Lisocabtagene Maraleucel in Patients With Relapsed or Refractory Marginal Zone Lymphoma in the Phase 2 TRANSCEND FL Study

CT-230

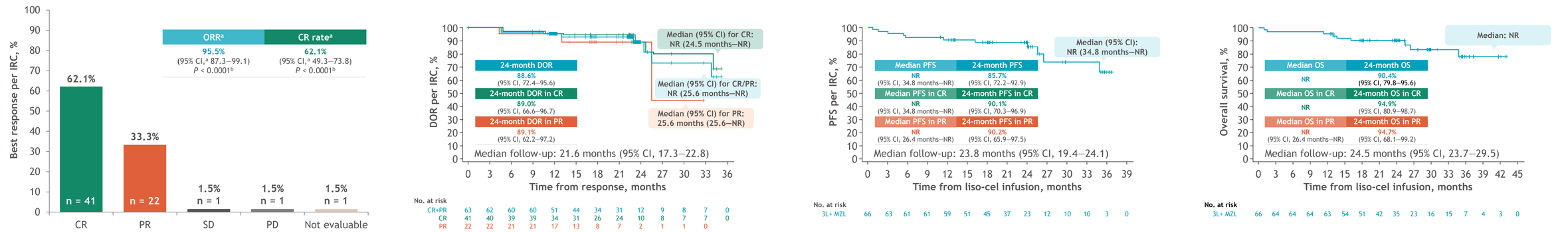
Oral presentation in XIII: Cellular Therapy
Saturday, September 6, 2025 | 9:30 AM–9:40 AM

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After a single administration of liso-cel, patients with 3L+ R/R MZL achieved deep and durable responses with high survival rates at 24 months
These clinically meaningful benefits, together with a manageable safety profile, underscore the potential role of liso-cel as a new standard of care in 3L+ R/R MZL

Figure 3. Efficacy outcomes (efficacy-evaluable set; n = 66)



[a]Two-sided 95% CI based on exact Clopper-Pearson method; [b]One-sided *P* value based on the exact binomial test (H_0 of ORR ≤ 50%; H_0 of CR rate ≤ 5%); [c]Median and 95% CIs of time-to-event estimates are based on the Kaplan-Meier method. Median follow-up and 95% CIs are based on reverse Kaplan-Meier method; [d]A total of 63 patients had CR or PR; 8 patients had events; 55 patients were censored. Among 5 patients with CR who had a DOR event, 3 died and 2 had PD. Among 3 patients with PR who had a DOR event, 2 died and 1 had PD; [e]Eleven patients had events and 55 patients were censored; [f]Nine patients had events and 57 patients were censored.
NR, not reached.

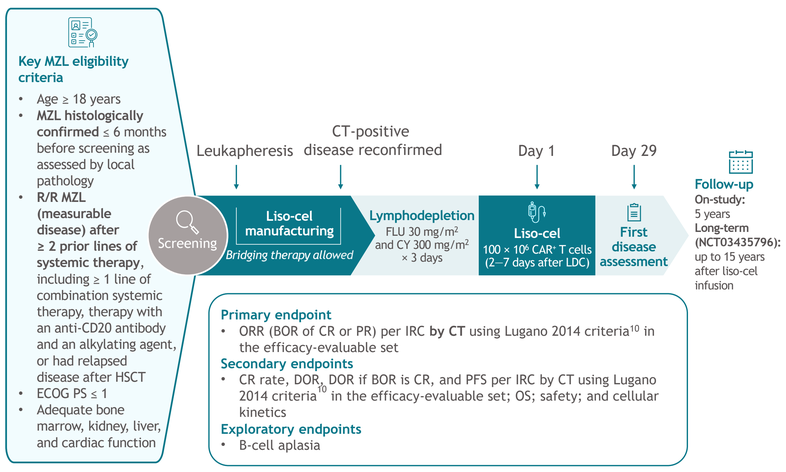
- The primary endpoint of ORR and secondary endpoint of CR rate per CT assessed by IRC were met (**Figure 3**)
- Among patients with PET-positive disease at baseline (n = 56), ORR was 98.2% and CR rate was 91.1%
  — ORR and CR rate per PET were derived from assessment of PET data reported by investigators

