



POST-ORLANDO 2025
Novità dal Meeting della Società Americana di Ematologia

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Torino
Centro Congressi Lingotto
19-21 febbraio 2026

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CAR-T nel Linfoma Follicolare e Mantellare

IRCSS Azienda Ospedaliero Universitaria di Bologna



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DICHIARAZIONE Beatrice Casadei

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Kite-Gilead					x	x	
Novartis					x	x	
Celgene-BMS					x	x	
Janssen						x	
Abbvie					x		
Beone					x		
Lilly					x		
Takeda						x	
Roche					x	x	



CAR T-cell Treatment in FL and MCL at ASH 2025

Follicular lymphoma

- 2 oral presentations: *Schuster S. et al, abs #468; Ahmed S. et al, abs #467*
- 6 poster presentations: *Major A. et al, abs #1798; Dahiya S. et al, abs#265; Budde E. et al, abs #254; Sharp J. et al, abs#2377; Srinagesh H. et al, abs #4159; Tun A. et al, abs#5356*

Mantle Cell Lymphoma

- 2 oral presentations: *Kersten M.J. et al, abs#662; Jain P. et al, abs#666*
- 5 poster presentations: *Van Meerten T. et al, abs #1798; Yang P. et al, abs#7125; Guidez S. et al, abs #3598; Beitinjaneh A. et al, abs#3606; Srinagesh H. et al, abs #4159.*



Introduction: CAR T-cells in R/R Follicular Lymphoma

Agent and trial	Ph	Pts n	POD24 %	Prior tx median	BT %	V2Vt, days	ORR/CR [^] %	Median f-up, mo	PFS, %	OS, %	CRS (any/ gr ≥3) %	ICANS (any/ gr ≥3) %
Tisa-cel (ELARA) ^{1,2,3}	II	97	63	4 (2-13)	45	46*	86 / 68	53	48mo: 50.2	48mo: 79.3	48/0	4/1
Axi-cel (ZUMA-5) ^{4,5}	II	124	56	3 (2-4)	4	40	90 / 75	64.6	60mo: 49.8	60mo: 69%	97/8	56/15
Liso-cel ^{6,7} (TRANSCEND-FL)	I/II	101 (3L) 23 (2L)	55	3 (2-10)	38	49	97 / 94	24	12mo: 83	12mo: 93	58/1	15/2

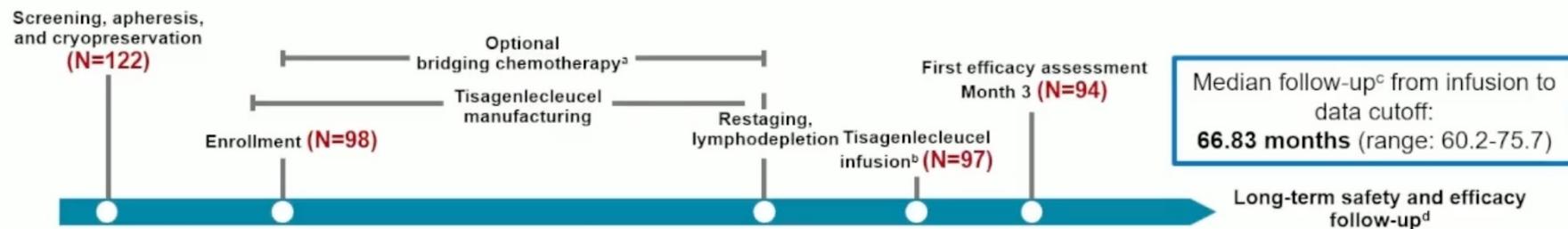
*median time from enrollment to infusion. ^consistent response rates were seen also in those patients with high-risk characteristics

1. Dreyling M. et al. Blood 2024. 2. Fowler N.H. et al, Nature Med 2022, 3. Thieblemont C. et al. ICML 2025; 4 Jacobson A.C. et al, Lancet Oncol 2022; 5 Neelapu S. et al. JCO 2025; 6. Morschauer F et al. Nature 2024 . 7. Nastoupil L. et al. ASH 2024



468. Clinical Outcomes of Tisagenlecleucel in Patients with Relapsed/Refractory Follicular Lymphoma (r/r FL): Phase 2 ELARA, 5-year update.

ELARA Study Design

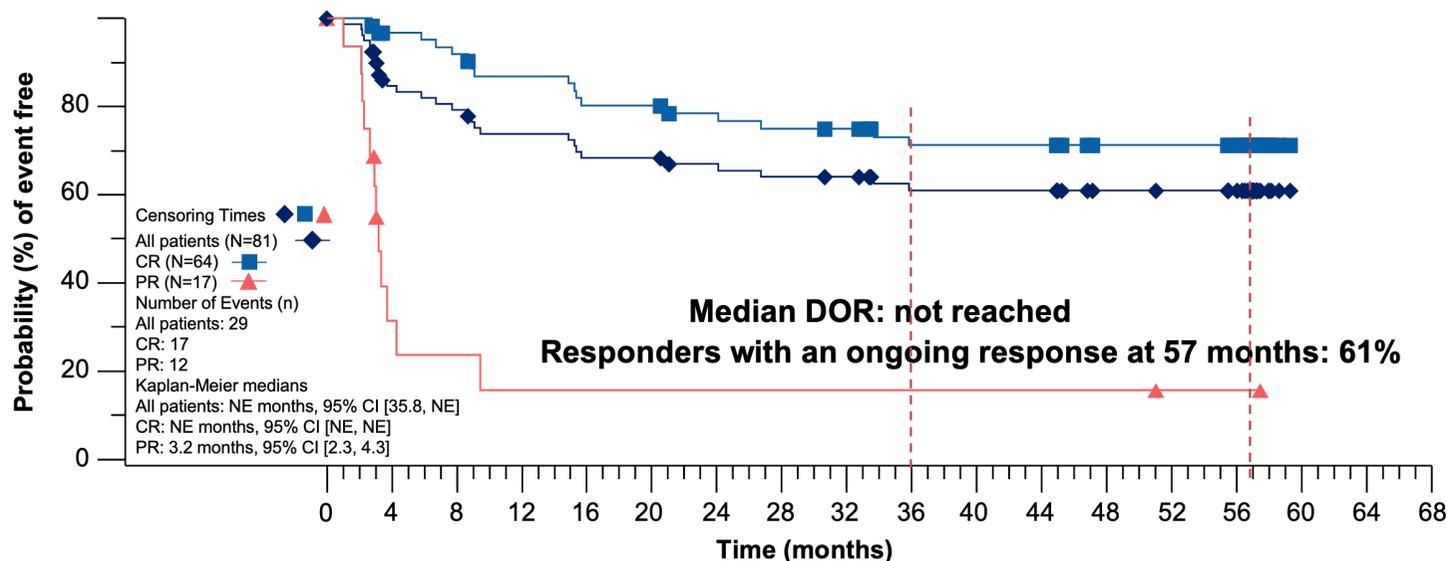


Key eligibility criteria	Study treatment	End points
<ul style="list-style-type: none">• ≥18 years of age• FL grade 1, 2, or 3A• Relapsed/refractory disease^e• No evidence of histological transformation/FL3B• No prior anti-CD19 therapy or allogeneic HSCT	Tisagenlecleucel dose range (single IV infusion) was 0.6-6×10 ⁸ CAR-positive viable T cells	Primary: CRR by IRC Secondary: ORR, DOR, PFS, OS, safety, cellular kinetics

- Bridging therapy was allowed and was followed by disease re-evaluation before tisagenlecleucel infusion
- Cellular kinetics were determined by measurement of transgene levels by qPCR



