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CAR T-cells as 2nd Line Therapy for Large B-cell Lymphomas: Update from the TRANSFORM trial

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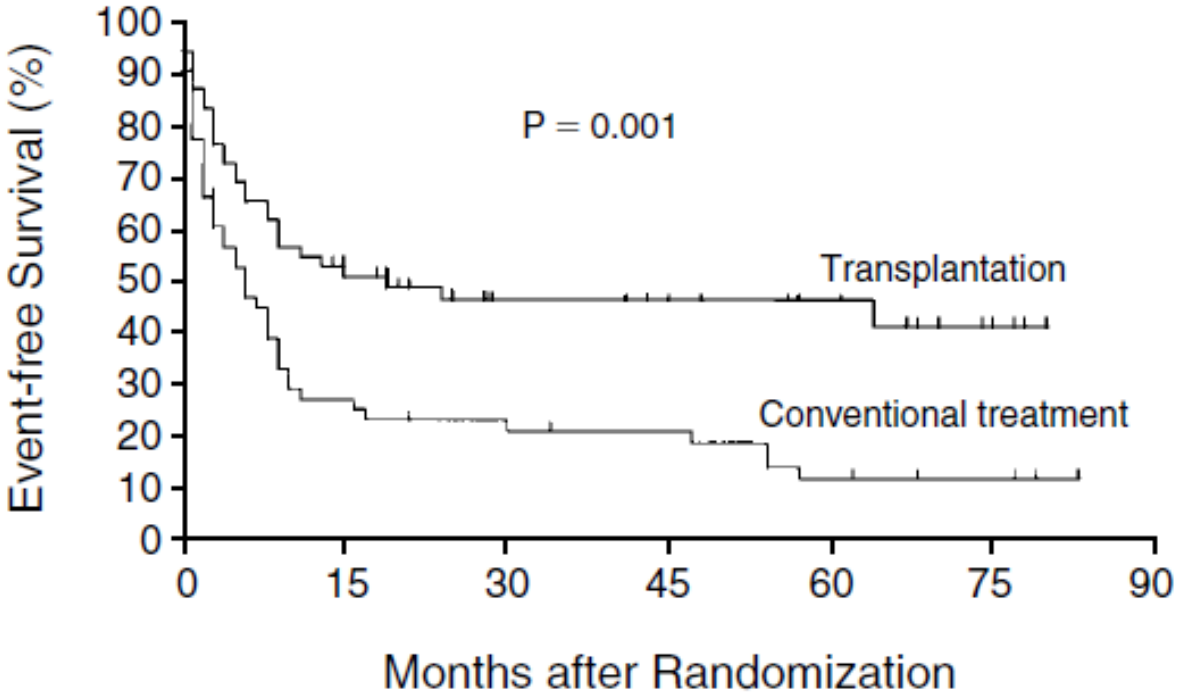
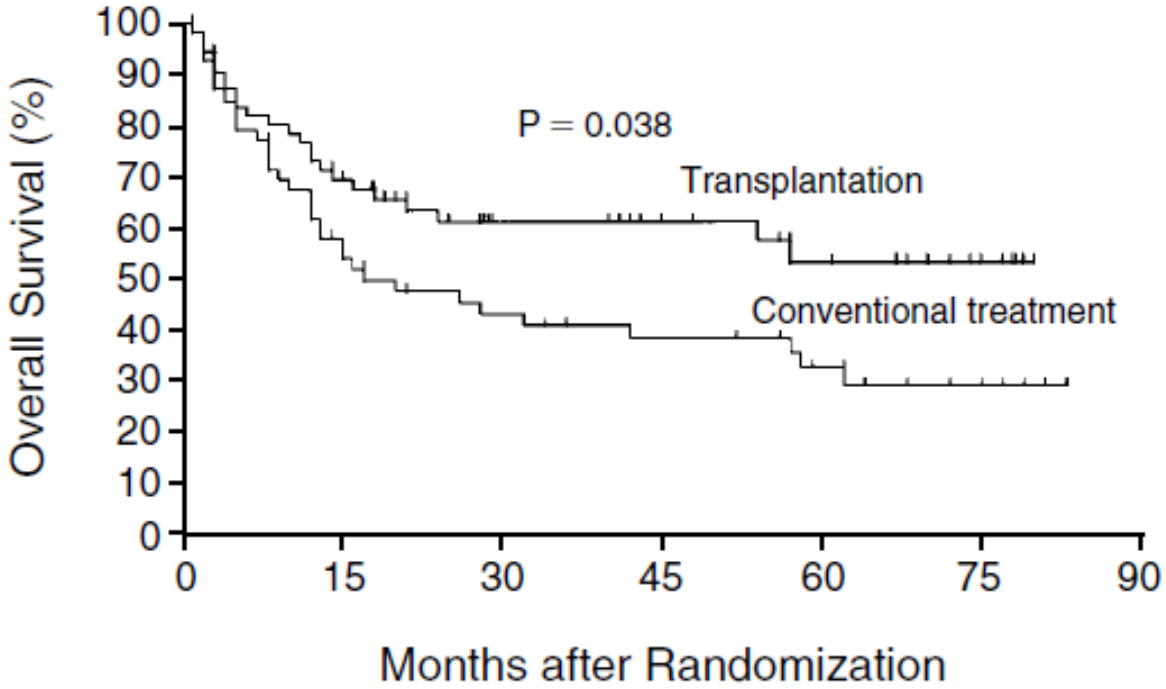
Disclosures for Jeremy Abramson

