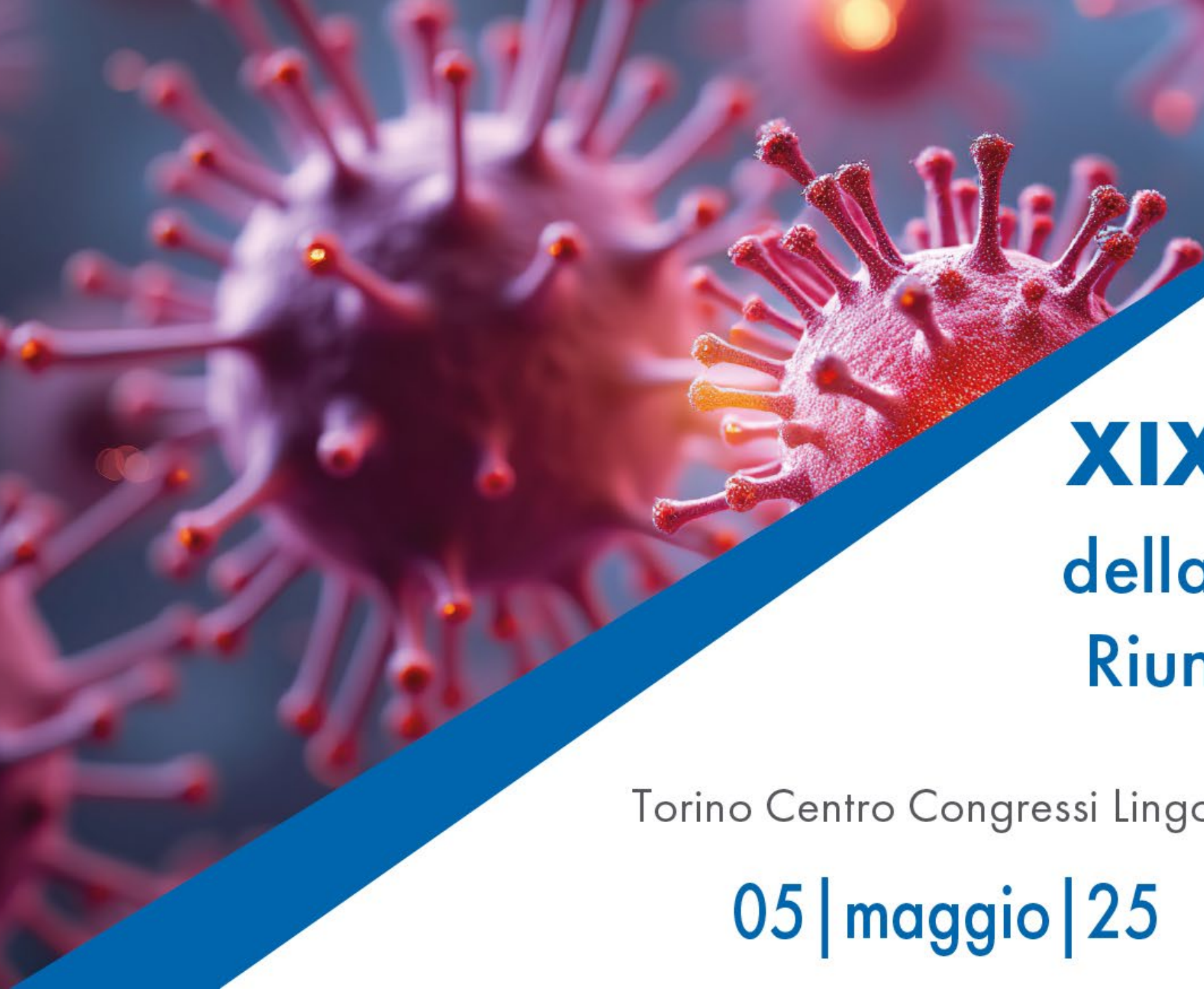

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XIX Congresso
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Torino Centro Congressi Lingotto

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relativo ai lavori del XIX congresso della Società GITMO del 5-6 Maggio 2025.

Disclosures of Simona Sica

Company name	Speakers bureau	Advisory Board	Travel/ Other
Kite Gilead	X		X
Novartis	X	X	X
Alexion	X	X	X
Incyte		X	X
Roche		X	X

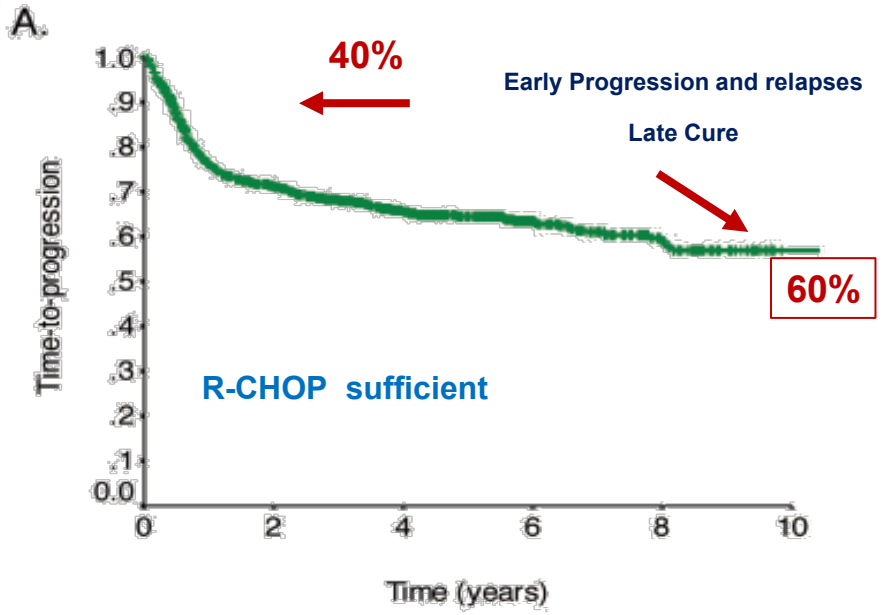
Axi-cel nel trattamento di seconda linea per il linfoma diffuso a grandi cellule B: dagli studi alla pratica clinica

Prof.ssa Simona Sica

Fondazione Policlinico Universitario A. Gemelli – IRCCS

Università Cattolica Sacro Cuore

Heterogeneity of outcomes in DLBCL treated with R-CHOP



Patients with DLBCL treated with R-CHOP-21 at BCCA (n = 1,476)

Relapse
22–30%

Refractory
10-12%

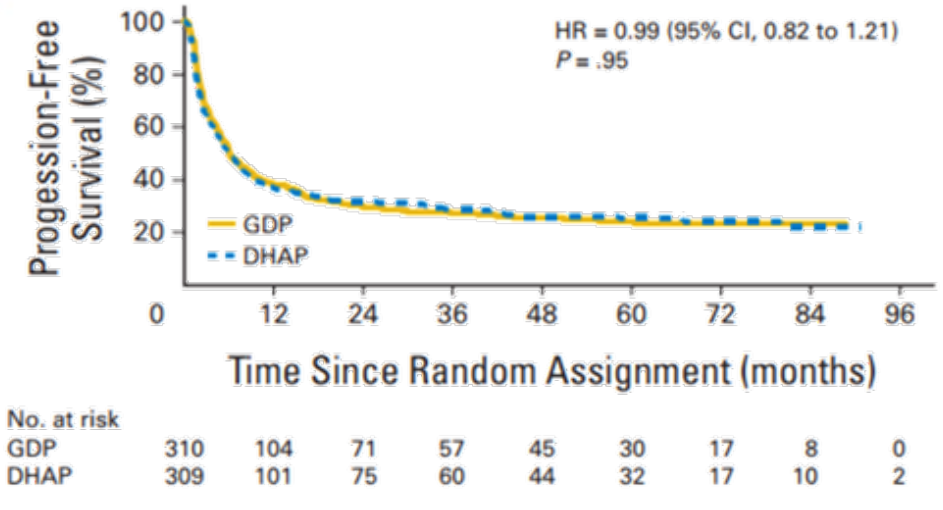
R-CHOP is insufficient in 40% of DLBCL:

- Clinical factors
  - IPI (R-IPI)
- GEP
  - ABC vs GCB
- Protein expression
  - MYC and BCL2
- TP-53 expression
- Chromosomal alterations
  - MYC, BCL2, BCL6
- Deep sequencing mutation/combined expression analysis

Sehn LH and Salles G N.Engl.J.Med 2021

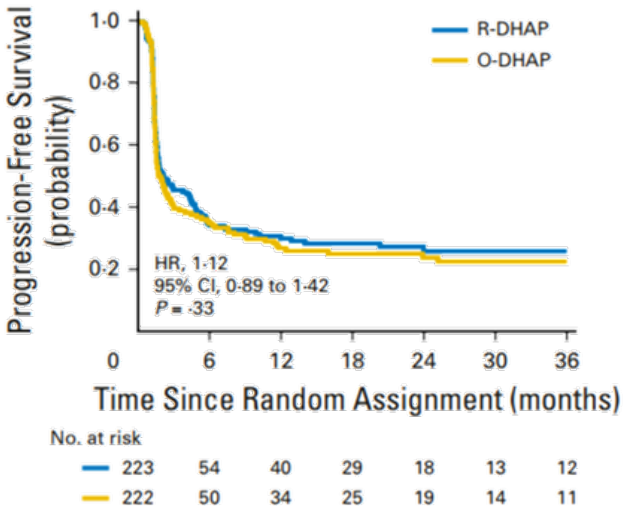
High dose chemo and ASCT: in the old era

NCIC-CTG LY.12



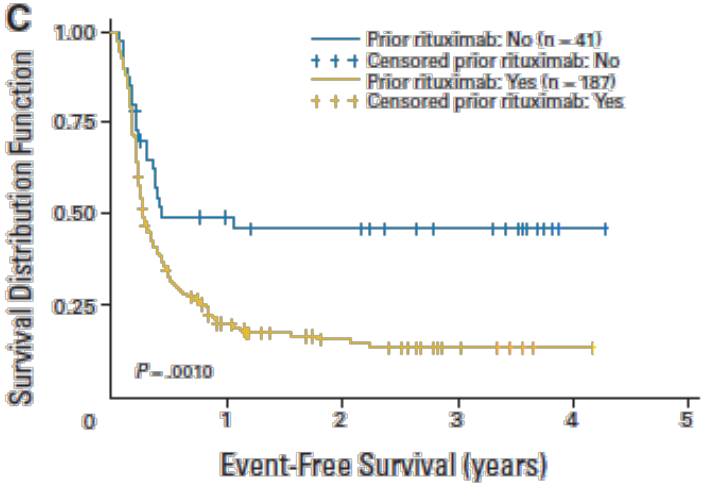
Crump, et al. JCO 2014

ORCHAARD



van Imhoff, et al. JCO 2017

CORAL (pts progressing ≤ 1 year)



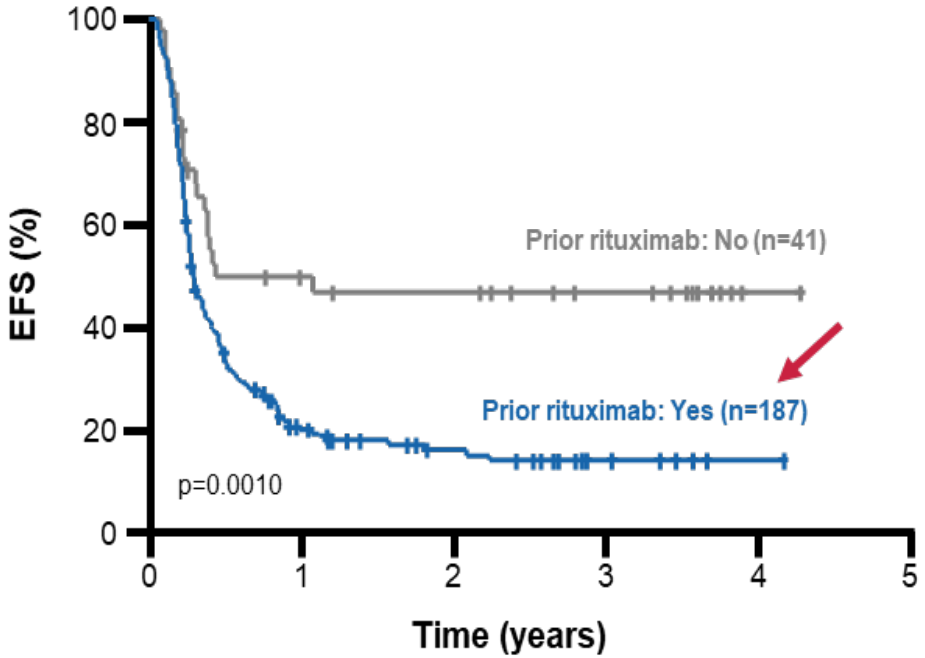
Gisselbrecht, et al. JCO 2010

- About 3/4 of DLBCL relapses happen within one year
- Plus, only half of relapsed DLBCL patients are candidates for HDT/ASCT due to age/comorbidities
- The SOC therefore fails in the vast majority of patients with relapsed DLBCL in the modern era

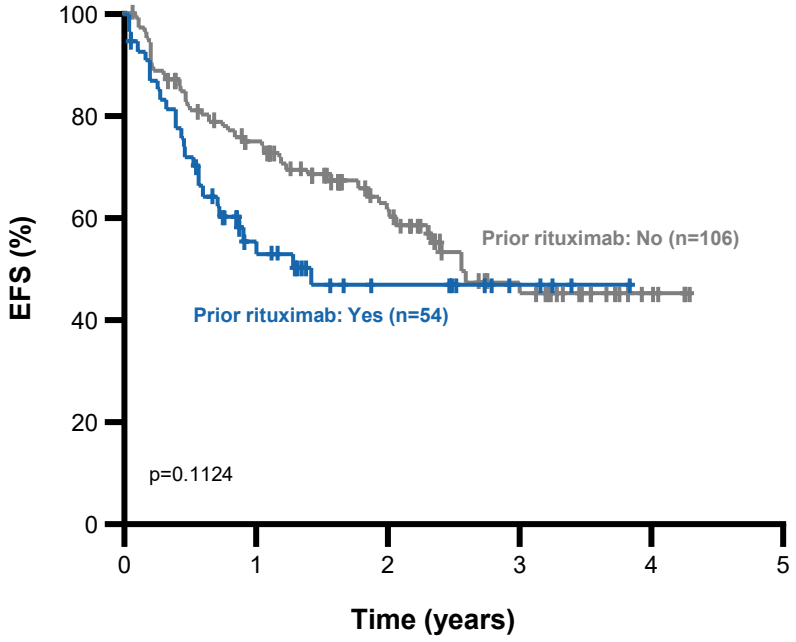
Patients relapsing <12 months after first-line CHT have a poor prognosis at 2L

CORAL: DLBCL at first relapse/primary refractory were randomly assigned to either R-ICE (n=202) or R-DHAP (n=194)