Median Duration of Response was Not Reached

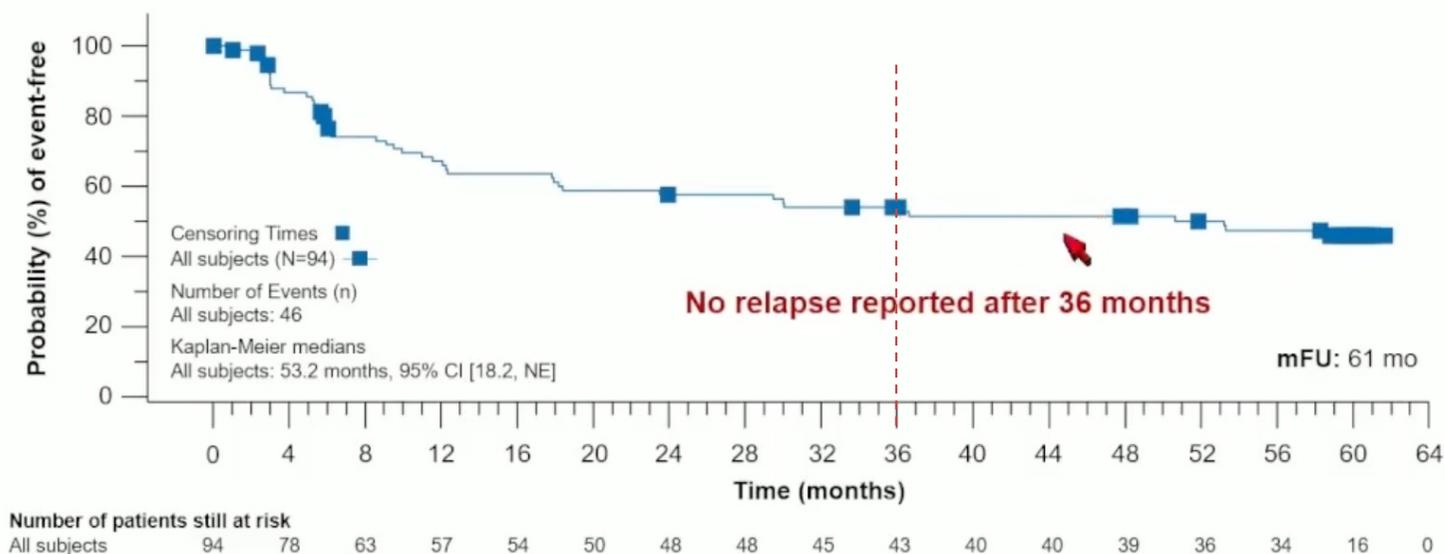


Number of patients still at risk	0	4	8	12	16	20	24	28	32	36	40	44	48	52	56	60	64	68
All patients	81	63	59	54	50	50	47	45	44	39	39	39	34	33	31	0	0	0
CR	64	59	56	52	48	48	45	43	42	37	37	37	32	32	30	0	0	0
PR	17	4	3	2	2	2	2	2	2	2	2	2	2	1	1	0	0	0

- The probability of maintaining CR/PR response at 48-mo was 61%
- The probability of maintaining CR at 48-mo was 71.2%



No Relapsed Events Were Reported after 36 Months

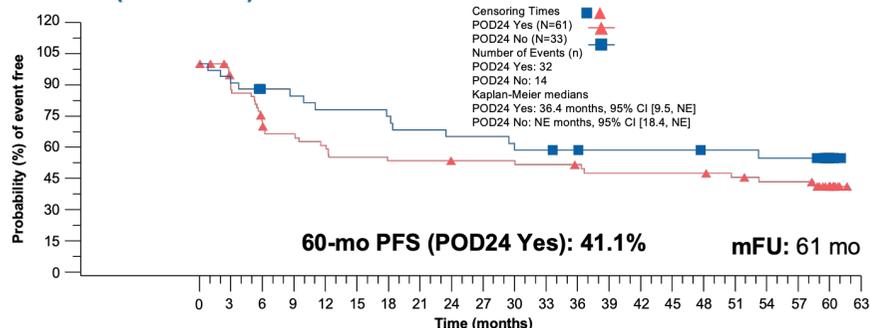


- The 60-mo PFS was 46% in all pts, and 59.8% in those who had CR
- The 60-mo OS was 74.1% in all pts, the median OS was NR



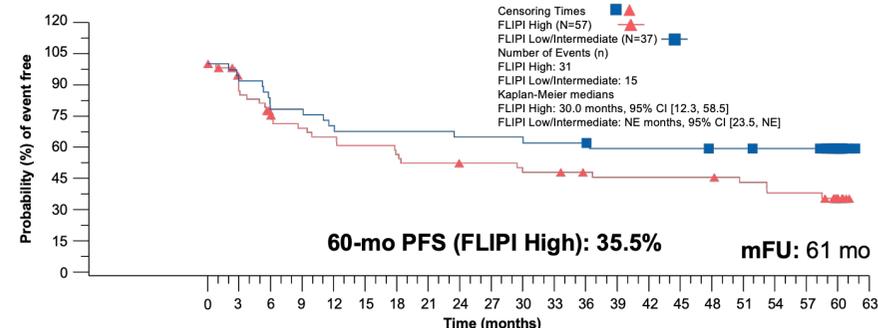
Prolonged and Sustained PFS and OS was Seen Across High-Risk Subgroups

POD24 (Yes vs No)



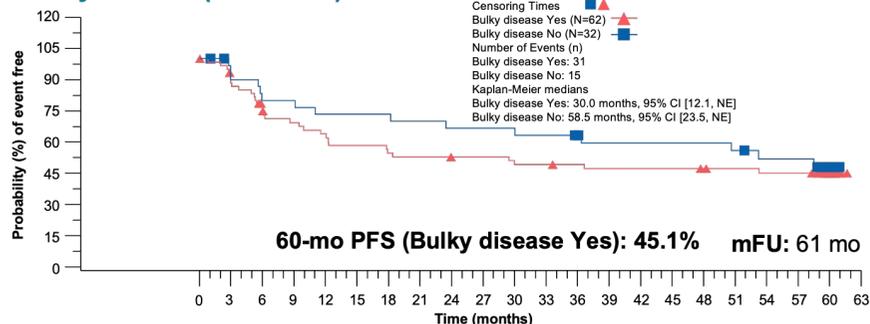
Time (months)	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63			
POD24 Yes	61	50	40	36	33	30	29	29	28	28	28	28	27	26	24	24	24	24	24	24	22	20	20	11	0
POD24 No	33	30	27	26	24	24	23	21	20	20	18	18	17	16	16	16	16	15	15	14	14	5	0	0	

FLIPI (High vs Low/Intermediate)



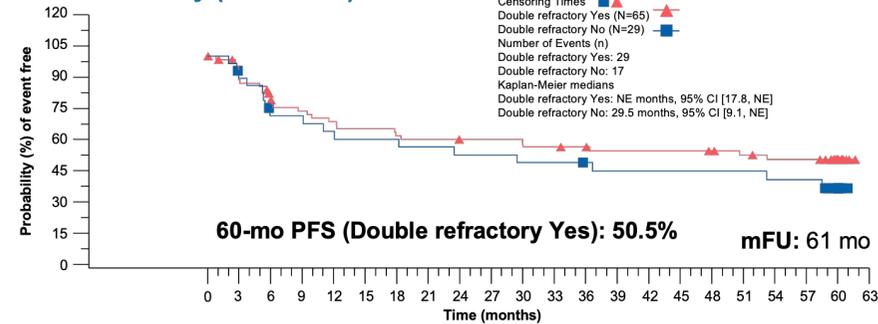
Time (months)	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	
FLIPI High	57	46	38	33	31	29	27	25	24	24	22	22	20	19	19	19	19	17	15	15	6	0	0
FLIPI Low/Intermediate	37	34	29	29	26	25	25	25	24	24	24	23	23	21	21	21	20	20	19	19	10	0	0

Bulky disease (Yes vs No)



Time (months)	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	
Bulky disease Yes	62	53	43	38	35	32	30	29	28	28	26	26	25	24	24	24	24	23	22	21	21	9	0
Bulky disease No	32	27	24	24	22	22	22	21	20	20	20	19	18	16	16	16	16	16	15	13	13	7	0

Double refractory (Yes vs No)

