

# Updates in CAR T-Cell Therapy

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November 11, 2023



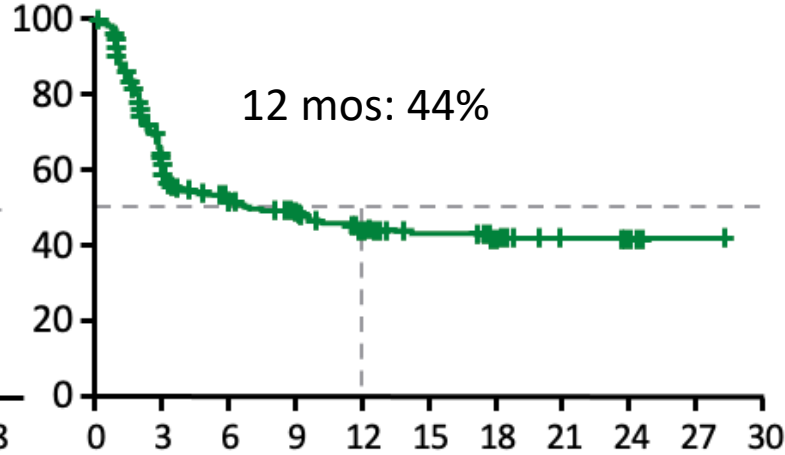
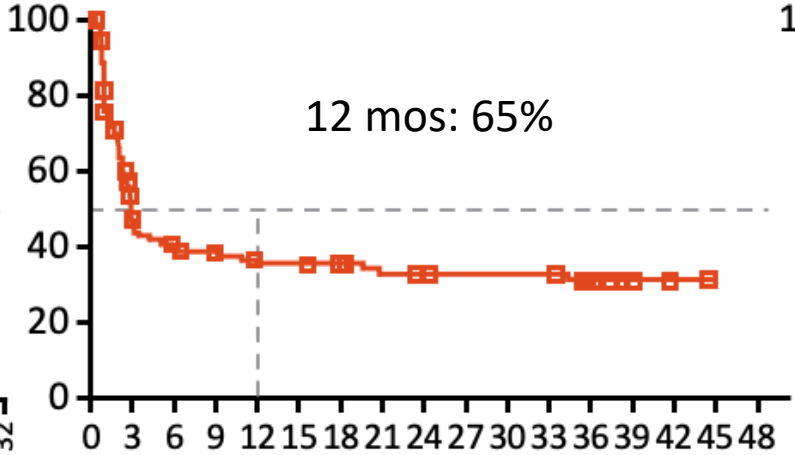
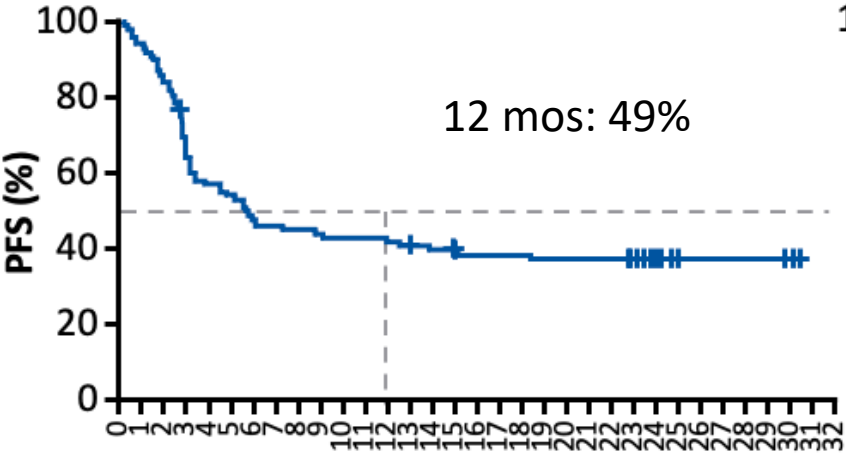
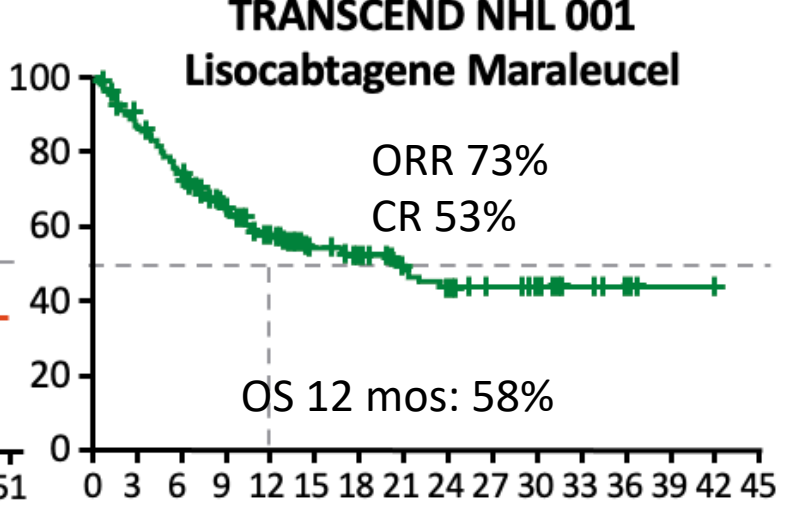
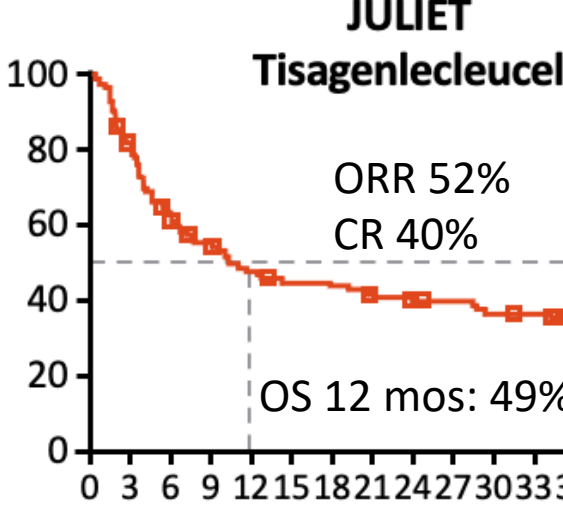
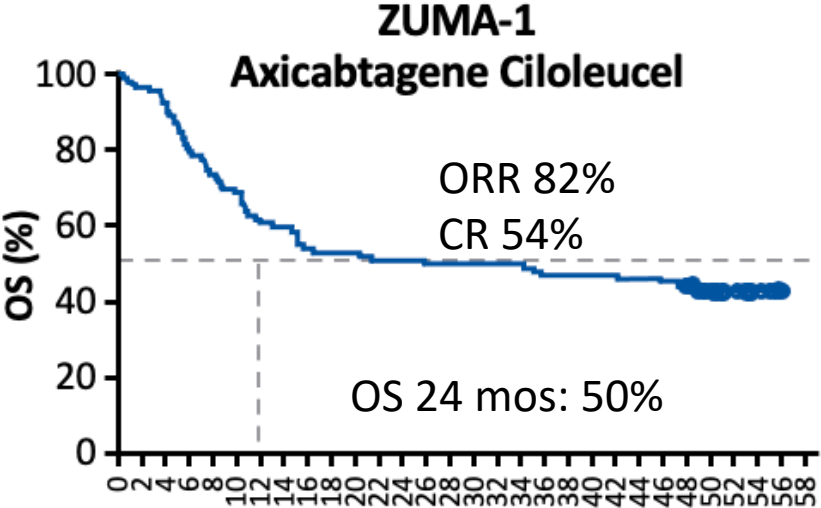
# Outline

- Updates in CAR T Therapies
  - Lymphoma
  - B-ALL
  - Multiple Myeloma
- Management of CRS, ICANS
- Ongoing studies

## Current FDA Approved CAR T Products

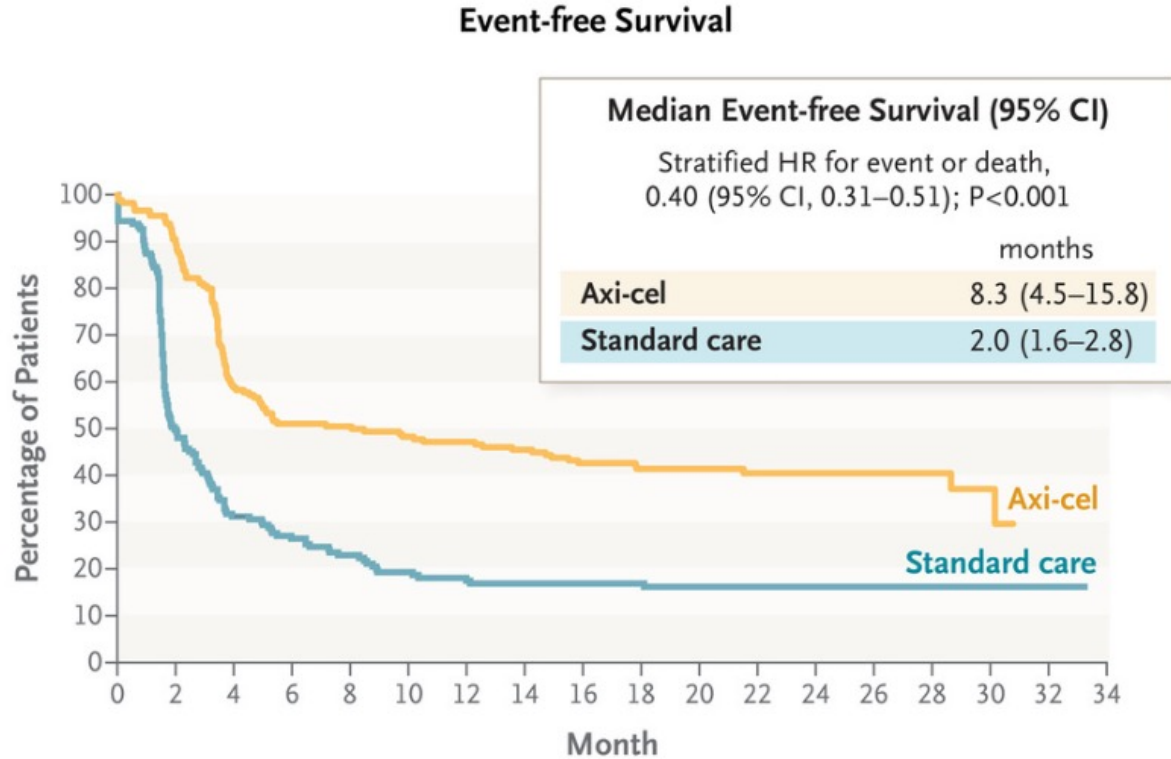
| Product                    | Disease               | Target | Indication                        | Approval           |
|----------------------------|-----------------------|--------|-----------------------------------|--------------------|
| Axicabtagene               | DLBCL<br>FL           | CD19   | 2 <sup>nd</sup> line<br>≥ 2 lines | 2017, 2022<br>2021 |
| Tisagenlecleucel           | DLBCL<br>B-ALL (≤ 25) | CD19   | ≥ 2 lines<br>≥ 2 lines            | 2018<br>2017       |
| Lisocabtagene<br>(Lisocel) | DLBCL                 | CD19   | 2 <sup>nd</sup> line              | 2021, 2022         |
| Brexucabtagene             | MCL<br>B-ALL (adults) | CD19   | ≥ 2 lines                         | 2020<br>2021       |
| Idecabtagene               | Multiple<br>Myeloma   | BCMA   | ≥ 4 lines                         | 2021               |
| Ciltacabtagene             | Multiple<br>Myeloma   | BCMA   | ≥ 4 lines                         | 2022               |

# Pivotal Phase I/II CD19 CAR T Trials: NHL



Locke. Lancet Oncol. 2019;20:31. Jacobson. ASH 2020. Abstr 1187. Jaeger. ASH 2020. Abstr 1194. Abramson. Lancet. 2020;396:839. Slide credit: [ProCE.com](http://ProCE.com) and [clinicaloptions.com](http://clinicaloptions.com)