Diagnosis to relapse <12 months



Diagnosis to relapse >12 months



Gisselbrecht, et al. JCO 2010

Outcomes in R/R-DLBCL in patients who respond to salvage therapy

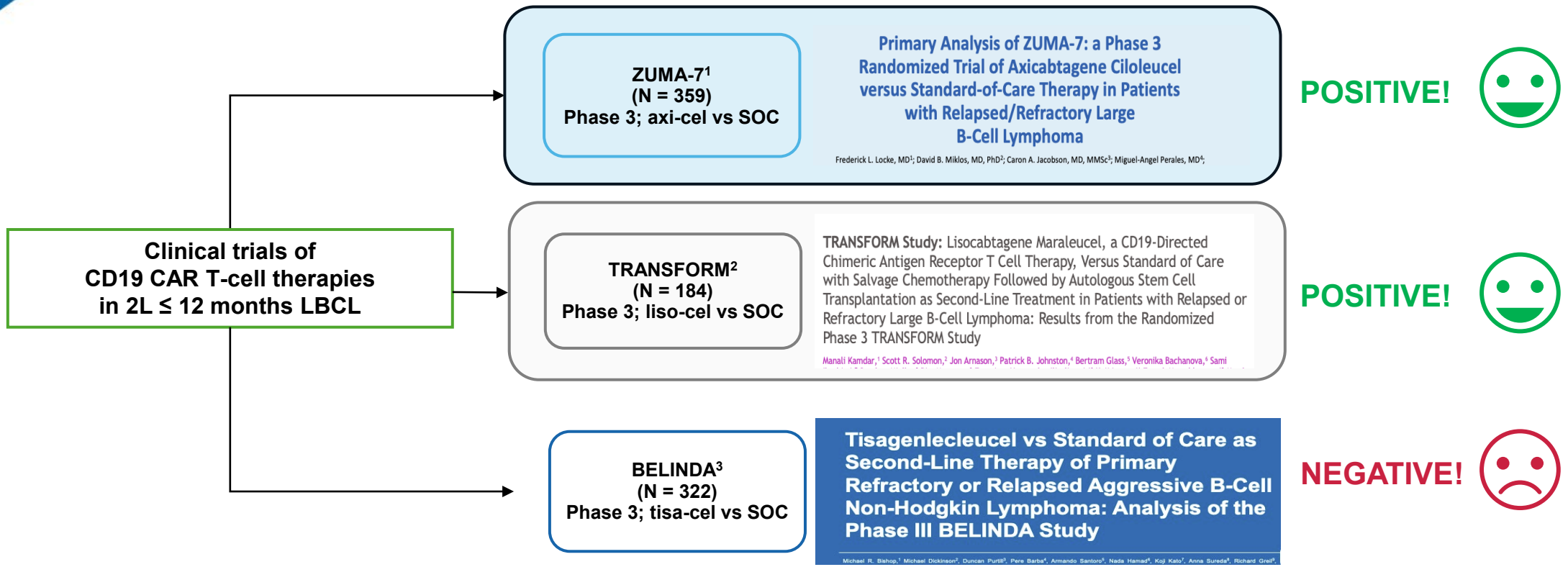
Platinum-based salvage therapy

~50% respond and proceed to ASCT

- **Various parameters greatly affect the results of ASCT, including:**
  - **Chemotherapy sensitivity before ASCT**
  - **Time from diagnosis to relapse of less than 12 months**
  - **Presence of prognostic factors at relapse**
  - **Age > 65 years**
- **The overall cure rate of ASCT-eligible patients is in the range of 20% to 25%**

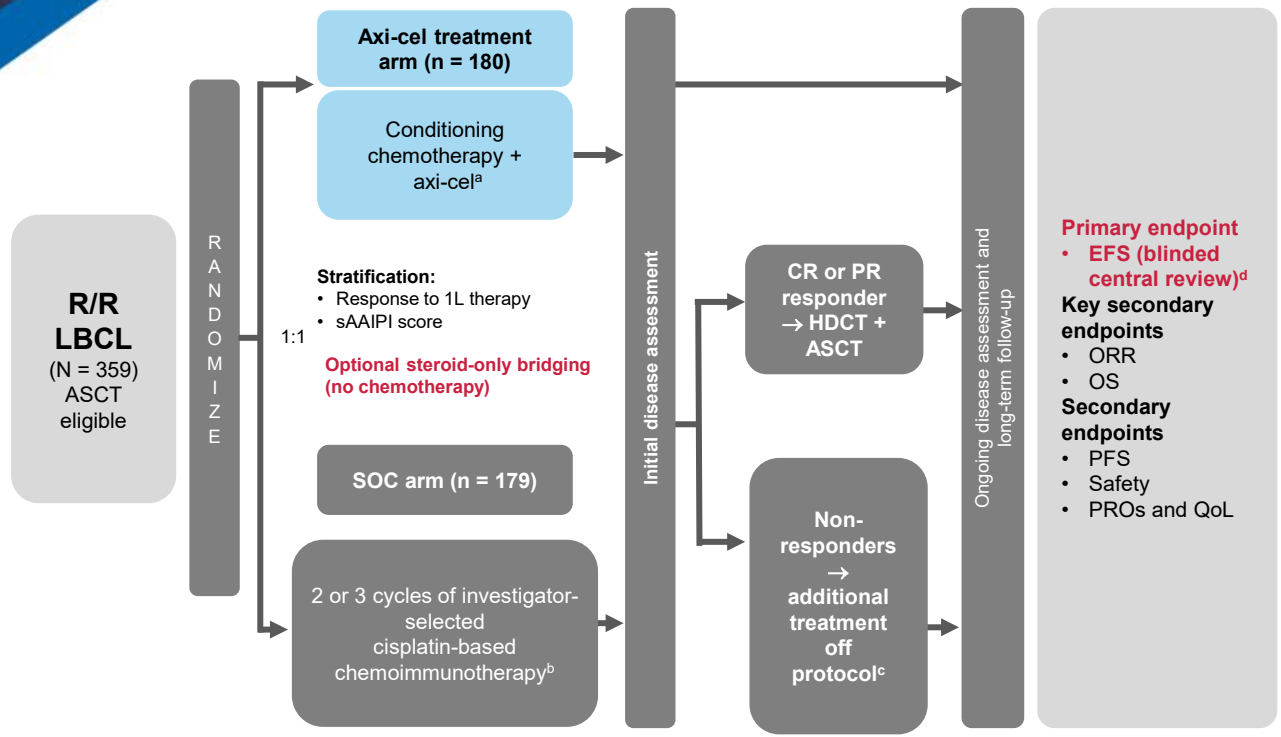
Sehn LH & Salles G. N Engl J Med 2021; 384:842–858; Gisselbrecht C, et al. J Clin Oncol 2010; 28:4184–4190; Crump M, et al. Blood 2017; 130:1800–1808

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



1. Locke FL et al. New Eng J Med 2022; 386:640-54; 2.The lancet. Vol 399 June 18, 2022; 3.Bishop MR et al. New Eng J Med 2022; 386:629-39

ZUMA-7: Axi-cel versus SOC in 2L LBCL



Characteristics	Axi-cel (n = 180)	SOC (n = 179)
Median age (range), years	58 (21–80)	60 (26–81)
Disease stage III-IV, n (%)	139 (77)	146 (82)
Primary refractory, n (%)	**133 (74)**	**131 (73)**
Relapse ≤ 12 months of 1L therapy, n (%)	**47 (26)**	**48 (27)**
HGBCL (incl. DHL/THL), n (%)	**31 (17)**	**25 (14)**
ECOG PS of 1	85 (47)	79 (44)
Elevated LDH level	101 (56)	94 (53)

Locke FL et al. New Eng J Med 2022; 386:640-54

The NEW ENGLAND JOURNAL of MEDICINE

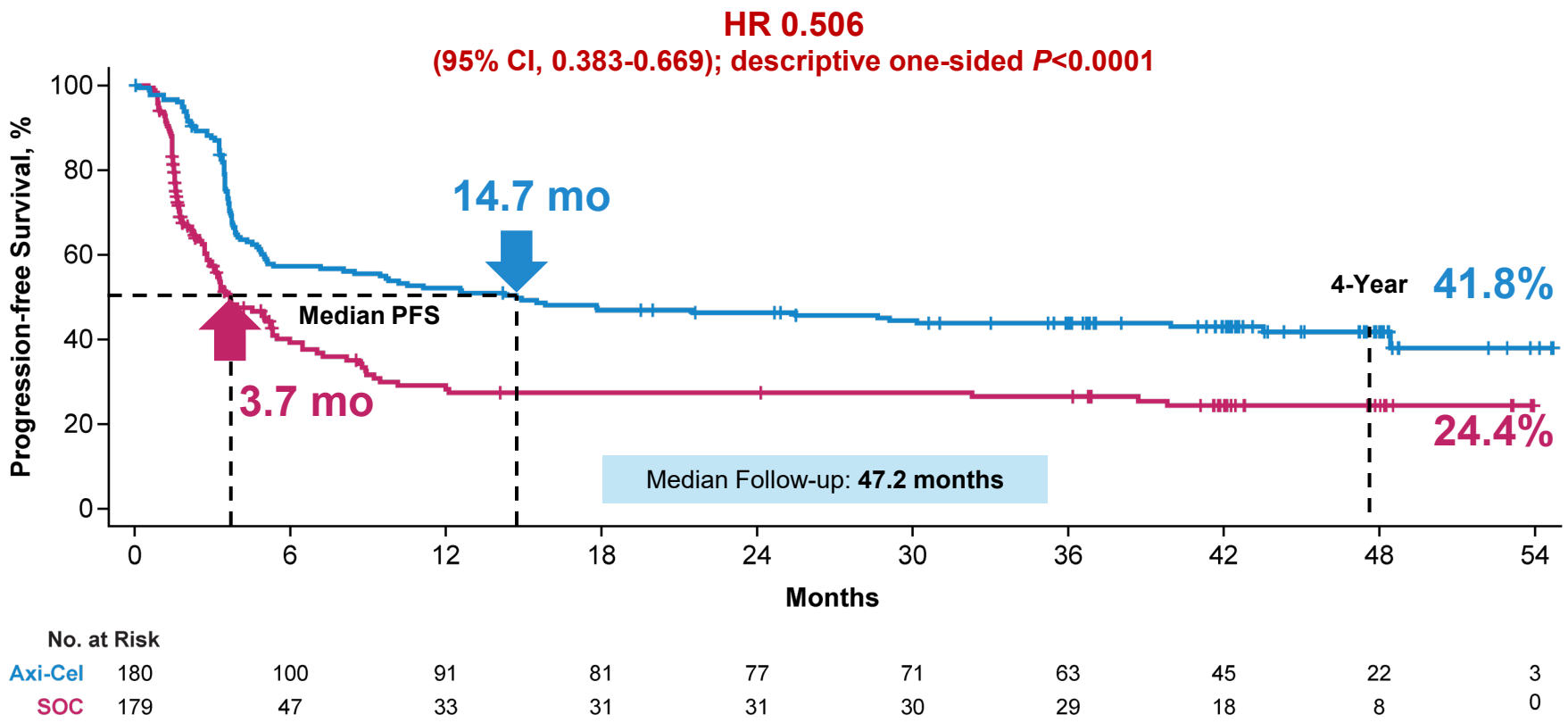
ORIGINAL ARTICLE

Survival with Axicabtagene Ciloleucel in Large B-Cell Lymphoma

J.R. Westin, O.O. Oluwole, M.J. Kersten, D.B. Miklos, M.-A. Perales, A. Ghobadi, A.P. Rapoport, A. Sureda, C.A. Jacobson, U. Farooq, T. van Meerten, M. Ulrickson, M. Elsawy, L.A. Leslie, S. Chaganti, M. Dickinson, K. Dorritie, P.M. Reagan, J. McGuirk, K.W. Song, P.A. Riedell, M.C. Minnema, Y. Yang, S. Vardhanabhuti, S. Filosto, P. Cheng, S.A. Shahani, M. Schupp, C. To, and F.L. Locke, for the ZUMA-7 Investigators and Kite Members*

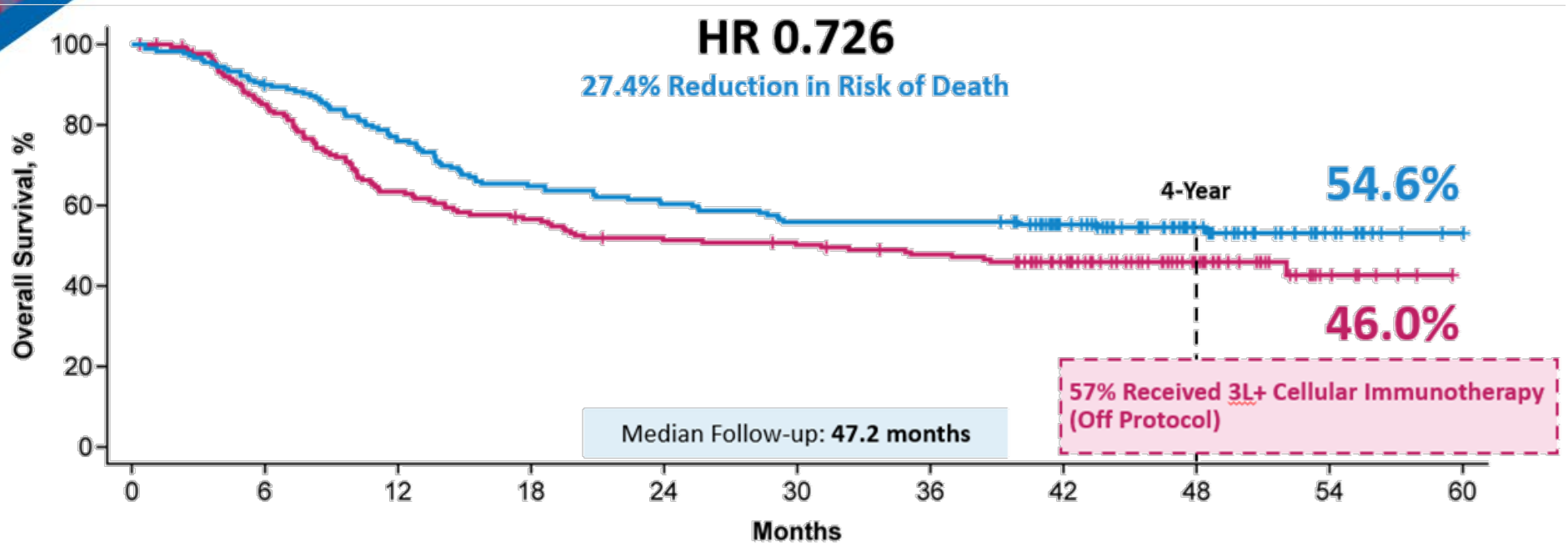
Westin JR , et al. N Engl J Med. 2023

PFS By Investigator Confirmed Benefit of Axi-Cel Over SOC



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

Axi-cel improved Overall Survival vs SoC



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

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

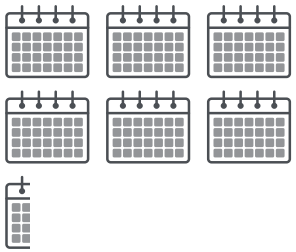
How does later use of axi-cel impact outcomes for patients with R/R LBCL?