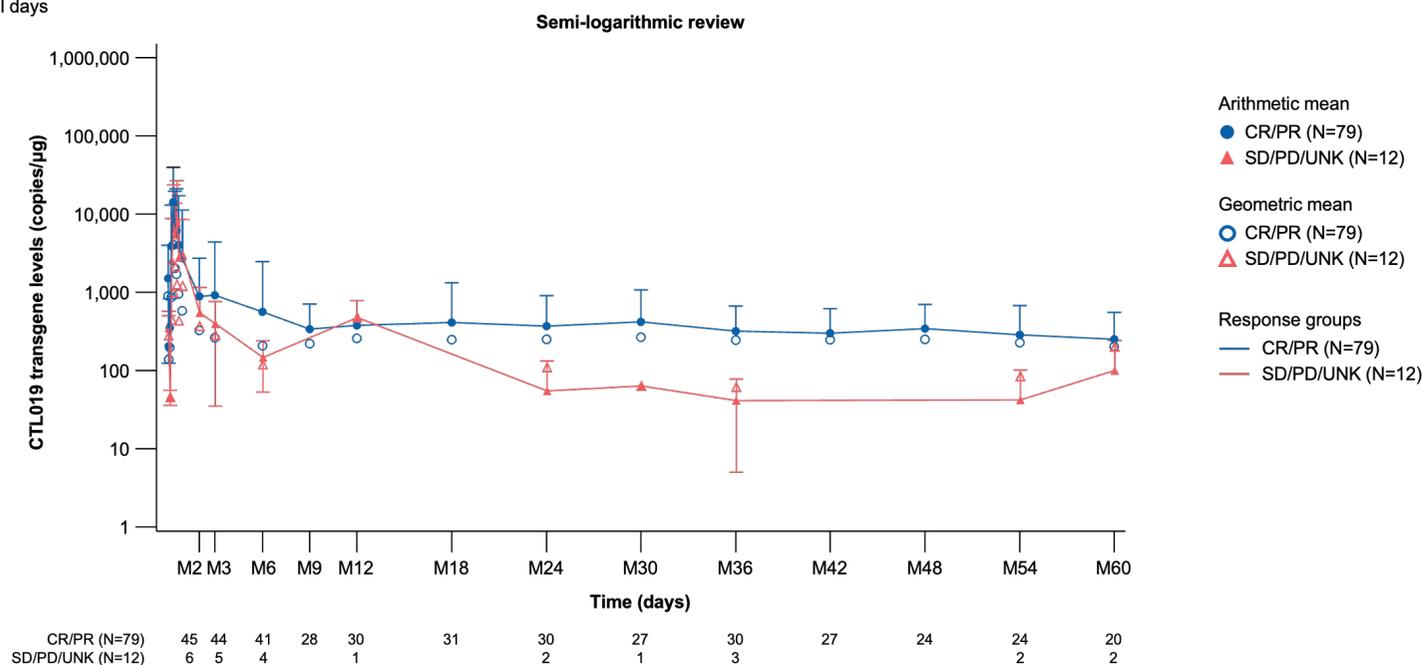


Time (months)	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63
Double refractory Yes	65	55	48	43	40	38	36	35	34	34	33	32	31	29	29	29	28	26	24	24	12	0
Double refractory No	29	25	19	19	17	16	16	15	14	14	13	13	12	11	11	11	11	11	10	10	4	0



Long-Term CAR-T Persistence was Observed

Variable: CTL019 transgene levels (copies/ μ g)
Timepoint: All days



- CAR transgene persistence (T_{last} ; time to last quantifiable transgene level) was observed up to 60.9 months
- The median T_{last} was 8.6 months (range: 0.6-60.9 months).



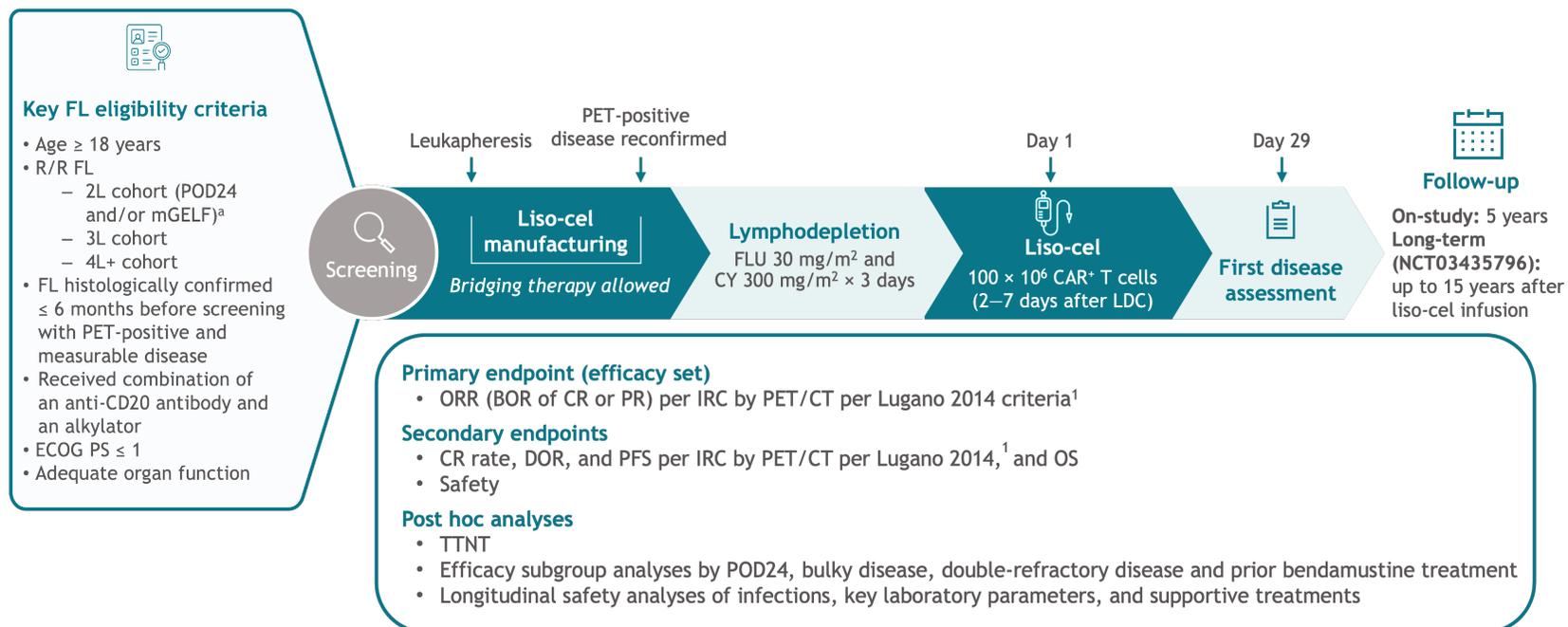
Summary

- After a median follow-up of >5 years, tisagenlecleucel continues to demonstrate
 - Robust and durable response rates (CRR: 68.1%; 61% patients were in response at 57 months)
 - Prolonged PFS (median PFS: 53.2 months)
- With **no relapse reported after 36 months**, which has translated into a durable survival in patients with r/r FL
- In patients with high-risk disease characteristics, consistent efficacy outcomes were reported compared to the overall population
- No new safety signals were reported, with very few patients reporting serious adverse events >4 years post-tisagenlecleucel infusion
- More than 75% of patients were alive, and approximately half remained progression-free at this final analysis, suggesting a curative potential for tisagenlecleucel in adult patients with r/r FL after two or more lines of systemic therapy



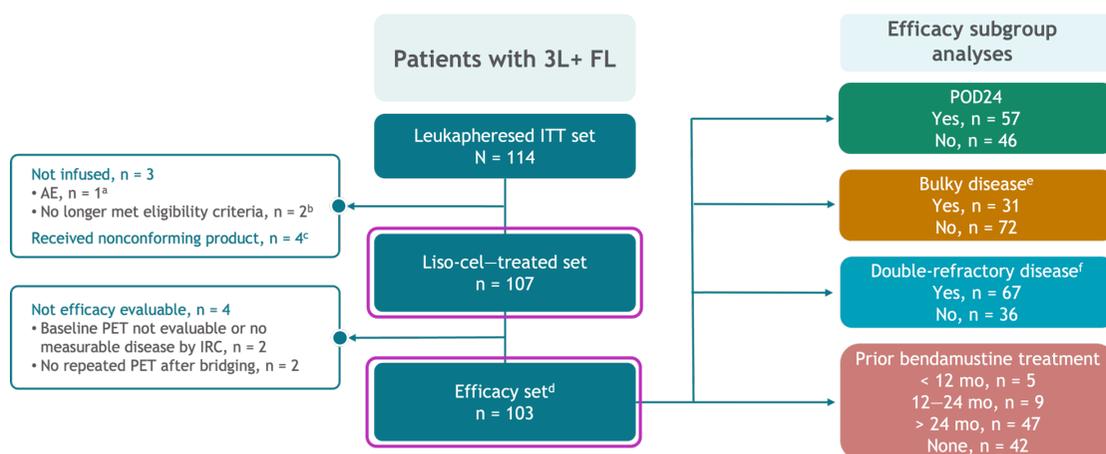
467. Three-Year Efficacy and Longitudinal Safety of Lisocabtagene Maraleucel in Patients with Third-Line or Later Follicular Lymphoma from TRANSCEND FL