# 2<sup>nd</sup> Line CAR T vs Autologous SCT: ZUMA-7

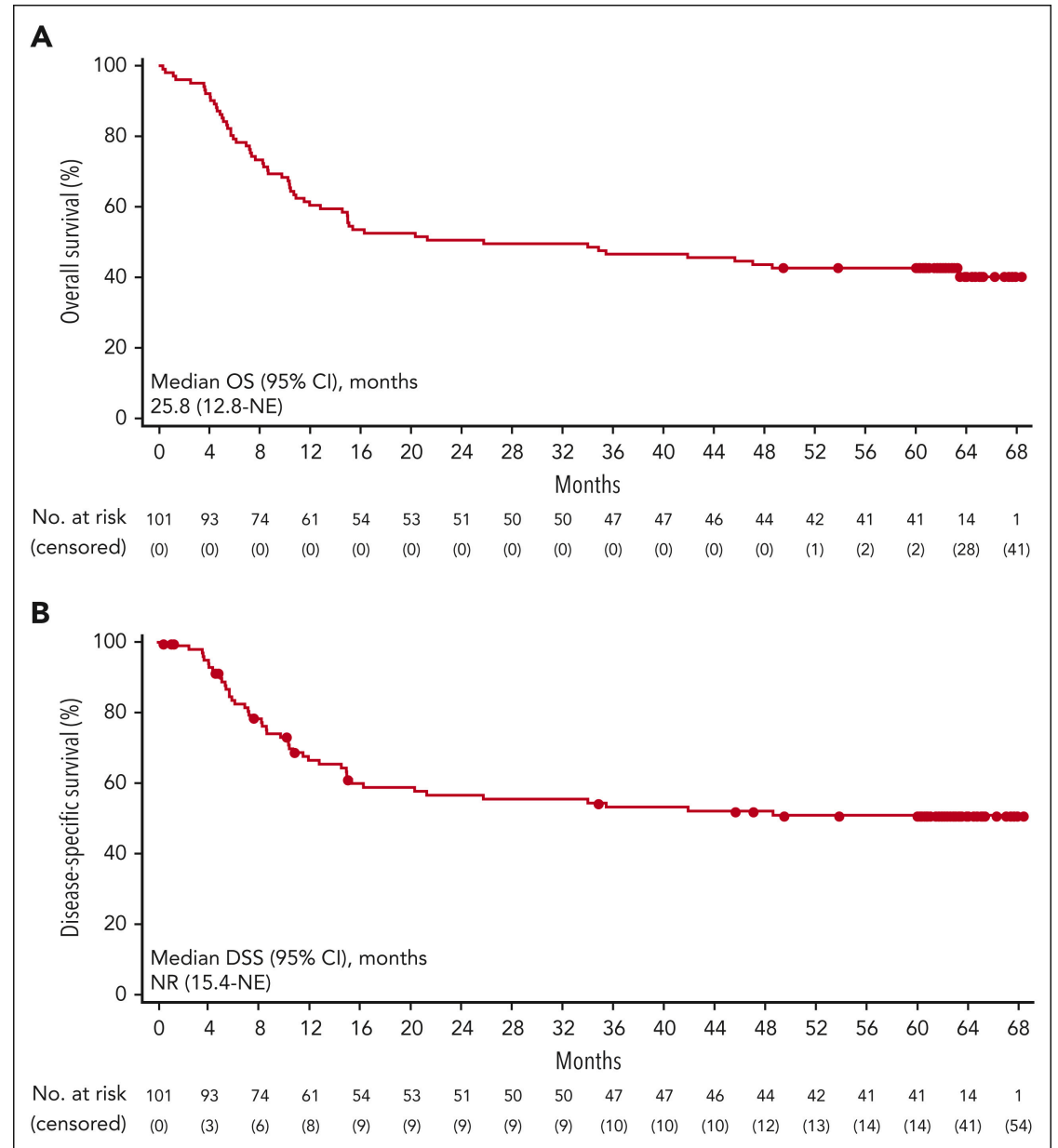


- 74% Primary Refractory disease
- No bridging chemo permitted

| End Point      | Axicabtagene           |
|----------------|------------------------|
| mEFS at 24 mos | <b>41%</b><br>(vs 16%) |
| PFS at 24 mos  | 14.7 mos<br>(vs 3.7)   |
| OS at 24 mos   | 61%<br>(vs 52%)        |
| ORR            | 83%                    |
| CR             | 65%<br>(vs 32%)        |

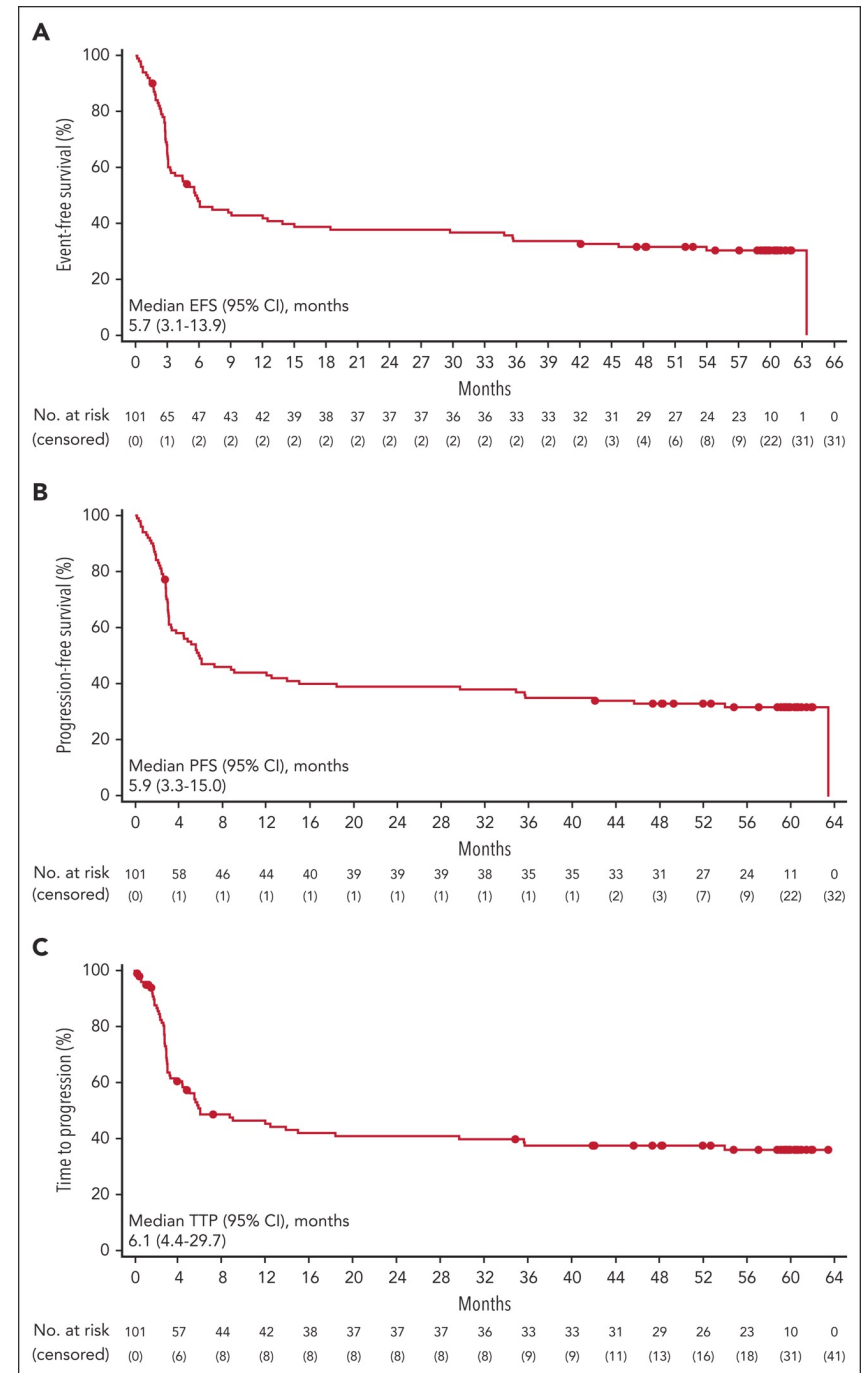
# ZUMA-1 Five-Year Follow Up

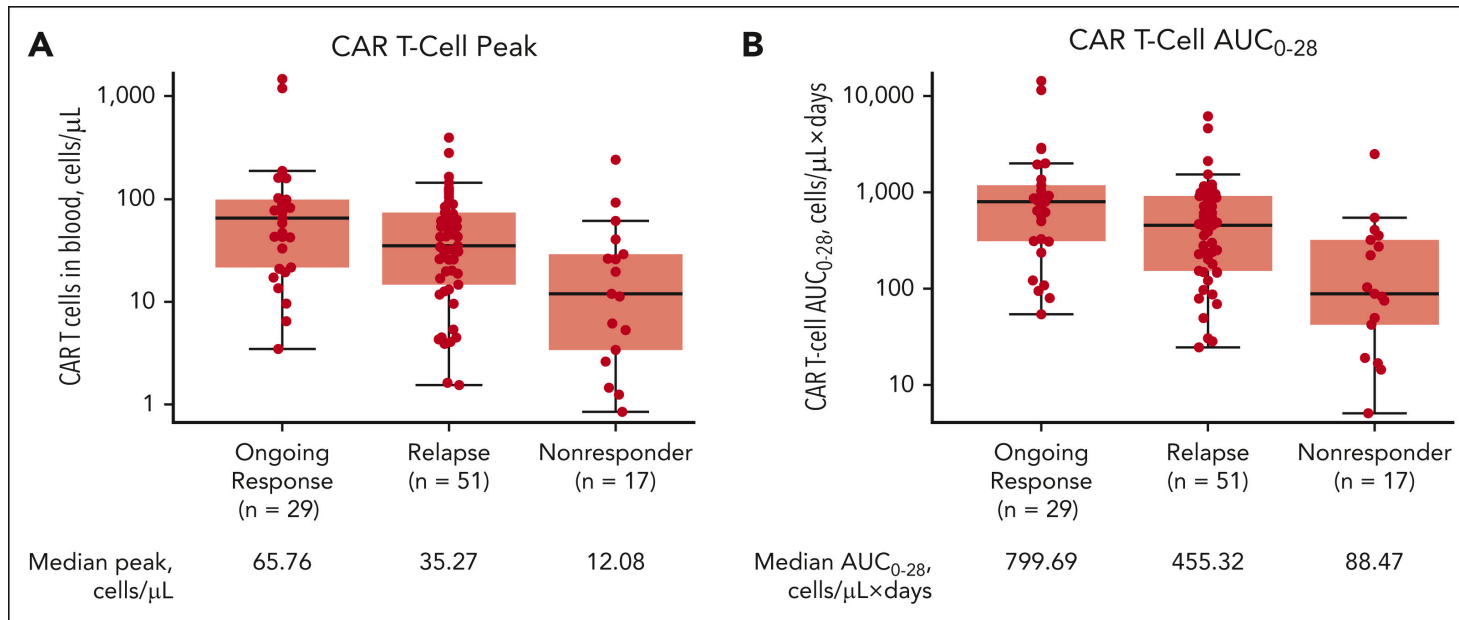
- Axicel Cohorts 1 and 2
  - LBCL, PMBCL, tFL
  - Primary refractory or relapse within 12 mos of autoSCT
- N =101. 63 months mFU
- mDOR 11 months
- mOS 25 months
- DSS 51%



# ZUMA-1 Five-Year Follow Up

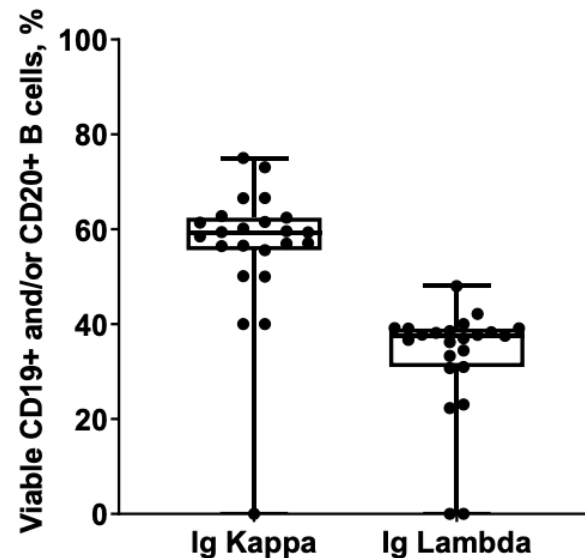
- 5-year EFS 30%
- 5-year PFS 31%
  
- 5-year OS 43%
- If CR, 5-year OS 64%





- Ongoing response associated with early CAR T expansion
- Polyclonal B-cell recovery and diversity in pts with ongoing responses
  - 91% at 3 years
- Protracted B-cell aplasia not required for response

