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CAR-T for follicular lymphoma: next generation

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10th Postgraduate Lymphoma Conference

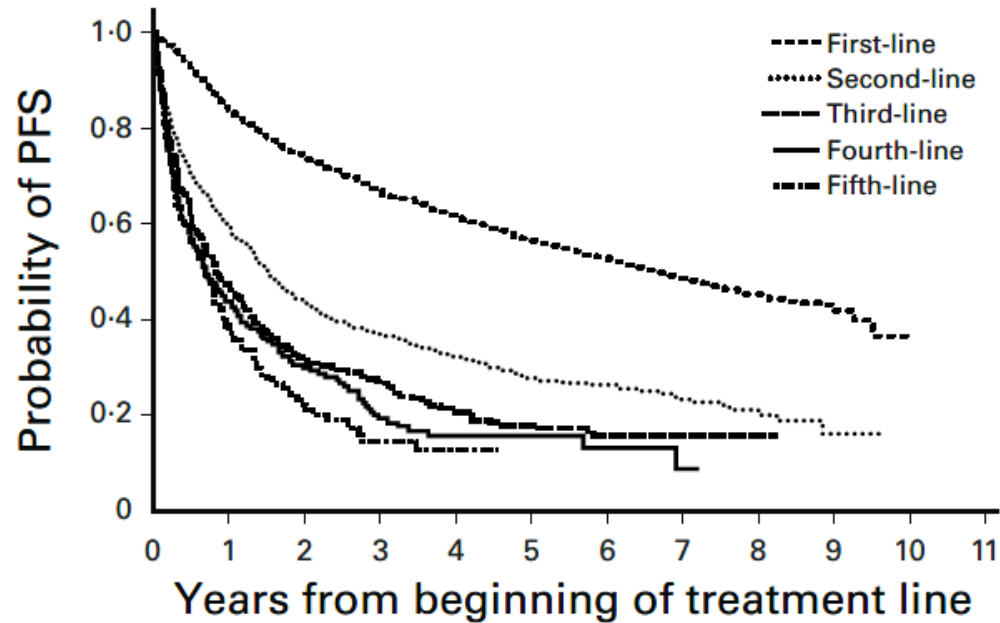
Venice, Hotel Monaco & Grand Canal, March 12-13, 2026

Disclosures

Disclosure	Company name
Research Support	Kite/Gilead, Allogene, Precision Biosciences, Adicet Bio, Sana Biotechnology, Cargo Therapeutics
Advisory Board / Consultant	Kite/Gilead, Sellas Life Sciences, Allogene, Adicet Bio, BMS, Fosun Kite, Caribou, Astellas Pharma, Morphosys, Janssen, Chimagen, ImmunoACT, Takeda, Synthekine, Carsgen, Appia Bio, GlaxoSmithKline, Galapagos, ModeX Therapeutics, Jazz Pharmaceuticals, ADC Therapeutics, BioOra Limited, Arovella Therapeutics, Merck, Pfizer, Poseida
Honoraria	MJH Life Sciences, PeerView, MD Education
Speaker's Bureau	None
Employment	None
Royalties	None
Stocks / Stock Options	None
Patents	Related to cell therapy

- I will discuss investigational use of CAR T-cell therapy

Outcomes in FL by line of therapy



No. at risk	0	1	2	3	4	5	6	7	8	9	10	11
First-line	2429	1916	1602	1381	1202	1035	869	635	329	96	1	0
Second-line	889	489	331	256	199	137	104	57	24	5	0	0
Third-line	438	181	109	78	50	30	18	5	1	0	0	0
Fourth-line	229	91	49	24	14	8	3	1	0	0	0	0
Fifth-line	123	42	19	9	5	0	0	0	0	0	0	0

Table I. Distribution of first-line to fifth-line treatment.

Treatment	Rx1 (n = 2429)	Rx2 (n = 889)	Rx3 (n = 438)	Rx4 (n = 229)	Rx5 (n = 121)
Rituximab	457 (19%)	279 (31%)	98 (22%)	35 (14%)	18 (15%)
R-chemo	1413 (58%)	345 (39%)	170 (39%)	79 (35%)	44 (36%)
Rituximab + anthracycline	828 (34%)	111 (12%)	51 (12%)	12 (5%)	8 (7%)
Rituximab + alkylator	424 (17%)	180 (20%)	89 (20%)	50 (22%)	25 (21%)
Rituximab + fludarabine	142 (6%)	43 (5%)	26 (6%)	11 (5%)	5 (4%)
Other R-chemo	19 (1%)	11 (1%)	4 (1%)	6 (3%)	6 (5%)
Chemotherapy	85 (3%)	77 (9%)	59 (13%)	37 (15%)	24 (20%)
BMT	6 (<1%)	17 (2%)	13 (3%)	17 (7%)	10 (8%)
Radiation (XRT)	261 (11%)	31 (7%)	31 (7%)	23 (10%)	15 (12%)
Radioimmunotherapy	10 (<1%)	45 (5%)	26 (6%)	11 (5%)	2 (2%)
Investigational	183 (8%)	45 (5%)	34 (8%)	21 (9%)	7 (6%)
Other therapies	14 (1%)	16 (2%)	7 (3%)	6 (5%)	1 (1%)

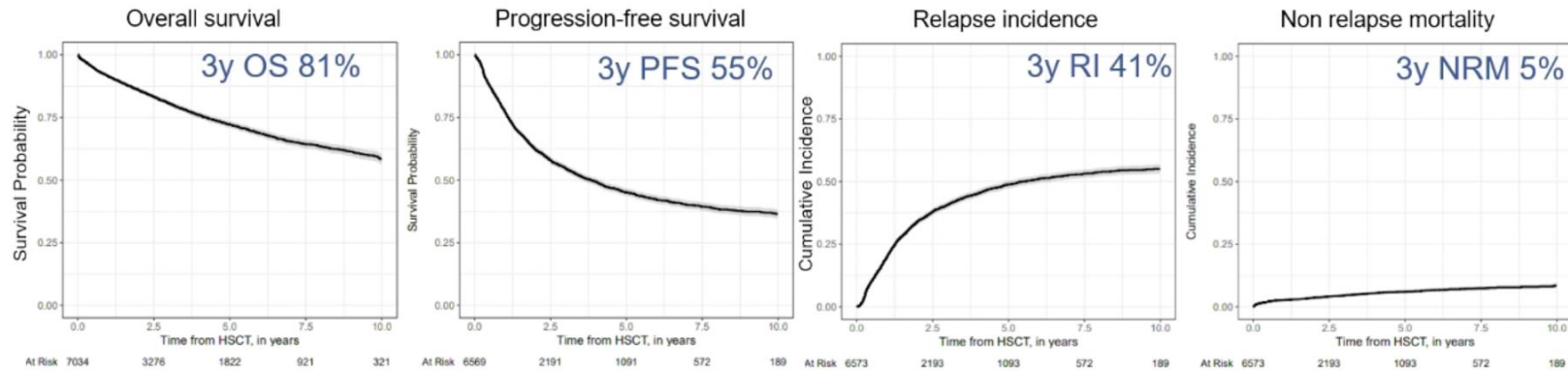
BMT, bone marrow transplant; R-chemo, rituximab plus chemotherapy; Rx, active treatment line; XRT, external beam radiation therapy.

Median PFS (yrs) 6.6 1.5 0.8 0.7 0.7

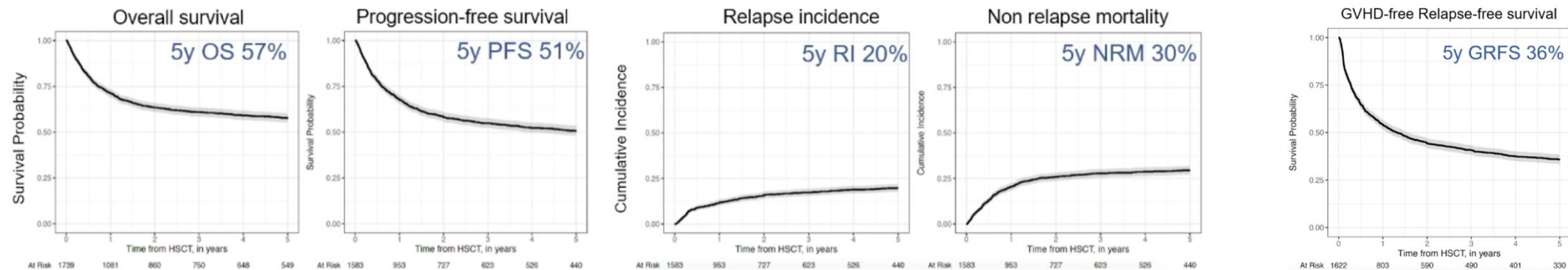
EBMT: Outcomes with autologous and allogeneic SCT in FL

- Auto- or Allo-SCT between 2010-2022 in FL (no transformation)

Autologous SCT (N = 7,034)



Allogeneic SCT (N = 1,739)



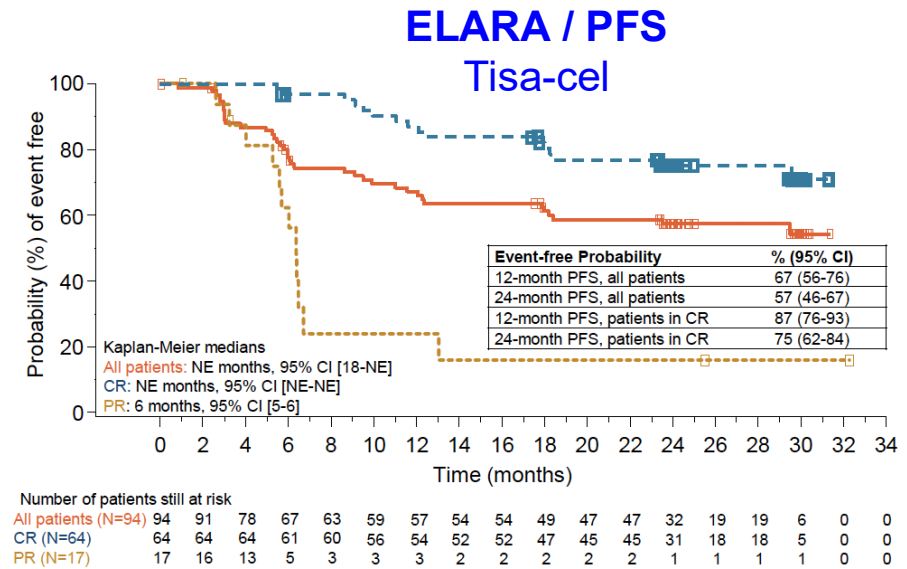
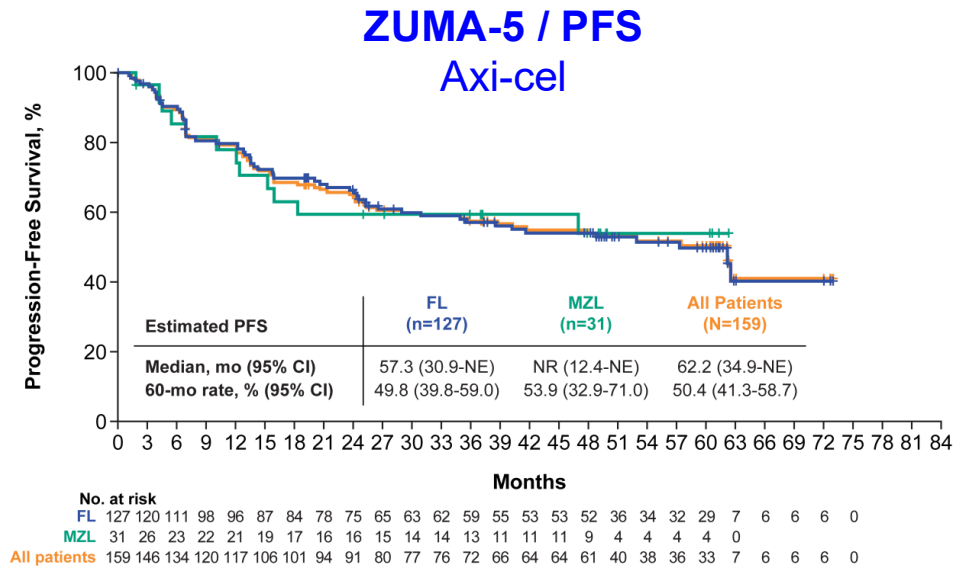
Autologous CD19 CAR T products approved in US for R/R FL

Characteristic	ZUMA-5	ELARA	TRANSCEND-FL
CAR-T product	Axi-cel	Tisa-cel	Liso-cel (3L+)
Histology	FL grade 1-3a	FL grade 1-3a	FL grade 1-3a
N	127	97	107
Median age	60	57	62
GELF criteria (%)	51	n/a	53
High-risk FLIPI (%)	44	60	57
Median prior lines	3	4	3
POD24 (%)	56	63	55
Refractory to last Rx (%)	69	78	67
Refs	Jacobson et al. <i>Lancet Oncol</i> 2022 Neelapu et al. <i>J Clin Oncol</i> 2025	Fowler et al. <i>Nat Med</i> 2022 Dreyling et al. <i>Blood</i> 2024	Morschhauser et al. <i>Nat Med</i> 2024 Ahmed et al. <i>ASH</i> 2025

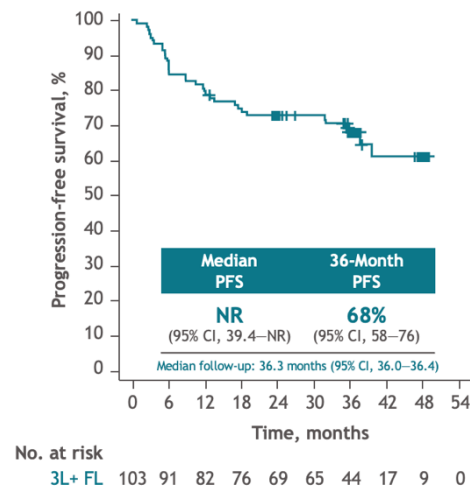
CD19 CAR T in FL: Safety and Response Rates

Characteristic	ZUMA-5	ELARA	TRANSCEND-FL
CAR-T product	Axi-cel	Tisa-cel	Liso-cel (3L+)
N	127	97	107
CRS, Any Gr/Gr ≥ 3 (%)	78/6	49/0	59/1
NE, Any Gr/Gr ≥ 3 (%)	56/15	37/3	16/2
ORR (%)	94	86	97
CR rate (%)	79	68	94
Refs	Jacobson et al. <i>Lancet Oncol</i> 2022 Neelapu et al. <i>J Clin Oncol</i> 2025	Fowler et al. <i>Nat Med</i> 2022 Dreyling et al. <i>Blood</i> 2024	Morschhauser et al. <i>Nat Med</i> 2024 Ahmed et al. <i>ASH</i> 2025

PFS outcomes with CD19 CAR-T in R/R FL



TRANSCEND FL / PFS Liso-cel

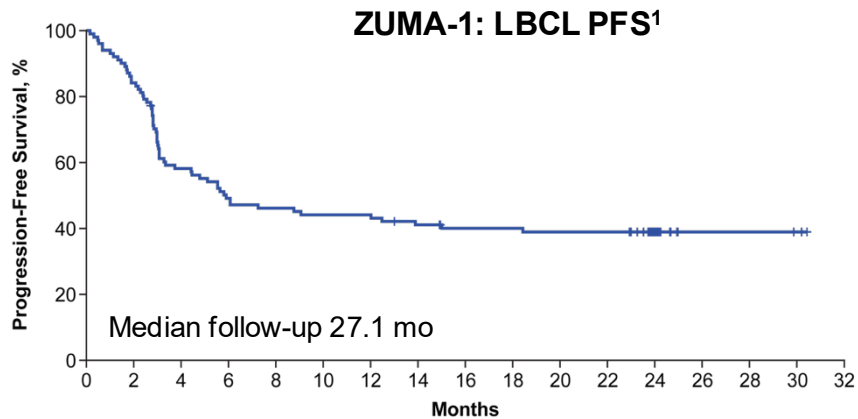
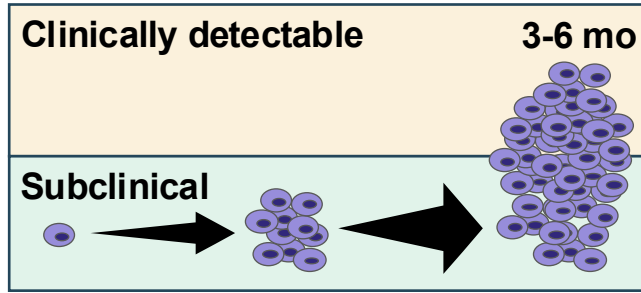


- Is CAR T cell therapy curative for FL?