Background

- There is an unmet need for new effective treatments with a manageable safety profile for patients with R/R MZL after 2 prior lines of therapy who have limited treatment options, particularly those with progression of disease ≤ 24 months (POD24) and poor prognosis[1–3]
- Lisocabtagene maraleucel (liso-cel), an autologous, CD19-directed, 4-1BB CAR T cell product, has previously demonstrated deep and durable responses with a manageable safety profile in patients with B-cell malignancies[4–9]
- The MZL cohort of TRANSCEND FL (NCT04245839), an open-label, single-arm, multicohort, multicenter, phase 2 study, assessed the efficacy and safety of liso-cel in adults with third-line or later (3L+) R/R MZL
- Here, we report the primary analysis for the MZL cohort of TRANSCEND FL

Methods

Figure 1. TRANSCEND FL study design: MZL cohort

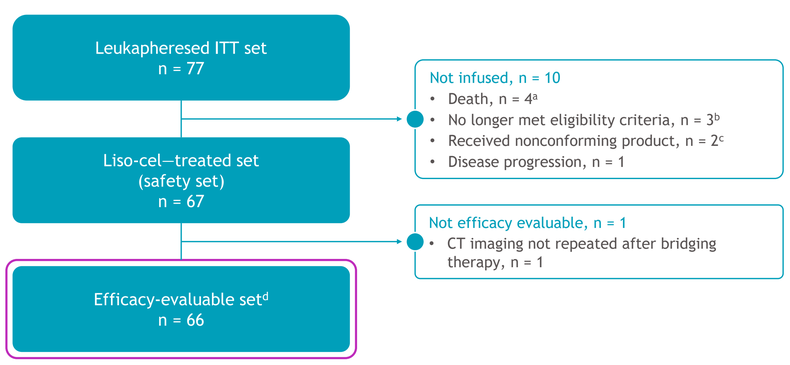


ClinicalTrials.gov identifier: NCT04245839.
BOR, best overall response; CY, cyclophosphamide; DOR, duration of response; FLU, fludarabine; IRC, independent review committee; LDC, lymphodepleting chemotherapy.

- In the MZL cohort of TRANSCEND FL (**Figure 1**), endpoints of ORR and CR rate were tested hierarchically in the following order at 1-sided α = 0.025 significance: ORR (null hypothesis [H_0]: ORR ≤ 50%) and then CR rate (H_0: CR rate ≤ 5%)

Results

Figure 2. Patient disposition and analysis sets



[a]Including 3 deaths due to disease progression and 1 due to suicide; for these 4 patients, death was the reason for study discontinuation; [b]Including 1 patient who did not have MZL histologically confirmed within 6 months of screening, 1 patient with a significant medical condition, and 1 patient with worsening ECOG PS; [c]Nonconforming product was defined as any product wherein one of the CD8 or CD4 cell components did not meet one of the requirements to be considered liso-cel, but could be considered appropriate for infusion; [d]Patients who received liso-cel and had positive disease present before liso-cel infusion per IRC.

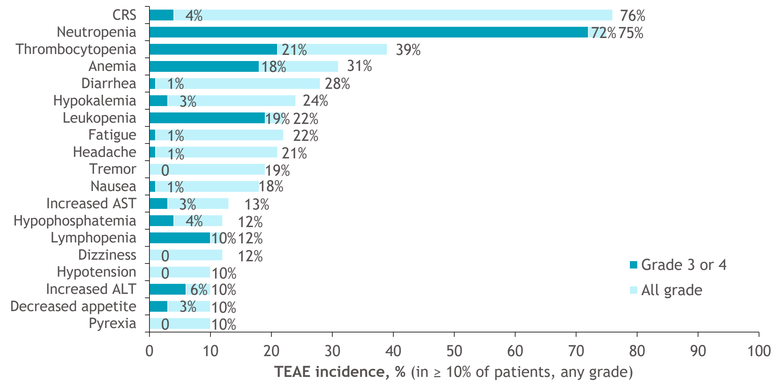
- A total of 13 (17%) patients were monitored in the outpatient setting (**Figure 2**)
- Median on-study follow-up was 24 months (range, 1–43)