### B-Cell Recovery

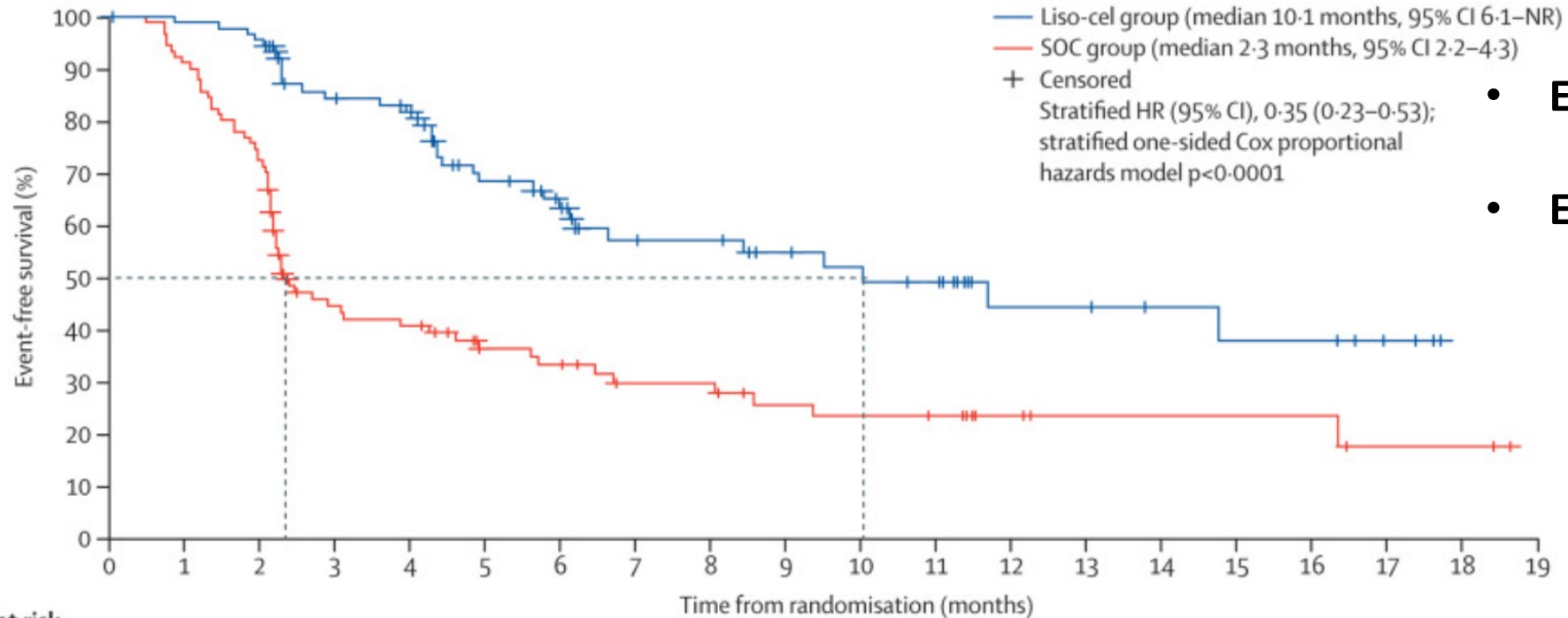




# TRANSFORM: Lisocabtagene 2<sup>nd</sup> line

- Lisocabtagene vs SOC in early relapsed ( $\leq 12$  mos) or refractory large B-cell lymphoma
  - SOC = 3 cycles platinum-containing salvage  $\rightarrow$  HD chemo + auto SCT

A

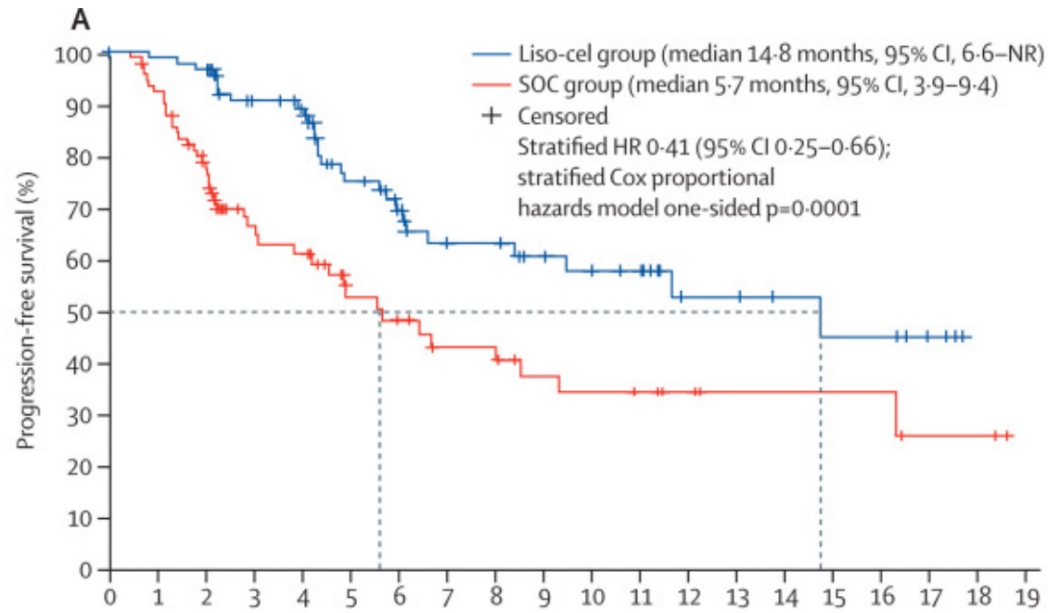


- **EFS 10 vs 2 mos**
- **EFS at 6 mos**
  - **63% v 33%**

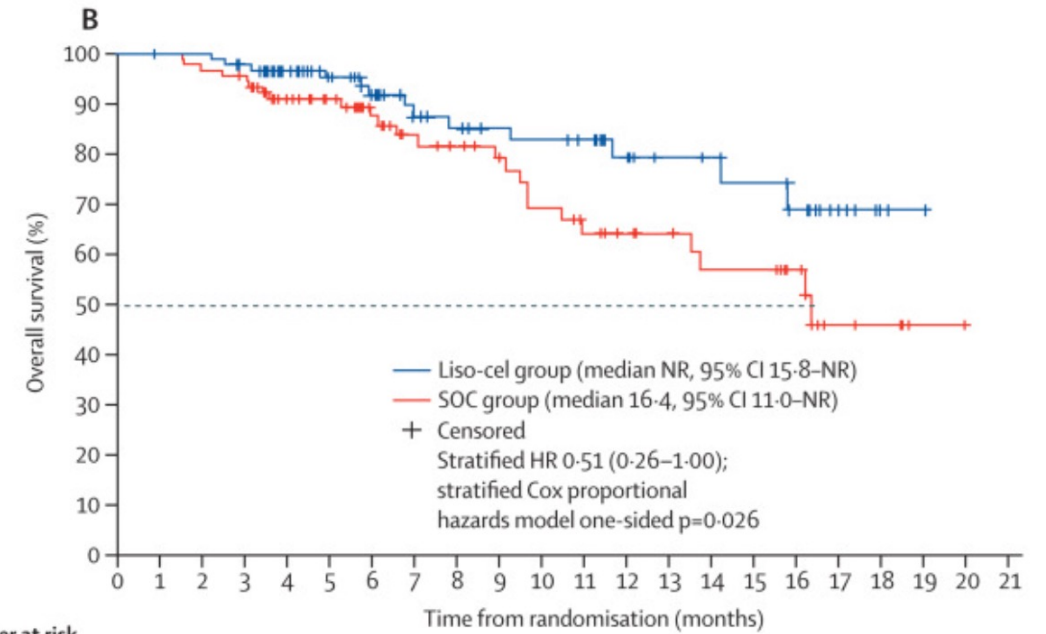
Number at risk  
(number censored)

|                     |        |        |        |         |         |         |         |         |         |         |         |         |        |        |        |        |        |        |        |         |
|---------------------|--------|--------|--------|---------|---------|---------|---------|---------|---------|---------|---------|---------|--------|--------|--------|--------|--------|--------|--------|---------|
| Lisocabtagene group | 92 (0) | 89 (2) | 86 (2) | 66 (13) | 62 (15) | 43 (25) | 36 (29) | 27 (35) | 26 (36) | 21 (40) | 19 (41) | 17 (42) | 9 (49) | 9 (49) | 7 (51) | 6 (51) | 6 (51) | 4 (53) | 0 (57) | .. (57) |
| SOC group           | 92 (0) | 83 (1) | 66 (1) | 35 (8)  | 32 (8)  | 23 (14) | 21 (14) | 16 (17) | 16 (17) | 12 (19) | 11 (19) | 10 (20) | 6 (24) | 4 (26) | 4 (26) | 4 (26) | 4 (26) | 2 (27) | 2 (27) | 0 (29)  |

# TRANSFORM: Lisocabtagene 2<sup>nd</sup> line



| Number at risk<br>(number censored) | 0         | 1         | 2         | 3          | 4          | 5          | 6          | 7          | 8          | 9          | 10         | 11         | 12        | 13        | 14        | 15        | 16        | 17        | 18        | 19        |
|-------------------------------------|-----------|-----------|-----------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Liso-cel group                      | 92<br>(0) | 89<br>(2) | 87<br>(2) | 69<br>(15) | 65<br>(18) | 44<br>(30) | 37<br>(34) | 28<br>(40) | 27<br>(41) | 22<br>(45) | 20<br>(46) | 18<br>(48) | 9<br>(56) | 9<br>(58) | 7<br>(58) | 6<br>(58) | 6<br>(60) | 4<br>(64) | 0<br>(64) | ..        |
| SOC group                           | 92<br>(0) | 82<br>(3) | 66<br>(7) | 37<br>(27) | 34<br>(27) | 23<br>(34) | 21<br>(34) | 16<br>(37) | 16<br>(37) | 12<br>(39) | 11<br>(39) | 10<br>(40) | 6<br>(44) | 4<br>(46) | 4<br>(46) | 4<br>(46) | 4<br>(46) | 2<br>(47) | 2<br>(47) | 0<br>(49) |