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





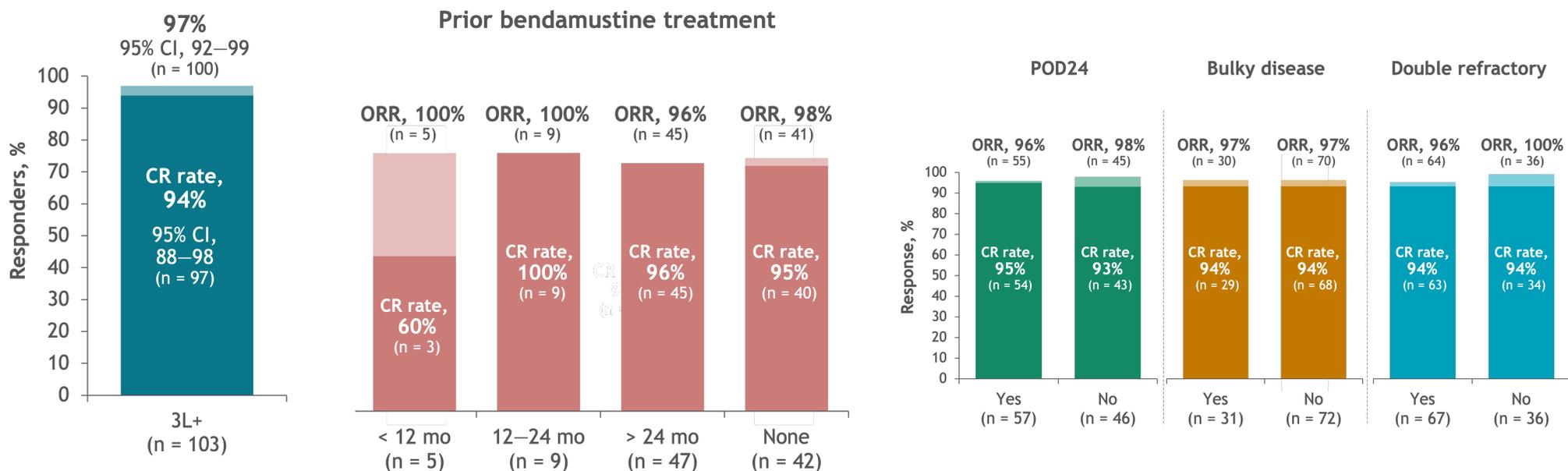
Patients Disposition and Characteristics



	3L+ FL (n = 107)
Median (range) age, y	62 (23–80)
Met mGELF criteria at most recent relapse, n (%)	57 (53)
Bulky disease, ^a n (%)	34 (32)
Median (range) prior lines of systemic therapy	3 (2–10)
Received prior HSCT, n (%)	33 (31)
Received prior rituximab and lenalidomide, n (%)	23 (21)
Received prior bendamustine, n (%)	65 (61)
Double refractory (anti-CD20 and alkylator), ^b n (%)	69 (64)
POD24 from initial immunochemotherapy, n (%)	59 (55)
Received bridging therapy, n (%)	44 (41)

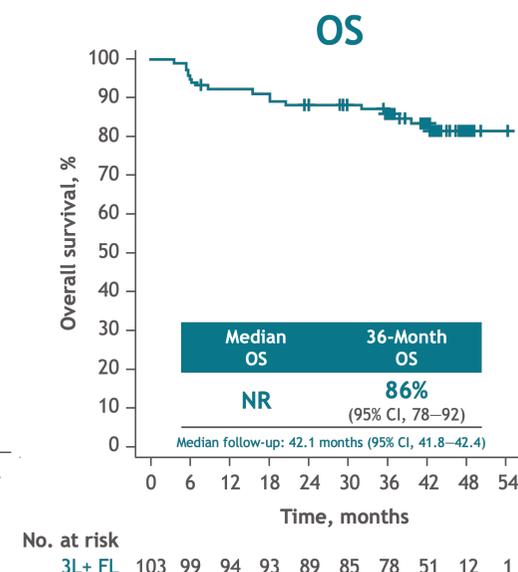
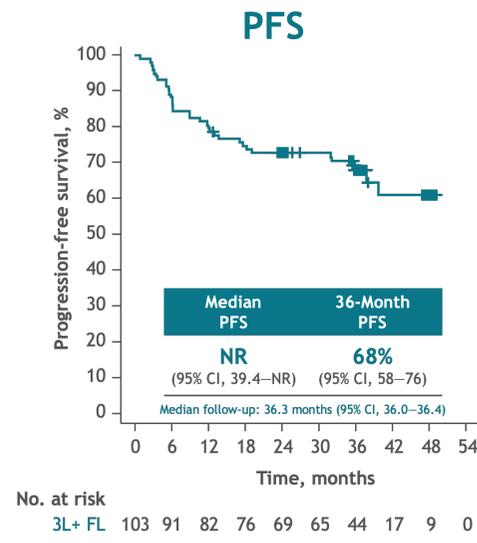
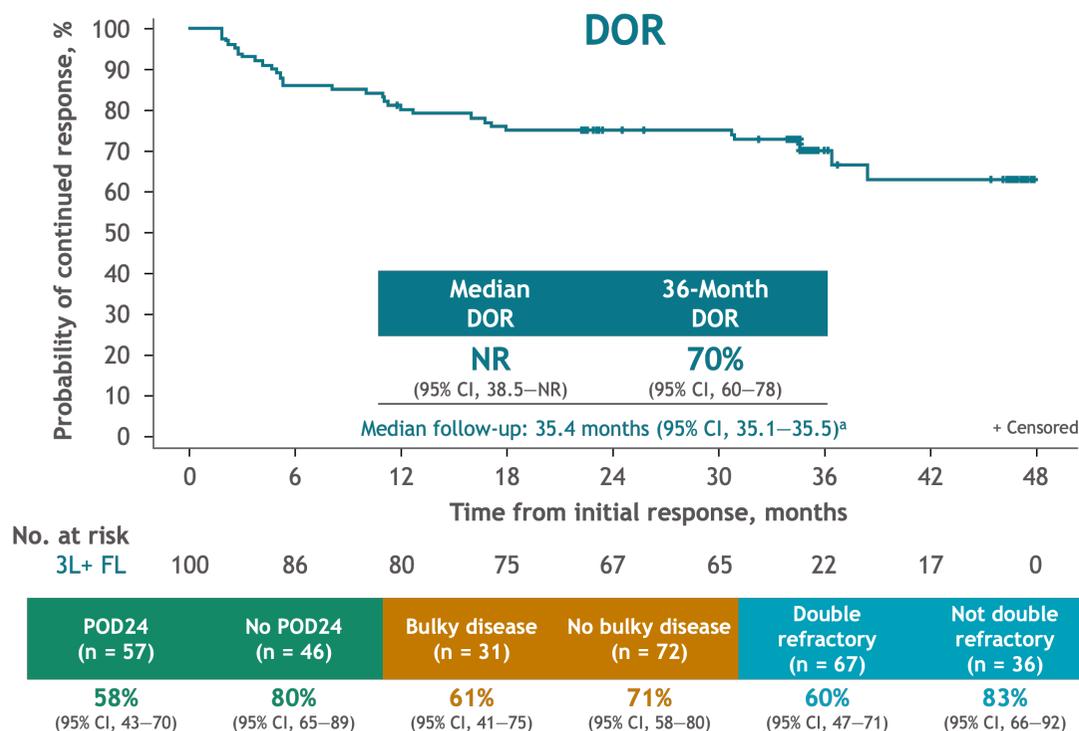


