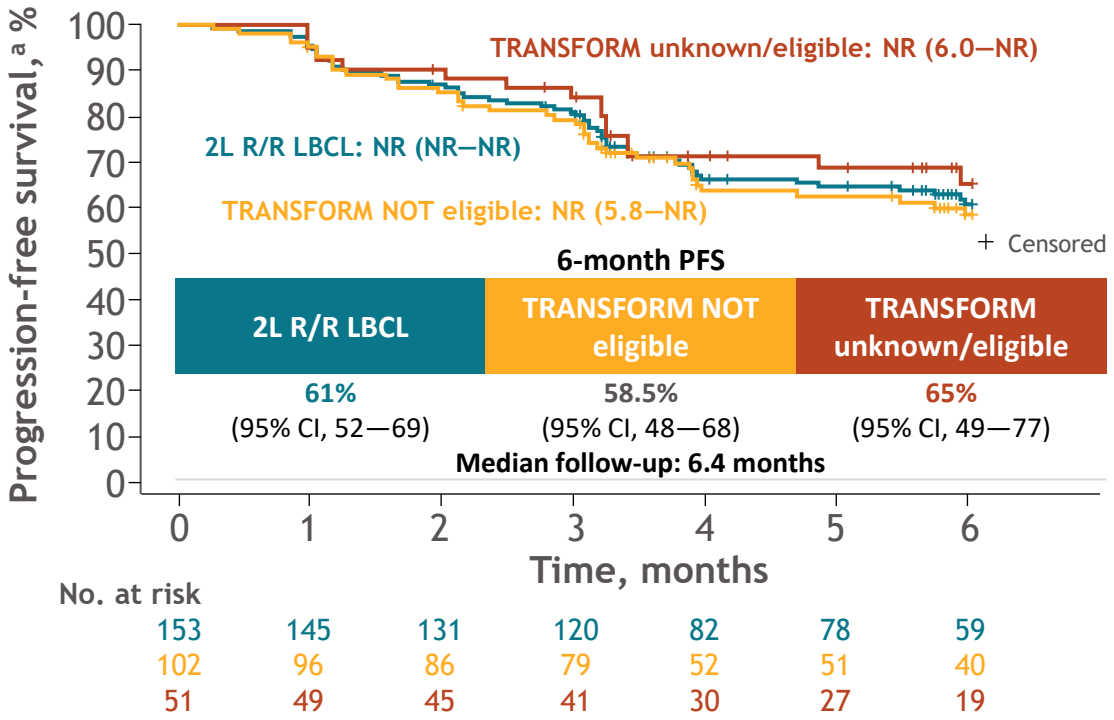


DOR

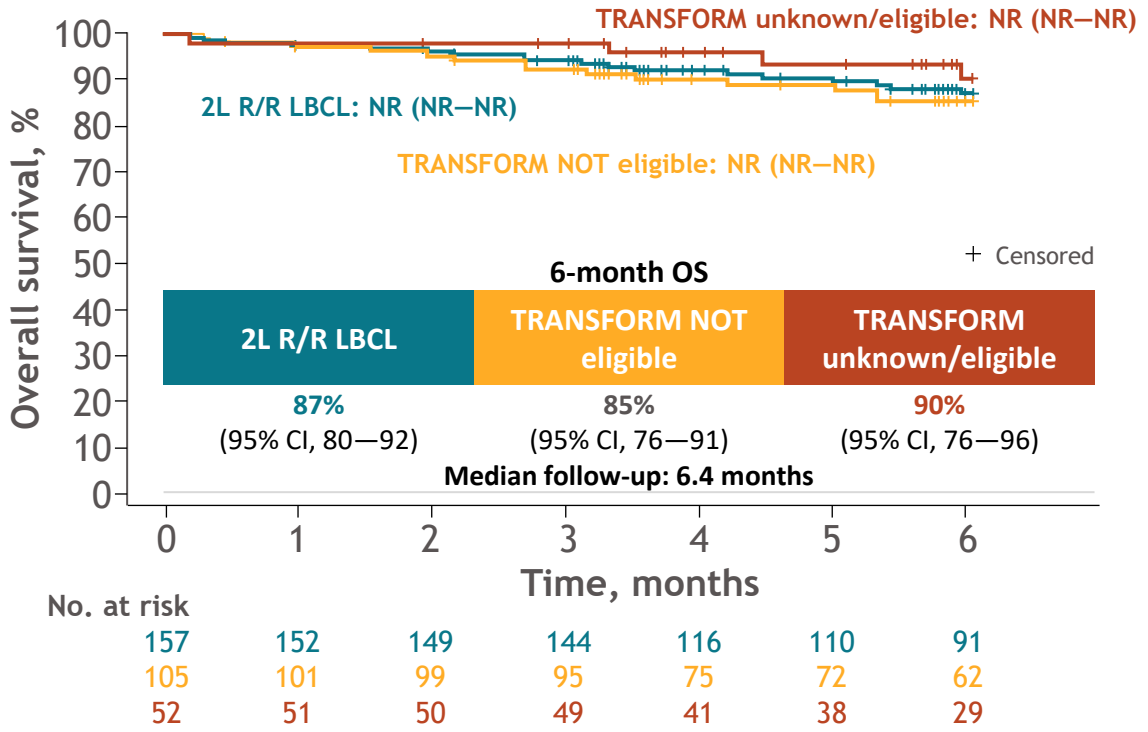


Progression-free survival and