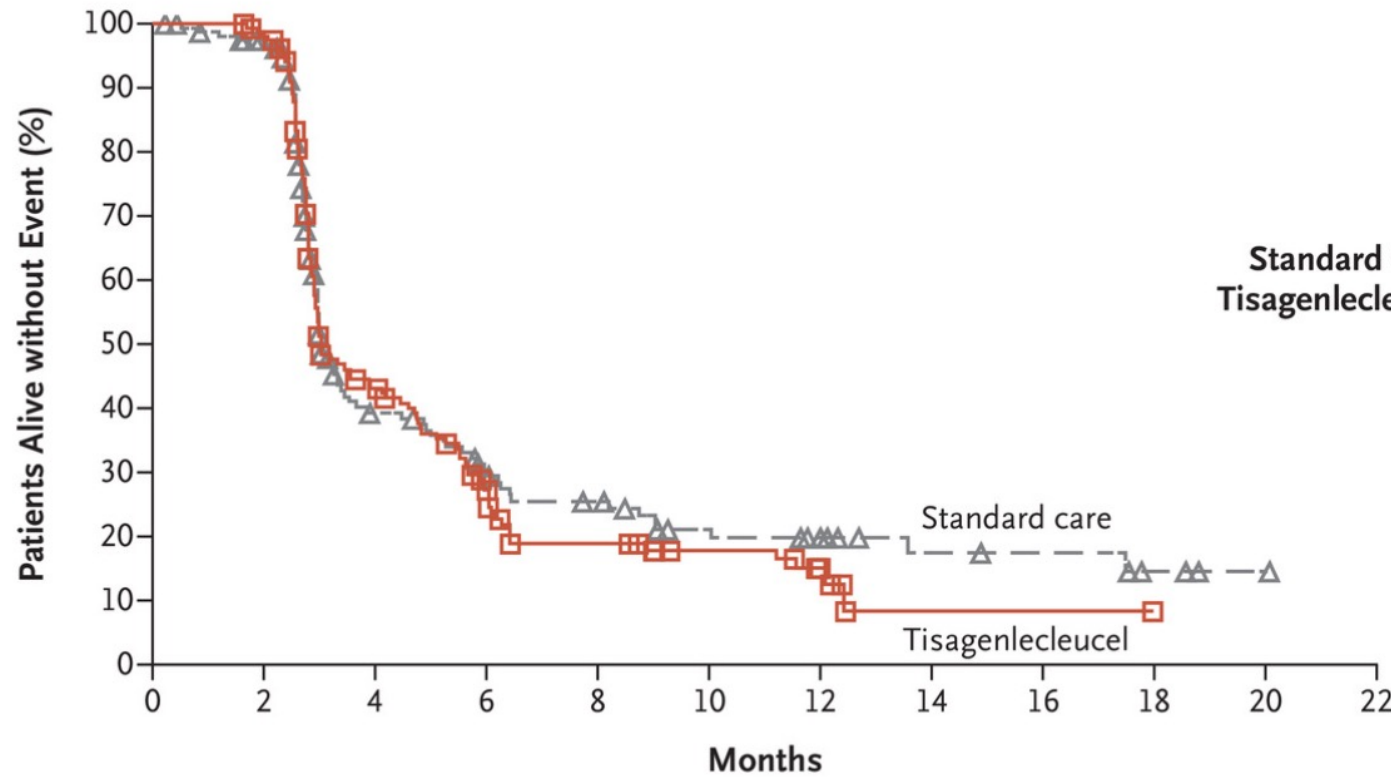


| Number at risk<br>(number censored) | 0         | 1         | 2         | 3          | 4          | 5          | 6          | 7          | 8          | 9          | 10         | 11         | 12         | 13         | 14         | 15         | 16         | 17        | 18        | 19        | 20        | 21        |
|-------------------------------------|-----------|-----------|-----------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-----------|-----------|-----------|-----------|-----------|
| Liso-cel group                      | 92<br>(0) | 91<br>(1) | 91<br>(1) | 87<br>(3)  | 75<br>(14) | 64<br>(24) | 53<br>(33) | 42<br>(43) | 37<br>(46) | 34<br>(49) | 33<br>(49) | 31<br>(51) | 22<br>(59) | 18<br>(63) | 17<br>(64) | 15<br>(65) | 12<br>(67) | 7<br>(72) | 2<br>(77) | 1<br>(78) | 0<br>(79) | ..        |
| SOC group                           | 92<br>(0) | 91<br>(1) | 89<br>(2) | 86<br>(12) | 72<br>(25) | 59<br>(35) | 48<br>(40) | 40<br>(42) | 37<br>(45) | 33<br>(46) | 28<br>(48) | 24<br>(51) | 21<br>(53) | 19<br>(54) | 16<br>(54) | 16<br>(58) | 12<br>(63) | 5<br>(64) | 4<br>(67) | 1<br>(67) | 1<br>(67) | 0<br>(68) |

**mPFS 14.8 v 5.7 months**  
**mOS NR v 16 months**

# BELINDA: Tisagenlecleucel 2<sup>nd</sup> line

- Optional bridging therapy
- Primary Endpoint: EFS



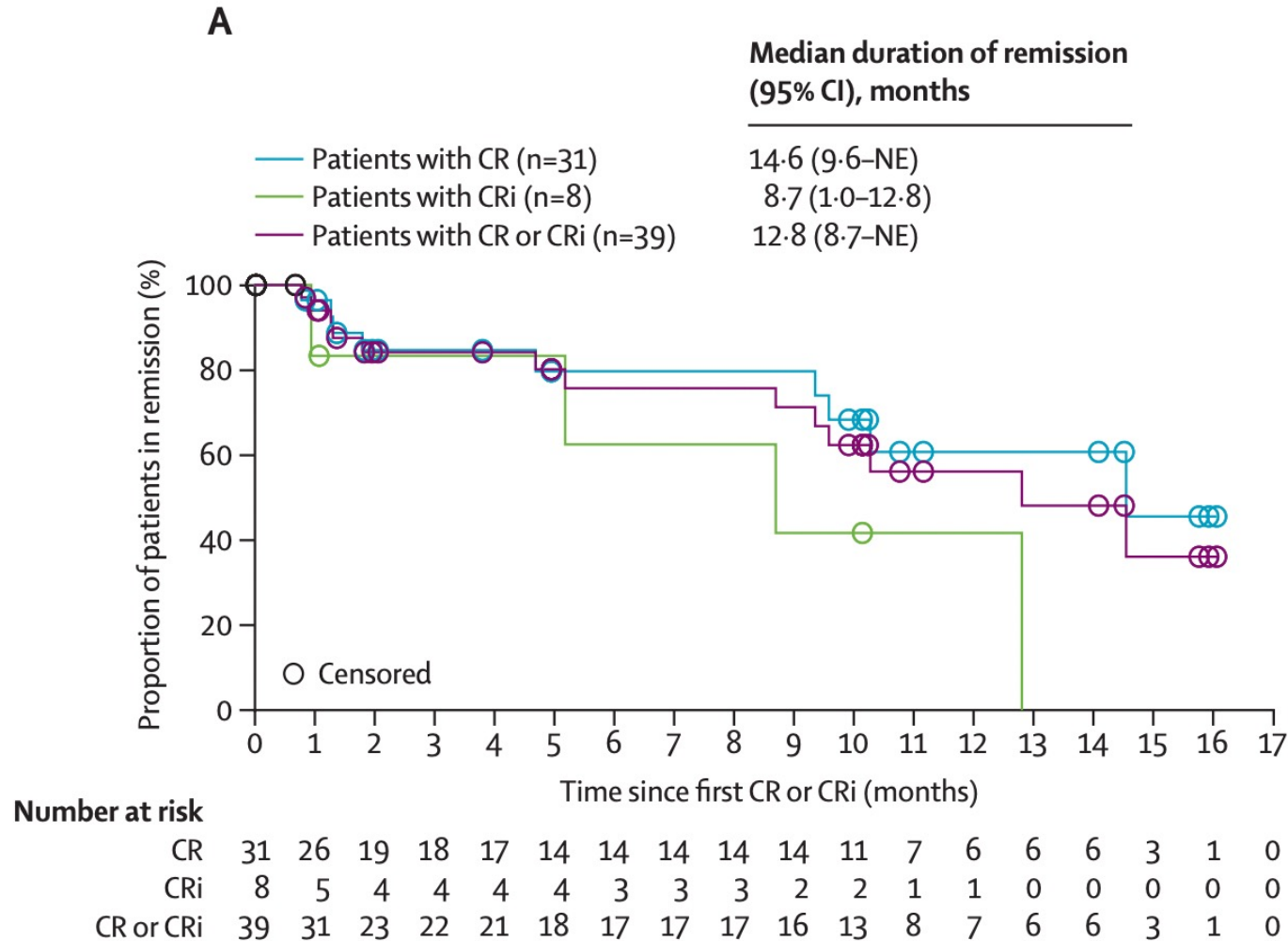
|                  | No. of Patients | No. of Events | Median Event-free Survival (95% CI) mo |
|------------------|-----------------|---------------|----------------------------------------|
| Standard Care    | 160             | 104           | 3.0 (3.0–3.5)                          |
| Tisagenlecleucel | 162             | 117           | 3.0 (2.9–4.2)                          |

Hazard ratio for event or death (tisagenlecleucel vs. standard care), 1.07 (95% CI, 0.82–1.40)  
P=0.61

## No. at Risk

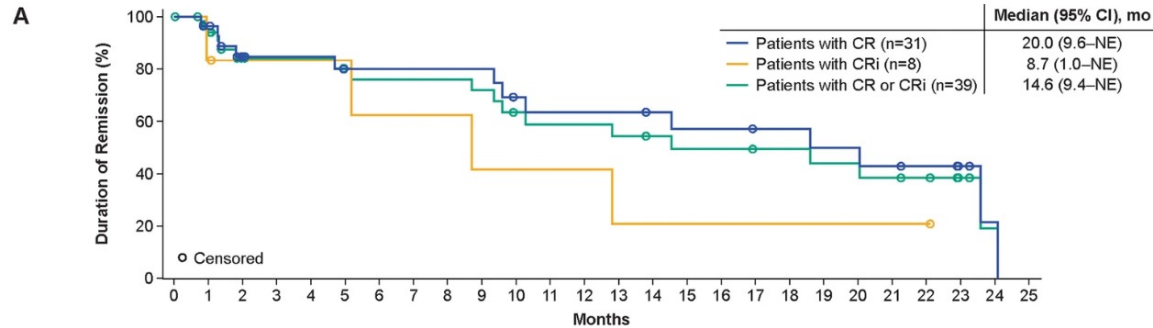
|                  |     |     |    |    |    |    |    |   |   |   |   |   |
|------------------|-----|-----|----|----|----|----|----|---|---|---|---|---|
| Standard care    | 160 | 148 | 45 | 31 | 25 | 17 | 12 | 7 | 6 | 3 | 1 | 0 |
| Tisagenlecleucel | 162 | 156 | 57 | 32 | 19 | 13 | 6  | 1 | 1 | 0 | 0 | 0 |

# ZUMA-3: Brexucabtagene in R/R B-ALL

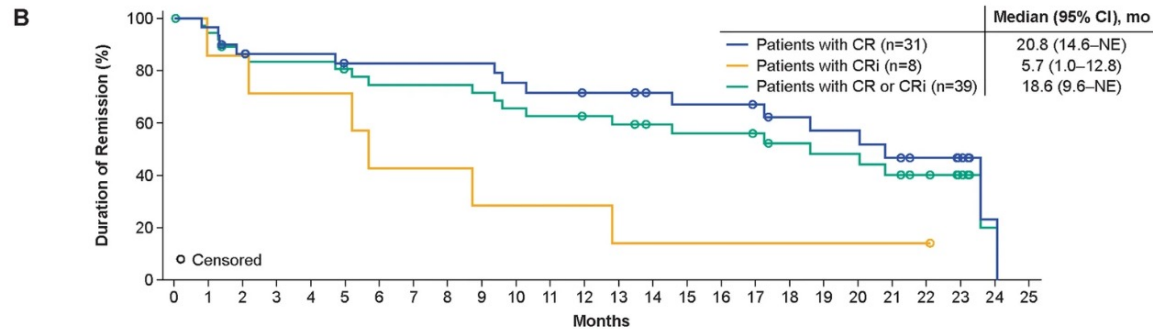


- $\geq 18$  years
- BM blasts  $\geq 5\%$
- 71% CR/CRi
- 12-month OS 71%
- Median OS 18 mos
  - NR in responders
  - 76% MRD negative (97% responders)
- Median RFS 11.6 mos

# ZUMA-3 Two-Year Follow Up



|                   |     |     |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
|-------------------|-----|-----|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| CR at risk        | 31  | 26  | 19   | 18   | 18   | 15   | 15   | 15   | 15   | 15   | 12   | 11   | 11   | 11   | 10   | 9    | 9    | 8    | 8    | 7    | 7    | 6    | 5    | 3    | 1    | 0    |
| (CR censored)     | (0) | (4) | (8)  | (9)  | (9)  | (11) | (11) | (11) | (11) | (11) | (12) | (12) | (12) | (12) | (13) | (13) | (13) | (14) | (14) | (14) | (14) | (14) | (15) | (17) | (18) | (18) |
| CRi at risk       | 8   | 5   | 4    | 4    | 4    | 4    | 3    | 3    | 3    | 2    | 2    | 2    | 2    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    |
| (CRi censored)    | (0) | (2) | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (3)  | (4)  | (4)  | (4)  |
| CR+CRi at risk    | 39  | 31  | 23   | 22   | 22   | 19   | 18   | 18   | 18   | 17   | 14   | 13   | 13   | 12   | 11   | 10   | 10   | 9    | 9    | 8    | 8    | 7    | 6    | 3    | 1    | 0    |
| (CR+CRi censored) | (0) | (6) | (11) | (12) | (12) | (14) | (14) | (14) | (14) | (14) | (15) | (15) | (15) | (15) | (16) | (16) | (16) | (17) | (17) | (17) | (17) | (17) | (18) | (21) | (22) | (22) |