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

The Good Old Days for ASCT in Relapsed/Refractory DLBCL

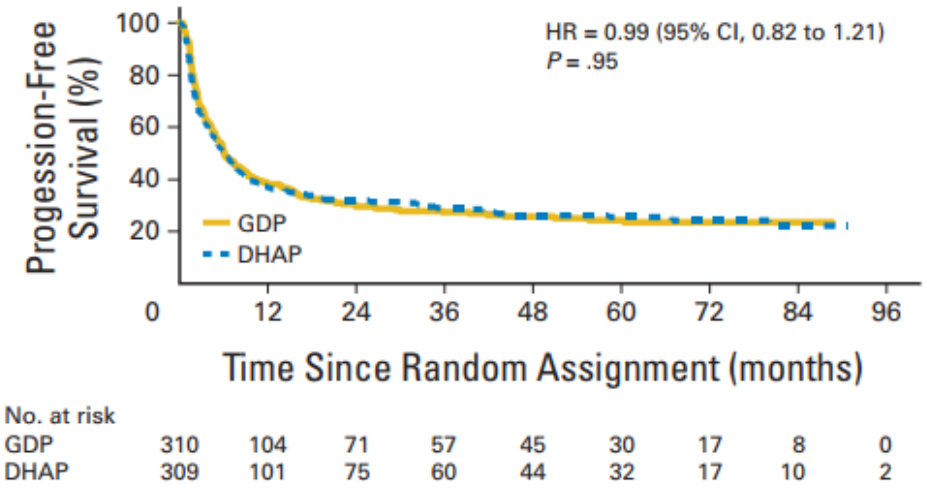




Philip, et al. NEJM. 1995

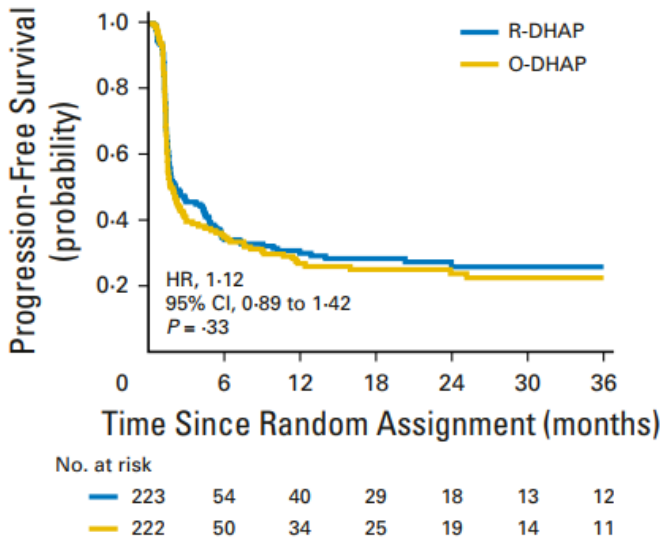
High dose chemo and ASCT: A flawed SOC in the Modern Era

NCIC-CTG LY.12



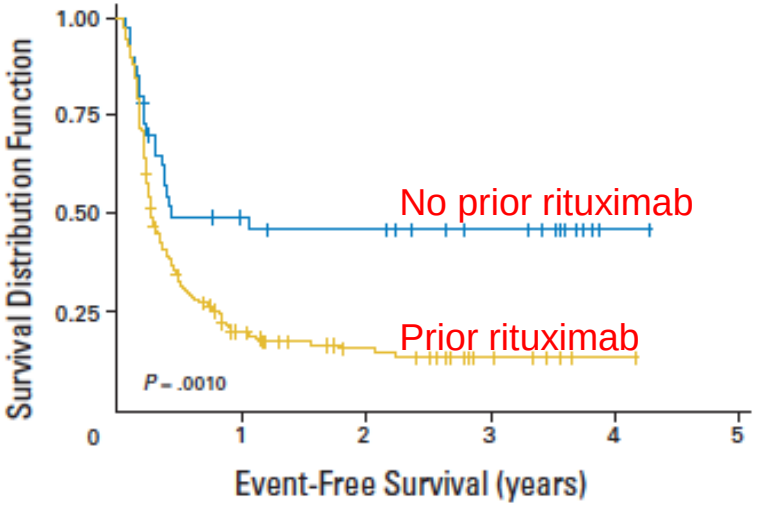
Crump, et al. JCO 2014

ORCHAARD



van Imhoff, et al. JCO 2017

CORAL (pts progressing ≤ 1 year)



