CAR-T and LBCL: Real World in 2^ line

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

Bologna, 10 Marzo 2025
Royal Hotel Carlton

Disclosures of Francesco Merli

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Roche						x	
Janssen						x	x
Gilead						x	
Takeda						x	x
Novartis						x	x
Incyte						x	
MSD						x	
Beigene							x
Kite							x
Astrazeneca						x	
Sandoz						x	

Approved CD19 CAR-T Cells in 2nd line for LBCL

Axi-cel

FDA, EMA and AIFA: DLBCL **refractory to first-line** chemoimmunotherapy or that **relapses within 12 months** of first-line chemoimmunotherapy

Liso-cel

EMA: DLBCL (and PMLBL, FL3B) **refractory to first-line** chemoimmunotherapy or that **relapses within 12 months** of first-line chemoimmunotherapy

FDA: DLBCL (and PMLBL, FL3B) **refractory to first-line** chemoimmunotherapy or that **relapses within 12 months** of first-line chemoimmunotherapy or **relapses after first-line** chemoimmunotherapy and are **not transplant eligible**

65th ASH Annual Meeting and Exhibition
December 9 – 12
San Diego, CA

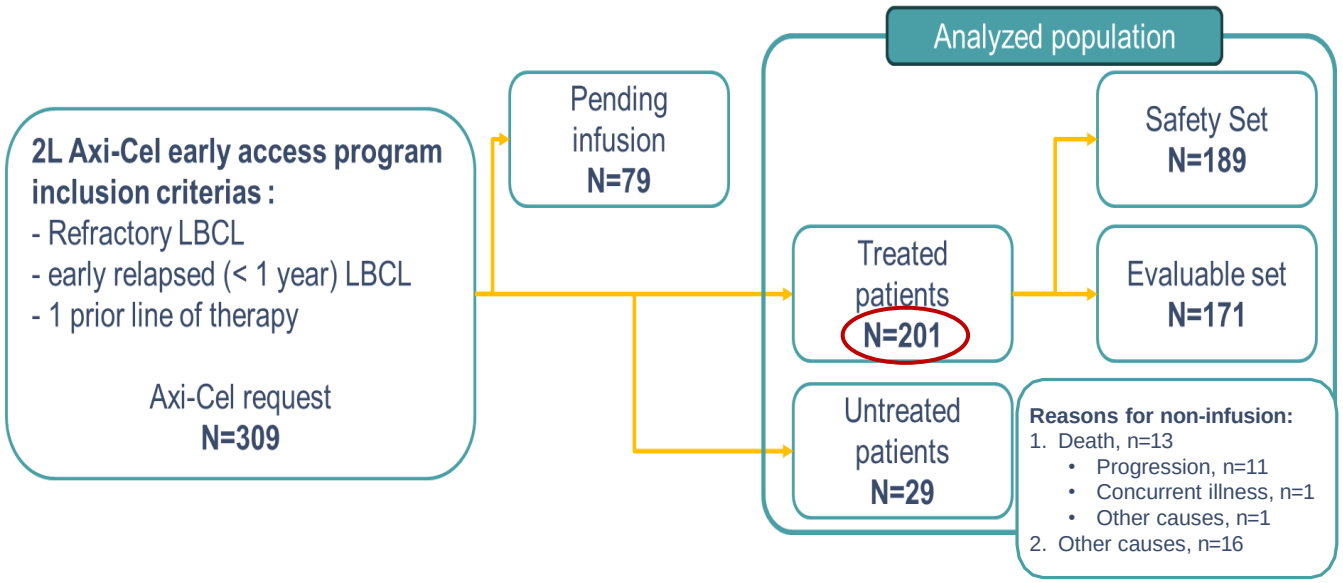
REAL WORLD DATA OF AXICABTAGENE CILOLEUCEL AS SECOND LINE THERAPY FOR PATIENTS WITH LARGE B CELL LYMPHOMA: FIRST RESULTS OF A LYSA STUDY FROM THE FRENCH DESCAR-T REGISTRY

Brisou G. et al. ASH 2023 [Abstract 905]

DESCAR-T :

French nationwide registry collecting real-life data of all patients treated with approved CAR T-cell therapies (NCT04328298)

Retrospective analysis → all patients included **between July 2022 and Aug 2023** in 2L Axi-Cel early access program



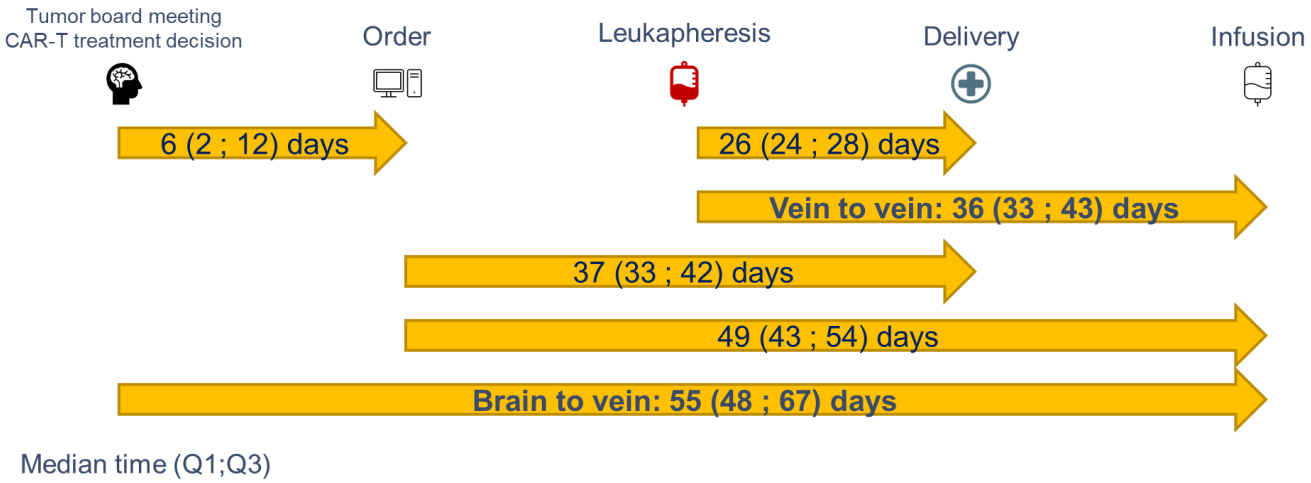
Patient Characteristics

	Treated patients N=201 (87.4%)		Untreated patients N=29 (12.6%)	
Sex Male	122	(60.7%)	16	(55.2%)
Age (years)				
Median (min; max)	61 (21; 82)		65 (34;80)	
Age >= 65 years	**77**	**(38.3%)**	**15**	**(51.7%)**
Bridging therapy	**177**	**(88.1%)**	**18**	**(62.1%)**
ECOG				
0-1	164	(81.6%)	14	(48.3%)
>=2	10	(5.0%)	3	(10.3%)
Missing	27	(13.4%)	12	(41.4%)
LDH > Normal				
No	75	(37.3%)	16	(55.2%)
Yes	122	(60.7%)	12	(41.4%)
Missing	4	(2.0%)	1	(3.4%)
Ann Arbor Stage				
I-II	30	(14.9%)	4	(13.8%)
III-IV	149	(74.1%)	20	(69.0%)
Unknown	22	(10.9%)	5	(17.2%)
Histology				
DLBCL	149	(74.1%)	22	(75.9%)
Transformed indolent	28	(13.9%)	6	(20.7%)
PMBL	6	(3.0%)	0	(0.0%)
HGBL	8	(4.0%)	1	(3.4%)
Other#	10	(5.0%)	0	(0.0%)
Primary refractory disease	**149**	**(74.1%)**	23	(79.3%)

DESCAR-T LBCL treated with Axi-cel in 2nd line

Brisou G. et al. ASH 2023 [Abstract 905]

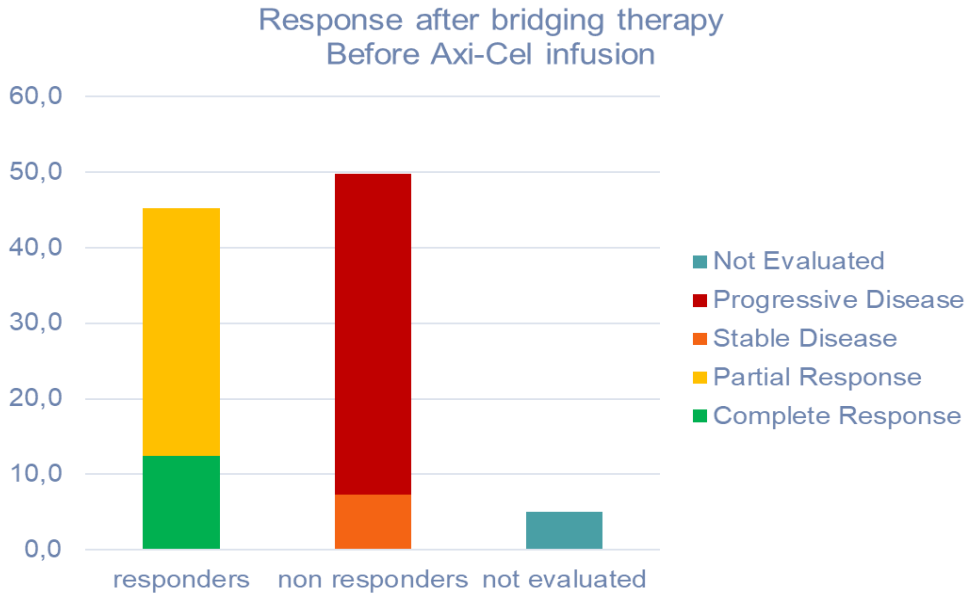
Time from decision to infusion



Bridging Therapies

Bridging therapy	**177**	**(88.1%)**
Number of bridging lines		
1	**153**	**(86.4%)**
2	19	(10.7%)
3	4	(2.3%)
4	1	(0.6%)
Type of treatment*		
Monoclonal antibody	**155**	**(87.6%)**
Anti-CD20	**153**	**(86.4%)**
Chemotherapy	**162**	**(91.5%)**
Platine-based regimen	**124**	**(70.1%)**
Radiotherapy	14	(7.9%)
IMiD	11	(6.2%)
Kinase inhibitor	14	(7.9%)
Corticosteroids	13	(7.3%)

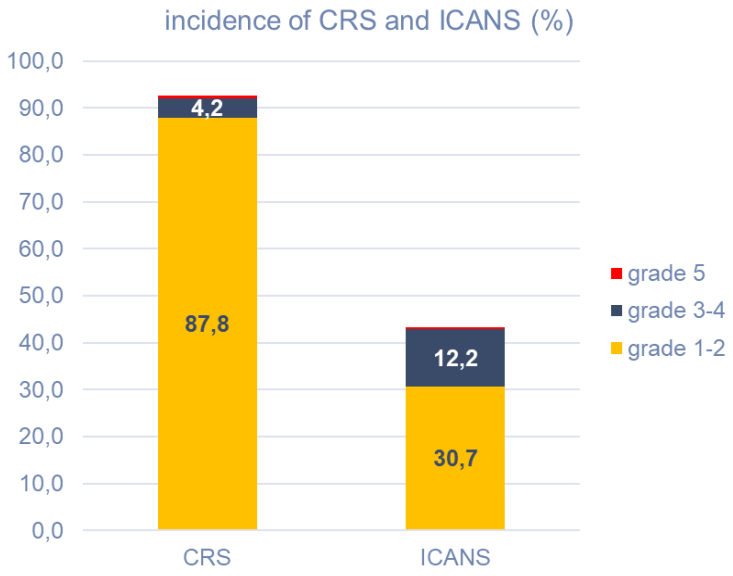
* Several treatment possible

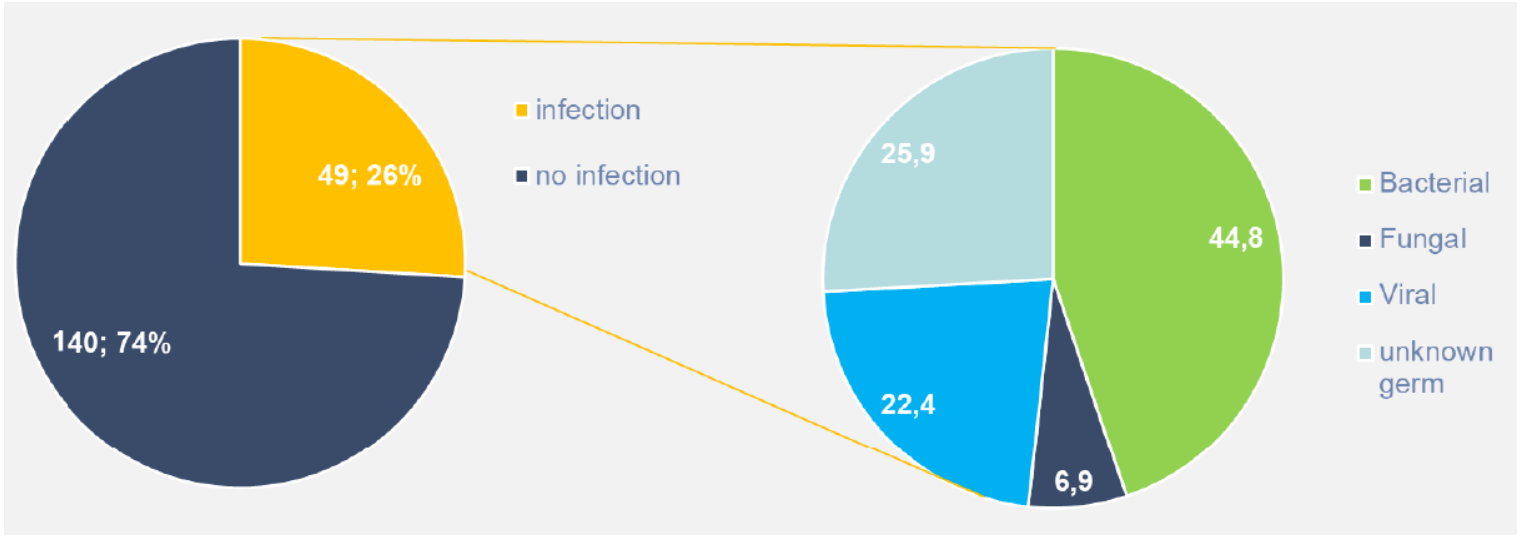


DESCAR-T LBCL treated with Axi-cel in 2nd line

Brisou G. et al. ASH 2023 [Abstract 905]

Toxicities

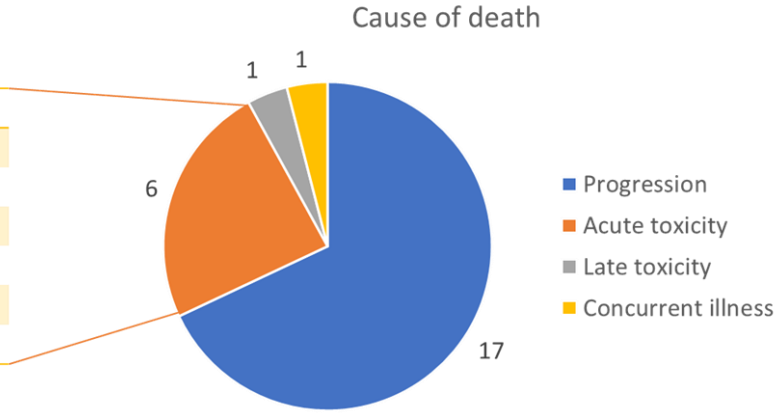




- **Most of these infections occurred during the first month post infusion**
- **Only 6 bacterial, 1 viral and 1 fungal infections occurred later**