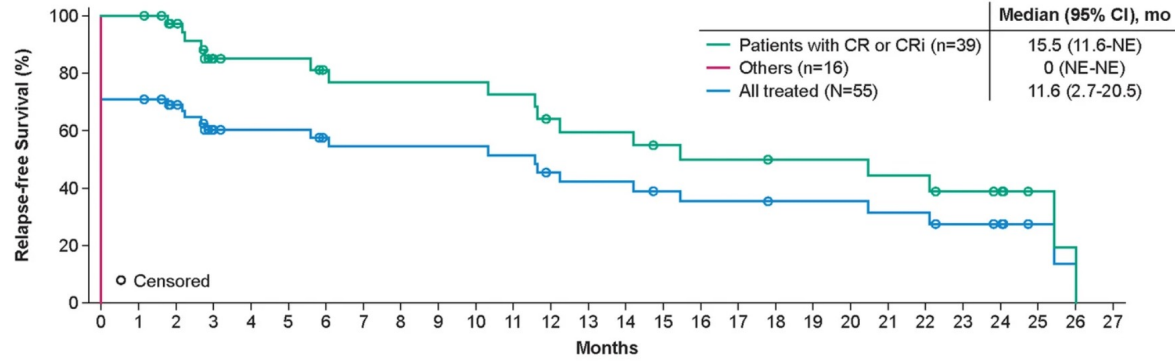


|                   |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |      |      |      |      |      |      |      |      |
|-------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|------|------|------|
| CR at risk        | 31  | 29  | 25  | 24  | 24  | 22  | 22  | 22  | 22  | 22  | 20  | 19  | 18  | 18  | 16  | 15  | 15  | 14  | 12   | 11   | 11   | 9    | 7    | 5    | 1    | 0    |
| (CR censored)     | (0) | (1) | (2) | (3) | (3) | (4) | (4) | (4) | (4) | (4) | (4) | (4) | (5) | (5) | (7) | (7) | (7) | (8) | (9)  | (9)  | (9)  | (9)  | (11) | (13) | (16) | (16) |
| CRi at risk       | 8   | 6   | 6   | 5   | 5   | 5   | 3   | 3   | 3   | 2   | 2   | 2   | 2   | 1   | 1   | 1   | 1   | 1   | 1    | 1    | 1    | 1    | 1    | 0    | 0    | 0    |
| (CRi censored)    | (0) | (1) | (1) | (1) | (1) | (1) | (1) | (1) | (1) | (1) | (1) | (1) | (1) | (1) | (1) | (1) | (1) | (1) | (1)  | (1)  | (1)  | (1)  | (1)  | (2)  | (2)  | (2)  |
| CR+CRi at risk    | 39  | 35  | 31  | 29  | 29  | 27  | 25  | 25  | 25  | 24  | 22  | 21  | 20  | 19  | 17  | 16  | 16  | 15  | 13   | 12   | 12   | 10   | 8    | 5    | 1    | 0    |
| (CR+CRi censored) | (0) | (2) | (3) | (4) | (4) | (5) | (5) | (5) | (5) | (5) | (5) | (5) | (6) | (6) | (8) | (8) | (8) | (9) | (10) | (10) | (10) | (10) | (12) | (15) | (18) | (18) |

- 71 enrolled
- 55 received CAR T infusion
- mFU 26 months
- CR/CRi remains 71%
- 11 (20%) proceeded to alloSCT
  - 8 CR, 2 CRi, 1 blast-free BM
- mDOR 14.6, 18.6 months w/wo censoring for alloSCT

# Relapse-Free Survival

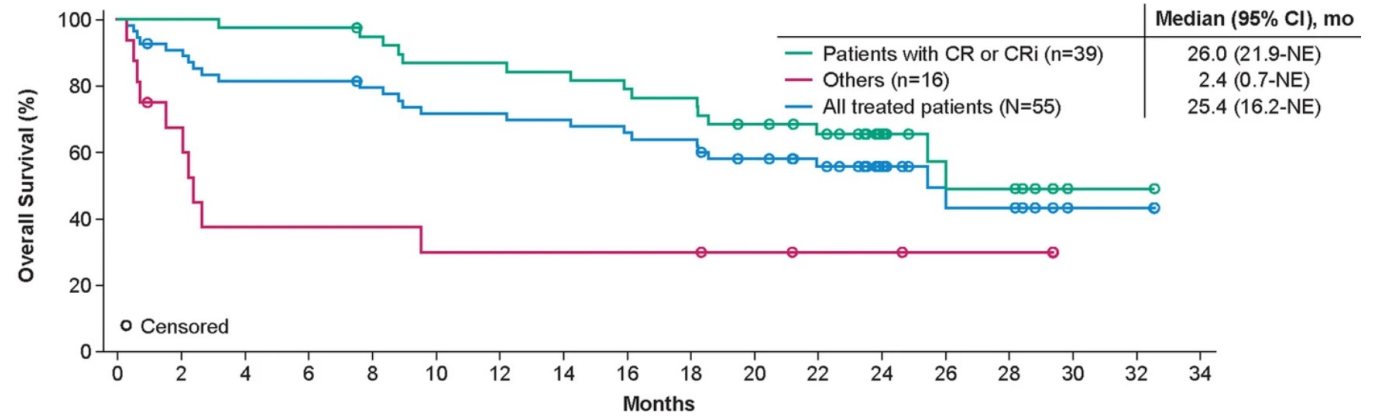
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|                        |     |     |     |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |      |
|------------------------|-----|-----|-----|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|
| CR+CRi at risk         | 39  | 39  | 33  | 24   | 22   | 22   | 19   | 18   | 18   | 18   | 18   | 17   | 14   | 13   | 13   | 11   | 10   | 10   | 9    | 9    | 9    | 8    | 8    | 6    | 5    | 2    | 1    | 0    |
| (CR+CRi censored)      | (0) | (0) | (5) | (10) | (12) | (12) | (14) | (14) | (14) | (14) | (14) | (14) | (15) | (15) | (15) | (16) | (16) | (16) | (17) | (17) | (17) | (17) | (17) | (18) | (19) | (22) | (22) | (22) |
| Others at risk         | 16  | 0   | 0   | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    | 0    |
| (Others censored)      | (0) | (0) | (0) | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  | (0)  |
| All treated at risk    | 55  | 39  | 33  | 24   | 22   | 22   | 19   | 18   | 18   | 18   | 18   | 17   | 14   | 13   | 13   | 11   | 10   | 10   | 9    | 9    | 9    | 8    | 8    | 6    | 5    | 2    | 1    | 0    |
| (All treated censored) | (0) | (0) | (5) | (10) | (12) | (12) | (14) | (14) | (14) | (14) | (14) | (14) | (15) | (15) | (15) | (16) | (16) | (16) | (17) | (17) | (17) | (17) | (17) | (18) | (19) | (22) | (22) | (22) |

# Overall Survival

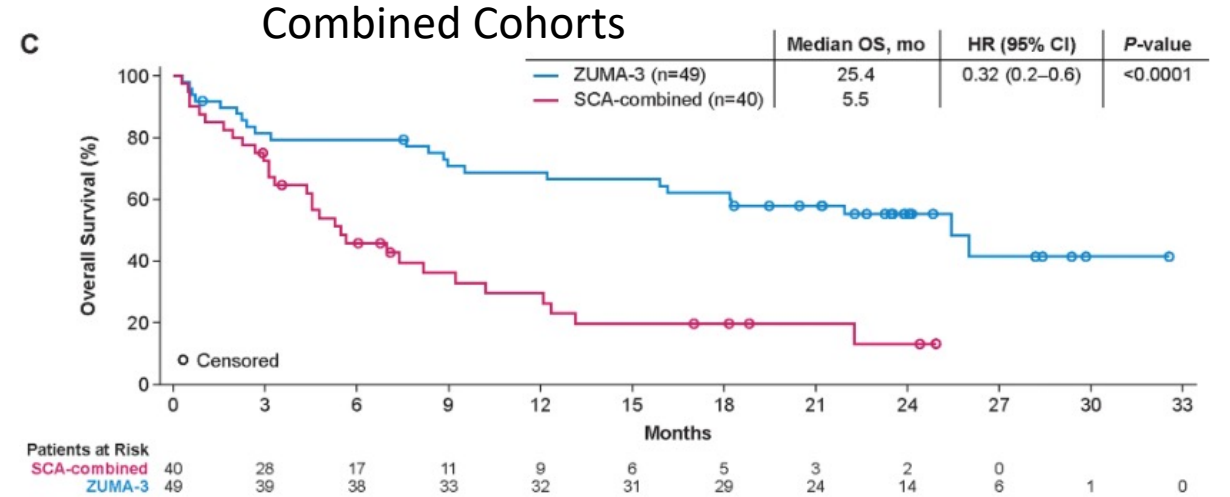
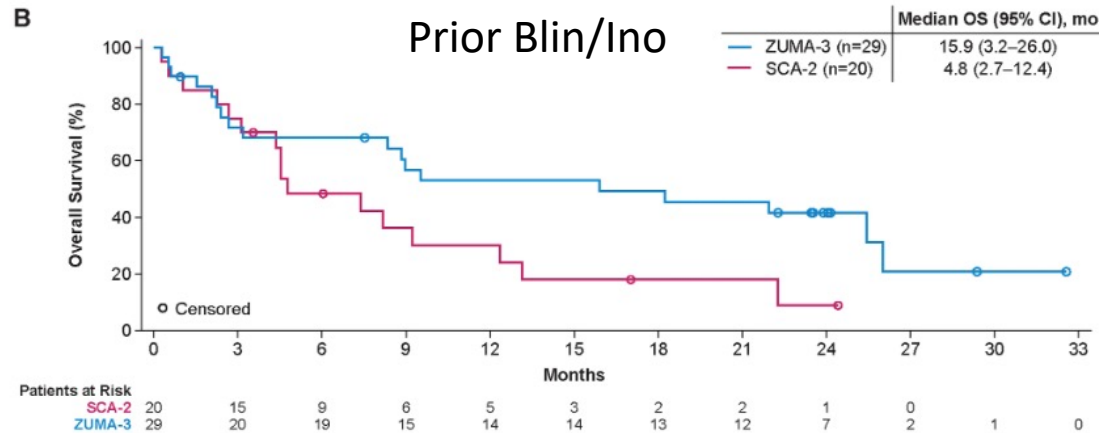
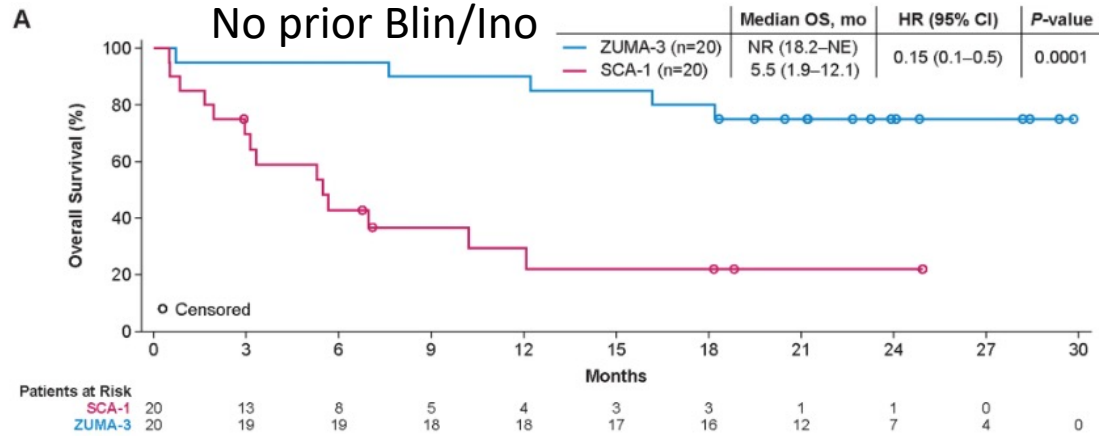
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|                        |     |     |     |     |     |     |     |     |     |     |     |     |      |      |      |      |      |      |
|------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|------|------|------|------|
| CR+CRi at risk         | 39  | 39  | 38  | 38  | 36  | 33  | 33  | 32  | 30  | 29  | 25  | 22  | 14   | 7    | 6    | 1    | 1    | 0    |
| (CR+CRi censored)      | (0) | (0) | (0) | (0) | (1) | (1) | (1) | (1) | (1) | (1) | (2) | (4) | (12) | (18) | (18) | (23) | (23) | (24) |
| Others at risk         | 16  | 9   | 5   | 5   | 5   | 4   | 4   | 4   | 4   | 4   | 3   | 2   | 2    | 1    | 1    | 0    | 0    | 0    |
| (Others censored)      | (0) | (2) | (2) | (2) | (2) | (2) | (2) | (2) | (2) | (2) | (3) | (4) | (4)  | (5)  | (5)  | (6)  | (6)  | (6)  |
| All treated at risk    | 55  | 48  | 43  | 43  | 41  | 37  | 37  | 36  | 34  | 33  | 28  | 24  | 16   | 8    | 7    | 1    | 1    | 0    |
| (All treated censored) | (0) | (2) | (2) | (2) | (3) | (3) | (3) | (3) | (3) | (3) | (5) | (8) | (16) | (23) | (23) | (29) | (29) | (30) |

