Clinical Outcomes of Lisocabtagene Maraleucel in Younger Patients With Relapsed or Refractory Large B-Cell Lymphoma

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Introduction

- The autologous, CD19-directed CAR T cell product, lisocabtagene maraleucel (liso-cel), has demonstrated consistent efficacy in a broad population of patients with B-cell malignancies, including R/R large B-cell lymphoma (LBCL)[1–7]
- While liso-cel can be used to treat a broad population of patients based on its favorable safety profile, understanding outcomes of liso-cel treatment in younger patients remains an area of interest

Objective

- To describe real-world effectiveness and safety outcomes for patients < 50 years of age with R/R LBCL who received liso-cel in the real-world or clinical trial setting

Methods

Table 1. Study populations and assessments

Real-world setting	Clinical trial setting
Liso-cel—treated patients with R/R LBCL who: • Received commercial liso-cel in the real-world setting in the United States as second-line or later treatment • Had ≥ 1 assessment for effectiveness and safety after infusion in the Center for International Blood and Marrow Transplant Research (CIBMTR) Registry between 02/2021 and 05/2025	Liso-cel—treated patients with R/R LBCL from the following clinical trials: • TRANSCEND NHL 001 (NCT02631044; data cutoff, 05/16/2024) • OUTREACH (NCT03744676; data cutoff, 09/22/2023) • TRANSCEND WORLD (NCT03484702; data cutoff, 12/15/2023) • TRANSFORM (NCT03575351; data cutoff, 10/13/2023)
Effectiveness assessments: • ORR, CR rate, DOR, PFS, and OS	Efficacy assessments: • ORR, CR rate, DOR, PFS, and OS
Safety assessments: • AEs of special interest (CRS, ICANS, clinically significant infections,[a] second primary malignancies, cytopenias) • NRM rates	Safety assessments: • AEs of special interest (CRS, NEs, grade ≥ 3 infections, second primary malignancies, cytopenias) • NRM rates

CRS, cytokine release syndrome; DOR, duration of response; ICANS, immune effector cell–associated neurotoxicity syndrome; NE, neurological events; NRM, nonrelapse mortality
[a]Any infection requiring treatment with certain exceptions as noted in the CIBMTR Forms Instruction Manual[8]

- All results are descriptive

Results

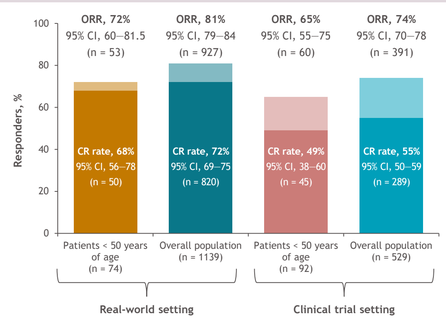
Table 2. Demographics and baseline characteristics

	Real-world setting		Clinical trial setting	
	Patients < 50 years of age (n = 74)	Overall population (n = 1144)	Patients < 50 years of age (n = 92)	Overall population (n = 529)
Median (range) age, y	41.7 (21.5–49.5)	71.3 (21.5–91.2)	41.0 (18.0–49.0)	63.0 (18.0–86.0)
Male, n (%)	46 (62)	683 (60)	55 (60)	326 (62)
ECOG PS, n (%)[a]				
0–1	62 (84)	1006 (88)	90 (98)	515 (97)
≥ 2	7 (9)	84 (7)	2 (2)	14 (3)
Not reported/unknown	5 (7)	54 (5)	0	0
Had ≥ 1 comorbidity,[b] n (%)	45 (61)[c]	618 (54)[d]	NA	NA
Elevated LDH preinfusion,[e] n (%)	35 (47)[f]	459 (40)[g]	21 (23)	106 (20)
Disease indication/histology, n (%)				
DLBCL	54 (73)	927 (81)	50 (54)	337 (64)
DLBCL NOS	13 (18)	172 (15)	29 (32)	187 (35)
DLBCL transformed	16 (22)	259 (23)	10 (11)	91 (17)
DLBCL or HGBCL	0	0	10 (11)	79 (15)
HGBCL	7 (9)	161 (14)	9 (10)	72 (14)
PMBCL	7 (9)	8 (1)	19 (21)	23 (4)
FL3B	0	9 (1)	2 (2)	8 (2)
Other B-cell lymphoma	6 (8)	39 (3)	2 (2)	10 (2)
Relapsed disease, n (%)	12 (16)[h]	420 (37)[i]	16 (17)	115 (22)
Refractory disease, n (%)	57 (77)	707 (62)	76 (83)	414 (78)
Chemotherapy refractory disease, n (%)	NA	NA	24 (26)	145 (27)
Received prior HSCT, n (%)	12 (16)	130 (11)	19 (21)	124 (23)
Autologous	10 (14)	127 (11)	19 (21)	124 (23)
Allogeneic	2 (3)	8 (1)	0	0
Autologous and allogeneic	0	1 (< 1)	0	0
Not provided	0	4 (< 1)	0	0
Median (range) number of lines of prior systemic therapy[j]	3 (1–13)	3 (1–16)	2 (1–9)	2 (0–9)
Secondary CNS lymphoma, n (%)	10 (14)	51 (4)	2 (2)	11 (2)
Received bridging therapy, n (%)	44 (59)[k]	710 (62)[l]	61 (66)	331 (63)
Outpatient treatment, n (%)	27 (36)	381 (33)	NA	NA

