Mass General Brigham
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CAR T-cells as 3rd Line Therapy for Large B-cell Lymphomas: Update from the TRANSCEND trial

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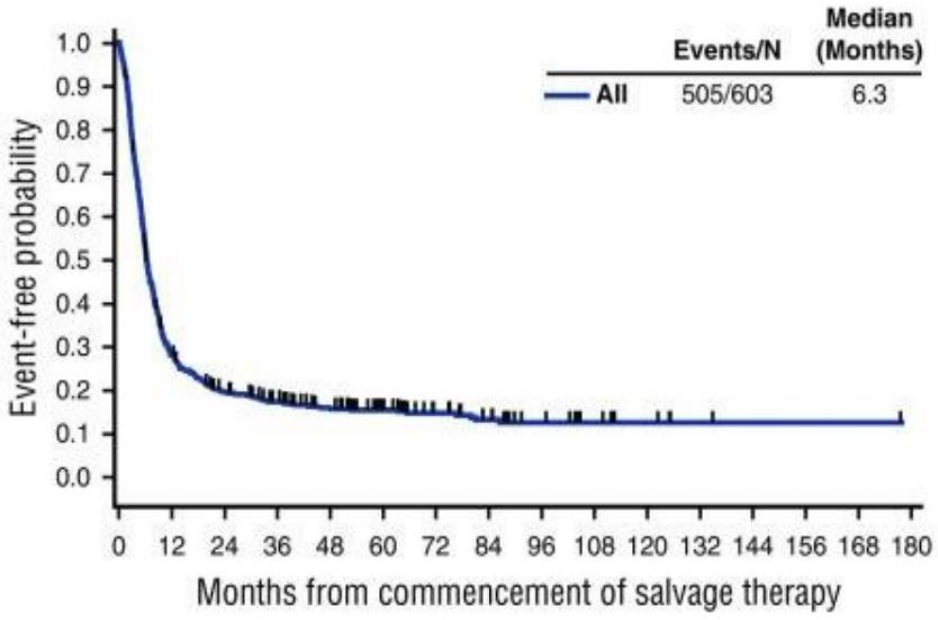
Disclosures for Jeremy Abramson

Consulting for AbbVie, Astra-Zeneca, BeiGene, Bristol Myers Squibb, Caribou Biosciences, Cellectar, Genentech, Incyte, Interius, Janssen, Kite Pharma, Lilly, Regeneron, Takeda

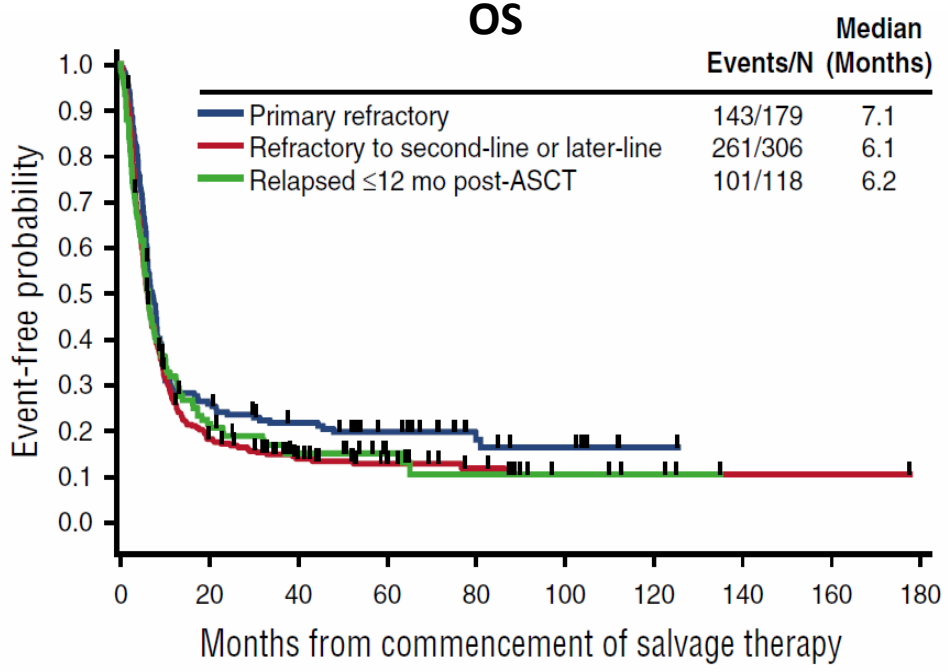
Chemotherapy-refractory DLBCL has a poor prognosis

