



POST-SAN DIEGO 2024

Novità dal Meeting della Società Americana di Ematologia

# Novità dal Meeting della Società Americana di Ematologia

Bologna

Palazzo Re Enzo

13-15 Febbraio 2025

COORDINATORI

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Beatrice Casadei

**CAR-T NEI LINFOMI INDOLENTI**

*IRCSS – Azienda Ospedaliero Universitaria di Bologna*



## Disclosures of Beatrice Casadei

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



# CAR T-cell Treatment and Indolent Lymphomas at ASH 2024

## Follicular lymphoma

- 2 oral presentations: *Neelapu S.S. et al, abs #864; Kersten M.J. et al, abs#93*
- 7 poster presentations: *Nastoupil L. et al, abs #4387; Thieblemont C. et al, abs#3034; Poddar S. et al, abs #4368; Sharp J. et al, abs#2377; Kramer A.M. et al, abs #2064; Marchetti M. et al, abs #2269; Boardman A.P. et al, abs#3028*

## Marginal zone lymphoma

- 2 oral presentations: *Neelapu S.S. et al, abs #864; Kersten M.J. et al, abs#93*

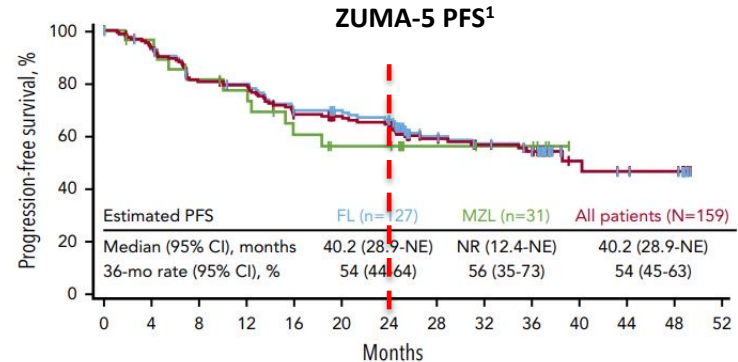
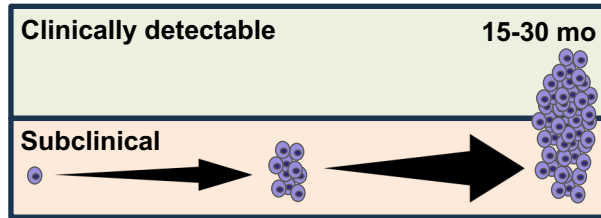
## Chronic lymphocytic leukemia

- 1 poster presentation: *Palma A.U. et al, abs #4607*



## 864. 5-Year Follow-up Analysis from ZUMA-5: A Phase 2 Trial of Axicabtagene Ciloleucel (Axi-Cel) in Patients with Relapsed/Refractory Indolent Non-Hodgkin Lymphoma. *Neelapu S.S. et al.* Oral presentation.

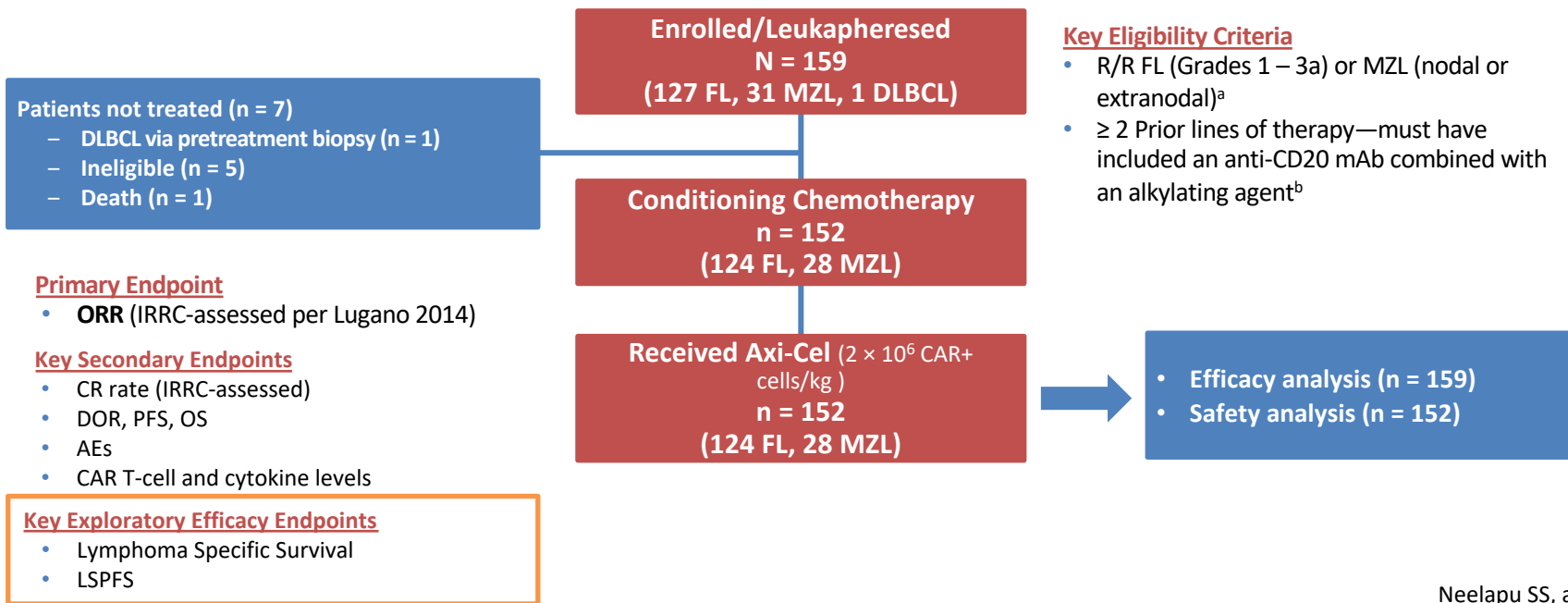
- This 5-year analysis occurred after the median follow-up of all enrolled patients reached  $\geq 60$  months post-infusion (data cut-off: 31 march 2024)



