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Patient-Reported Outcomes with Lisocabtagene Maraleucel in Patients with Third-Line or Later Relapsed or Refractory Marginal Zone Lymphoma from the Phase 2 TRANSCEND FL Study

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ASH 2025, Presentation 709

Introduction

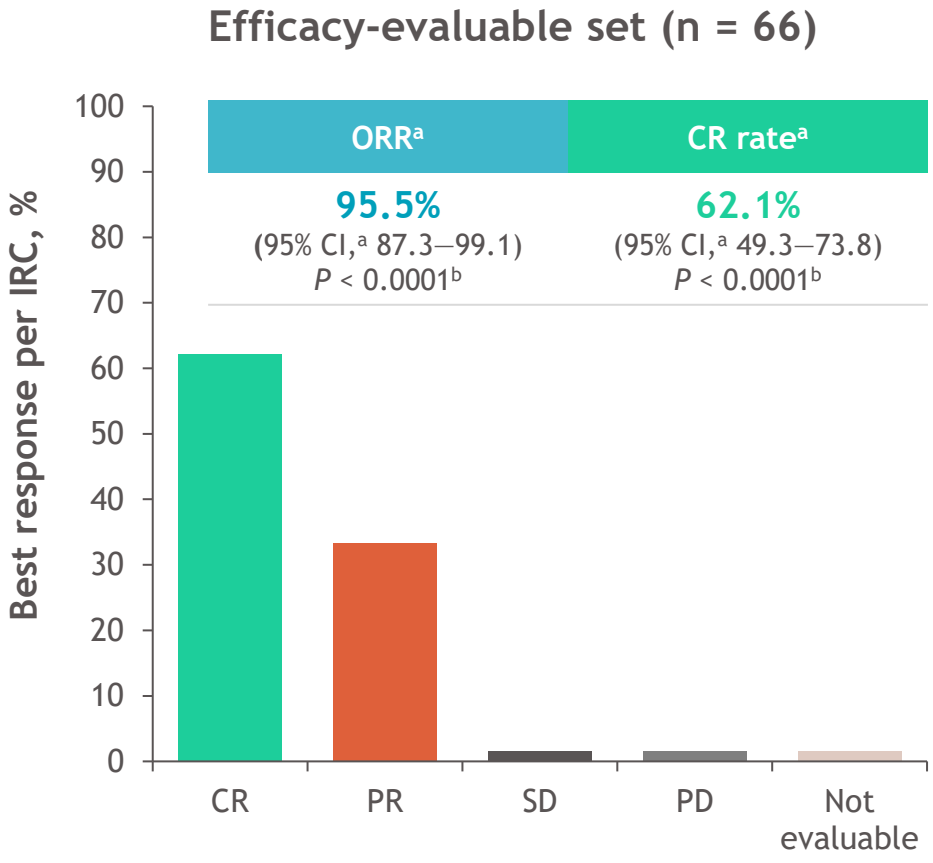
- Lisocabtagene maraleucel (liso-cel) is an autologous, CD19-directed, 4-1BB CAR T cell product
- We previously reported the results of the primary analysis of the MZL cohort of TRANSCEND FL (NCT04245839), an open-label, single-arm, multicohort, multicenter, phase 2, pivotal study of liso-cel[1]
  - Robust efficacy (ORR = 95.5%; CR rate = 62.1%) was observed with high 24-month DOR, PFS, and OS rates of 88.6%, 85.7%, and 90.4%, respectively[1]
  - The safety profile was manageable and consistent with prior reports in other B-cell malignancies[1–7]
- Patient-reported outcomes (PRO) from clinical studies of patients with R/R MZL treated with CD19-directed CAR T cell therapy have not been previously reported
- Here, we report PROs from patients with 3L+ MZL treated with liso-cel in the TRANSCEND FL study