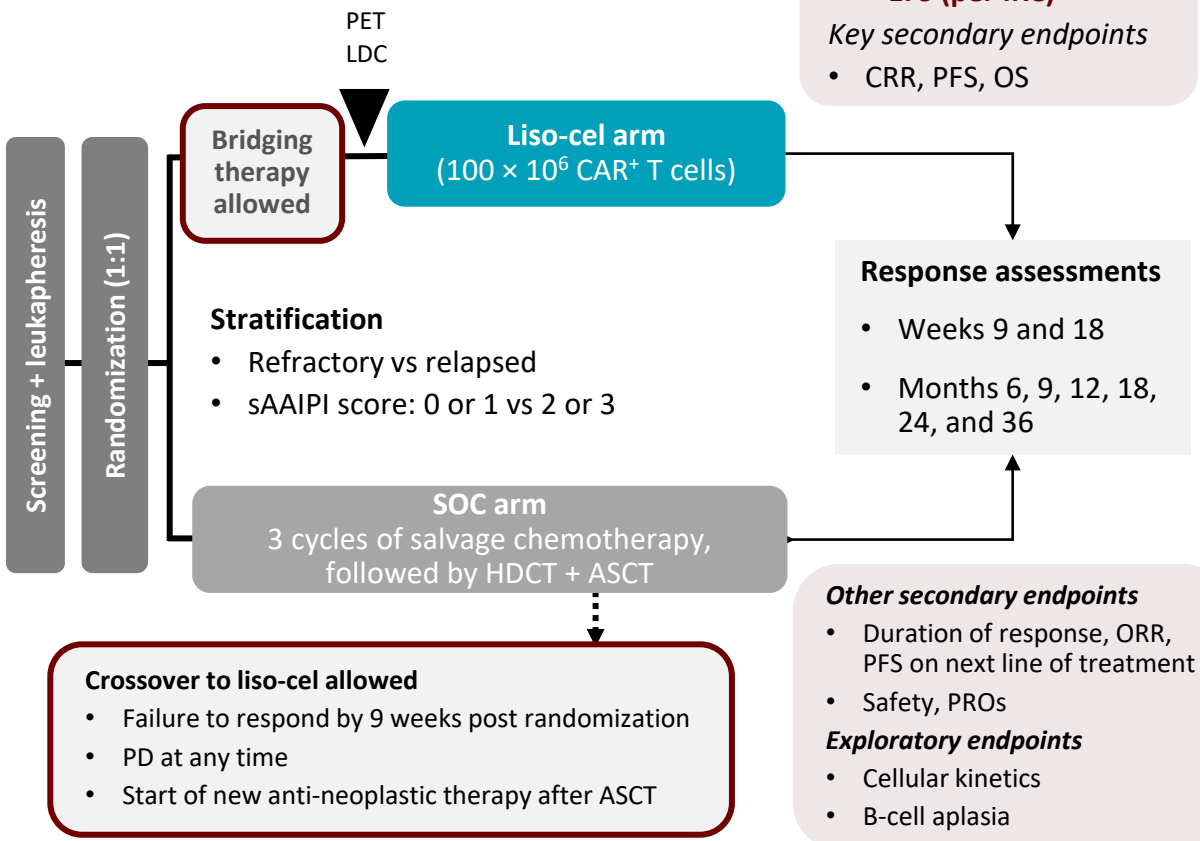
Gisselbrecht, et al. JCO 2010

- About 3/4 of DLBCL relapses happen within one year
- Plus, only half of relapsed DLBCL patients are candidates for HDT/ASCT due to age/comorbidities
- The SOC therefore fails in the vast majority of patients with relapsed DLBCL in the modern era

TRANSFORM: liso-cel versus SOC in 2L LBCL

Key eligibility

- Age 18–75 years
- Aggressive NHL
  - DLBCL NOS (de novo or transformed from iNHL), HGBCL (DHL/THL) with DLBCL histology, grade 3B FL, PMBCL, THRBCL
- R/R ≤ 12 months after 1L treatment containing an anthracycline and a CD20-targeted agent
- ECOG PS score ≤ 1
- Eligible for HSCT
- Secondary CNS lymphoma allowed
- LVEF > 40% for inclusion
- No minimum ALC



Characteristic	Liso-cel (n = 92)	SOC (n = 92)
Median age (range), years	60 (53.5–67.5)	58 (42–65)
LBCL subtypes, n (%)		
DLBCL NOS	53 (58)	49 (53)
HGBCL (DHL/THL), n (%)	**22 (24)**	**21 (23)**
PMBCL	8 (9)	10 (11)
DLBCL transformed from iNHL	7 (8)	8 (9)
Primary refractory, n (%)	**67 (73)**	**68 (74)**
Relapsed, n (%)	**25 (27)**	**24 (26)**
sAAIPI score, n (%)		
0 or 1	56 (61)	55 (60)
2 or 3	36 (39)	37 (40)
ECOG PS score of 1, n (%)	44 (48)	35 (38)

