

Updates on CAR-T cell therapy in DLBCL

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◆ Disclosure

- Honoraria: AstraZeneca, Ono Pharmaceuticals, Eisai, Chugai, Janssen, Symbio, Bristol Myers Squibb, Daiichi Sankyo, Otsuka, Abbvie, Takeda, Eli Lilly, Genmab, Kyowa Kirin, MSD, Astellas, Pfizer, MeijiSeika Pharma, Novartis, Nihon Kayaku, Gilead
- Consulting: AstraZeneca, Ono Pharmaceuticals, Mitsubishi Tanabe Pharma, Eisai, Chugai, Bristol Myers Squibb, Takeda, Otsuka, Abbvie, Zenyaku, Kyowa Kirin, MSD, Carna Biosciences, Novartis, Yakult, Nihon Shinyaku, Beigene
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Contents

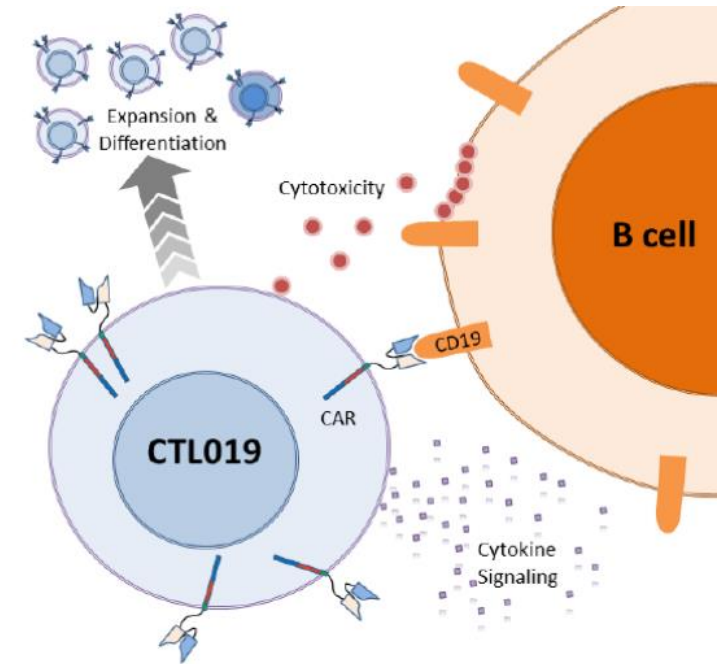
- ◆ Latest Updates from Key Clinical Trials
- ◆ Cross Products Comparison
- ◆ Current Real-World Practice of CAR-T for DLBCL in Japan

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Current Role of CD19 CAR-T in DLBCL

- SOC for R/R DLBCL after ≥ 2 lines of therapy
- Preferred 2L option in early relapse/refractory disease (vs. ASCT)



FDA Briefing Document ODAC Meeting BLA 125646 tisagenlecleucel

Region	Yescarta (axi-cel)	Kymriah (tisa-cel)	Breyanzi (liso-cel)
United States	2017	2018	2021
Europe	2018	2018	2022
Japan	2021	2019	2021
Singapore	2024	2021	–

CD19 CAR-T for 3L+ DLBCL long-term results

	Tisa-cel	Axi-cel	Liso-cel
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Even with single-arm evidence, CAR-T is regarded as more effective than SOC in 3L+ LBCL and may cure some patients.

Phase 3 studies of CAR-T vs SOC for high-risk 2L DLBCL

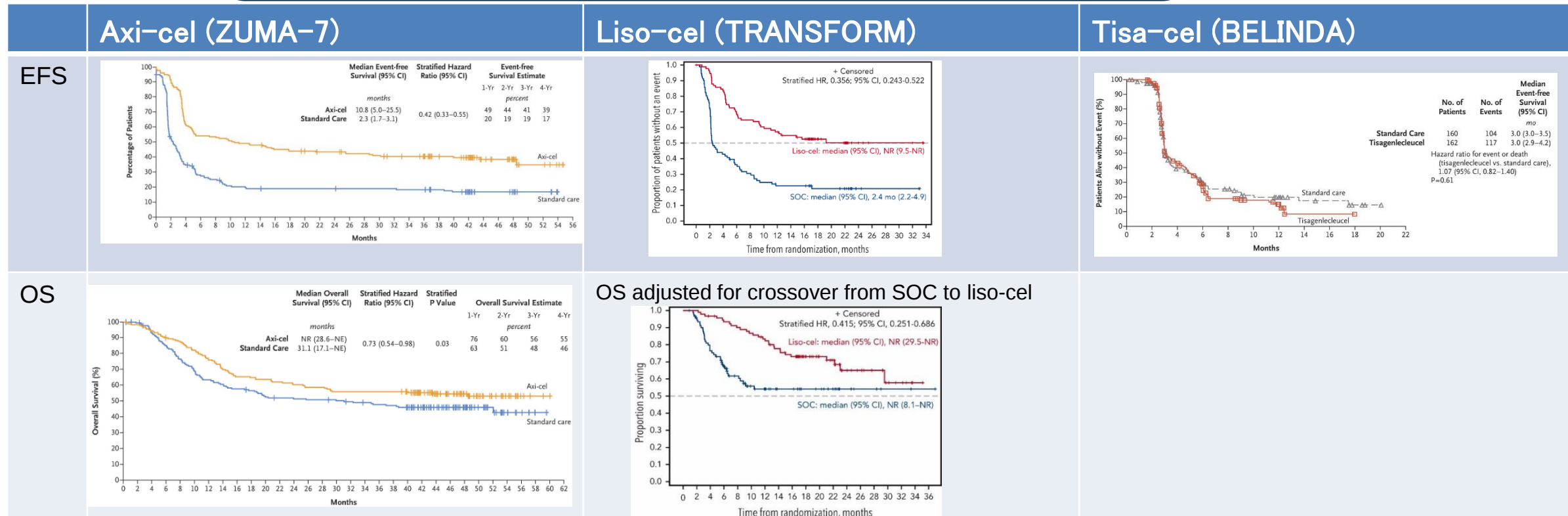
High-risk 2L-DLBCL

- <CR to 1L R-CHOP
- CR < 12 mo

R

CAR-T

SOC: multi-agent chemo → ASCT

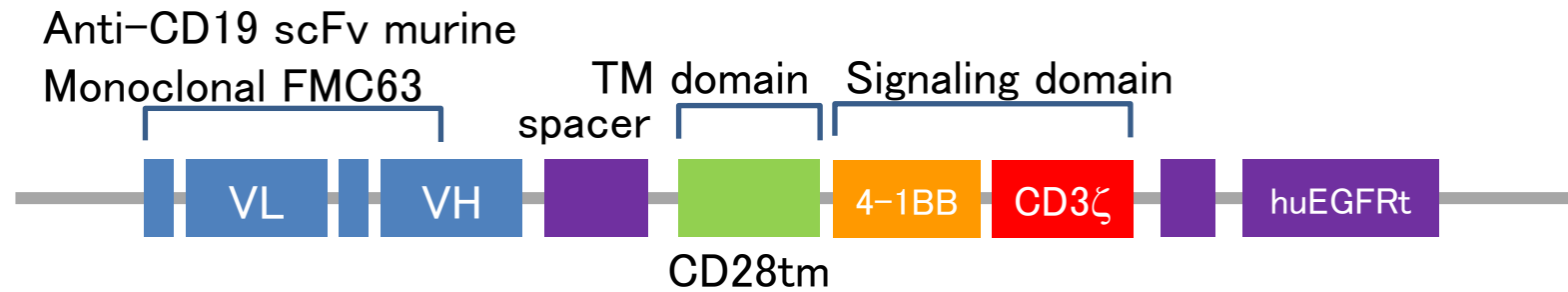


Locke FL et al. N Engl J Med 2022; 386:640-54, Westin JR et al. N Engl J Med 2023; 389:148-57

Kamdar M et al. Lancet 2022; 399:2294-308, Abramson JS et al. Blood 2023; 141:1675-84, Bishop MR et al. N Engl J Med 2022;386:629

Lisocabtagene maraleucel (Liso-cel)

- CAR construct



TRANSFORM: study design

Key eligibility criteria

- Age 18–75 years
- Aggressive NHL: DLBCL NOS, tDLBCL from indolent NHL, HGBCL (double/triple hit), FL3B, PMBCL, THRBCL
- Disease refractory or relapsed^a ≤ 12 mo after 1L treatment containing an anthracycline and a CD20-targeted agent
- ECOG PS ≤ 1
- Eligible for HSCT

Screening +
leukapheresis

PET (if bridging therapy received)

*Bridging
therapy
optional^a*

Lymphodepletion
FLU 30 mg/m² and
CY 300 mg/m² × 3 days

Liso-cel^b
100 × 10⁶ CAR⁺ T cells
(2–7 days
after FLU/CY)

**Disease
assessments**
(up to 36 months
after randomization)

43 (47%) patients
continued to LTFU

89 (97%) patients received liso-cel

1:1 randomization (n = 92 in each arm)

SOC

*3 cycles of salvage immunochemotherapy^a
followed by HDCT + HSCT*

**Disease
assessments**
(up to 36 months
after randomization)

*Crossover to receive
liso-cel allowed if SOC
failed based on IRC-
confirmed EFS event*