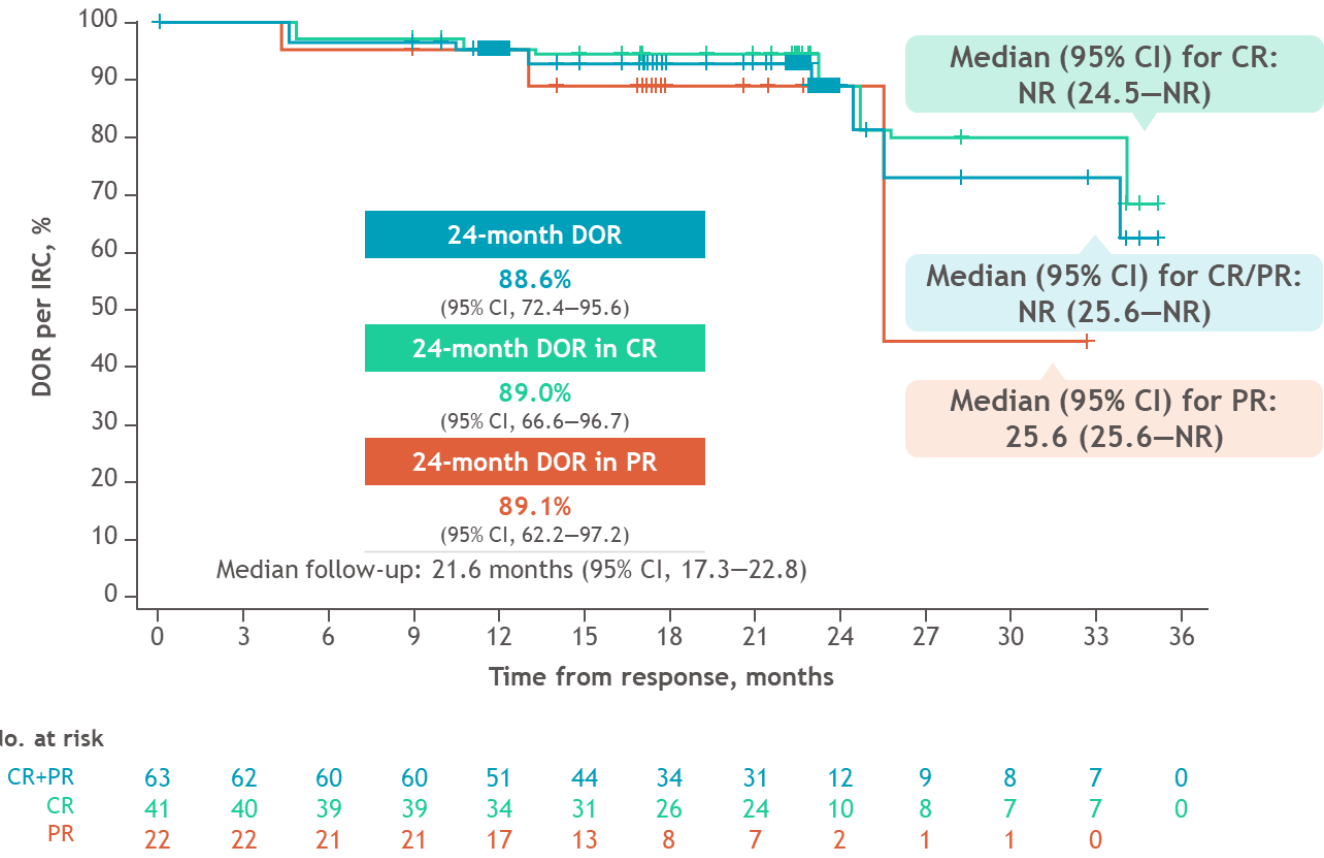
3L+, third line or later; DOR, duration of response.

1. Palomba ML, et al. *Hematol Oncol* 2025;43(S3):55—58; 2. Abramson JS, et al. *Blood* 2023;141:1675—1684; 3. Abramson JS, et al. *Lancet* 2020;396:839—852; 4. Sehgal A, et al. *Lancet Oncol* 2022;23:1066—1077; 5. Siddiqi T, et al. *Lancet* 2023;402:641—654; 6. Morschhauser F, et al. *Nat Med* 2024;30:2199—2207; 7. Wang M, et al. *J Clin Oncol* 2024;42:1146—1157.

Liso-cel delivered high rates of durable responses in 3L+ MZL

- In the primary analysis of the MZL cohort from TRANSCEND FL, liso-cel demonstrated high response rates with sustained disease control at 2 years in 3L+ MZL





No. at risk

CR+PR	63	62	60	60	51	44	34	31	12	9	8	7	0
CR	41	40	39	39	34	31	26	24	10	8	7	7	0
PR	22	22	21	21	17	13	8	7	2	1	1	0	

[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%).
H_0, null hypothesis; IRC, independent review committee; NR, not reached; SD, stable disease.
Palomba ML, et al. *Clin Lymphoma Myeloma Leuk* 2025;25(suppl 1):S1006–S1007.

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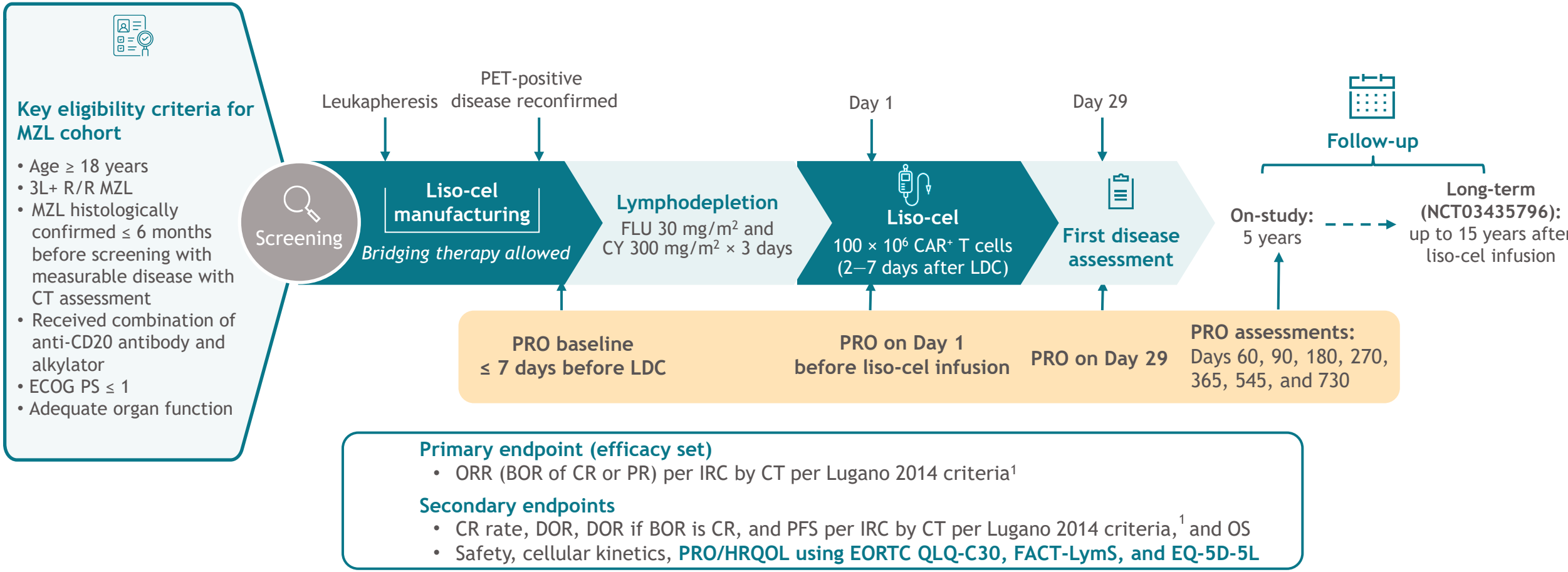
TRANSCEND FL: phase 2, open-label, multicenter study



ClinicalTrials.gov identifier: NCT04245839.