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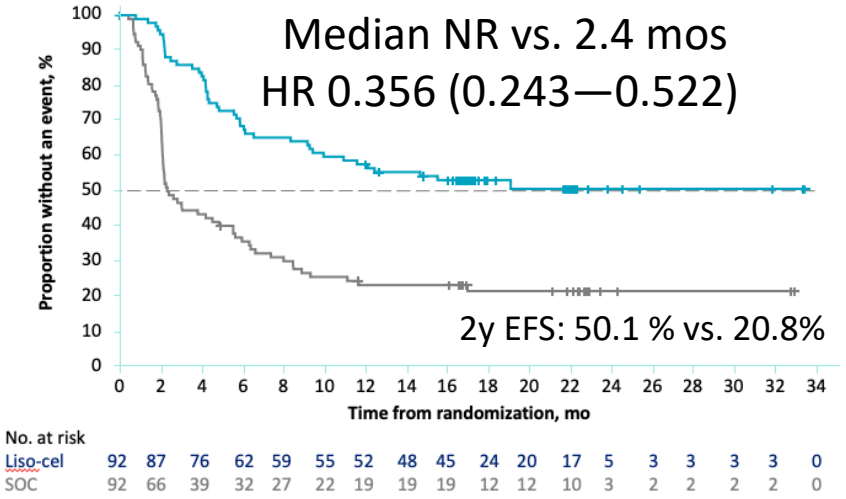
Liso-cel vs. SOC as 2nd line therapy in primary refractory or early relapsed large B-cell lymphomas

ORR: 87% vs. 49%
CRR: 74% vs. 43%

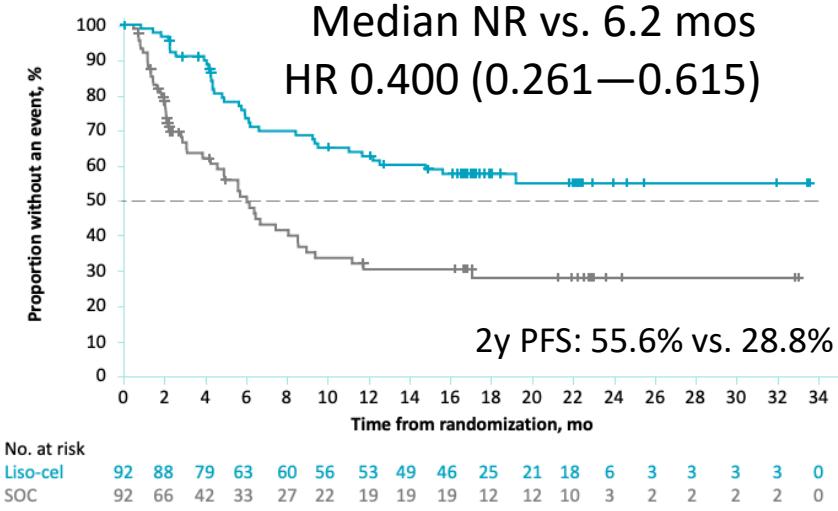
EFS

Median NR vs. 2.4 mos
HR 0.356 (0.243—0.522)



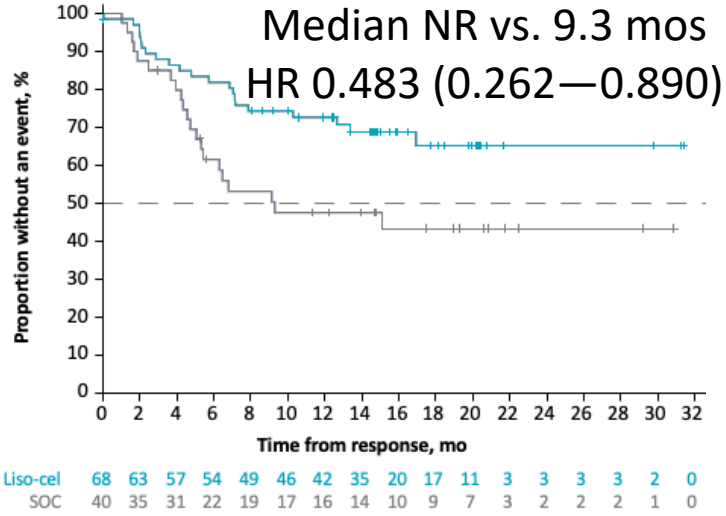
PFS

Median NR vs. 6.2 mos
HR 0.400 (0.261—0.615)



DoCR

Median NR vs. 9.3 mos
HR 0.483 (0.262—0.890)