overall survival were NR

PFS

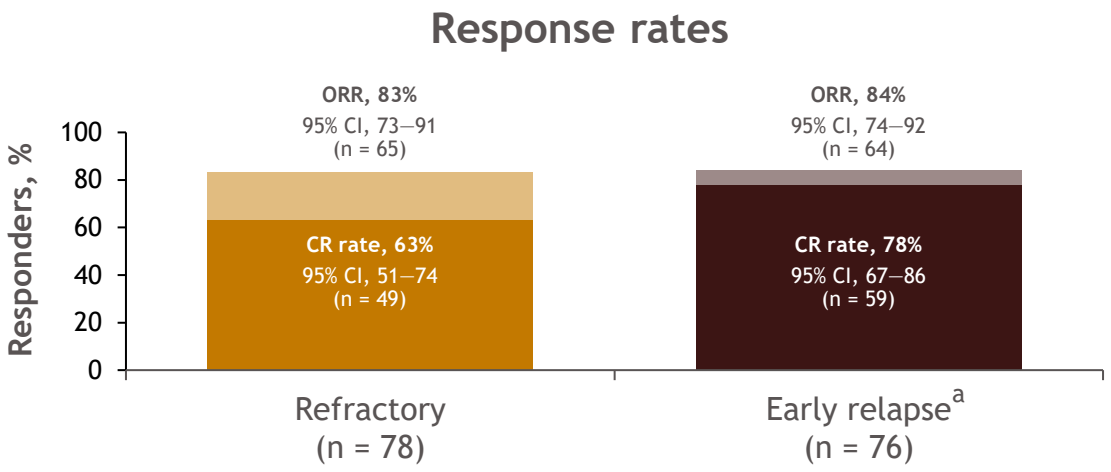


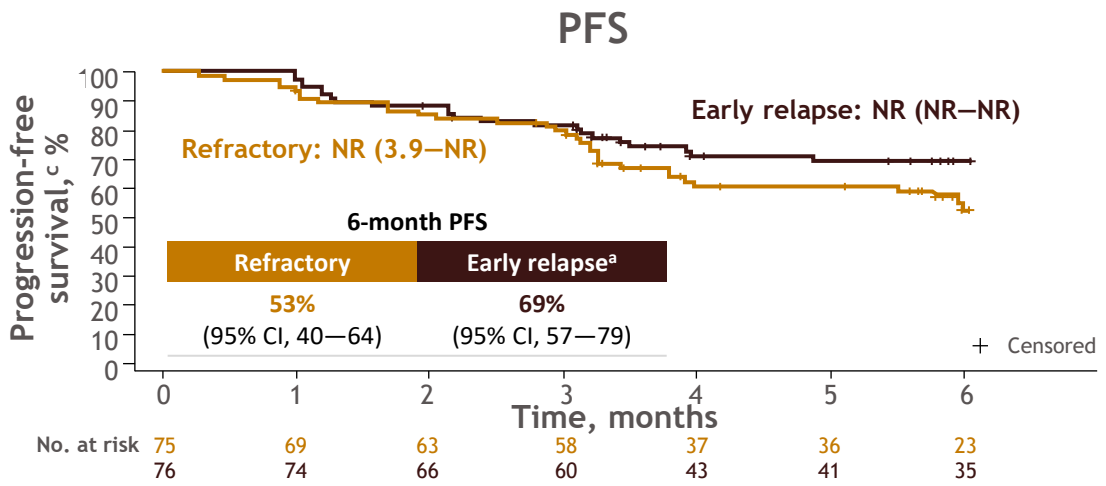
OS

