Lisocabtagene Maraleucel in Relapsed or Refractory Follicular Lymphoma (TRANSCEND FL): Impact of Prior Lines of Therapy, Bendamustine Exposure, and Disease Progression ≤ 24 Months of Initial Systemic Therapy

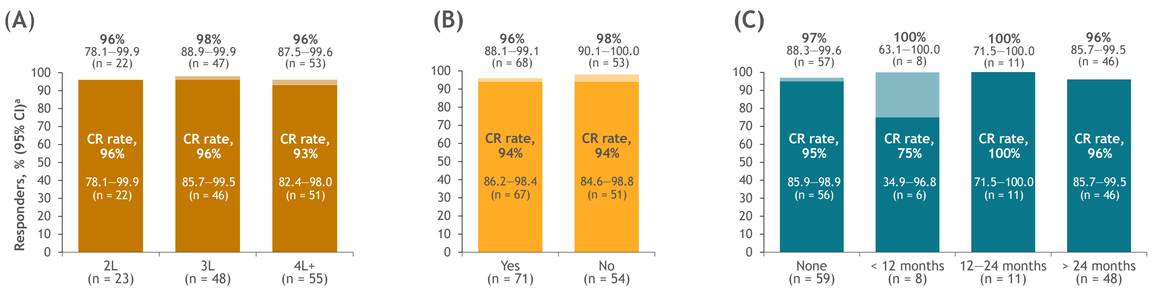
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Liso-cel demonstrated high response rates across a broad population of patients with R/R FL from TRANSCEND FL

Figure 2. ORR and CR rate per IRC by (A) number of prior LOTs, (B) POD24 status (2L+), and (C) prior bendamustine exposure before leukapheresis (2L+)



[a]Two-sided 95% CI based on exact Clopper-Pearson method.

- ORR was 96%—100% across all subgroups
- CR rate was similar across prior LOTs (**Figure 2A**) and POD24 subgroups (**Figure 2B**), but lower in patients with prior bendamustine exposure < 12 months (75%) versus other bendamustine subgroups (≥ 95%) (**Figure 2C**), though sample size was small in the < 12-month and 12- to 24-month subgroups

Table 2. Time-to-event efficacy outcomes by subgroup

	Number of prior LOTs			POD24 (2L+)[a]		Prior bendamustine exposure before leukapheresis (2L+)				Total 2L+ population (N = 126)
	2L (n = 23)	3L (n = 48)	4L+ (n = 55)	Yes (n = 71)	No (n = 54)	None (n = 59)	< 12 mo (n = 8)	12–24 mo (n = 11)	> 24 mo (n = 48)	
Median DOR, months[b]	NR	NR	30.9	30.9	NR	NR	NR	NR	NR	NR
24-month DOR rate, %	86	76	73	70	87	77	50	72	82	77
Median (95% CI) PFS, months[b]	NR	NR	31.8	31.8	NR	31.8	NR	NR	NR	NR
24-month PFS rate, %	83	75	71	67	85	74	50	72	79	74
24-month OS rate, %	96	89	87	86	94	93	71	91	88	90
Free of next treatment at 24-month rate, %	91	85	76	78	89	85	58	91	81	82

Median OS and TTNT were NR across all subgroups.
[a]POD24 status was not estimable for 1 patient; [b]Medians were estimated from Kaplan-Meier product-limit estimates.
NR, not reached.

- A trend toward better outcomes was observed with liso-cel in earlier versus later (4L+) LOTs (**Table 2; see also Table S2 using QR code**)
- The 24-month rates were generally better for patients without POD24 but still clinically meaningful in patients with POD24
- Outcomes were consistently high for all prior bendamustine subgroups except for the < 12-month subgroup where a trend for lower 24-month rates was observed; results should be interpreted with caution due to small sample size (n = 8)