Causes of Death

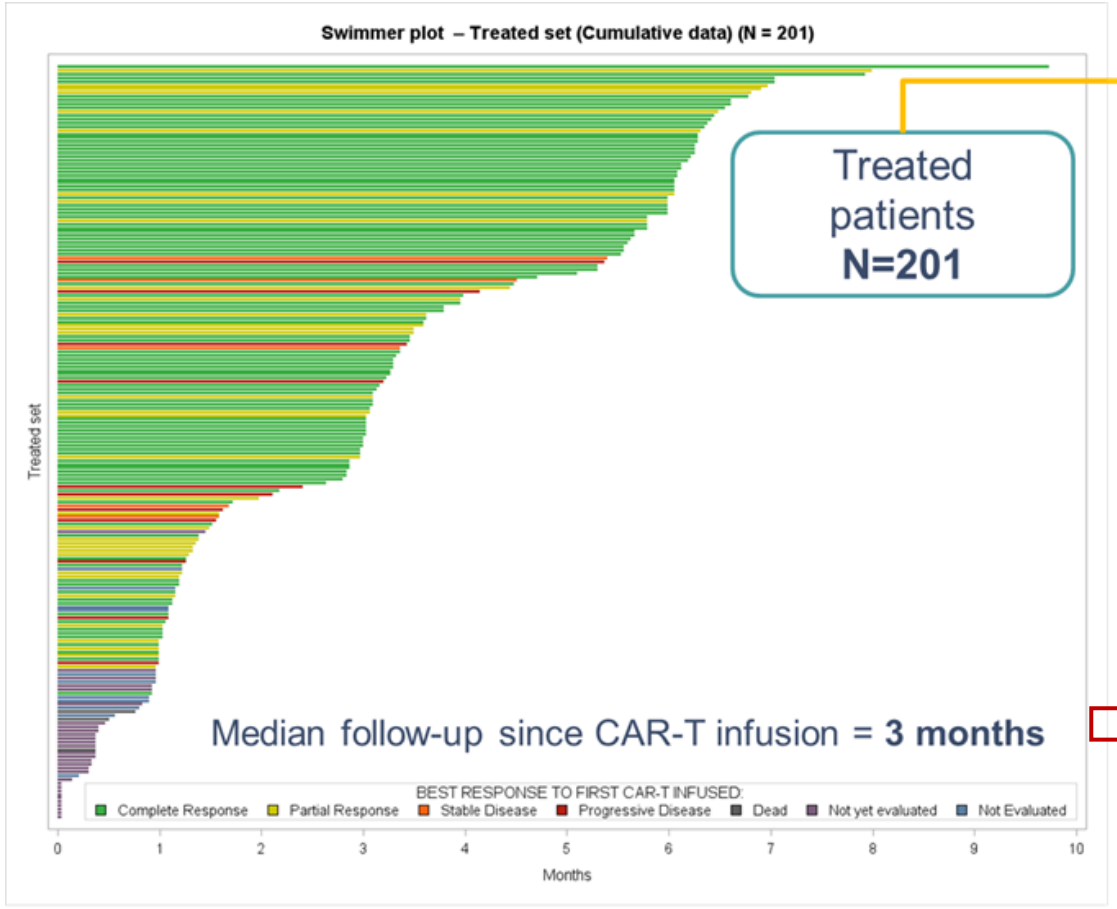
Cause of death	n
UNKNOWN	1
NEUROLOGICAL TOXICITY	1
ACUTE HEMATOTOXICITY (DEEP PANCYTOPENIA)	1
CRS	1
MULTIVISCERAL FAILURE	1
SEPTIC SHOCK	1

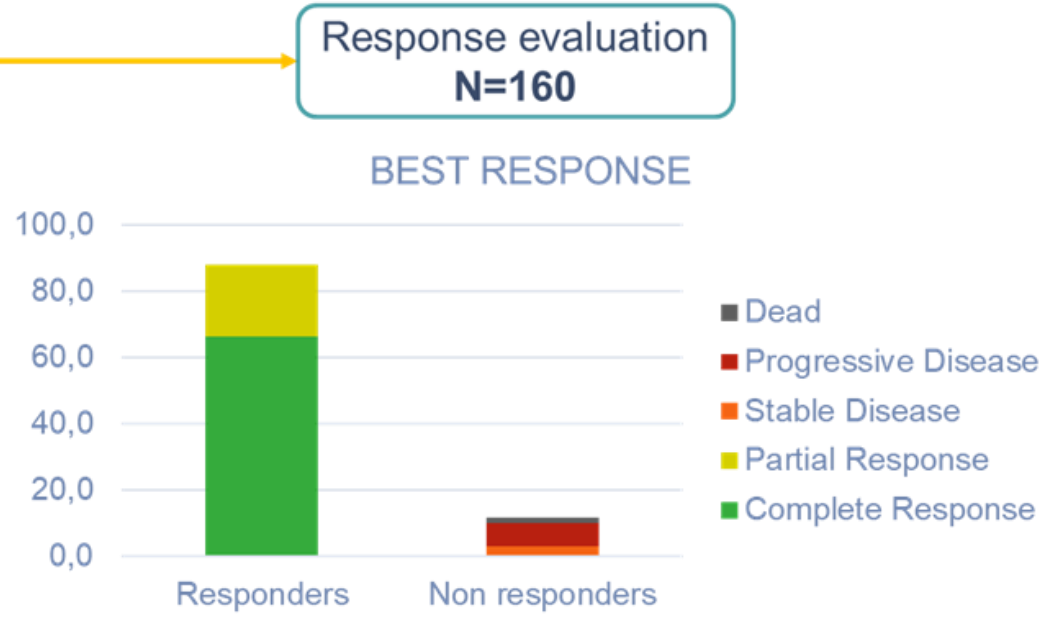


DESCAR-T LBCL treated with Axi-cel in 2nd line

Brisou G. et al. ASH 2023 [Abstract 905]

Response



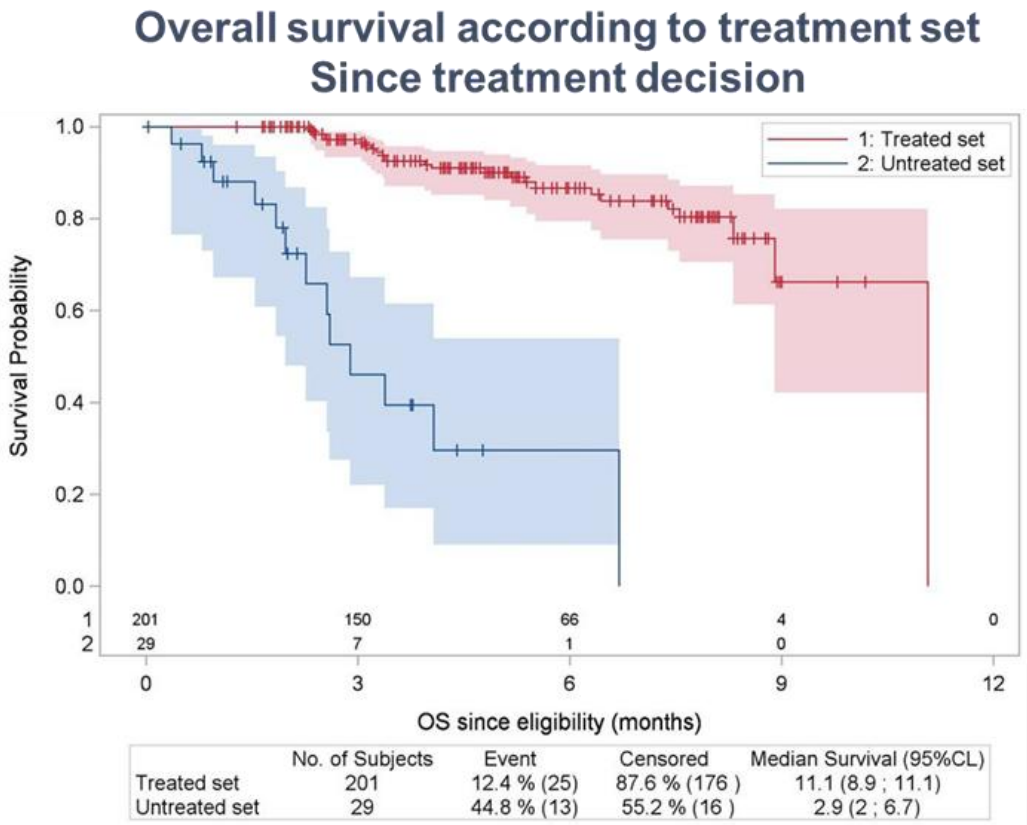


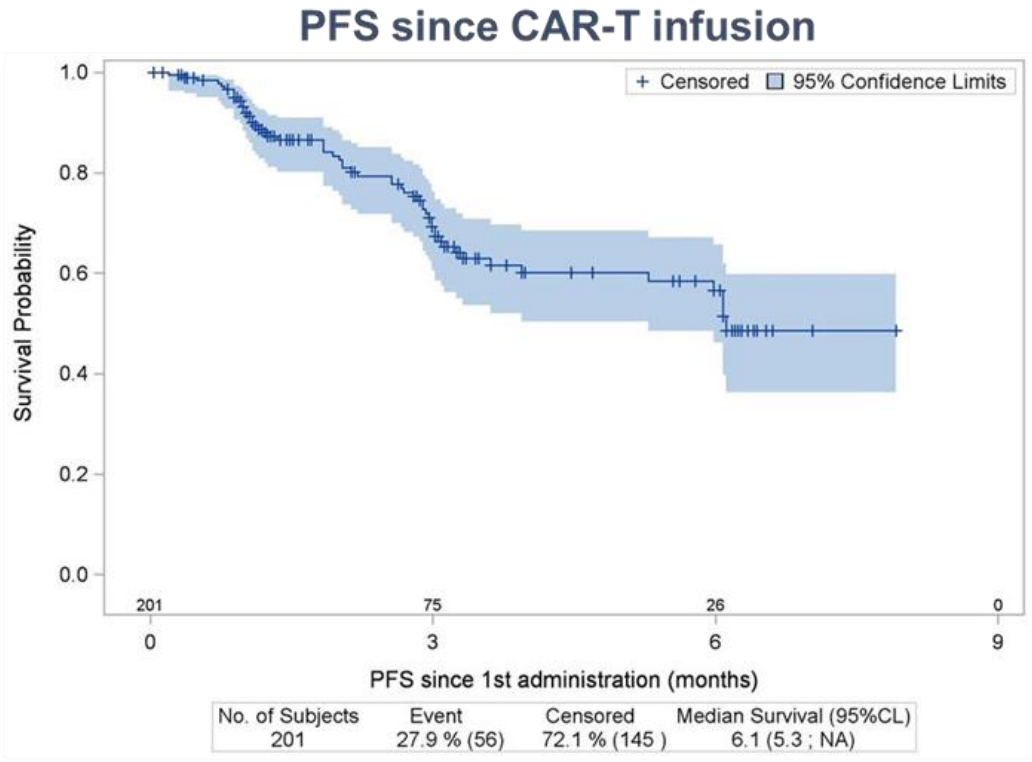
	n	%
Complete Response	106	66.3
Partial Response	35	21.9
Stable Disease	5	3.1
Progressive Disease	11	6.9
Dead	3	1.9

DESCAR-T LBCL treated with Axi-cel in 2nd line

Brisou G. et al. ASH 2023 [Abstract 905]

Survival





median OS since eligibility

- treated set: 11.1 (8.9-11.1) months
- untreated set: 2.9 (2-6.7) months

median PFS since 1° administration: 6.1 (5.3-NA) months

DESCAR-T LBCL treated with Axi-cel in 2nd line

Brisou G. et al. ASH 2023 [Abstract 905]

KEY MESSAGES

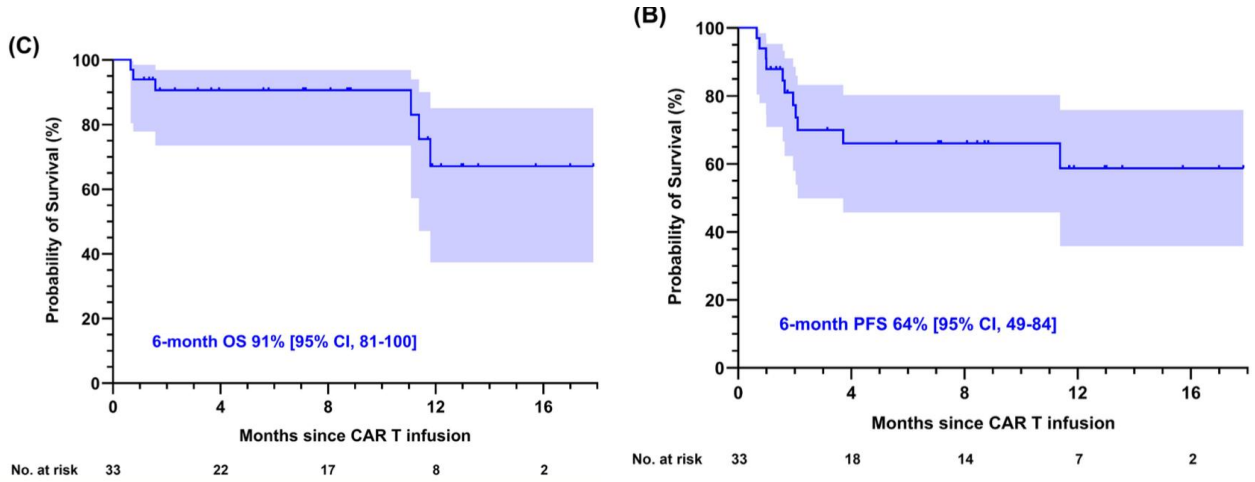
- Inclusion in DESCART registry for 2L LBCL patients is on-going with rapid accrual
- The vast majority of patients were primary refractory and received bridging chemotherapy
- Axi-cel in 2L for R/R LBCL is feasible and safe in real-life
- No new toxicity signals were observed
- Early assessments of response are in line with those described in ZUMA-7 and ALYCANTE studies
- Further follow up is needed and ongoing

Real-world experience of axicabtagene ciloleucel, a CD19-directed CAR T-cell therapy, in the second-line treatment of early relapsed or primary refractory large B-cell lymphoma

Othman T, et al Br J Haematol. 2024

	N = 33 (%)
(A)	
Median age at infusion, years (range)	64 (20–86)
≤60	11 (33)
>60	22 (67)
Gender	
Female	11 (33)
Male	22 (67)
ECOG performance status at infusion	
0–1	28 (85)
Unknown	5 (15)
Diagnosis	
Diffuse large B-cell lymphoma	23 (70)
High-grade B-cell lymphoma with *MYC* and *BCL2* rearrangement	3 (9)
Transformed follicular lymphoma	7 (21)
Stage	
I–II	7 (21)
III–IV	25 (76)
Unknown	1 (3)
Bulky disease by Lugano criteria	
Yes	9 (27)
No	16 (49)
Unknown	8 (24)
IPI score at infusion	
0–2	20 (61)
3–5	5 (15)
Unknown	6 (18)
Cell of origin	
GCB	19 (58)
Non-GCB	14 (42)
Double expressor	
Yes	11 (33)
No	11 (33)
Unknown	11 (33)
Active CNS disease at infusion	1 (3)
Disease status at leucapheresis	
Early relapse	18 (55)
Primary refractory	15 (45)
Bridging therapy	
Polatuzumab-containing regimen[a]	7 (21)
Platinum-containing regimen[b]	10 (30)
Radiation ranging from 2400 to 3750 cGy	3 (9)
Steroids alone	3 (9)
None	10 (30)
Lymphodepletion	
Fludarabine/cyclophosphamide	26 (79)
Bendamustine/rituximab	7 (21)
Ineligible by ZUMA-7 criteria	20 (61)
Received bridging therapy not restricted to steroids[c]	20 (61)
Impaired organ function[d]	7 (21)
Foley catheter inserted at time of CAR T infusion	2 (6)
Active CNS disease at the time of CAR T infusion	1 (3)
Deep vein thrombosis within 6 months of CAR T infusion	1 (3)
History of cancer excluding non-melanoma skin cancer or carcinoma in situ and active within 3 years of CAR T infusion	1 (3)

Real-word experience: single-center experience of City of Hope (Duarte, California, USA)



Bridging therapy: 70%

Survival outcomes:

- Median EF, OS, PFS not reached after mFU of 7.2 months
- 6-month EFS and PFS were both 64%,
- 6-month OS: 91%, 6-month NRM: 10%, 6-month Cum.Inc.Rel. (CIR) 24%

Safety:

- CRS >2: 3% (vs 6% of ZUMA-7)
- ICANS >2: 24% (vs 21% but lower disease burden)

Therapy succesfully provided to 64% of patients in the outpatient setting

- Hospital stay reduction of 6 days per patient
- Necessity of outpatient immune effector cell (IEC) care team

What's new in second-line CAR-T therapies for DLBCL from the 66th ASH Annual Meeting?