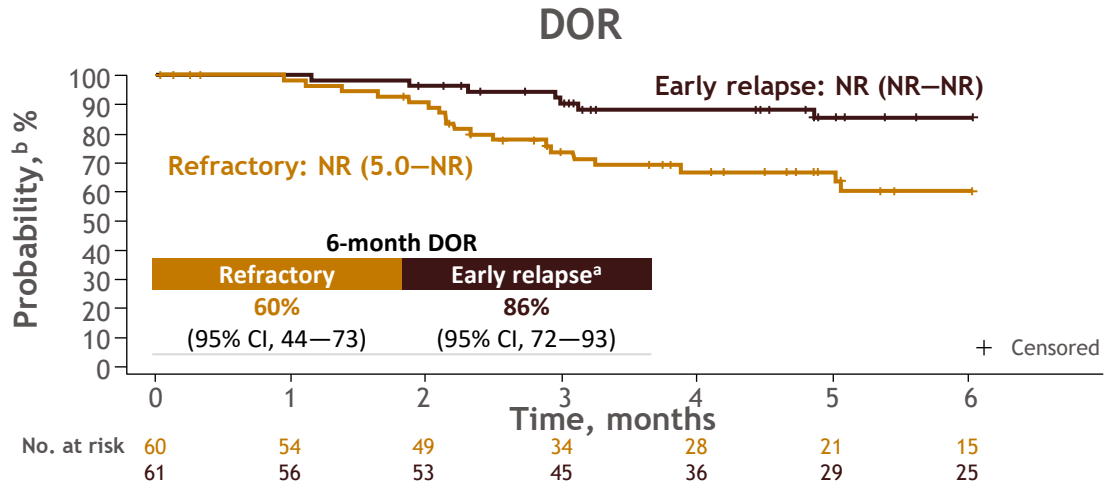


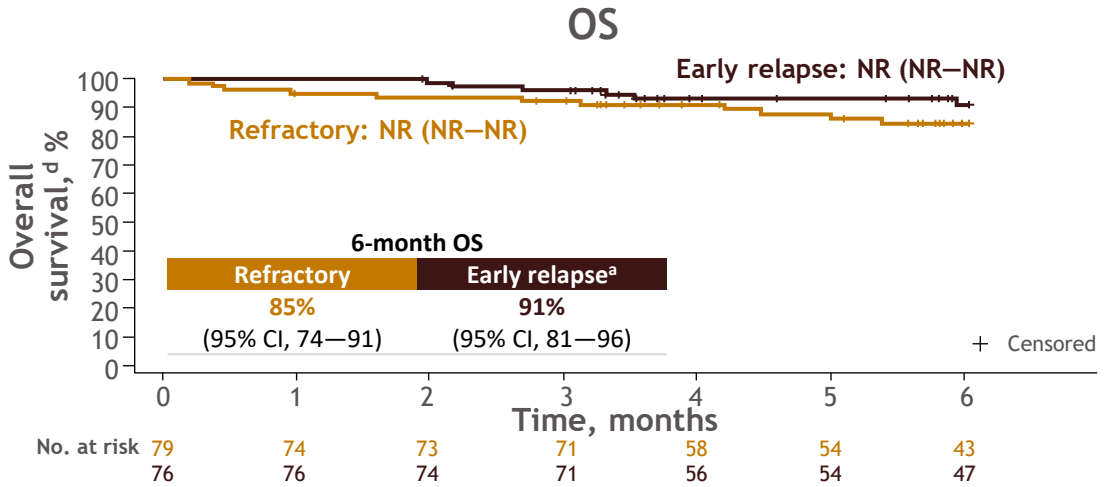
[a]Patients with available PFS data.