# ZUMA-3 vs SCHOLAR-3

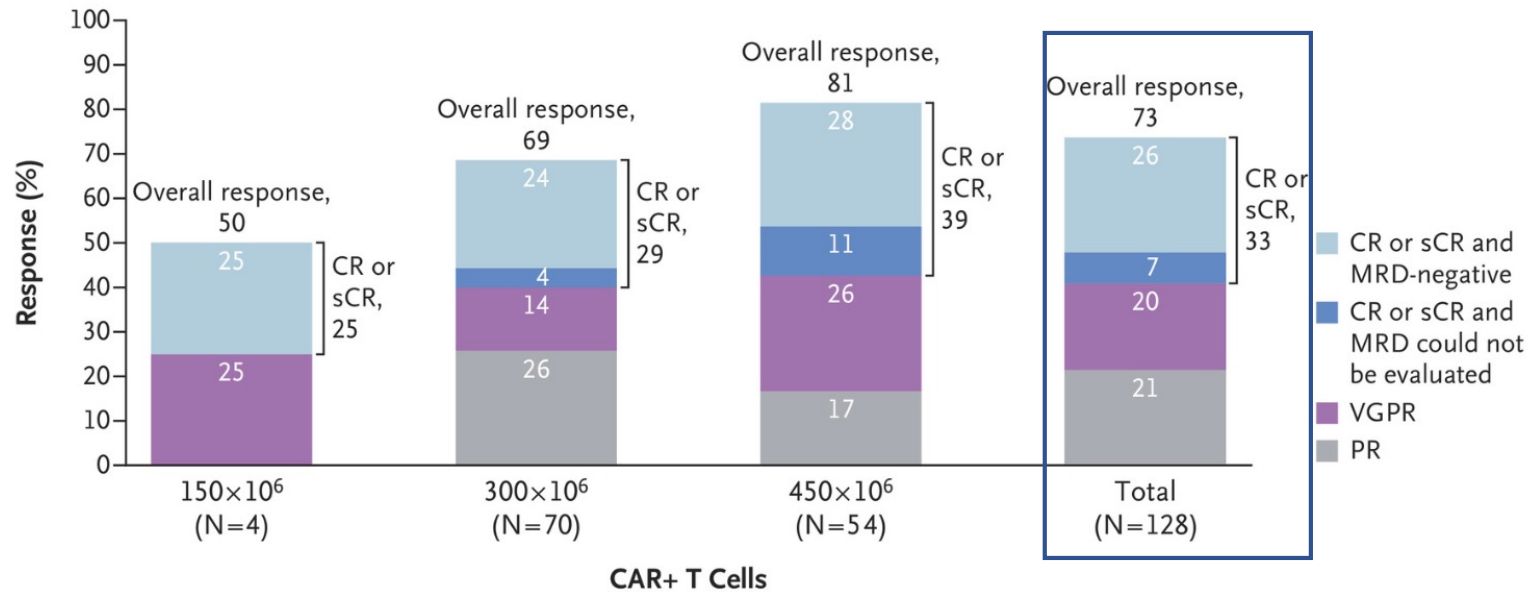
- Patients compared to matched historical controls from SCHOLAR-3
  - SCHOLAR-3: R/R B-ALL in historical clinical trials
  - 1 – no prior Blin/Ino
  - 2 – prior Blin/Ino
  - 3 - combined cohort



# Idecabtagene Vicleucel: KarMMa Phase 2

- $\geq 4$  lines of therapy
- Median 6 prior lines of therapy
  - 94% prior auto SCT
- mDOR 10.7 mos
- mPFS 8.8 mos
- OS 19.7 mos
- MRD-negativity 26%
- CRS 84%
  - 5%  $\geq$  G3
- Neurotoxicity 18%
  - 3%  $\geq$  G3

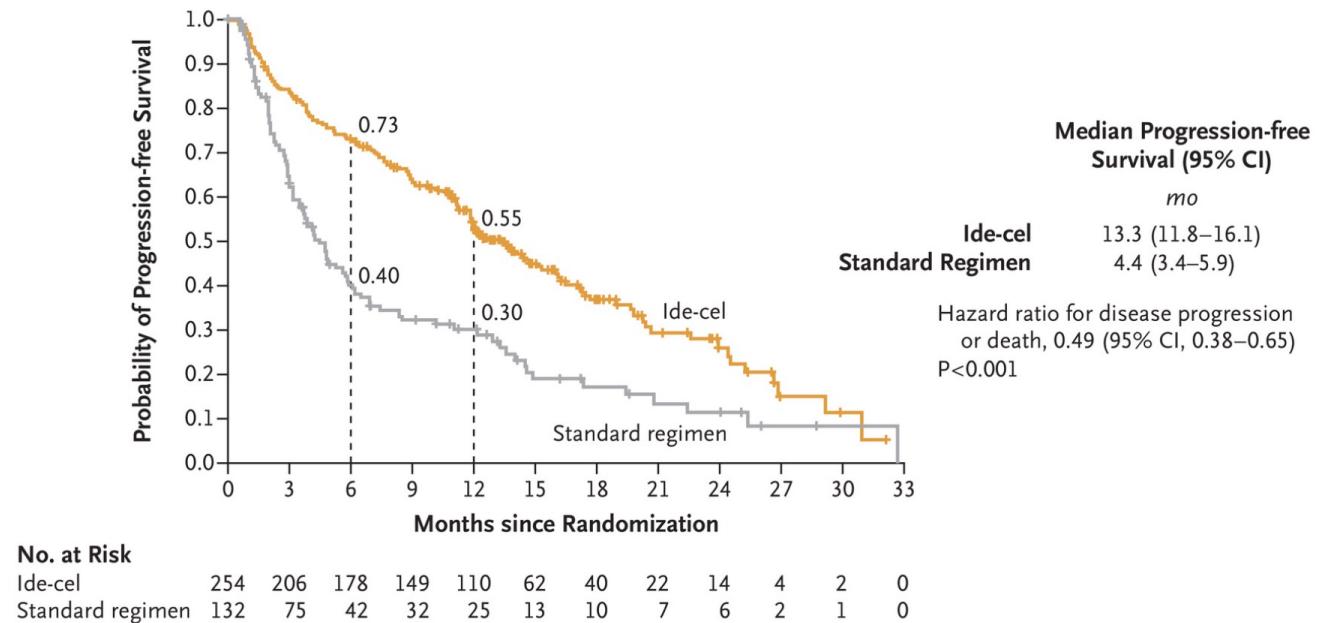
Tumor Response, Overall and According to Target Dose





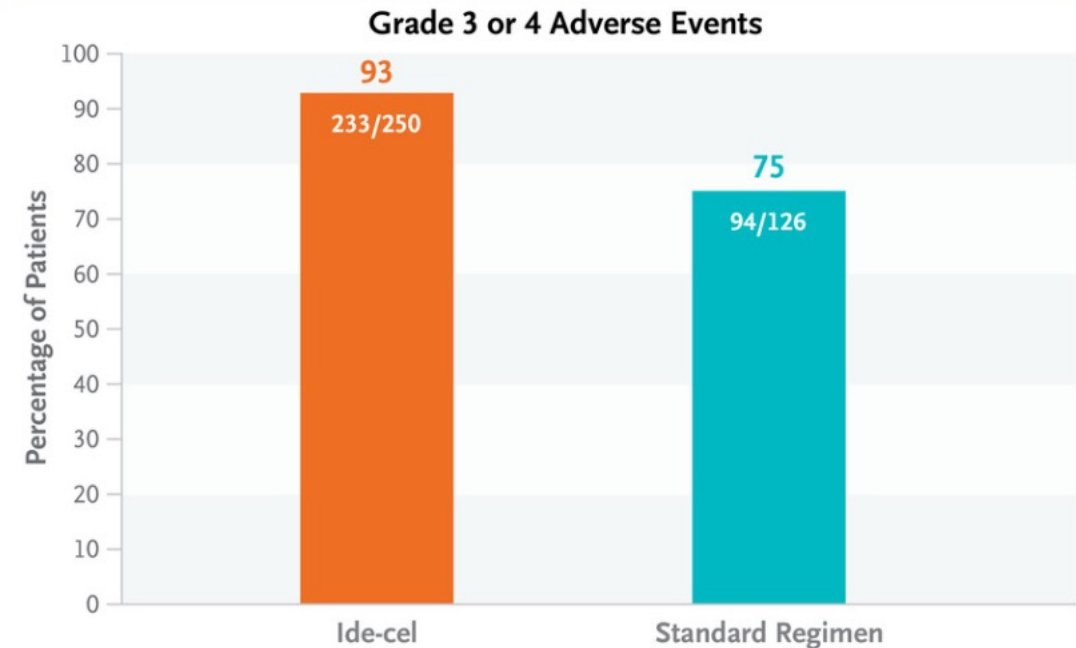
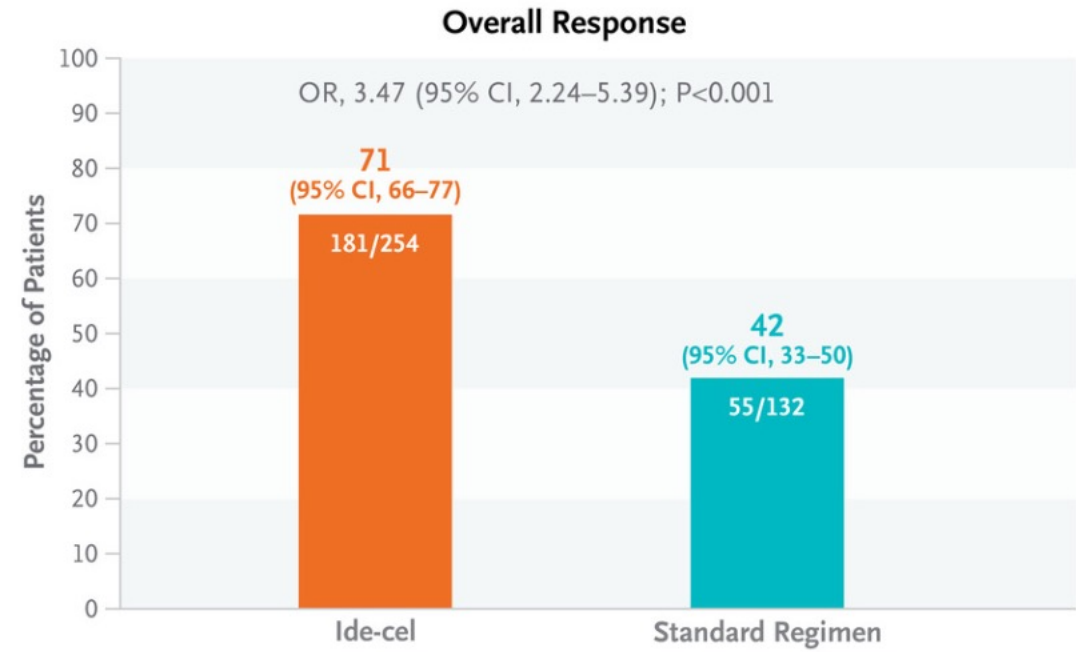
# KarMMa-3: Idecel vs SOC

- Triple-class exposed, R/R MM patients
- 2-4 prior lines including Dara, Imid, PI  $\geq 2$  cycles and disease progression within 60 days
- 2:1 Idecel vs SOC
- Stratification by age, prior lines, high-risk cytogenetics