[a]At infusion for patients treated in the real-world setting and at screening for patients treated in clinical trials; [b]Based on criteria from the Hematopoietic Cell Transplantation-Comorbidity Index; [c]Comorbidity data were NA for 18 patients; [d]Comorbidity data were NA for 265 patients; [e]Elevated LDH was defined as > ULN in the real-world setting and ≥ 500 U/L in clinical trials; [f]LDH data preinfusion were NA for 7 patients; [g]LDH data preinfusion were NA for 108 patients; [h]Relapsed versus refractory disease status data were NA for 5 patients; [i]Relapsed versus refractory disease status data were NA for 17 patients; [j]Prior lines of therapy included bridging therapies for patients treated in the real-world setting; [k]History of bridging therapy was NA for 2 patients; [l]History of bridging therapy was NA for 32 patients.
FL3B, follicular lymphoma grade 3B; HGBCL, high grade B-cell lymphoma; NA, not available; NOS, not otherwise specified; PMBCL, primary mediastinal large B-cell lymphoma.

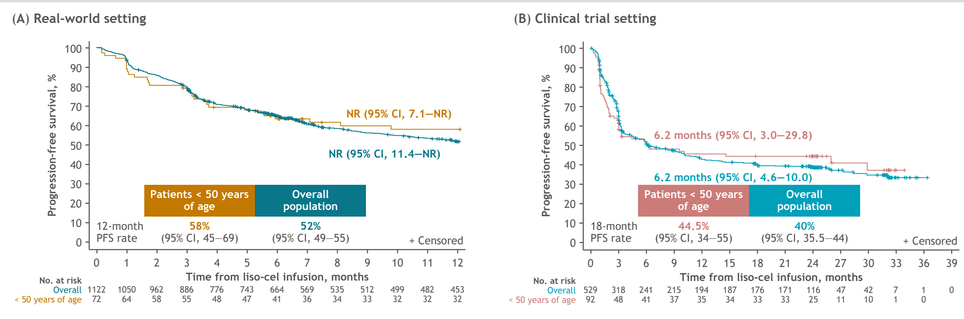
In younger patients with R/R LBCL < 50 years of age from real-world and clinical trial settings, responses were deep and durable after treatment with liso-cel, consistent with outcomes in the overall populations

Figure 1. Response rates[a]



Response assessments for patients treated with liso-cel in the real-world setting were as reported by treating physicians to the CIBMTR Registry; response assessments for patients in clinical trials were by independent review committee assessment based on Lugano 2014 criteria.[8]
[a]Patients with best overall response "not assessed" or "not provided" (missing) were considered as nonresponders when relapse, progression, or death was reported for these patients ≤ 90 days after CAR T cell infusion. Otherwise, they were not considered for the computation of ORR/CR rate.

Figure 2. Progression-free survival



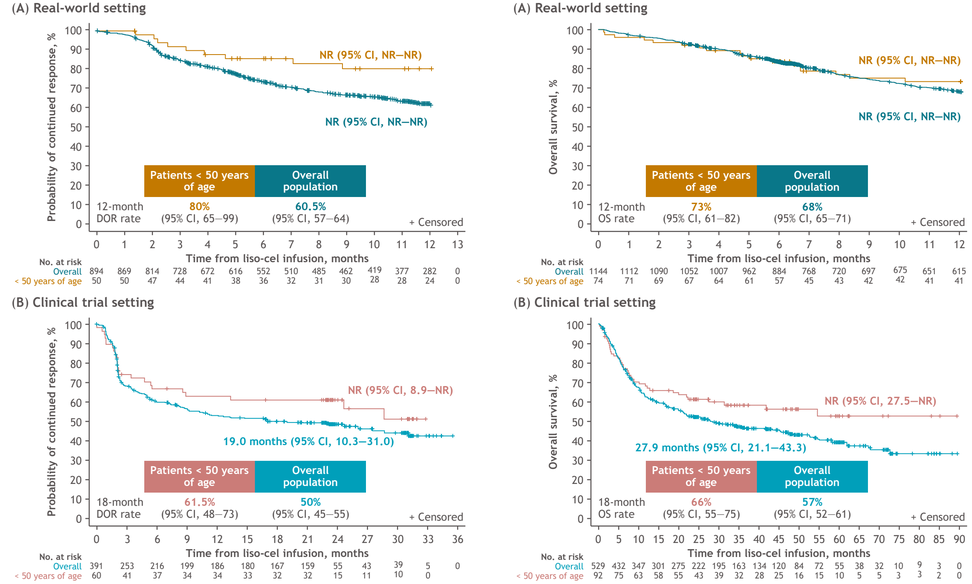
Data in figures are median (95% CI). PFS was defined as the time from date of infusion to relapse, progression, or death for the real-world setting, and as the time from liso-cel infusion to disease progression or death from any cause for clinical trials.
NR, not reached.