Subgroup analysis by disease status in the second-line setting





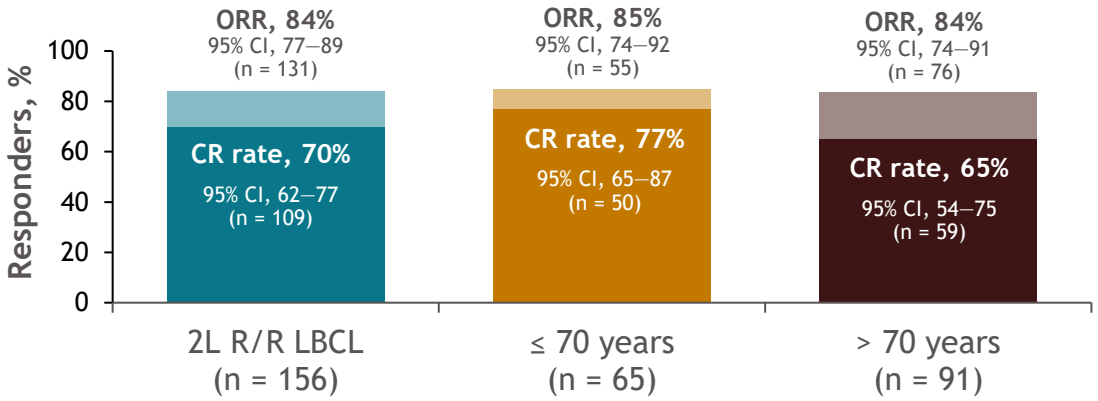




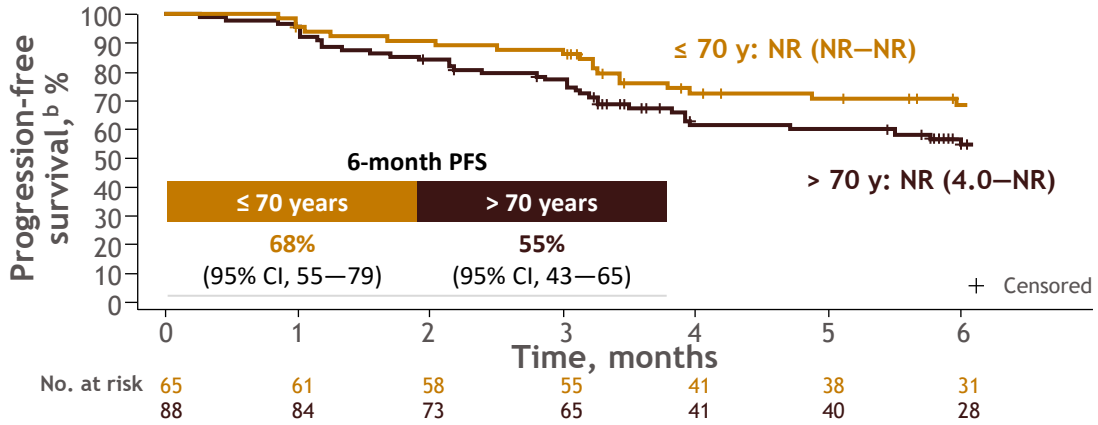
- While higher CR rates were reported for patients with early relapsed disease, median DOR, PFS, or OS were NR in either subgroup