ZUMA-7

Exploratory *post-hoc* analysis of 127 patients in the **SoC** arm of **ZUMA-7** who went on to receive subsequent therapy. 68 patients received 3L cellular immunotherapy.[1]

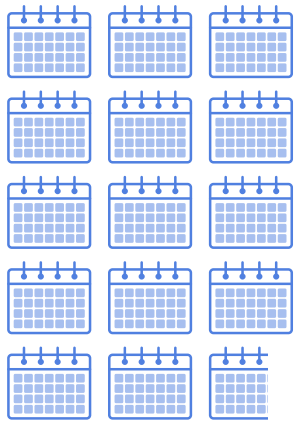
Median PFS[1a]

3L CAR T post-SoC (n=68)

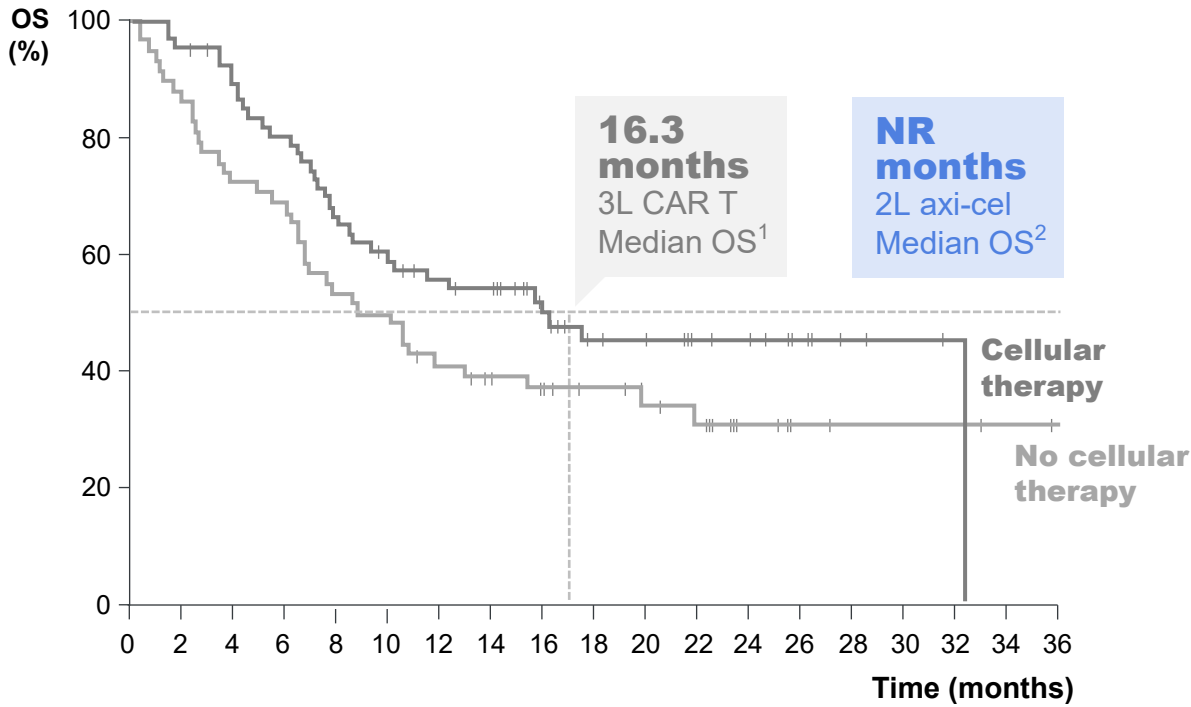


6.3 months

2L axi-cel (n=179)



14.7 months



N at risk

Yes	68	65	61	53	44	39	34	32	24	17	15	11	10	6	3	2	1	0
No	59	51	42	40	31	29	23	20	17	14	11	9	5	3	2	2	2	1	0

Earlier CAR T-cell intervention may provide greater patient benefit versus later intervention

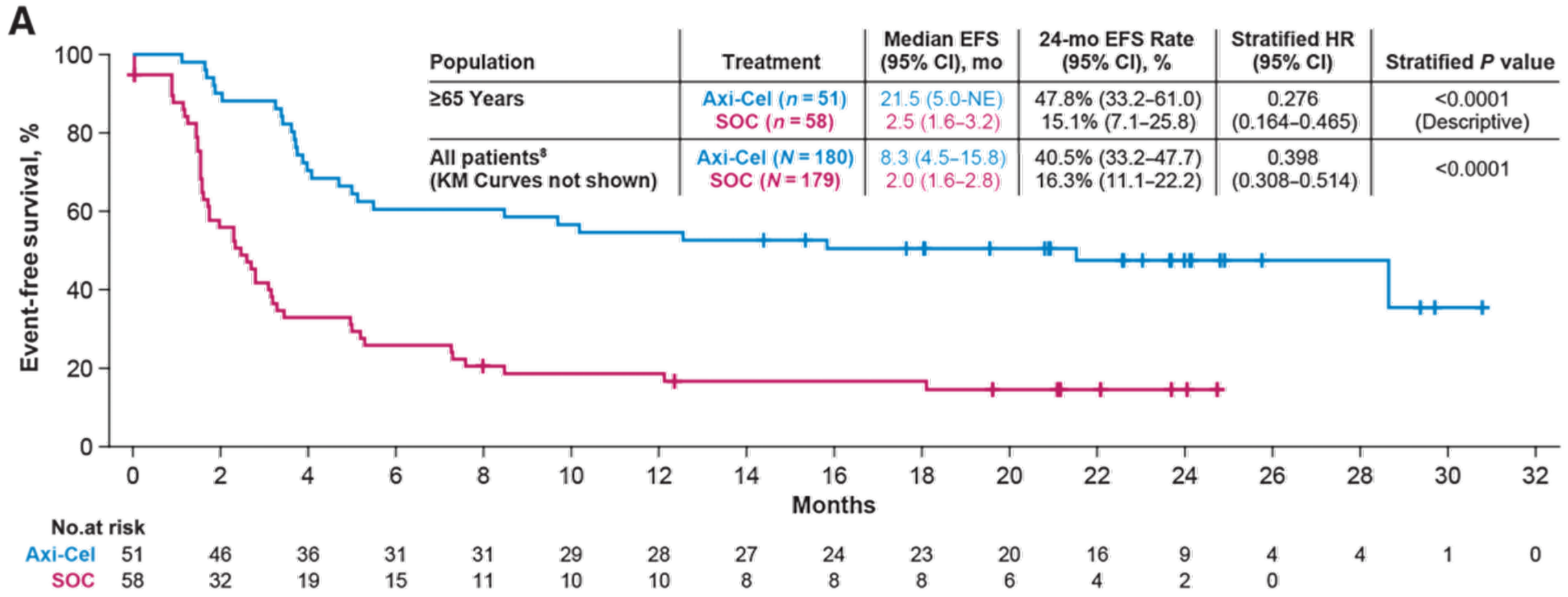
[a]Comparison of outcomes for patients who received subsequent cellular therapy with those who received axi-cel as 2L therapy were not part of the formal analysis.

2L: second-line; 3L: third-line; CAR: chimeric antigen receptor; LBCL: large B-cell lymphoma; mFU: median follow-up; OS: overall survival; PFS: progression-free survival; R/R: relapsed or refractory; SoC: standard of care.

1. Ghobadi A, *et al. Blood Adv*. 2024 ;8:2982–2990. 2. Westin JR, *et al. N Engl J Med* 2023; 389:148–157.

Older Age is not a contraindication for CAR-T Cell Therapy

ZUMA-7 analysis 109 patients >65 yrs



Population	Treatment	Median EFS (95% CI), mo	24-mo EFS Rate (95% CI), %	Stratified HR (95% CI)	Stratified *P* value
≥65 Years	Axi-Cel (*n* = 51)	21.5 (5.0-NE)	47.8% (33.2–61.0)	0.276 (0.164–0.465)	<0.0001 (Descriptive)
	SOC (*n* = 58)	2.5 (1.6–3.2)	15.1% (7.1–25.8)		
All patients[8] (KM Curves not shown)	Axi-Cel (*N* = 180)	8.3 (4.5–15.8)	40.5% (33.2–47.7)	0.398 (0.308–0.514)	<0.0001
	SOC (*N* = 179)	2.0 (1.6–2.8)	16.3% (11.1–22.2)		

Westin JR. et al. Clin Canc Res 2023

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

- Data were collected from the CIBMTR database
- 446 patients
- 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

2L, second line; axi-cel, axicabtagene ciloleucel; LBCL, large B-cell lymphoma; R/R, relapsed or refractory.
Lee *et al.* ASH 2024 (Abstract 526; oral presentation)

Baseline patient and disease characteristics

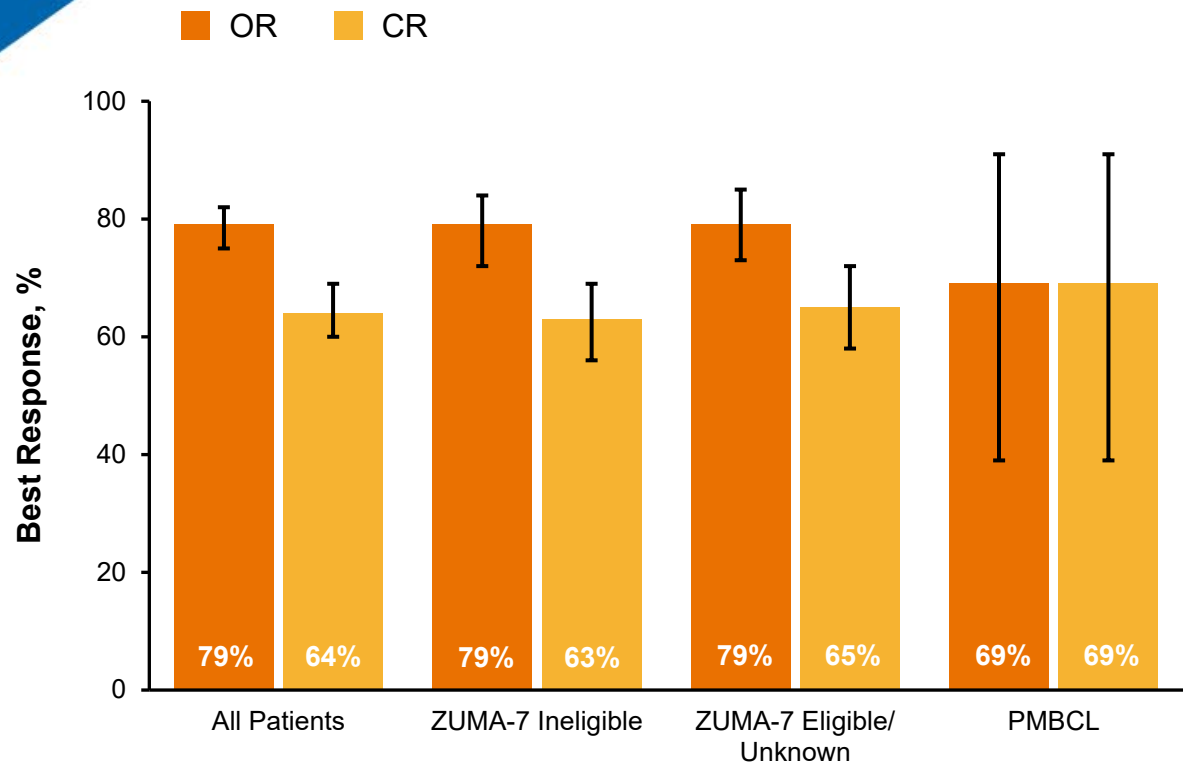
Characteristic	All Patients N=446
Median age, years (range)	63.9 (19.5-86.0)
≥65 to <70, n (%)	74 (17)
≥70, n (%)	137 (31)
Male sex, n (%)	285 (64)
ECOG performance status 0-1,[a] n (%)	401 (97)
Disease type, n (%)	
DLBCL	349 (78)
PMBCL	13 (3)
HGBCL	79 (18)
FL Grade 3B	5 (1)
Elevated lactate dehydrogenase 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)

- A total of 446 patients with R/R LBCL received axi-cel in 2L between April 2022 and July 2023
- Most patients had non-Hispanic ethnicity (White, 72%; Black, 5%; Asian, 6%); 12% were Hispanic
- 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)
  - PMBCL: 10.3 months (95% CI, 6.1-12.3)

[a] Unknown or not reported was excluded from the denominator in percentage calculations. [b] Response defined as complete response (25%) or partial response (36%). [c] Vein-to-vein time is defined as the time from leukapheresis to axi-cel infusion. [d] Most common bridging therapies were systemic (53%) or radiation (16%). 2L, second line; axi-cel, axicabtagene ciloleucel; ECOG, Eastern Cooperative Oncology Group; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HCT-CI, hematopoietic cell transplantation comorbidity index; HGBCL, high-grade B-cell lymphoma; IQR, interquartile range; PMBCL, primary mediastinal B-cell lymphoma.

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

Results - Baseline patient and disease characteristics

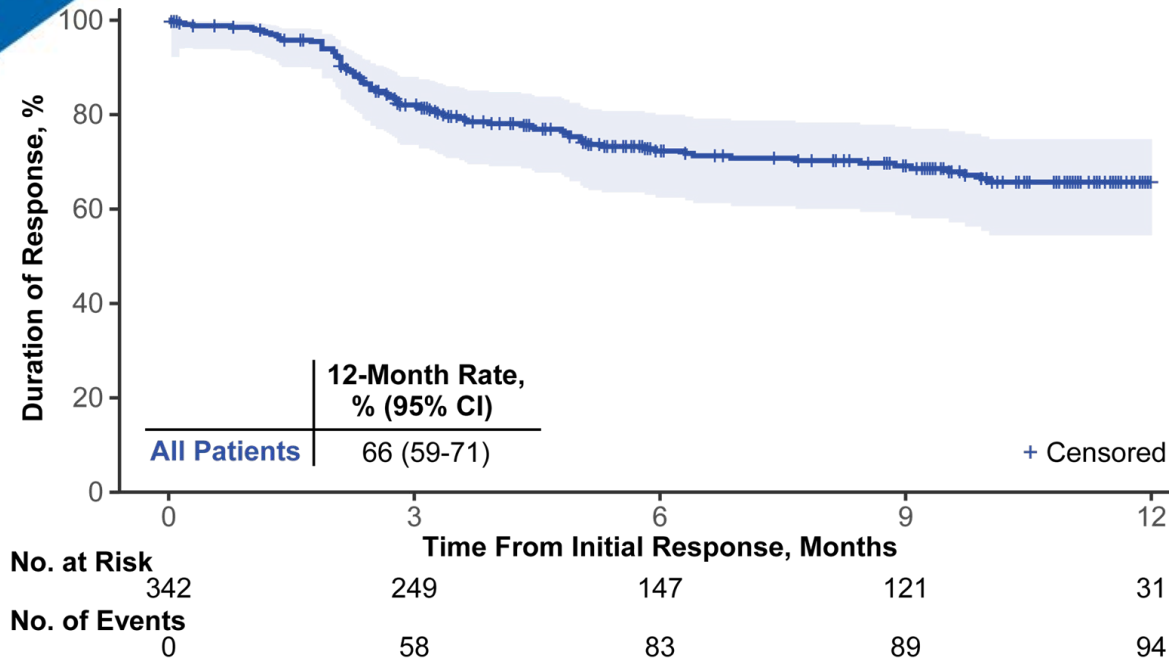


- ORs and CRs were similar across all patient groups[a,b]
- Median time to OR in all patients was 2.1 months (IQR, 1.0-3.6)
  - ZUMA-7 ineligible: 1.8 months (IQR, 1.0-3.4)
  - ZUMA-7 eligible/unknown: 2.4 months (IQR, 1.0-3.7)
  - PMBCL: 3.0 months (IQR, 1.2-NE)
- Median time to CR in all patients was 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)

Error bars denote 95% CIs.
[a] Patients with missing response assessment were excluded.
[b] Analysis by ZUMA-7 eligibility was among patients with DLBCL, HGBCL, and FL Grade 3B; patients with PMBCL were analyzed separately. [c] Total number of evaluable patients.
CR, complete response; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; IQR, interquartile range; NE, not estimable; OR, objective response; PMBCL, primary mediastinal B-cell lymphoma.
Lee et al. ASH 2024 (Abstract 526; oral presentation)

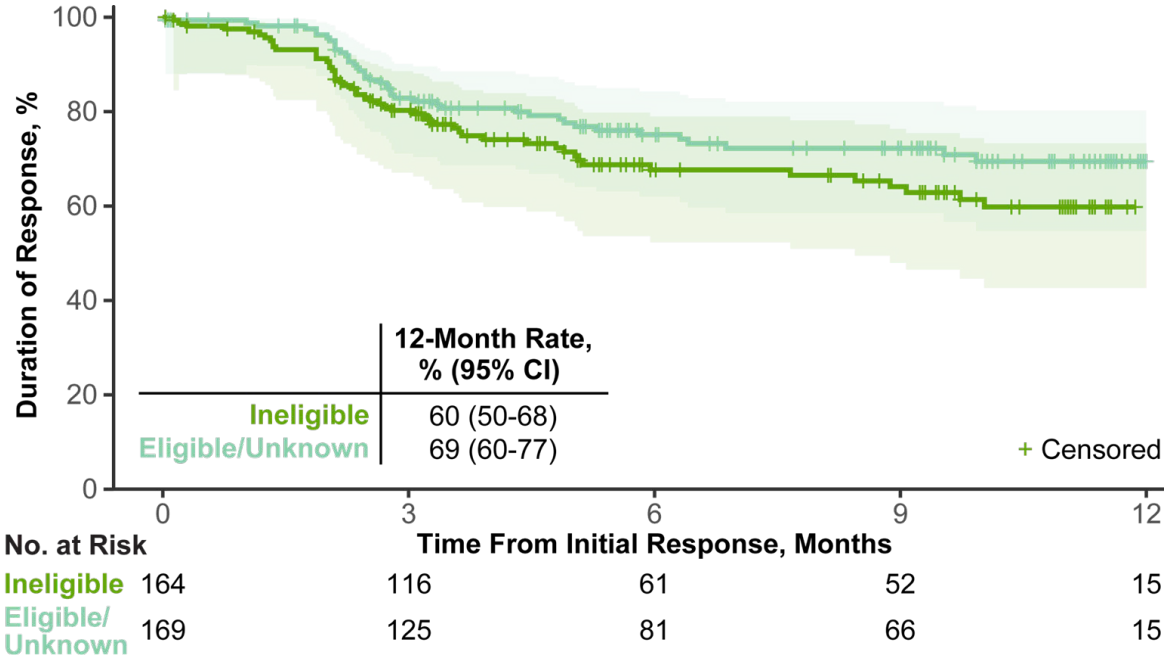
Results - Duration of Response

DOR in All Patients



No. at Risk					
	342	249	147	121	31
No. of Events					
	0	58	83	89	94

DOR by ZUMA-7 Eligibility[a]