Table 1. Patient demographics and baseline characteristics

	Liso-cel–treated set (n = 67)
Median (range) age, y	62 (37–81)
< 65 y	37 (55)
≥ 65 y to < 75 y	20 (30)
≥ 75 y	10 (15)
Male, n (%)	39 (58)
MZL subtype, n (%)	
Nodal	32 (48)
Splenic	18 (27)
Extranodal/Mucosa-associated lymphoid tissue	17 (25)
Ann Arbor stage at screening, n (%)	
Stage I/II	3 (4)/7 (10)
Stage III/IV	8 (12)/49 (73)
FL International Prognostic Index at screening, n (%)	
Low risk (0–1)	11 (16)
Intermediate risk (2)	13 (19)
High risk (3–5)	41 (61)
Not available	2 (3)
LDH > ULN before LDC, n (%)	35 (52)
Bone marrow involvement before infusion, n (%)	28 (42)
Bulky disease (modified GELF criteria),[a] n (%)	15 (22)
POD24,[b] n (%)	24 (36)
Median (range) prior lines of systemic therapy[c]	3 (2–12)
Received prior rituximab and lenalidomide, n (%)	15 (22)
Received prior bendamustine, n (%)	52 (78)
Received prior BTKi, n (%)	26 (39)
Prior HSCT,[d] n (%)	11 (16)
Refractory to last systemic therapy,[e] n (%)	26 (39)
Received bridging therapy,[f] n (%)	30 (45)

[a]Any mass > 7 cm, or ≥ 3 masses (each > 3 cm) based on investigator assessment; [b]Defined as progression of disease within 24 months from initiation of first-line chemoimmunotherapy; [c]Including chemotherapy, immunotherapy, and radioimmunotherapy; [d]All autologous; HSCT was grouped with a preceding chemotherapy regimen and any intervening conditioning regimen, including radiation, and considered together as 1 line of therapy. Prior anticancer surgeries were not considered as lines of prior therapies for nodal and extranodal MZL subtypes, but splenectomy was considered a line of therapy for splenic MZL subtype; [e]Refractory defined as a best response of SD or PD after prior therapy; [f]Including systemic treatment only (n = 26; most commonly rituximab [n = 15], CY [n = 9], and prednisone [n = 7]), radiation therapy only (n = 3), and both systemic treatment and radiation therapy (n = 1).
GELF, Groupe d'Etude des Lymphomes Folliculaires; SD, stable disease.

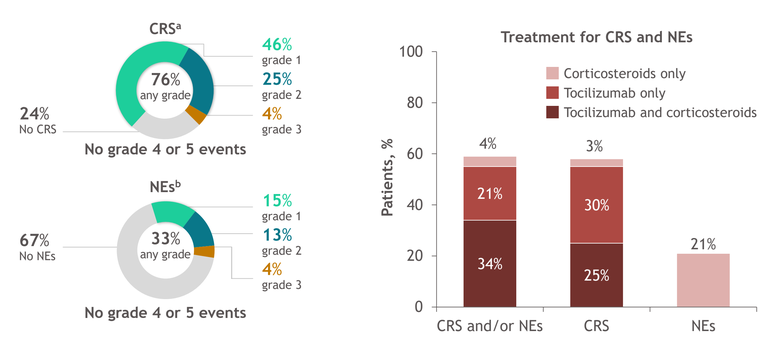
Figure 4. Most common (≥ 10%) TEAEs[a] (liso-cel–treated set, n = 67)



[a]TEAE period was defined as the time from initiation of liso-cel administration through and including study Day 90. AEs occurring after initiation of another anticancer treatment were not included.
CRS, cytokine release syndrome; TEAE, treatment-emergent adverse event.

- The most common any-grade TEAEs were CRS and cytopenias (**Figure 4**)
- Two grade 5 TEAEs occurred
  — T-cell lymphoma on Day 32. Liso-cel transgene testing and integration site analysis suggested that the T-cell lymphoma was not derived from CAR T cells
  — Neutropenic sepsis on Day 47

Figure 5. Cytokine release syndrome and neurological events (liso-cel–treated set, n = 67)



[a]Graded according to the Lee 2014 criteria; [b]Defined as investigator-identified neurological AEs related to liso-cel and graded per the NCI CTCAE, version 5.0.
NE, neurological event.