- Lymphoma-specific assessment of survival may be necessary to determine curative potential in FL



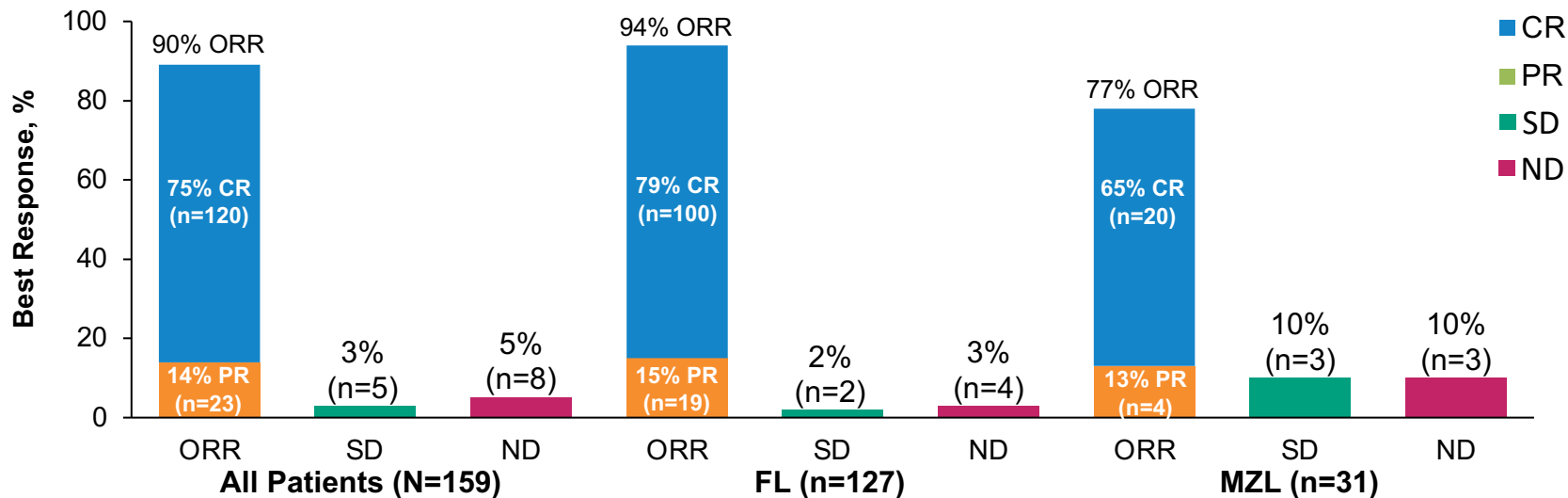
## ZUMA-5 \_ Study Design



Neelapu SS, abs#864