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

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

STUDY DESIGN AND ANALYSIS

Data Source	• Data were collected from the CIBMTR database • **Study population:** consecutive, consenting adult patients with R/R LBCL (including DLBCL, HGBCL, FL Grade 3B, PMBCL) who received axi-cel in 2L between April 2022 and July 2023 from 89 centers in the United States and enrolled in the CIBMTR data registry
Outcomes of Interest	• **Effectiveness:** OR and CR rate, DOR, EFS, OS • **Safety:** CRS, ICANS, cytopenias, infections, non-relapse mortality, cause of death, therapies to manage CRS and ICANS

Statistical Analysis	• Descriptive statistics summarized baseline patient characteristics and outcomes in the overall population, by ZUMA-7 eligibility among patients with DLBCL, HGBCL, and FL Grade 3B (ineligible vs eligible/unknown), and in patients with PMBCL
	  ○ Patients with PMBCL were ineligible for ZUMA-7 and were analyzed separately
	• Time-to-event outcomes were assessed using Kaplan–Meier methodology
	  ○ When sufficient data were available, 12-month data were reported; otherwise, 6-month data were reported

Real-World Early Outcomes of Second-Line Axicabtagene Ciloleucel Therapy in Patients With R/R LBCL

Lee *et al.* ASH 2024 (Abstract 526)

Baseline patient and disease characteristics

- N=**446 patients**
- axi-cel in 2L between **April 2022 and July 2023**
- **Median follow-up for all patients was 12.0 months** (95% CI, 11.5-12.1)
  - ZUMA-7 ineligible: 11.8 months (95% CI, 7.2-12.1)
  - ZUMA-7 eligible/unknown: 12.1 months (95% CI, 11.8-12.3)

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 LDH levels pre-infusion, n (%)	199 (48)
Response to last line of therapy pre-leukapheresis, n (%)	228 (51)
Median vein-to-vein time, days, (IQR)	29.0 (27.0-35.0)
Bridging therapy,[a,d] n (%)	286 (66)

Eligibility and transplant ineligibility

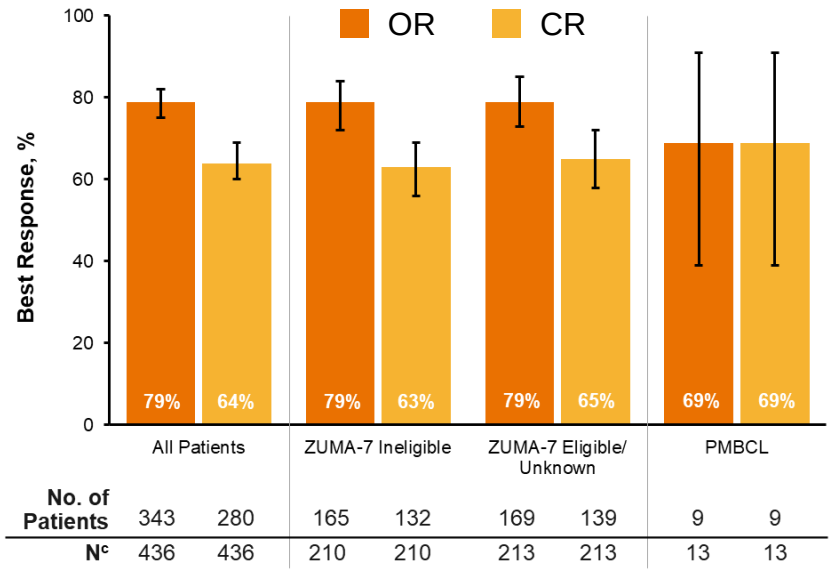
Characteristic	All Patients N=446
ZUMA-7 eligibility,[a] n (%)	
Eligible	214 (48)
Not eligible	219 (49)
Organ impairment	150 (34)
Pulmonary (moderate/severe)	81 (18)
Cardiac	49 (11)
Bone marrow (platelets, ANC, and/or ALC)	37 (8)
Arrhythmia	26 (6)
Cerebrovascular disease	14 (3)
Renal (moderate/severe)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

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

Real-World Early Outcomes of Second-Line Axicabtagene Ciloleucel Therapy in Patients With R/R LBCL

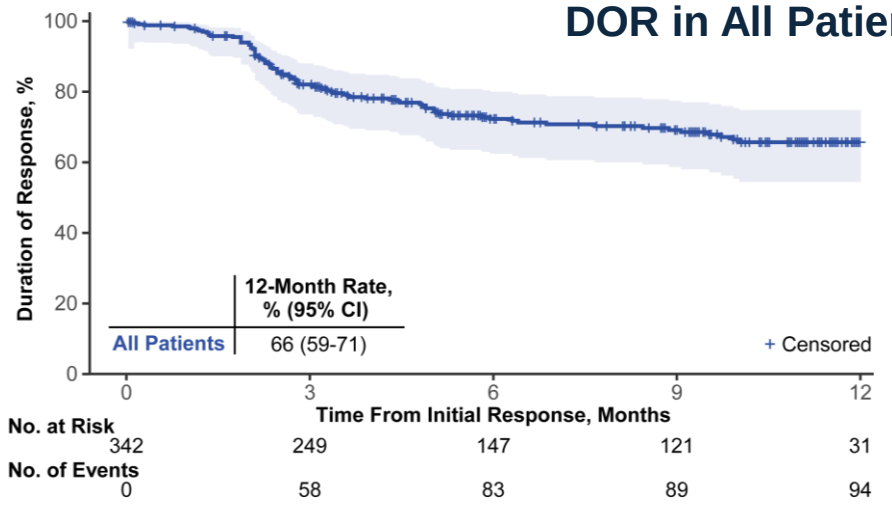
Lee *et al.* ASH 2024 (Abstract 526)

ORs and CRs were similar across all patient groups

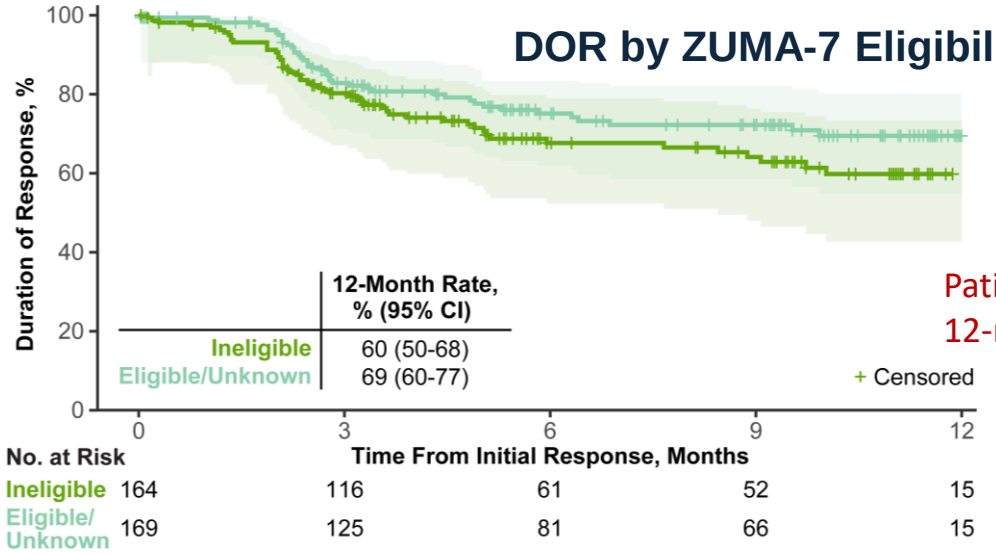


- Median time to OR in all patients was 2.1 months (IQR, 1.0-3.6)
  - ZUMA-7 ineligible: 1.8 months (IQR, 1.0-3.4)
  - ZUMA-7 eligible/unknown: 2.4 months (IQR, 1.0-3.7)
  - PMBCL: 3.0 months (IQR, 1.2-NE)
- Median time to CR in all patients was 3.1 months (IQR, 1.1-NE)
  - ZUMA-7 ineligible: 3.2 months (IQR, 1.1-NE)
  - ZUMA-7 eligible/unknown: 3.1 months (IQR, 1.1-NE)
  - PMBCL: 3.0 months (IQR, 1.2-NE)

median fup: 12 months



All patients:
12-month DOR: 66%



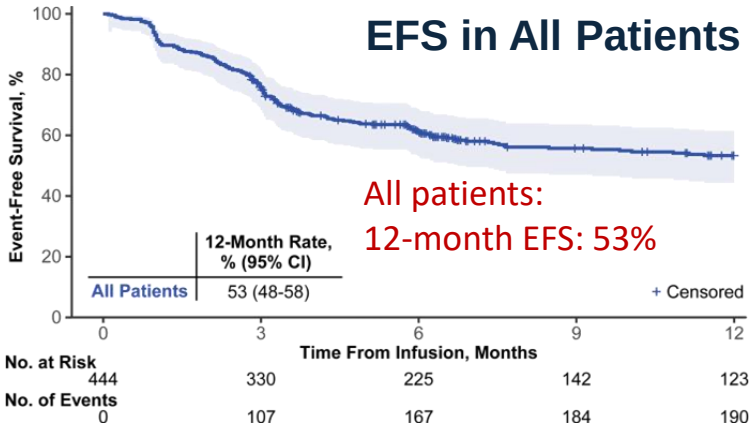
Patients ZUMA eligible:
12-month DOR: 69%

Patients ZUMA ineligible:
12-month DOR: 60%

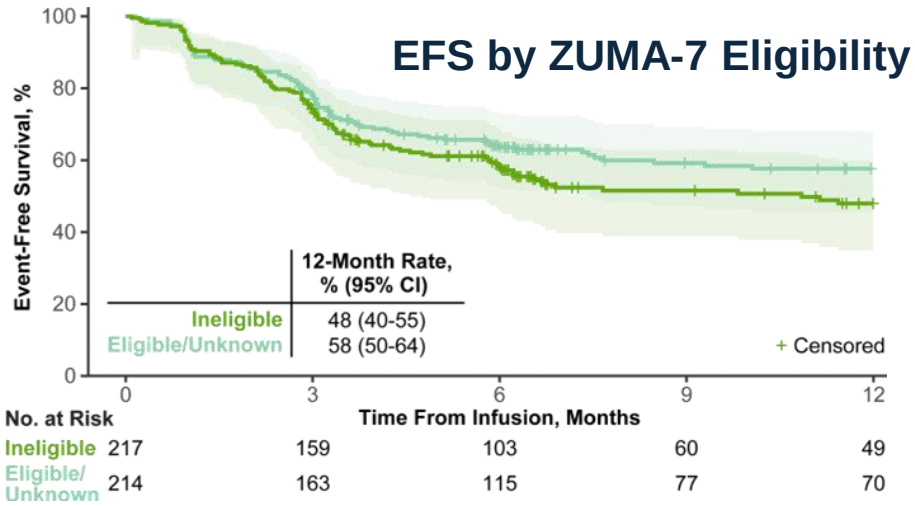
Real-World Early Outcomes of Second-Line Axicabtagene Ciloleucel Therapy in Patients With R/R LBCL

Lee *et al.* ASH 2024 (Abstract 526)

Event-free survival



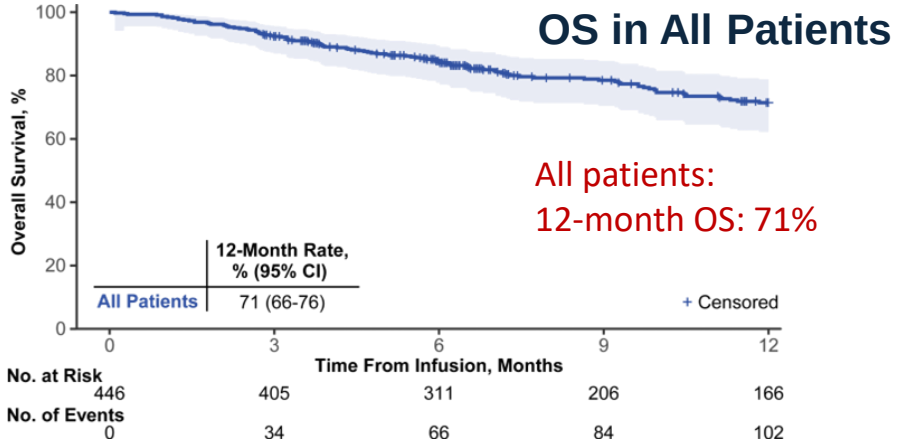
All patients:
12-month EFS: 53%



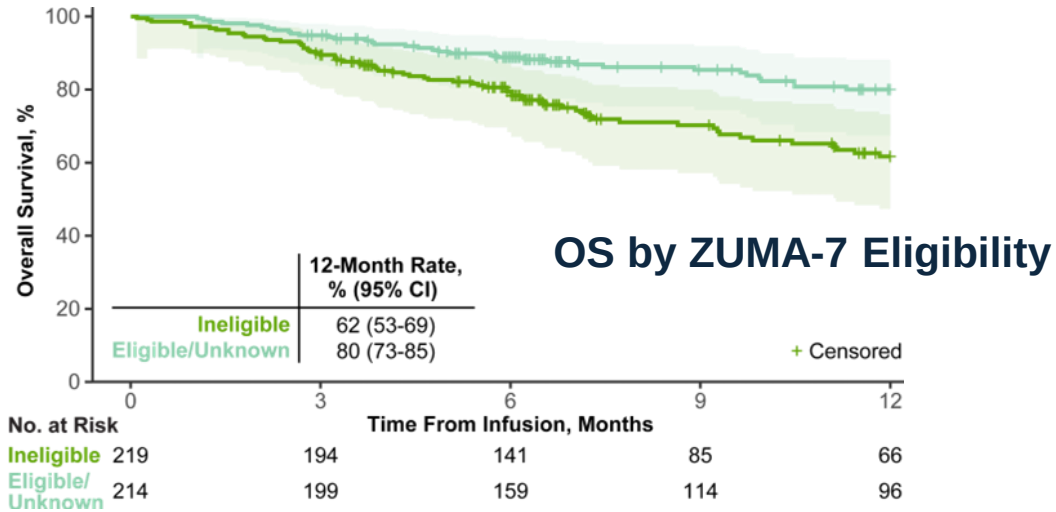
Patients ZUMA eligible:
12-month EFS: 58%