BOR, best overall response; CY, cyclophosphamide; EORTC QLQ-C30, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 items; EQ-5D-5L, EuroQol 5-dimensional, 5-level; FACT-LymS, Functional Assessment of Cancer Therapy - Lymphoma Subscale; FLU, fludarabine; HRQOL, health-related quality of life; LDC, lymphodepleting chemotherapy.

1. Cheson BD, et al. *J Clin Oncol* 2014;32:3059—3068.

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PRO instruments

PRO instrument	Domains	Range	Notes
EORTC QLQ-C30	Primary: global health status/QOL, physical, role, and cognitive functioning, fatigue, pain Exploratory: remaining domains	0—100	↑ Global health status and functioning domain scores = better HRQOL ↑ Symptom domain scores = higher level of symptomatology or problems
FACT-LymS	Lymphoma-specific symptoms	0—60	15 items rated 0—4 0: not at all 4: very much ↑ Score = better HRQOL
EQ-5D-5L	Health utility index (derived based on scores for 5 dimensions)	0—1	0: death 1: to full health Negative scores = state perceived to be worse than death
	EQ-VAS	0—100	0: worst imaginable health 100: best imaginable health

EQ-5D-5L dimensions

QOL, quality of life; VAS, visual analog scale.

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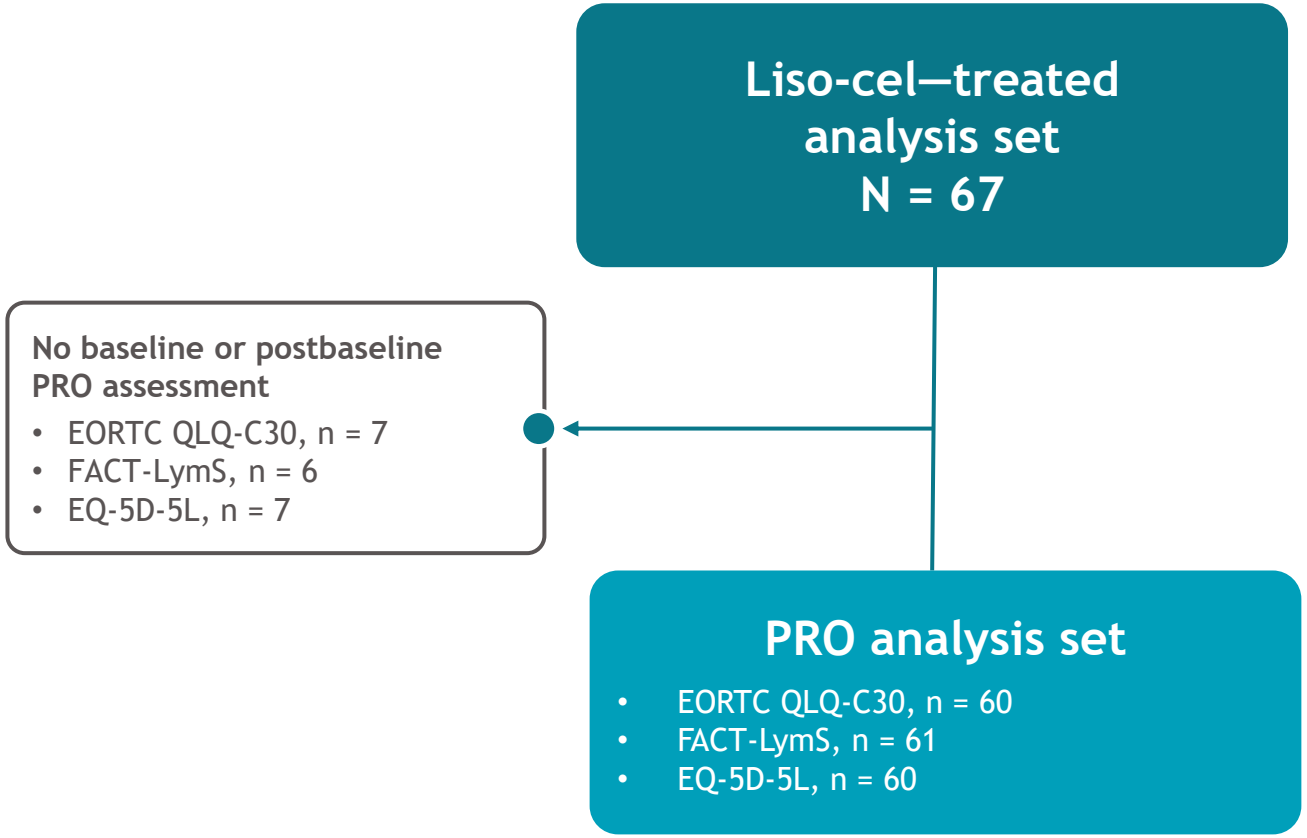
Patient disposition and analysis groups



- PRO completion rates were > 80% through 18 months

Data cutoff: November 29, 2024. First patient first visit: July 14, 2020; last patient last treatment: October 31, 2023.
PRO-evaluable set included all patients with baseline and ≥ 1 postbaseline assessment. The PRO completion rate was defined as the number of patients submitting a valid PRO assessment at a given time point over the number of patients who were still expected to submit a PRO assessment at that time point.