Neelapu et al. *ASH 2024*, Abstract 864
 Dreyling M et al. *ASH 2022*, Abstract 608
 Ahmed et al. *ASH 2025*, Abstract 467

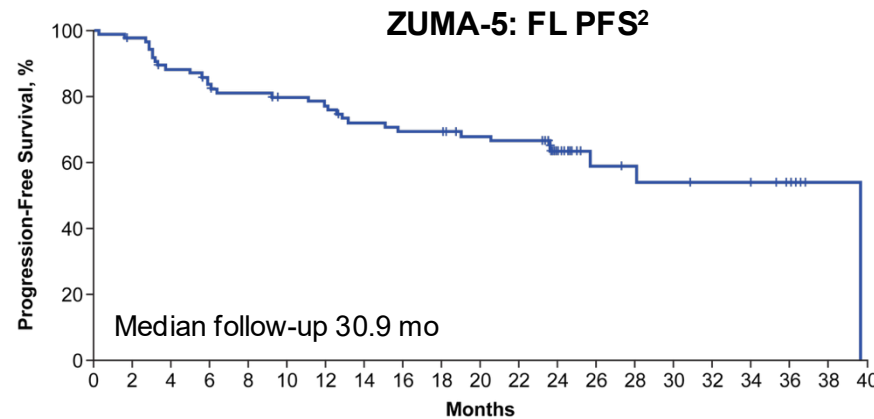
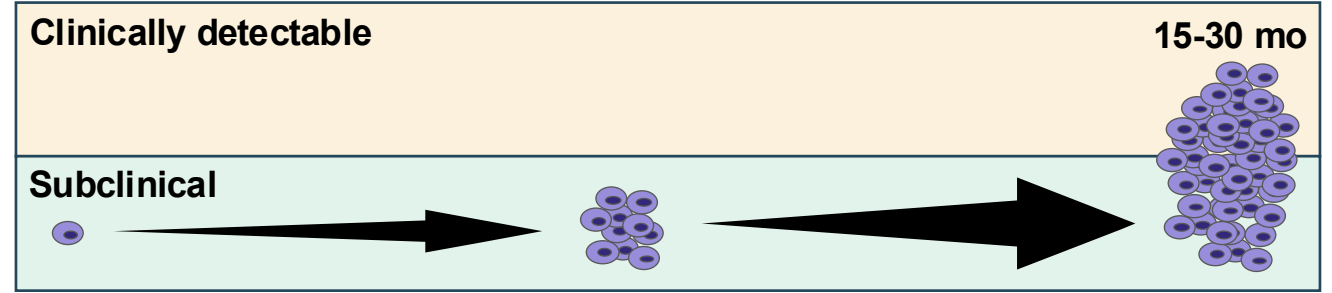
Difference in relapse pattern between LBCL and FL

LBCL



- With curative therapies in LBCL, most PFS events are PD-related, occurring early and resulting in a plateau within 2 years

FL



- In FL, PFS events are likely to occur over a longer period, including PD- and non-PD-related events, with no obvious plateau within 2 years
- Lymphoma-specific assessment of survival may be necessary to determine curative potential in FL
- Outcomes from ZUMA-5 after a median follow-up of ≥ 5 years, including lymphoma-specific survival analyses

ZUMA-5: Five-year analysis methods

- The 5-year analysis occurred after the median follow-up of all enrolled patients reached ≥ 60 months post-infusion (N=159; FL, n=127; MZL, n=31)

Events	PFS	Lymphoma-specific PFS	Competing risks
Disease progression	Yes	Yes	No
Death due to lymphoma	Yes	Yes	No
Death due to study treatment	Yes	Yes	No
Death due to other causes	Yes	No	Yes

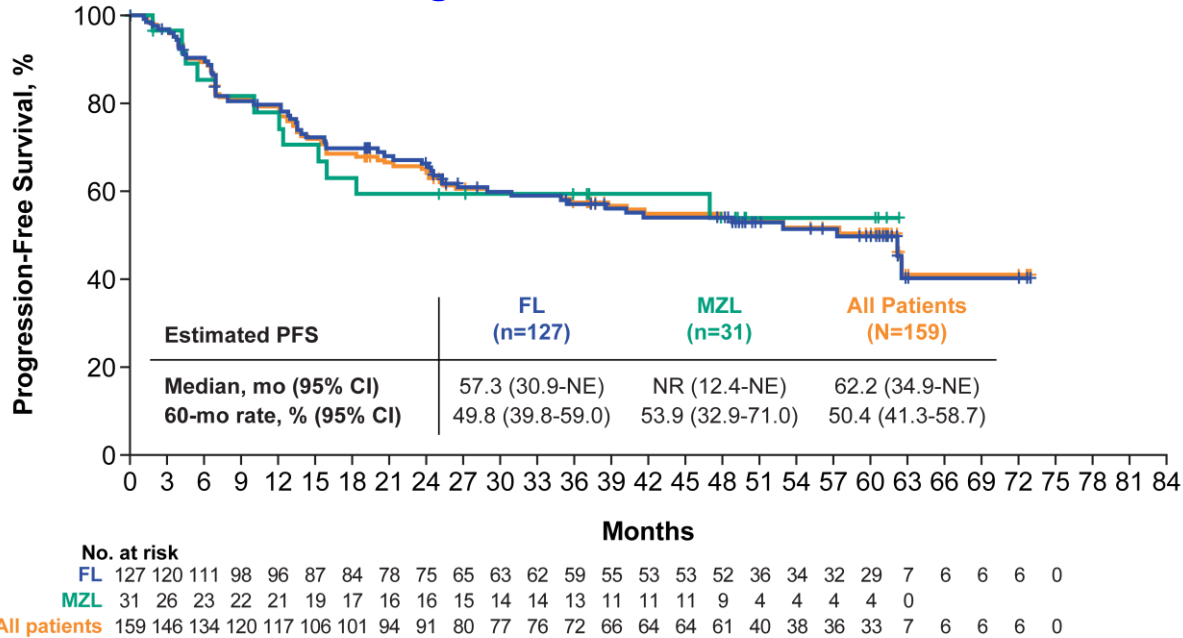
ZUMA-5: Five-year analysis methods

- The 5-year analysis occurred after the median follow-up of all enrolled patients reached ≥ 60 months post-infusion (N=159; FL, n=127; MZL, n=31)

Events	PFS	Lymphoma-specific PFS	Competing risks	OS	Lymphoma-specific survival	Competing risks
Disease progression	Yes	Yes	No	No	No	No
Death due to lymphoma	Yes	Yes	No	Yes	Yes	No
Death due to study treatment	Yes	Yes	No	Yes	Yes	No
Death due to other causes	Yes	No	Yes	Yes	No	Yes

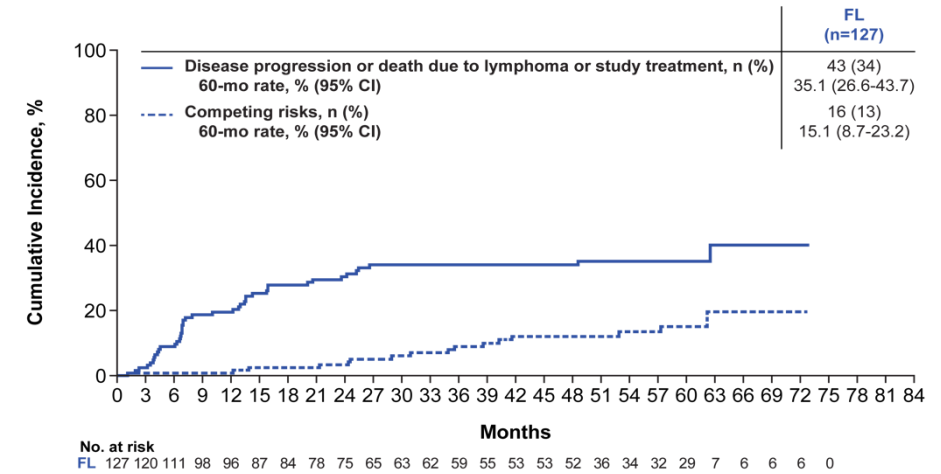
ZUMA-5: PFS and Lymphoma-specific PFS in FL