Age subgroup analyses in the second-line setting

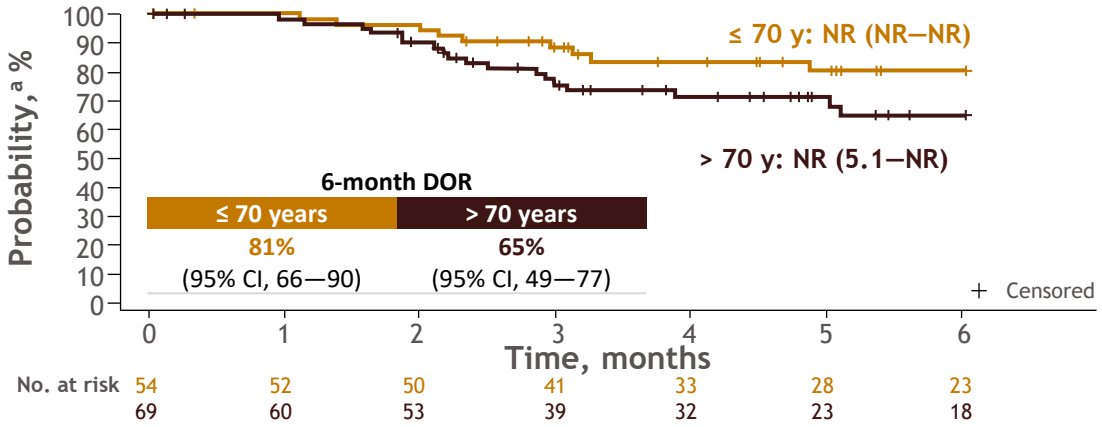
Response rates



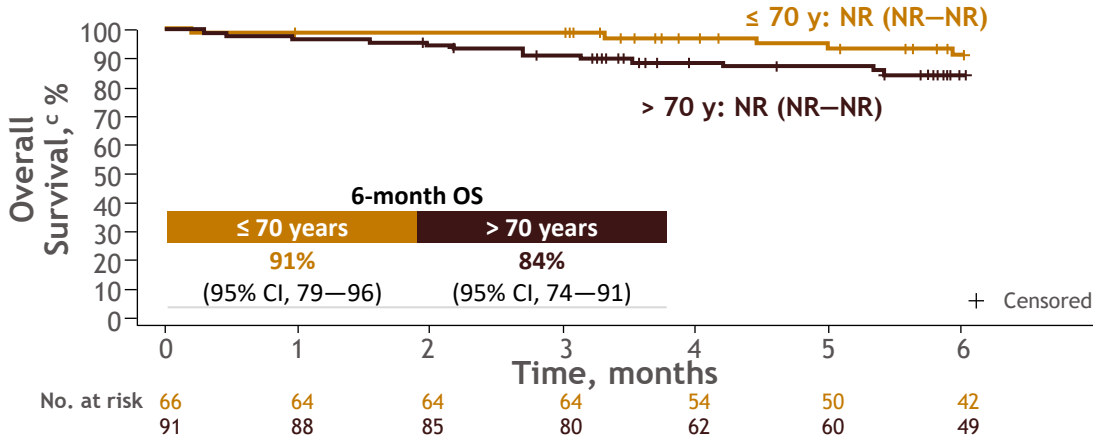
PFS



DOR



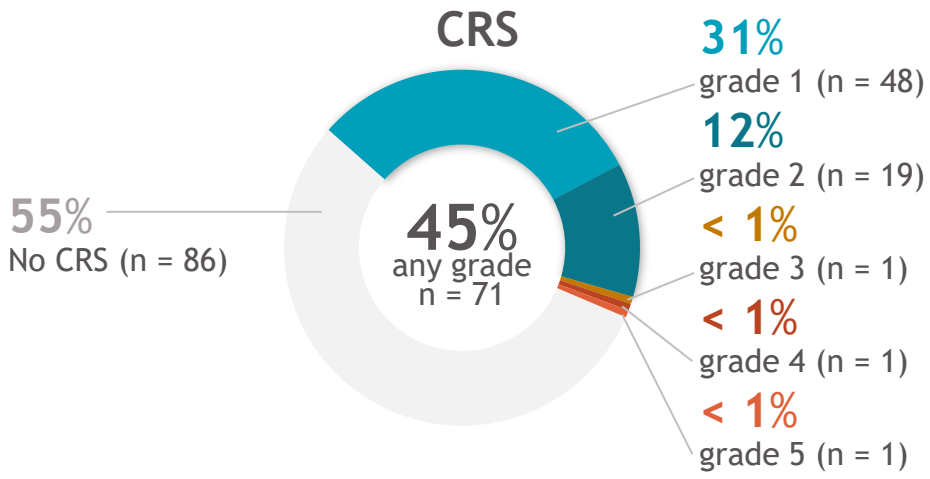
OS

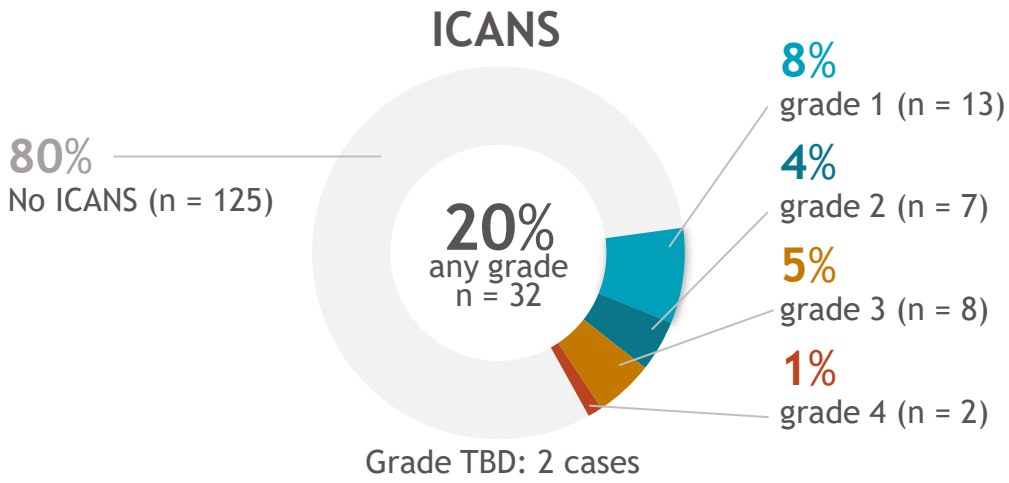


- Liso-cel was effective across both age subgroups

[a]Responders with available DOR data; [b]Patients with available PFS data; [c]Patients with available OS data.