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Baseline characteristics (EORTC QLQ-C30 analysis set)

	Liso-cel–treated analysis set (n = 67)	EORTC QLQ-C30 analysis set (n = 60)
Median (IQR) age, y	62 (57–71)	63 (57–71)
Male, n (%)	39 (58)	34 (57)
Race, n (%)		
Asian	4 (6)	4 (7)
Black or African American	1 (2)	1 (2)
White	38 (57)	33 (55)
Unknown or missing	24 (36)	22 (37)
Histological subtype, n (%)		
Extranodal MZL/MALT	17 (25)	14 (23)
Nodal	32 (48)	29 (48)
Splenic	17 (25)	17 (28)
ECOG PS at screening, n (%)		
0	37 (55)	37 (62)
1	30 (45)	23 (38)
Ann Arbor stage, n (%)		
Stage I/II	10 (15)	9 (15)
Stage III/IV	57 (85)	51 (85)
FLIPI risk category, n (%)[a]		
Low (0–1)	11 (16)	10 (17)
Intermediate (2)	13 (19)	11 (18)
High (3–5)	41 (61)	37 (62)
Disease status after last systemic treatment before liso-cel, n (%)		
Refractory	26 (39)	20 (33)
Relapsed	41 (61)	40 (67)
Median (IQR) no. of prior systemic lines of therapy	3 (2–5)	3 (2–5)

- Baseline PRO scores were similar to or slightly better than the European and US general populations

[a]Data unavailable for 2 (3%) patients each in the liso-cel–treated analysis set and EORTC QLQ-C30 analysis set.
FLIPI, Follicular Lymphoma International Prognostic Index; MALT, mucosa-associated lymphoid tissue; US, United States.

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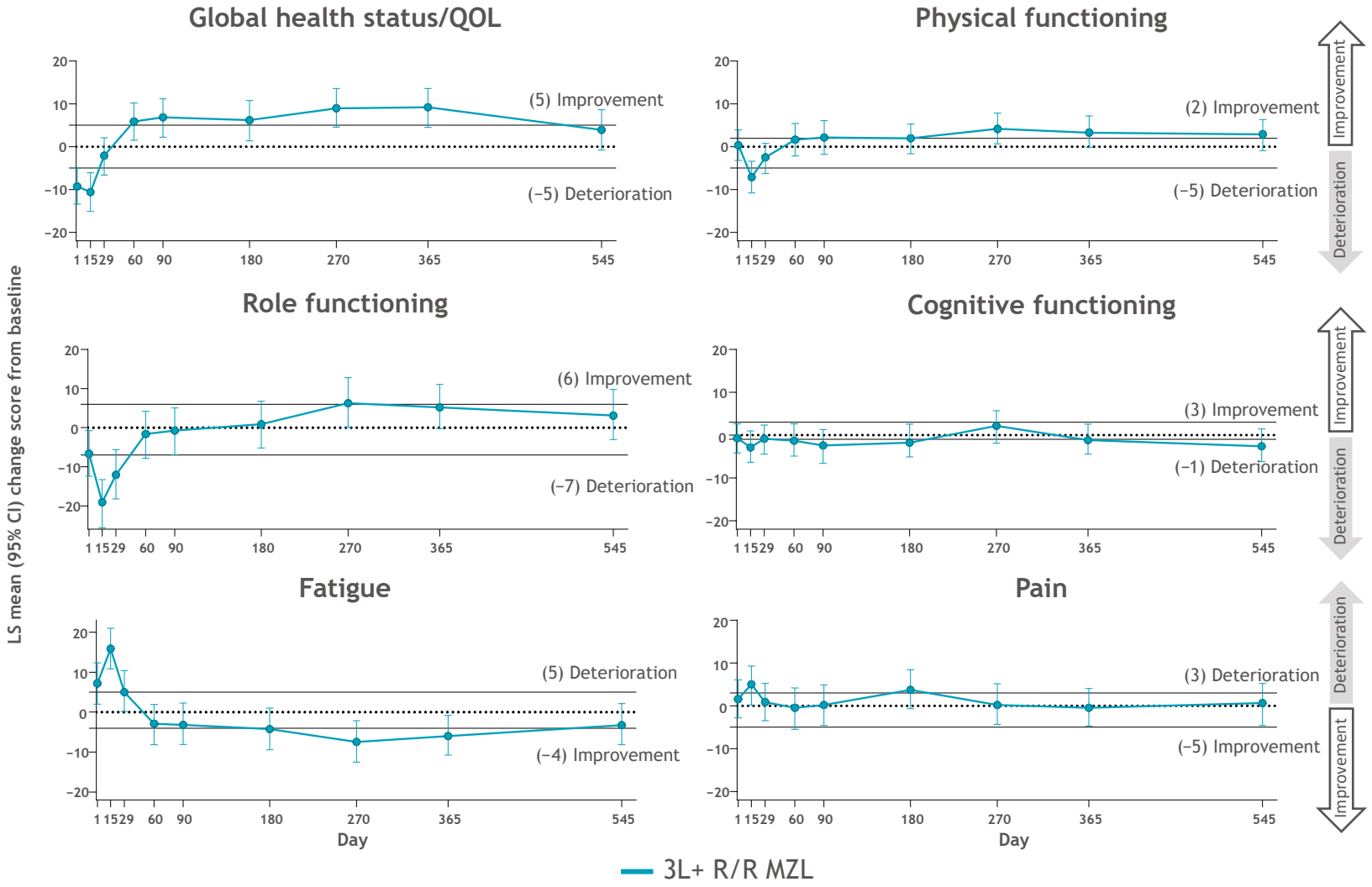
Most EORTC QLQ-C30 domains improved over time