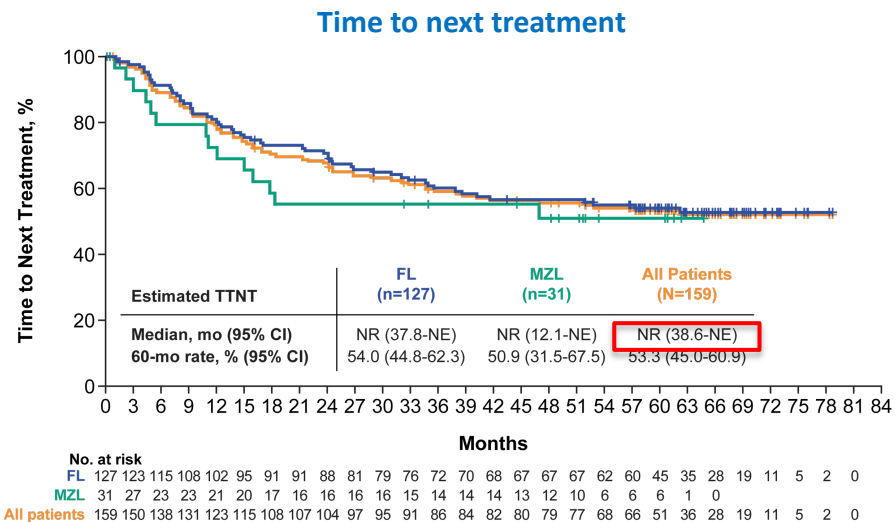
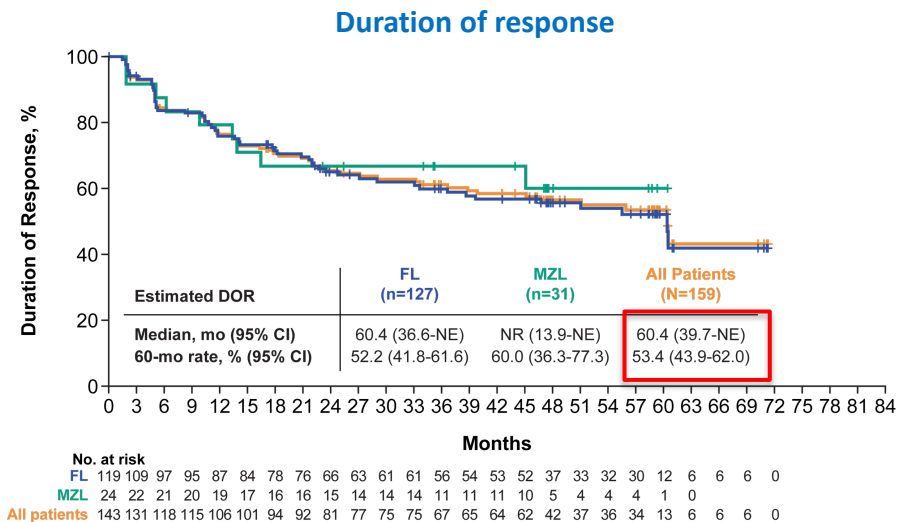


## ZUMA-5 \_ Overall and Complete Response Rate



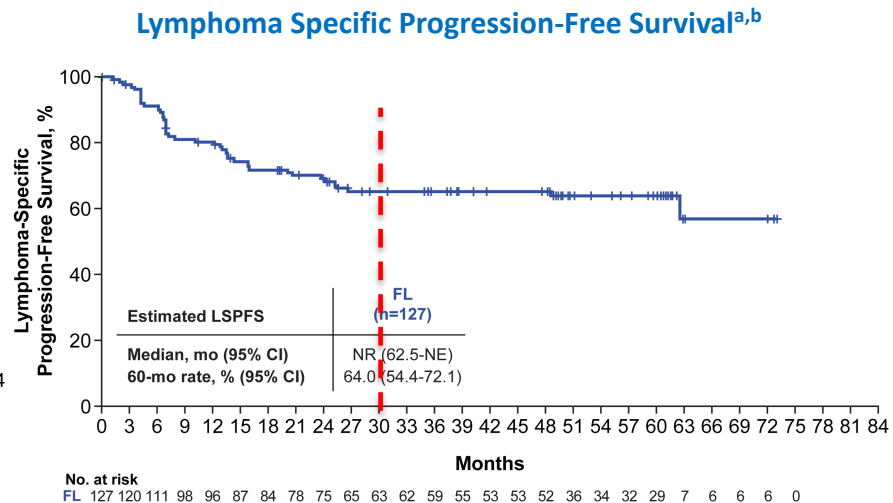
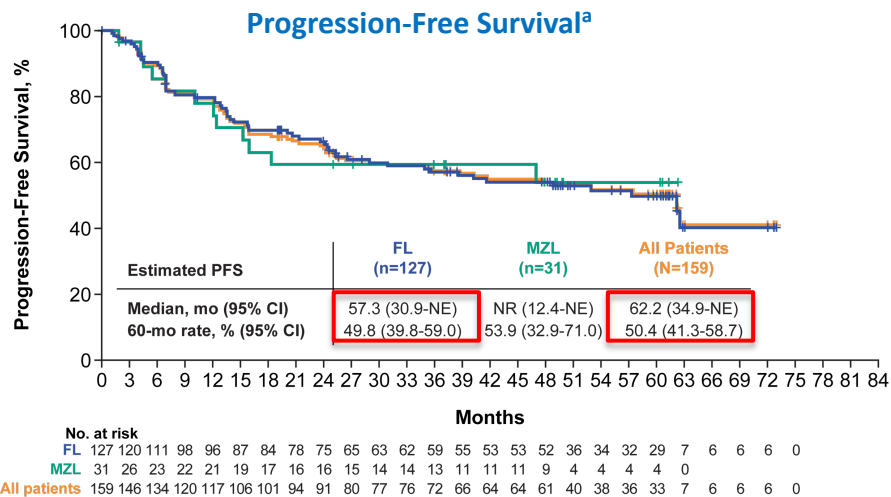