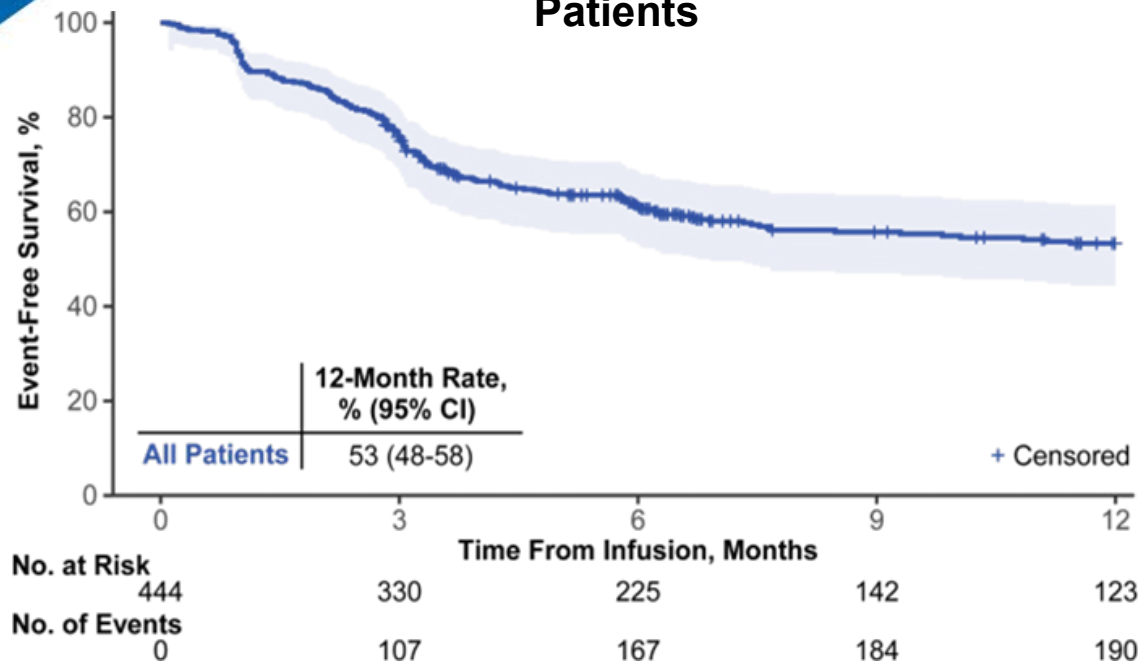
No. at Risk					
Ineligible	164	116	61	52	15
Eligible/ Unknown	169	125	81	66	15

- Among all patients (median follow-up, 12 months), the 12-month DOR rate was 66%
  - Among patients who were ZUMA-7 ineligible, the 12-month DOR rate was 60%
  - Among patients who were ZUMA-7 eligible/unknown, the 12-month DOR rate was 69%
  - Among patients with PMBCL, the 6-month DOR rate was 100%

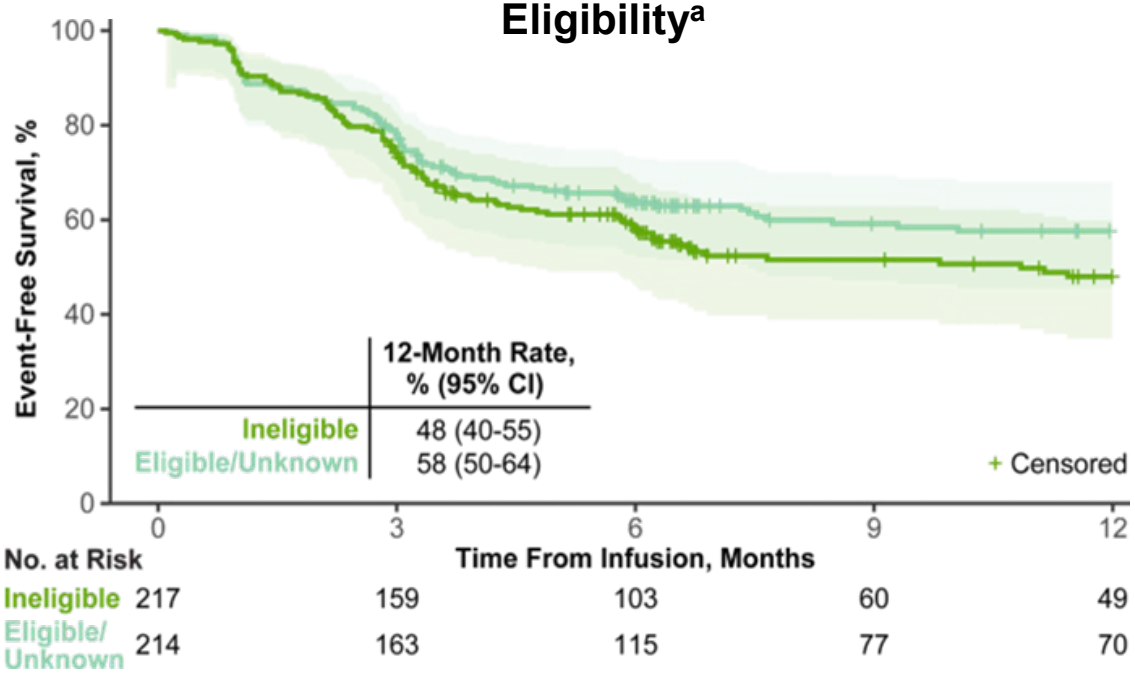
Shaded areas represent confidence bands.
[a] Analysis by ZUMA-7 eligibility was among patients with DLBCL, HGBCL, and FL Grade 3B; patients with PMBCL were analyzed separately.
DOR, duration of response; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; PMBCL, primary mediastinal B-cell lymphoma.
Lee *et al.* ASH 2024 (Abstract 526; oral presentation)

Results - Event Free Survival

EFS in All Patients



EFS by ZUMA-7 Eligibility[a]

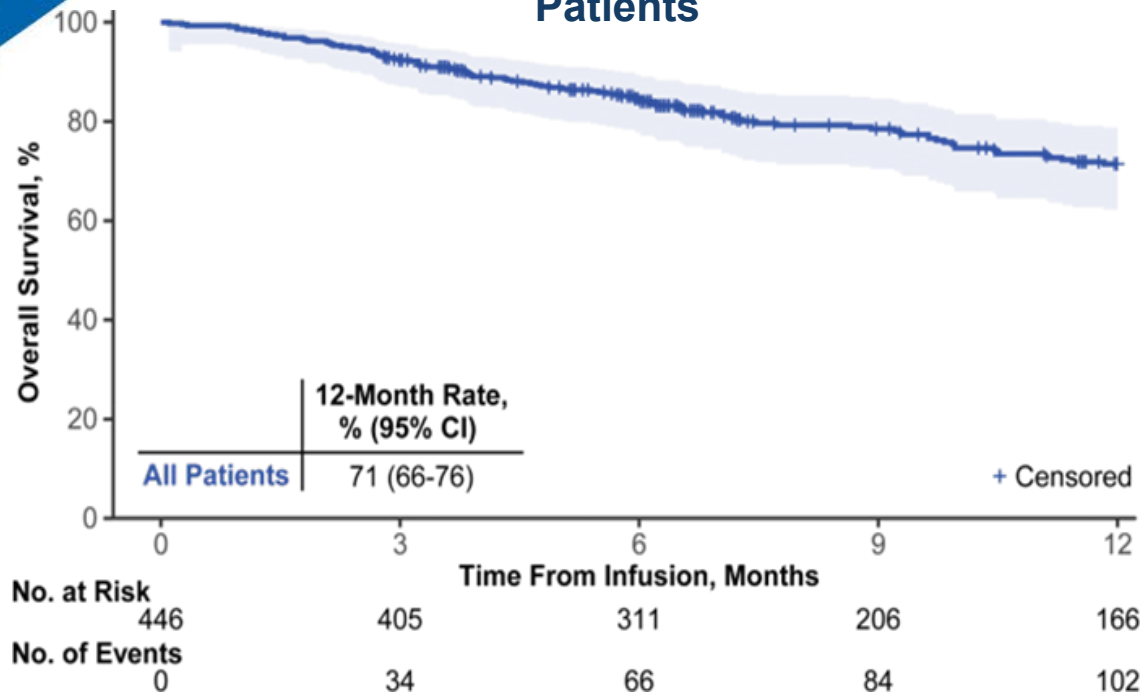


- Among all patients, the 12-month EFS rate was 53%
  - Among patients who were ZUMA-7 ineligible, the 12-month EFS rate was 48%
  - Among patients who were ZUMA-7 eligible/unknown, the 12-month EFS rate was 58%
  - Among patients with PMBCL, the 6-month EFS rate was 68% (95% CI, 36-87)

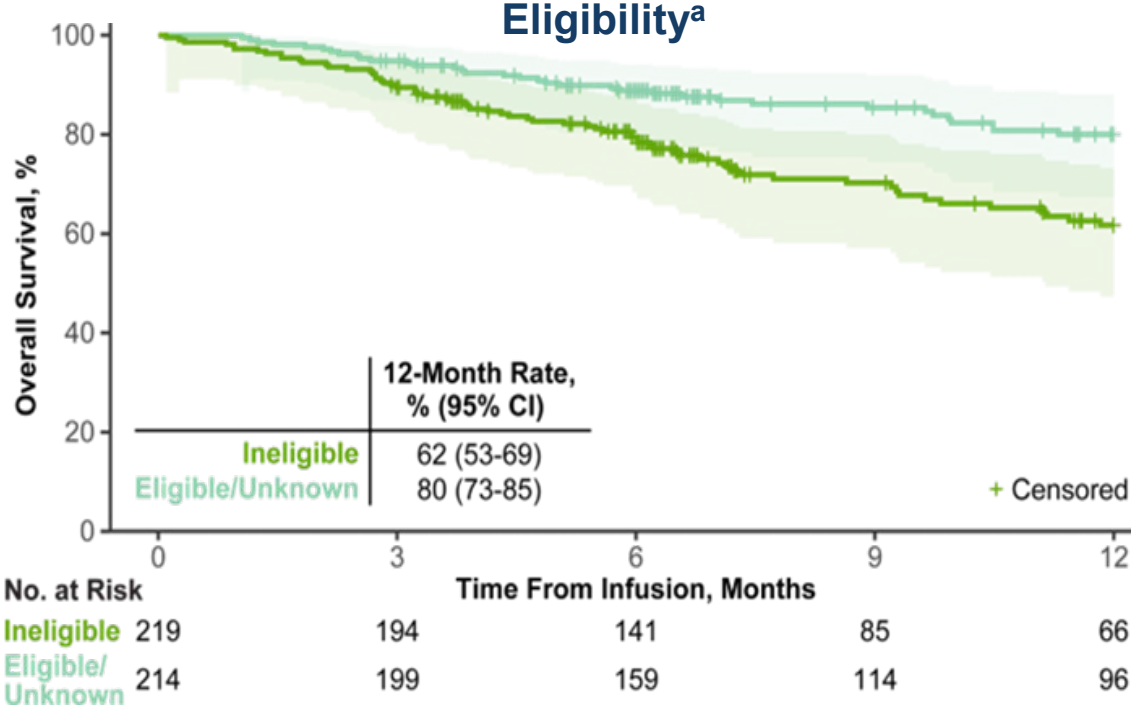
Shaded areas represent confidence bands.
[a] Analysis by ZUMA-7 eligibility was among patients with DLBCL, HGBCL, and FL Grade 3B; patients with PMBCL were analyzed separately.
DOR, duration of response; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; PMBCL, primary mediastinal B-cell lymphoma.
Lee *et al.* ASH 2024 (Abstract 526; oral presentation)

Results - Overall Survival

OS in All Patients



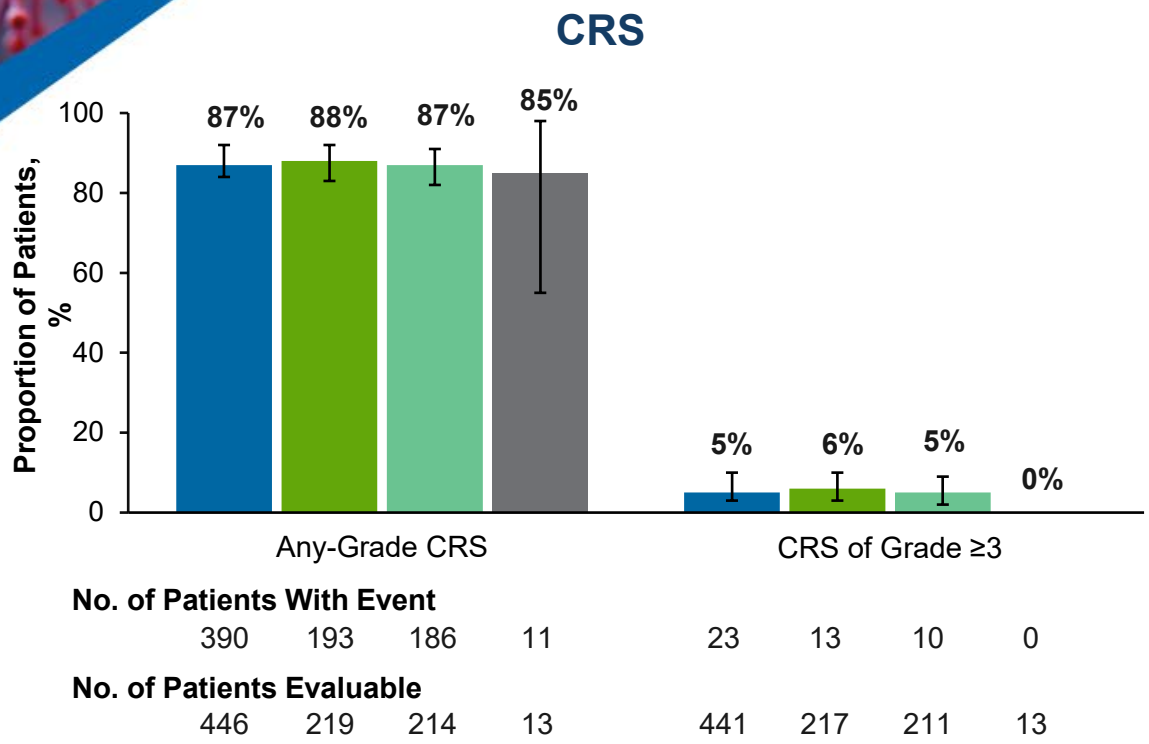
OS by ZUMA-7 Eligibility[a]



- Among all patients, the 12-month OS rate was 71%
  - Among patients who were ZUMA-7 ineligible, the 12-month OS rate was 62%
  - Among patients who were ZUMA-7 eligible/unknown, the 12-month OS rate was 80%
  - Among patients with PMBCL, the 6-month OS rate was 100%

Shaded areas represent confidence bands.
[a] Analysis by ZUMA-7 eligibility was among patients with DLBCL, HGBCL, and FL Grade 3B; patients with PMBCL were analyzed separately.
DOR, duration of response; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; PMBCL, primary mediastinal B-cell lymphoma.
Lee *et al.* ASH 2024 (Abstract 526; oral presentation)