- After an initial transient deterioration between Day 1 and Day 15, mean scores improved between Day 15 and Day 60 on 5 EORTC QLQ-C30 domains (all except cognitive functioning, which remained stable throughout, reflecting consistently higher baseline score)
- These improvements were generally maintained or further enhanced beyond Day 90
- Median time to confirmed improvement in EORTC QLQ-C30 domains occurred between 6 and 16 weeks after infusion

EORTC QLQ-C30 analysis set. Dashed line represents baseline (change = 0); solid lines represent the minimally important difference thresholds for clinically meaningful change (improvement or deterioration) from baseline in mean scores.[1,2] LS, least squares.

1. Cocks K, et al. *Eur J Cancer* 2012;48:1713–1721; 2. Johnston BC, et al. *BMJ Open* 2015;5:e007953.

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Most patients had clinically meaningful improvement or stable scores in all EORTC QLQ-C30 domains over time

- After treatment with liso-cel for 3L+ MZL, more patients had improved or stable scores across domains (58%—90%) than those who experienced deterioration (10%—42%)

EORTC QLQ-C30 analysis set. Improvement, no change, and worsening were defined by score changes from baseline of ≥ 5, < 5 to > −5, and ≤ −5 for global health status/QOL and physical functioning; ≤ −10, < 10 to > −10, and ≥ 10 for fatigue; ≤ −15, < 15 to > −15, and ≥ 15 for pain; and ≥ 15, < 15 to > −15, and ≤ −15 for cognitive functioning and role functioning, respectively.

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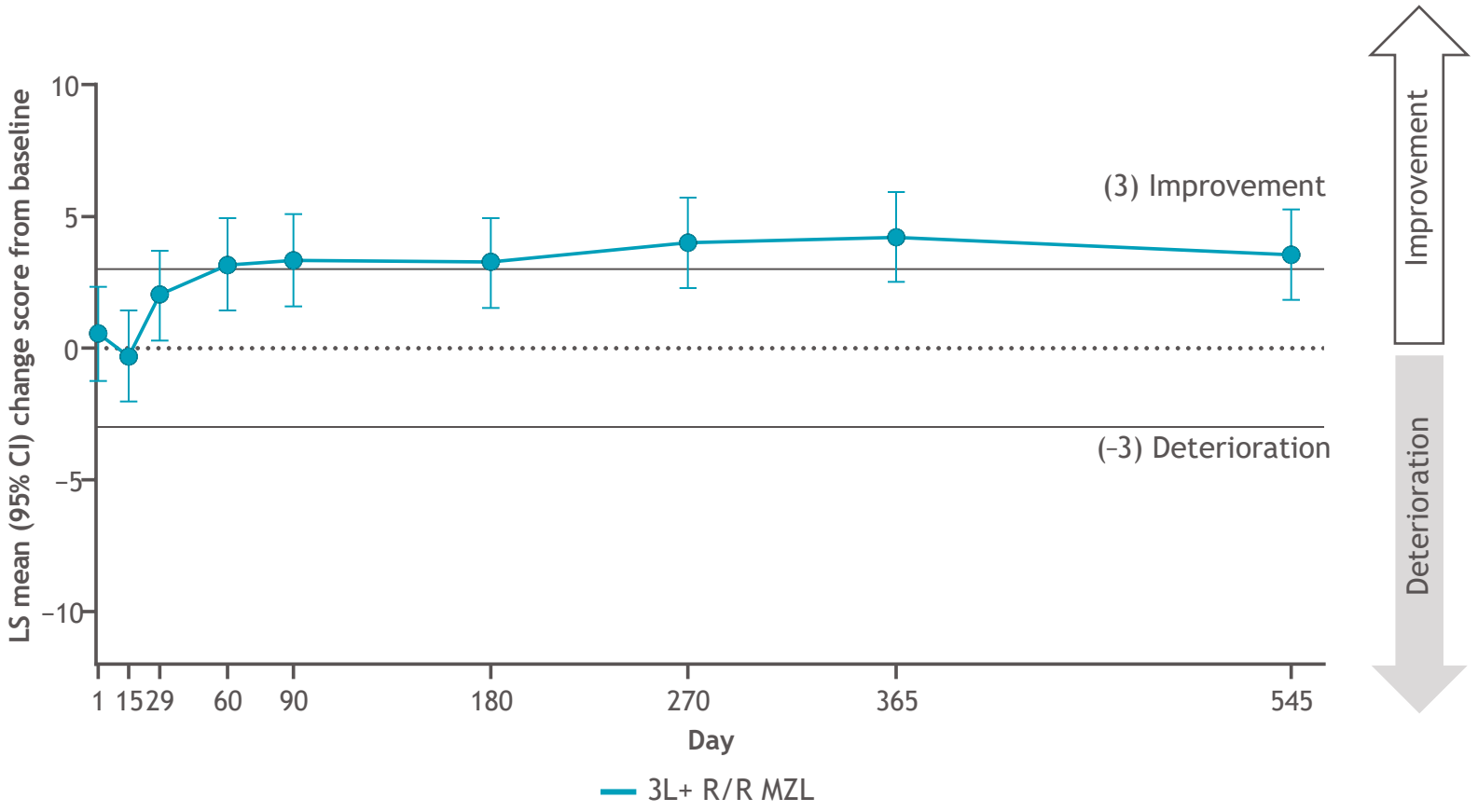
FACT-LymS score improved over time