Progression-Free Survival

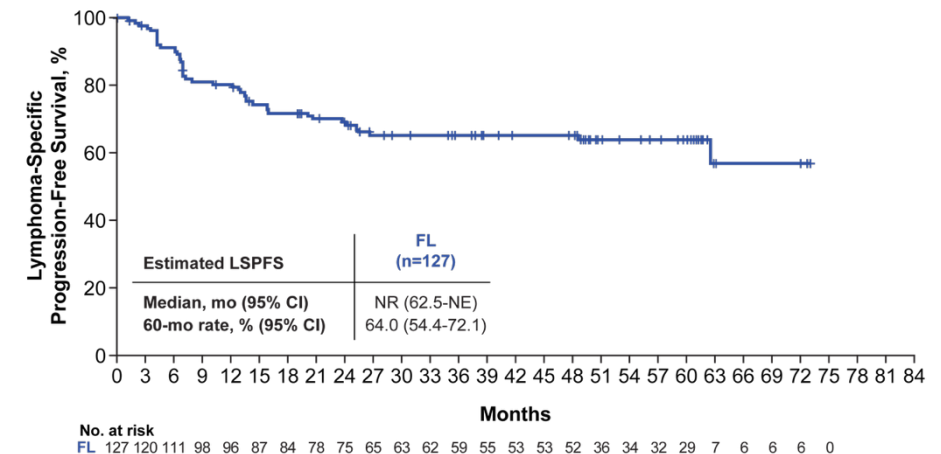


- 60-month PFS rate in FL was 49.8%
- 60-month lymphoma-specific PFS was 64.0%

Cumulative Incidence of Progression and Lymphoma-Specific Death in FL

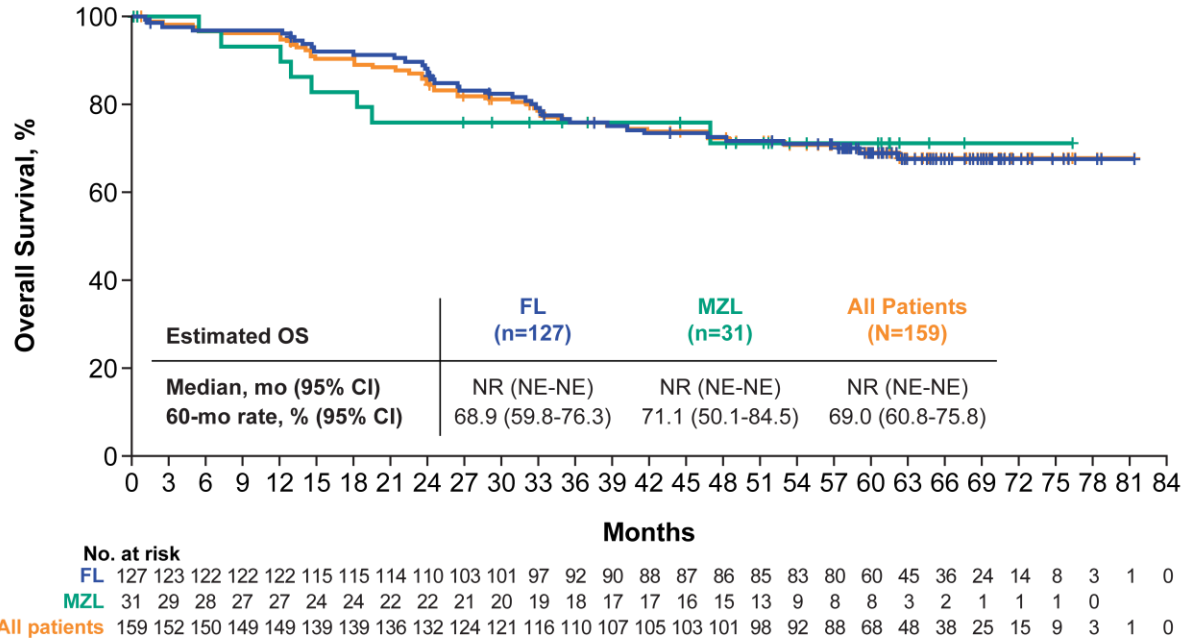


Lymphoma-Specific PFS

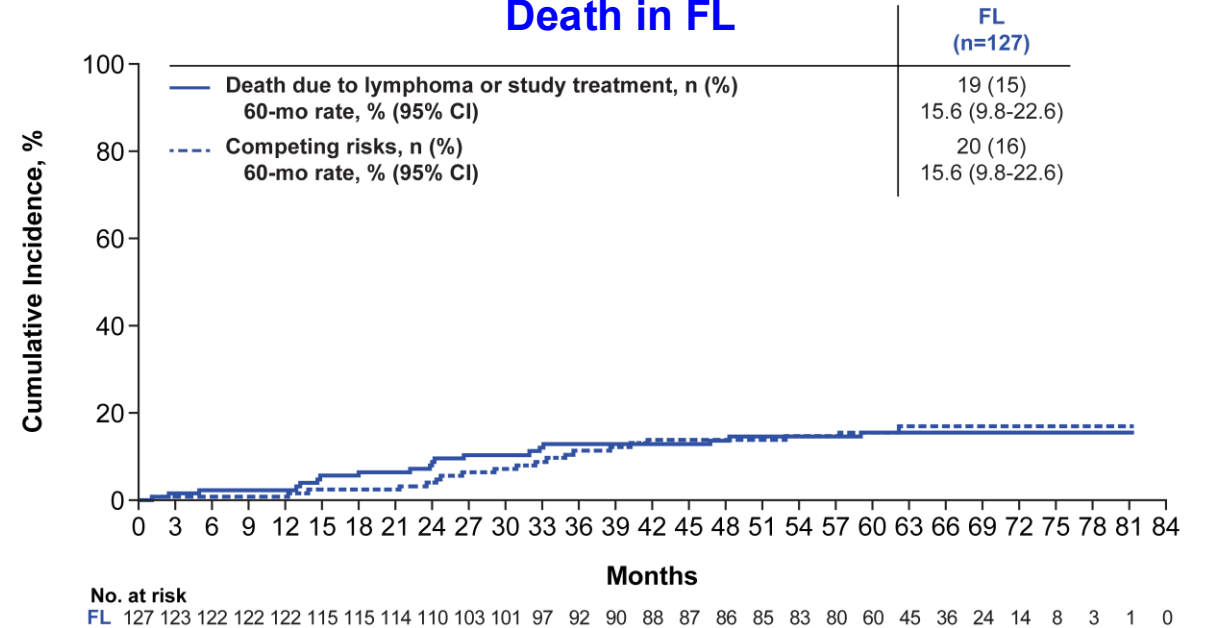


ZUMA-5: OS and Cumulative incidence of lymphoma-specific death

Overall Survival



Cumulative Incidence of Lymphoma-Specific Death in FL

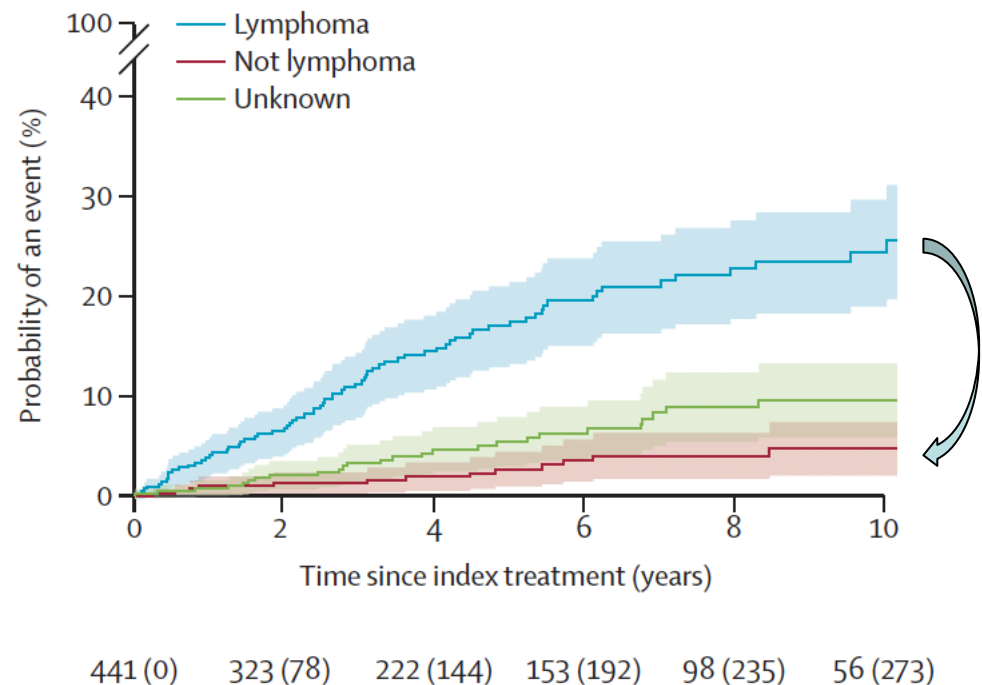


- Median OS was not reached
- The rate of lymphoma-specific death at 60 months in FL was 15.6%

Cumulative incidence of lymphoma-specific death: ZUMA-5 vs. Historical

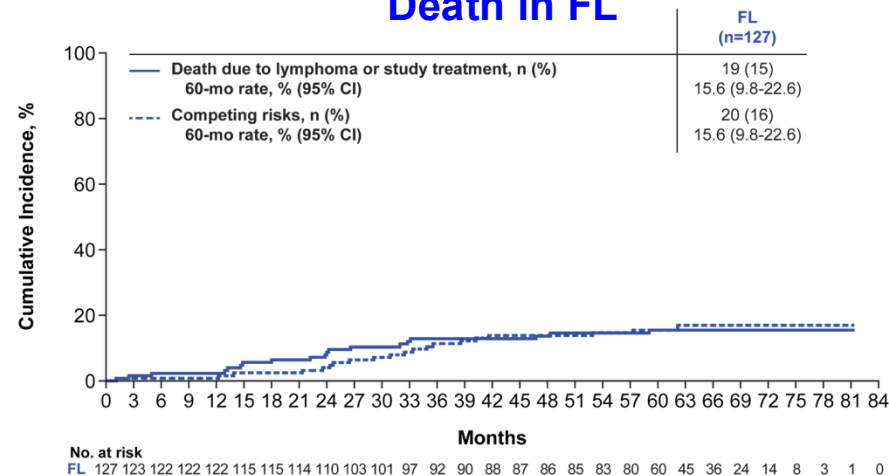
Treatment patterns and outcomes of patients with relapsed or refractory follicular lymphoma receiving three or more lines of systemic therapy (LEO CReWE): a multicentre cohort study

Carla Casulo, Melissa C Larson, Julianne J Lunde, Thomas M Habermann, Izidore S Lossos, Yucal Wang, Loretta J Nastoupil, Christopher Strouse, Dai Chihara, Peter Martin, Jonathon B Cohen, Brad S Kahl, W Richard Burack, Jean L Koff, Yong Mun, Anthony Masaquel, Mei Wu, Michael C Wei, Ashwini Shewade, Jia Li, James Cerhan, Christopher R Flowers, Brian K Link, Matthew J Maurer

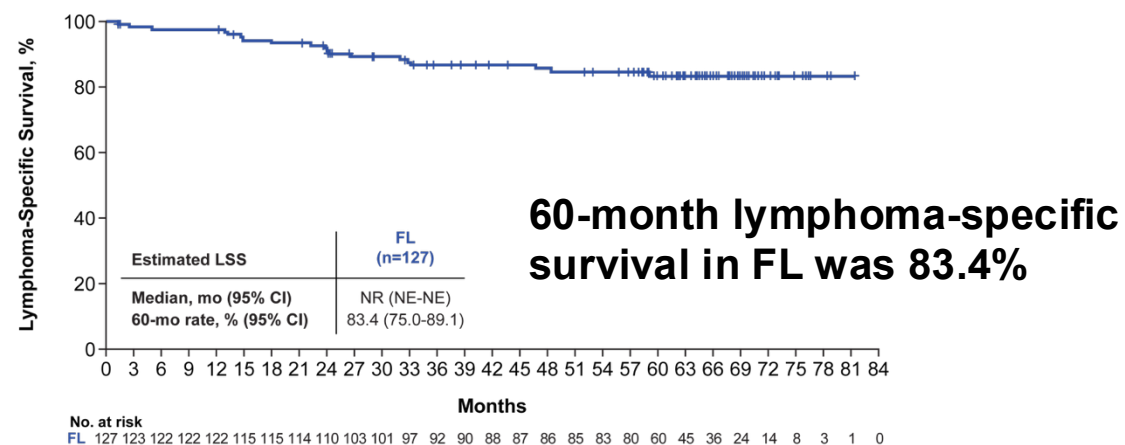


Casulo C et al. *Lancet Haematol* 2022 Apr;9(4):e289-e300

Cumulative Incidence of Lymphoma-Specific Death in FL



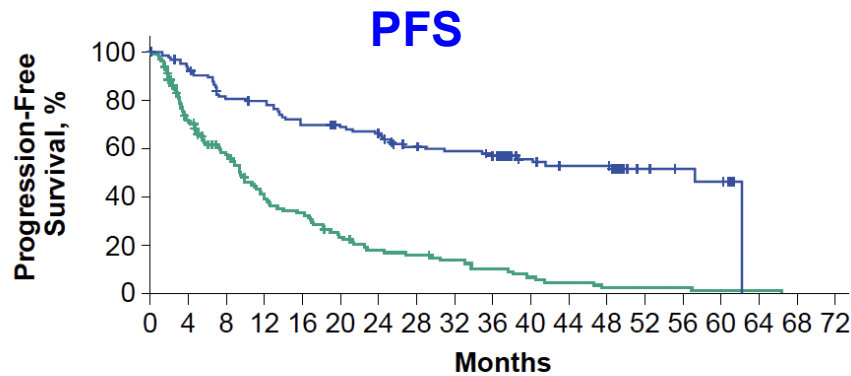
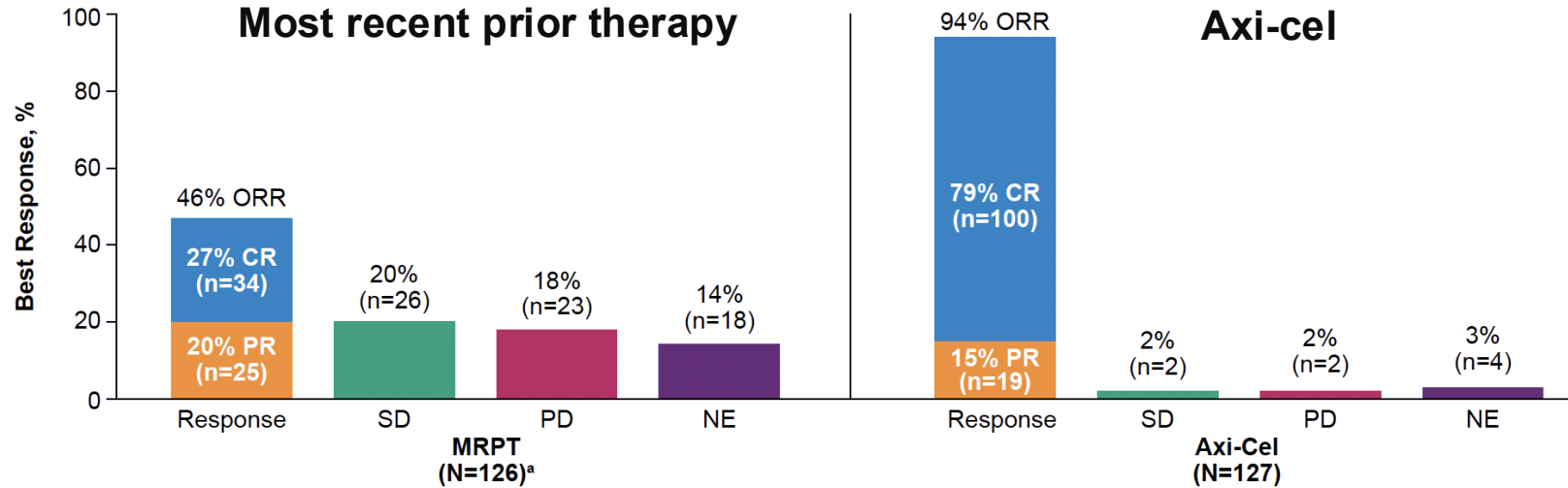
Lymphoma-Specific Survival



Neelapu et al. *ASH* 2024, Abstract 864
Neelapu et al. *J Clin Oncol* 2025

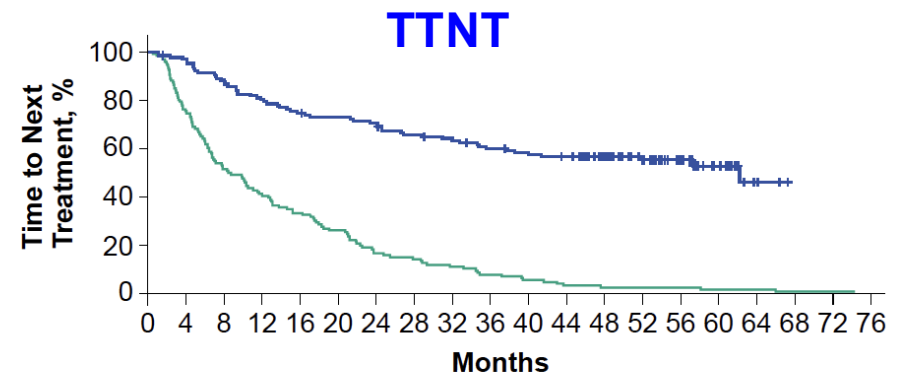
Intrapatent analysis from ZUMA-5: Axi-cel vs prior SOC therapy in FL

Best response



No. at Risk

Months	0	4	8	12	16	20	24	28	32	36	40	44	48	52	56	60	64	68	72
Axi-Cel	127	115	98	96	84	80	75	64	61	57	42	38	38	12	10	9	1	0	
MRPT ^a	126	84	61	41	34	23	17	15	12	9	6	4	2	2	2	1	1	0	



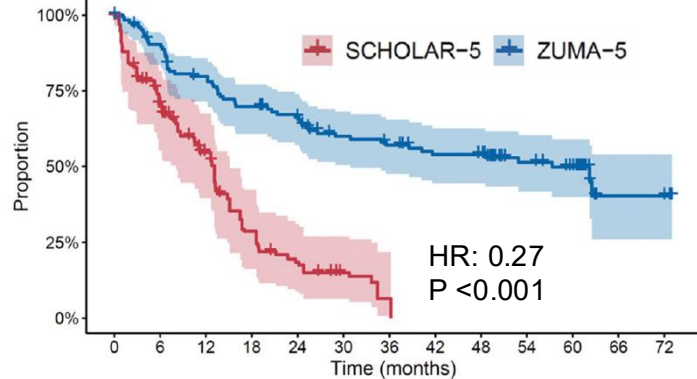
No. at Risk

Months	0	4	8	12	16	20	24	28	32	36	40	44	48	52	56	60	64	68	72	76
Axi-Cel	127	122	111	102	94	91	88	81	78	72	69	66	52	40	27	14	5	0		
MRPT ^a	126	95	65	52	42	33	21	18	14	10	7	4	3	3	3	2	2	1	1	0