- Grade 3 CRS and NEs occurred in 4% of patients each; no grade 4 or 5 CRS/NEs occurred (**Figure 5**)
  — Median time to onset and resolution of CRS were both 4 days
  — Median time to onset and resolution of NEs were 8.5 and 8 days, respectively

Table 2. Other adverse events of special interest

	Liso-cel–treated set (n = 67)
Grade ≥ 3 cytopenia at Day 29 visit, n (%)[a]	28 (42)
Second primary malignancy, n (%)	8 (12)[b]
Grade ≥ 3 infection, n (%)	11 (16)[c]
TE period (≤ 90 days after infusion)	6 (9)[d]
Post-TE period (> 90 days after infusion)	7 (10)[e]
MAS/HLH (all grade 3 and all resolved), n (%)	3 (4)
Tumor lysis syndrome, n (%)	1 (1)

[a]Grade ≥ 3 laboratory results of decreased hemoglobin, neutrophil, or platelet count at the Day 29 (±2 days) visit; [b]Including 4 patients with nonmelanoma skin cancer, 2 patients with AML, 1 patient with T-cell lymphoma, and 1 patient with MDS; [c]Some patients may have grade ≥ 3 infections in both TE and post-TE periods; [d]Including 5 patients with grade 3 infections and 1 patient with grade 5 neutropenic sepsis. The grade 3 infections were pneumonia, COVID-19 infection, sepsis, sinusitis, and staphylococcal sepsis (n = 1 each); all grade 3 infections resolved; [e]Seven patients experienced 9 events of grade ≥ 3 infection during the post-TE period: COVID-19 (n = 4; including pneumonia [n = 1]) and other pneumonia (n = 5). All events resolved.
AML, acute myeloid leukemia; HLH, hemophagocytic lymphohistiocytosis; MAS, macrophage activation syndrome; MDS, myelodysplastic syndromes; TE, treatment emergent.

- Grade ≥ 3 cytopenia at Day 29 was reported in 42% of patients (**Table 2**)
- Most cytopenia events at Day 29 recovered to grade ≤ 2 by Day 90 and all recovered to grade ≤ 2 by data cutoff of November 2024 (**see Table S1 using QR code**)
- Among 77 leukapheresed patients, 16 (21%) deaths occurred on-study (**see Table S2 using QR code**)
- Liso-cel exhibited rapid expansion with a median time to maximum transgene levels of 10 days after infusion (**see Figure S1 using QR code**)
- Results for B-cell aplasia and hypogammaglobulinemia are available (**see Figure S2 using QR code**)

Conclusions

- **After a single administration of liso-cel, patients with 3L+ R/R MZL achieved deep and durable responses with high survival rates at 24 months**
  — Primary and key secondary endpoints were met with an **ORR of 95.5%** and **CR rate of 62.1%**, respectively, assessed by IRC per CT
  — The 24-month rates were 88.6% for DOR, 85.7% for PFS, and 90.4% for OS
  — Outcomes were similar among patients who had CR and PR by IRC per CT
- **The safety profile of liso-cel was manageable, and no new safety signals were identified[4–9]**
  — Grade 3 CRS and NEs occurred in 4% of patients each; no grade 4 or 5 CRS/NEs occurred
- **Liso-cel demonstrated clinically meaningful benefit in patients with 3L+ R/R MZL, underscoring its potential role as a new standard of care in this patient population**

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Acknowledgments

- This study was previously presented at the 18th International Conference on Malignant Lymphoma (ICML); June 17–21, 2025; Lugano, Switzerland
- We would like to thank the patients, caregivers, investigators, and study personnel
- This study was funded by Celgene, a Bristol-Myers Squibb Company
- All authors contributed to and approved the presentation; writing and editorial assistance were provided by Bu Reinen, PhD, CMPP, of The Lockwood Group (Stamford, CT, USA), funded by Bristol Myers Squibb

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Presented at the Society of Hematologic Oncology (SOHO) 2025 Annual Meeting; September 3–6, 2025; Houston, TX, USA

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