Patients ZUMA ineligible:
12-month EFS: 48%

Overall survival



All patients:
12-month OS: 71%



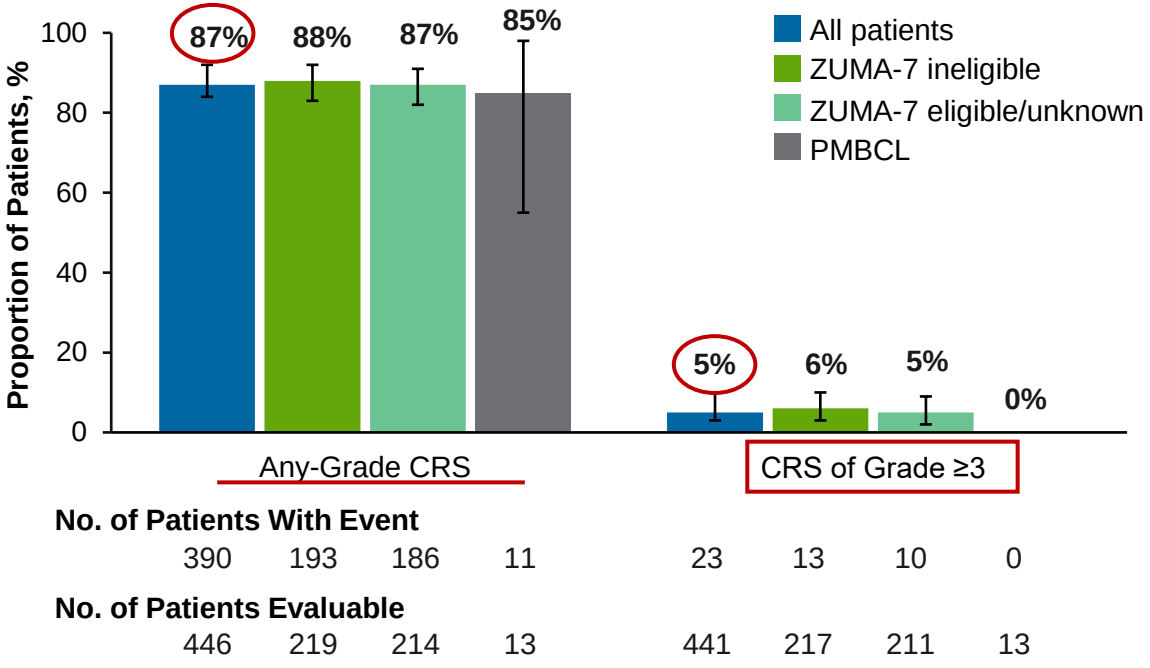
Patients ZUMA eligible:
12-month OS: 80%

Patients ZUMA ineligible:
12-month OS: 62%

Real-World Early Outcomes of Second-Line Axicabtagene Ciloleucel Therapy in Patients With R/R LBCL

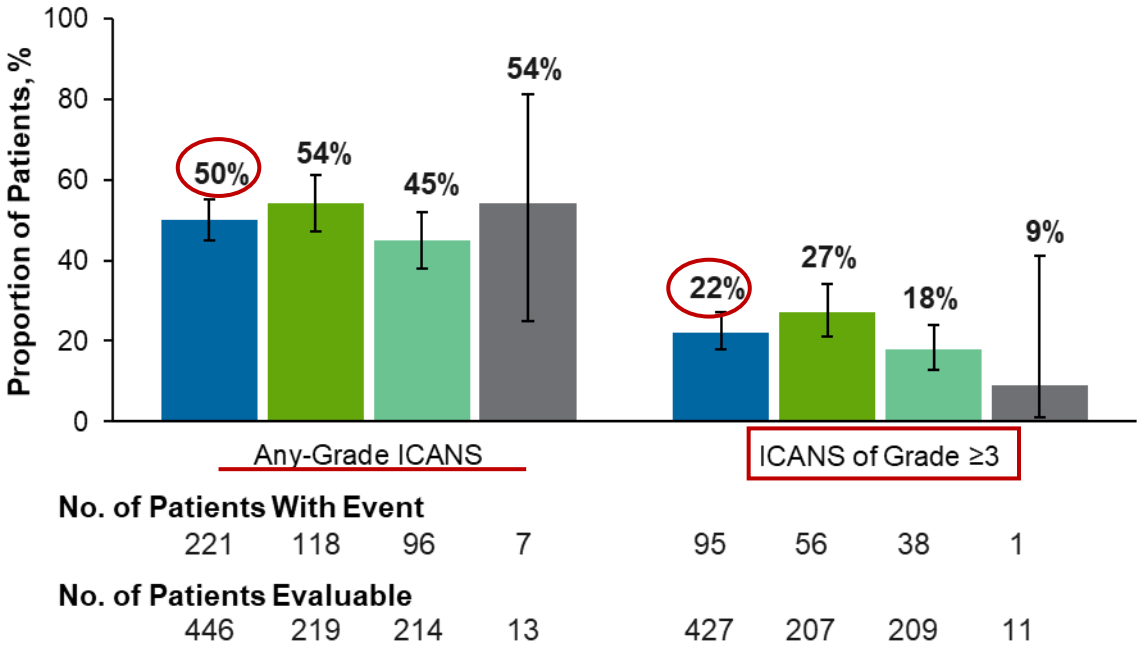
Lee *et al.* ASH 2024 (Abstract 526)

Incidence of CRS



Incidence of any-grade CRS and Grade ≥3 CRS were similar across patient groups

Incidence of ICANS



Incidence of any-grade ICANS and Grade ≥3 ICANS were similar across patient groups

The most common treatments given for CRS and/or ICANS were tocilizumab (80%), corticosteroids (65%), antiepileptics (19%), and anakinra (18%)

Real-World Early Outcomes of Second-Line Axicabtagene Ciloleucel Therapy in Patients With R/R LBCL

Lee *et al.* ASH 2024 (Abstract 526)

Patient deaths

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)

Conclusions:

- This is the largest real-world analysis of patients with R/R LBCL who received 2L commercial axi-cel
  - 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
- A limitation of this study is that some patients receiving bridging therapy may have been misclassified as third line or later by the algorithm used to define line of therapy and therefore excluded from this analysis
- Future work will assess real-world outcomes with a longer follow-up
- Overall, these findings support the use of axi-cel as a 2L therapy for patients with R/R LBCL, including many patients who would have been considered ineligible for ZUMA-7, in the real-world setting

Welcome to the 66th ASH® Annual Meeting and Exposition

Multi-centre real-world outcomes of large B-cell lymphoma patients treated with 2L axicabtagene ciloleucel in the UK

Kuhnl A, et al. ASH 2024 (Abstract 2342; poster presentation)

N=195

LBCL R/R ≤12 months since 1L therapy approved for axi-cel as 2L therapy

Outcomes

- ORR, PFS and OS
- Tolerability

Median follow-up: 9.1 months

Methods

Consecutive patients approved for SOC axi-cel by the UK National CAR T Clinical panel (UKNCCP) between May 2023 and March 2024 across 15 CAR T centres

Baseline patient characteristics

	Patients approved for axi-cel (N=195)
Median age, years (range)	61 (22–76)
LBCL subtype De novo DLBCL NOS HGBCL Transformed FL	 71% 9% 12%
Advanced stage disease	76%
Extranodal involvement ≥2 sites	32%
Elevated LDH	63%
Bulky disease	25%
1L CIT R-CHOP Polatuzumab-R-CHP	 71% 16%

Results

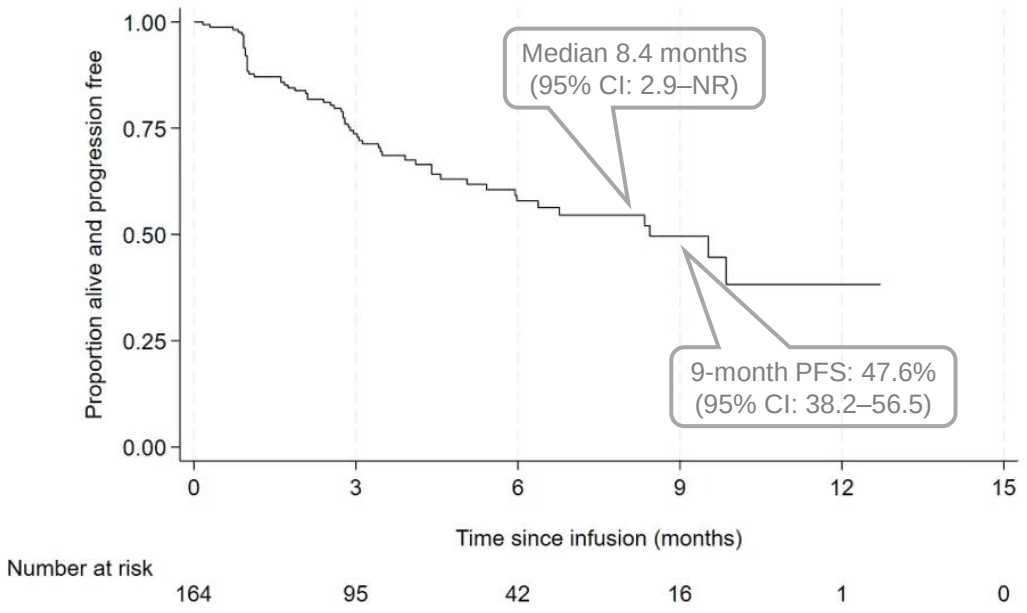
- Of 195 patients. 189 (97%) underwent leukapheresis and 176 (90%) were infused
- Median time from approval to infusion: 49 days (IQR 42–60)
- Median vein-to-vein time: 36 day (IQR 33–47)
- Time interval from 1L CIT to axi-cel approval: at end of 1L treatment 56%; within 3 months 20%; 3–6 months 9%; 6–12 months 15%
- Holding therapy: 47% (majority systemic CIT)
- Bridging therapy: 97% (systemic BT 67%; radiotherapy 20%; combined modality treatment 11%)
- ORR to systemic BT: 52% (13% CR)
- **Best response (N=176): 61.1% CR; 26.9% PR; 88.0% ORR**

Response rates were comparable with those reported in the ZUMA-7 trial

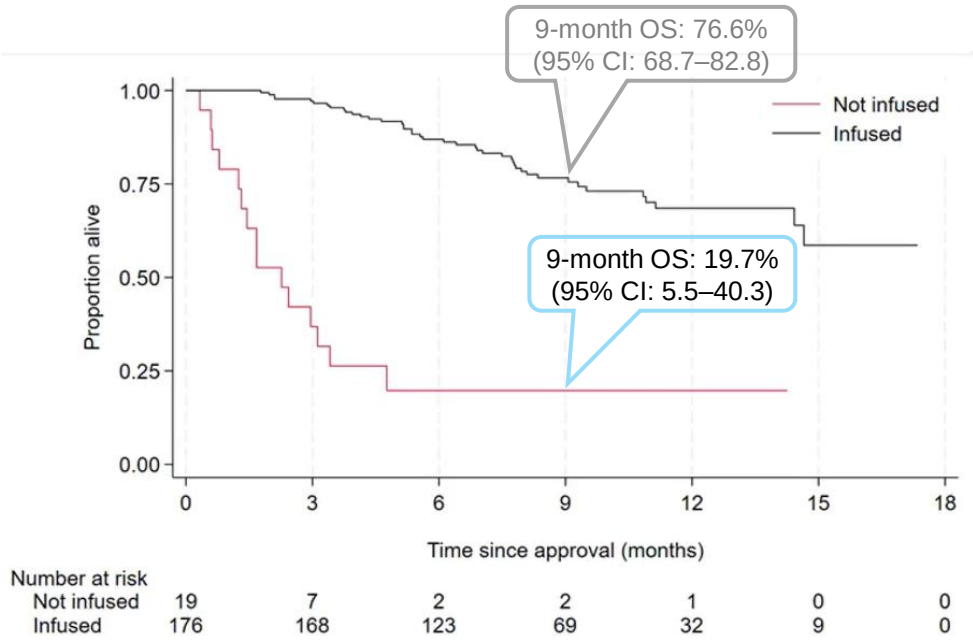
Multi-centre real-world outcomes of large B-cell lymphoma patients treated with 2L axicabtagene ciloleucel in the UK

Kuhnl A, et al. ASH 2024 (Abstract 2342)

PFS



OS



Safety

- CRS any-grade 98%; Grade ≥3 4%
- ICANS any-grade 44%; Grade ≥3 17%
- 90% of patients received tocilizumab, 60% corticosteroids and 17% anakinra
- Cumulative incidence NRM at 9 months: 5.4% (95% CI: 2.7–10.8)

With limited follow-up, PFS and OS are encouraging despite 47% of patients requiring urgent pre-apheresis holding therapy and 97% receiving post-apheresis bridging therapy

Real-World Outcomes of Lisocabtagene Maraleucel as Second-Line Therapy in Patients with R/R LBCL: First Results from the Center for International Blood and Marrow Transplant Research Registry (CIBMTR)

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

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

June 2022 — August 2024: Study period

Data cutoff August 4, 2024

Study outcomes and endpoints

- **Effectiveness outcomes:** ORR, CR rate, DOR, PFS, and OS
- **Safety outcomes:** AEs of special interest, NRM,[b] and deaths

Subgroup analyses

- ORR, CR rate, DOR, PFS, and OS by TRANSFORM eligibility criteria, refractory or relapsed disease status, and age

Median follow-up[c] of 6.4 months (95% CI, 6.1–6.5; range, 0.2–14.8)

N=157 patients

N=105 (67%) patients were ineligible for TRANSFORM (primarily due to age and/or severity of comorbidities)

	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)

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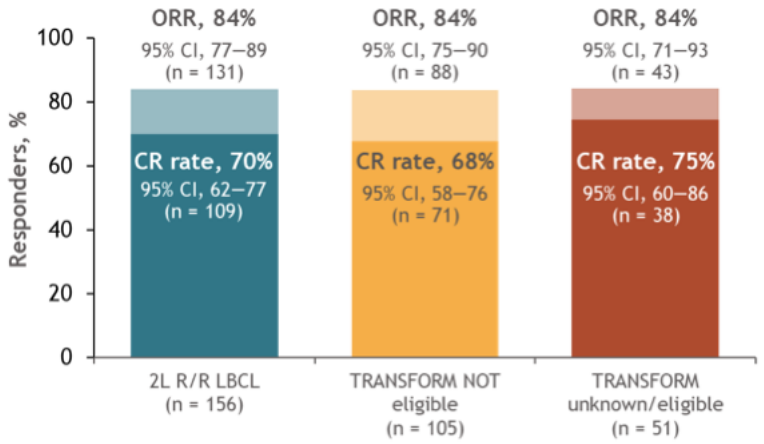
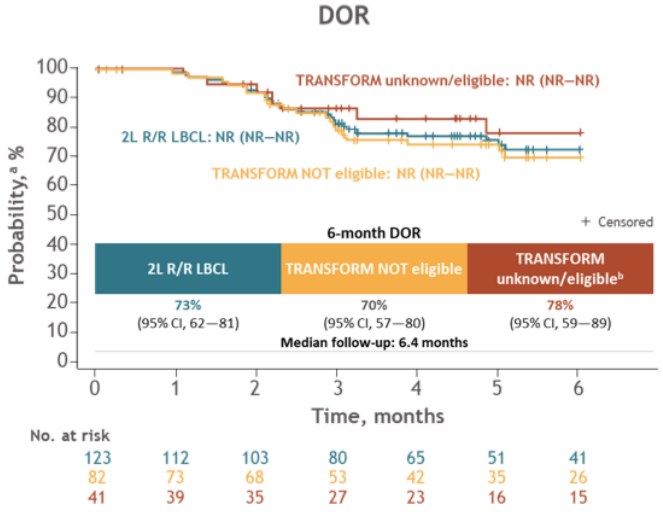
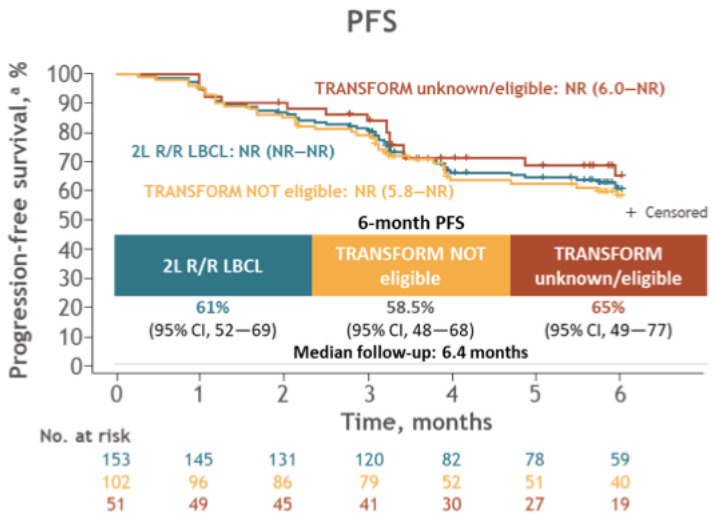
Real-World Outcomes of Lisocabtagene Maraleucel as Second-Line Therapy in Patients with R/R LBCL: First Results from the Center for International Blood and Marrow Transplant Research Registry (CIBMTR)