- Similar outcomes were observed in POD24 group

ZUMA-5 vs. SCHOLAR-5 comparison of outcomes at 5 years in R/R FL after ≥ 2 lines of therapy

Progression-free survival

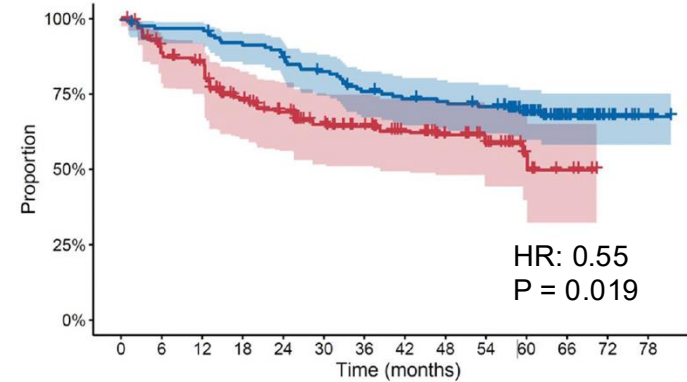


Number at risk

SCHOLAR-5	89	45	23	11	7	3	1	0	0	0	0	0
ZUMA-5	127	111	96	84	75	63	59	53	52	34	29	6

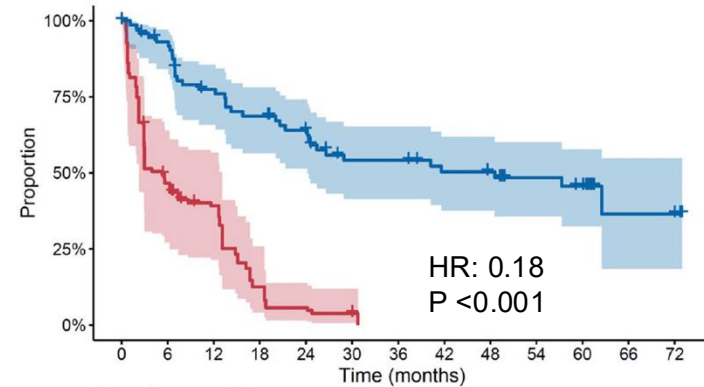
3rd line+

Overall survival



Number at risk

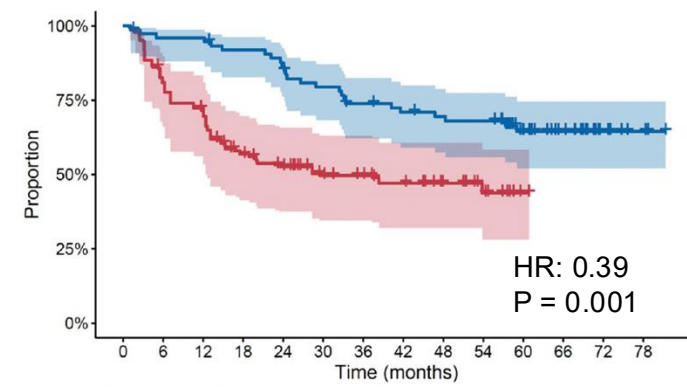
SCHOLAR-5	128	110	105	80	71	60	50	43	33	27	9	2	0	0
ZUMA-5	127	122	122	115	110	101	92	88	86	83	60	36	14	3



Number at risk

SCHOLAR-5	50	15	11	3	2	1	0	0	0	0	0	0
ZUMA-5	75	66	53	47	40	31	31	27	26	17	15	4

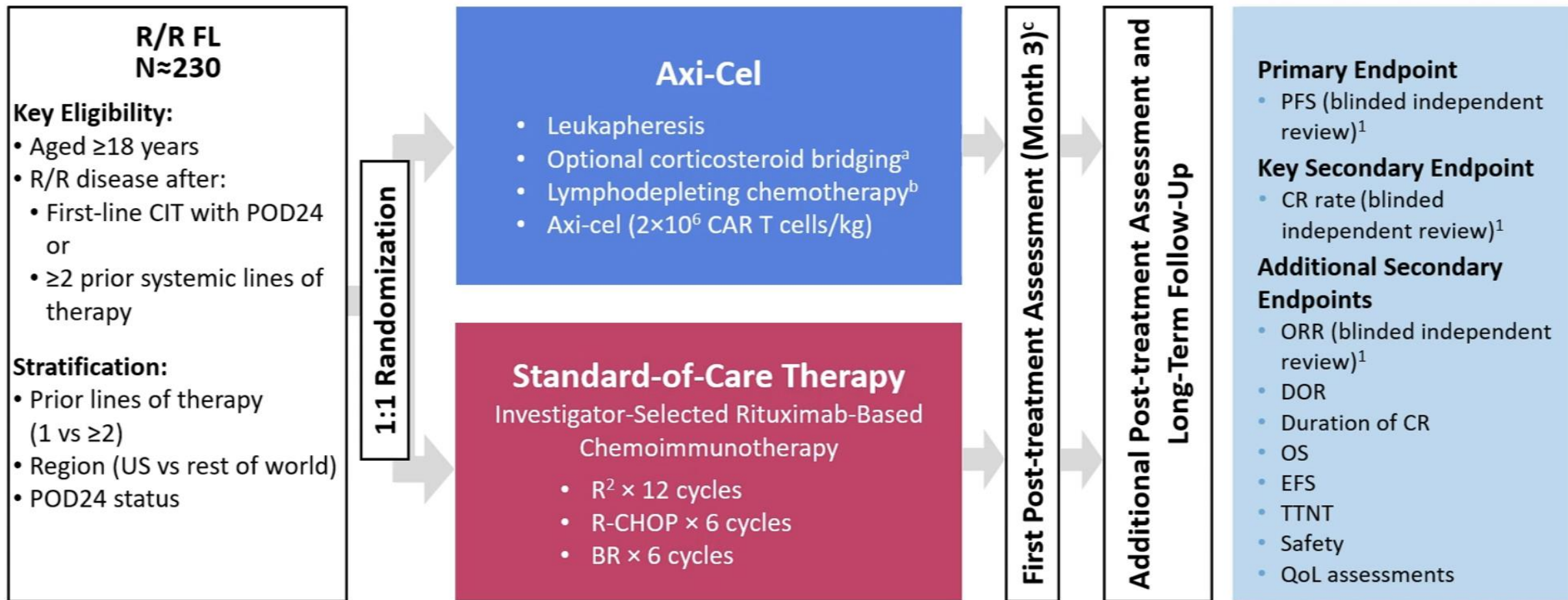
4th line+



Number at risk

SCHOLAR-5	74	58	52	36	31	23	19	17	14	9	2	0	0	0
ZUMA-5	75	71	71	67	63	57	52	49	47	46	31	21	8	3

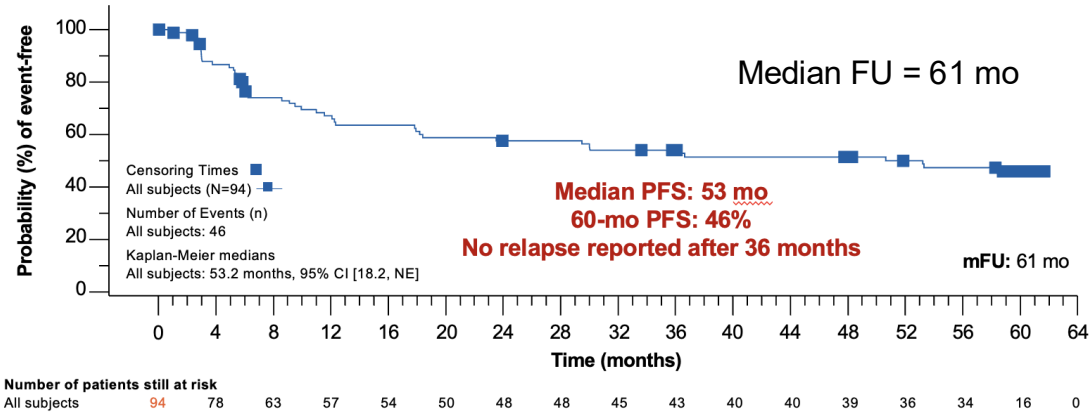
ZUMA-22: Study design



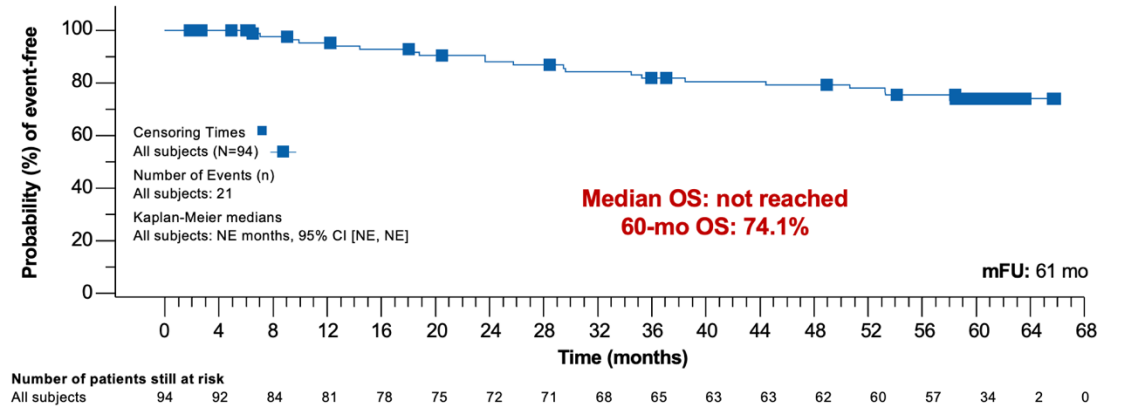
PFS and OS in ELARA and TRANSCEND-FL

Progression-free survival

ELARA

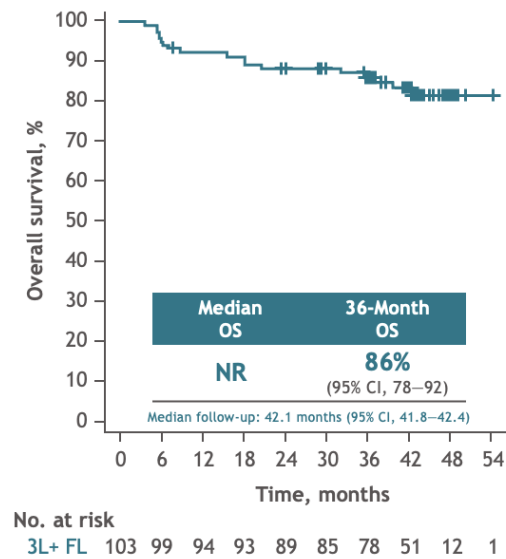
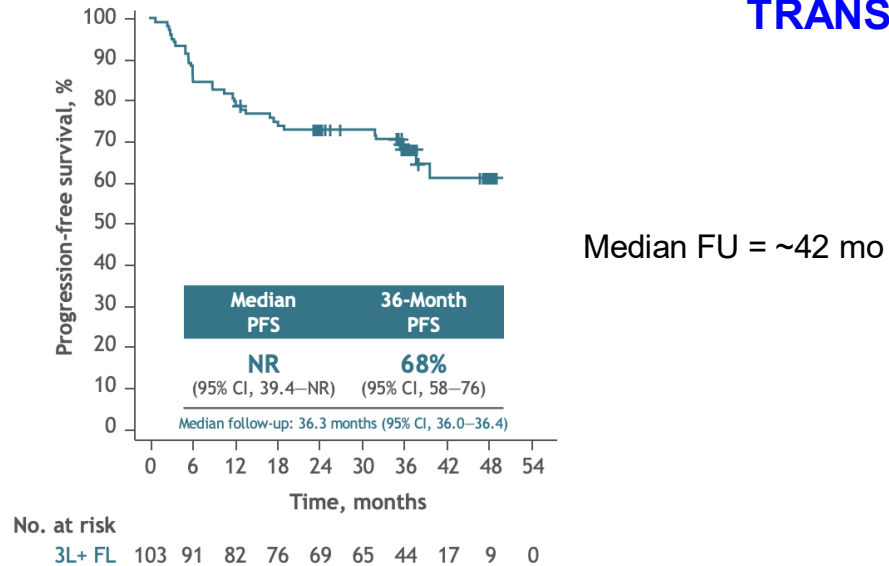