Responses were Deep and Consistent Across Subgroups



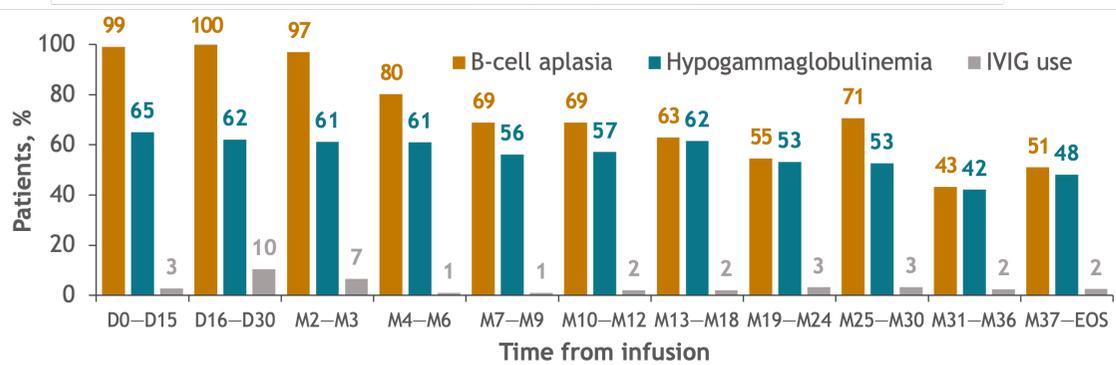
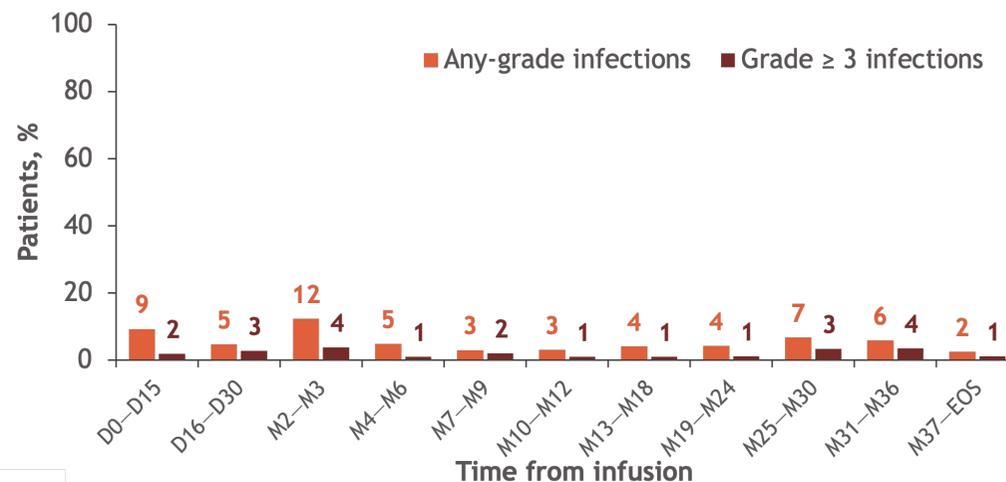
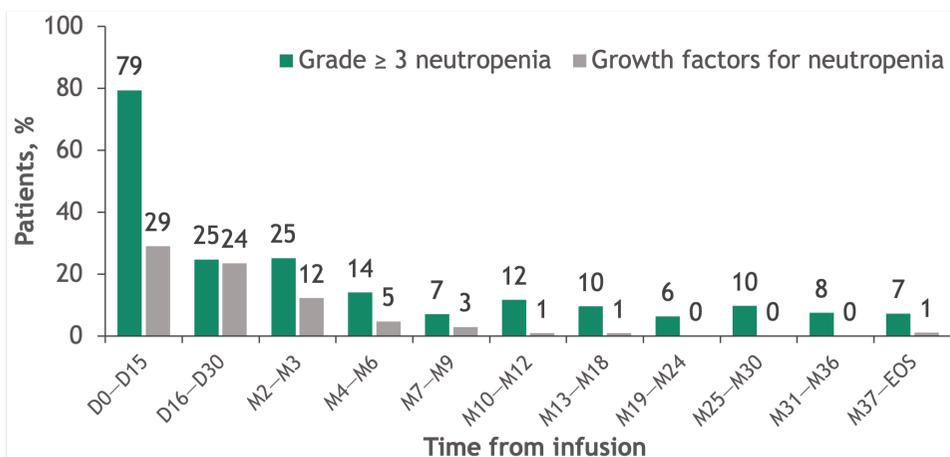


Responses were Durable even in Patients with High-Risk Disease





Liso-cel Showed Favorable Long-term Safety



Use of growth factors, transfusions, and IVIG therapy, n (%)	3L+ FL (n = 107)
Growth factors for neutropenia	54 (50)
Erythropoiesis stimulating agents	5 (5)
RBC transfusions for anemia	24 (22)
Platelet transfusions ^a	16 (15)
IVIG therapy	29 (27)



Summary

- After 3 years of follow-up, a single infusion of liso-cel continued to show high rates of deep (CR rate, 94%) and durable responses (36-month DOR, 70%) with sustained survival (36-month OS, 86%) in patients with 3L+ R/R FL
- Liso-cel demonstrated consistently high efficacy across subgroups with ORR of 96%—100% and 3-year ongoing response rates of 60%—83%, even among patients with high-risk characteristics (POD24, bulky disease, double-refractory disease)
- Patients who received bendamustine \geq 12 months before leukapheresis had durable responses and high 3-year PFS rates, similar to the overall population and consistent with patients without prior bendamustine exposure
- Longitudinal safety analyses demonstrate a favorable long-term safety profile with liso-cel in patients with 3L+ FL
- Low infections, high rates of hematologic recovery, and modest supportive care needs reinforce the feasibility of outpatient management and the potential for low health care resource utilization with liso-cel in clinical practice
- Three-year follow-up from TRANSCEND FL confirm the high efficacy and sustained favorable safety with a single infusion of liso-cel, positioning it as a key therapeutic option for 3L+ R/R FL