- After a transient worsening between Day 1 and Day 15, the LS mean change in FACT-LymS score started to improve between Day 15 and Day 60 and remained consistent thereafter
  - Improvements exceeded the minimally important difference after Day 60
- Median time to improvement in FACT-LymS score was 10 weeks

FACT-LymS analysis set. Dashed line represents baseline (change = 0); solid lines represent the minimally important difference thresholds for clinically meaningful change (improvement or deterioration) from baseline in mean scores.[1,2] FACT-LymS includes lymphoma-relevant symptoms, including pain, lumps/swelling, fevers, night sweats, itching, fatigue, weight loss, loss of appetite, trouble concentrating, worry about infections, and emotional well-being.[3]

1. Cocks K, et al. *Eur J Cancer* 2012;48:1713—1721; 2. Johnston BC, et al. *BMJ Open* 2015;5:e007953; 3. Hlubocky FJ, et al. *Leuk Lymphoma* 2013;54:1942—1946.

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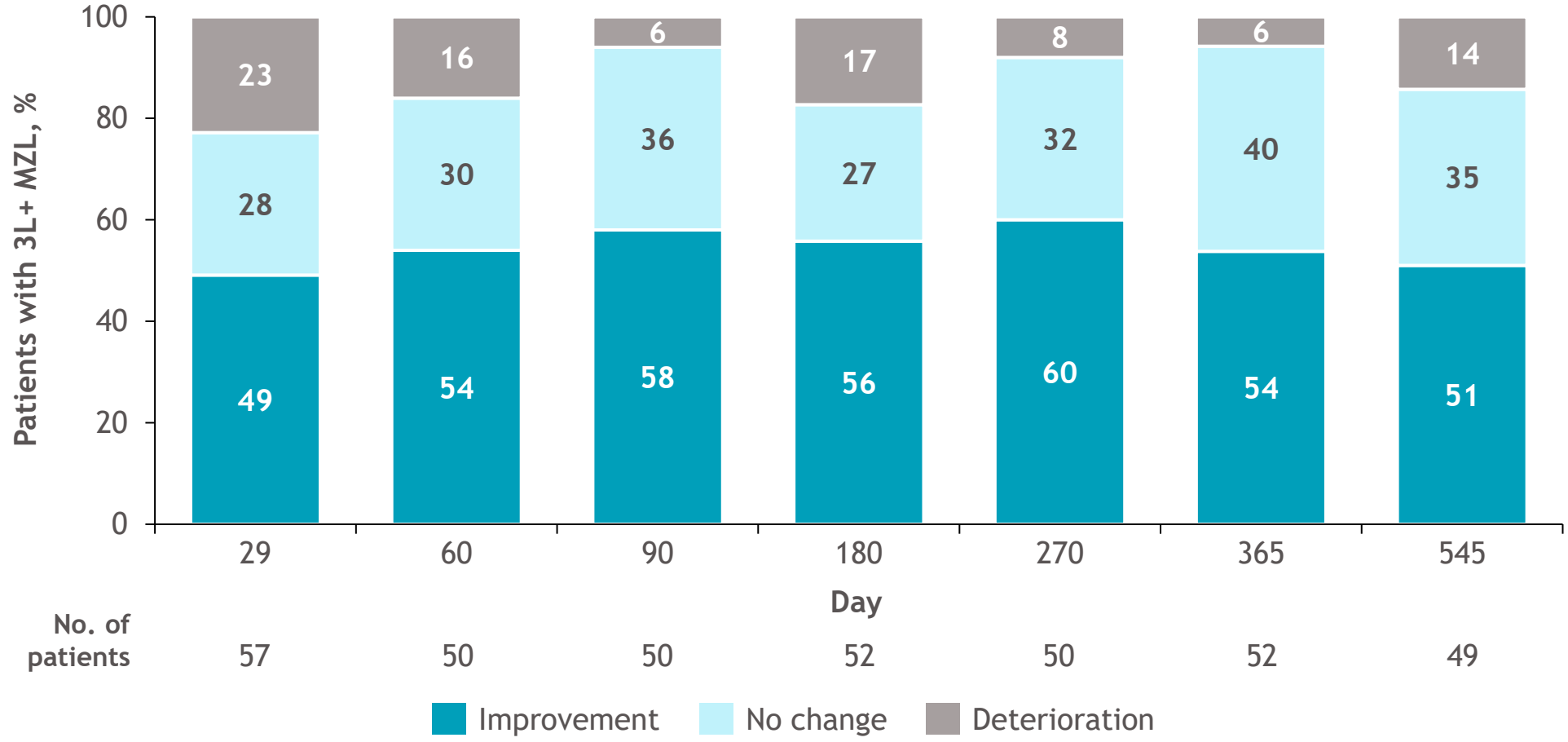
Most patients had clinically meaningful improvement or stable FACT-LymS scores over time

- In patients with 3L+ MZL, the proportion of patients with clinically meaningful improvements remained consistently above 50% as early as Day 60 after infusion, and most patients without improvement had stable scores over time



FACT-LymS analysis set. Improvement, no change, and worsening were defined by score changes from baseline of ≥ 3, < 3 to > −3, and ≤ −3, respectively.
The denominator for the percentage calculation in each category is based on the number of patients who answered ≥ 50% of the items for the domain (ie, a minimum of 8 of the 15 items).