Patients refractory to chemotherapy or relapsing ≤12 months after ASCT have low response rates to next therapy and an OS of 6 months

EFS



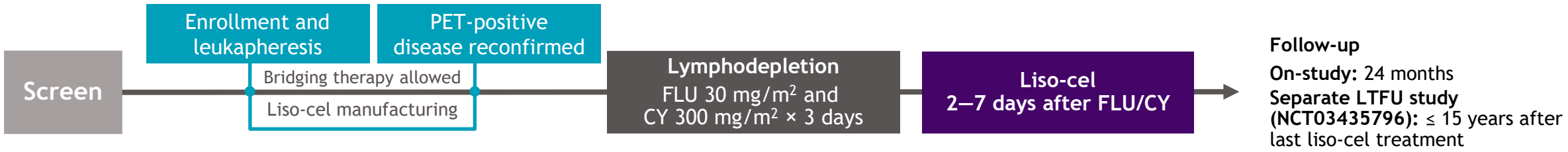
OS



ASCT, autologous stem cell transplantation; DLBCL, diffuse large B-cell lymphoma OS, overall survival.

Crump M, et al. Blood. 2017;130:1800-8.

TRANSCEND NHL 001, a seamless design, pivotal, phase 1 study



	N = 270
Age, median (range), y	63 (18—86)
NHL subtypes, n (%)	
DLBCL NOS	137 (51)
Transformed from FL / other indolent lymphomas	60 (22) / 18 (7)
HGBCL / PMBCL / FL3B	36 (13) / 15 (6) / 4 (1)
Secondary CNS lymphoma, n (%)	7 (3)
Prior lines of systemic therapy, median (range)	3 (1—8)
Chemotherapy refractory, n (%)	181 (67)
Prior autologous / allogeneic HSCT, n (%)	90 (33) / 9 (3)
Received bridging therapy, n (%)	159 (59)

Only CAR T-cell pivotal trial to include: secondary CNS DLBCL; prior allo SCT; transformed non-follicular iNHL; grade 3B FL; no minimal ALC, ANC, Hgb or platelets; moderate renal or cardiac dysfunction

	N = 270
Cytokine release syndrome (CRS)	
Any grade / grade 3—4, %	42% / 2%
Neurological events (NE)	
Any grade / grade 3—4, %	30% / 10%
Grade 3-4 cytopenia at Day 29, %	37%

- **Overall median follow-up was 19.9 months (range, 0.2—45.2)**
- **Total on-study follow-up time was 352 patient-years**