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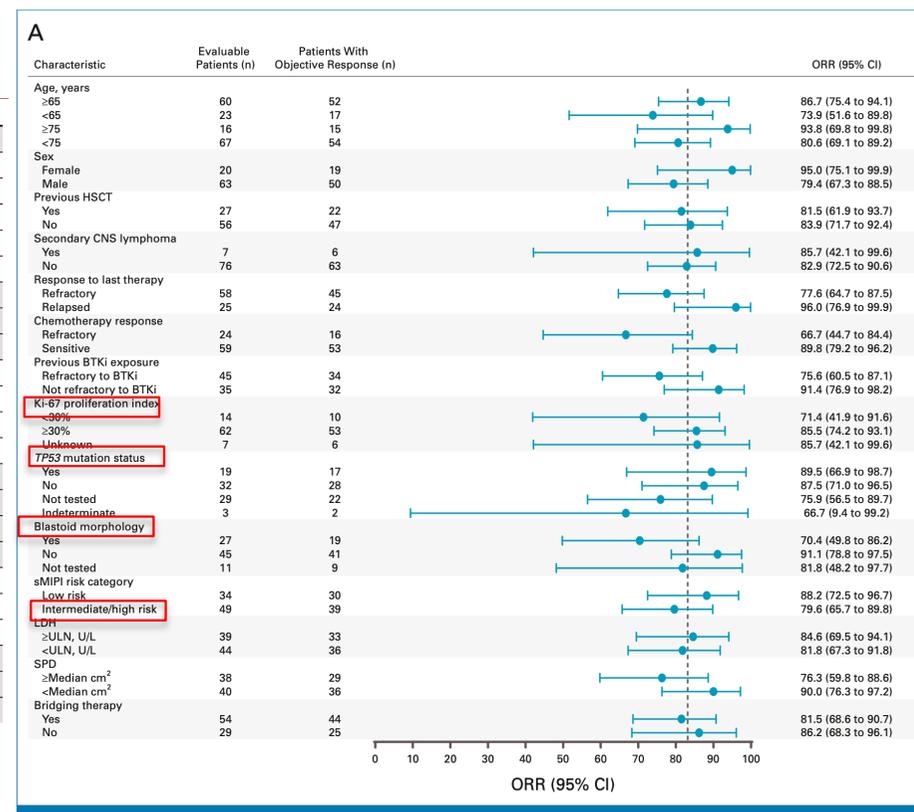
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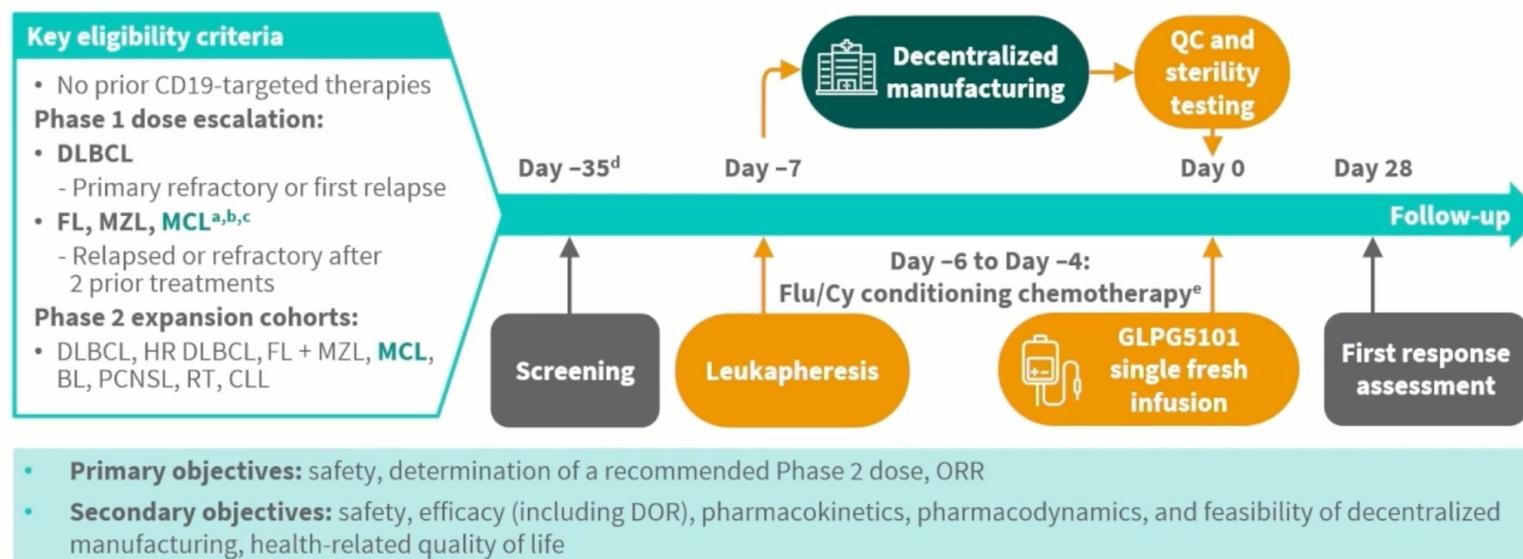
Introduction: CAR T-cells in R/R Mantle Cell Lymphoma

Characteristic	No.	ORR, No. (%)	CR, No. (%)	PR, No. (%)	SD, No. (%)	PD, No. (%)	mDOR, Months (95% CI) [No.]	mPFS, Months (95% CI) [No.]	mOS, Months (95% CI) [No.]
All-treated*	68	62 (91)	46 (68)	16 (24)	3 (4)	3 (4)	28.2 (13.5 to 47.1) [62]	25.8 (9.6 to 47.6) [68]	46.6 (24.9 to NE) [68]
Ki-67 PI, %									
< 30	9	9 (100)	7 (78)	2 (22)	0	0	26.5 (3.6 to NE) [9]	27.5 (4.4 to NE) [9]	NR (4.4 to NE) [9]
≥ 30	43	39 (91)	31 (72)	8 (19)	2 (5)	2 (5)	45.6 (14.4 to NE) [39]	46.6 (9.6 to 48.0) [43]	47.6 (34.9 to NE) [43]
TP53 mutation status									
Mutation	6	6 (100)	6 (100)	0	0	0	NR (5.4 to NE) [6]	NR (6.4 to NE) [6]	NR (19.9 to NE) [6]
Wild-type	30	30 (100)	21 (70)	9 (30)	0	0	46.7 (8.3 to NE) [30]	47.6 (9.2 to NE) [30]	NR (37.5 to NE) [30]
MCL morphology									
Classical	40	37 (93)	26 (65)	11 (28)	1 (3)	2 (5)	24.8 (8.2 to 46.7) [37]	18.2 (7.8 to 47.6) [40]	47.6 (24.0 to NE) [40]
Pleomorphic	4	4 (100)	3 (75)	1 (25)	0	0	NR (1.6 to NE) [4]	NR (2.6 to NE) [4]	NR (12.6 to NE) [4]
Blastoid	17	14 (82)	9 (53)	5 (29)	2 (12)	1 (6)	13.5 (2.0 to NE) [14]	14.5 (3.0 to 48.0) [17]	22.9 (5.5 to NE) [17]
Prior BTKi									
Ibrutinib	52	48 (92)	35 (67)	13 (25)	2 (4)	2 (4)	28.2 (10.4 to 46.7) [48]	25.8 (9.6 to 47.6) [52]	46.4 (22.9 to NE) [52]
Acalabrutinib	10	8 (80)	5 (50)	3 (30)	1 (10)	1 (10)	5.0 (1.6 to NE) [8]	5.6 (0.9 to NE) [10]	NR (4.8 to NE) [10]
Both	6	6 (100)	6 (100)	0	0	0	NR (NE to NE) [6]	NR (NE to NE) [6]	NR (NE to NE) [6]
POD24 status									
With POD24	33	31 (94)	22 (67)	9 (27)	1 (3)	1 (3)	17.1 (5.4 to 47.1) [31]	14.5 (6.4 to 47.6) [33]	36.1 (13.7 to NE) [33]
Without POD24	35	31 (89)	24 (69)	7 (20)	2 (6)	2 (6)	45.6 (14.4 to NE) [31]	29.3 (14.5 to NE) [35]	NR (25.3 to NE) [35]
MRD status at month 6									
Positive	4	3 (75)	2 (50)	1 (25)	0	1 (25)	6.1 (5.4 to NE) [3]	7.1 (0.9 to NE) [4]	27.0 (13.5 to NE) [4]
Negative	15	15 (100)	14 (93)	1 (7)	0	0	NR (10.4 to NE) [15]	NR (11.3 to NE) [15]	NR (46.4 to NE) [15]



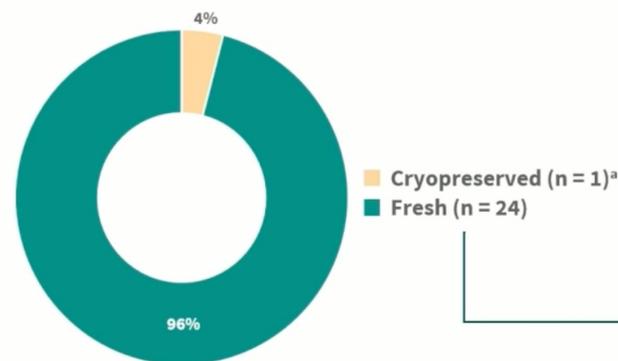
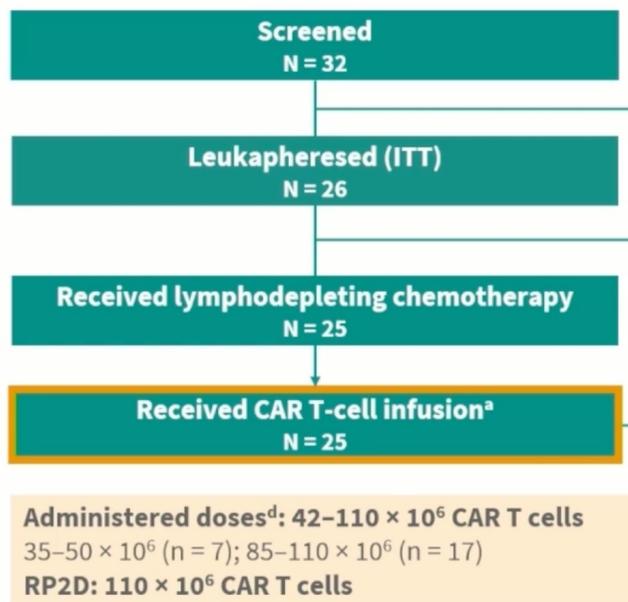


662. High Complete Response Rates and Minimal Residual Disease (MRD) Negativity, With Durable Responses, in High-Risk Mantle Cell Lymphoma (MCL) with GLPG5101, a Fresh, Early Memory-Enriched CAR T-Cell Therapy With a 7-Day Vein-to-Vein Time: Results From the ATALANTA-1 MCL Cohort





ATALANTA-1: High Rate of Fresh Infusions with Short Vein-to-Vein Time



- 24/25 (96%) patients who received an infusion were given a fresh product
- A **vein-to-vein time of 7 days** was achieved in 23/24 (96%) patients who received a fresh product
- Short vein-to-vein time **eliminated the need for cytotoxic bridging therapy^b** for all patients who received a fresh product



The decentralized manufacturing platform delivers a CAR T-cell product with enrichment of early memory phenotype CD8+ CAR T-cells and reduction of terminally differentiated effectors.