Overall survival



Schuster et al. ASH 2025; Abstract 468

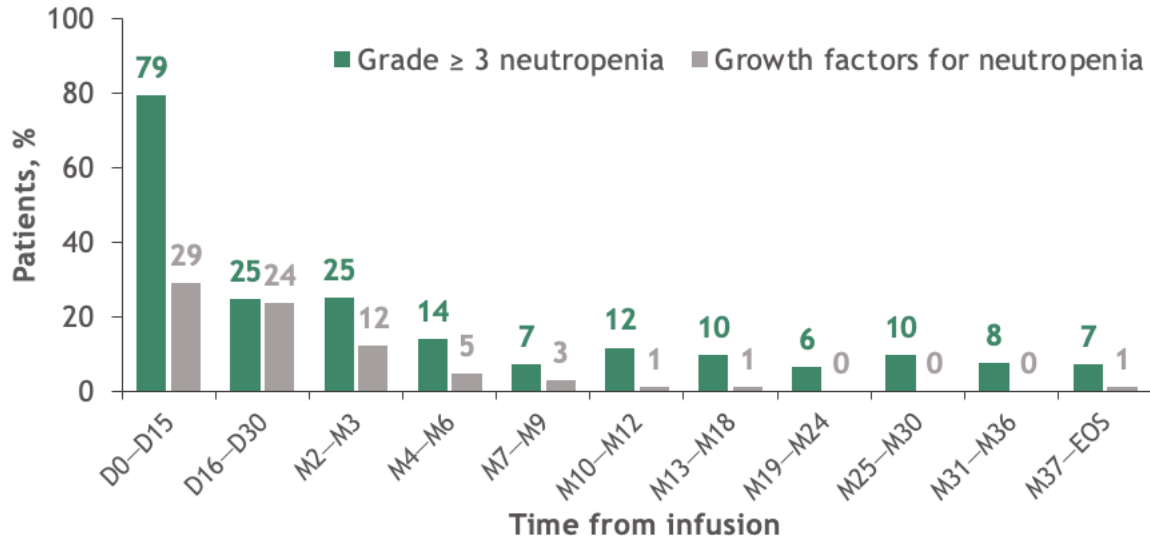
TRANSCEND-FL



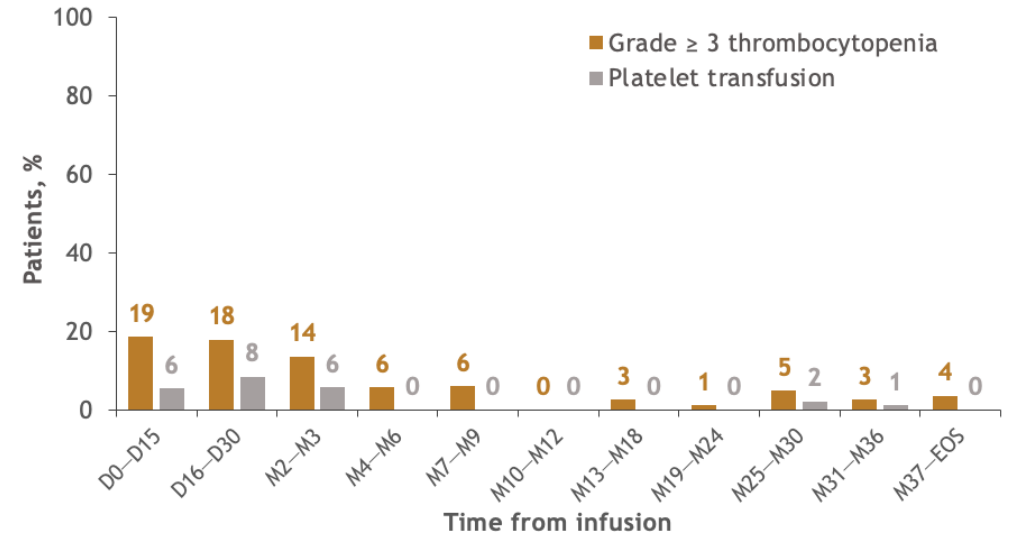
Ahmed et al. ASH 2025; Abstract 467

TRANSCEND-FL: Long-term safety

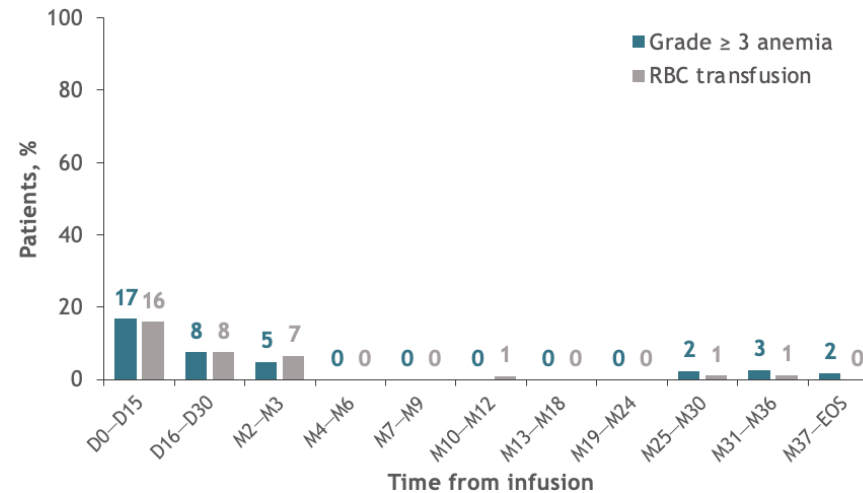
Neutropenia / Growth factor



Thrombocytopenia / Transfusion

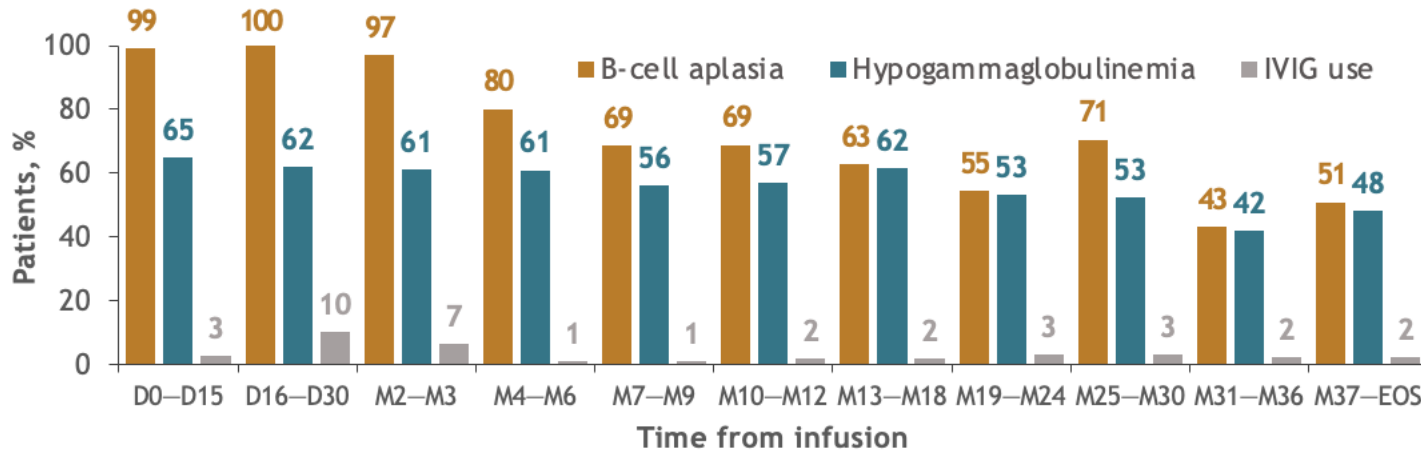


Anemia / Transfusion

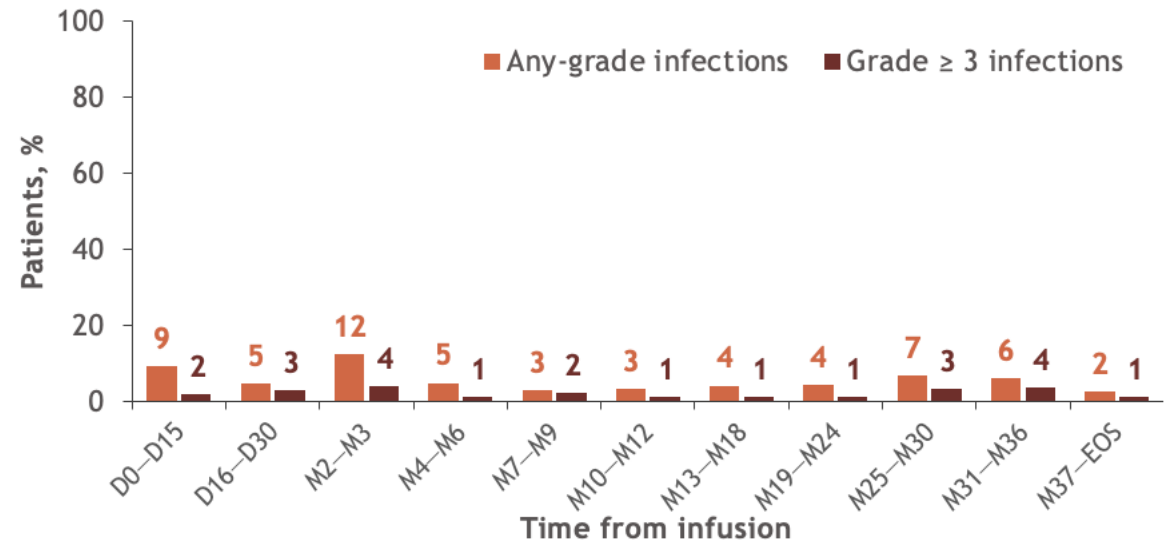


TRANSCEND-FL: Long-term safety

B-cell aplasia / Hypogammaglobulinemia / IVIG

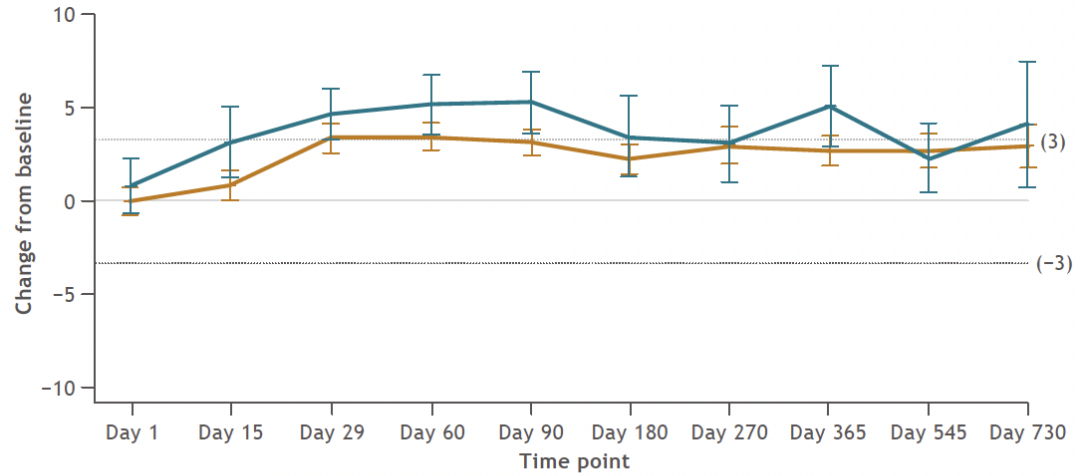


Any grade / Grade ≥ 3 infections



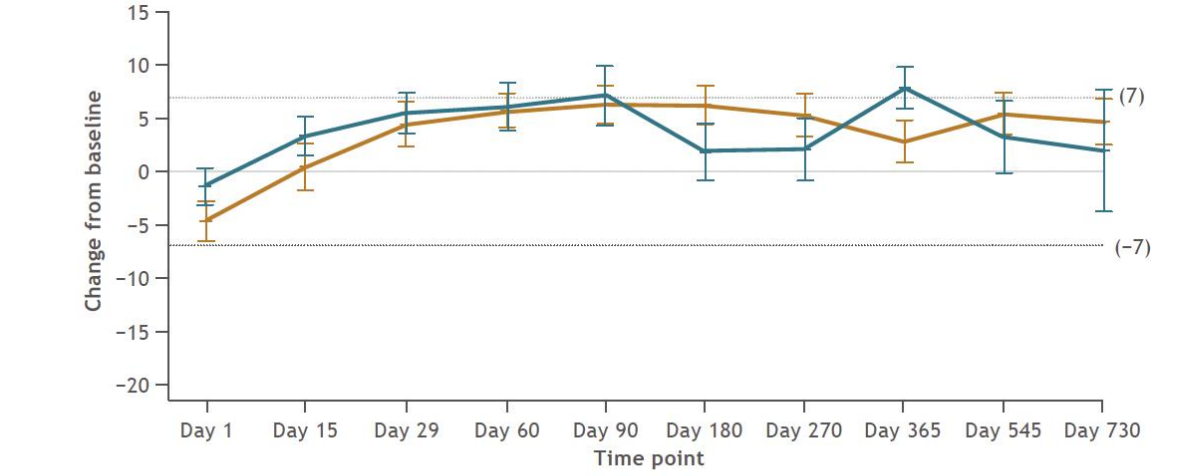
TRANSCEND-FL: Patient-reported outcomes showed early and durable improvement in health-related quality of life

FACT-LymS



	Day 1	Day 15	Day 29	Day 60	Day 90	Day 180	Day 270	Day 365	Day 545	Day 730
2L FL	19	16	18	16	18	18	15	15	17	15
3L+ FL	88	88	91	92	92	85	86	82	75	70

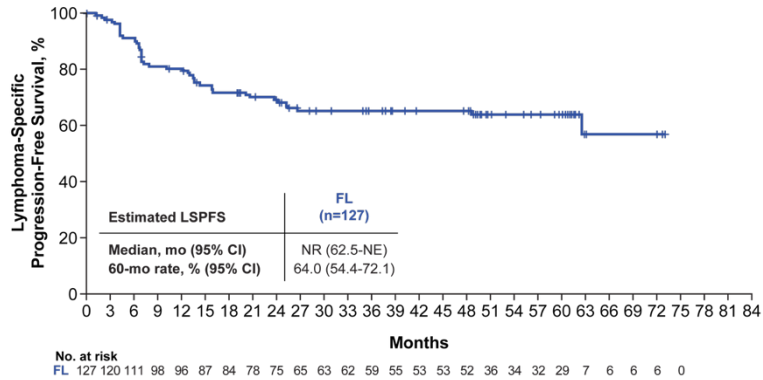
EQ VAS



No. of patients	Day 1	Day 15	Day 29	Day 60	Day 90	Day 180	Day 270	Day 365	Day 545	Day 730
2L FL	16	15	17	15	17	17	14	15	16	16
3L+ FL	86	83	86	88	87	82	80	78	67	66

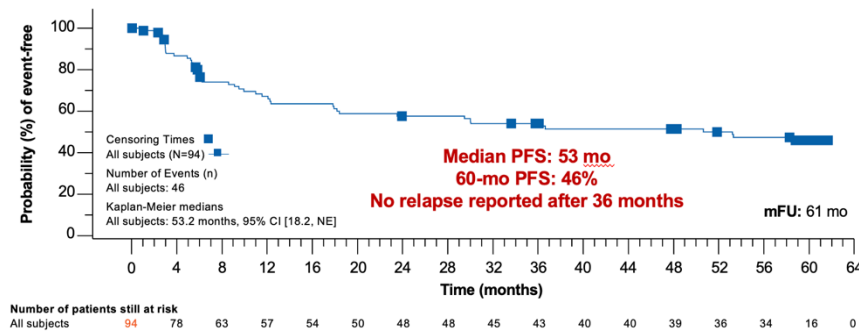
CD19 CAR T cell therapy is potentially curative in R/R FL