Results - Incidence of CRS

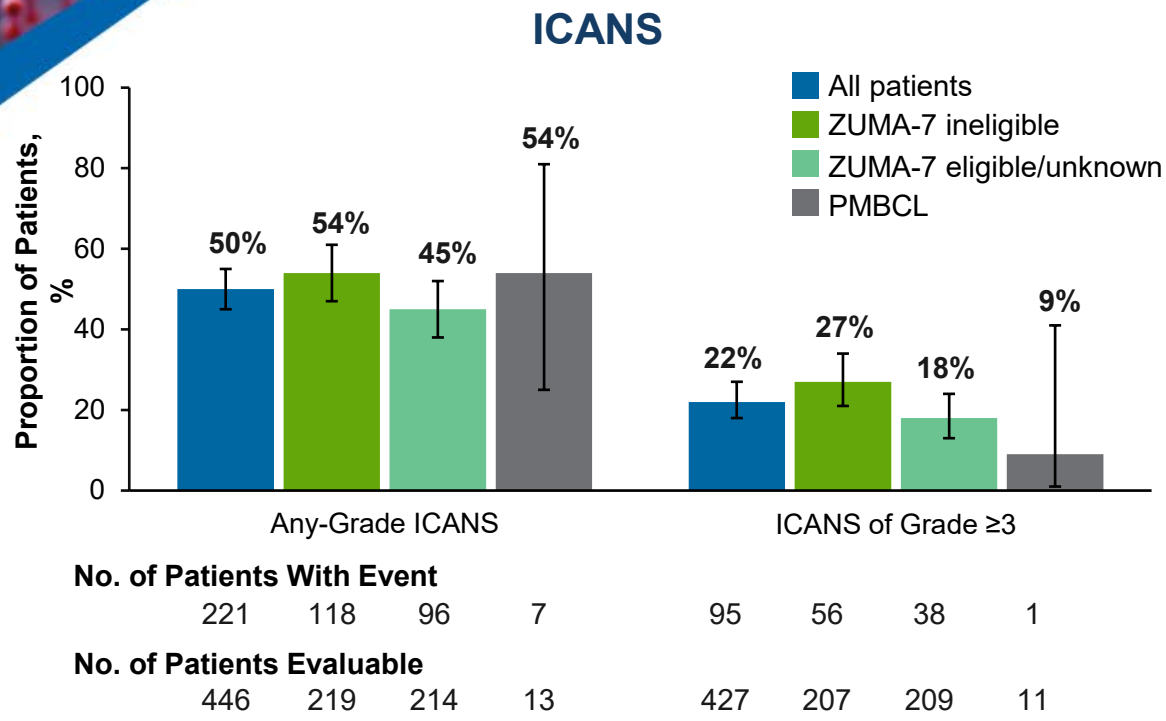


Characteristic	All Patients N=446	ZUMA-7 Eligibility[a]		Patients With PMBCL n=13
		Ineligible n=219	Eligible/ Unknown n=214	
Any-grade CRS, n (%)	390 (87)	193 (88)	186 (87)	11 (85)
Median time from infusion to CRS onset, days (IQR)	4 (2-6)	4 (2-5)	4 (2-6)	4 (2-6)
Median time from CRS onset to resolution, 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)	-	-	-

- Incidence of any-grade CRS and Grade ≥3 CRS were similar across patient groups[b,c]
- Among all patients, 390 (87%) had any-grade CRS; Grade ≥3 CRS occurred in 5%

Error bars denote 95% CIs.
[a] Analysis by ZUMA-7 eligibility was among patients with DLBCL, HGBCL, and FL Grade 3B; patients with PMBCL were analyzed separately.
[b] CRS and ICANS were graded per ASTCT consensus criteria. [c] Missing were excluded.
ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; ICANS, immune effector cell-associated neurotoxicity syndrome; IQR, interquartile range; PMBCL, primary mediastinal B-cell lymphoma.
Lee *et al.* ASH 2024 (Abstract 526; oral presentation)

Results - Incidence of ICANS



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)	-	-	-

- Incidence of any-grade ICANS and Grade ≥3 ICANS were similar across patient groups[b,c]
- The most common treatments given for CRS and/or ICANS were tocilizumab (80%), corticosteroids (65%), antiepileptics (19%), and anakinra (18%)

Error bars denote 95% CIs.
[a] Analysis by ZUMA-7 eligibility was among patients with DLBCL, HGBCL, and FL Grade 3B; patients with PMBCL were analyzed separately.
[b] CRS and ICANS were graded per ASTCT consensus criteria. [c] Missing were excluded.
ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; ICANS, immune effector cell-associated neurotoxicity syndrome; IQR, interquartile range; PMBCL, primary mediastinal B-cell lymphoma.
Lee *et al.* ASH 2024 (Abstract 526; oral presentation)

Results - 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)

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

[a] Analysis by ZUMA-7 eligibility was among patients with DLBCL, HGBCL, and FL Grade 3B; patients with PMBCL were analyzed separately.
[b] Unknown or not reported was excluded from the denominator in percentage calculations. c REL/PD and treatment for REL/PD was treated as a competing risk; HSCT was censored.
CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma;
HSCT, hematopoietic stem cell transplantation; NE, not estimable; PMBCL, primary mediastinal B-cell lymphoma; REL/PD, relapsed or progressive disease.
Lee *et al.* ASH 2024 (Abstract 526; oral presentation)

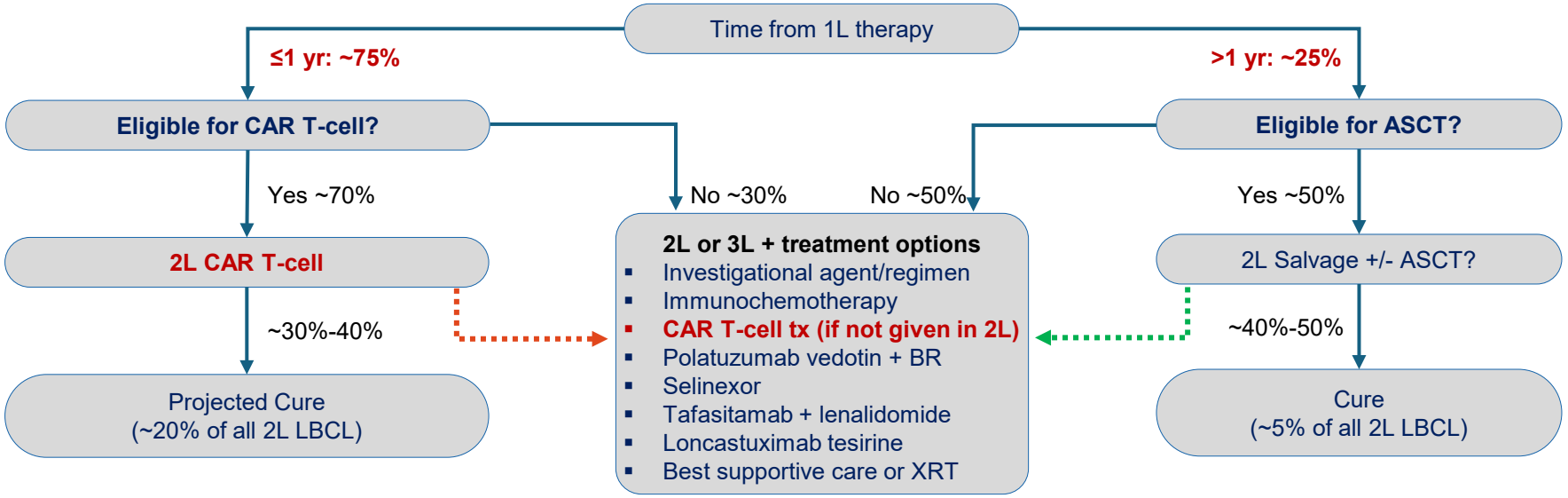
Axi-cel role in 2L setting

- Axi-cel is an autologous anti-CD19 CAR T-cell therapy approved in many countries for treating patients with LBCL that is refractory to 1L therapy or relapses within 12 months of 1L therapy[1,2]
  - Axi-cel has demonstrated curative potential in the 2L (ZUMA-7) and 3L+ settings (ZUMA-1) for patients with R/R LBCL[3,4]
- In the Phase 3 ZUMA-7 study, axi-cel showed superior EFS, response rate, and OS versus standard of care in transplant-intended R/R LBCL[3,5]
- The Phase 2 ALYCANTE study (NCT04531046) additionally demonstrated high response and durable remissions in transplant-ineligible patients[6]
- In the real-world setting, despite a broader patient population beyond the ZUMA-7 trial, effectiveness and safety outcomes were consistent with those observed in ZUMA-7 supporting the use of axi-cel as a 2L therapy for patients with R/R LBCL[7]

1. YESCARTA® (axicabtagene ciloleucel) Prescribing information. Kite Pharma, Inc; 2024. 2. YESCARTA® (axicabtagene ciloleucel) [summary of product characteristics]. Amsterdam, The Netherlands: Kite Pharma EU B.V.; 2024. 3. Westin JR, et al. N Engl J Med. 2023;389:148-157. 4. Neelapu SS, et al. Blood. 2023;141:2307-2315.
5. Locke FL, et al. N Engl J Med. 2022;386:640-654. 6. Houot R, et al. Nat Med. 2023;29:2593-2601.; 7. Lee *et al.* ASH 2024 (Abstract 526; oral presentation)
1L, first line; 2L, second line; 3L+, third line or later; axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; EFS, event-free survival; LBCL, large B-cell lymphoma; OS, overall survival; R/R, relapsed or refractory.

CD19-Targeted CAR T-Cell Therapy Has Dichotomized the Management of R/R DLBCL

New algorithm for Second-line Therapy of LBCL



Timing of relapse is a key decision factor for selecting 2L therapy CART vs SOC within 12 months

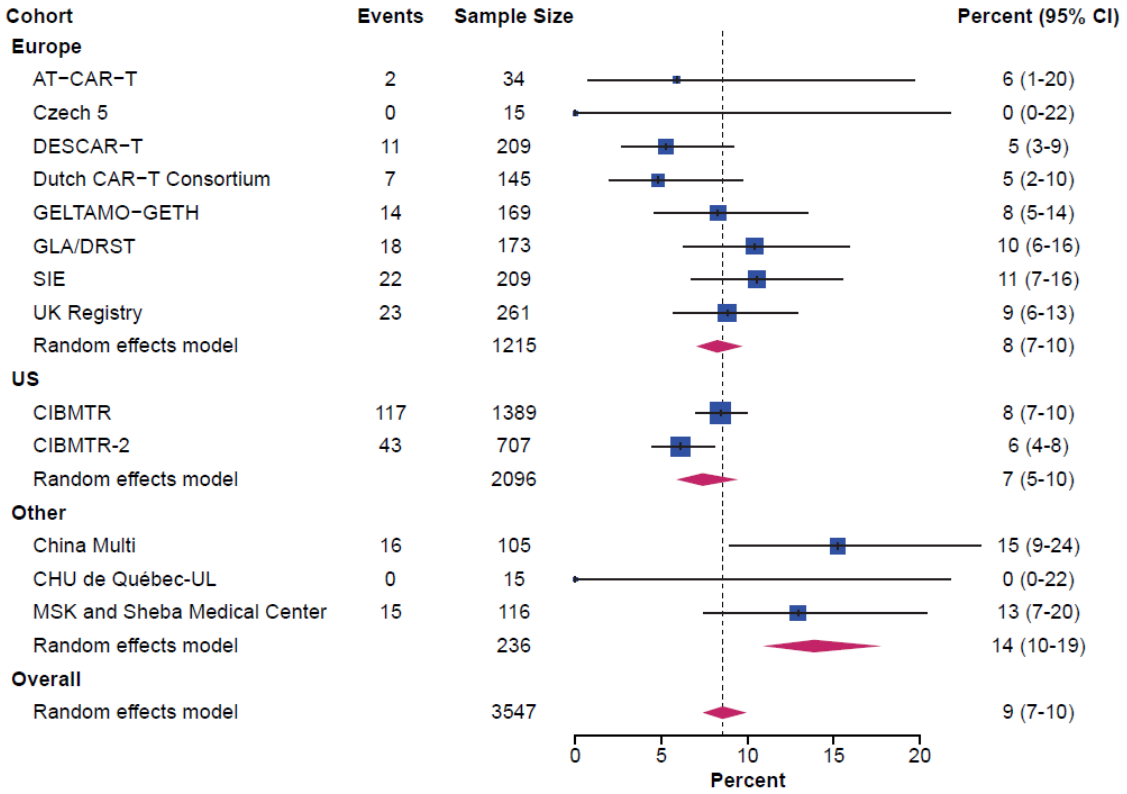
Westin. Blood. 2022;139:2737

Real-World Safety Outcomes of Axicabtagene Ciloleucel in Patients With Diffuse Large B-Cell Lymphoma and Follicular Lymphoma in Europe and United States: A Systematic Review and Meta-Analysis

Robin Sanderson, FRCPath, PhD[1];
Javier Munoz, MD, MS, MBA, FACP[2]; Francis Ayuk, MD[3];
Francis Nissen, MD, PhD[4]; Fang Sun, MD, PhD[4];
Eve H. Limbrick-Oldfield, PhD[5]; David Wennersbusch, MPP[5]; Grace Lee, PharmD, MAS[4]; and Caron A. Jacobson, MD, MMSc[6]

[1]King's College Hospital, London, UK; [2]Mayo Clinic, Phoenix, USA; [3]Department of Stem Cell Transplantation, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; [4]Kite, a Gilead Company, Santa Monica, USA; [5]RainCity Analytics, Vancouver, Canada; and [6]Dana-Farber Cancer Institute, Boston, USA

Results - Meta-Analysis of Grade ≥3 CRS by Geography

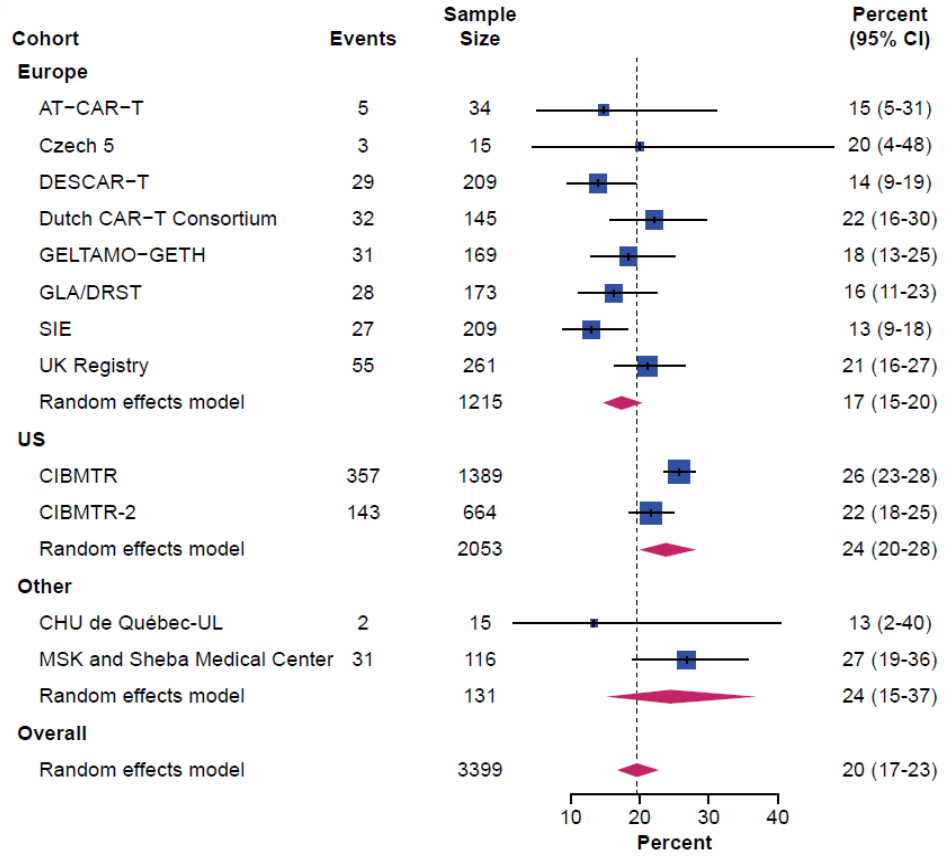


- Estimated incidence of any grade cytokine release syndrome (CRS) was 88% (95% CI, 85-91) for Europe and 82% (95% CI, 81-84) for the US
- Grade ≥3 CRS was estimated at 8% (95% CI, 7-10) for Europe and 7% (95% CI, 5-10) for the US
- The rate of Grade ≥3 CRS numerically reduced from 11% (95% CI, 7-16) before December 2019 to 8% (95% CI, 5-12) afterward