91 (99%) patients started SOC (43 [47%] received HDCT/HSCT)

57 (62%) patients received
liso-cel in crossover

25 (27%) patients
continued to LTFU

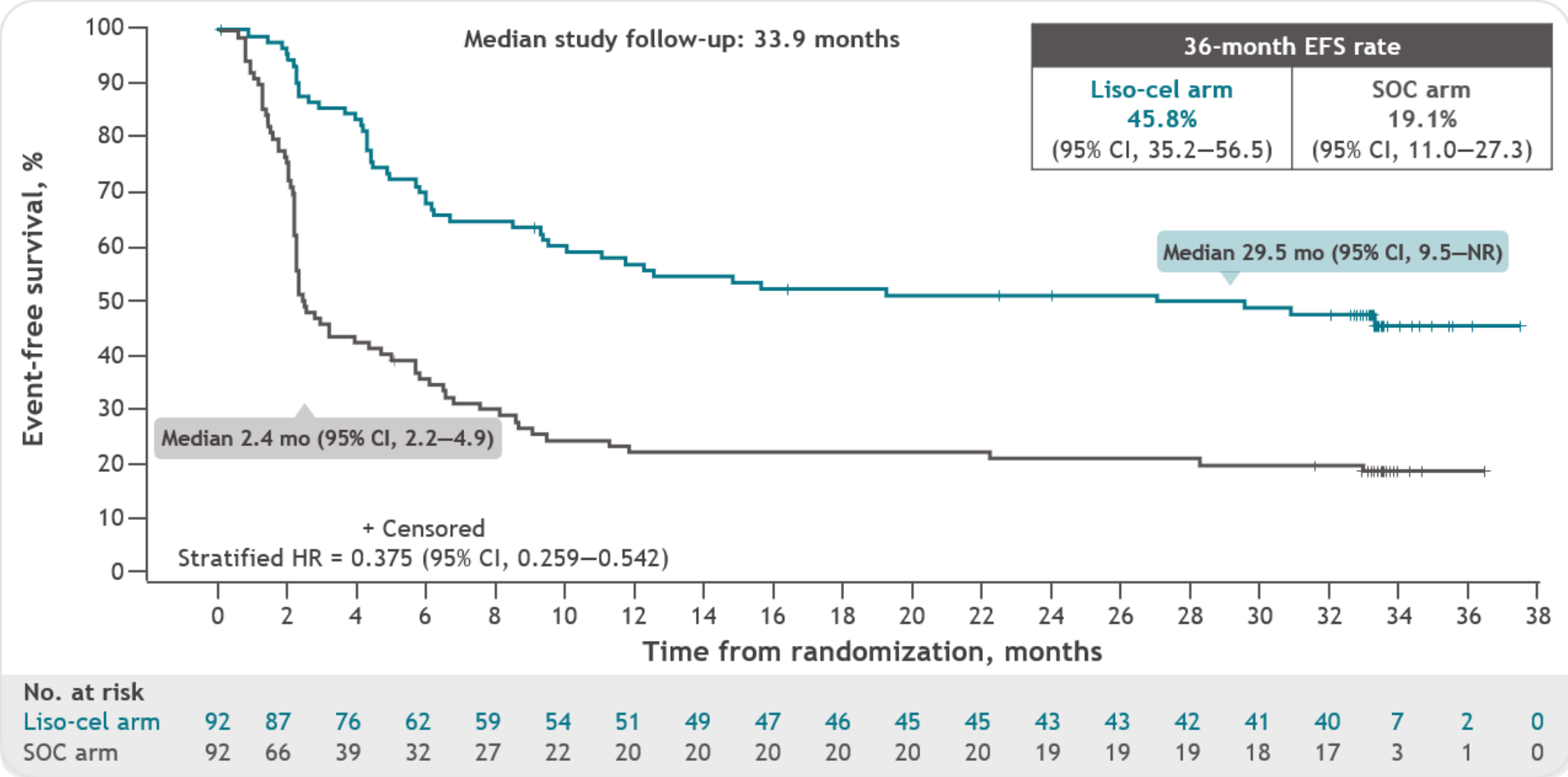
Primary endpoint: EFS per IRC assessment by Lugano 2014 criteria¹

Key secondary endpoints: CR rate, PFS, and OS

Demographics and baseline disease characteristics (ITT set)

	Liso-cel arm (n = 92)	SOC arm (n = 92)
Male, n (%)	44 (48)	61 (66)
Age, y		
Median (range)	60 (20–74)	58 (26–75)
≥ 65, n (%)	36 (39)	25 (27)
LBCL subtypes, n (%)		
DLBCL NOS	53 (58)	50 (54)
HGBCL with rearrangements in <i>MYC</i> and <i>BCL2</i> , <i>BCL6</i> , or both	22 (24)	21 (23)
PMBCL	8 (9)	9 (10)
tDLBCL from any indolent lymphoma	7 (8)	8 (9)
THRBCL	1 (1)	4 (4)
FL3B	1 (1)	0
LBCL subtype based on cell of origin, n (%)		
GCB	45 (49)	40 (43)
ABC, non-GCB	21 (23)	29 (32)
ECOG PS at screening, n (%)		
0	48 (52)	57 (62)
1	44 (48)	35 (38)
sAAIPI, n (%)		
0 or 1	56 (61)	55 (60)
2 or 3	36 (39)	37 (40)
Prior response status, n (%)		
Refractory ^a	67 (73)	70 (76)
Relapsed ^b	25 (27)	22 (24)

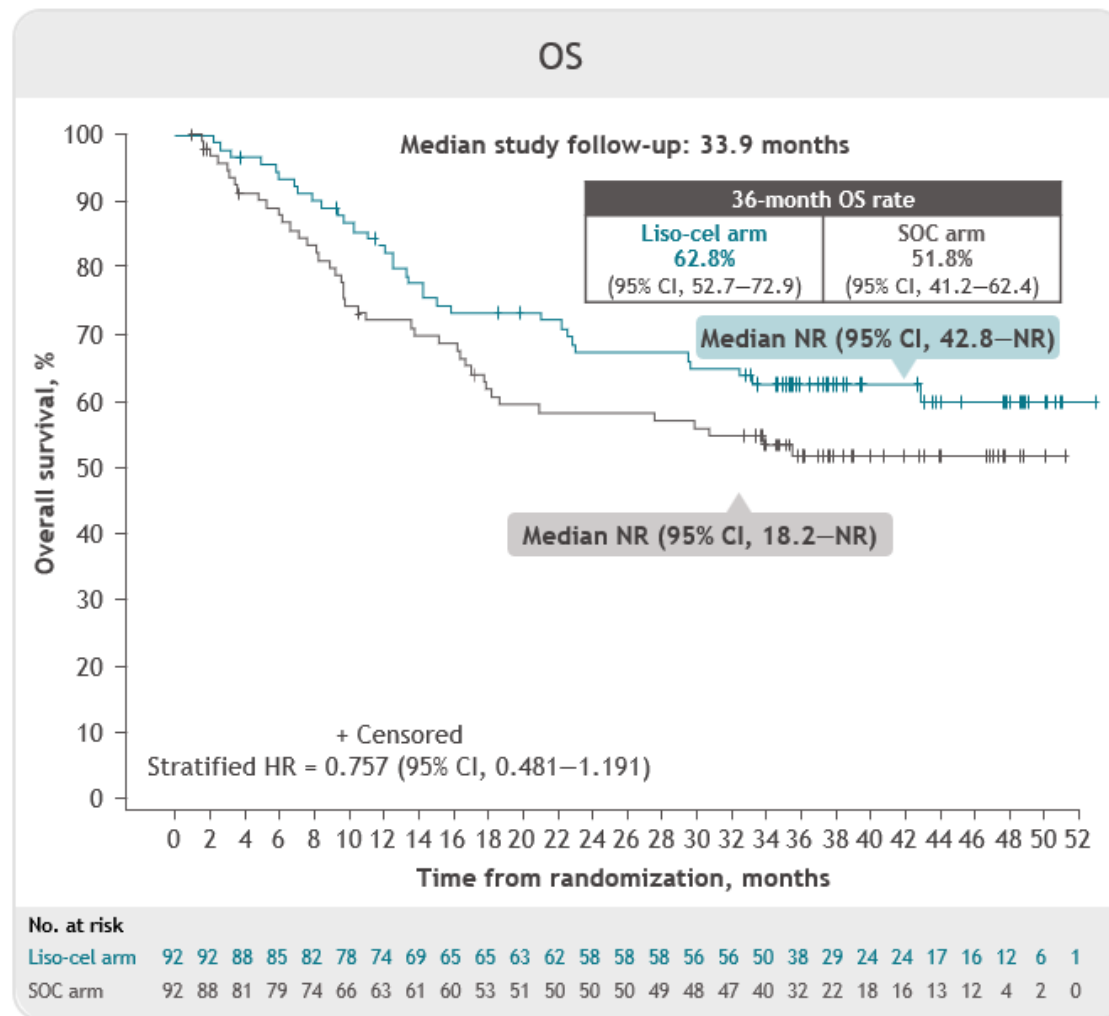
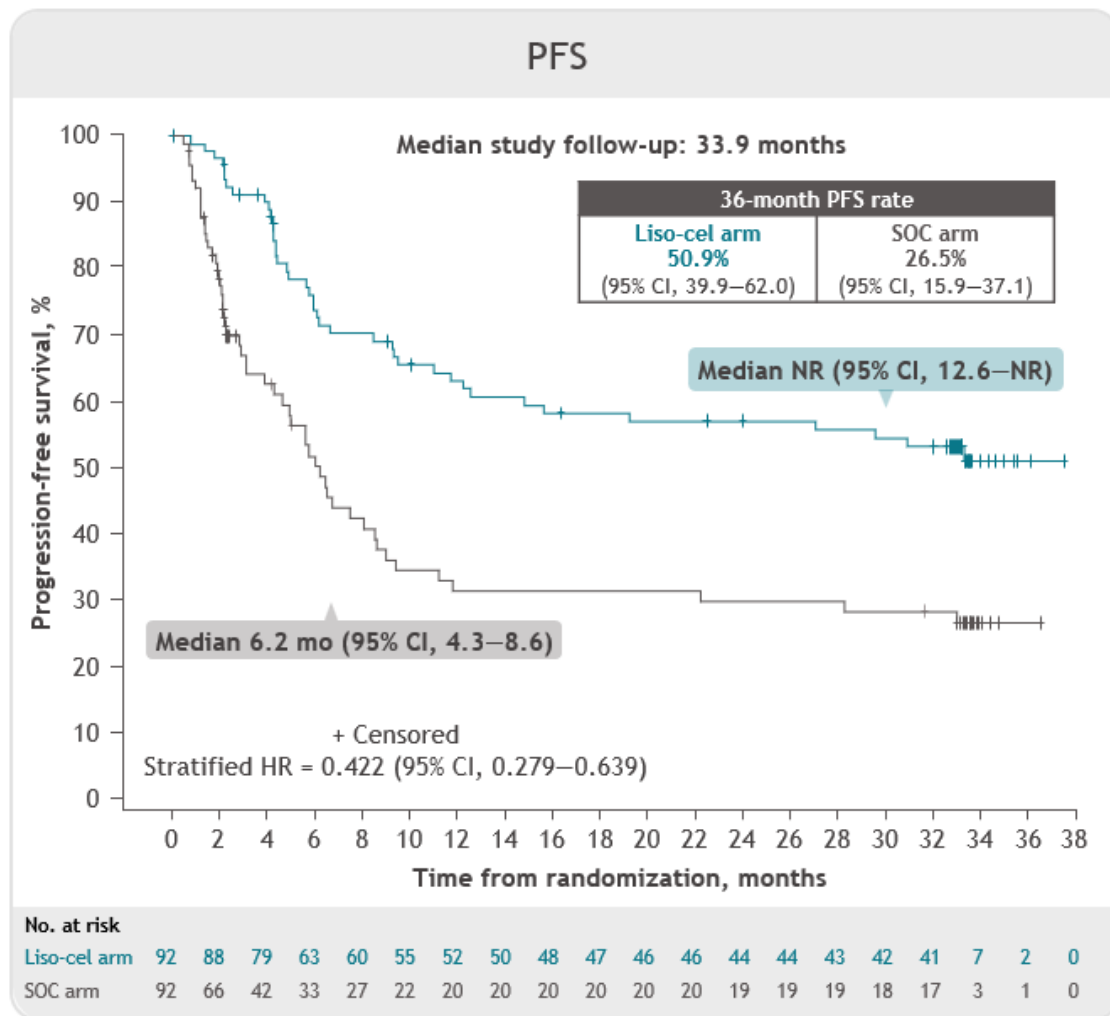
Event-free survival based on IRC assessment (ITT set)