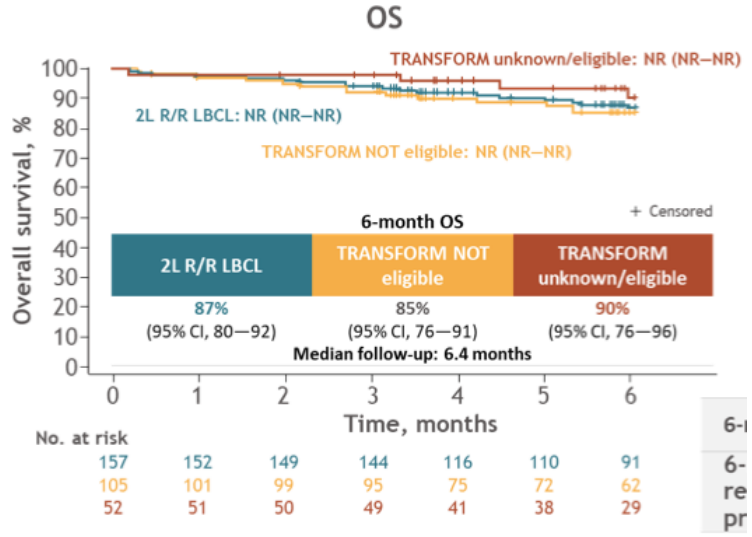
Bobillo MS, et al. ASH 2024 [Abstract 470]

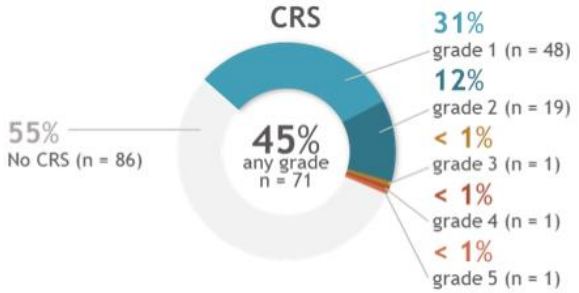
median FU 6.4 (0.3-13.8) months

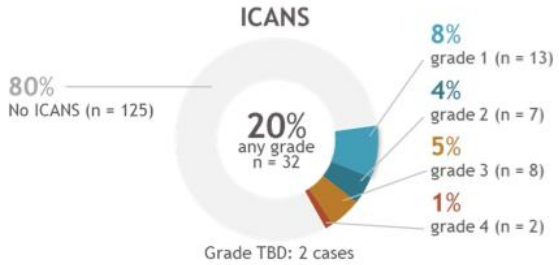












	2L R/R LBCL (n = 157)
6-mo cumulative incidence of NRM (95% CI)	1.3 (0.3–4.3)
6-mo cumulative incidence of relapse/progression or death due to primary disease (95% CI)	37.9 (29.6–46.0)

Results support Liso-cel as 2^SOC for pts, young and old alike with R/R LBLC for ASCT

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CAR-T Cell Therapy in **Early Relapsed/Refractory** Large B-Cell Lymphoma: Real World Analysis from the Cell Therapy Consortium

Rojek A.E. et al. ASH 2024 [Abstract 628]

retrospective multicenter study to evaluate the real-world outcomes of early R/R LBCL pts treated with **CAR-T in 2L as compared to the 3L+ setting**

Table 1: Patient Characteristics

	All pts, N = 155	2L CAR T, N = 53	3L+ CAR T, N = 102
Age at apheresis			
Median, yrs (IQR)	63 (56-70)	63 (55-70)	63 (56-70)
> 70 years, %	25	28	24
Male, %	67	62	70
ECOG PS ≥ 2, %	15	19	14
Non-Caucasian ethnicity, %	11	6	14
Disease stage III/IV, %	77	81	75
Active secondary CNS lymphoma, %	13	9	15
Elevated pre-LDc LDH, %	45	45	45
Disease status at time of referral, %			
Primary refractory	30	51	25
Relapsed, then refractory	27	0	35
Relapsed	31	42	26
Received bridging therapy, %	75	78	73
CAR T cell product, %			
Axi-cel	57	74	48
Tisa-cel	16	0	25
Liso-cel	27	26	27

Table 2: Toxicities and Outcomes

Toxicity	All pts, N = 155	2L CAR T, N = 53	3L+ CAR T, N = 102
CRS, %			
Any grade	68	60	71
Grade 3-4	6	6	6
ICANS, %			
Any grade	35	40	33
Grade 3-4	15	15	15
Outcomes			
30-day response*, %			
CR	54	67	49
ORR	80	84	78
90-day response†, %			
CR	57	59	55
ORR	70	73	68
9-month PFS, % (95% CI)	48 (41-57)	56 (44-71)	45 (36-56)
9-month OS, % (95% CI)	64 (57-72)	75 (63-88)	59 (50-69)

* out of 137 evaluable pts at 30 days post CAR T infusion

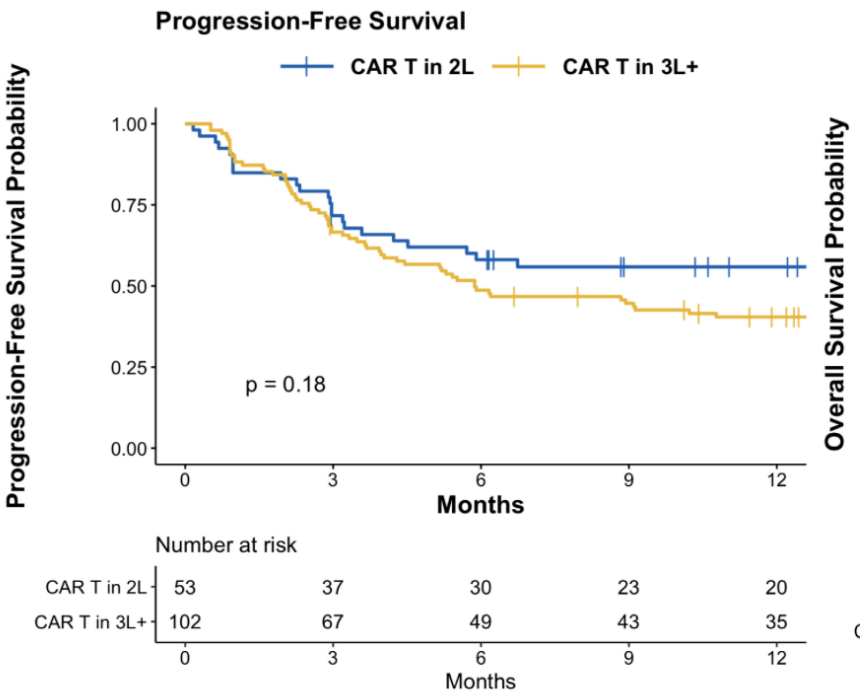
† out of 122 evaluable pts at 90 days post CAR T infusion

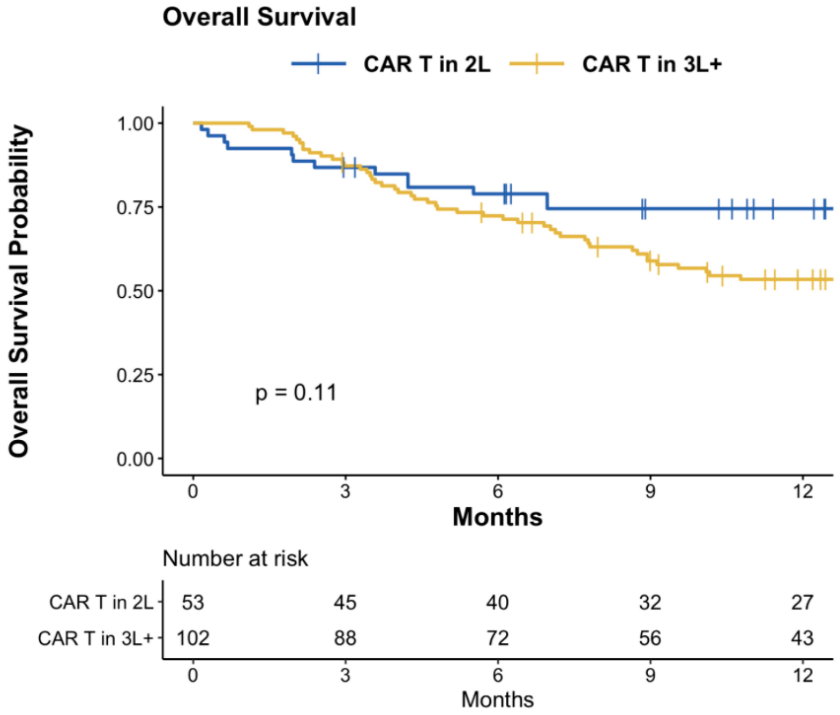
- **no differences in rates of CRS or ICANS** between pts receiving 2L vs 3L+ CAR-T
- **no significant difference in either ORR or CR rate** for those treated with 2L or 3L+ CAR-T.

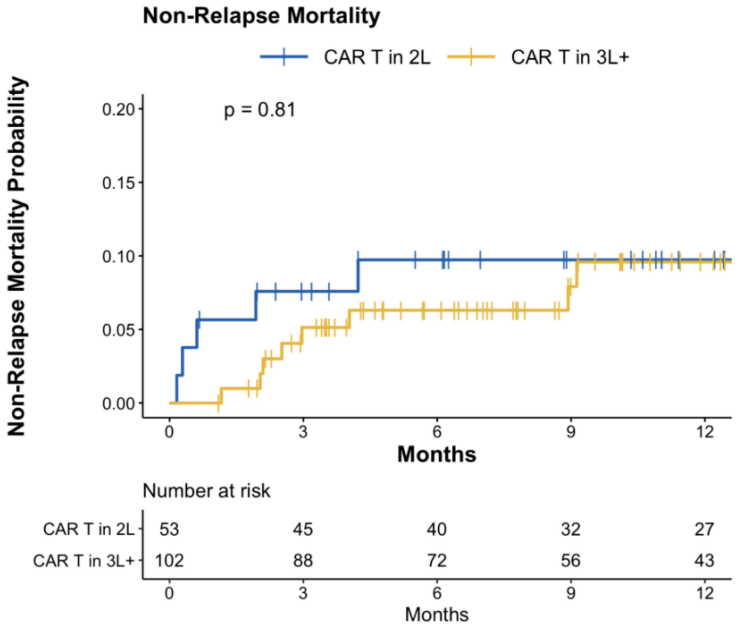
CAR-T Cell Therapy in Early Relapsed/Refractory Large B-Cell Lymphoma: Real World Analysis from the Cell Therapy Consortium

Rojek A.E. et al. ASH 2024 [Abstract 628]

Survival outcomes







- outcomes of pts treated with commercial CAR-T in both the 2L and 3L+ setting yield **favorable response and survival outcomes**

- selection of **more fit pts** and **efforts to reduce disease burden** prior to infusion **may improve survival outcomes** for early R/R LBCL pts treated with CAR-T **regardless of line of therapy**

THE COST-EFFECTIVENESS OF AXICABTAGENE CILOLEUCEL VERSUS STANDARD OF CARE AS SECOND-LINE THERAPY IN PATIENTS WITH LARGE B-CELL LYMPHOMA IN ITALY

Rodriguez-Guadarrama YA et al, EBMT 2024

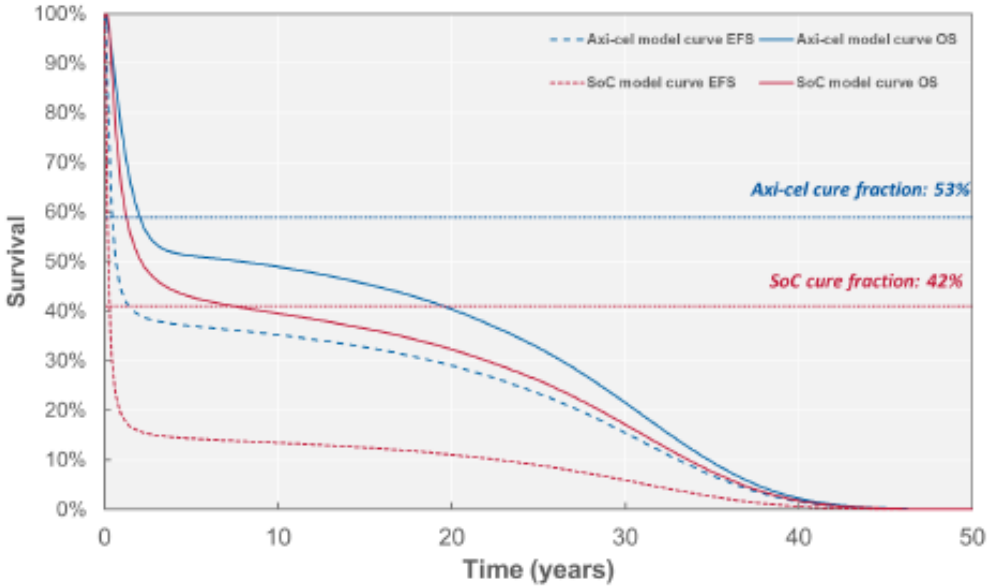
Objective: The objective of this study was to estimate the cost-effectiveness of axi-cel versus SOC in 2L LBCL from an Italian National Health Service (NHS) perspective.

RESULTS:

Axi-cel treatment of patients with 2L LBCL (time to event data obtained from ZUMA-7) was associated with

- a per patient incremental QALY (Quality Adjusted Life Year) gain of 1.92
- incremental costs of €70,577 compared to SOC.
- As a result, **axi-cel was cost-effective with an ICER (Incremental Cost- Effectiveness Ratio) of €36,811 per QALY versus SOC**

Figure 1. Modelled extrapolated survival



- The difference in 5-year projected OS was 8.3% (51.2% vs. 42.9% for axi-cel and SOC, respectively)

- The model estimated 5-year EFS to be 37% and 14.3% for axi-cel and SOC, respectively.

- The results were driven by better long-term survival of patients in the axi-cel arm, more time spent in the event-free state, and the avoidance of subsequent lines of CAR T-cell.