# ZUMA-5 \_ Duration of Response and Time To Next Treatment





# ZUMA-5 \_ PFS and Lymphoma Specific PFS



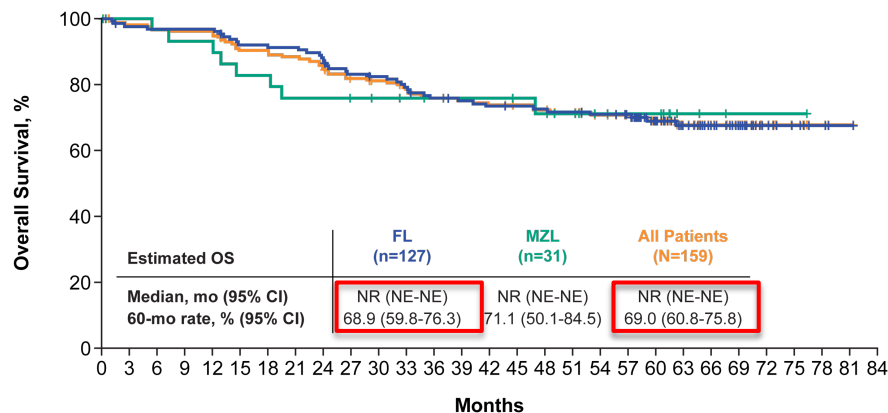
<sup>a</sup> Progression events were determined by the investigator. <sup>b</sup> Death due to lymphoma included death due to disease progression or determined to be disease related. Death due to study treatment complications included death determined to be related to axi-cel or lymphodepleting chemotherapy. These were analyzed per investigator assessment. Deaths not related to lymphoma or study treatment were censored.





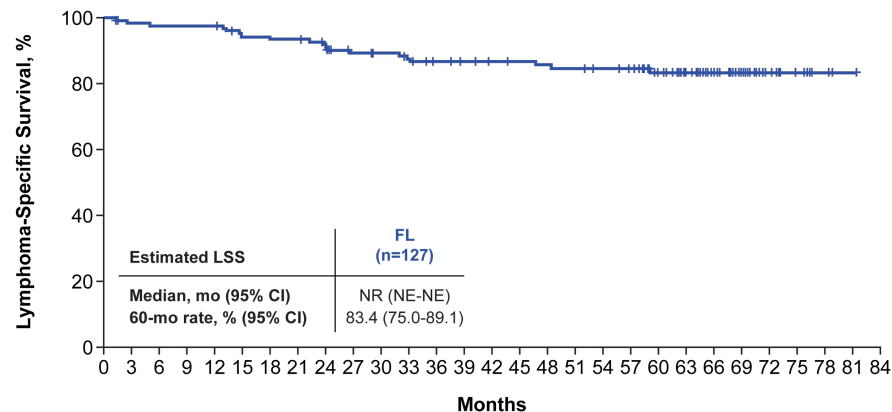
# ZUMA-5 \_ OS and Lymphoma Specific Survival

Overall Survival



No. at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75	78	81	84
FL	127	123	122	122	122	115	115	114	110	103	101	97	92	90	88	87	86	85	83	80	60	45	36	24	14	8	3	1	0
MZL	31	29	28	27	27	24	24	22	22	21	20	19	18	17	17	16	15	13	9	8	8	3	2	1	1	1	1	0	0
All patients	159	152	150	149	149	139	136	132	124	121	116	110	107	105	103	101	98	92	88	68	48	38	25	15	9	3	1	0	0