NR, not reached.

Progression-free survival based on IRC assessment and overall survival (ITT set)

TRANSFORM

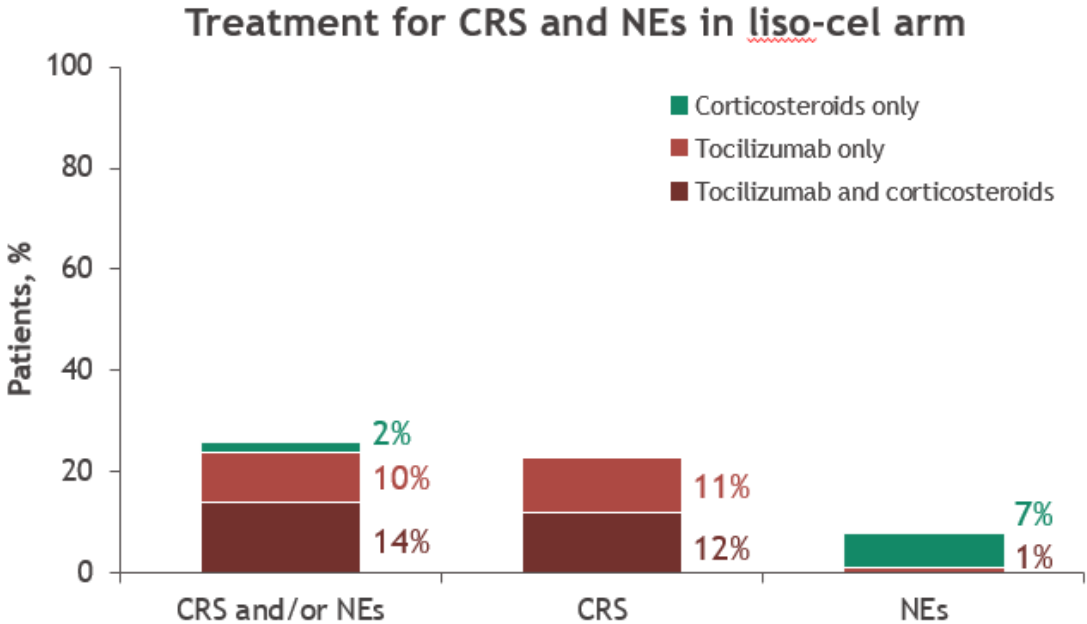
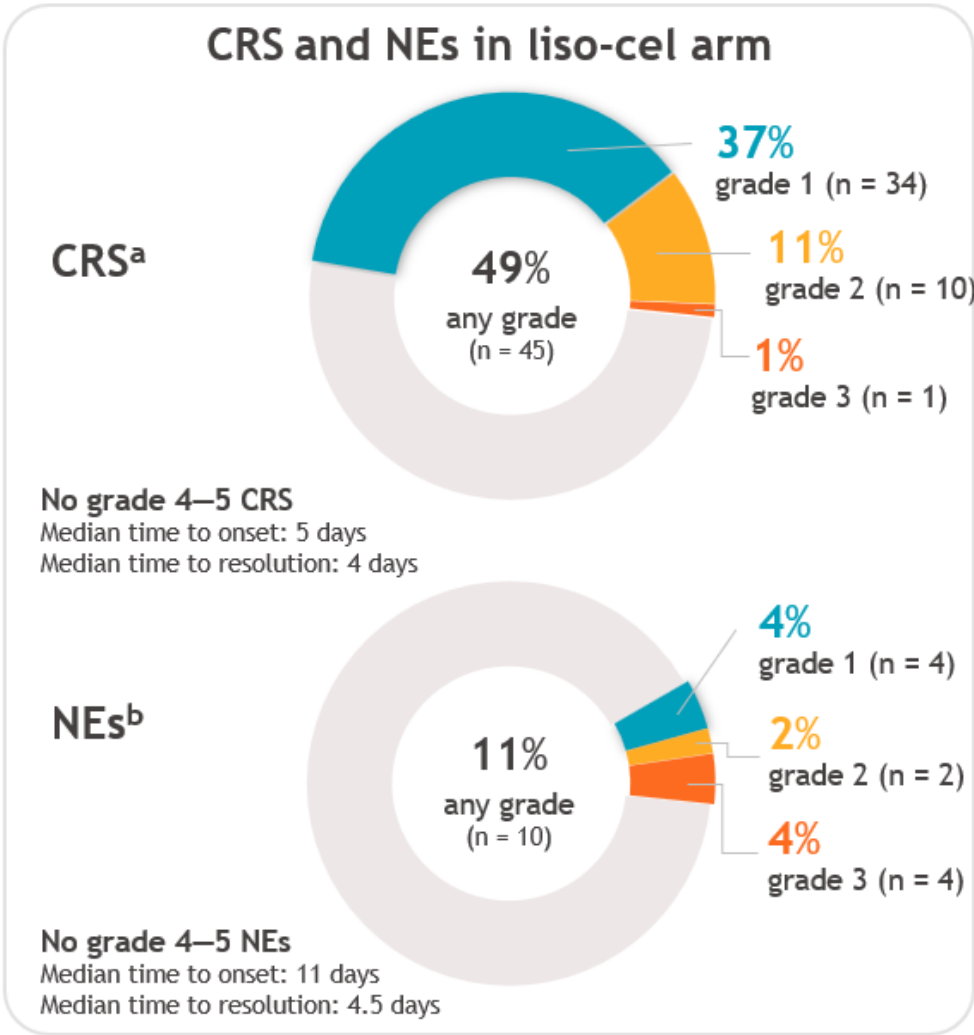


- 57 (62%) patients in SOC arm crossed over to receive liso-cel

Kamdar M et al. ASCO 2024 #7013

Kamdar M et al. J Clin Oncol 2025; 43:2671

Treatment-emergent adverse events of special interest (safety set)



	Liso-cel arm (n = 92)	SOC arm (n = 91)
Prolonged cytopenia, ^c n (%)	40 (43)	3 (3)
Grade ≥ 3 infections, n (%)	14 (15)	19 (21)

^aGraded according to the Lee 2014 criteria; ^bDefined as investigator-identified neurological AEs related to liso-cel. These were graded per the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03; ^cGrade ≥ 3 anemia, neutropenia, or thrombocytopenia at 35 days after liso-cel infusion for the liso-cel arm or at 35 days after the start of the last chemotherapy for the SOC arm. NE, neurological event.