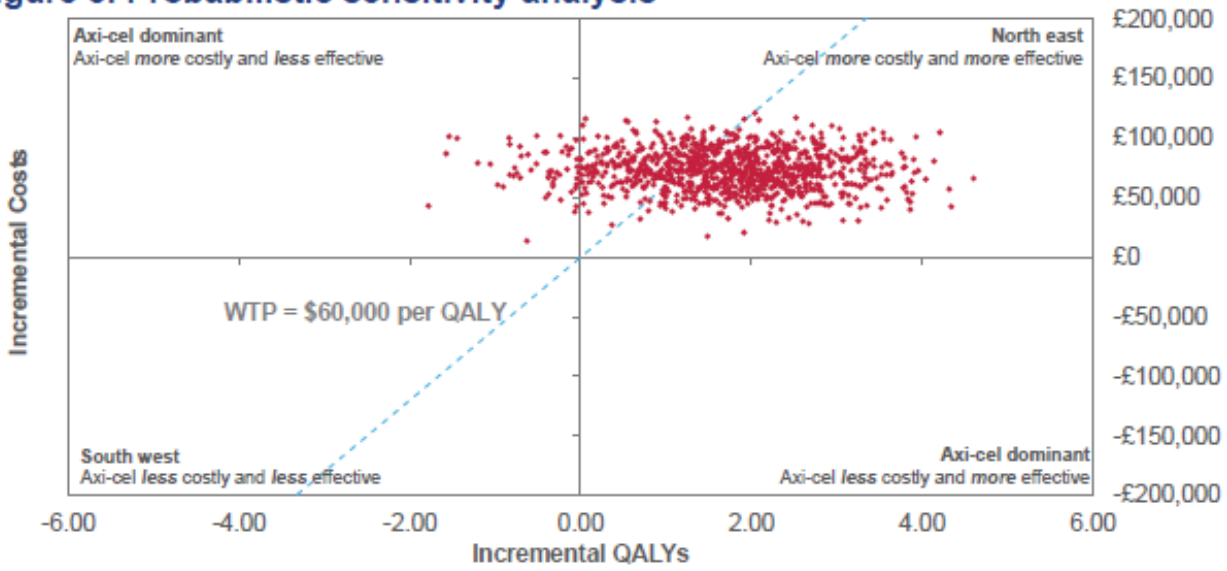
THE COST-EFFECTIVENESS OF AXICABTAGENE CILOLEUCEL VERSUS STANDARD OF CARE AS SECOND-LINE THERAPY IN PATIENTS WITH LARGE B-CELL LYMPHOMA IN ITALY

Rodriguez-Guadarrama YA et al, EBMT 2024

RESULTS:

In probabilistic sensitivity analyses,
axi-cel was 68% likely to be cost-effective at a willingness to pay threshold of €60,000 per QALY gained

Figure 3. Probabilistic sensitivity analysis



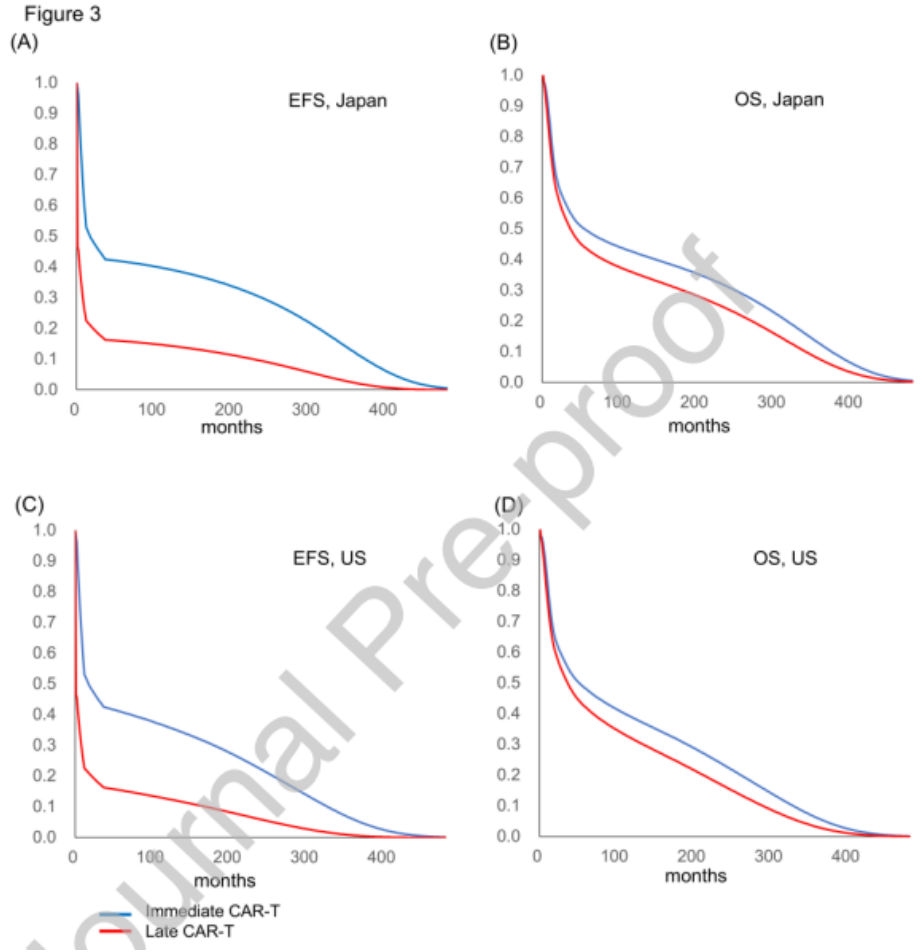
axi-cel, axicabtagene ciloleucel; QALYs, quality-adjusted life years; WTP, willingness to pay

CONCLUSIONS:

- Over a lifetime horizon of 50 years, treatment of patients with 2L LBCL with axi-cel is cost-effective, with an ICER well below the €60,000 per QALY willingness-to-pay threshold relevant in Italy.
- This is because by treating in the 2L setting, patients experience a survival benefit and a better QoL in the long-term, whilst avoidance of CAR-T-cell in subsequent lines of treatment offsets incremental costs.
- Reducing delays and barriers to access and increasing patient awareness of CAR T-cell therapies are remaining challenges to address.

Impact of real-world clinical factors on an analysis of the cost-effectiveness of 'immediate CAR-T' versus 'late CAR-T' as second-line treatment for DLBCL patients

Estimated survival curves of the 'immediate CAR-T' and 'late CAR-T' strategies in Japan and the US using the model.



Conclusion:

Incorporating various clinical factors, the analysis showed that 'immediate CAR-T' is more cost-effective than 'late CAR-T.'

However, this conclusion should be interpreted with caution, as the ICERs were very close to the WTP thresholds, and the results were highly sensitive to parameter changes.

Yamamoto C. et al; Transplantation and Cellular Therapy; 2025

Comparison between studies on Real World experiences of CAR-T Therapy in 2° line for R/R LBCL

Study	CAR-T	N° pts	mFU in mo.	ORR %	CR %	PFS	OS	CRS %	ICANS %
PILOT TRIAL	Liso-cel	61	18 (range, 1.2-32.8)	80.3% [68.2-89.4]	54.1% [40.8-66.9]	18-mo PFS: 42.9% [29.9-55.2] at mFU (24.0 mos)	18-mo OS: 59% [45.2-70-4] at mFU (24.24 mos)	38	31
Alycante Trial	Axi-cel	62	12 (range, 2.1-17.9)	69.4% [56.4– 80.4%]	71.0% [58.1–81.8%]	12-mo estim. PFS: 48.8% [34.0-62.0]	12-mo estim. PFS: 78.3% [64.7-87.1]	95.1	51.6
Descar-T	Axi-cel	201	3	88.2%	66.3%	median PFS: 6.1 mos [5.3-NA]	median OS: 11.1 mos [8.9-11.1]	92	43
City of Hope experience	Axi-cel	33	7.2	85%	76%	median PFS NR 6-mo PFS: 64% [49-84]	median OS NR 6-mo OS: 91% [81-100]	91	58
Lee DC et al. ASH 2024	Axi-cel	446	12	79%	64%	12-mo EFS: 53% [48-58]	12-mo OS: 71% [66–76]	87	50
Bobillo MS et al. ASH 2024	Liso-cel	157	6.4 (range, 0.3-13.8)	84% [77-89]	70% [62-77]	61% [52-69] at mFU (6.4 mos)	87% [80-92] at mFU (6.4 mos)	45	20
Rojek AE et al. ASH 2024	Axi-cel and Liso-cel	53	11.1 (range, 0.2-63)	73%*	59%*	9-mo PFS: 56% [44-71]	9-mo OS: 75% [63-88]	60	40

Legend: Pts: patients; mFU: Median follow-up; mo: months; ORR: overall response rate; CR: complete response; PFS: progression free survival; OS: overall survival; CRS: Cytokine Realease Syndrome; ICANS: Immune Cell–Associated Neurologic Syndrome,

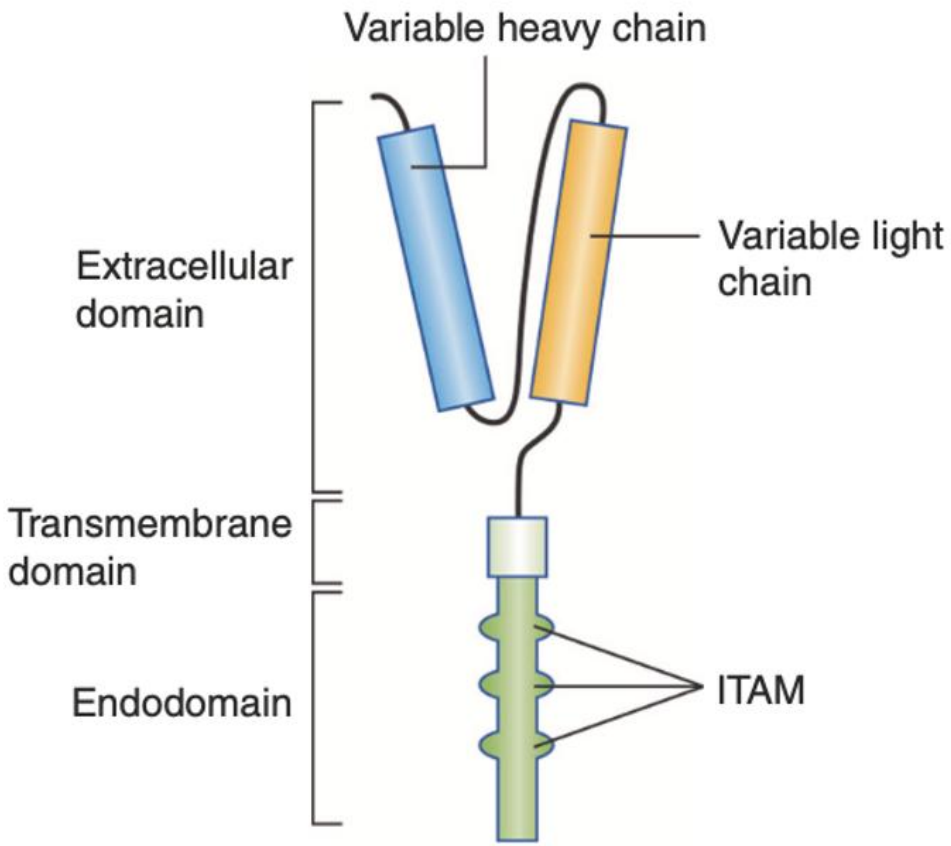
*At 3 months

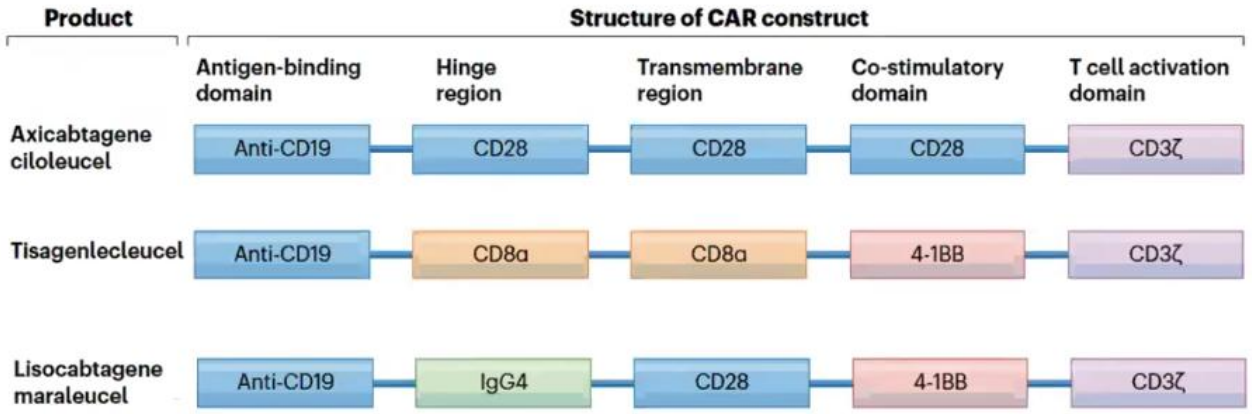
Take home messages

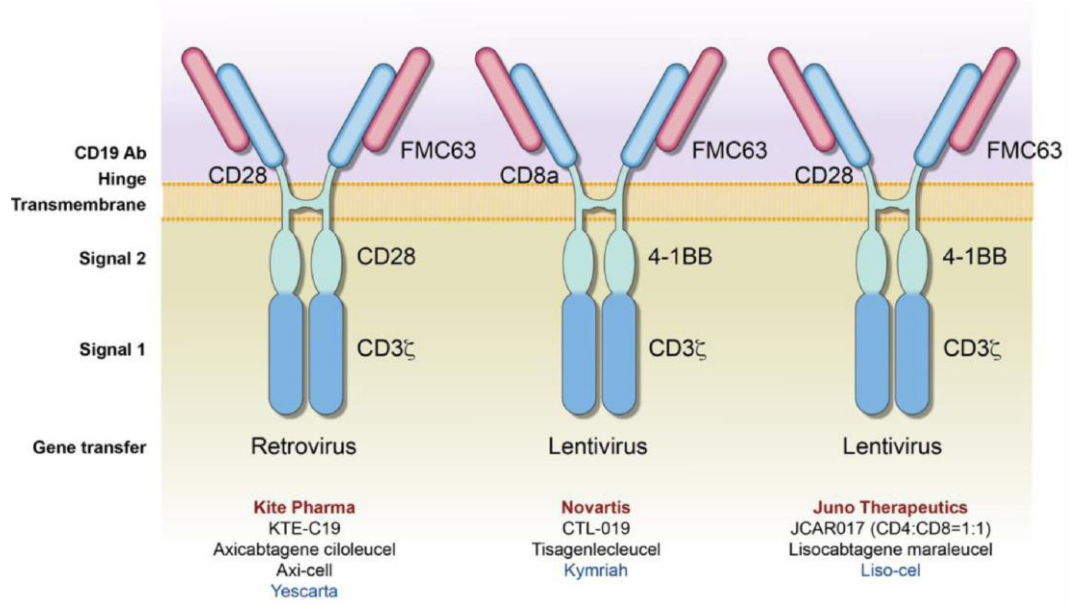
- The vast majority of real-world studies on CAR-T in DLBCL have focused on third-line treatment or included patients receiving CAR-T regardless of the treatment line.
- Since CAR-T therapies were approved for second-line treatment (ZUMA-7 and TRANSFORM), data collection has also started focusing on second-line use.
- **Real-world study results confirm those of registration trials**, showing greater efficacy of CAR-T compared to standard therapy even in second-line DLBCL patients
- In real-world studies, **Axi-cel and Liso-cel have shown similar results in terms of response and survival outcomes; Liso-cel seems to have a better safety profile.**
- **Second line-CAR-T therapy represents cost-effective alternative to standard-of-care** (SOC) for adult patients with relapsed or refractory LBCL, making it a valuable use of healthcare resources from a global perspective