Lymphoma Specific Survival<sup>a</sup>



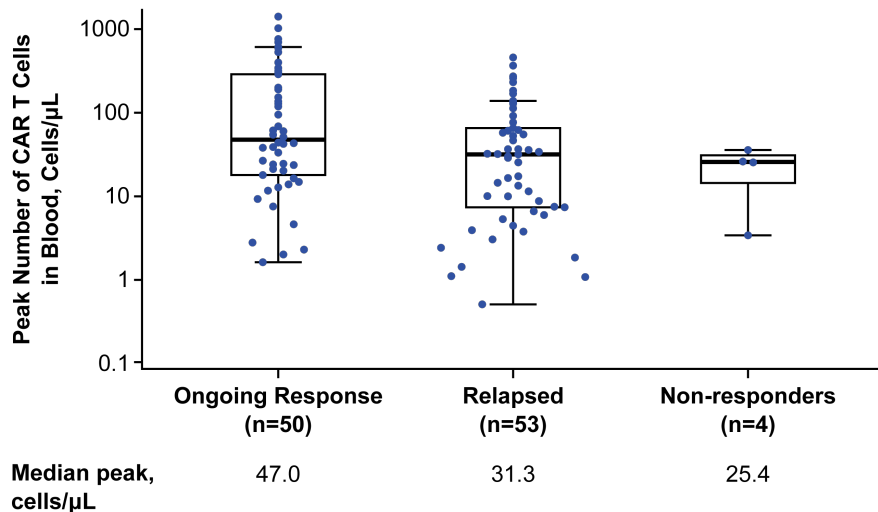
No. at risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63	66	69	72	75	78	81	84
FL	127	123	122	122	122	115	115	114	110	103	101	97	92	90	88	87	86	85	83	80	60	45	36	24	14	8	3	1	0

<sup>a</sup> Death due to lymphoma included death due to disease progression or determined to be disease related. Death due to study treatment complications included death determined to be related to axi-cel or lymphodepleting chemotherapy. These were analyzed per investigator assessment. Deaths not related to lymphoma or study treatment were censored.