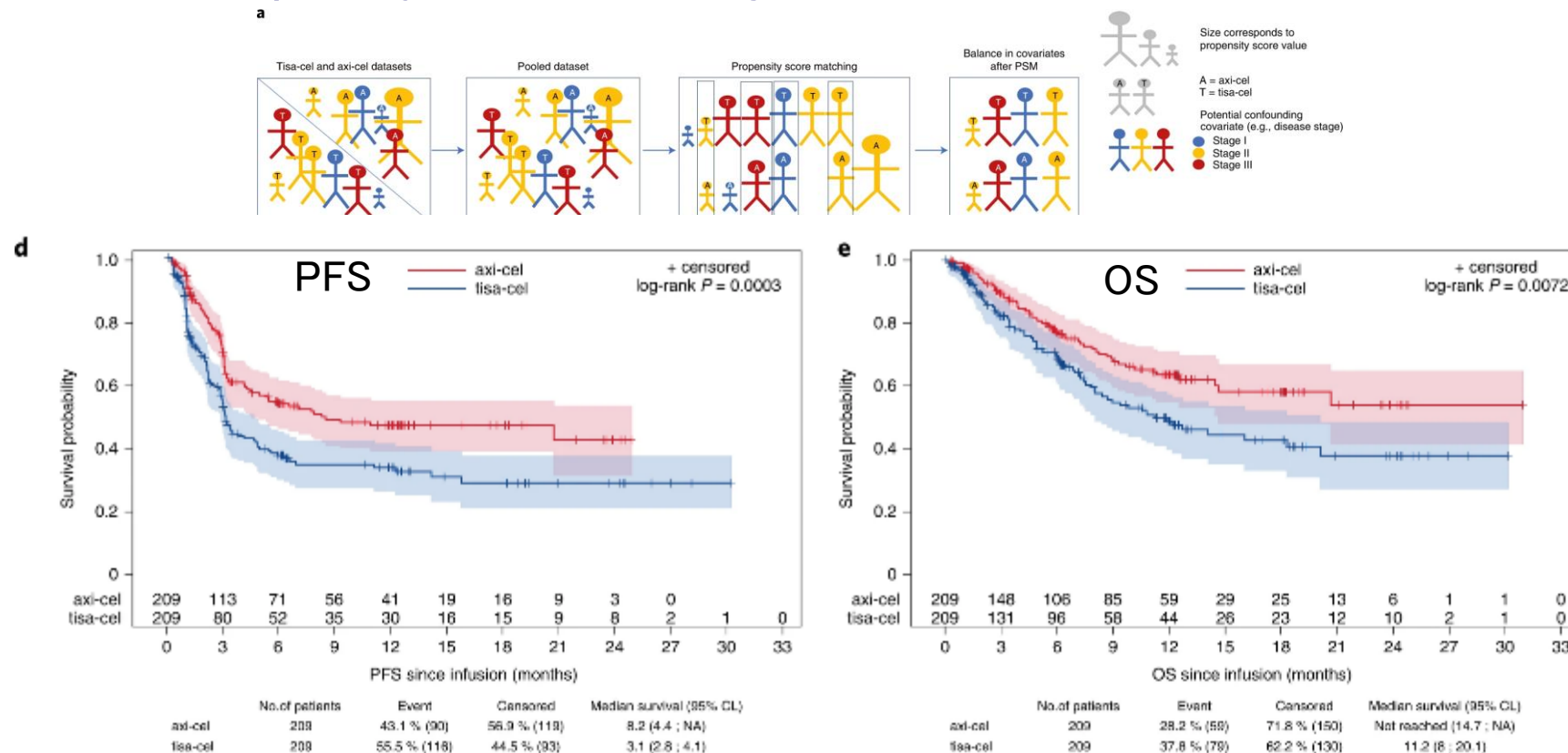
Contents

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Matching-adjusted indirect comparison of Axi-cel vs Tisa-cel in 3L+ LBCL

DESCAR-T (French Registry)

Propensity score matching



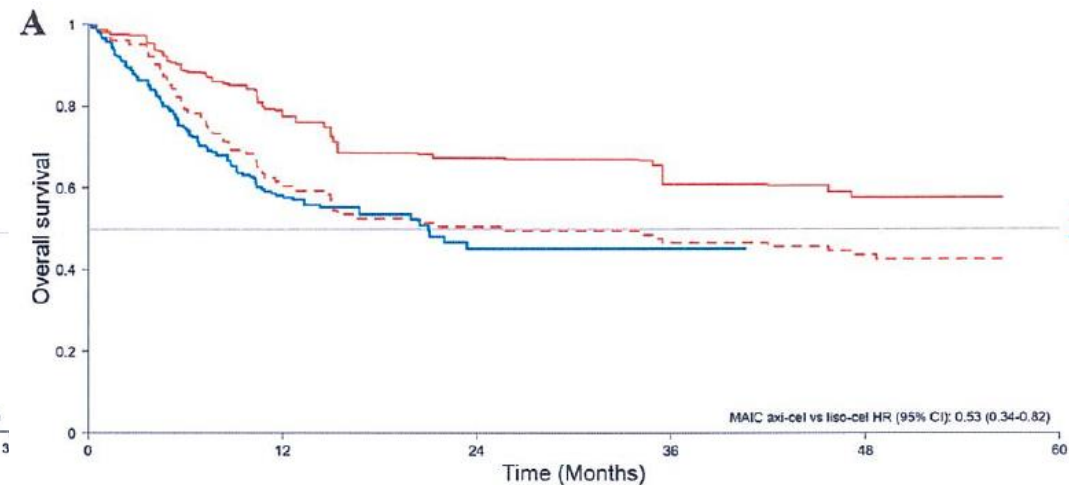
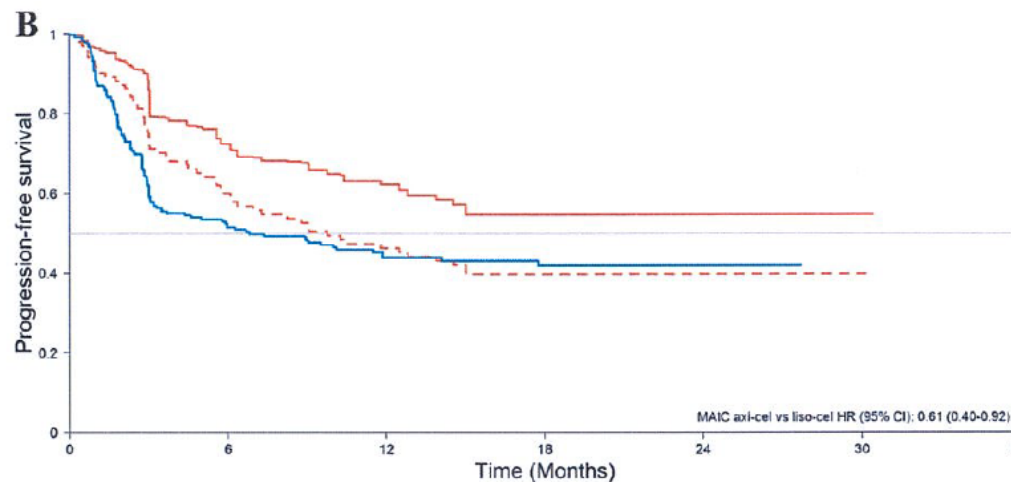
	axi-cel		tisa-cel		P
	n = 209		n = 209		
CRS of any grade	180	(86.1%)	158	(75.6%)	0.006
Grade 1-2	169	(80.9%)	139	(66.5%)	<0.001
Grade ≥3	11	(5.3%)	19	(9.1%)	0.130
ICANS of any grade	102	(48.8%)	46	(22.0%)	<0.001
Grade 1-2	73	(34.9%)	40	(19.1%)	<0.001
Grade ≥3	29	(13.9%)	6	(2.9%)	<0.001
Cytopenia of any grade at M1	135	(64.6%)	82	(39.2%)	<0.001
Grade 1-2	64	(30.6%)	56	(26.8%)	0.387
Grade ≥3	71	(34.0%)	26	(12.4%)	<0.001
Neutropenia of any grade at M1	124	(59.3%)	57	(27.3%)	<0.001
Grade 1-2	71	(34.0%)	37	(17.7%)	<0.001
Grade ≥3	53	(25.4%)	20	(9.6%)	<0.001
Anemia of any grade at M1	94	(45.0%)	58	(27.8%)	<0.001
Grade 1-2	90	(43.1%)	58	(27.8%)	0.001
Grade ≥3	4	(1.9%)	0	(0.0%)	0.044
Thrombocytopenia of any grade at M1	116	(55.5%)	62	(29.7%)	<0.001
Grade 1-2	70	(33.5%)	43	(20.6%)	0.003
Grade ≥3	46	(22.0%)	19	(9.1%)	<0.001