Grazie per l’attenzione

Anti-CD19 CAR T-Cell therapy for r/r LBCL



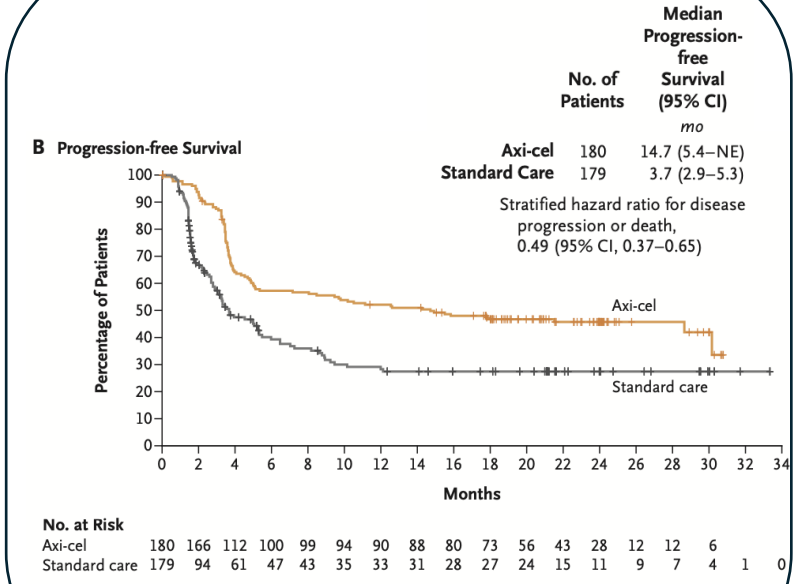




Tokarew N, Ogonek J, Endres S, et al. Teaching an old dog new tricks: next-generation CAR T cells. Br J Cancer. 2019. Kathryn M. Cappell, Nature Reviews Clinical Oncology 2023; Peihua Lu et al. CAR-T and other adoptive cell therapies for B cell malignancies, JCO 2021

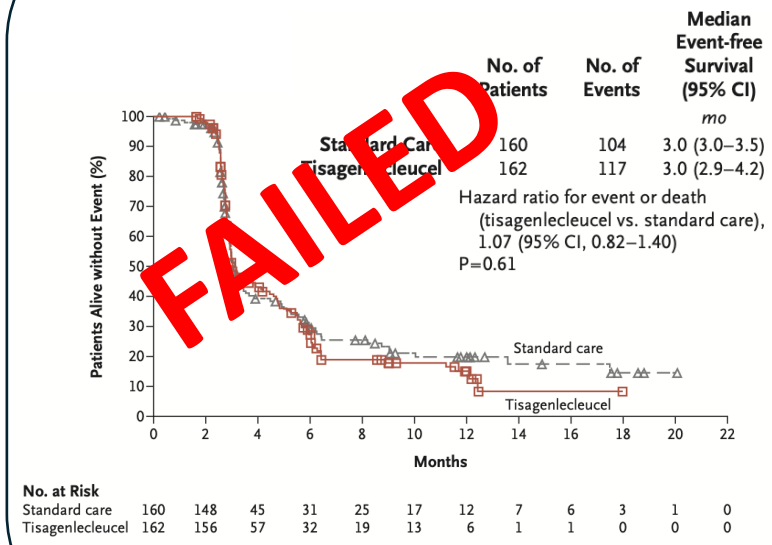
CD19 CAR-T Cells for R/R LBCL: moving to 2nd line

ZUMA-7
Axicabtagene Ciloleucel



Locke et al, NEJM 2022

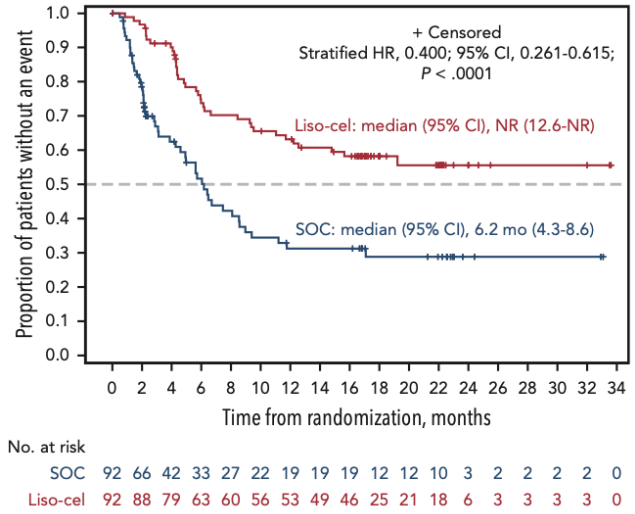
BELINDA
Tisagenlecleucel



Bishop et al, NEJM 2022

TRANSFORM
Lisocabtagene Maraleucel

Median FU 17.5 months



Abramson et al, Blood 2022

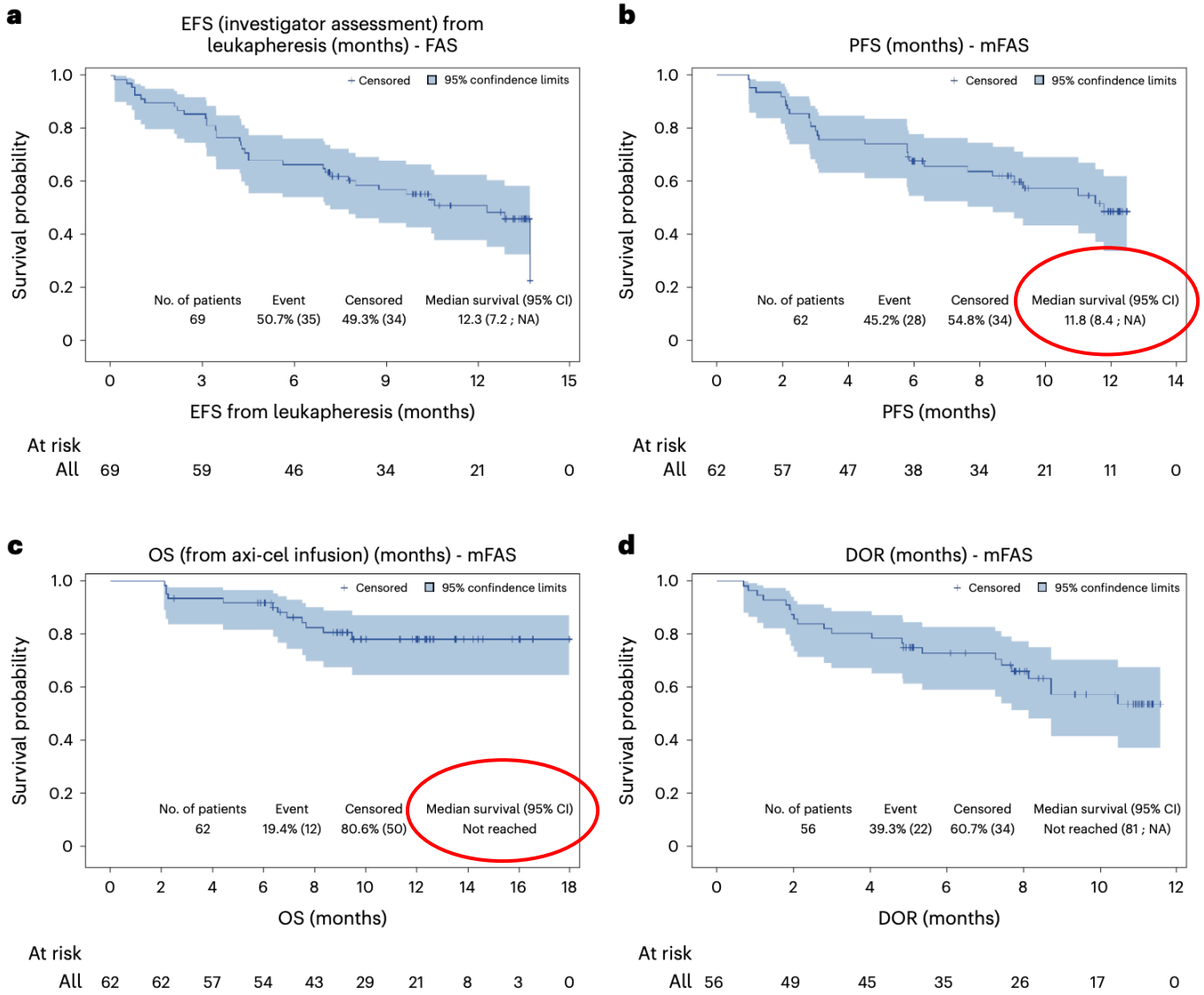
ALYCANTE Trial – Axi-Cel in R/R ineligible for ASCT

Houot, R., e al. *Nat Med* **2023**

- phase 2 trial
- adult patients with **R/R LBCL INELIGIBLE for ASCT**
- primary end point: complete metabolic response (CMR) after 3 months from Axi-Cel infusion

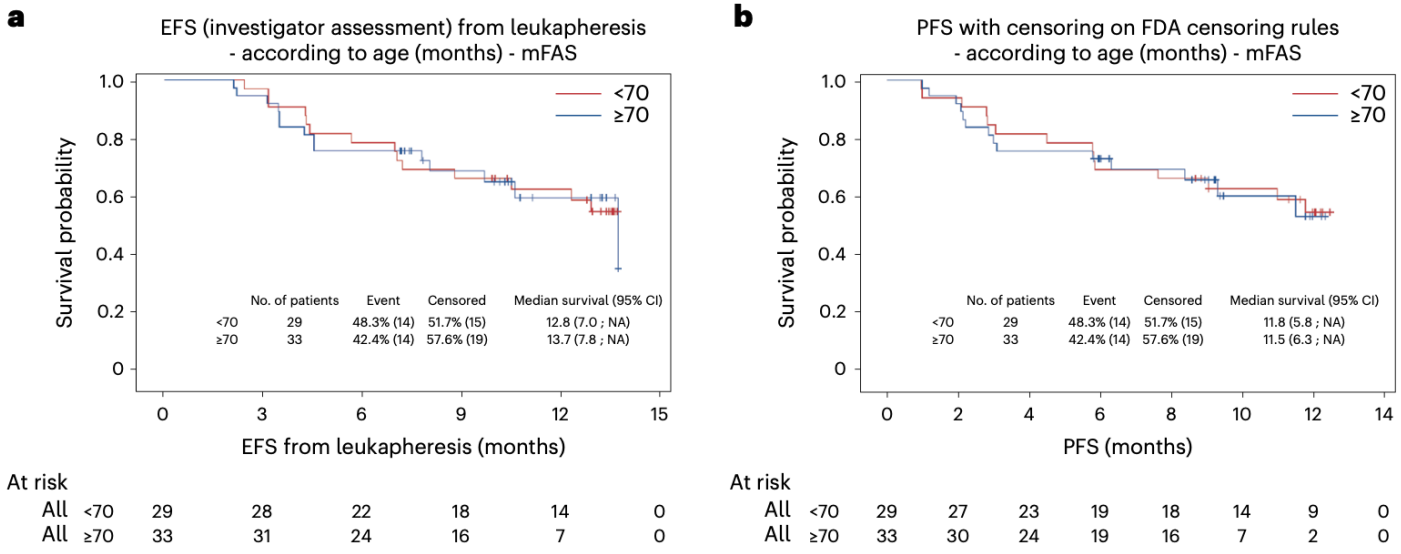
Response	Investigator-assessed (%)	Assessed by a central review panel (%)
Response at 3 months		
Objective response	47 (75.8)	43 (69.4)
Complete response	44 (71.0)	41 (66.1)
Partial response	3 (4.8)	2 (3.2)
Stable disease	0	1 (1.6)
Progressive disease	7 (11.3)	9 (14.5)
Not evaluated	8[a] (12.9)	9 (14.5)
Best response		
Objective response	56 (90.3)	57 (91.9)
Complete response	49 (79.0)	51 (82.3)
Partial response	7 (11.3)	6 (9.7)
Stable disease	3 (4.8)	1 (1.6)
Progressive disease	3 (4.8)	4 (6.5)
Not evaluated	0	0

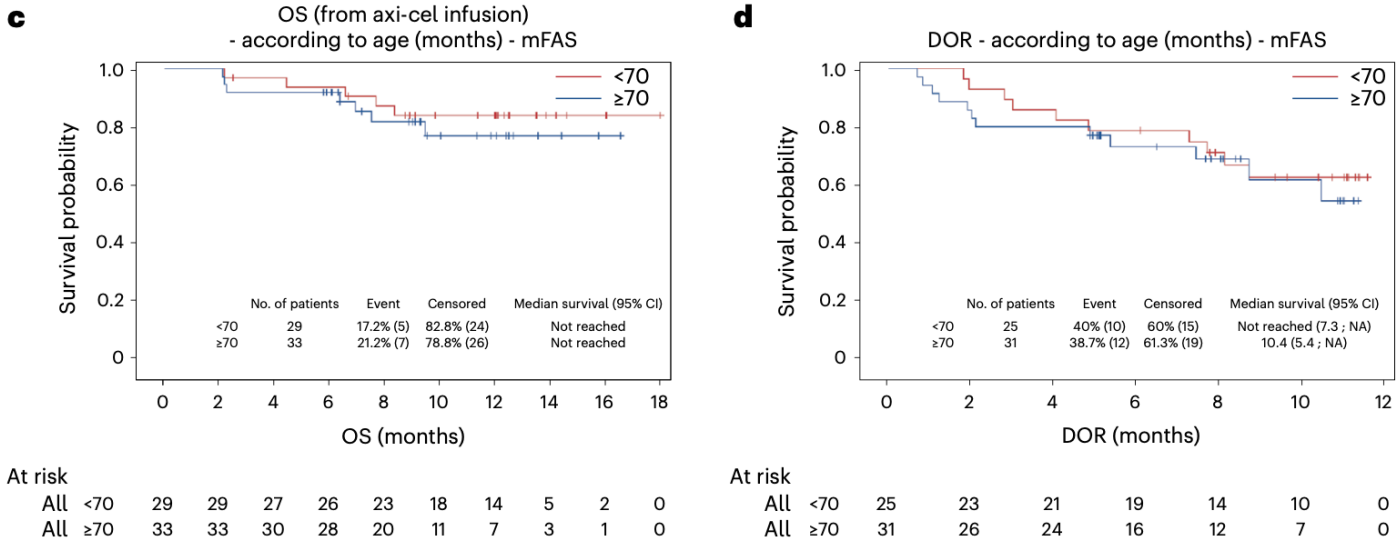
at a median follow-up of 12 months (range, 2.1-17.9)



ALYCANTE Trial – Axi-Cel in R/R ineligible for ASCT

no differences in term of response, survival outcomes and toxicity between >70y and <70y





Adverse events >2 in 95.2% of patients

- neutropenia 66%
- thrombocytopenia 38%.
- CRS 95.5% (grade >2 8%)
- ICANS 51.6% (grade >2 14.5%)

At the time of data cutoff, 12 patients died, 5 of whom from lymphoma and 1 of unknown reason

results support axi-cel as 2^ line therapy in patients with R/R LBCL ineligible for ASCT