CRS and ICANS





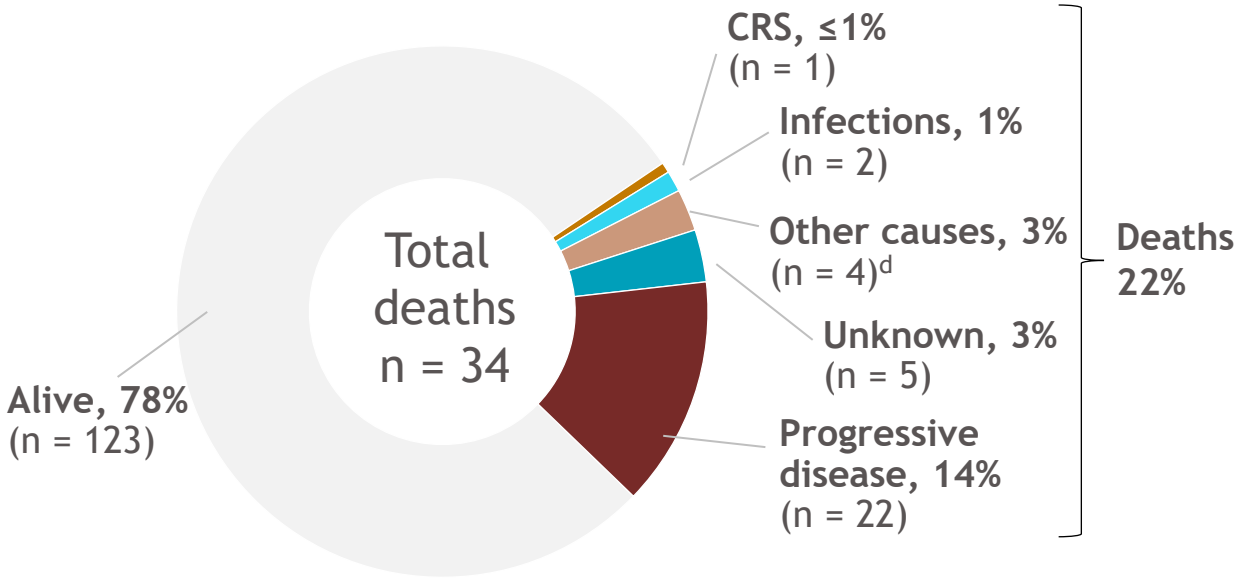
	2L R/R LBCL (n = 157)	
	CRS	ICANS
Median (IQR) time to onset, days	4.0 (3.0—7.0)	8.0 (5.0—9.0)
Median (IQR) duration, days	3.0 (2.0—5.0)	10 (4.0—378.0)
Patients who received treatment, n/N (%)	58/71 (82)	29/32 (91)
Treatments, n (%)		
Tocilizumab alone	34 (59)	1 (3)
Corticosteroids alone	2 (3)	14 (48)
Tocilizumab + corticosteroids	20 (34)	0
Antiepileptics alone or with other agents	0	10 (34)
Other	2 (3)	3 (10)

- Most patients experienced either no or low-grade CRS and ICANS
  - Higher incidence of CRS and ICANS were reported for the TRANSFORM ineligible, refractory disease, or ≥ 70 years cohorts. These differences were not statistically significant, except for incidence of ICANS that was significantly higher in patients ≥ 70 years of age

Other adverse events, nonrelapse mortality, and deaths

	2L R/R LBCL (n = 157)
Prolonged cytopenia, n/N (%)[a]	16/152 (11)
Clinically significant infections, n (%)	52 (33)
Secondary Malignanciess, n (%)	6 (4) 1 case of MDS[b]
Grade 3/4 organ toxicity, n (%)	8 (5)
Tumor lysis syndrome, n (%)	1 (0.6)

Survival status of patients with 2L R/R LBCL[c]



	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]

«Chiedo scusa alle grandi domande per le piccole risposte »
Wislawa Symborska

CAR-T TEAM

HUMANITAS RESEARCH HOSPITAL

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