Median Follow-up: 17.5 mo

Toxicity	Grade	%
CRS	Any grade Grade 3	49 1
Neurotox	Any grade Grade 3	11 4

Liso-cel associated with improved QOL by PRO

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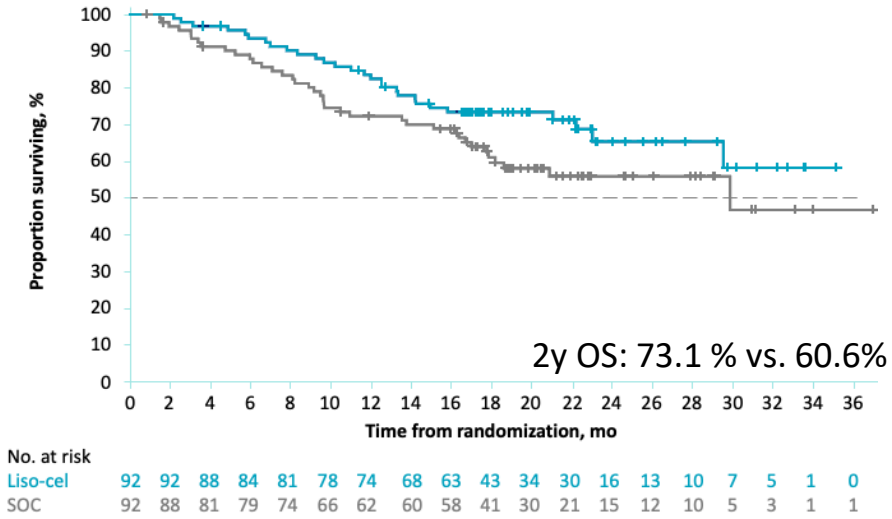
Liso-cel vs. SOC as 2nd line therapy: Overall Survival and Crossover

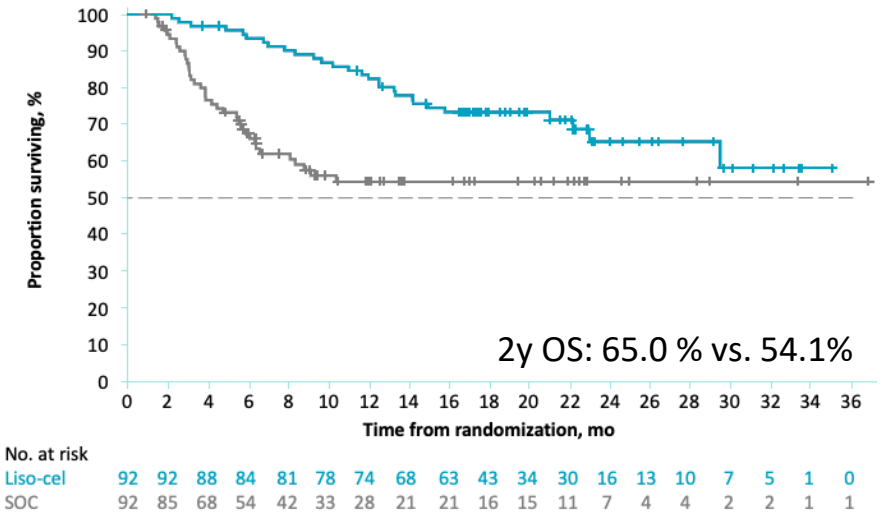
OS

Median NR vs. 29.9 mos
HR 0.724 (0.443—1.183)



OS adjusted for crossover

Median NR vs. NR
HR 0.415 (0.251—0.686)



Crossover subgroup

N=61 (66% of SOC)

	Crossover subgroup (n = 57 treated)
Median f/u	12.0 m (1.4—28.1)
ORR / CRR	61% / 53%
Median EFS	5.9 m (3.1—15.1)
Median PFS	5.9 m (3.2—26.5)
Median OS	15.8 m (11.8—NR)

Median Follow-up: 17.5 mo

66% of SOC pts crossed over

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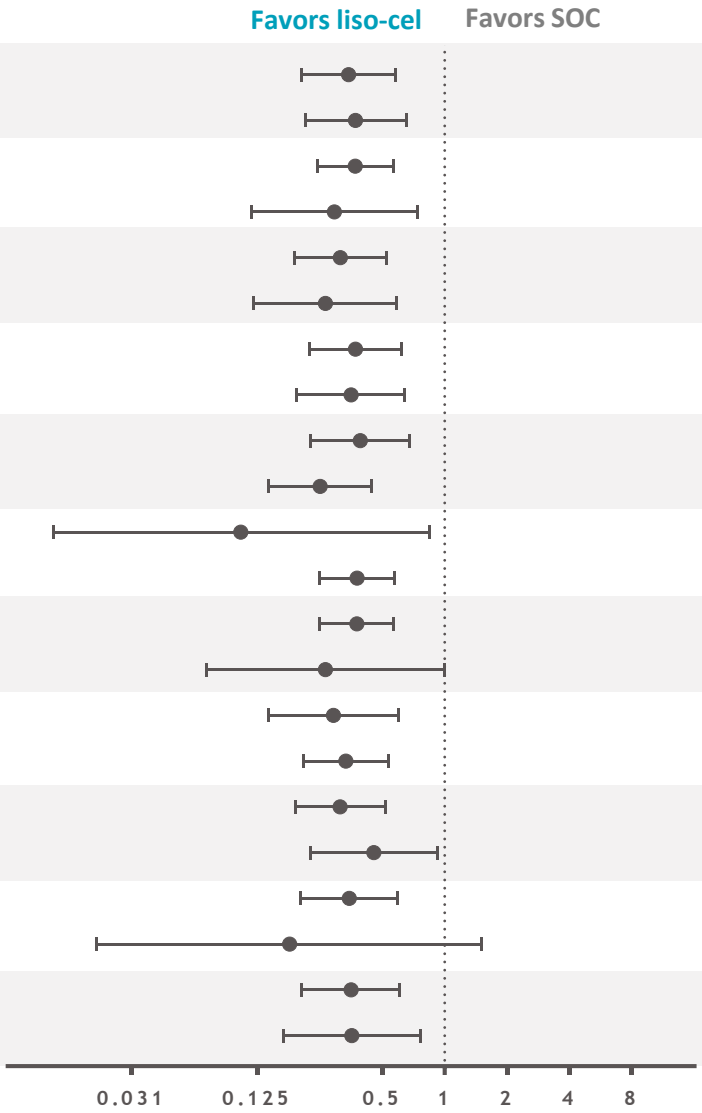
TRANSFORM: EFS per IRC by subgroup (ITT)