- Of the 1144 patients in the real-world overall population, 74 (6%) were < 50 years of age at infusion, and of the 529 patients in the clinical trial overall population, 92 (17%) were < 50 years of age at infusion
- In the real-world cohort, patients < 50 years of age had a lower prevalence of DLBCL and a higher prevalence of PMBCL, refractory disease, elevated LDH, and comorbidities, but similar ECOG PS, number of prior lines of therapy, secondary CNS lymphoma, and receipt of bridging therapy compared with the overall population (**Table 2**)
- In the clinical trials cohort, patients < 50 years of age had a higher prevalence of PMBCL and a lower prevalence of HGBCL than the overall population but similar ECOG PS, number of prior lines of therapy, and proportions with refractory disease (**Table 2**)
- In real-world patients < 50 years of age, median follow-up was 14.8 months (95% CI, 12.7—24.0); median follow-up, 13.0 months [95% CI, 12.9—13.2] in the overall population) and in clinical trial patients < 50 years of age, median follow-up was 42.0 months (95% CI, 32.9—48.3; median follow-up, 46.0 months [95% CI, 38.6—48.0] in the overall population)

Table 3. Time-to-event outcome rates in the real-world and clinical trial settings

	Real-world setting		Clinical trial setting	
	Patients < 50 years of age (n = 74)	Overall population (n = 1144)	Patients < 50 years of age (n = 92)	Overall population (n = 529)
PFS rates, % (95% CI)				
12-month rate	58 (45–69)	52 (49–55)	46 (35–56)	43 (38–47)
18-month rate	NA	NA	44.5 (34–55)	40 (35.5–44)
DOR rates, % (95% CI)				
12-month rate	80 (65–89)	60.5 (57–64)	63 (49.5–74)	53 (48–58)
18-month rate	NA	NA	61.5 (48–73)	50 (45–55)
OS rates, % (95% CI)				
12-month rate	73 (61–82)	68 (65–71)	68 (57–77)	62.5 (58–66.5)
18-month rate	NA	NA	66 (55–75)	57 (52–61)

Figure 3. Duration of response



Data in figures are median (95% CI). DOR was defined as time from initial response (continued CR [patients already in CR at the start of the preparative regimen]/CR/PR) to relapse, progression, or death for patients treated in the real-world setting and as time from first response (CR/PR) after liso-cel infusion to disease progression, or death (TRANSCEND NHL 001, OUTREACH, TRANSCEND WORLD, TRANSFORM) or additionally until start of new antineoplastic therapy due to efficacy concerns (TRANSFORM), whichever occurred first, in clinical trials.
[a]Patients with best overall response "not assessed" or "not provided" (missing) were considered as nonresponders when relapse, progression, or death was reported for these patients ≤ 90 days after CAR T cell infusion. Otherwise, they were not considered for the computation of ORR/CR rate.

- In real-world patients, median PFS was NR in both younger patients and the overall population, with similar 12-month rates (**Figure 2A, Table 3**)
- In clinical trial patients, median PFS was 6.2 months in both younger patients and the overall population, with similar 18-month rates (**Figure 2B, Table 3**)

Figure 4. Overall survival

Data in figures are median (95% CI). OS was defined as the time from infusion to death or last follow-up for the real-world setting, and as the time from liso-cel infusion to death from any cause for clinical trials.