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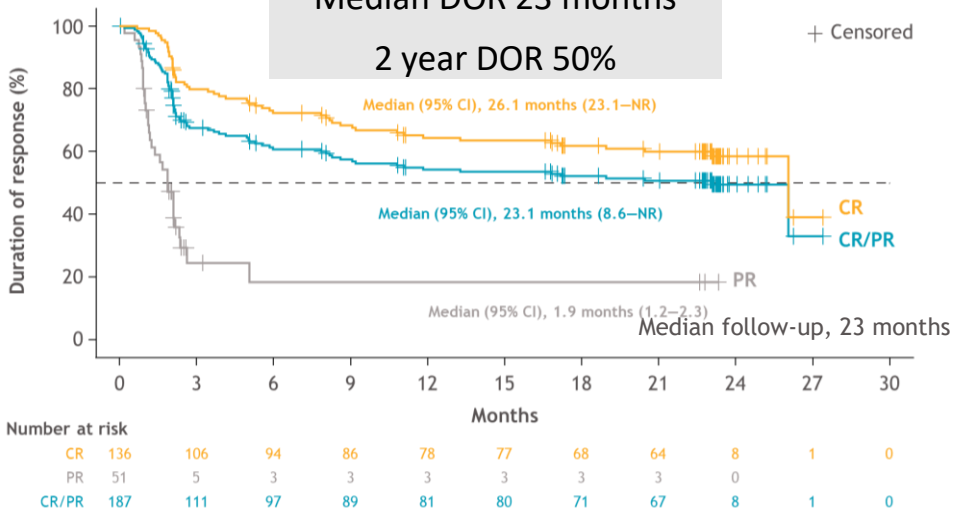
Efficacy follow-up at 2 years