CIBMTR-2 was a more recent cohort, with infusion dates not overlapping with CIBMTR.
AT-CAR-T: Austrian CAR-T Network; CAR-T: chimeric antigen receptor T-cell therapy; CHU de Québec-UL: Centre Hospitalier Universitaire de Québec-Université Laval; CI: confidence interval; CIBMTR: Center for International Blood and Marrow Transplant Research; CRS: cytokine release syndrome; Czech 5: five treatment centers in Czechia; DESCAR-T: Dispositif d'Enregistrement et Suivi des patients traités par CAR-T; GELTAMO-GETH: Grupo Español de Trasplante Hematopoyético y Terapia Celular; GLA / DRST: German Lymphoma Alliance / Deutsches Register für Stammzelltransplantation; MSK: Memorial Sloan Kettering; SIE: Societa Italiana di Ematologia; UK: United Kingdom; US: United States

Sanderson *et al.* EHA 2024 (Abstract P2088; poster)

Results - Meta-Analysis of Grade ≥3 ICANS by Geography

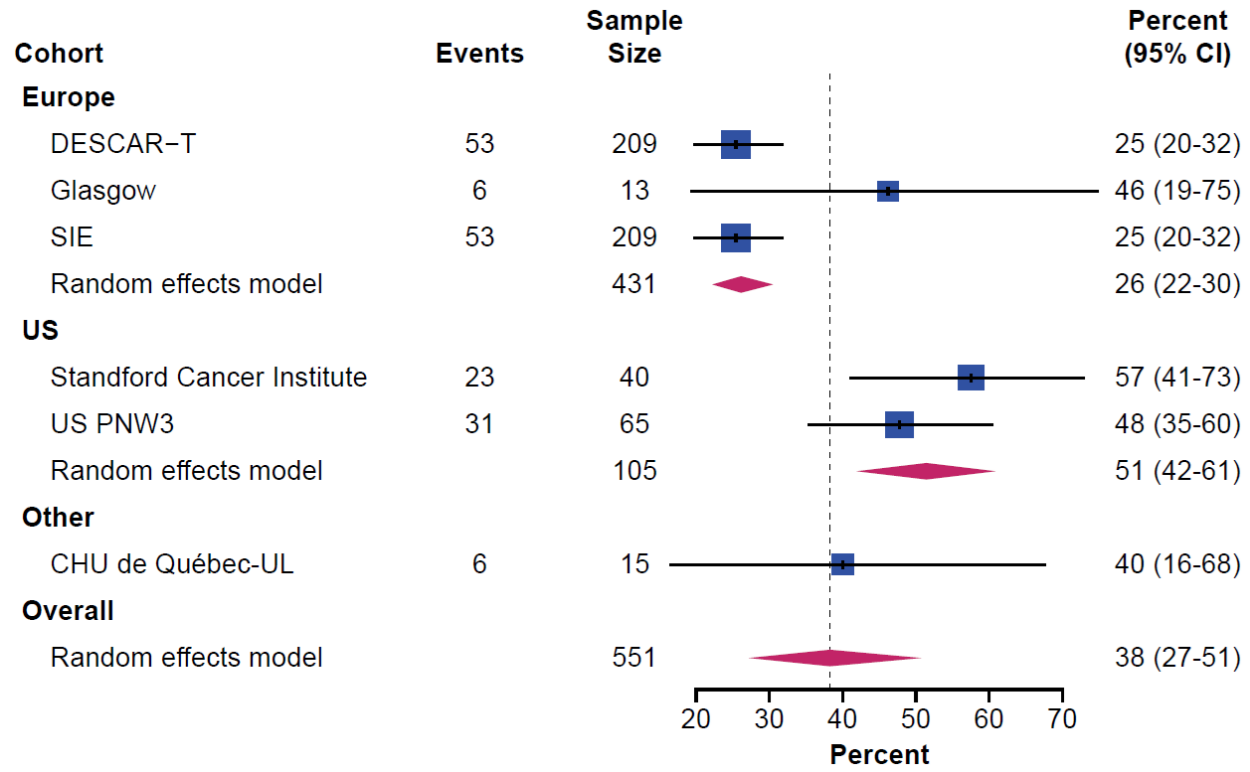


- *Estimated incidence of any grade ICANS was 47% (95% CI, 41-53) for Europe and 50% (95% CI, 40-60) for the US*
- The incidence of Grade ≥3 ICANS was numerically lower in Europe (17% [95% CI, 15-20]) than the US (24% [95% CI, 20-28])
  - The estimates for Grade ≥3 ICANS for both the US and Europe were within the range of the ZUMA-1 rates
- Grade ≥3 ICANS numerically reduced after December 2019 from 24% (95% CI, 17-33) to 20% (95% CI, 16-25)

CIBMTR-2 was a more recent cohort, with infusion dates not overlapping with CIBMTR.
AT-CAR-T: Austrian CAR-T Network; CAR-T: chimeric antigen receptor T-cell therapy; CHU de Québec-UL: Centre Hospitalier Universitaire de Québec-Université Laval; CI: confidence interval; CIBMTR: Center for International Blood and Marrow Transplant Research; CRS: cytokine release syndrome; Czech 5: five treatment centers in Czechia; DESCAR-T: Dispositif d'Enregistrement et Suivi des patients traités par CAR-T; GELTAMO-GETH: Grupo Español de Trasplante Hematopoyético y Terapia Celular; GLA / DRST: German Lymphoma Alliance / Deutsches Register für Stammzelltransplantation; MSK: Memorial Sloan Kettering; SIE: Societa Italiana di Ematologia; UK: United Kingdom; US: United States

Sanderson *et al.* EHA 2024 (Abstract P2088; poster)

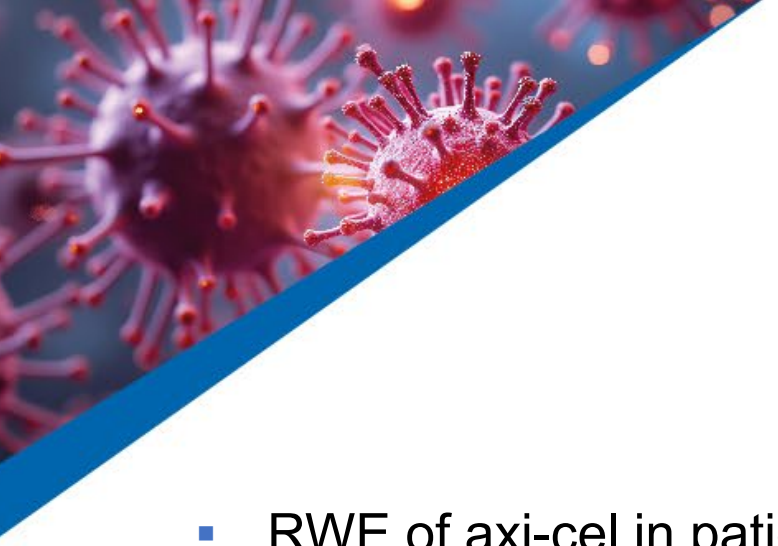
Results - Meta-Analysis of Prolonged Grade ≥3 Neutropenia by Geography



- Estimated incidence of any grade prolonged neutropenia in Europe was 47% (95% CI, 31-63; US-based data were not available)
- *Estimated incidence of Grade ≥3 prolonged neutropenia (present at or after 1 month post-infusion) was higher in the US (51% [95% CI, 42-61]) than in Europe (26% [95% CI, 22-30];*
- A similar trend between regions was observed with thrombocytopenia and anemia

Prolonged neutropenias were those present at or after 1 month post-infusion (Day 28 or 30).
CI: confidence interval; CHU de Québec-UL: Centre Hospitalier Universitaire de Québec-Université Laval; DESCAR-T: Dispositif d'Enregistrement et Suivi des patients traités par CAR-T; PNW3: Seattle Cancer Care Alliance, and Fred Hutchinson Cancer Research Center; SIE: Societa Italiana di Ematologia; US: United States

Sanderson *et al.* EHA 2024 (Abstract P2088; poster)



Conclusions

- RWE of axi-cel in patients with R / R DLBCL and FL was robust, with a marked increase in quantity and quality from Europe since the prior analysis[1]
- Overall, safety was manageable and consistent between regions and with clinical trials[2-3]
- Evolving management in the real world may have correlated with improved safety over time

axi-cel: axicabtagene ciloleucel; DLBCL: diffuse large B-cell lymphoma; FL: follicular lymphoma; R / R: relapsed / refractory; RWE: real-world evidence

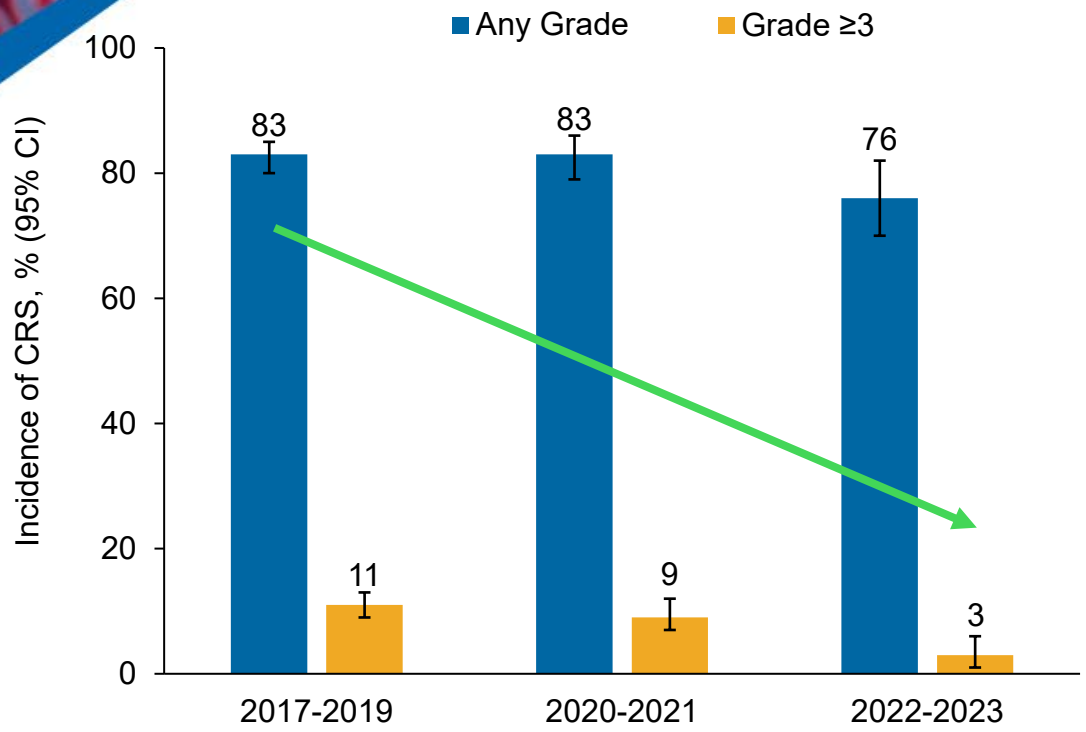
Sanderson *et al.* EHA 2024 (Abstract P2088; poster)
Jacobson C, et al. Transplant Cell Ther. 2024;30:77. E1-77.e15.
1.Neelapu SS, et al. N Engl J Med. 2017;377:2531-2544.
2.Jacobson CA, et al. Lancet Oncol. 2022;23:91-103.
3.Oluwole OO, et al. Br J Haematol. 2021;194:690-700.

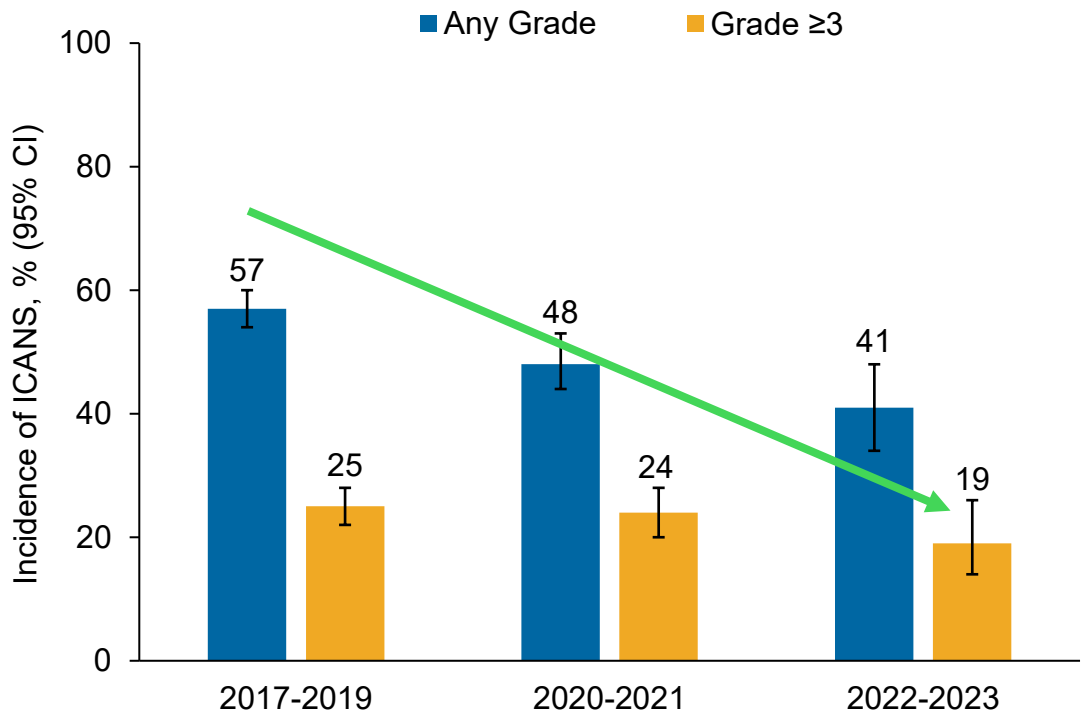
Baseline patient and disease characteristics

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 et al. ASH 2024 (Abstract 527; oral presentation) – A CIBMTR Report

Treatment trends for CRS/ICANS across study periods



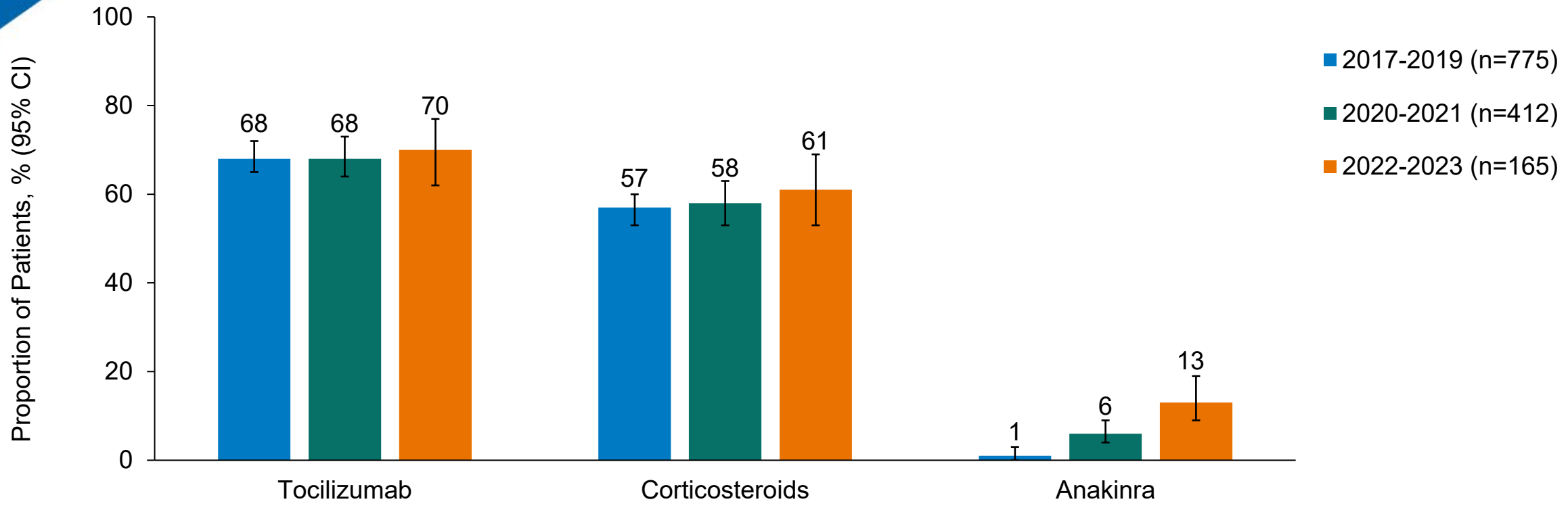


	2017-2019 n=923	2020-2021 n=486	2022-2023 n=206
Median time to onset (IQR), days	4 (2-6)	4 (2-6)	4 (2-6)
Median duration (IQR), days	7 (4-10)	6 (4-8)	5 (4-8)