ZUMA-5: Lymphoma-Specific PFS



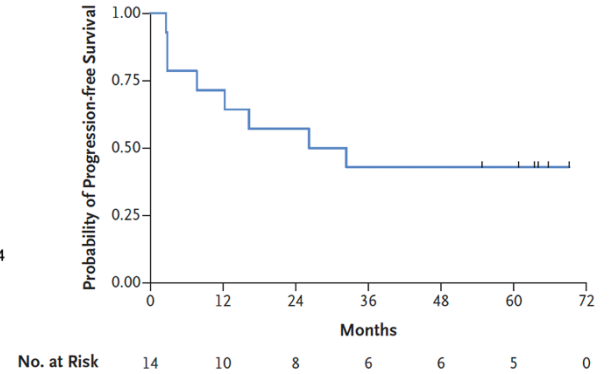
Neelapu et al. ASH 2024, Abstract 864

ELARA: PFS



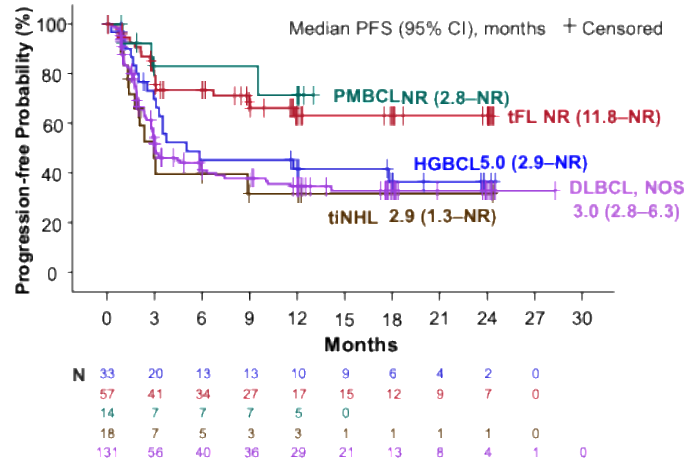
Schuster et al. ASH 2025; Abstract 468

U Penn / CTL019: FL PFS



Chong EA et al. *N Engl J Med.* 2021 Feb 18;384(7):673-674

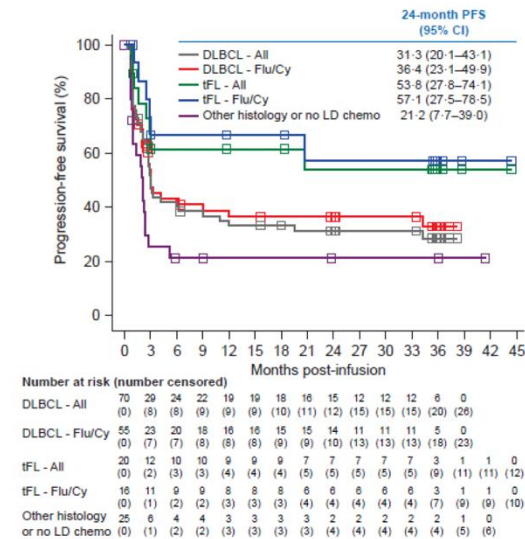
TRANSCEND tFL PFS



Abramson et al. ASH 2019, Abstract 241

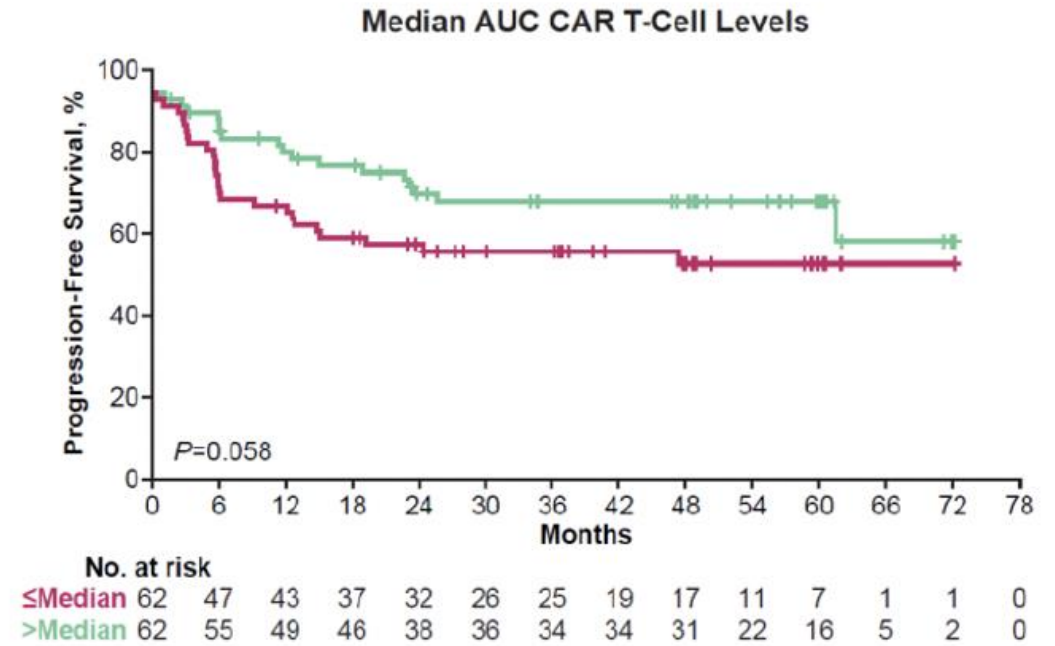
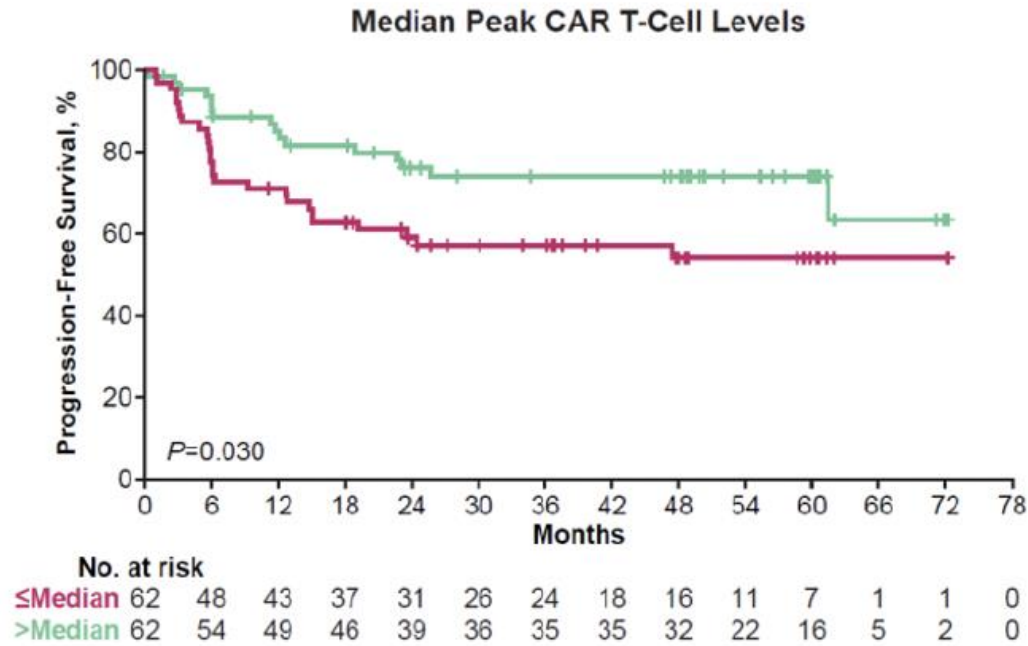
Cure in
~60% of R/R FL

JULIET tFL PFS



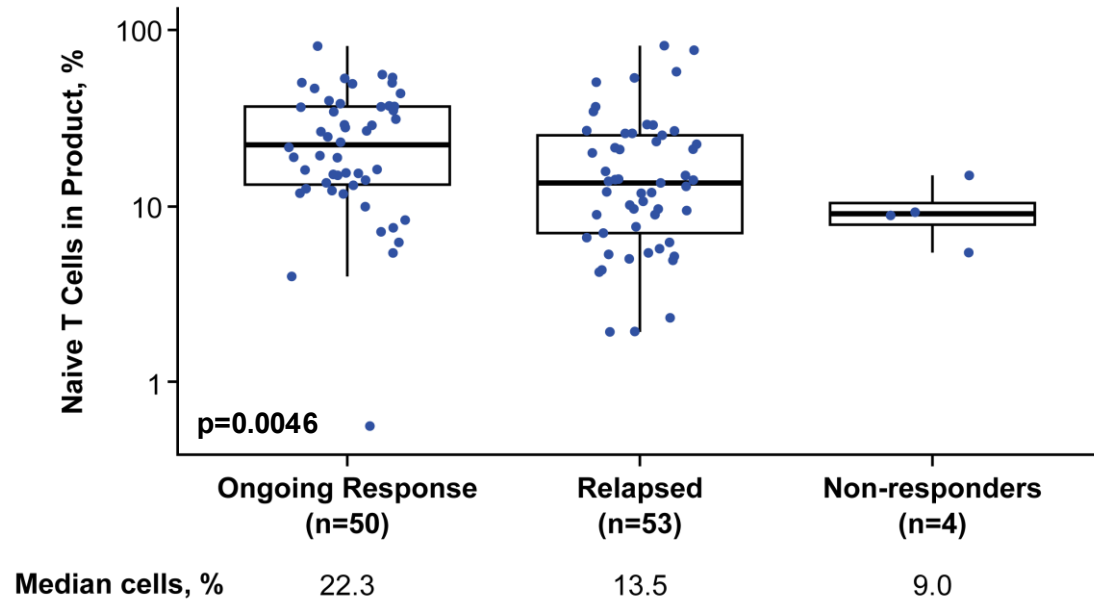
Schuster SJ et al, *Lancet Oncol* 2021 Oct;22(10):1403-1415

ZUMA-5: Peak CAR-T expansion and AUC₀₋₂₈ associated with PFS in FL

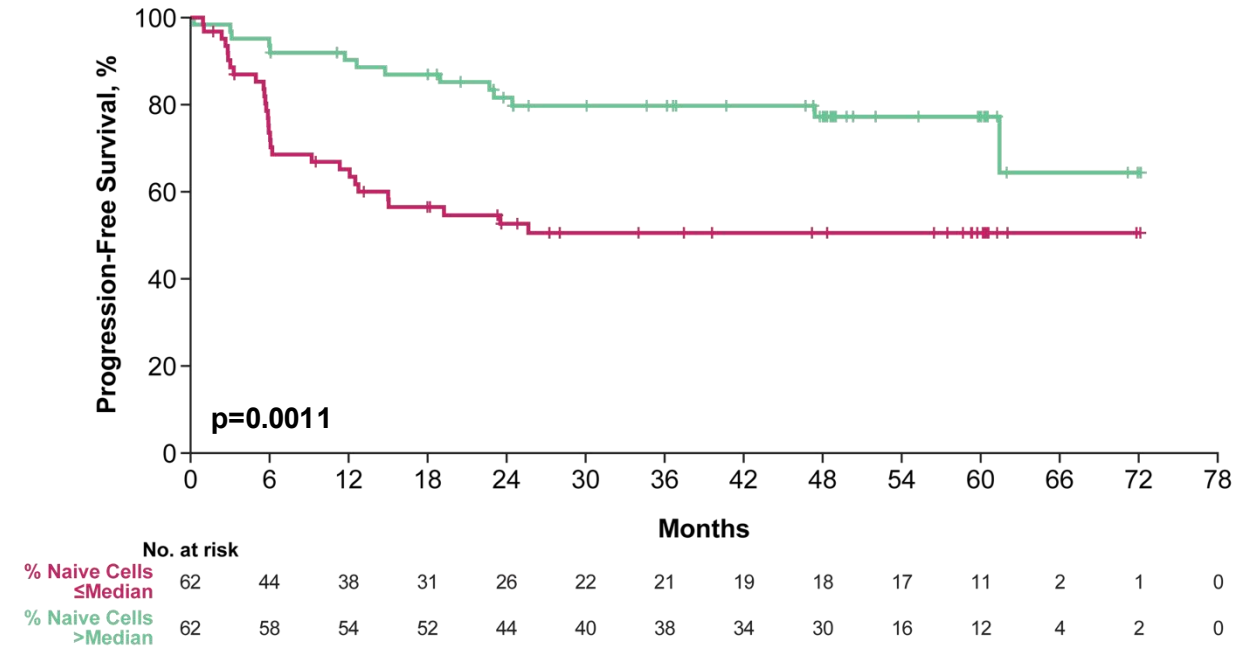


ZUMA-5: Impact of naïve T cells in product in FL

Naive T Cells in Product



PFS by Median Naive T Cells in Product



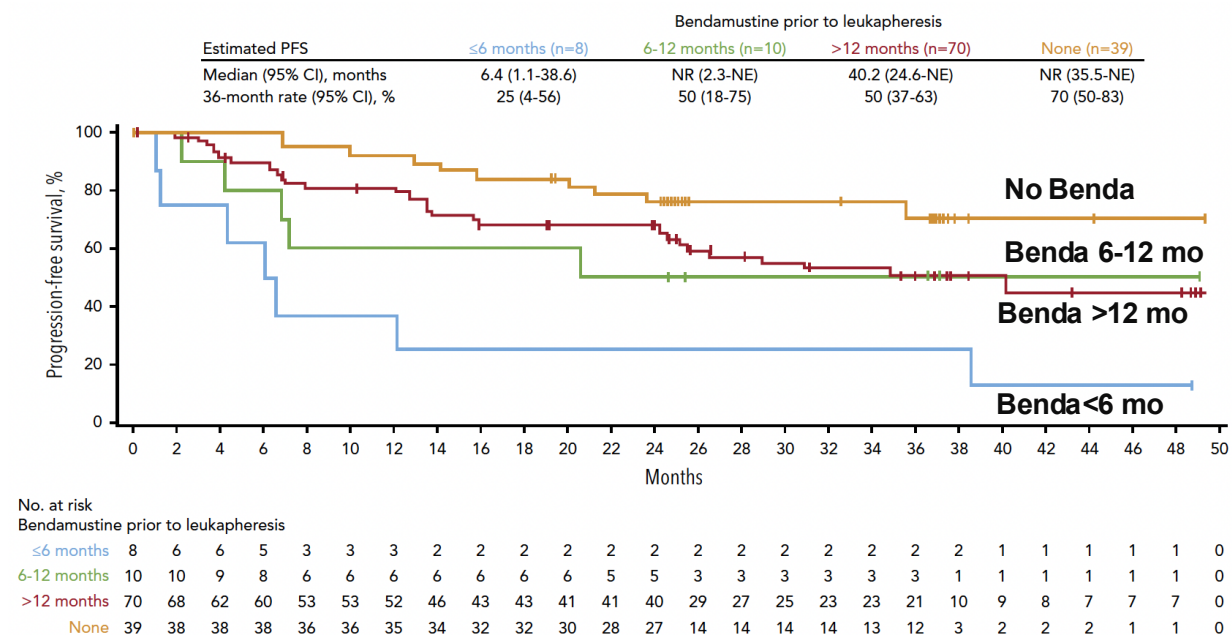
- Among patients with FL, a higher percentage of naïve T cells (CCR7+CD45RA+) in axi-cel product, indicative of naïve phenotype, was associated with ongoing response at 60 months and longer PFS