Response	Response Evaluable Set N = 257
Overall	**73%**
Complete	**53%**

Duration of Response

Median DOR 23 months

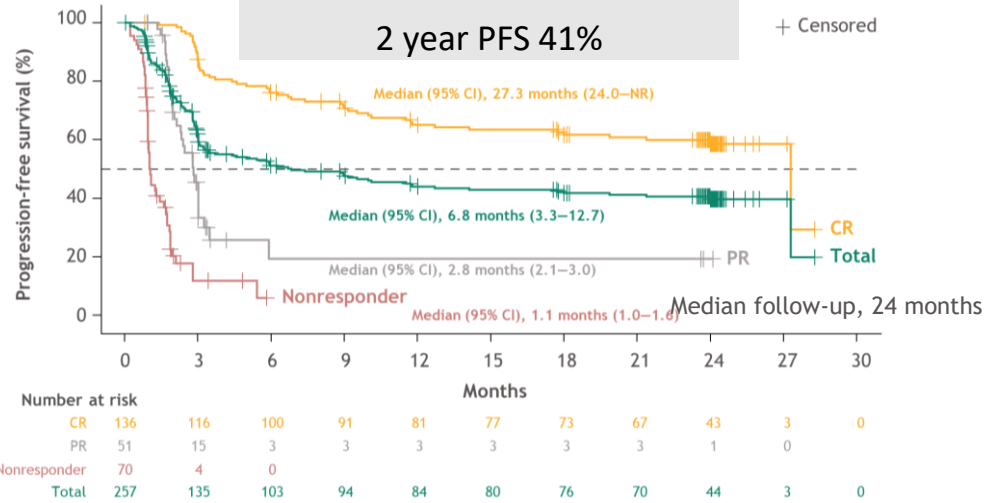
2 year DOR 50%



Progression-Free Survival

Median PFS 7 months

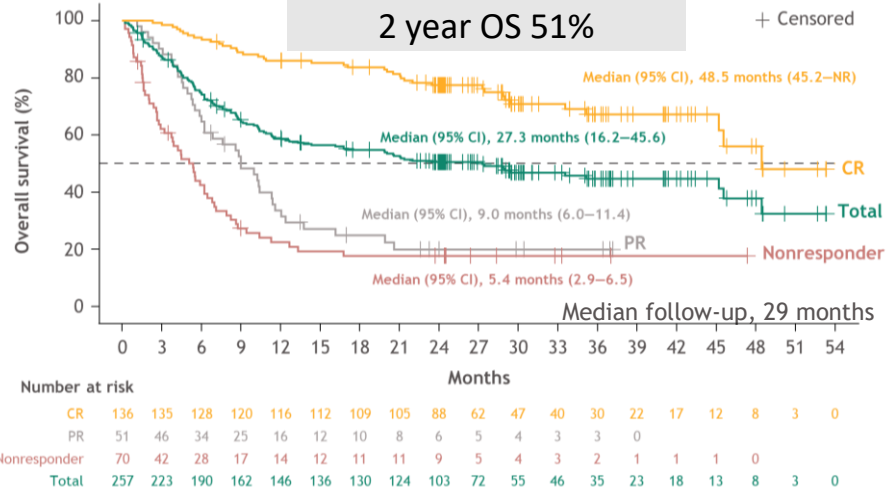