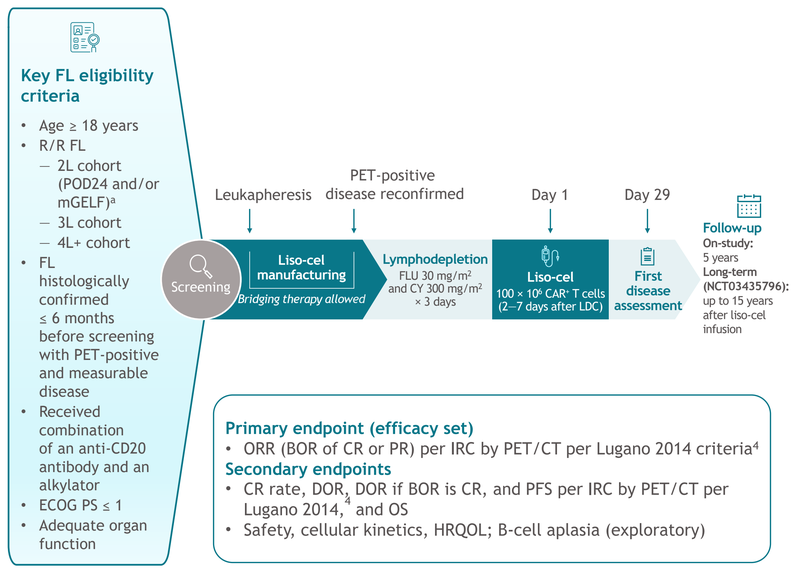
Background

- In the primary analysis of the TRANSCEND FL study (NCT04245839; data cutoff date of January 10, 2024), lisocabtagene maraleucel (liso-cel) showed an ORR of 97%, CR rate of 94%, and favorable safety in patients with third-line (3L) or later (3L+) R/R FL[1]
  - In patients with second-line (2L), high-risk FL (progression of disease ≤ 24 months [POD24] from initial immunochemotherapy and/or meeting ≥ 1 modified Groupe d'Etude des Lymphomes Folliculaires [mGELF] criteria), ORR was 96% and all responders achieved CR[1]
- In patients with R/R FL, increasing lines of therapy (LOT), POD24 from initial immunochemotherapy, and recent exposure to bendamustine before CAR T cell therapy may impact patient outcomes[2,3]
- Here, we report post hoc analyses of efficacy and safety outcomes in patients with R/R FL from TRANSCEND FL by number of prior LOTs, POD24 status from first-line therapy with an anti-CD20 antibody and an alkylator, and prior bendamustine exposure before leukapheresis with a median (range) on-study follow-up of 29.7 months (0.3—39.6)
  - Cellular kinetic outcomes were also assessed in patient subgroups by prior bendamustine exposure before leukapheresis

Methods

Study design

Figure 1. TRANSCEND FL: phase 2, open-label, multicenter, multicohort study



[a]POD24 was defined as progression within 24 months of diagnosis after treatment with an anti-CD20 antibody and an alkylating agent within the first 6 months of initial FL diagnosis. Patients who did not meet criteria of POD24 had to meet ≥ 1 of the mGELF criteria (symptoms attributable to FL; threatened end-organ function, or cytopenia secondary to lymphoma or bulky disease [single mass > 7 cm, or ≥ 3 masses > 3 cm]; splenomegaly; or steady progression over ≥ 6 months).
4L+, fourth line or later; BOR, best overall response; CY, cyclophosphamide; DOR, duration of response; FLU, fludarabine; HRQOL, health-related quality of life; IRC, independent review committee; LDC, lymphodepleting chemotherapy.

- TRANSCEND FL enrolled patients who were ≥ 18 years of age with 2L or later (2L+) FL (**Figure 1**)
- All patients received ≥ 1 prior lines of combination systemic therapy with an anti-CD20 antibody and an alkylator; patients with 2L FL met POD24 criteria and/or ≥ 1 mGELF criteria
- Post hoc subgroup analyses were performed by number of prior LOTs (2L, 3L, 4L+), POD24 status (yes, no), and prior bendamustine exposure (no prior bendamustine or < 12 months, 12—24 months, or > 24 months before leukapheresis)
- Outcomes included ORR, CR rate, DOR, and PFS (all by IRC), OS, time to next treatment (TTNT), and safety; cellular kinetics were also assessed in the bendamustine subgroups

Results

Patients

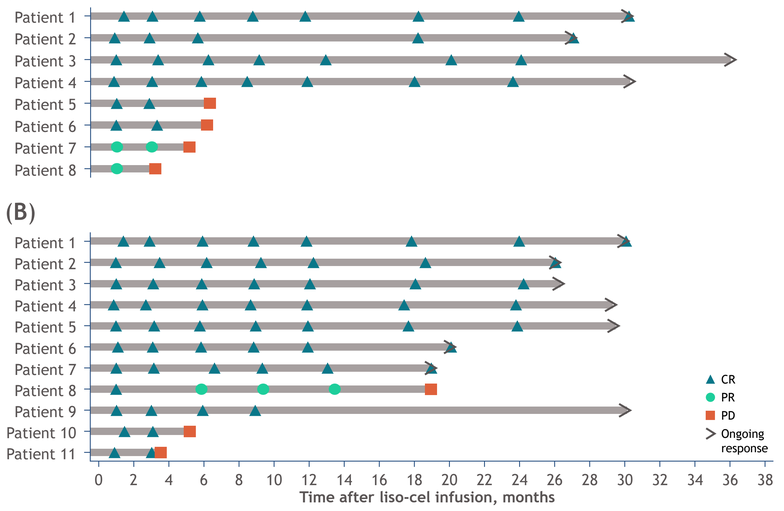
Table 1. Patient demographics and baseline characteristics