- Median DOR was NR in both younger patient populations and was NR and 19.0 months in the overall real-world and clinical trials populations, respectively (**Figure 3**)
- OS outcomes were also similar in younger patients compared with the overall populations in both the real-world and clinical trial settings, with similar 12-month and 18-month OS rates, respectively (**Figure 4, Table 3**)

Table 4. AEs of special interest

	Real-world setting		Clinical trial setting[a]	
	Patients < 50 years of age (n = 74)	Overall population (n = 1144)	Patients < 50 years of age (n = 92)	Overall population (n = 529)
CRS, n (%)[b]	43 (58)	586 (51)	48 (52)	226 (43)
Grade 1	31 (42)	394 (34)	33 (36)	143 (27)
Grade 2	8 (11)	158 (14)	12 (13)	74 (14)
Grade 3	0	3 (< 1)	2 (2)	5 (1)
Grade 4	1 (1)	17 (1)	1 (1)	4 (1)
Grade 5	2 (3)	8 (1)	0	0
Not provided	1 (1)	6 (1)	0	0
ICANS/NEs, n (%)[c]	21 (28)	305 (27)	24 (26)	128 (24)
Grade 1	11 (15)	121 (11)	8 (9)	41 (8)
Grade 2	0	56 (5)	6 (7)	42 (8)
Grade 3	3 (4)	72 (6)	8 (9)	38 (7)
Grade 4	5 (7)	28 (2)	2 (2)	7 (1)
Grade 5	1 (1)	6 (1)	0	0
Under review	1 (1)	18 (2)	0	0
Clinically significant infections/ grade ≥ 3 infections, n (%)[d]	41 (55)	545 (48)	12 (13)	69 (13)
Second primary malignancy, n (%)	1 (1)	72 (6)	1 (1)	8 (2)
Prolonged cytopenia, n (%)[e]	8 (11)	144 (13)	29 (32)	198 (37)

[a]Includes treatment-emergent AEs, defined as AEs that started any time from liso-cel administration to within 90 days after infusion (TRANSCEND NHL 001, OUTREACH, TRANSCEND WORLD) and AEs occurring or worsening on or after the date of randomization and within 90 days after liso-cel infusion or start of new antineoplastic therapy, whichever occurs first as well as those occurring anytime thereafter suspected of being related to study treatment (TRANSFORM); [b]CRS was graded according to Lee 2014 criteria[10]; [c]For patients treated in the real-world setting, ICANS was graded according to the American Society for Transplantation and Cellular Therapy 2019 criteria,[11] and grade data reflect the maximum ICANS grade at 100 days; for clinical trials, NEs were defined as investigator-identified neurological AEs related to liso-cel; [d]For infections data, clinically significant infections, were reported in the CIBMTR Registry for patients treated in the real-world setting and grade ≥ 3 infections were reported for clinical trials; [e]Defined as grade 4 thrombocytopenia and/or neutropenia persistent at 30 days after liso-cel infusion for patients treated in the real-world setting and as grade ≥ 3 laboratory result of anemia, neutropenia, or thrombocytopenia not resolved at the Day 29 study visit after liso-cel infusion for clinical trials.

Table 5. Deaths and NRM rates

	Real-world setting		Clinical trial setting	
	Patients < 50 years of age (n = 74)	Overall population (n = 1144)	Patients < 50 years of age (n = 92)	Overall population (n = 529)
Deaths, n (%)	22 (30)	424 (37)	39 (42)	292 (55)
12-month incidence of NRM, % (95% CI)	NR	6 (5–8)	2 (0.5–8)	4 (2–6)
12-month cumulative incidence of relapse or progression, % (95% CI)	42 (30–54)	42 (39–45)	52 (41–62)	54 (49–58)

In the real-world setting, NRM was defined as the cumulative incidence of death without prior relapse; for clinical trials, NRM was defined as the cumulative incidence of death without prior progression, while patients remain on study treatment and before starting any new anticancer therapy.

- Overall rates of CRS and ICANS/NEs were consistent across real-world and clinical trial treatment settings, with low rates of grade ≥ 3 events in younger patients and the overall populations in both settings (**Table 4**)
- Incidences of grade ≥ 3 cytopenias and serious infections were similar in younger patients and the overall populations within both treatment settings; however, comparisons between settings are limited by differences in reporting and definitions for these AEs
- Second primary malignancies were uncommon in both real-world and clinical trial patients, regardless of age
- Among real-world patients < 50 years of age, 22 (30%) died, most commonly due to PD (n = 19/22 [86%]); 12-month NRM rate was NR (**Table 5**)
- Among clinical trial patients < 50 years of age, 39 (42%) died, most commonly due to PD (29/39 [74%]); 2 (5%) patients died without prior relapse due to COVID-19 (3%) and unknown cause (3%); 12-month NRM rate was 2% (95% CI, 0.5–8)

Conclusions

- Efficacy outcomes were similar to the overall population in both settings despite some high-risk disease features being more prevalent in the younger populations
- Responses were deep and durable in younger patients from the real-world and clinical trial settings, with 12-month and 18-month DOR rates of 80% and 61.5%, respectively
- Rates of CRS and ICANS/NEs were similar in both settings, and most events were low grade
- These data show that liso-cel maintains strong efficacy and a favorable safety profile in younger patients in the real-world setting, consistent with clinical trial findings, supporting its use in all eligible patients, including in outpatient care

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