2 year PFS 41%



Overall Survival

Median OS 27 months

2 year OS 51%



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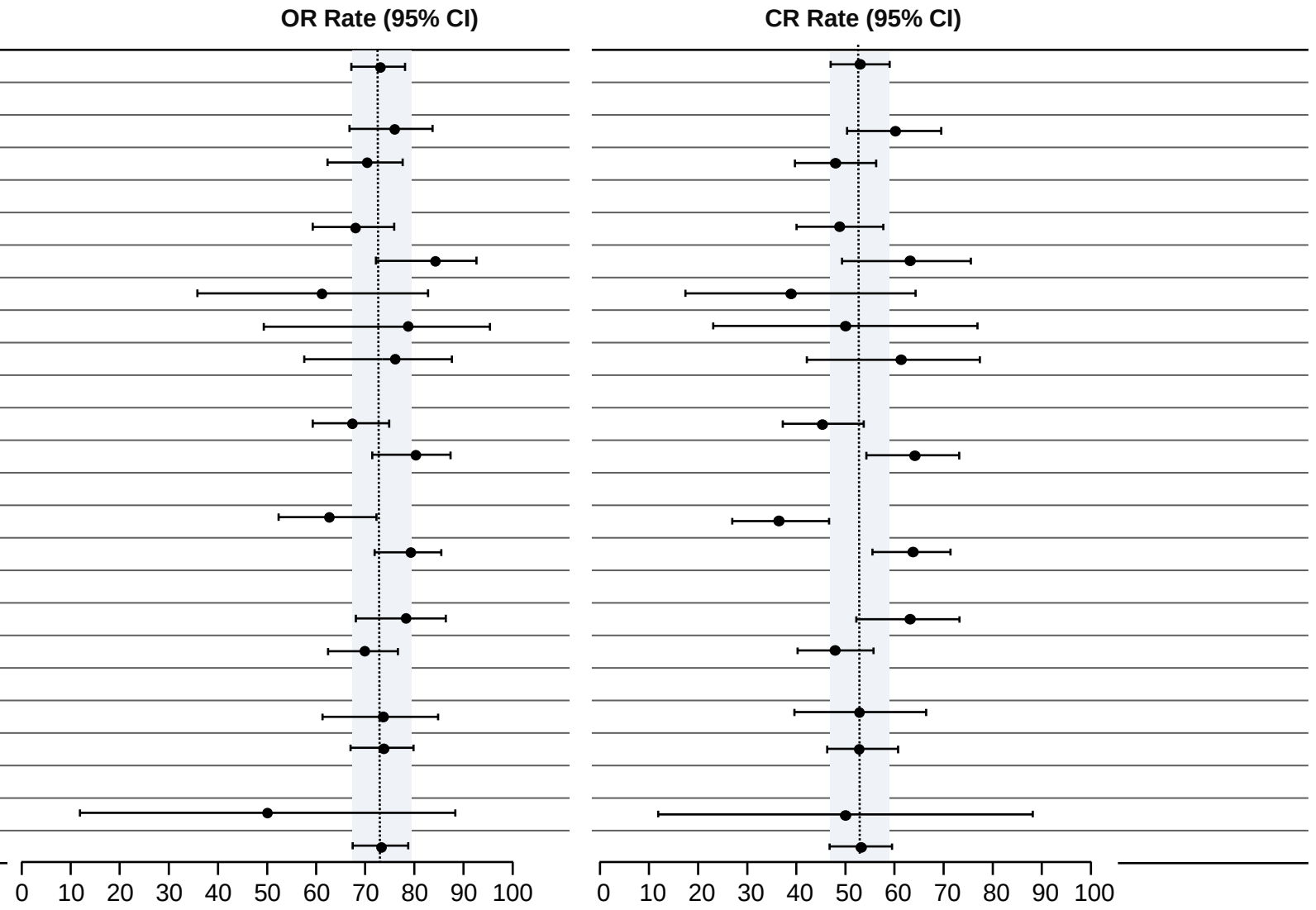
Objective and Complete Responses by Patient and Clinical Characteristics