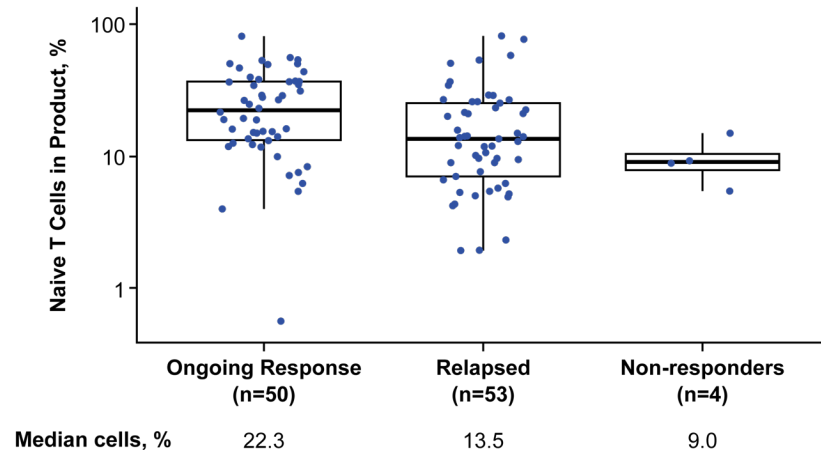


# ZUMA-5 \_ Correlative Analysis (FL)

## Peak CAR T-Cell Expansion



## Naive T Cells in Product





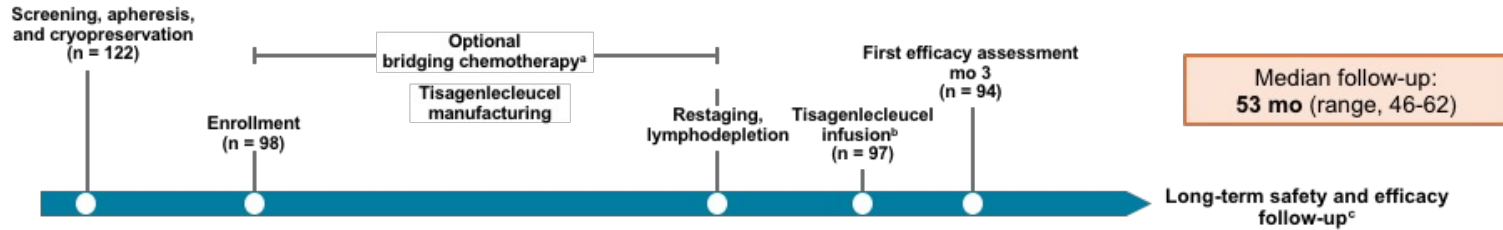
## ZUMA-5 \_ Conclusions

- After a median follow-up of >5 years, axi-cel continued to demonstrate durable responses and long-term survival in patients with R/R iNHL
  - Over half of patients were alive at data cutoff without the need for a subsequent therapy
  - The plateau in lymphoma-specific PFS, with only two progression events after month 30, indicates the curative potential of axi-cel in FL
- Safety outcomes with axi-cel remained consistent with previous analyses, and no new safety signals were observed
- Elevated early CAR T-cell expansion and a naive product phenotype continued to be associated with durable response
- **Collectively, these long-term data support axi-cel as a highly effective therapeutic approach for patients with R/R iNHL, with a curative potential.**



## 3034. Clinical Outcomes of Patients with High-risk Relapsed/Refractory Follicular Lymphoma Treated With Tisagenlecleucel: Phase 2 Elara 4-year Update.

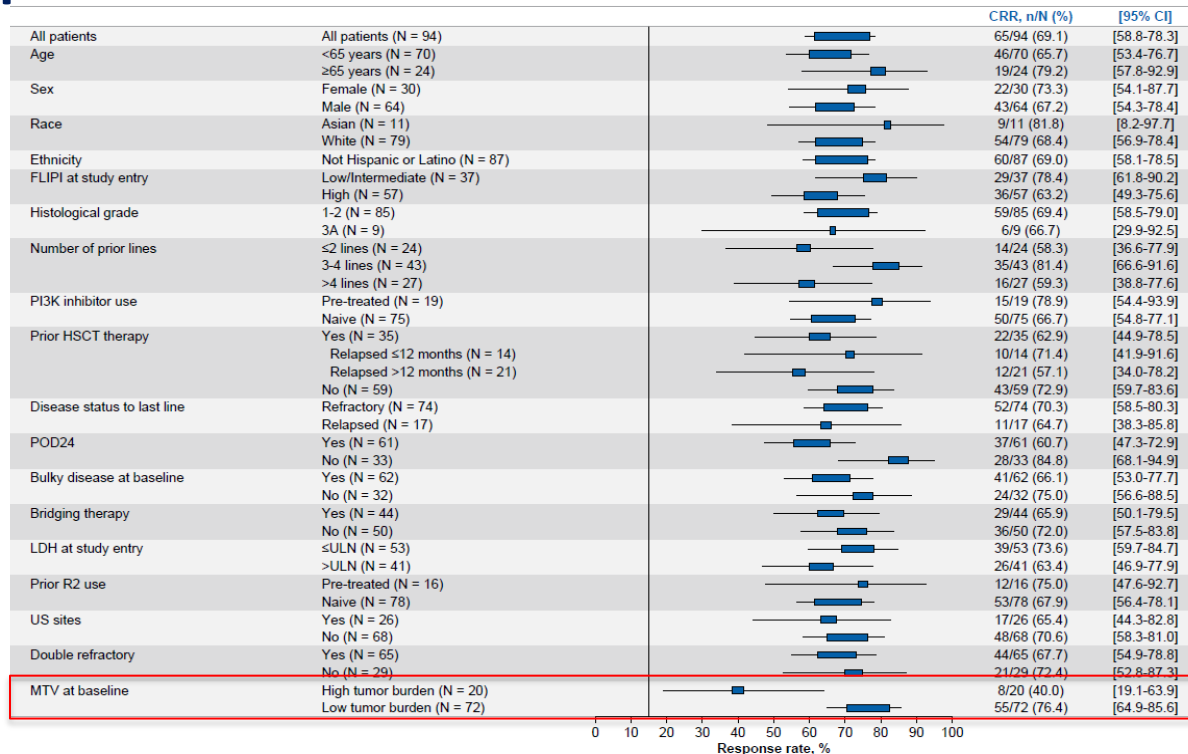
*Thieblemont C. et al.* Poster presentation.