	Number of prior LOTs			POD24 (2L+)[a]		Prior bendamustine exposure before leukapheresis (2L+)				Total 2L+ population (N = 130)
	2L (n = 23)	3L (n = 48)	4L+ (n = 59)	Yes (n = 73)	No (n = 56)	None (n = 59)	< 12 mo (n = 11)	12—24 mo (n = 11)	> 24 mo (n = 49)	
Median age, y	53	60	64	59	62	60	56	66	61	60
FLIPI at screening, n (%)										
Low risk (0—1)	12 (52)	3 (6)	9 (15)	16 (22)	8 (14)	14 (24)	3 (27)	1 (9)	6 (12)	24 (18)
Intermediate risk (2)	4 (17)	20 (42)	14 (24)	19 (26)	19 (34)	20 (34)	2 (18)	2 (18)	14 (29)	38 (29)
High risk (3—5)	7 (30)	25 (52)	36 (61)	38 (52)	29 (52)	25 (42)	6 (55)	8 (73)	29 (59)	68 (52)
Double refractory (anti-CD20 + alkylator), n (%)	11 (48)	33 (69)	36 (61)	55 (75)	24 (43)	32 (54)	7 (64)	8 (73)	33 (67)	80 (62)
POD24 from initial chemoimmunotherapy, n (%)	15 (65)	31 (65)	27 (46)	73 (100)	0	34 (58)	7 (64)	10 (91)	22 (45)	73 (56)

[a]POD24 status was not estimable for 1 patient.
FLIPI, Follicular Lymphoma International Prognostic Index.

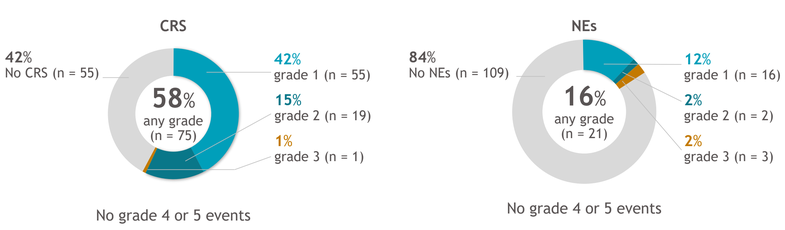
- Most patients had double-refractory disease or POD24 from initial chemoimmunotherapy (**Table 1**)
- There were no major differences in baseline characteristics across subgroups (**see Table S1 using QR code**)

Figure 3. Swimmer plots of response in patients with prior bendamustine exposure (A) < 12 months before leukapheresis (n = 8) and (B) 12—24 months before leukapheresis (n = 11)



- Liso-cel showed deep and durable responses in patients with more recent bendamustine exposure, including those with exposure < 12 months before leukapheresis (**Figure 3**)
- No apparent differences in liso-cel cellular kinetics or persistence were observed in the prior bendamustine subgroups (**see Figure S1, Figure S2, and Table S3 using QR code**)

Figure 4. CRS and NEs in the total 2L+ population (N = 130)



CRS, cytokine release syndrome; NE, neurological event.