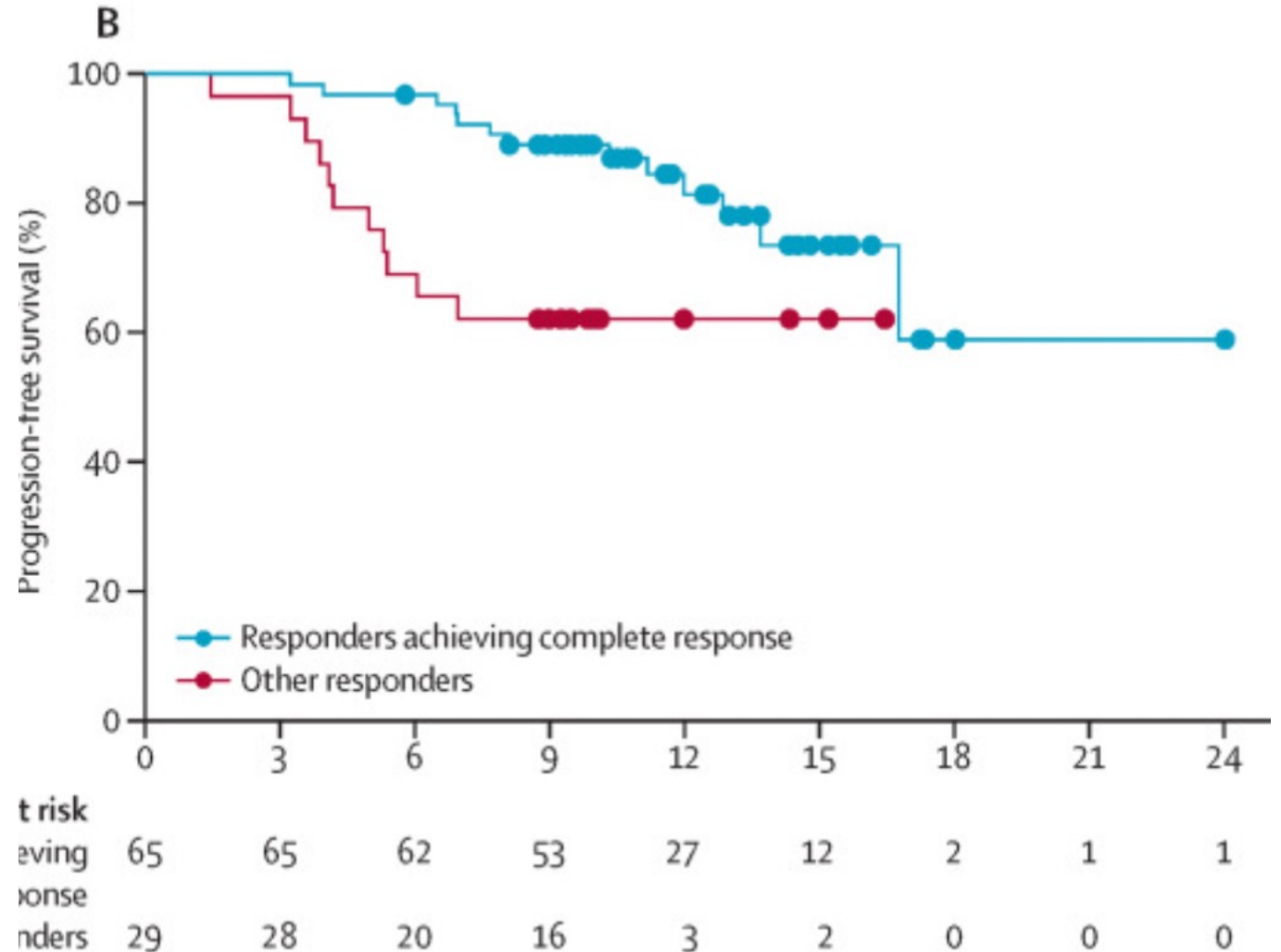
# KarMMa-3: Idecel vs SOC

- CR or SCR 39% vs 5%
- Med Time to Response 2.9 mos vs 2.1 mos
- mDOR 14.8 os vs 9.7 mos
- MRD-negative status within 3 months of at least CR: 20% vs 1%
  
- Neutropenia 78% vs 44%
- Thrombocytopenia 54% vs 29%
- Infections 58% vs 54%
- CRS 88% (5% G3+)
- Neurotoxicity 15% (3% G3+)
- Deaths: 30% vs 26%

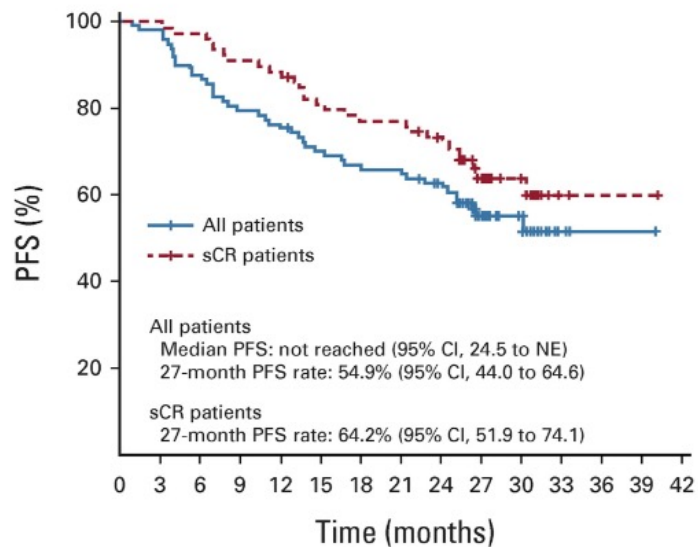


# Ciltacabtagene Autoleucel: CARTITUDE Phase 1b/2

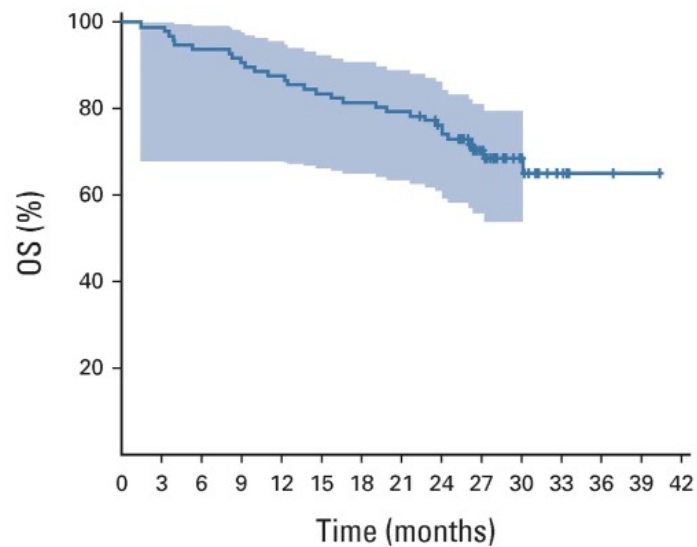
- $\geq 4$  lines of therapy
- 6-month PFS 90%
- 12-month:
  - PFS 77%
  - OS 89%
- Neurotoxicity 21%
  - 17% ICANS
  - 2%  $\geq$  Grade 3 ICANS
- CRS 95% (4%  $\geq$  Grade 3)



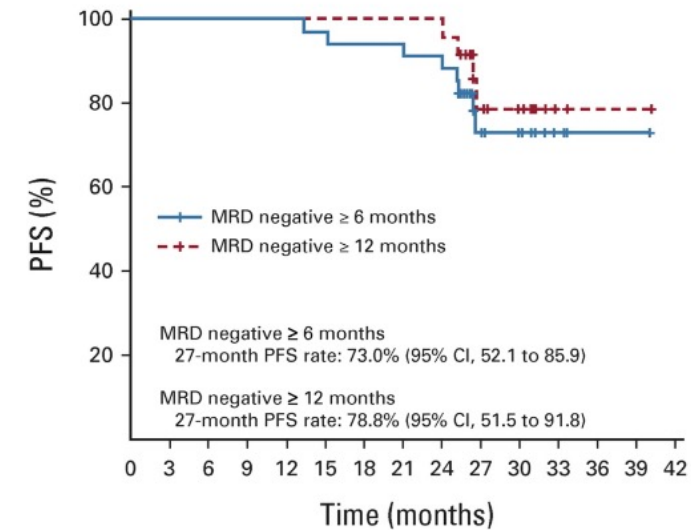
# Ciltacel: 2-year Follow Up



| No. at risk: | 0  | 3  | 6  | 9  | 12 | 15 | 18 | 21 | 24 | 27 | 30 | 33 | 36 | 39 | 42 |
|--------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| All patients | 97 | 95 | 85 | 77 | 74 | 67 | 64 | 63 | 57 | 27 | 17 | 3  | 1  | 1  | 0  |
| sCR patients | 80 | 80 | 78 | 73 | 71 | 64 | 62 | 61 | 55 | 27 | 17 | 3  | 1  | 1  | 0  |



| No. at risk: | 0  | 3  | 6  | 9  | 12 | 15 | 18 | 21 | 24 | 27 | 30 | 33 | 36 | 39 | 42 |
|--------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| All patients | 97 | 96 | 91 | 88 | 85 | 81 | 79 | 77 | 71 | 42 | 22 | 6  | 2  | 1  | 0  |



| No. at risk:                  | 0  | 3  | 6  | 9  | 12 | 15 | 18 | 21 | 24 | 27 | 30 | 33 | 36 | 39 | 42 |
|-------------------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| MRD negative $\geq 6$ months  | 34 | 34 | 34 | 34 | 34 | 33 | 32 | 32 | 31 | 13 | 10 | 3  | 1  | 1  | 0  |
| MRD negative $\geq 12$ months | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 24 | 11 | 8  | 2  | 1  | 1  | 0  |

- Median FU 27.7 months
- ORR 97.9%
- 82.5% SCR
- mDOR NR
- 27-month PFS 55%, OS 70%
- Safety profile: 1 additional case of Parkinsonism (total 6)

# Management of Toxicities

|                            | <b>Tisagenleucel</b>                                                                                                                                         | <b>Axicabtagene ciloleucel</b>                                                                                                                   | <b>Brexucabtagene autoleucel</b>                                                             | <b>Lisocabtagene maraleucel</b>                                                               | <b>Idecabtagene autoleucel</b>                                                           |
|----------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| Approval Date              | 8/30/2017                                                                                                                                                    | 10/18/2017                                                                                                                                       | 6/24/2020                                                                                    | 2/5/2021                                                                                      | 3/26/2021                                                                                |
| Indication(s)              | <ul style="list-style-type: none"> <li>• B-cell precursor acute lymphoblastic leukemia (ALL)</li> <li>• Relapsed/refractory large B-cell lymphoma</li> </ul> | <ul style="list-style-type: none"> <li>• Relapsed/refractory large B-cell lymphoma</li> <li>• Relapsed/refractory follicular lymphoma</li> </ul> | <ul style="list-style-type: none"> <li>• Relapsed/refractory mantle cell lymphoma</li> </ul> | <ul style="list-style-type: none"> <li>• Relapsed/refractory large B-cell lymphoma</li> </ul> | <ul style="list-style-type: none"> <li>• Relapsed/refractory multiple myeloma</li> </ul> |
| Target Antigen             | CD-19                                                                                                                                                        | CD-19                                                                                                                                            | CD-19                                                                                        | CD-19                                                                                         | BCMA                                                                                     |
| Incidence of CRS           | Any: 74-77%<br>≥ Grade 3: 23-48%                                                                                                                             | Any: 84-94%<br>≥ Grade 3: 8-13%                                                                                                                  | Any: 91%<br>≥ Grade 3: 18%                                                                   | Any: 46%<br>≥ Grade 3: 4%                                                                     | Any: 85%<br>≥ Grade 3: 9%                                                                |
| Incidence of Neurotoxicity | Any: 60-71%<br>≥ Grade 3: 19-22%                                                                                                                             | Any: 77-87%<br>≥ Grade 3: 21-31%                                                                                                                 | Any: 81%<br>≥ Grade 3: 37%                                                                   | Any: 35%<br>≥ Grade 3: 12%                                                                    | Any: 28%<br>≥ Grade 3: 4%                                                                |

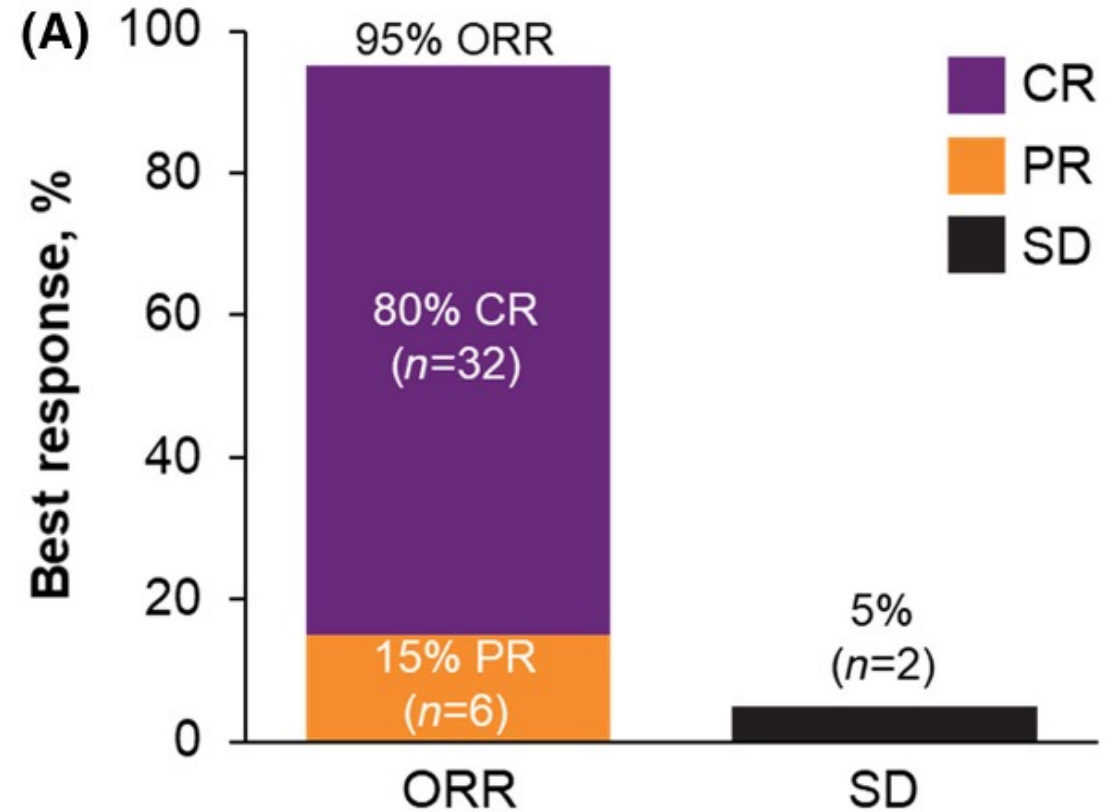
# Prophylactic steroid Use: Cohort 6 ZUMA-1