	2017-2019 n=923	2020-2021 n=486	2022-2023 n=206
Median time to onset (IQR), days	7 (5-9)	6 (4-9)	7 (5-10)
Median duration (IQR), days	7.5 (4-13)	7.0 (4-12)	6.0 (4-11)

Wang et al. ASH 2024 (Abstract 527; oral presentation) – A CIBMTR Report

Treatment trends for CRS/ICANS across study periods

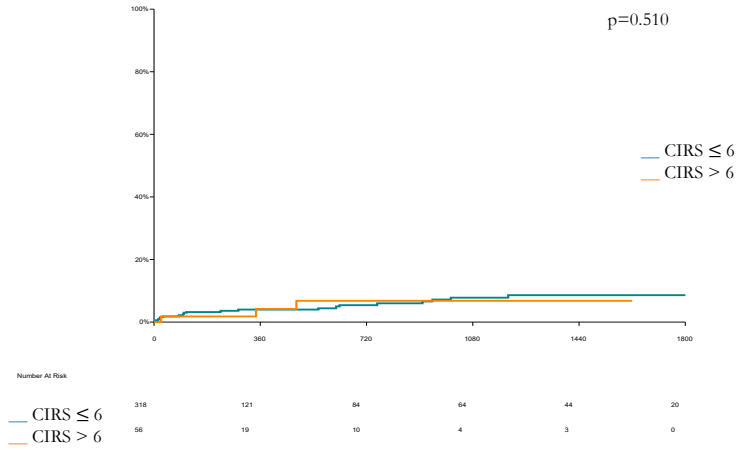


- In univariate analysis, rates of tocilizumab and corticosteroid use were consistent for the 3 periods, with a trend for increased anakinra use (1%, 6%, and 13%, respectively)

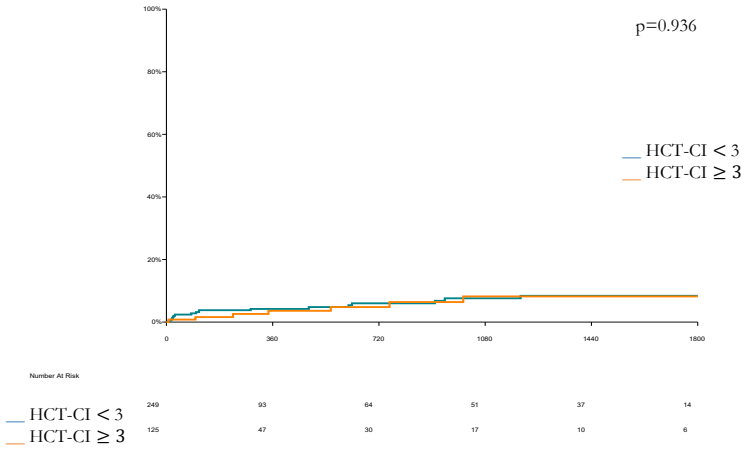
Percentages reflect the proportion of patients who experienced CRS/ICANS and had treatment reported (yes or no). CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

High Comorbidity Burden does not impact Non-Relapse Mortality in patients with LBCL treated with CAR-T

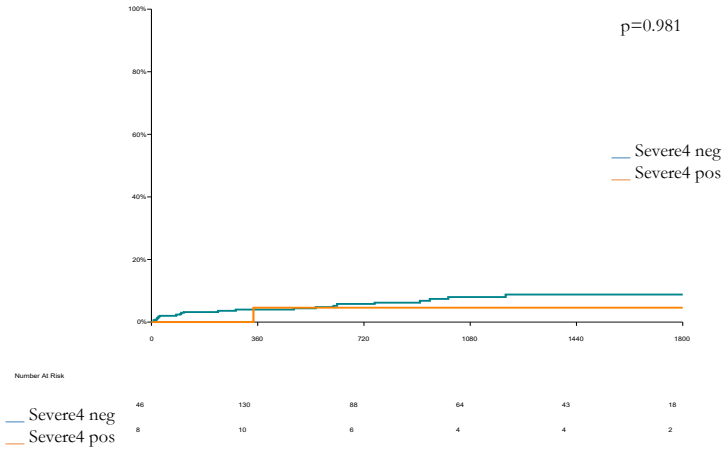
NRM by CIRS



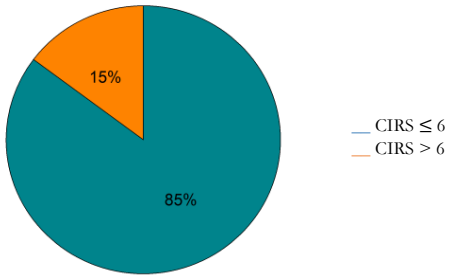
NRM by HCT-CI



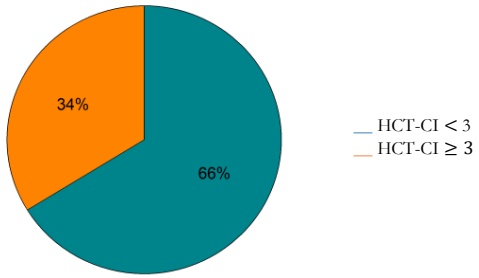
NRM by Severe4



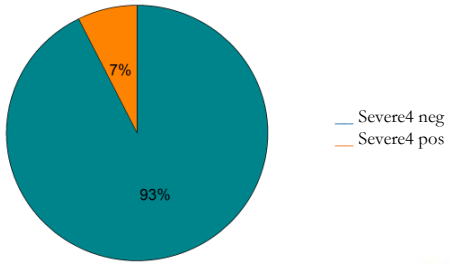
Comorbidity Burden assessed by CIRS



Comorbidity Burden assessed by HCT-CI

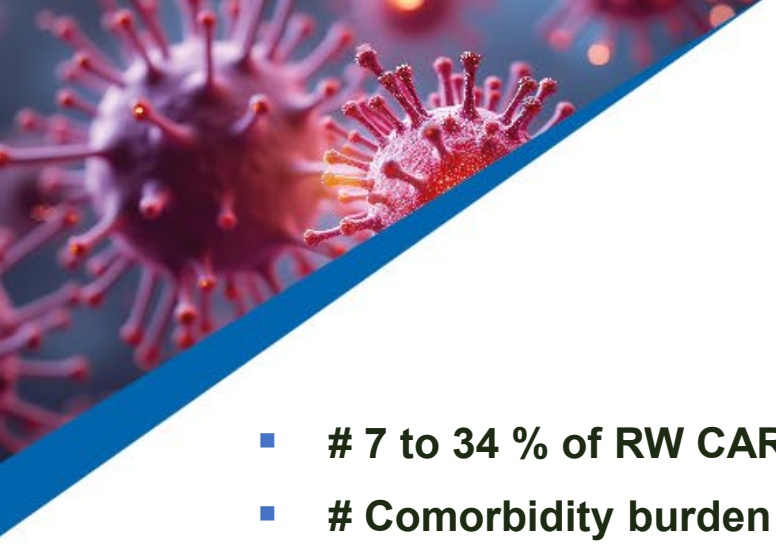


Comorbidity Burden assessed by Severe4



Galli E. et al… and Sica S., EBMT 2025 Oral presentation

In 379 LBCL patients from 2 centers



- **# 7 to 34 % of RW CAR-T patients are highly comorbid (@CIRS / HCT-CI / Severe4)**
- **# Comorbidity burden does not impact**
  - CRS G2+
  - ICANS G2+
  - Early ICAHT G2+
  - Late ICAHT G2+
  - Intensive treatments (Toci / Steroids / ICU admission)
- **# Comorbid patients show a NRM of 4-8% comparable to “fit” patients**

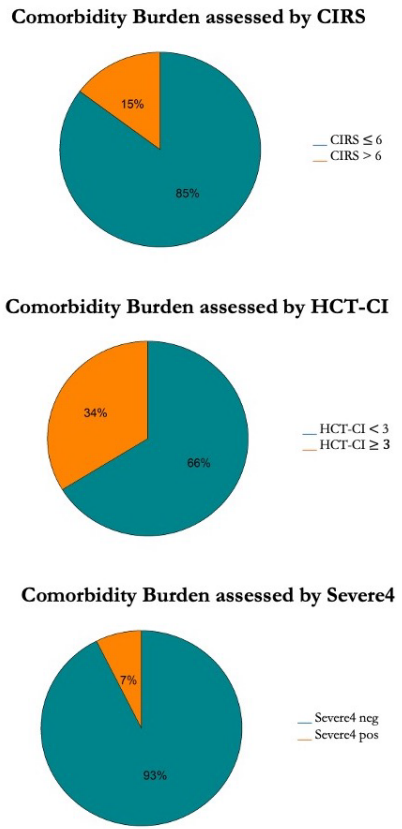
Comorbidities do not affect Non-Relapse Mortality or Toxicity in CD19 CAR-T Therapy

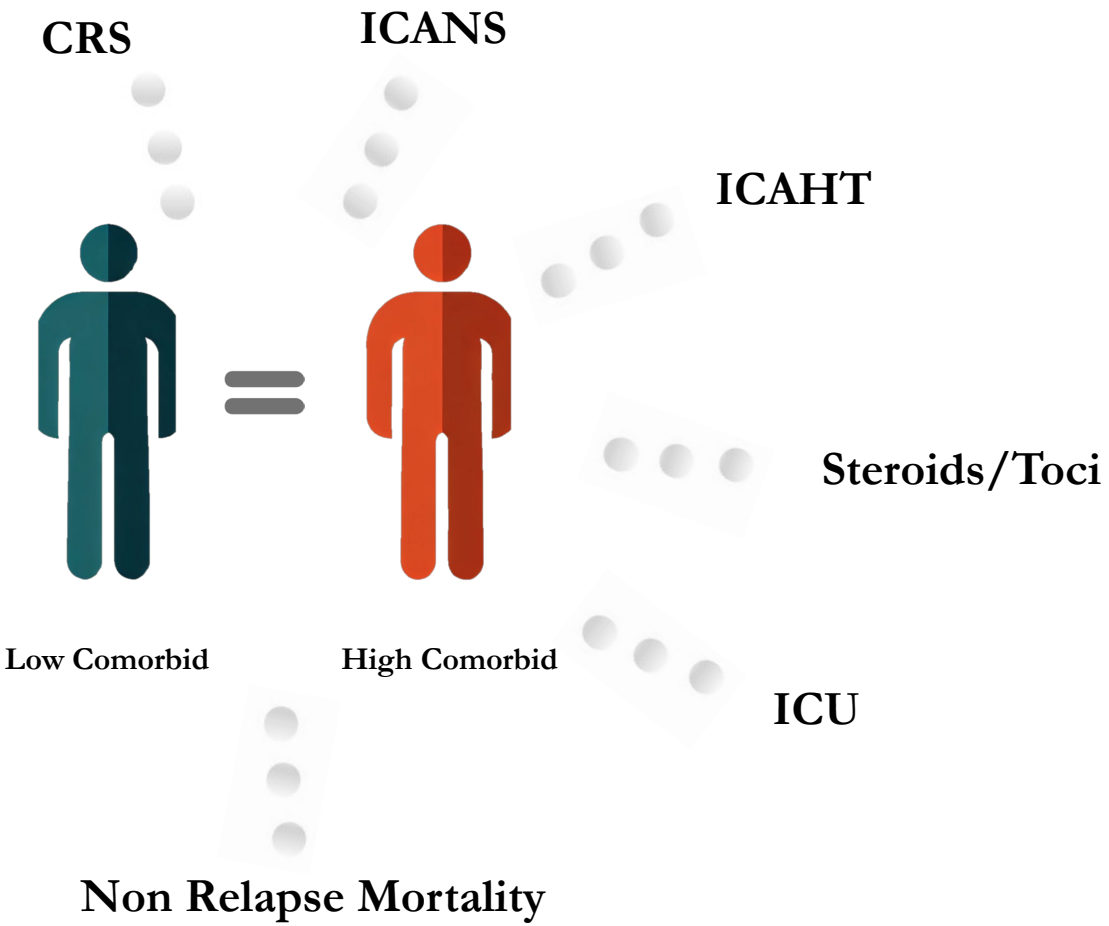
Galli E. et al… and Sica S., EBMT 2025 Oral presentation

In 379 LBCL patients from 2 centers

High Comorbidity Burden does not impact tolerability of CAR-T therapy in terms of Non-Relapse Mortality, toxicities and intensive treatments

In 379 LBCL patients from 2 centers





Galli E. et al… and Sica S., EBMT 2025 Oral presentation

REGULAR ARTICLE

blood advances

11 FEBRUARY 2025 •

A real-world comparison of commercial-use axicabtagene ciloleucel and lisocabtagene maraleucel in large B-cell lymphoma

Key Points

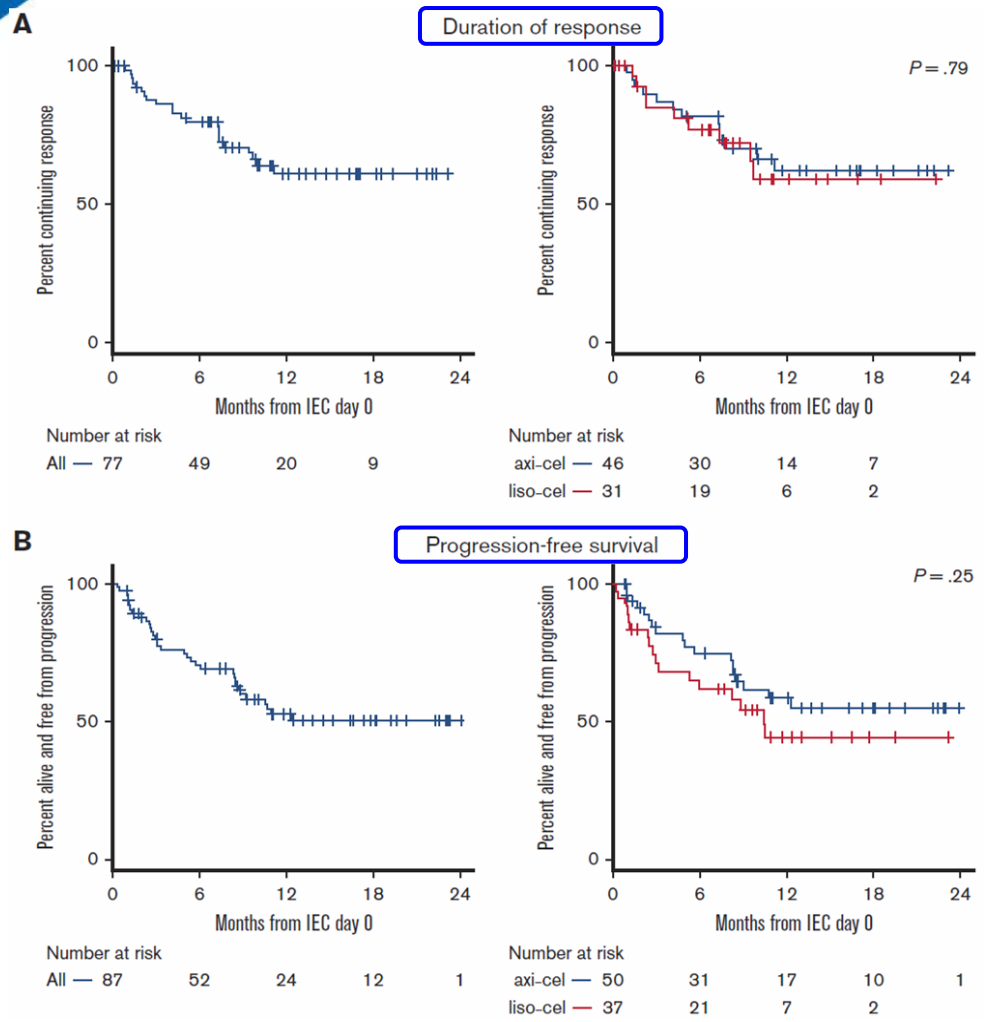
- Axi-cel and liso-cel had similar outcomes, but when accounting for differences in risk factors, axi-cel was associated with superior PFS.