Subgroup	Evaluable Patients, n
Overall	256
Age	
≥65 years	108
<65 years	148
Subtype	
DLBCL NOS	131
tFL	57
Transformed iNHL	18
PMBCL	14
HGBCL	33
Bridging therapy	
Yes	150
No	106
High disease burden[a]	
Yes	99
No	149
HSCT	
Yes	87
No	169
Comorbidities[b]	
Yes	60
No	196
Secondary CNS lymphoma	
Yes	6
No	250



[a]Patients with LDC SPD ≥50 cm^2 or LDH ≥500 U/L. [b]Patients with CrCl >30 but <60 mg/min or with LVEF ≥40% to <50%.
CI, confidence interval; CNS, central nervous system; CR, complete response; DLBCL, diffuse large B-cell lymphoma; HGBCL, high-grade B-cell lymphoma; HSCT, hematopoietic stem cell transplantation; iNHL, indolent non-Hodgkin lymphoma; NOS, not otherwise specified; PMBCL, primary mediastinal large B-cell lymphoma; tFL, transformed from follicular lymphoma.

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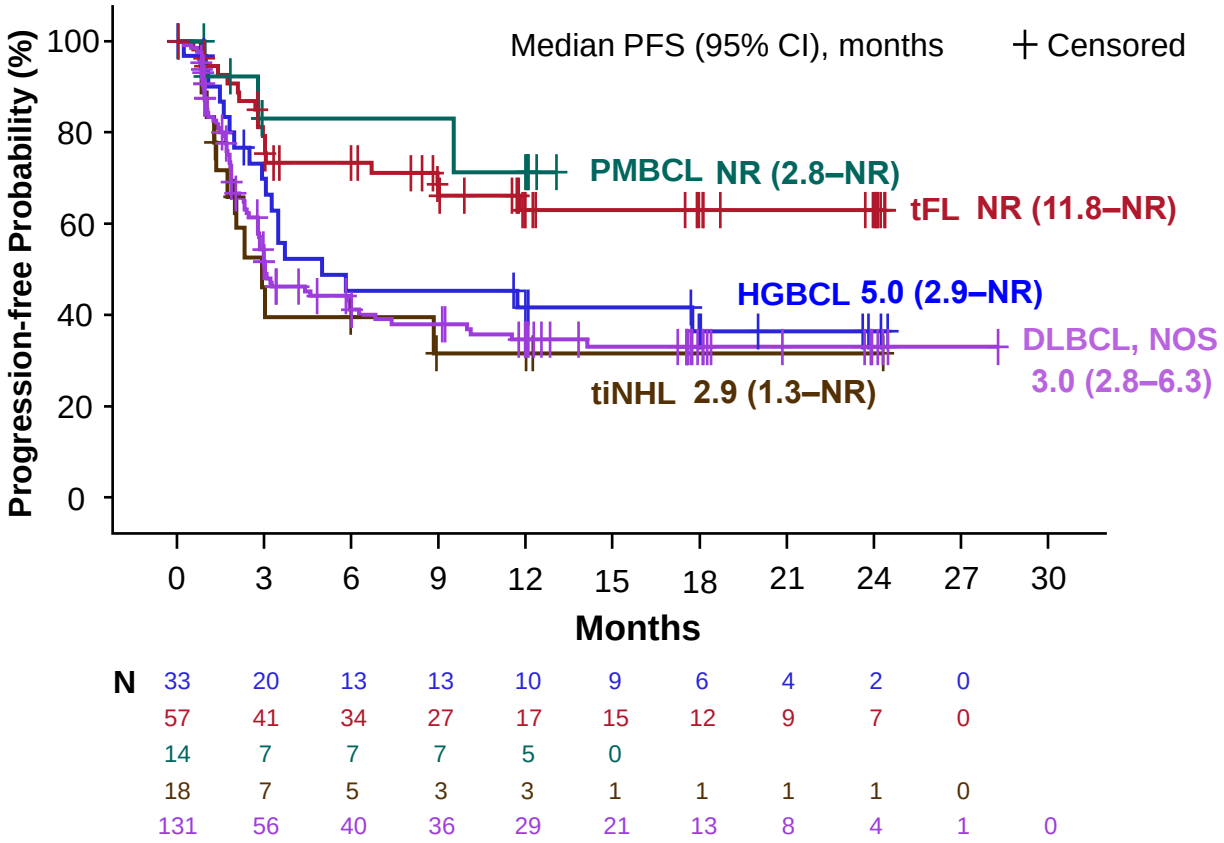
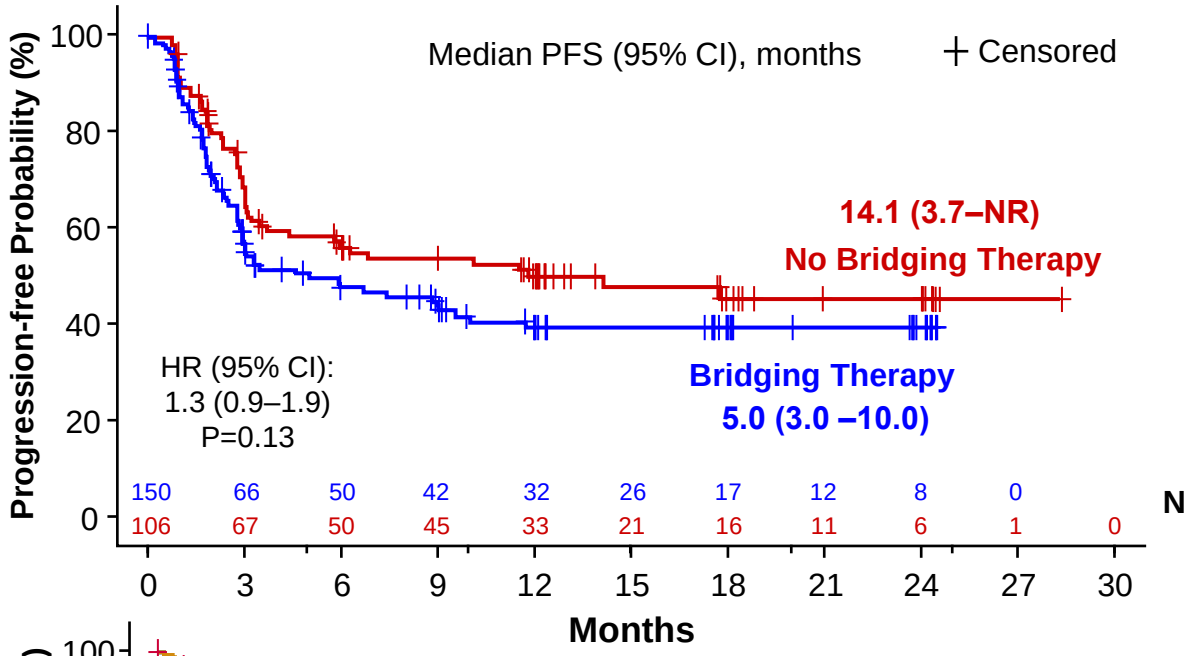
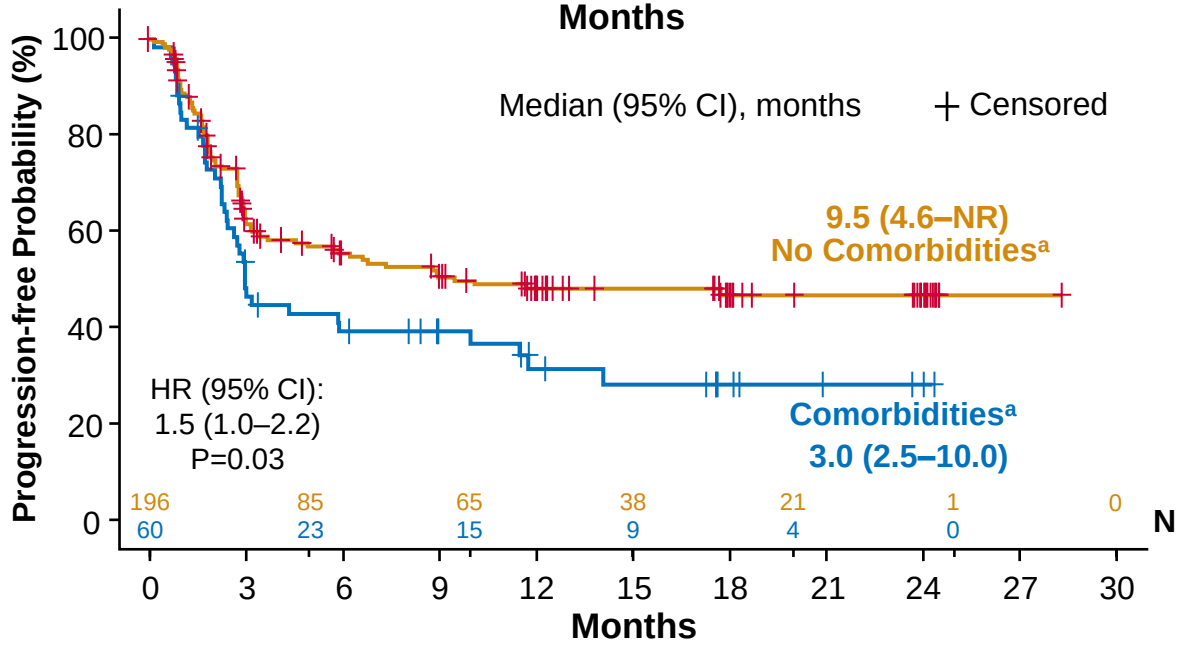
Progression-Free Survival by Subgroups