	Liso-cel, n/N	SOC, n/N	Stratified HR (95% CI)
sAAIPI: 0 or 1	23/56	39/55	0.34 (0.21—0.58)
sAAIPI: 2 or 3	21/36	32/37	0.37 (0.21—0.65)
Prior response status: refractory	37/67	57/70	0.37 (0.24—0.57)
Prior response status: relapse to last prior therapy	7/25	14/22	0.29 (0.12—0.74)
Age group, years: < 65	23/56	51/67	0.31 (0.19—0.52)
Age group, years: ≥ 65 to < 75	21/36	18/23	0.27 (0.12—0.59)
Sex: male	23/44	47/61	0.37 (0.22—0.62)
Sex: female	21/48	24/31	0.35 (0.19—0.64)
ECOG PS (at screening): 0	20/48	40/57	0.39 (0.23—0.68)
ECOG PS (at screening): 1	24/44	31/35	0.25 (0.14—0.44)
SPD: > 50 cm^2	3/10	9/10	0.10 (0.01—0.85)
SPD: ≤ 50 cm^2	38/77	59/76	0.38 (0.25—0.57)
Lactate dehydrogenase: < 500 unit/L	38/79	60/81	0.38 (0.25—0.57)
Lactate dehydrogenase: ≥ 500 unit/L	5/10	11/11	0.27 (0.07—1.00)
Prior CT response status: chemorefractory (PD, SD)	18/26	17/18	0.29 (0.14—0.60)
Prior CT response status: chemosensitive (PR, CR)	26/66	54/74	0.33 (0.21—0.54)
NHL type: DLBCL	25/60	46/58	0.31 (0.19—0.52)
NHL type: HGBCL	18/22	18/21	0.46 (0.23—0.92)
DLBCL subtype: DLBCL NOS de novo	23/53	39/50	0.35 (0.20—0.59)
DLBCL subtype: DLBCL transformed from indolent NHL	2/7	7/8	0.18 (0.02—1.51)
DLBCL subtype based on cell of origin: GCB	27/45	32/40	0.35 (0.21—0.61)
DLBCL subtype based on cell of origin: ABC, non-GCB	10/21	26/29	0.36 (0.17—0.76)

CT, chemotherapy; SD, stable disease; SPD, sum of the product of perpendicular diameters.

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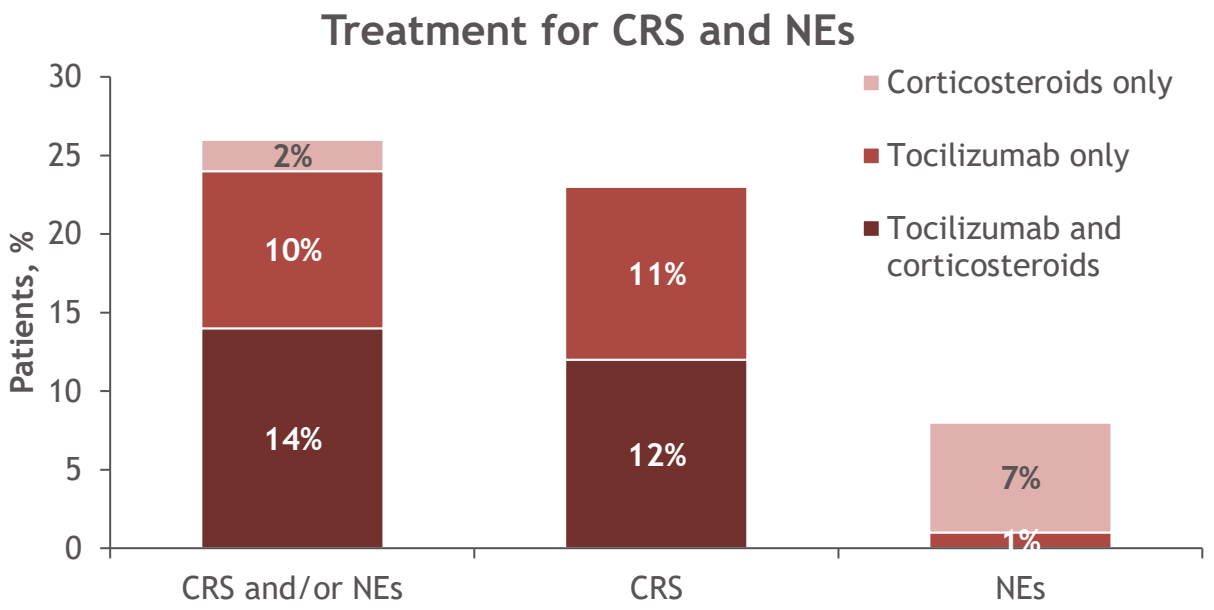
TRANSFORM: Primary Mediastinal B-cell Lymphoma