Impact of bendamustine exposure pre-apheresis in FL

ZUMA-5: Propensity score matching in FL

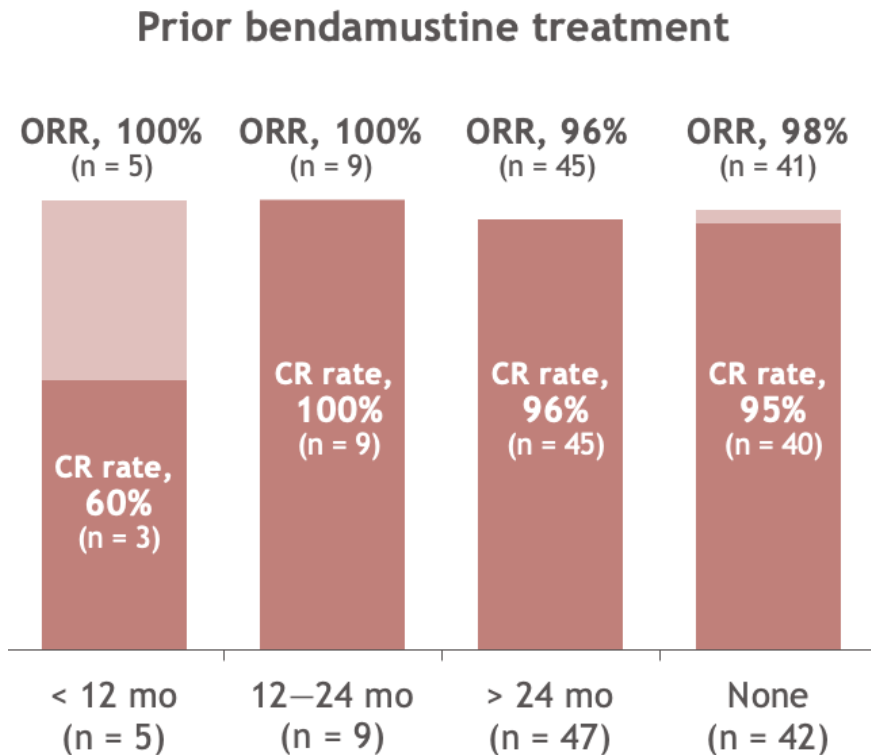
Bendamustine Use Prior to Leukapheresis	≤12 Months (n=15)	None (n=15)	P Value
ORR, n (%)	12 (85.7)	15 (100.0)	.2241
CR	8 (57.1)	12 (80.0)	.2451
Ongoing response at 36 months, n (%)	4 (28.6)	9 (60.0)	.1394
Grade ≥3 neurologic events, n (%)	1 (6.7)	2 (13.3)	1
Grade ≥3 CRS, n (%)	1 (6.7)	2 (13.3)	1
Peak CAR T-cell level, median (IQR), cells/μL	17.1 (3.0-48.4)	42.5 (5.7-62.6)	.3046
AUC CAR T-cell level, median (IQR), cells/μL×days	181.1 (45.3-414.4)	507.0 [99.1-745.9]	.1485
Total number of CD4 cells infused, median (IQR), n×10 ⁶	149.3 (70.0-176.1)	121.1 (93.0 -205.0)	.5409
Total number of CD8 cells infused, median (IQR), n×10 ⁶	131.9 (90.0-183.5)	130.4 (92.2-176.0)	.8743
Total number of CCR7+CD45RA+ T cells infused, median (IQR), n×10⁶	21.7 (17.4-45.5)	44.9 (24.0-89.7)	.1781
IFN-γ in co-culture, median (IQR), pg/mL	2871.0 (2272.5-4360.0)	6973.0 (5348.0-10403.0)	.001665