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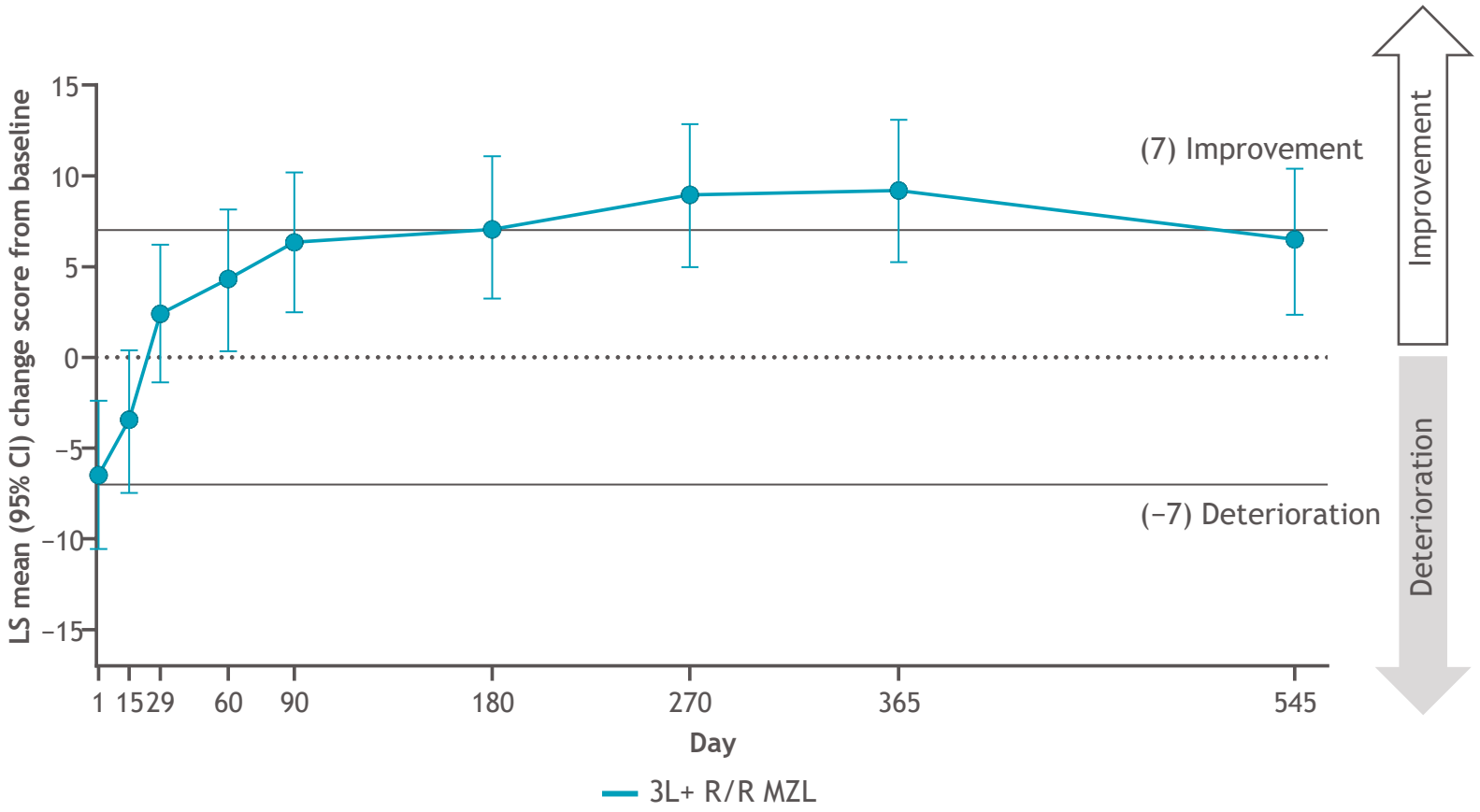
EQ-5D-5L VAS score improved over time



- Patients showed improvement in the EQ-5D-5L VAS as early as Day 15 reaching the minimum threshold to be considered clinically meaningful at Day 180 and remained largely consistent thereafter
- The median time to confirmed improvement was 26.6 weeks

EQ-5D-5L analysis set. Dashed line represents baseline (change = 0); solid lines represent the MID thresholds for clinically meaningful change (improvement or deterioration) from baseline in mean scores.[1,2]