	Liso-cel arm (n = 8)	SOC arm (n = 9)
EFS		
Patients with events, n (%)	1 (12.5)	6 (67)
Median (95% CI) EFS, months	NR (11.0–NR)	2.2 (1.0–NR)
18-month EFS rate, % (95% CI)	87.5 (64.6–100.0)	33.3 (2.5–64.1)
ORR, n (%)	8 (100)	3 (33)
Two-sided 95% CI	63.1–100.0	7.5–70.1
CR rate, n (%)	8 (100)	3 (33)
Two-sided 95% CI	63.1–100.0	7.5–70.1
PFS		
Patients with events, n (%)	1 (12.5)	3 (33)
Median (95% CI) PFS, months	NR (11.0–NR)	NR (1.0–NR)
18-month PFS rate, % (95% CI)	87.5 (64.6–100.0)	66.7 (35.9–97.5)
OS		
Patients with events, n (%)	1 (12.5)	1 (11)
Median (95% CI) OS, months	NR (11.0–NR)	NR (17.9–NR)
18-month OS rate, % (95% CI)	87.5 (64.6–100.0)	83.3 (53.5–100.0)

- In the subgroup of patients with PMBCL, efficacy outcomes were similar to the overall population, favoring liso-cel over SOC

TRANSFORM: TEAEs of special interest (safety set)

Patients with CRS and NEs	Liso-cel arm (n = 92)
CRS,[a] n (%)	
Any grade	45 (49)
Grade 1	34 (37)
Grade 2	10 (11)
Grade 3	**1 (1)**
Grade 4/5	**0**
Time to onset, days, median (range)	5.0 (1–63)
Time to resolution, days, median (range)	4.0 (1–16)
NE,[b] n (%)	
Any grade	10 (11)
Grade 1	4 (4)
Grade 2	2 (2)
Grade 3	**4 (4)**
Grade 4/5	**0**
Time to onset, days, median (range)	11.0 (7–17)
Time to resolution, days, median (range)	4.5 (1–30)



- No vasopressors or prophylactic corticosteroids were used

Other adverse events of special interest	Liso-cel arm (n = 92)	SOC arm (n = 91)
Prolonged cytopenia[c]	40 (43)	3 (3)
Grade ≥ 3 infection	14 (15)	19 (21)

[a]Graded according to the Lee 2014 criteria; [b]Defined as investigator-identified neurological adverse events related to liso-cel. These were graded per the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03; [c]Grade ≥ 3 anemia, neutropenia, or thrombocytopenia at 35 days after liso-cel infusion for the liso-cel arm or at 35 days after the start of the last CT for the SOC arm. NE, neurological event.

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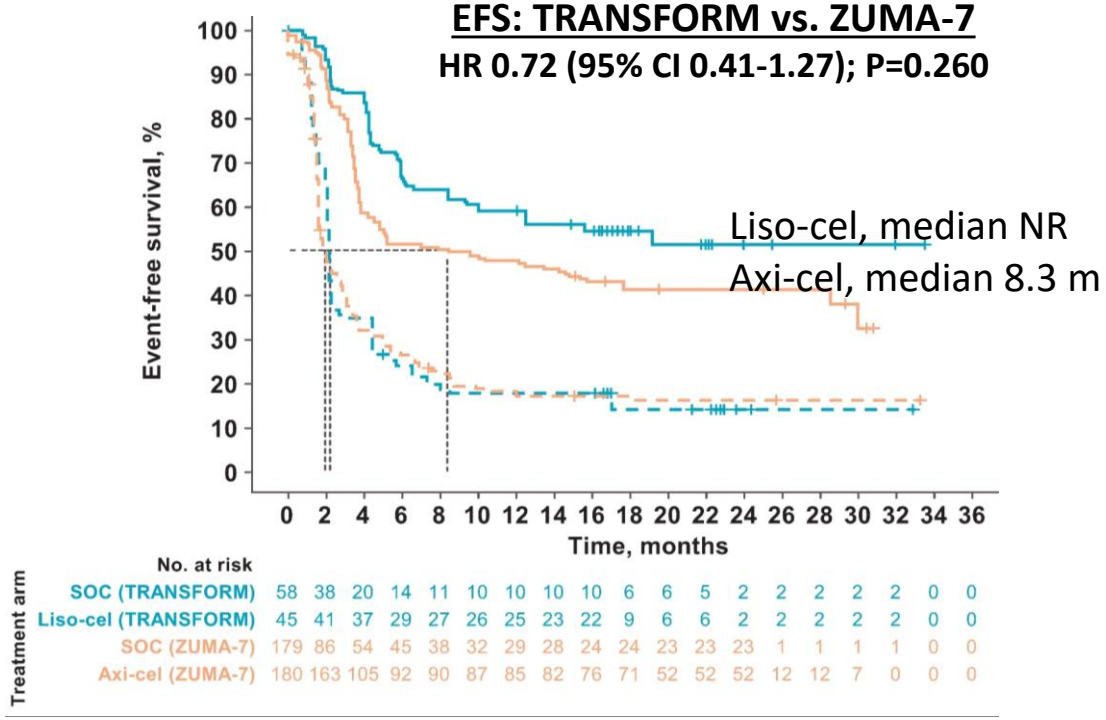
Matched Adjusted Indirect Comparison of TRANSFORM vs. ZUMA-7