Houot, R., e al. *Nat Med* **2023**

PILOT trial – Liso-Cel in R/R ineligible for ASCT

- phase 2 trial
- primary end point: **ORR**

key eligibility criteria

- age: ≥ 18 yrs
- LBCL: DLBCL NOS (de novo; transformed FL), HGBCL (double/triple hit), FL3b
- one prior line with anthracycline and anti CD20
- ineligible for ASCT by investigator and met > 1 of the following:
  - age ≥ 70 years
  - ECOG PS =2
  - DLCO ≤ 60%
  - LVEF ≤ 50%
  - CrCl < 60 mL/min
  - AST/ALT > 2 x ULN
- Patients with secondary CNS lymphoma were allowed

N=**61**

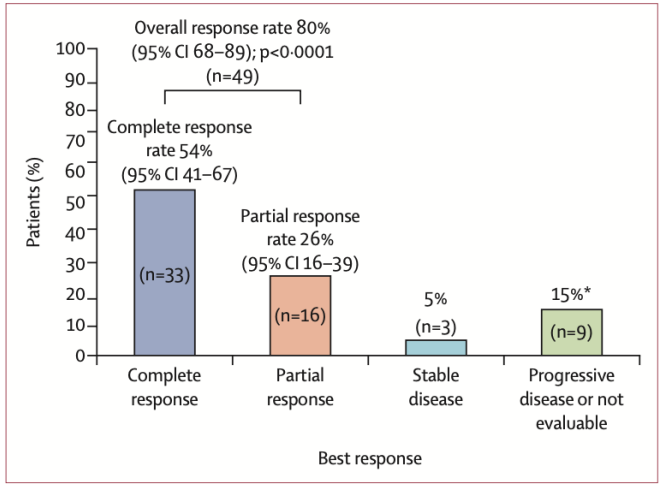
DLBCL:	33 (54%)
High grade:	18 (30%)
Double o triple hit:	20 (33%)
Refractory:	33 (54%)
Relapsed ≤ 12 months:	13 (21%)
Relapsed > 12 months:	15 (25%)

First-line treatment for LBCL: 84% CHOP

Response after first line:

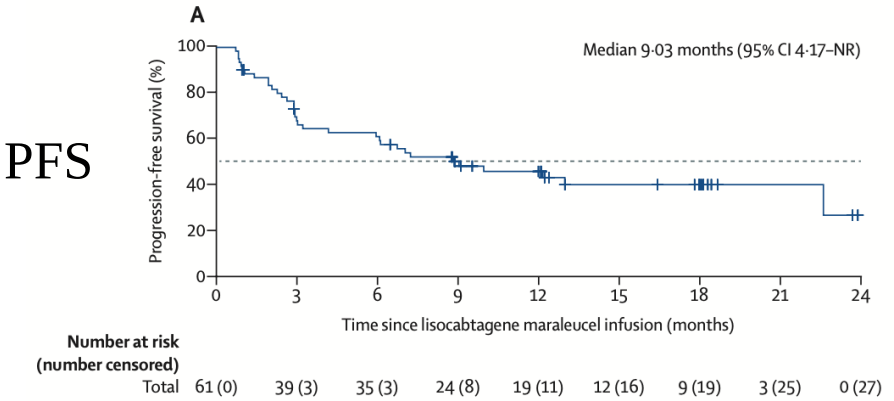
CR:	28 (46%)
PR:	15 (25%)
SD:	5 (8%)
PD:	13 (21%)

Bridging therapy: 32 (52%)

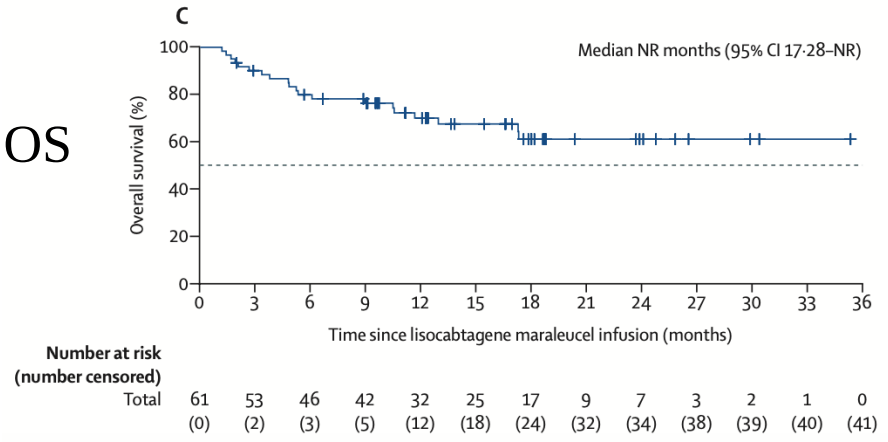


median follow-up: **12.3 months (1.2 – 26.5)**

PFS



OS



Sehgal, Alison et al . The Lancet Oncology, 2022

65th ASH Annual Meeting and Exhibition
December 9 – 12
San Diego, CA

Final Analysis of the Phase 2 PILOT Study

median follow-up of **18.2 months** (range, 1.2-32.8)

Table. Summary of efficacy (liso-cel–treated efficacy analysis set) and safety (liso-cel–treated analysis set) outcomes

Efficacy outcomes	Liso-cel–treated efficacy analysis set (N = 61)
ORR (CR + PR), n (%) [95% CI][a]	49 (80.3) [68.2–89.4]
CR rate, n (%) [95% CI][a]	33 (54.1) [40.8–66.9]
BOR, n (%)	
CR	33 (54.1)
PR	16 (26.2)
SD	3 (4.9)
PD	8 (13.1)
NE	1 (1.6)
DOR	
Continued response at 12 mo, % (95% CI)[b]	54.9 (39.6–67.9)
Continued response at 18 mo, % (95% CI)[b]	52.6 (37.4–65.8)
Median follow-up, mo (95% CI)[c]	23.1 (22.9–23.3)
PFS	
18-mo PFS rate, % (95% CI)[b]	42.9 (29.9–55.2)
Median follow-up, mo (95% CI)[c]	24.0 (23.8–24.15)
OS	
18-mo OS rate, % (95% CI)[b]	59.0 (45.2–70.4)
Median follow-up, mo (95% CI)[c]	24.25 (23.95–24.8)
Summary of AEs[d]	**Post-TE period[e] (n = 57)**
Any AE, n (%)	29 (50.9)
Grade 3–4	9 (15.8)
Grade 5	1 (1.8)
Any serious AE	5 (8.8)
Most common (> 3%) grade ≥ 3 AEs, n (%)	
Anemia	3 (5.3)
Thrombocytopenia	3 (5.3)
Lymphopenia	2 (3.5)

These results support lisocabtagene maraleucel as a potential second-line treatment in patients with large B-cell lymphoma for whom HSCT is not intended.

Sehgal A. et al ASH 2023 [Abstract 705]

The cost-effectiveness of CAR-T vs SOC as second-line therapy in R/R LBCL. Experiences of Singapore and Sweden

	Abstract P1217 (Singapore)	Abstract S334 (Sweden)
Objective	Evaluation of the lifetime cost-effectiveness and budget impact of treatment with axi-cel compared to the current SOC in patients with LBCL refractory to or relapse within 12 months of first-line (1L) chemoimmunotherapy.	
Methods	Partitioned survival model with three health states: 'event-free', 'post-event', and 'death'.	
Data Inputs	Efficacy and safety data from ZUMA-7. Healthcare resource use and costs obtained from ZUMA-7, literature, and Singaporean price lists.	Efficacy and safety data from ZUMA-7, including EFS, TTNT, and OS (median follow-up: 47.2 months). Mixture cure models used for extrapolation.
Health Metrics Considered	QALYs, LYs, and costs, with utility values estimated from published literature.	
Results	Axi-cel generated 8.24 QALYs compared to 6.52 QALYs with SOC at an incremental cost of S$130,433 (~US$95,423), resulting in an ICER of S$75,910 (~US$55,534) per QALY gained.	Axi-cel resulted in an incremental gain of 1.65 QALYs and incremental costs of SEK 964,786 per patient compared to SOC, leading to an ICER of SEK 585,663 per QALY gained. At a willingness-to-pay of SEK 1,000,000 per QALY gained, **axi-cel is 84% likely to be cost-effective (avoiding the need for subsequent treatments)**
Key Cost Effectivenes Drivers	**Improved long-term survival, extended event-free time, and reduction of additional treatment costs in the axi-cel arm.**	

ICER: cost-effectiveness ratio

QALY: Quality-Adjusted Life Year

Francesca Lim et al. EHA 2024 [Abstract P1217]. Kanje V.H. el al. EHA [Abstract S334]

The cost-effectiveness of CAR-T vs SOC as second-line therapy in R/R LBCL. Experiences of Singapore and Sweden

	Abstract P1217 (Singapore)	Abstract S334 (Sweden)
Budget Impact	Axi-cel introduction in Singapore's healthcare system is expected to increase the annual budget impact by ~17% from S$21.7 million (US$15.9M) to S$25.4 million (US$18.6M) in Year 5, mitigated by a reduction in subsequent treatment-related costs	
Key message	Axi-cel can be considered a **highly cost-effective allocation of resources** in Singapore with **manageable budget impact** compared to SOC in patients with LBCL R/R.	Axi-cel is a **cost-effective alternative compared to SOC** for adult patients with R/R LBCL and can be considered an **efficient use of resources** from a Swedish health care perspective.

Francesca Lim et al. EHA 2024 [Abstract P1217]. Kanje V.H. el al. EHA [Abstract S334]

blood advances

Cost-effectiveness of second-line lisocabtagene maraleucel in relapsed or refractory diffuse large B-cell lymphoma

Choe JH et al, Blood Advances 2024

Table 3. Estimated base case cost and utility outcomes over the lifetime horizon

Treatment	Costs	Life-years	QALYs	Incremental Costs	Incremental QALYs	ICER per QALY
Health care sector perspective						
Liso-cel	$668 624	5.34	3.64	$201 001	2.02	$99 669
SC	$467 624	2.47	1.62	–	–	–
Societal perspective						
Liso-cel	$882 475	5.34	3.64	$137 560	2.02	$68 212
SC	$744 914	2.47	1.62	–	–	–

All costs were adjusted to 2022 USD; values in the table are rounded, which may result in minor discrepancies in summation.
ICER is calculated as incremental costs divided by incremental QALYs.

quality of life and life expectancy analysis:

→ patients receiving liso-cel therapy exhibited an average life expectancy of 5.34 years, compared with 2.47 years for those on SC

→ additionally, patients receiving liso-cel achieved an average of 3.64 QALYs compared with 1.62 QALYs for SC recipients

In conclusion, liso-cel demonstrates cost-effectiveness in treating patients with R/R DLBCL within the $100 000 per QALY willingness-to-pay threshold, particularly when analyzed over a lifetime horizon from both health care sector and societal perspectives.
However, this cost-effectiveness is less certain under a 5-year horizon and when considering the therapy's list price increase from 2022 to 2023.
The inclusion of broader societal costs suggests a potential economic advantage for CAR T-cell therapies, contingent on sustained clinical outcomes and corroborating real-world evidence

Cost-effectiveness of second-line lisocabtagene maraleucel in relapsed or refractory diffuse large B-cell lymphoma

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Choe JH et al, Blood Advances 2024

AIM: to evaluate the cost-effectiveness of liso-cel aganist platinum-based chemotherapy followed by high-dose chemotherapy and autologous hematopoietic stem cell transplantation over a lifetime horizon

→ our model revealed distinct differences in survival outcomes between liso-cel and SC.

- estimated 40 months after treatment EFS:

23% for liso-cel
10% for SC

- estimated 40 months after treatment OS:

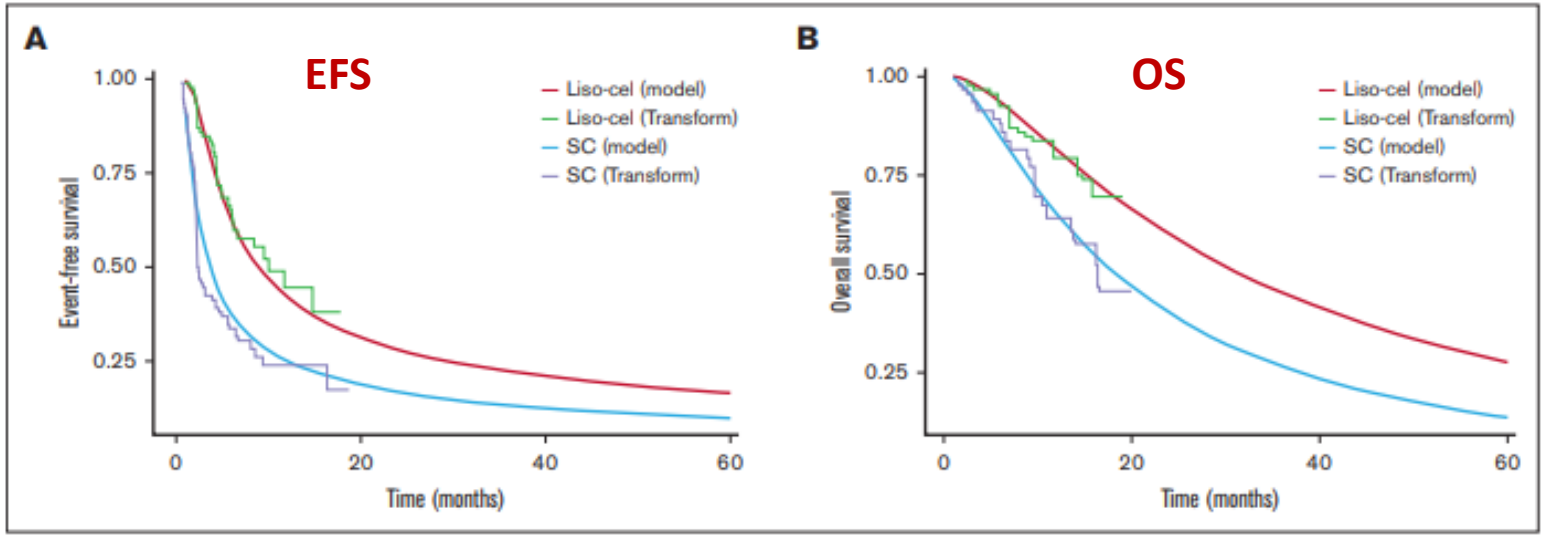
45% for liso-cel
22% for SC

- estimated 5-year EFS:

18% for liso-cel
8% for SC

- estimated 5-year OS:

32% for liso-cel
12% for SC



Impact of real-world clinical factors on an analysis of the cost-effectiveness of 'immediate CAR-T' versus 'late CAR-T' as second-line treatment for DLBCL patients

Study design:

- The analysis was performed for both Japanese and US settings using a Markov model. Lifetime horizon analysis.
- Life expentancy, age variation (40-70 years), choice of CAR-T, opportunity to receive 3°-line CAR-T were incorporeted
- Outcome was measured based on incremental cost-effectiveness ratio (ICER), with willingness-to-pay (WTP) thresholds of ¥7,500,000 and $150,000 per QALY in Japan and the US, respectively, with an annual discount rate of 3%.

Results:

- Compared with 'late CAR-T,' the **'immediate CAR-T' strategy gained QALYs of 0.97 and 0.89 with an incremental cost of ¥5,998,354 and $88,440 in Japan and the US, respectively.**
- The ICERs were ¥6,170,058/QALY in Japan and $99,596/QALY in the US
- In the probabilistic sensitivity analysis for patients aged 60, 'immediate CAR-T' was cost-effective in 54.8% and 61.7% of the 10,000 Monte Carlo iterations in Japan and the US, respectively.
- Sensitivity analyses showed that **'immediate CAR-T' was not cost-effective when patients were over 68.4** in Japan, **when the standardized mortality ratio of CAR-T and ASCT survivors was close, and when utility during treatment-free remission was low.**

Yamamoto C. et al; Transplantation and Cellular Therapy; 2025