Key Points

- We observed longer time from apheresis to treatment with liso-cel and more frequent CRS, ICANS, and prolonged neutropenia with axi-cel.

Survival outcomes

Kaplan-Meier curves illustrating time-to-event for the overall cohort and comparing axi-cel and liso-cel cohorts. (A) DOR curves for patients who achieved a CR or PR at first restaging after therapy. (B) PFS curves. (C) OS curves



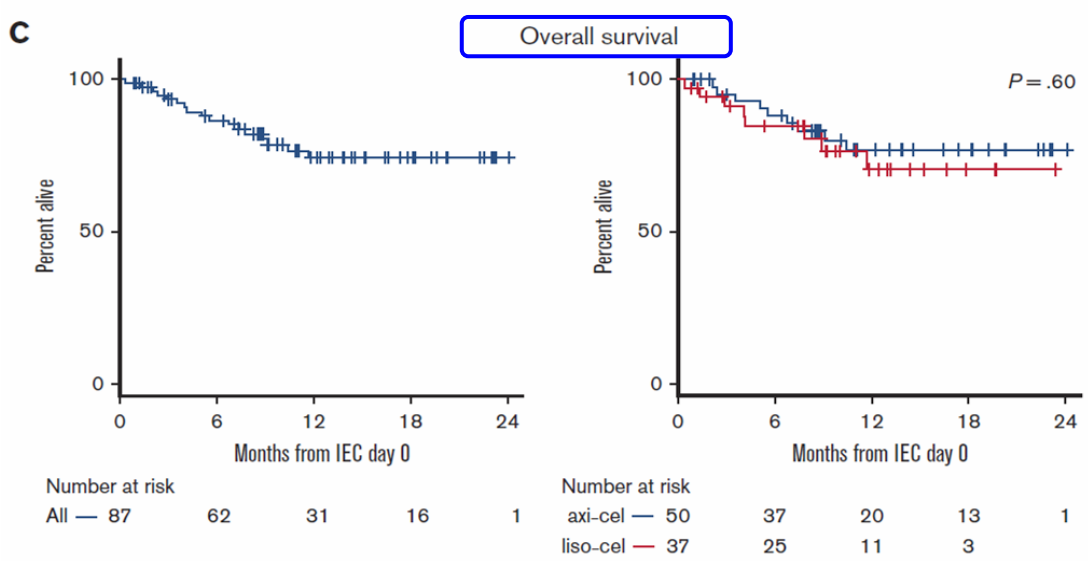


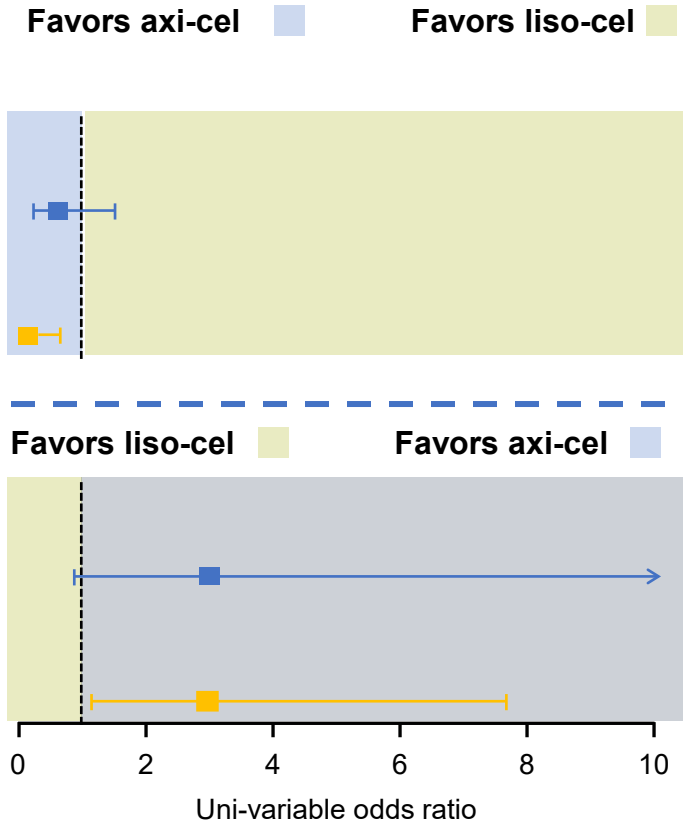
Figure 1

Looka et al. Blood Adv 2025

How do efficacy outcomes compare in a propensity score-weighted analysis?

	N(%)	OR (95% CI)	p-value
Complete response			
Axi-cel	50 (57)	Reference	
Liso-cel	37 (43)	0.60 (0.24, 1.52)	0.29
Overall response (CR/PR)			
Axi-cel	50 (57)	Reference	
Liso-cel	37 (43)	0.16 (0.02, 0.67)	0.025

	N(%)	HR (95% CI)	p-value
Overall survival			
Axi-cel	50 (57)	Reference	
Liso-cel	37 (43)	2.95 (0.84, 10.43)	0.092
Progression-free survival			
Axi-cel	50 (57)	Reference	
Liso-cel	37 (43)	2.95 (1.14, 7.60)	0.025



Propensity scoring factors:

- Age
- IPI pre-LDT
- Bridging therapy (Y/N)
- # of prior LoT
- LDH prior to LDT
- ECOG PS
- SPD
- Day 0 CRP
- Day 0 IL-6

A lower rate of overall response and inferior PFS were observed in the liso-cel cohort vs. axi-cel when comparing after propensity score weighted comparison

CRP: C-reactive protein; CR, complete response; ECOG PS: Eastern Cooperative Oncology Group performance status; HR, hazard ratio; IL-6: interleukin 6; IPI: International Prognostic Index; LDH: lactate dehydrogenase; LDT, lymphodepleting chemotherapy; LoT: line of therapy; OS, overall survival; OR, odds ratio; PFS, progression-free survival; PR, partial response; SPD: sum of product of diameters

Looka A, *et al. Blood Adv* 2024; ePub ahead of print.

Responses to CAR T-cell therapy and survival

	Total (N = 87)	Axi-cel (n = 50)	Liso-cel (n = 37)
Median follow-up (95% CI), mo	11 (10-14)	12 (10-18)	10 (9-14)
Best response			
CR	68% (57-77)	72% (58-84)	62% (45-78)
PR	21% (13-31)	20% (10-34)	22% (10-38)
1-mo response			
CR	54% (43-65)	62% (47-75)	43% (27-61)
PR	28% (19-38)	26% (15-40)	30% (16-47)
PFS, median (95% CI)	NR (9 to NR)	NR (9 to NR)	11 (6 to NR)
12-mo PFS	53%, (42-66)	59% (45-76)	44% (29-68)
DOR, median (95% CI)	NR (11 to NR)	NR (11 to NR)	NR (9 to NR)
12-mo DOR	61% (49-76)	62% (48-81)	59% (41-86)
OS, median (95% CI)	NR (NR to NR)	NR (NR to NR)	NR (NR to NR)
12-mo OS	74% (64-86)	77% (65-92)	71% (55-91)

Values are presented as rate (95% CI) unless otherwise stated.
NR, not reached.

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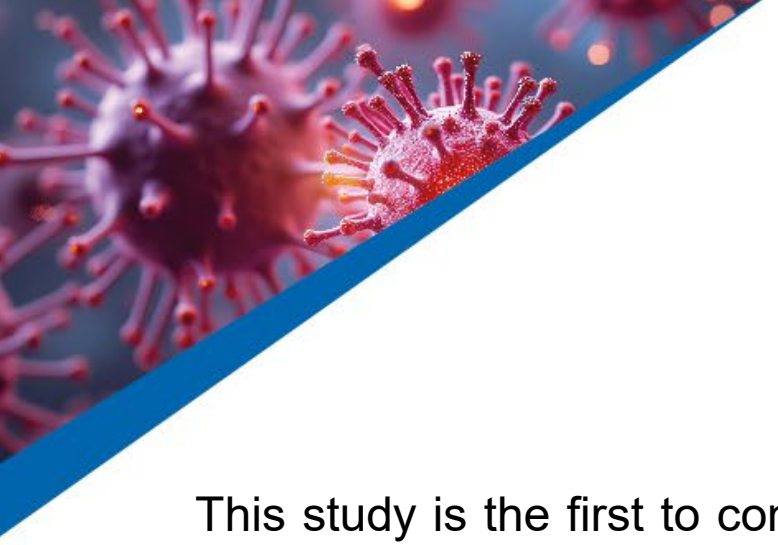

Conclusions

This study is the first to compare the efficacy and toxicities of axi-cel and liso-cel for the treatment of R/R LBCL in the commercial setting.

Overall, direct comparison of axi-cel and liso-cel cohorts shows similar key outcomes including response rate and PFS, but prolonged wait times for liso-cel may have resulted in biased selection of patients with more favorable characteristics for liso-cel. When accounting for these higher-risk characteristics, an inferior PFS is observed with liso-cel compared with axi-cel. These findings warrant further evaluation in a multicenter setting.

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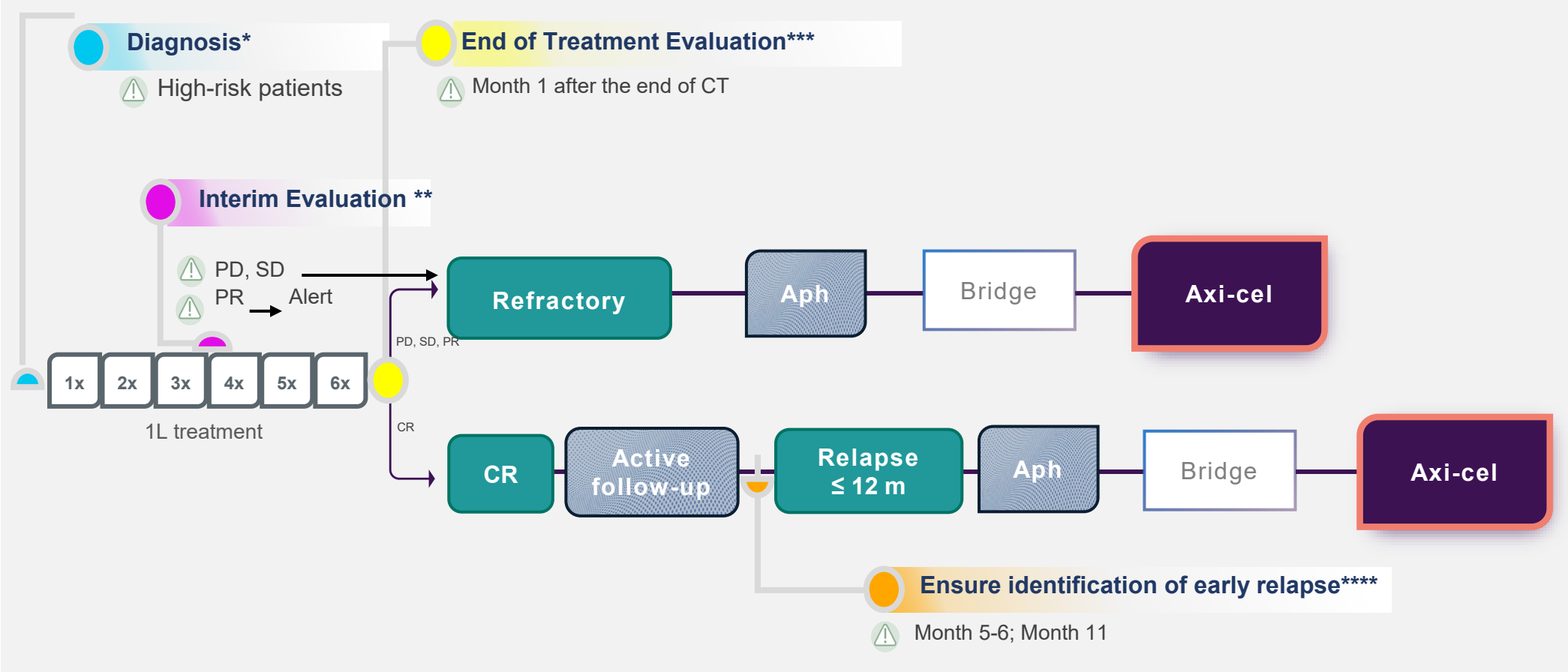
Patient Journey to axi-cel in 2L DLBCL



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Summary: how to improve survival outcomes in chemorefractory and/or early relapsed LBCL patients in 2L

Risk factors at diagnosis

- IPI score
- Cell of origin
- Genetic signatures
- TMTV
- ctDNA

- Alert qualified center for high risk patients
- Early planning of PET/TAC evaluation timings

Interim evaluation during 1L therapy

- Recommended by most Guidelines after 2-4 cycles
- PET result is predictive of outcome

- Refer patients in PD or SD
- Alert QTC for patients in PR

End of treatment evaluation and follow-up after 1L therapy

- EOT 3-6 weeks after the last 1L cycle
- Follow-up evaluations for CR patients at 5-6 and 11 months after the last 1L cycle

- Refer patients in PD, SD or PR
- Early planning for follow-up evaluations for patients in CR
- Refer patients with signs of progression before 12 months

Speaker's view

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Characteristics at ASCT	
Median age at ASCT (range)	56 (18-76)
Disease status at salvage therapy:	
Late relapse	314 (40%)
Early relapse	128 (16%)
Primary refractory	349 (44%)
Treatment line at ASCT:	
Second line	617 (78%)
Third line	147 (19%)
Frontline in transformed	27 (3%)
Disease status at ASCT:	
CR	481 (61%)
PR	275 (35%)
SD	21 (3%)
Not evaluated	14 (2%)

Autologous Stem Cell Transplantation for Relapsed/Refractory Large B Cell Lymphoma: Multicenter GETH-TC/GELTAMO Study

- Retrospective multicenter study including 791 patients with relapsed/refractory (R/R) large B cell lymphoma (LBCL) all histologies
- ASCT from 2010-2021
- All the patients received rituximab anthracycline-based frontline therapy
- After a median follow-up of 74 months (95%CI 68-81) from infusion, 65% of 21 the patients were alive and 84% of them free of disease
- Progression-free survival (PFS) and overall survival (OS) at 6 years were 51% (95%CI 47-54) and 63% (95%CI 23 60-67), respectively
- Non-relapse mortality (NRM) at 1 year was 9% (95%CI 7-11)

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	PFS (HR, 95%CI)	p	OS (HR, 95%CI)	p
>60 years at ASCT	1.31 (1.06-1.62)	**0.011**	1.66 (1.30-2.12)	**<0.001**
Time period before 1-nov-2012	---	---	1.40 (1.07-1.83)	**0.014**
3th line versus 2nd line at ASCT	1.81 (1.42-2.31)	**<0.001**	1.90 (1.44-2.5)	**<0.001**
PR versus CR pre-ASCT	1.46 (1.18-1.81)	**<0.001**	1.56 (1.21-1.99)	**<0.001**
SD versus CR pre-ASCT	---	---	3.01 (1.61-5.62)	**<0.001**

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Autologous Stem Cell Transplantation for Relapsed/Refractory Large B Cell Lymphoma: Multicenter GETH-TC/GELTAMO Study

- Forty percent of the patients had primary refractory disease pre-ASCT, 16% experienced early relapse and 40% late relapse
- PFS was significantly influenced by age at ASCT, the number of lines prior to ASCT and disease status at ASCT (p<0.01)
- In the multivariate analysis, age >60 years at ASCT [HR 1.31 (95%CI 1.06-1.62), p=0.011], ASCT as ≥3rd line [HR 1.81 (95%CI 1.42-2.31), p6-year-PFS and OS of 51% (95%CI 47-54) and 63% (95%CI 60-67), respectively with NRM at 1 year of 9% (95%CI 7-11)
- These results indicate that ASCT is a curative option for patients with chemosensitive disease (especially in CR after salvage), regardless of the timing of relapse after frontline treatment
- ASCT could be an option in chemosensitive relapses regardless of the period of time until treatment failure in centers without availability for CAR-T therapy provided the disease is sensitive to salvage therapy
- From 307 patients who relapsed after ASCT (39%), 59 received CAR-T therapy (19%) with a 1y-OS of 79% (95%CI: 69-90) and 1y-NRM of 8% (95%CI: 0-15). Sixty-eight patients received allo-SCT (22%) with 1y-OS of 50% (95%CI: 38-62) and 1y-NRM of 38% (95%CI: 26-51)

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