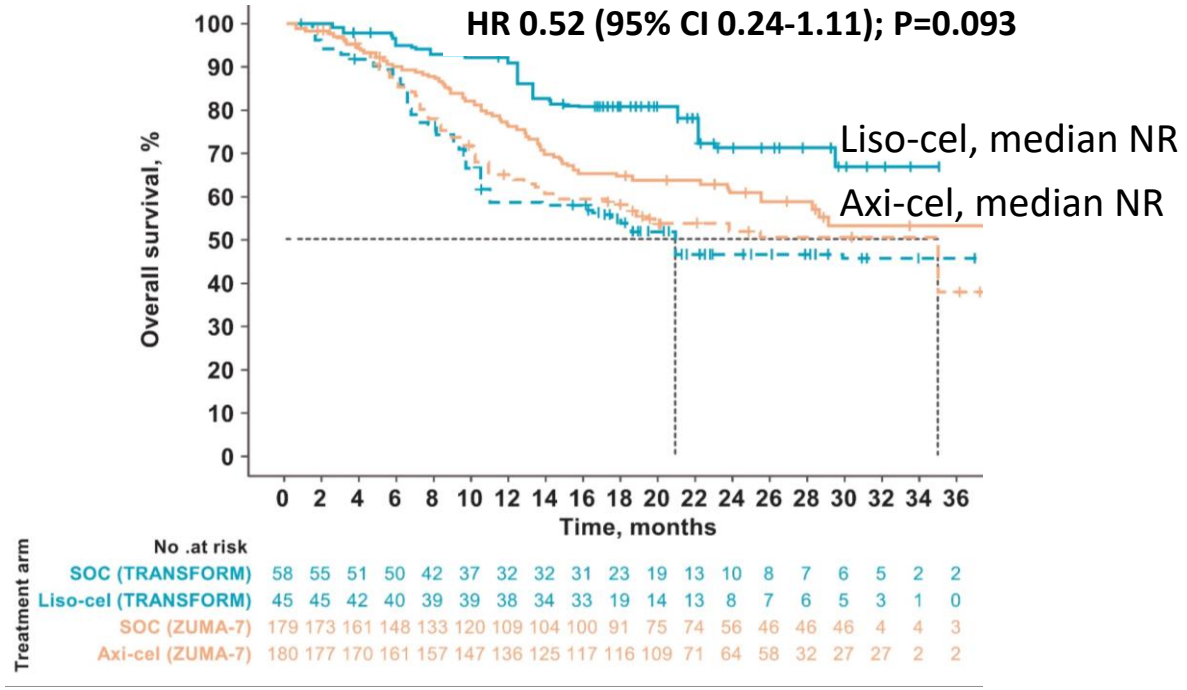
EFS: TRANSFORM vs. ZUMA-7

HR 0.72 (95% CI 0.41-1.27); P=0.260

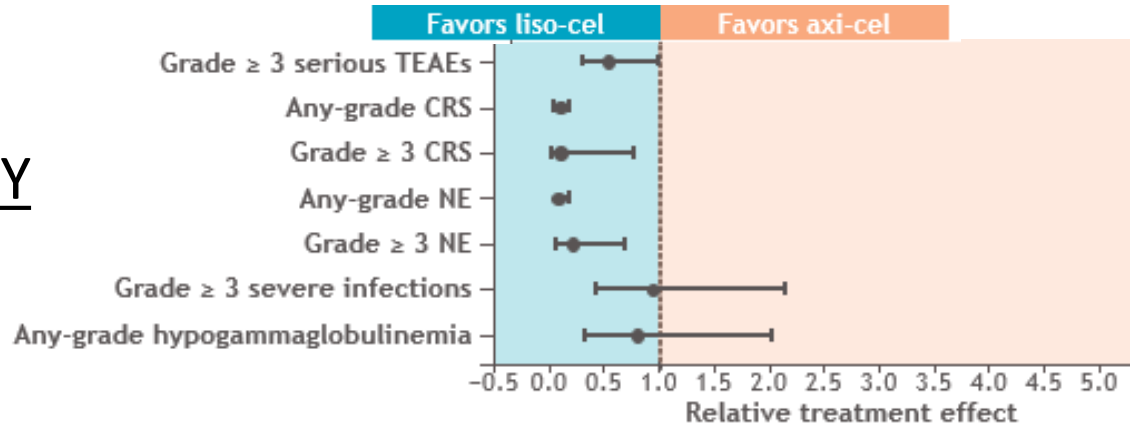


OS: TRANSFORM vs. ZUMA-7

HR 0.52 (95% CI 0.24-1.11); P=0.093



SAFETY



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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

Acknowledgments

- Patients and caregivers

- Investigators and study personnel at all participating study sites

Thank you for your attention!

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