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Incidence of AEs in the TE and post-TE period

	TE period (within 90 days of liso-cel infusion; N = 270)	
	Any grade	Grade ≥ 3
Patients with AEs, n (%)[a]	**268 (99)**	**213 (79)**
Patients with liso-cel–related AEs, n (%)	**201 (74)**	**94 (35)**
Most frequent AEs (≥ 20% in any grade), n (%)		
Neutropenia	169 (63)	161 (60)
Anemia	129 (48)	101 (37)
Fatigue	119 (44)	4 (1)
Cytokine release syndrome	113 (42)	6 (2)
Nausea	90 (33)	4 (1)
Thrombocytopenia	85 (31)	73 (27)
Headache	80 (30)	3 (1)
Decrease appetite	77 (29)	7 (3)
Diarrhea	71 (26)	1 (< 1)
Constipation	63 (23)	0
Dizziness	60 (22)	1 (< 1)
Hypotension	60 (22)	8 (3)
Cough	57 (21)	0
Vomiting	56 (21)	1 (< 1)
Infections and infestations SOC, n (%)	**111 (41)**	**33 (12)**

	Post-TE period (Day 91 to end of study; N = 249)	
	Any grade	Grade ≥ 3
Patients with AEs, n (%)	**105 (42)**	**57 (23)**
Patients with liso-cel–related AEs, n (%)	**42 (17)**	**21 (8)**
Most frequent AEs (≥ 4% in any grade), n (%)		
Neutropenia	21 (8)	17 (7)
Anemia	19 (8)	16 (6)
Fatigue	18 (7)	1 (< 1)
Thrombocytopenia	16 (6)	10 (4)
Nausea	15 (6)	0
Hypogammaglobulinemia	13 (5)	0
Diarrhea	13 (5)	2 (1)
Pyrexia	11 (4)	0
Febrile neutropenia	10 (4)	9 (4)
Decreased appetite	10 (4)	1 (< 1)
Infections and infestations SOC, n (%)	**24 (10)**	**12 (5)**

- Few AEs occurred after the 90-day TE reporting period

[a]AEs were graded using National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03; CRS was graded per Lee 2014 criteria (Lee DW, et al. *Blood* 2014;124:188—195).
SOC, system organ class; TE, treatment emergent.

Incidence of AEs of special interest

	Liso-cel—treated set (N = 270)
CRS[a]	
Any grade / grade 3—4, n (%)	113 (42) / 6 (2)
Median (range) days to onset / resolution of first CRS	5 (1—14) / 5 (1—17)
NE[b]	
Any grade / grade 3—4, n (%)	80 (30) / 27 (10)
Median (range) days to onset / resolution of first NE	9 (1—66) / 11 (1—86)
CRS or NE, n (%)	127 (47)
Prolonged cytopenia[c] **at Day 29**	101 (37)
Grade 3—4 decreased hemoglobin, n (%)	17 (6)
Median (range) time to recovery to grade ≤ 2 in 10 patients,[d] days	26 (3—150)
Grade 3—4 decreased platelets, n (%)	81 (30)
Median (range) time to recovery to grade ≤ 2 in 47 patients,[d] days	35 (5—328)
Grade 3—4 decreased neutrophils, n (%)	53 (20)
Median (range) time to recovery to grade ≤ 2 in 42 patients,[d] days	25.5 (2—336)

- Most CRS and NEs were of grade 1 or 2
- No grade 5 CRS or NEs were reported
- Among patients with prolonged cytopenia who had laboratory results after Day 29, recovery to grade ≤ 2 anemia, thrombocytopenia, and neutropenia occurred in all patients at a median of 26, 35, and 25.5 days, respectively

[a]CRS was graded per Lee 2014 criteria (Lee DW, et al. *Blood* 2014;124:188—195); [b]NEs were defined as investigator-identified neurological AEs related to liso-cel were graded using National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03; [c]Prolonged cytopenia is defined as grade ≥ 3 laboratory result of decreased hemoglobin, decreased neutrophil count, or decreased platelet count at the Day 29 visit; [d]Recovery data are presented for patients who had hematology laboratory results after Day 29.

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Deaths during the TE and post-TE period

	Liso-cel—treated set (N = 270)		
	≤ 30 days after **last liso-cel infusion**	> 30 days and ≤ 90 days after last liso-cel infusion	> 90 days after last liso-cel infusion
Any death, n (%)	9 (3)	24 (9)	100 (37)
Disease progression	6 (2)	18 (7)	86 (32)
Adverse event	3 (1)	5 (2)	3 (1)
Unknown	0	1 (< 1)	4 (1)
Other	0	0	7 (3)[a]

- Few deaths due to AEs occurred anytime on study
- No patient died of COVID-19

[a]Stroke, pneumonia, sepsis/pneumonia, disseminated aspergillosis, septic shock, heart attack, diffuse intra-abdominal ischemia; n = 1 for each.

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Conclusions

- In this extended follow-up analysis of TRANSCEND, responses to liso-cel were durable, with a median DOR of 23.1 months and an estimated rate of continued response at 2 years of 49.5%
- The estimated 2-year PFS and OS rates were 40.6% and 50.5%, respectively
- Liso-cel treatment was associated with low incidences of severe (grade ≥ 3) CRS and NE
- Few AEs occurred after the 90-day TE period
- No new safety signals were observed during long-term follow-up

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Acknowledgments

- Patients and caregivers

- Investigators and study personnel at all participating sites

Thank you for your attention!

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