1. Pickard AS, et al. *Health Qual Life Outcomes* 2007;5:70; 2. Johnston BC, et al. *BMJ Open* 2015;5:e007953.

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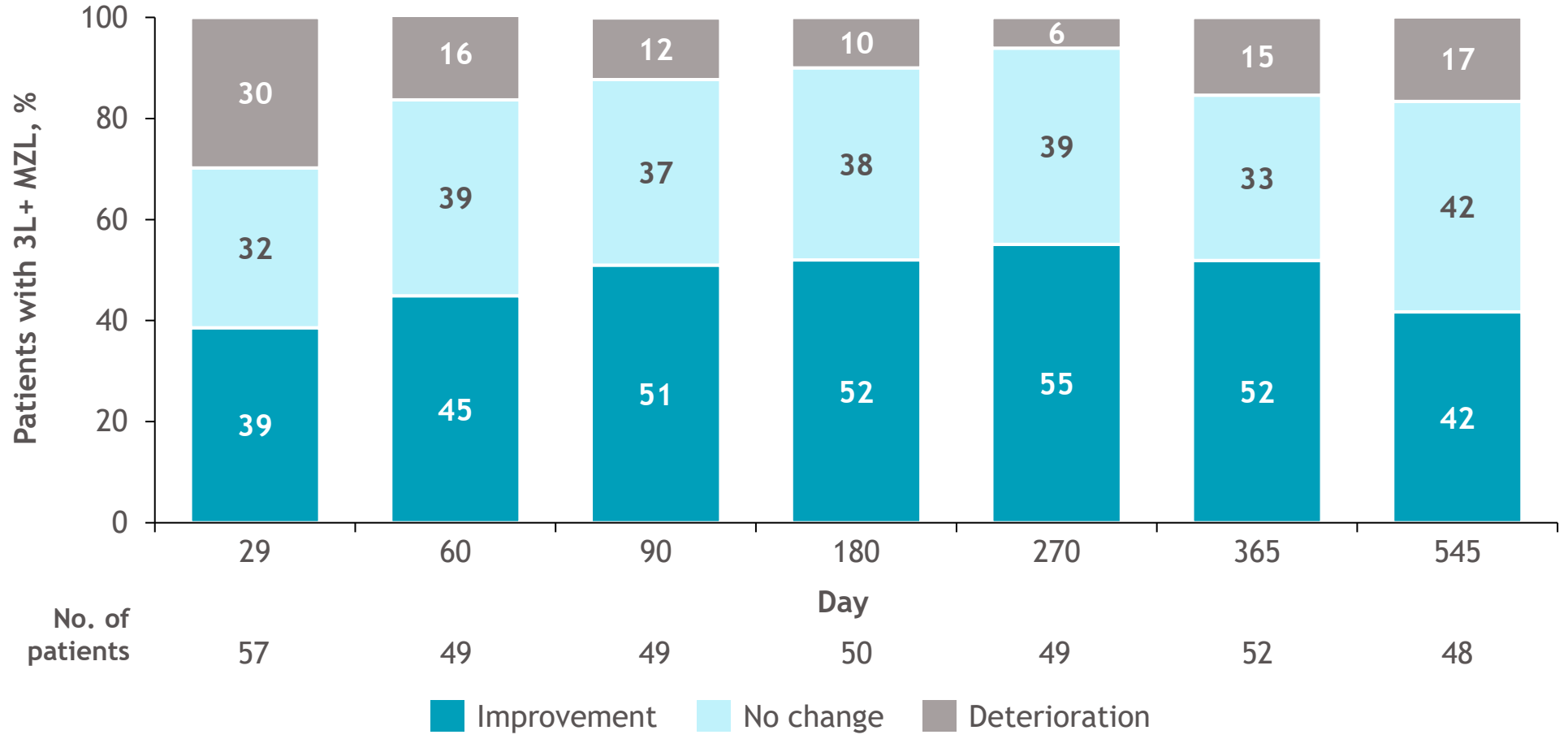
Most patients had clinically meaningful improvement or stable EQ-5D-5L VAS scores over time

- In patients with 3L+ MZL across all visits, approximately half of patients improved over time, about one-third remained stable, and only 6%—30% experienced deterioration



EQ-5D-5L analysis set. Improvement, no change, and worsening were defined by score changes from baseline of ≥ 7, < 7 to > −7, and ≤ −7, respectively.

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Summary

- The PRO analyses from the MZL cohort in TRANSCEND FL represent one of the largest efforts to characterize PROs in 3L+ R/R MZL
  - This finding provides valuable insight into the direct patient experience with liso-cel and complement the high efficacy and favorable safety from the primary analysis
- Following a transient decline immediately after treatment, PROs were either maintained or showed improvement over time
- These PRO results further support liso-cel as a new treatment in 3L+ R/R MZL, offering deep and durable responses with manageable safety accompanied by meaningful QOL benefits after a 1-time infusion

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Announcements

FDA-approved in the United States:

- BREYANZI® is indicated for the treatment of adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least 2 prior lines of systemic therapy
  - https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-lisocabtagene-maraleucel-relapsed-or-refractory-marginal-zone-lymphoma

Accepted for publication in *The Lancet*:

- "Lisocabtagene maraleucel in patients with relapsed or refractory marginal zone lymphoma: primary analysis results from the global, multicohort, single-arm, phase 2 TRANSCEND FL study"
  - M. Lia Palomba, Stephen J. Schuster, Reem Karmali, Alan P. Skarbnik, Jeremy S. Abramson, Kirit Ardeshna, Peter Borchmann, Brian T. Hill, Alejandro Martin García-Sancho, Gianpaolo Marcacci, Aaron P. Rapoport, Guillaume Cartron, Isabelle Fleury, Koji Izutsu, Manali Kamdar, Stephan Mielke, Anna Maria Barbui, Juan Luis Reguera Ortega, Loretta J. Nastoupil, Sairah Ahmed, Merav Bar, Lizbeth Diaz, Ulrika Furustrand, Victoria Diab, Min Vedal, Ariel Avilion, Jinender Kumar, Rina Nishii, Silvia Colicino, Franck Morschhauser

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Acknowledgments

- We would like to thank the patients, caregivers, investigators, and study personnel
- The study was funded by Celgene, a Bristol-Myers Squibb Company
- All authors contributed to and approved the presentation; analysis support was provided by Ling Shi, PhD, and Shien Guo, PhD, of Evidera (Bethesda, MD, USA), and writing and editorial assistance were provided by Marco Emanuele Favretto, PhD, of The Lockwood Group (Stamford, CT, USA), funded by Bristol Myers Squibb