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

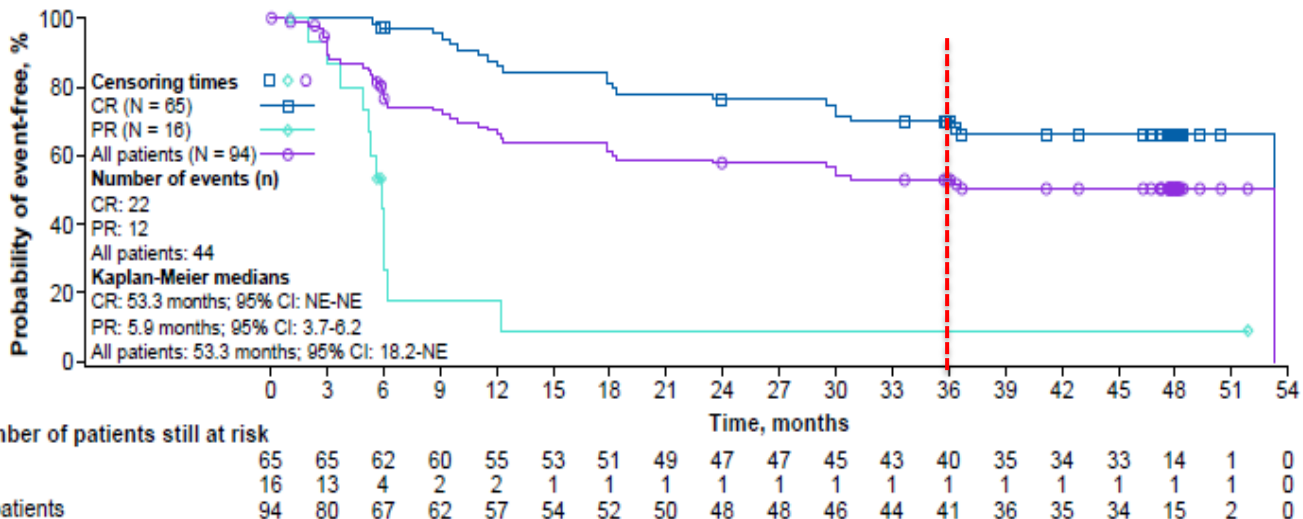


# ELARA \_ Response Rate



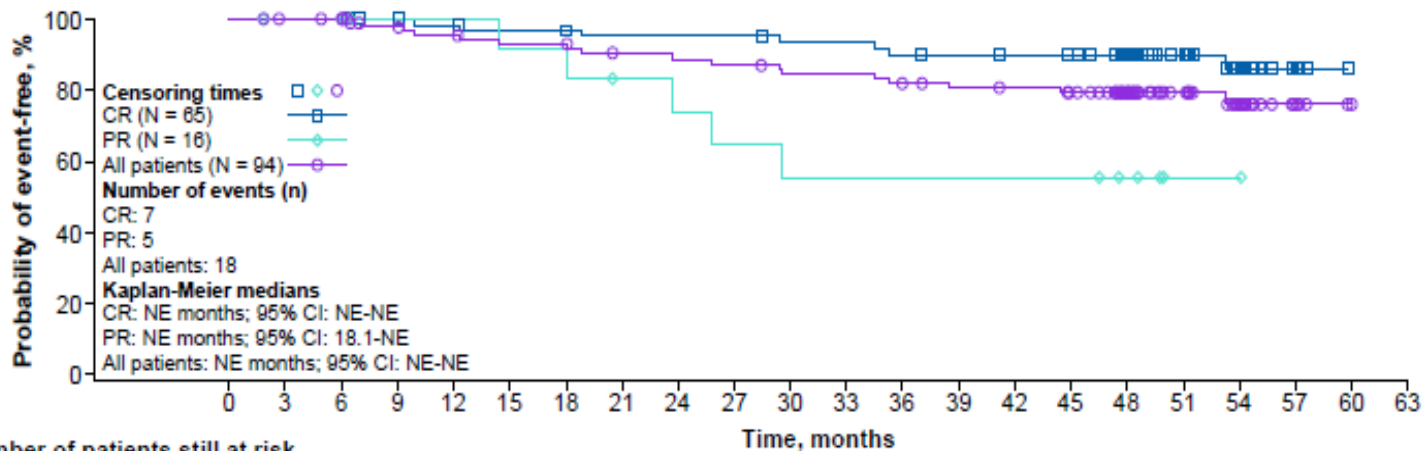


# ELARA \_ Progression Free Survival





# ELARA \_ Overall Survival



**Number of patients still at risk**

	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	60	63
CR	65	65	65	63	61	59	59	57	57	57	55	55	53	52	51	50	40	27	17	4	0	0
PR	16	15	15	12	12	11	11	9	8	7	6	6	6	6	6	6	4	1	1	0	0	0
All patients	94	92	91	84	81	78	78	74	72	71	68	68	65	63	62	59	45	29	19	5	1	0



## ELARA \_ Conclusions

- Updated long-term follow-up from the ELARA trial continues to demonstrate robust durable responses >4 years post-infusion, alongside a favorable safety profile
- Subgroup analyses suggest that most baseline high-risk disease characteristics are not associated with inferior CRR, 48-mo PFS, or 48-mo OS
  - Although lower CRR, 48-mo PFS, and 48-mo OS rates were reported for patients with high tumor burden, it is important to remember that high-risk subgroup analyses were exploratory, and some subgroups (i.e. high tumor burden) had very limited patient numbers





## 2377. Evaluation of Outcome and Toxicities of Commercial axi-cel and tisa-cel for Relapsed or Refractory Follicular Lymphoma: Real-World Evidence from 10 US Academic Center. *Sharp J. et al.* Poster presentation.