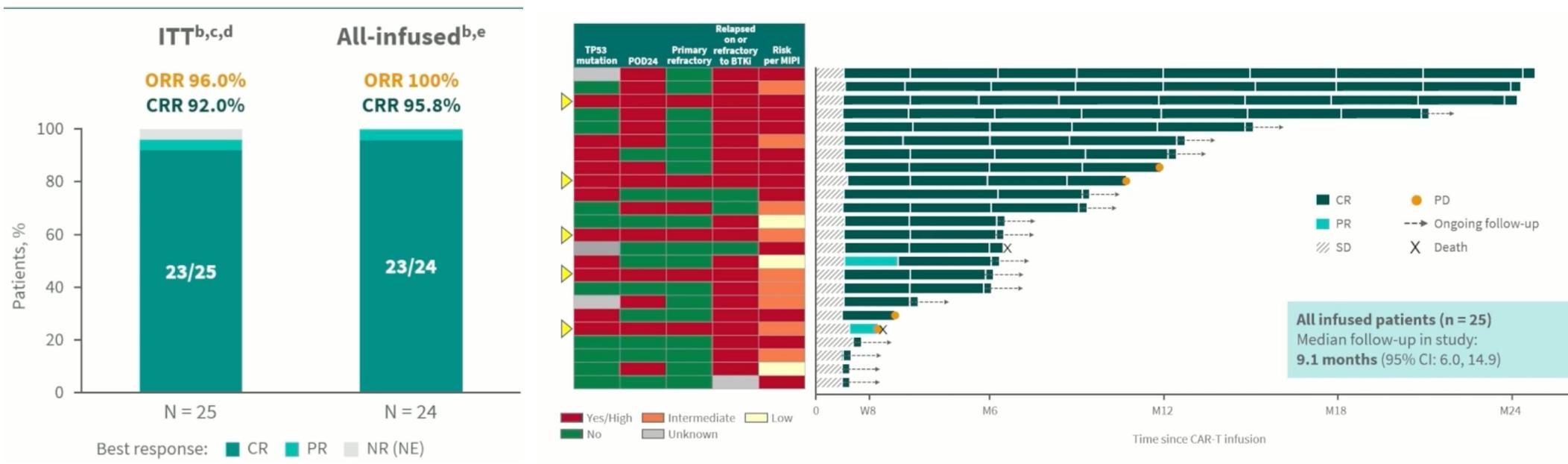


R/R MCL Patients had High-Risk Disease and were Refractory to SOC

	All patients ^a N = 25
Age, median (range), years	67 (48-81)
Male sex, n (%)	22 (88)
Female sex, n (%)	3 (12)
MCL variant, n (%)	
Classic	18 (72)
Blastoid	3 (12)
Leukemic	4 (16)
MIPI score at screening, n (%)	
Low risk	3 (12)
Intermediate risk	9 (36)
High risk	13 (52)
TP53 mutated, n/n available (%)	12/22 (55) ^b
Ki-67: ≥ 30%, n/n available (%)	10/15 (67)
POD24, n (%)	15 (60)
Elevated LDH, n (%)	11 (44)
Ann Arbor disease stage: III-IV, n (%)	24 (96)
Bone marrow involvement, n/n available (%)	18/23 (78)
Prior systemic therapies, median (range)	2 (1-6)
1 prior line, n (%)	1 (4)
≥ 2 prior lines, n (%)	24 (96)
Prior BTKi, n (%)	24 (96)
Prior ASCT, n (%)	9 (36)
Relapsed ^a after last line, n (%)	10 (40)
Refractory ^a to last line, n (%)	14 (56)
Relapsed on or refractory to BTKi, ^b n (%)	21 (84) ^c
Time from diagnosis to leukapheresis, median (range), years	3.7 (0.6-11.8)



High ORR/CRR and Durable Response were Seen in High-Risk, 3L+ R/R MCL



- 90% (9/10) of MRD-evaluable patients were MRD-negative at CR
- 7/9 MRD-negative patients remained in CR at time of data cutoff
- **At 9 mo the estimated DoR and PFS were 83%**



Safety and TEAEs related to GLPG5101

	All patients ^a N = 24		All patients ^a N = 24		All patients ^a N = 24
Any TEAE, n (%)	23 (96)	Hematologic Grade ≥ 3 TEAEs, n (%)		CRS, n (%)	15 (63)
GLPG5101-related TEAE, n (%)	23 (96)	Neutropenia ^b	15 (63)	Grade 1	9 (38)
Serious TEAE, n (%)	10 (42)	Thrombocytopenia ^c	5 (21)	Grade 2	6 (25)
TEAE leading to death, n (%)	0	Anemia ^d	4 (17)	Grade 3	0
Grade ≥ 3 TEAE, n (%)	20 (83)	Leukopenia ^e	2 (8)	ICANS, n (%)	6 (25)
Grade ≥ 3 infections, n (%)	5 (21)	Lymphopenia ^f	2 (8)	Grade 1	5 (21)
Device-related infection	2 (8)	Prolonged cytopenia,^{g,h} Grade ≥ 3, n/n available (%)		Grade 2	0
Pneumonia	2 (8)	28 days post-infusion	8/24 (33)	Grade 3	1 (4)
Bronchopulmonary aspergillosis	1 (4)	56 days post-infusion	5/22 (23)		
COVID-19	1 (4)	98 days post-infusion	6/19 (32)		
<i>Pseudomonas</i> infection	1 (4)	183 days post-infusion	5/17 (29)		