Table 3. AEs of special interest by subgroup

	Number of prior LOTs			POD24 (2L+)[a]		Prior bendamustine exposure before leukapheresis (2L+)				Total 2L+ population (N = 130)[b]
	2L (n = 23)	3L (n = 48)	4L+ (n = 59)	Yes (n = 73)	No (n = 56)	None (n = 59)	< 12 mo (n = 11)	12—24 mo (n = 11)	> 24 mo (n = 49)	
CRS, n (%)	12 (52)	28 (58)	35 (59)	41 (56)	33 (59)	36 (61)	5 (45)	7 (64)	27 (55)	75 (58)
Grade 1	7 (30)	20 (42)	28 (47)	29 (40)	26 (46)	28 (47)	2 (18)	5 (45)	20 (42)	55 (42)
Grade 2	5 (22)	8 (17)	6 (10)	12 (16)	6 (11)	7 (12)	3 (27)	2 (18)	6 (12.5)	19 (15)
Grade ≥ 3[c]	0	0	1 (2)	0	1 (2)	1 (2)	0	0	0	1 (1)
NE, n (%)	4 (17)	8 (17)	9 (15)	8 (11)	13 (23)	10 (17)	1 (9)	2 (18)	8 (16)	21 (16)
Grade 1	3 (13)	6 (12.5)	6 (10)	6 (8)	9 (16)	9 (15)	0	1 (9)	5 (10)	16 (12)
Grade 2	0	0	2 (3)	0	2 (4)	1 (2)	0	0	1 (2)	2 (2)
Grade ≥ 3[c]	1 (4)	1 (2)	1 (2)	2 (3)	1 (2)	0	1 (9)	1 (9)	1 (2)	3 (2)
SPM, n (%)[d]	2 (9)	3 (6)	4 (7)	3 (4)	6 (11)	4 (7)	2 (18)	0	3 (6)	9 (7)
Grade ≥ 3 infections, n (%)	1 (4)	6 (12.5)	6 (10)	10 (14)	3 (5)	5 (8)	2 (18)	1 (9)	5 (10)	13 (10)
Hypogammaglobulinemia, n/N (%)[e]										
Baseline	2/21 (10)	18/43 (42)	25/53 (47)	25/64 (39)	20/52 (38)	19/54 (35)	3/9 (33)	4/9 (44)	19/45 (42)	45/117 (38)
Day 365	8/20 (40)	19/41 (46)	31/47 (66)	29/56 (52)	29/51 (57)	25/53 (47)	4/7 (57)	6/8 (75)	23/40 (57.5)	58/108 (54)
Day 730	4/19 (21)	19/36 (53)	22/42 (52)	24/51 (47)	20/45 (44)	19/45 (42)	2/8 (25)	4/7 (57)	20/37 (54)	45/97 (46)

All percentages are rounded to whole numbers except those with ".5%".
[a]POD24 status was not estimable for 1 patient; [b]In the total 2L+ population, 100 (77%) patients experienced grade ≥ 3 treatment-emergent AEs; [c]All events were grade 3 with no grade 4 or 5 events reported; [d]Included events of acute myeloid leukemia (n = 2), rectal cancer (n = 1), colon adenocarcinoma (n = 1), malignant melanoma (n = 1), colorectal cancer (n = 1), mucoepidermoid carcinoma (n = 1), myelodysplastic syndrome (n = 1), and basal cell carcinoma (n = 1). No secondary T-cell malignancies were reported; [e]Percentages are calculated as the number of patients with IgG < 500 mg/dL over the number of patients with samples available for evaluation at each time point.
IgG, immunoglobulin G; SPM, second primary malignancy.

- Rates of CRS and NEs were consistent across subgroups with low rates of grade 3 and no grade 4 or 5 events in the total population (**Table 3; Figure 4**)
- The overall SPM rate was similar to the rate observed after non-CAR T cell therapies in R/R FL[5,6] (**Table 3**)
- While hypogammaglobulinemia was reported in 46% of patients at Day 730 (2 years), the overall rate of grade ≥ 3 infections in the total 2L+ population was low (10%)
- The overall proportion of patients with grade ≥ 3 cytopenia at Day 90 was low (18%) in the total 2L+ population, with recovery to grade ≤ 2 occurring by Day 365 after infusion for the vast majority of patients (**see Table S4 using QR code**)

Conclusions

- In TRANSCEND FL, liso-cel demonstrated meaningful clinical benefit across a broad population of patients with R/R FL, regardless of POD24 status and prior bendamustine exposure, with a trend towards better outcomes when used in earlier LOTs
  - Patients with more recent bendamustine exposure before leukapheresis (< 24 months) also experienced deep and durable responses with liso-cel
- Liso-cel showed a favorable benefit/risk profile in patients with R/R FL, with low rates of severe CRS and NEs across subgroups, and no new safety signals observed
- After a single infusion with liso-cel, patients with R/R FL benefited from high efficacy outcomes and a favorable safety profile regardless of baseline and disease characteristics
  - Results suggest that use of liso-cel in earlier versus later lines of treatment may lead to better patient outcomes in R/R FL, providing rationale for incorporation of liso-cel early in the FL treatment journey

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