CRS, ICANS, and cytopenias are more frequent with axi-cel

Matching-adjusted indirect comparison of Axi-cel vs Liso-cel in LBCL

□ ZUMA-1 & TRANSCEND-NHL-001

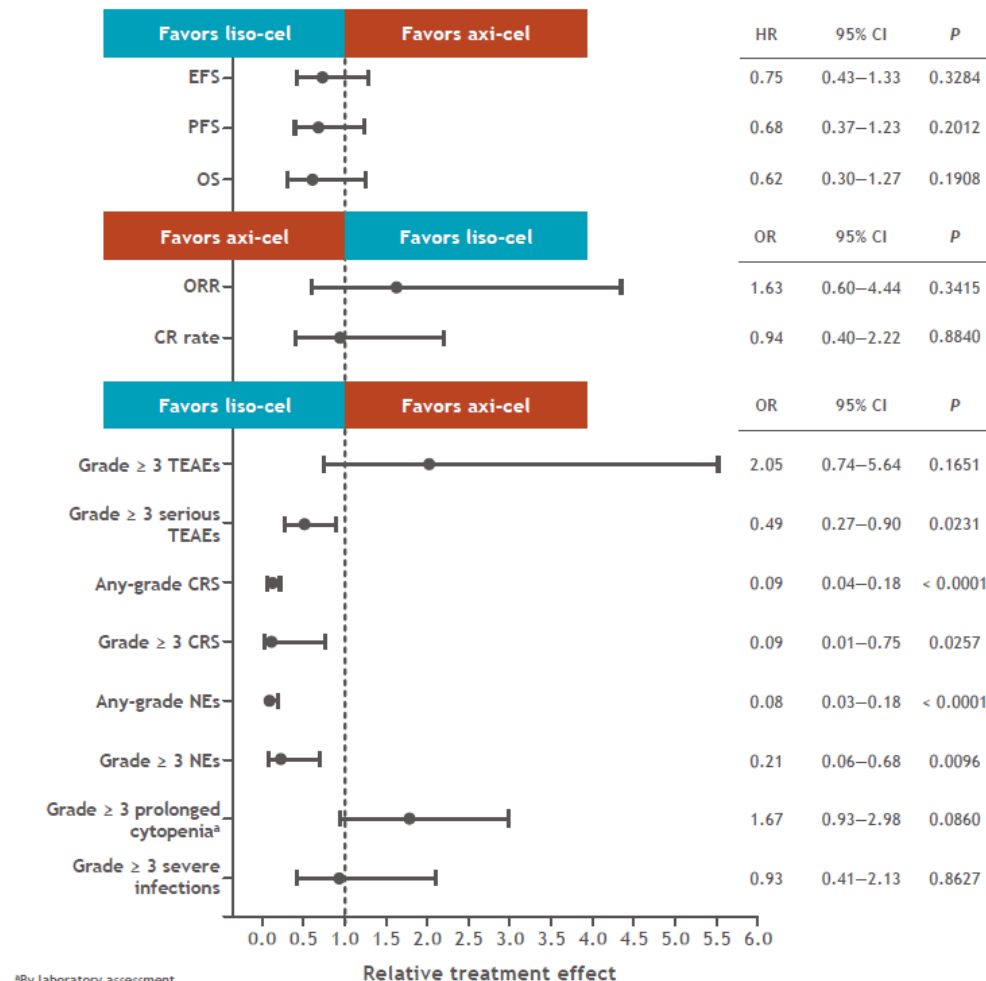
- ORR: comparable
- PFS: Axi-cel > Liso-cel, HR: 0.61 (95% CI: 0.40-0.92)
- OS: Axi-cel > Liso-cel, HR 0.53 (95% CI 0.34-0.82)
- Grade ≥ 3 CRS: more frequent with Axi-cel, OR: 3.64 (95% CI 1.04-12.76)
- Neurological events: more frequent with Axi-cel, , OR: 3.45 (95% CI: 1.65-7.19)



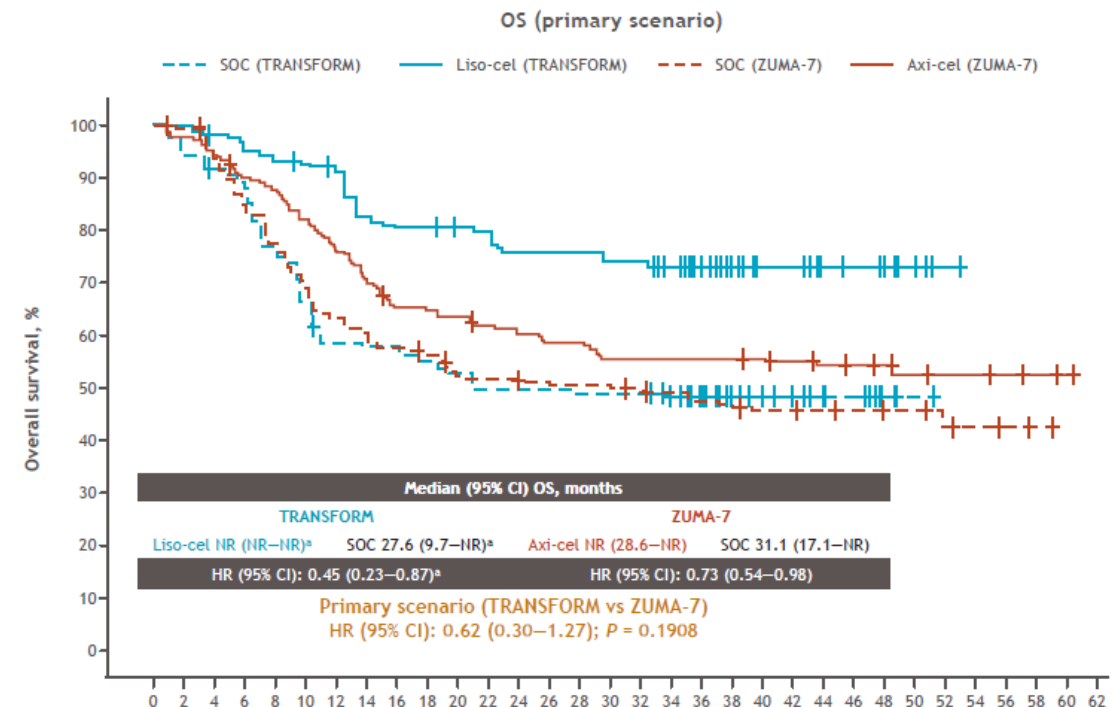
Matching-adjusted indirect comparison of Axi-cel vs Liso-cel in LBCL

TRANSFORM & ZUMA-7

- liso-cel and axi-cel had no statistically significant differences in efficacy (ORR, CR rate, EFS, PFS, OS)
- Liso-cel had fewer $\geq$ Gr 3 serious TEAEs and events of CRS and NEs (any grade and $\geq$ Gr 3) than axi-cel



^aBy laboratory assessment.
OR, odds ratio.