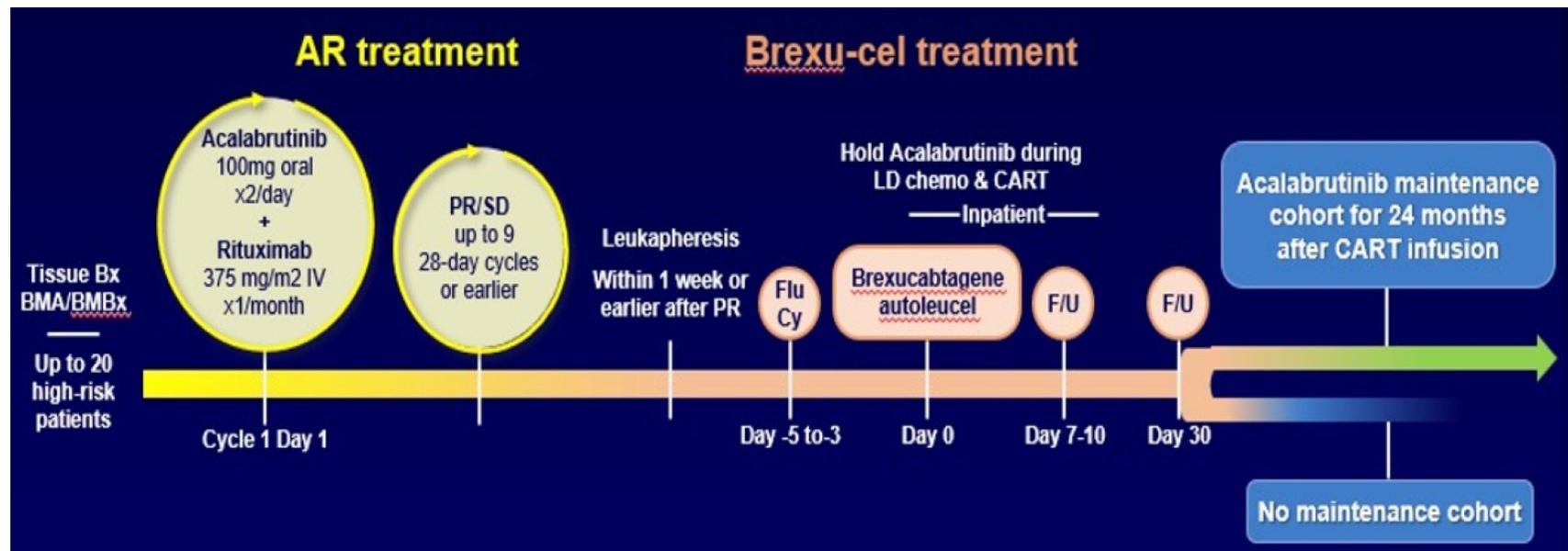
Summary

- GLPG5101 achieved deep and durable responses in patients with R/R MCL, including patients with high-risk features
- In patients receiving a CAR T-cell infusion, 100% ORR and 96% CRR were observed, with DOR and PFS rates of 83%, respectively, at a median follow-up of 9 months
- The safety profile of GLPG5101 was favorable, with no grade ≥ 3 CRS, and 1 grade ≥ 3 ICANS, suggesting its potential use in the outpatient setting
- GLPG5101, a fresh, early memory-enriched phenotype CD19 CAR-T product, yields robust expansion, retention of early memory phenotypes, and long-term persistence, with high rates of MRD negativity
- The short 7-day vein-to-vein time enabled a low dropout rate (4%) and eliminated the need for BT, allowing for more patients to receive treatment that otherwise would not have been able to receive

GLPG5101 offers **timely** treatment, with **durable efficacy and low rates of high-grade toxicities** for patients with R/R MCL, supporting its further development



666. Acalabrutinib plus Rituximab Followed by Brexucabtagene Autoleucel for Frontline Treatment of High-Risk Mantle Cell Lymphoma: The Window-3 Clinical Trial



- Primary objective: safety; Secondary objectives: ORR, CRR, PFS and OS
- Exploratory: MRD, multiomic analysis and immune profiling from blood/tissue

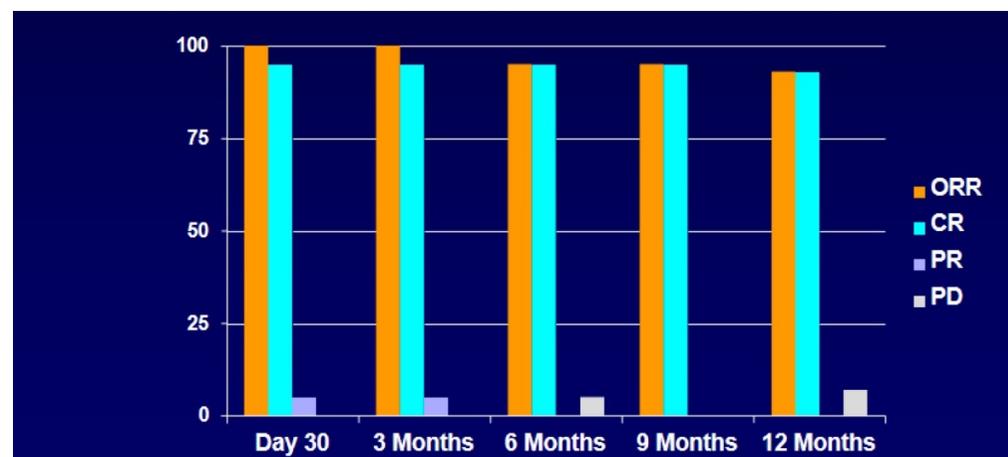


Despite Patients Characteristics, Response Rate was Deep and Persistent

Baseline Patient Characteristics* (N=20)

Median Age (Range)	62(44-73)
Male n (%)	17(85%)
Bone Marrow Involvement n (%)	19(95%)
GI involvement	19(95%)
MIPI n (%)	
Low Risk	1(5%)
Intermediate Risk	6(30%)
High Risk	13(65%)
Serum LDH > ULN, n (%)	11(55%)
Blastoid/Pleomorphic/Classic	5/5/10 (25/25/50%)
TP53 aberrant*	10/20 (50%)
SOX-11 positive, n (%)	18/20(90%)
Ki-67% (<30%)/ (<50%)	5/20(25%)/12/20 (60%)
Ki-67% (≥30%)/ (≥50%)	15/20(75%)/8/20 (40%)

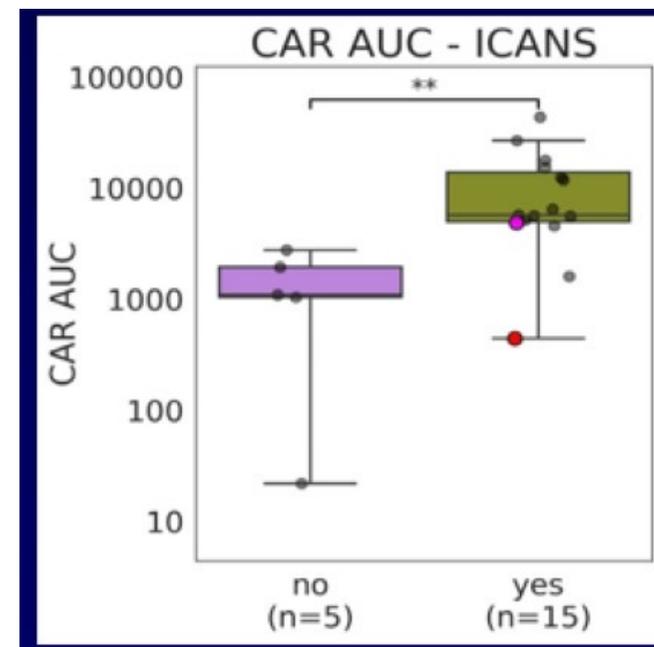
- 2 pts progressed at 6 and 12 mo and 2 came off tx
- Day30: ORR 100%, CR 95%
- With a median follow-up of 17 mo, 2y PFS and OS were 89% and 100%





Safety: gr ≥ 3 CRS and ICANS

Safety	All Patients N=20
During AR treatment	
Grade 3 AEs, n	1 (skin rash)
Grade 4 AEs, n	0
After brexu-cel infusion	
Any-grade CRS, %	100
Max grade 3, %	5
Max grade 4, %	10
Median time to CRS onset, d (range)	3 (0-7)
Any-grade ICANS, %	75
Max grade 3, %	30
Max grade 4, %	15
Median time to ICANS onset, d (range)	6 (2-15)
Resolved ICANS events, %	100
Median time to ICANS resolution, d (range)	3 (1-37)
Requiring intensive care, %	40
Median duration, d (range)	3 (2-25)
Neutropenia (grade 3 or 4), %	60
Thrombocytopenia (grade 3 or 4), %	20
Infections (grade 3 or 4), %	20
Grade 5 events	0



Peak of expansion significantly correlated with any gr of ICANS



Summary

- AR followed by brexucel demonstrates strong efficacy, leading to early and notably high rates of undetectable MRD in untreated high risk MCL
- The incidence of gr 3 or higher CRS and ICANS was consistent, however toxicities were manageable
- The limited sample size and absence of a control arm constrain definitive attribution of aca effects on CAR-T fitness and toxicity
- Extended follow-up and translational analyses are underway to assess response durability and the impact of aca maintenance on long-term safety and efficacy



Conclusions of CAR T-cell in FL and MCL at ASH25

RR FL:

- Curative potential of CAR T-cell in RR FL (3L+) [no relapse after 36 mo, 50% progression free and 80% alive at 5 years]
- In patients with high-risk disease characteristics, consistent efficacy outcome were reported
- Bendamustine < 12 mo before apheresis seems to influence response rates
- Long term CART persistence seems to correlate with duration of response

High risk MCL:

- GLPG5101, a fresh, early memory-enriched phenotype CD19 CAR-T product, yields robust expansion, retention of early memory phenotypes, and long-term persistence, with high rates of response and MRD negativity with a good safety profile
- The short 7-day vein-to-vein time enabled a low dropout rate (4%) and eliminated the need for BT, allowing for more patients to receive treatment that otherwise would not have been able to receive
- The role of BTKi + CART in untreated patients, is still a question due to a very good efficacy but higher rate of toxicity



POST-ORLANDO 2025
Novità dal Meeting della Società Americana di Ematologia

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Torino, 19-21 Febbraio 2026

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