ZUMA-5: PFS in FL

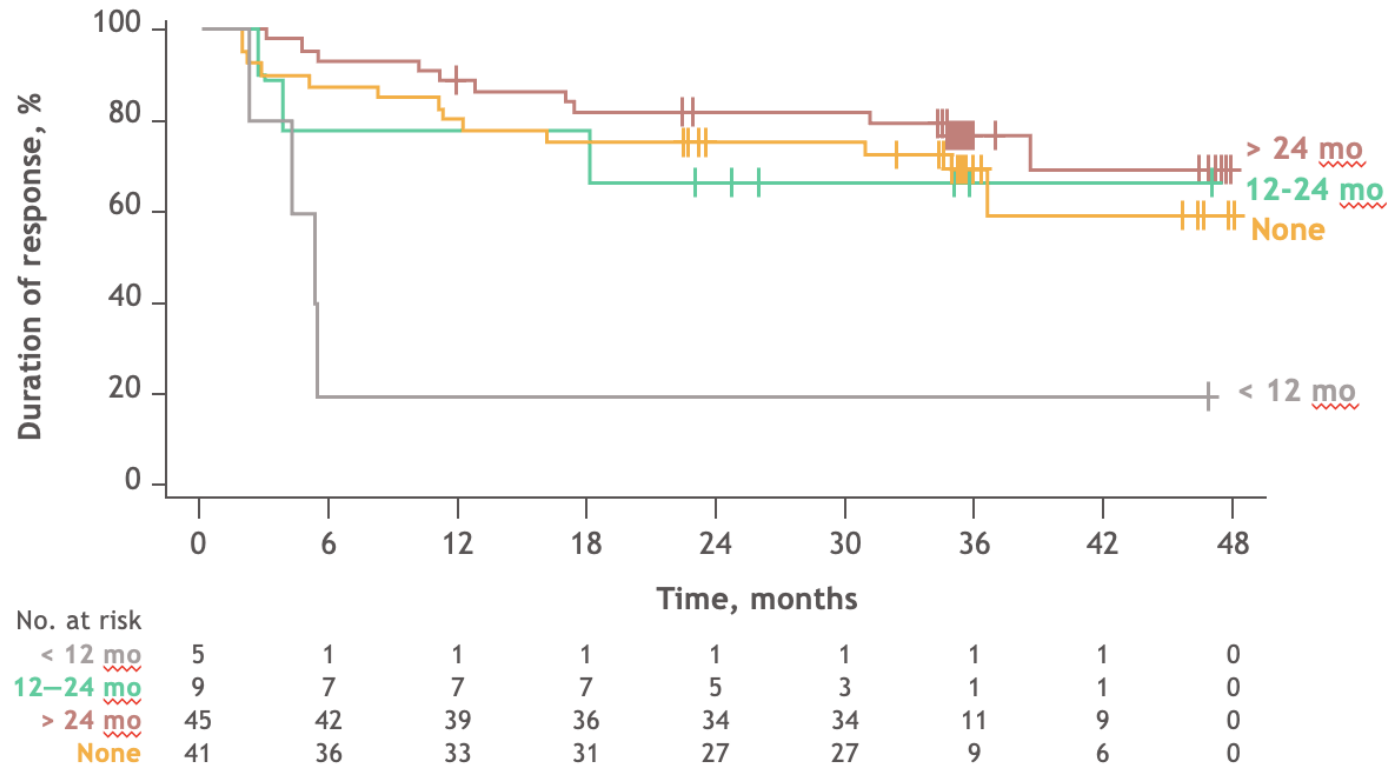


TRANSCEND-FL: Impact of prior bendamustine exposure

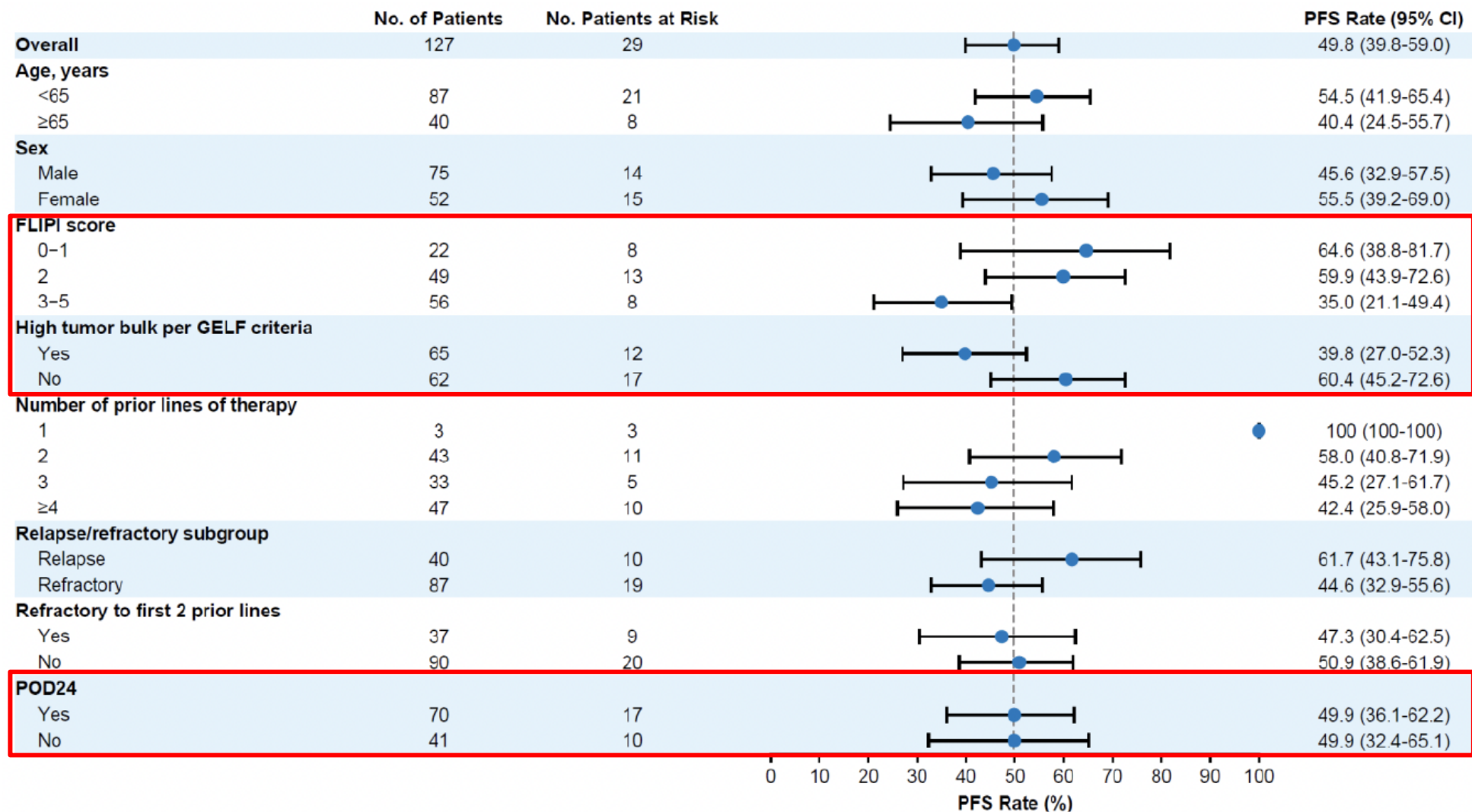
ORR/CR rate



DoR

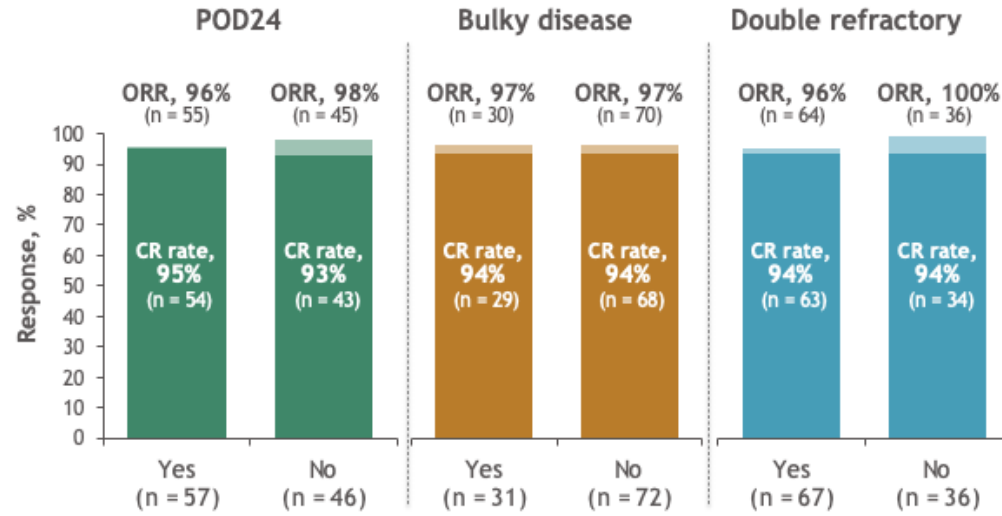


ZUMA-5: PFS rates at 60 mo in key subgroups in FL

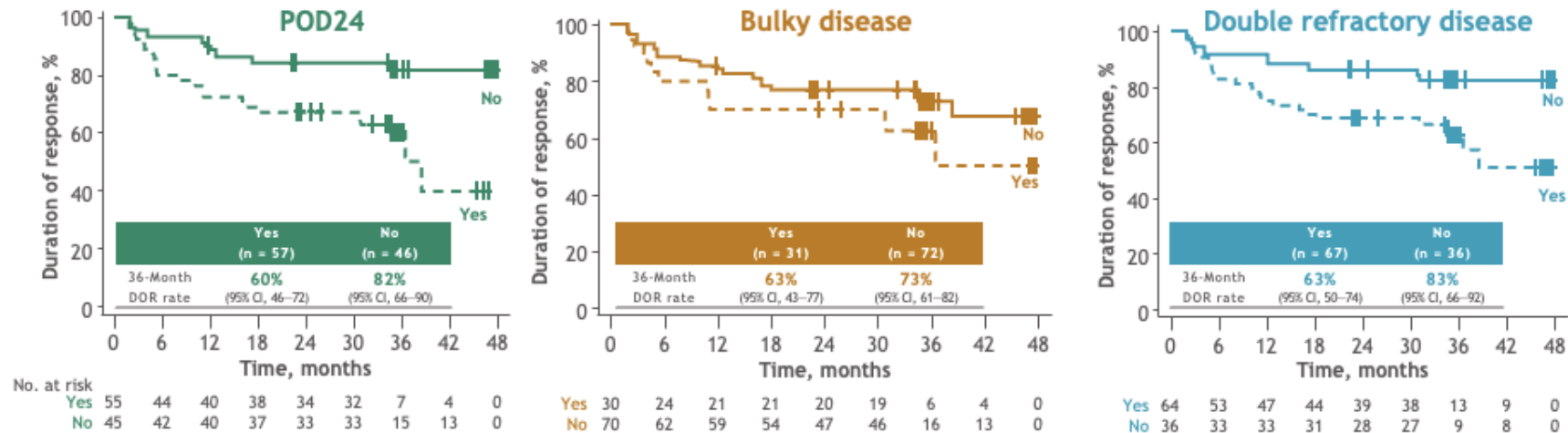


TRANSCEND-FL: Outcomes by subgroups

ORR/CR rate



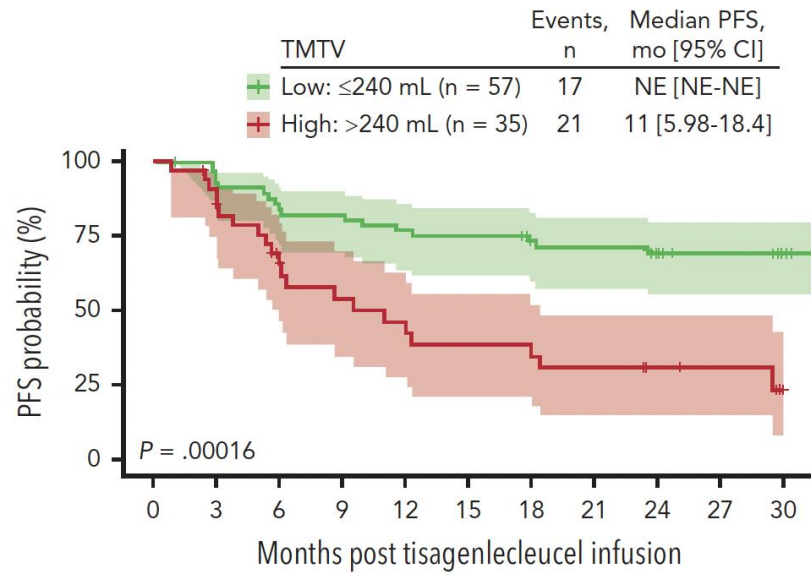
DoR



ELARA: TMTV, naïve CD8+ T cells, and CAR expansion are associated with PFS after tisa-cel in R/R FL

PFS by TMTV

Kaplan-Meier plots of PFS by TMTV

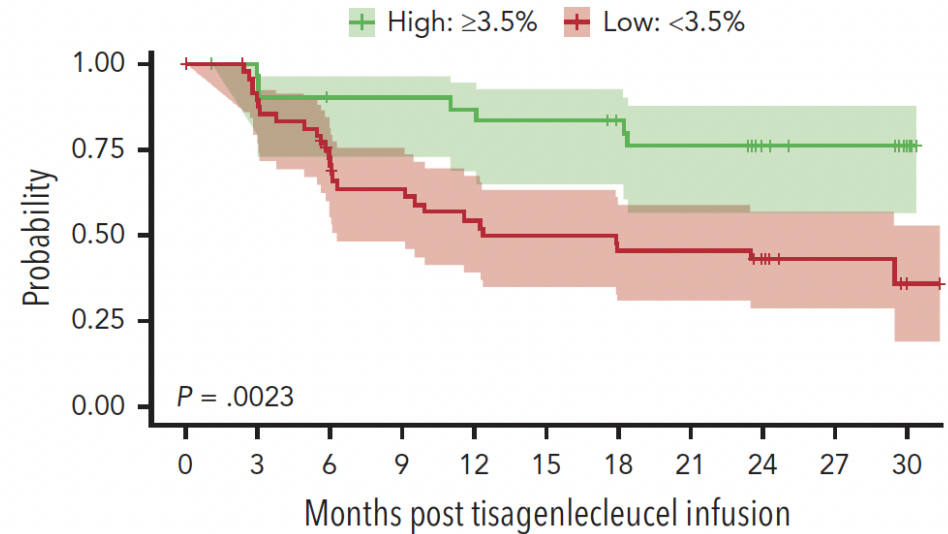


Number at risk (number of events)

	0	3	6	9	12	15	18	21	24	27	30
Low: ≤240 mL	57 (0)	51 (5)	47 (9)	46 (10)	43 (13)	42 (14)	38 (15)	37 (16)	26 (17)	15 (17)	6 (17)
High: >240 mL	34 (0)	27 (5)	18 (11)	14 (14)	12 (16)	10 (18)	9 (19)	8 (20)	5 (20)	4 (20)	0 (21)

PFS by % naïve CD8+ T in apheresis

PFS by percentage of naïve CD8+ T cells

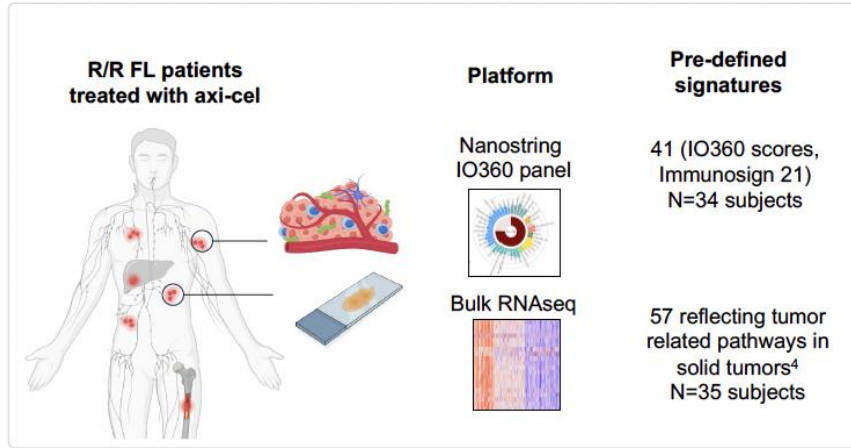


Number at risk (number of events)

	0	3	6	9	12	15	18	21	24	27	30
High: ≥3.5%	32 (0)	28 (3)	27 (3)	27 (3)	26 (4)	25 (5)	23 (5)	21 (7)	13 (7)	11 (7)	5 (7)
Low: <3.5%	50 (0)	42 (6)	32 (14)	28 (17)	24 (21)	22 (23)	20 (25)	20 (25)	15 (26)	6 (26)	1 (27)

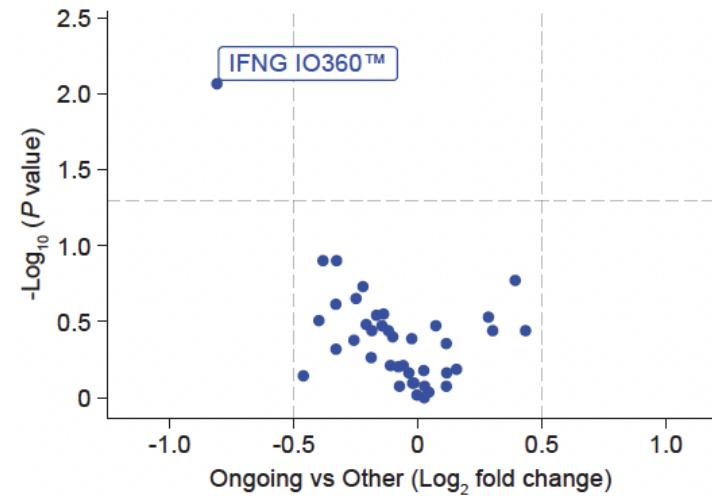
IFN signaling in the TME was associated with inferior PFS after axi-cel in R/R FL (ZUMA-5)

Pre-treatment tumor profiling

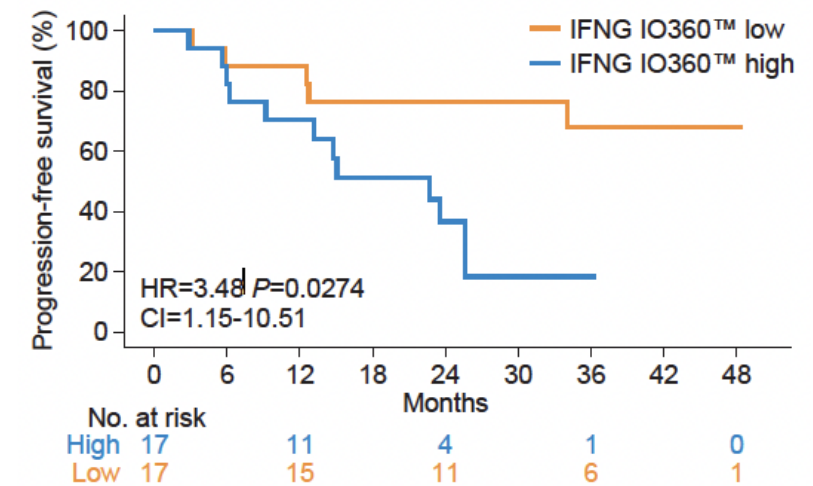


R/R, relapsed/refractory; 30 subjects were overlapping in nanostring and RNAseq analysis;

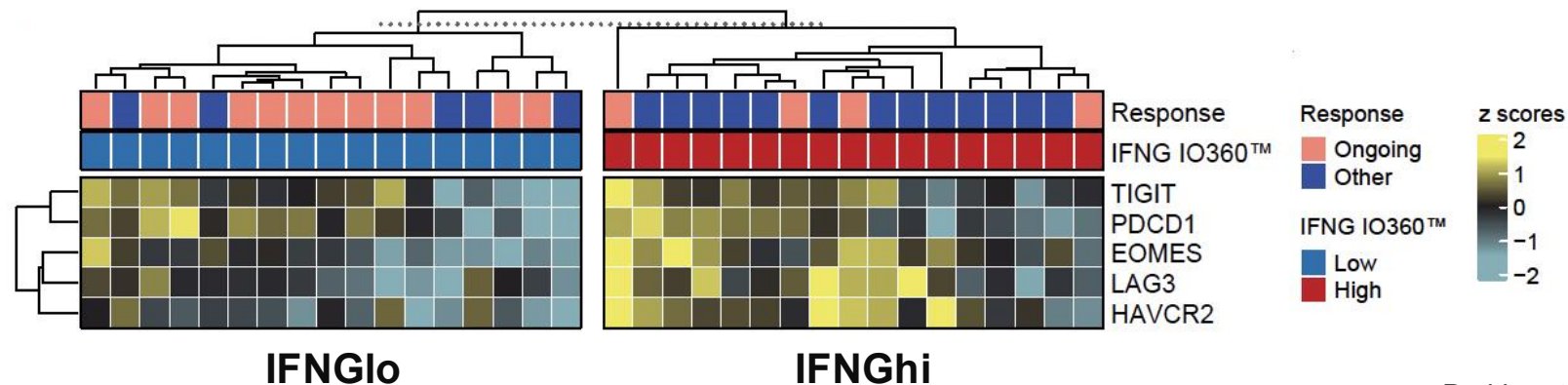
GES association with relapse



IFNG GES association with PFS

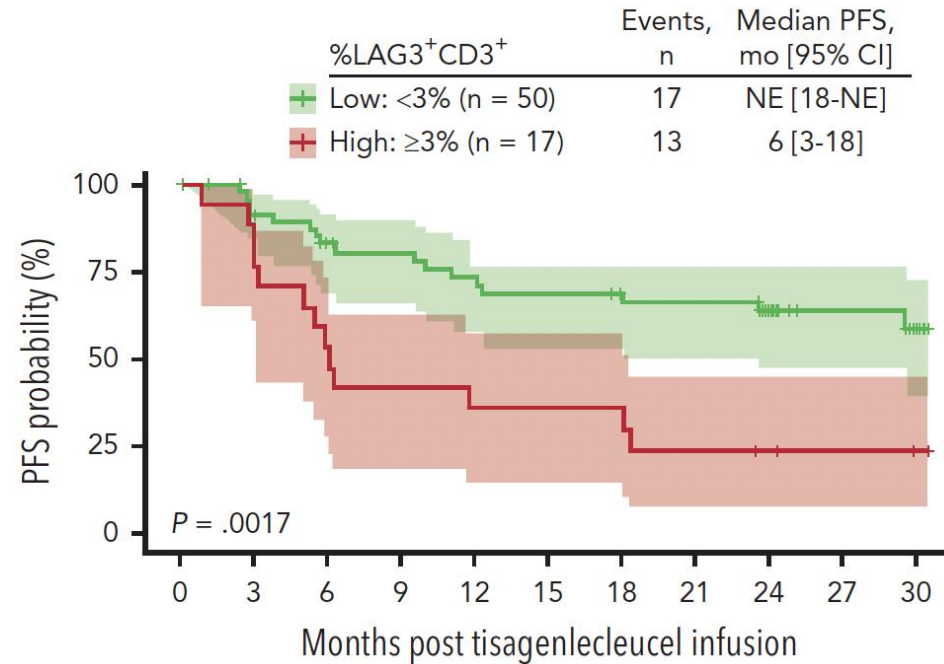


High LAG3, TIM3, and EOMES in IFNG^{hi} tumors



Higher percent of LAG3⁺ T cells in the TME was associated with inferior PFS after tisa-cel in R/R FL (ELARA)

Kaplan-Meier plots of PFS associated with %LAG3⁺CD3⁺ cells in baseline tumors



Number at risk
(number of events)

Low: <3%	50 (0)	42 (4)	36 (8)	34 (9)	31 (12)	29 (14)	26 (15)	26 (15)	19 (16)	11 (16)	3 (17)
High: ≥3%	17 (0)	13 (4)	8 (9)	7 (10)	6 (11)	6 (11)	5 (12)	4 (13)	3 (13)	2 (13)	1 (13)
	0	3	6	9	12	15	18	21	24	27	30
	Months post tisagenlecleucel infusion										

Summary

- The plateau in lymphoma-specific PFS indicates **curative potential of CD19 CAR-T in ~60% of R/R FL**
 - Phase 3 trials are ongoing in 2nd and 3rd line FL
- Longitudinal analyses demonstrate a favorable **long-term safety** profile with CD19 CAR-T in 3L+ FL
- **Peak CAR T expansion** and **naïve product phenotype** impact efficacy and are affected by prior bendamustine exposure within 12 months of apheresis
- **IFN gene expression signature** in TME was associated with higher expression of inhibitory receptors and inferior PFS
- **Avoiding bendamustine and combination strategies** with immune checkpoint blockade may further improve outcomes with CD19 CAR T cell therapy in FL

Thank you for your attention!

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