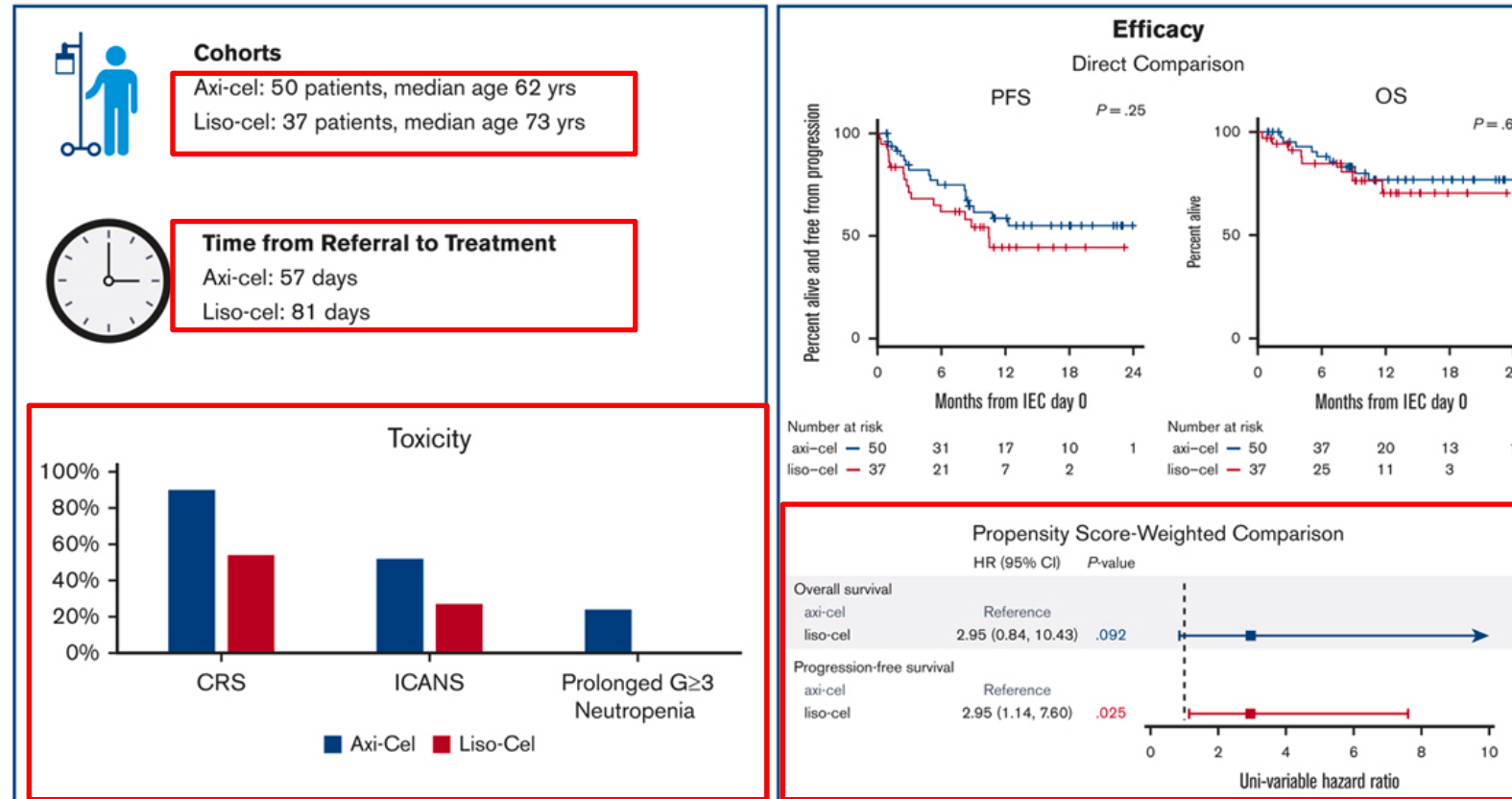
Abramson JS et al. ASH 2024 Poster 3130

Leuk Lymphoma 2025; 2025 Jul 24:1-14. doi: 10.1080/10428194.2025.2532674.

Real-world comparison of commercial-use Axi-cel vs Liso-cel in LBCL

□ Single center retrospective analysis (DFCI)

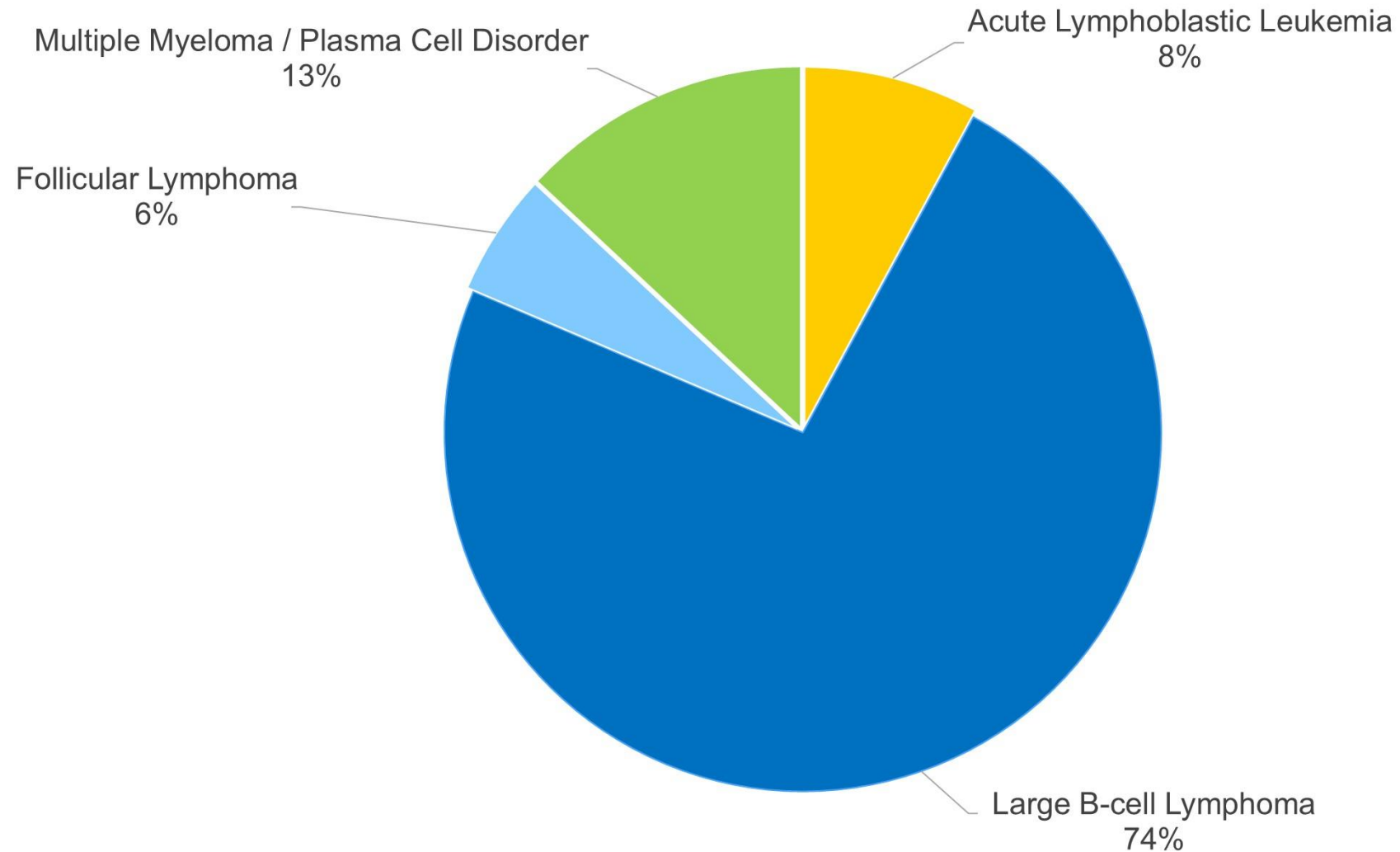
- When accounting for differences in risk factors, axi-cel was associated with superior PFS.
- Longer time from apheresis to treatment with liso-cel and more frequent CRS, ICANS, and prolonged neutropenia with axi-cel.



Contents

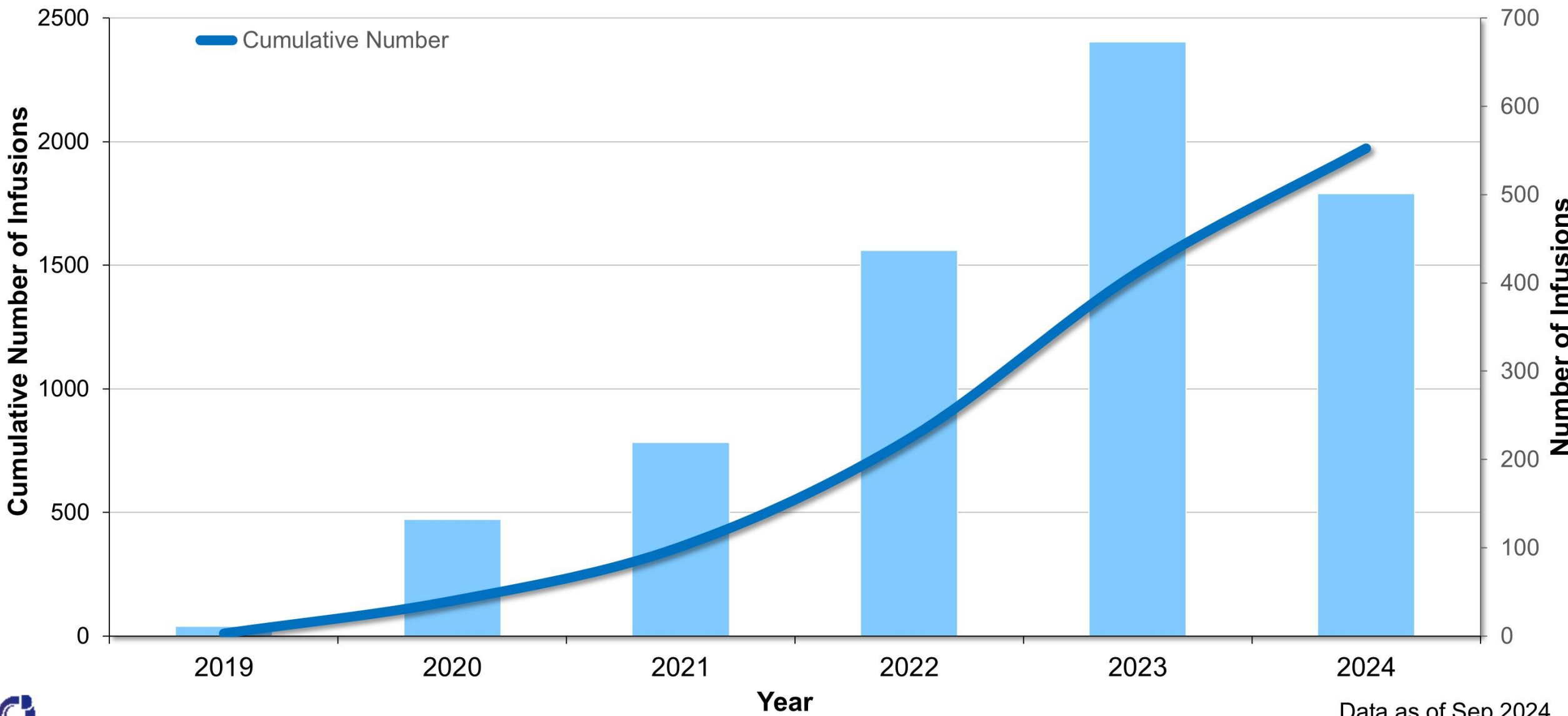
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CAR-T cell Indications