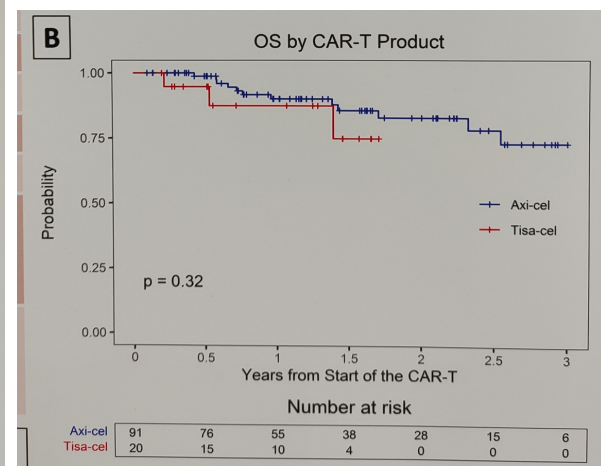
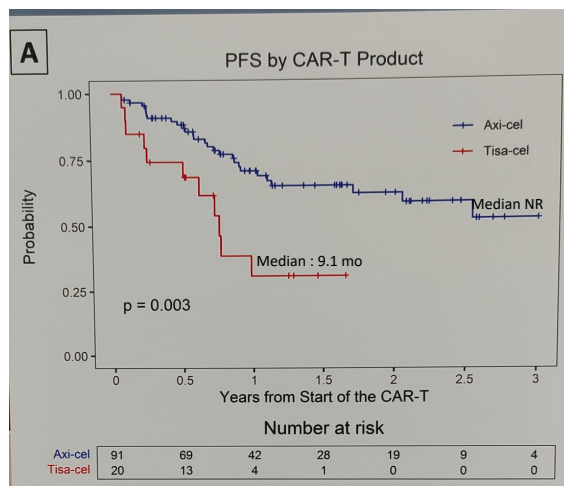
- 111 patients included:
  - 82% received axicel
  - 18% received tisacel
- Median follow-up 14.1 mo
- Tisa-cel group: older, higher proportion of female, more likely to receive benda LD, and receive CART outpatient

Parameter	Axi-cel	Tisa-cel	P value
Median age, years	60	74	<0.001
Female, %	23	60	0.003
LD Bendamustine, %	3	35	<0.001
Disease stage III/IV, %	29/52	25/63	0.82
Prior LoT, median	3	3	0.57
ECOG PS: 0-1 / $\geq 2$ %	96/4	100/0	1.0
Bulky disease, %	44	53	0.71
Primary refractory, %	24	16	0.56
POD24, %	62	56	0.83
CR/PR prior to CAR-T, %	21	16	1.0



## Real World Evidence - Results

	Axi-cel (n=91)	Tisa-cel (n=20)	P value
ORR, % (Day 90+)	89	83	0.43
CRR, % (Day 90+)	85	71	0.16
Median OS, mo	NR	NR	--
1-year OS, %	90	87	0.32
Median PFS, mo	NR	9.1	<b>0.003</b>
1-year PFS, %	71%	31%	--





## Real World Evidence – Results and Conclusions

Toxicities – n (%)	Axi-cel (n=91, 82%)	Tisa-cel (n=20, 18%)	P- value
Cytokine release syndrome, any	71 (78%)	14 (70%)	0.44
CRS Grade 1-2	66 (73%)	13 (65%)	0.50
CRS Grade ≥3	5 (6%)	1 (5%)	1.0
ICANS Grade, any	39 (43%)	4 (20%)	0.03
ICANS Grade 1-2	21 (23%)	3 (15%)	0.55
ICANS Grade ≥3	18 (20%)	1 (5%)	0.19
Unexpected inpatient stay within 30 days of CAR-T*	6 (75%)	5 (63%)	1.0
Unexpected re-admission within 30 days of CAR-T**	20 (24%)	1 (8%)	0.29

- First RWE analysing outcomes and toxicities of axicel and tisacel for RR FL
- Response rates were comparable in the two cohorts
- PFS inferior with tisa-cel but no OS difference
- Small number of tisa-cel patients is a limitation



## **SSD LINFOMI E SDR LINFOPROLIFERATIVE CRONICHE, UOC EMATOLOGIA**

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