Aggregated data from 2019 to 2024

Number of CAR-T cell Infusions



Data as of Sep 2024

CD19-directed CAR-T therapies approved in Japan

Indications for LBCL

	Kymriah (Tisa-cel)	Yescarta (Axi-cel)	Breyanzi (Liso-cel)
◆ Approval for LBCL	Mar 2019	Jan 2021 (3L+) Dec 2022 (2L)	Mar 2021 (3L+) Dec 2022 (2L)
◆ Indication			
• Treatment line			
3L+	✓	✓	✓
2L	-	SCT-eligible, CR<1y Refractory to 1L	SCT-eligible, CR<1y SCT-ineligible
• Special conditions			
Active SCNSL	-	-	✓
History of allo SCT	-	-	✓

Certification of CAR-T sites and individual patients

- Site accreditation by the pharmaceutical company for CAR-T therapy
- No individual pre-authorization process by health insurance for CAR-T in Japan
- Optimal Use Guidelines (Ministry of Health, Labour and Welfare)
 - Patient eligibility criteria
 - Approved institutions
 - Physician qualifications



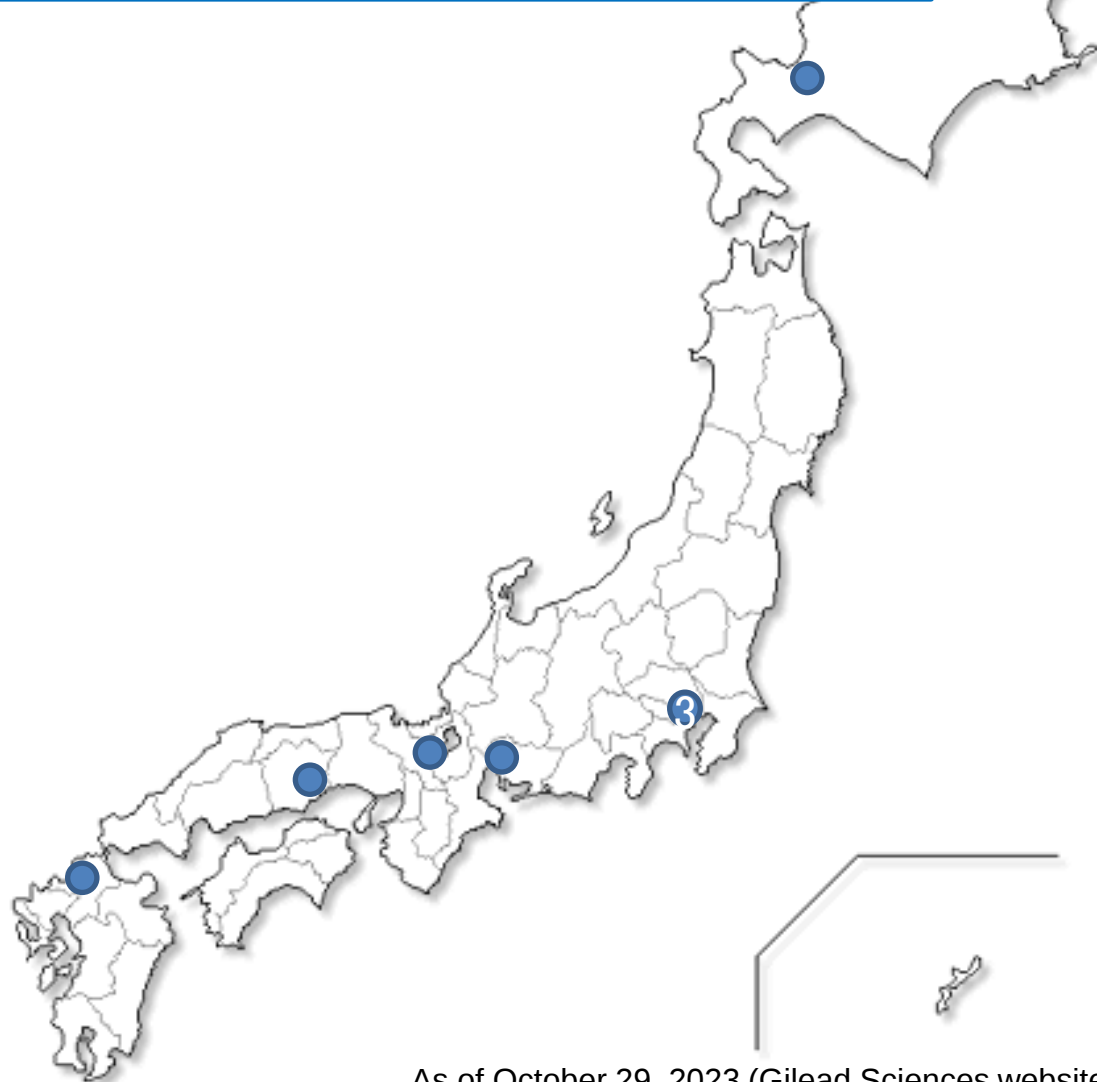
<https://www.pmda.go.jp/files/000270020.pdf>

List price of Yescarta, Breyanzi, Kymriah:
32,647,761 JPY = 226,700 USD

Rapid Expansion of Yescarta Treatment Centers in Japan

Oct 2023

Yescarta-accredited centers: 8 across Japan

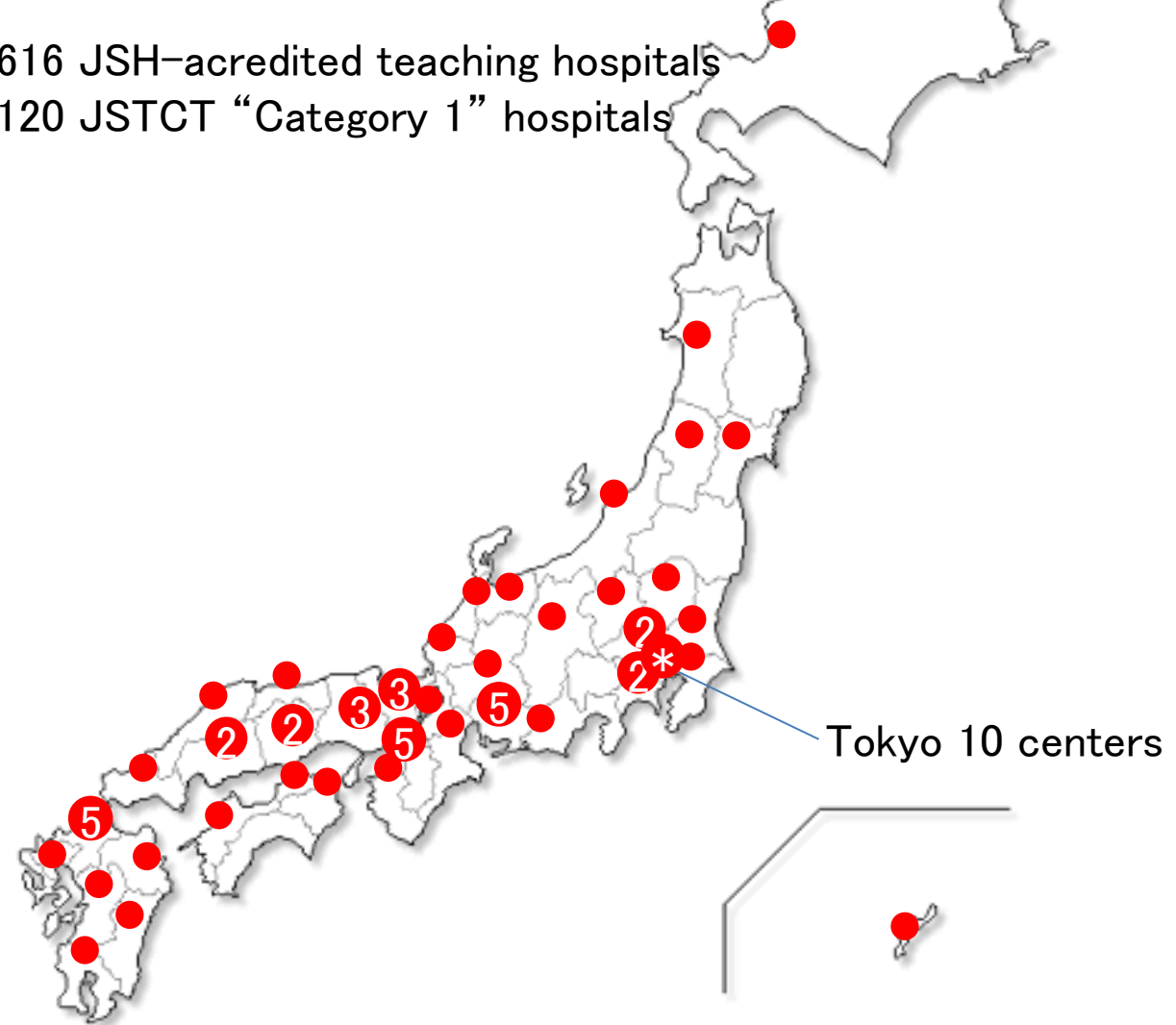


As of October 29, 2023 (Gilead Sciences website)

Aug 2025

Yescarta-accredited centers: 69 across Japan

616 JSH-accredited teaching hospitals
120 JSTCT “Category 1” hospitals



As of May 29, 2025 (Gilead Sciences website)

Clinical Outcomes of Commercial CAR-T at NCCH

		Axi-cel (n=43)	Liso-cel (N=56)
Leukapheresis		Apr 2023-Dec 2024	Oct 2021-Oct 2024
Age, median (range)		61 (20-74)	66.5 (18-77)
Female, n(%)		25 (58.1)	24 (42.9)
ECOG-PS 0/1, n(%)		29 (67)/14 (33)	55 (98.2)
Lines of previous therapy, median (range)		1 (1-4)	2 (1-7)
- Second line therapy, n(%)		25 (58)	14 (25)
Histologic subtype	DLBCL, NOS/Transformed FL HGBCL [‡] /PMBCL	22 (53)/5(12) 11 (26)/5(12)	44 (78.6) 5 (8.8)/7 (12.2)
LDH level (U/L) > UNL at the time of apheresis, n(%)		21 (49)	28 (50)
Received bridging therapy, n(%)		37 (86)	50 (89.3)
- Response before infusion, n(%)	CR/PR	10 (23)/18 (42)	46 (82.1)
	SD/PD	5 (12)/10 (23)	10 (17.9)
Primary refractory to initial therapy, n(%)		19 (44)	31 (55.4)
Time from apheresis to infusion, median days (range)		34 (28-47)	45 (35-139)

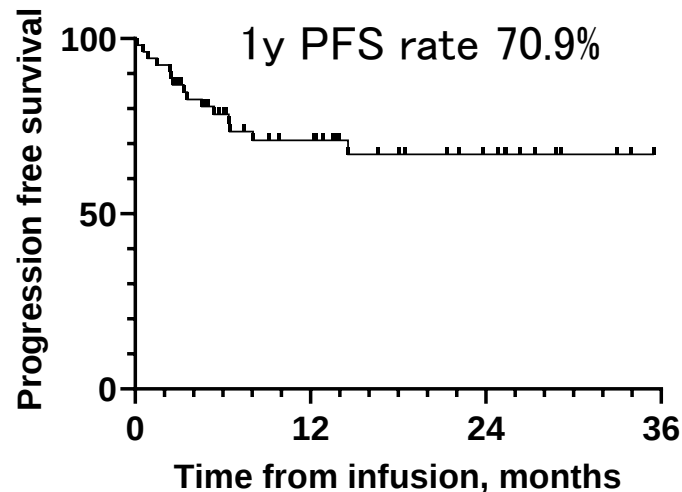
Clinical Outcomes of Commercial Liso-cel at NCCH

Leukapheresis Oct 2021-Oct 2024

● Efficacy evaluable patients (n=53)

	Best response	Ongoing response	
		At 3 months	At 6 months
ORR; n (%)	44 (83.0)	43 (81.1)	29 (54.7)
CR; n (%)	43 (81.1)	39 (73.6)	28 (52.8)
PR; n (%)	1 (1.9)	4 (7.5)	1 (1.9)

Median follow up duration: 12.4 months



● Safety evaluable patients (n=56)

CRS Any Grade; n (%)	44 (78.6)
Grade1	29 (51.8)
Grade2	14 (25.0)
Grade3	1 (1.8)
Grade4	0 (0)
Use of tocilizumab; n (%)	25 (44.6)
Use of steroid; n (%)	6 (10.7)

ICANS; Any Grade n (%)	5 (8.9)
Grade1	2 (3.6)
Grade2	2 (3.6)
Grade3	1 (1.8)
Grade4	0 (0)
Use of tocilizumab; n (%)	0 (0)
Use of steroid; n (%)	3 (5.4)

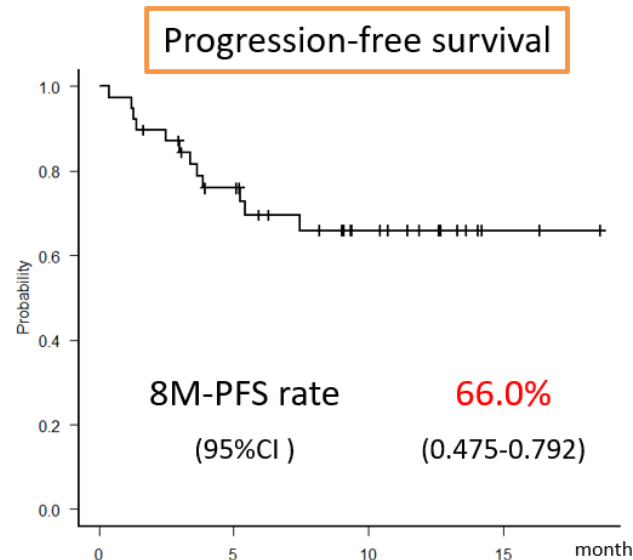
Clinical Outcomes of Commercial Axi-cel at NCCH

Leukapheresis Apr 2023-Oct 2024

● Efficacy evaluable patients (n=39)

	Best response	Ongoing response	
		At 3 months	At 6 months
ORR; n (%)	34 (87)	30 (77)	21 (54)
CR; n (%)	28 (72)	28 (72)	21 (54)
PR; n (%)	6 (15)	2 (5)	0

Median follow up duration: 8.7 months



● Safety evaluable patients (n=43)

CRS Any Grade; n (%)	41 (95)
Grade1	14 (33)
Grade2	21 (49)
Grade3	3 (7)
Grade4	3 (7)
Use of tocilizumab; n (%)	35 (81)
Use of steroid; n (%)	36 (84)

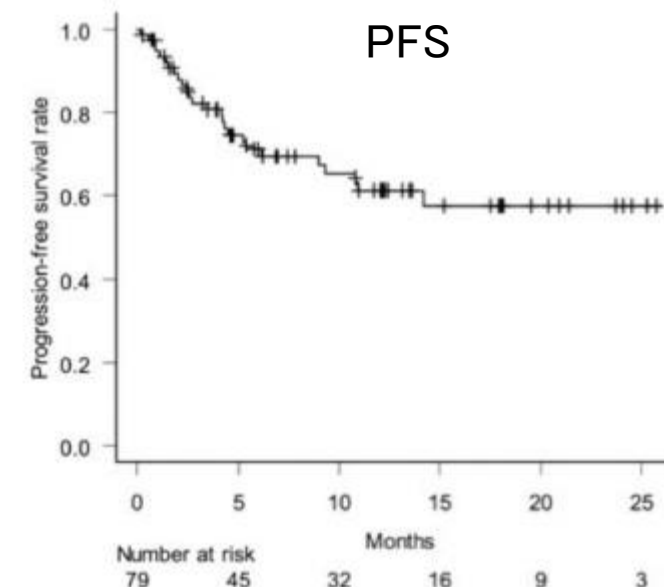
ICANS; Any Grade n (%)	13 (30)
Grade1	5 (12)
Grade2	3 (7)
Grade3	1 (2)
Grade4	4 (9)
Use of tocilizumab; n (%)	0 (0)
Use of steroid; n (%)	13 (30)

Real-World Data of Liso-cel for LBCL in Japan

JSCT-CART23 Study

		Liso-cel (N=160)
Registered from 17 centers		Mar 2021-Sep 2024
Treatment line 3L+/2L		107/53
Data available		N=79
Age, median (range)		66 (22-78)
Lines of previous therapy, median (range)		3
≥3		60.8%
Histologic subtype	DLBCL	55.7%
	Transformed FL	25.3%
	PMBCL	12.7%
	HGBCL	5.1%
Received bridging therapy, n(%)		96.2%
- Response before infusion, n(%)	ORR	49.3%
	SD/PD	26.6%
Time from apheresis to infusion, median days (range)		56 (40-156)

ORR	79.7%
CR rate	62.0%
CRS any grade	77.2%
grade ≥3	1.3%
ICANS any grade	12.7%
grade ≥3	8.9%



Take Home Messages

- CAR-T cell therapy has transformed the treatment of relapsed/refractory DLBCL and is potentially curative for a subset of patients.
- Comparative data highlight differences among products: axi-cel shows higher efficacy but also higher toxicity, whereas liso-cel demonstrates a more favorable safety profile.
- In Japan, approvals are largely consistent with the US and Europe; notably, liso-cel has broader indications, including SCT-ineligible second-line patients and secondary CNS lymphoma.
- CAR-T use in Japan is rapidly expanding, with ~900 infusions estimated in 2024 and over 1,000 projected for 2025, supported by an increasing number of certified centers and registry data confirming real-world effectiveness and safety.

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