## Dexamethasone 10 mg daily Day 0, +1, +2

|                     |     | AE Grade                                                |                                                         |                                                             |                                                             |
|---------------------|-----|---------------------------------------------------------|---------------------------------------------------------|-------------------------------------------------------------|-------------------------------------------------------------|
|                     |     | 1                                                       | 2                                                       | 3                                                           | 4                                                           |
| Original<br>AE Mgmt | CRS | Tocilizumab: <b>No</b><br>Corticosteroid: <b>No</b>     | Tocilizumab: <b>Yes*</b><br>Corticosteroid: <b>Yes*</b> | Tocilizumab: <b>Yes</b><br>Corticosteroid: <b>Yes</b>       | Tocilizumab: <b>Yes</b><br>Corticosteroid: <b>Yes</b>       |
|                     | NE  | Tocilizumab: <b>No</b><br>Corticosteroid: <b>No</b>     | Tocilizumab: <b>Yes</b><br>Corticosteroid: <b>No</b>    | Tocilizumab: <b>Yes</b><br>Corticosteroid: <b>Yes†</b>      | Tocilizumab: <b>Yes</b><br>Corticosteroid: <b>Yes</b>       |
| Cohort 6<br>AE Mgmt | CRS | Tocilizumab: <b>Yes‡</b><br>Corticosteroid: <b>Yes§</b> | Tocilizumab: <b>Yes</b><br>Corticosteroid: <b>Yes</b>   | Tocilizumab: <b>Yes</b><br>Corticosteroid: <b>Yes</b>       | Tocilizumab: <b>Yes</b><br>Corticosteroid: <b>Yes, HD</b>   |
|                     | NEs | Tocilizumab: <b>No</b><br>Corticosteroid: <b>Yes</b>    | Tocilizumab: <b>Yes  </b><br>Corticosteroid: <b>Yes</b> | Tocilizumab: <b>Yes  </b><br>Corticosteroid: <b>Yes, HD</b> | Tocilizumab: <b>Yes  </b><br>Corticosteroid: <b>Yes, HD</b> |

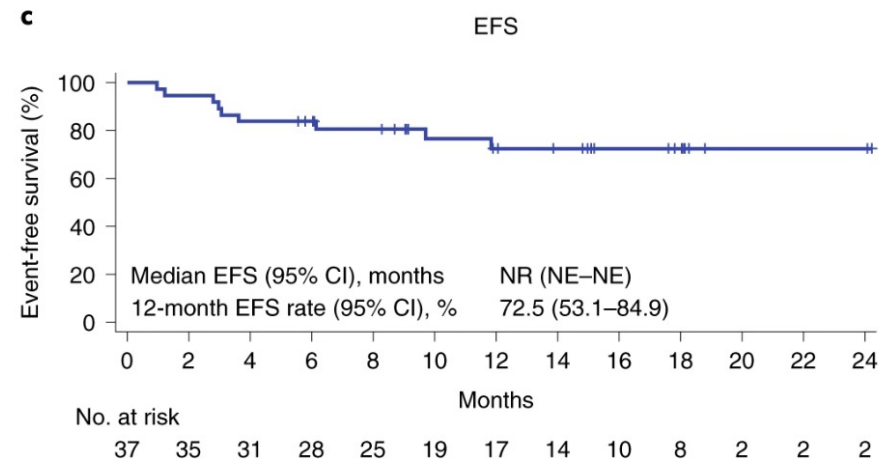
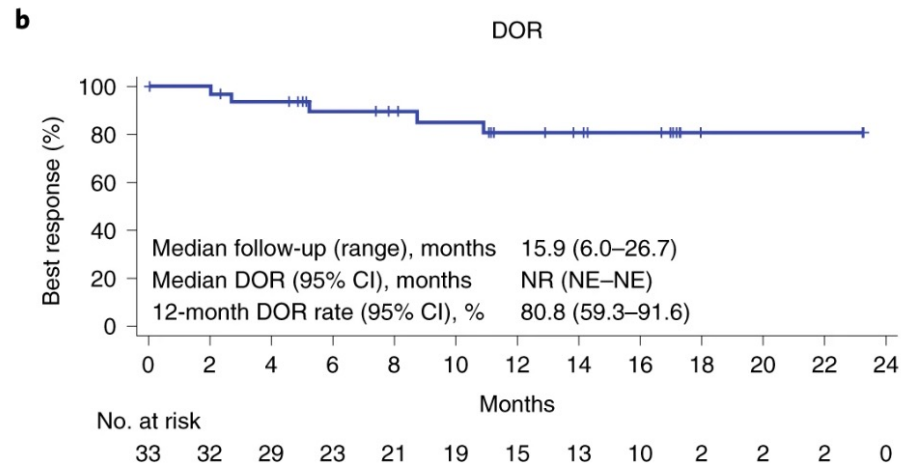
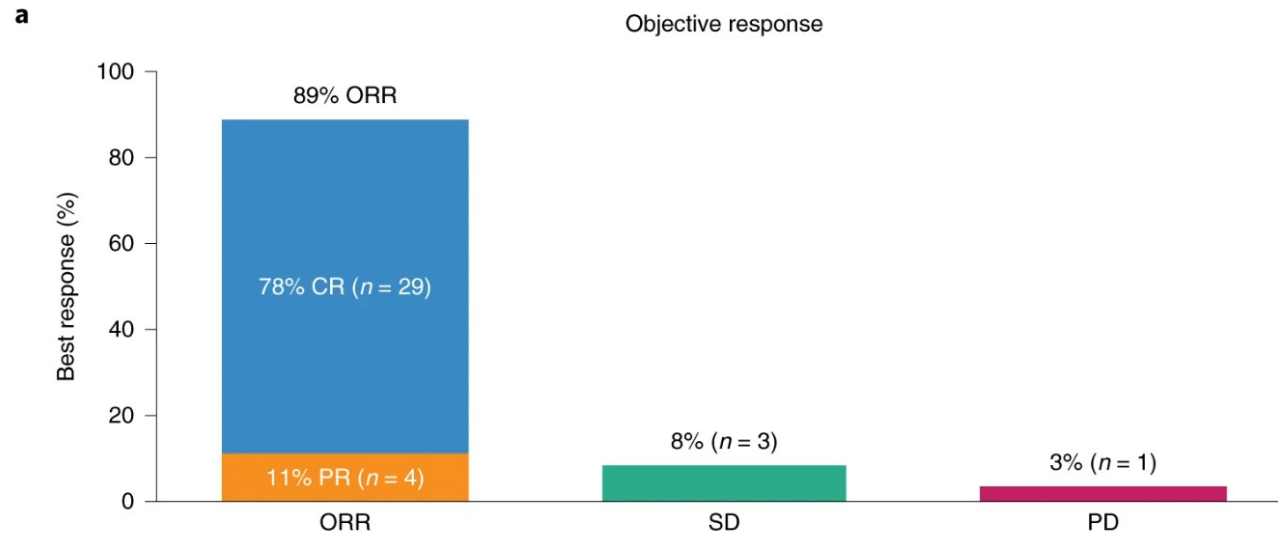
# Prophylactic steroid Use: Cohort 6 ZUMA-1

- 80% incidence CRS
  - No Grade 3-4 events
- Neurotoxicity 58%
  - 13% Grade  $\geq 3$
- Lower cumulative steroid dose to treat CRS and ICANS
- CAR T expansion and efficacy maintained



# ZUMA-12

- Phase II, single-arm, high-risk LBCL
  - DHL/THL or IPI  $\geq 3$
  - PET2-Positive
- 2 cycles SOC chemo  $\rightarrow$  Axicel
- Estimated at 12 mos:
  - DOR 81%
  - PFS 75%
  - EFS 73%

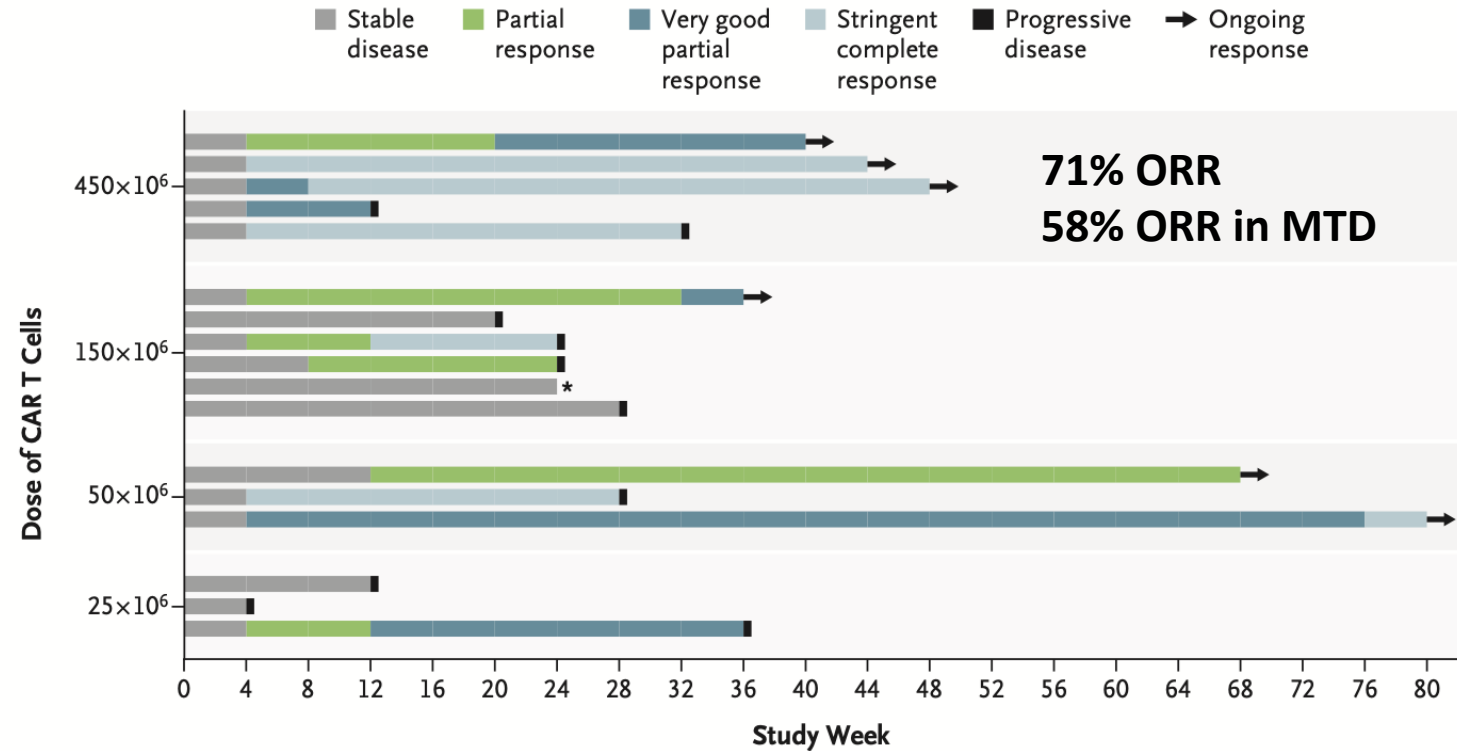




# GPRC5D-Targeted CAR T cells for MM

- Phase I dose-escalation study
- R/R MM, including prior BCMA CAR T therapy
- Median 6 lines prior therapy
- 47% prior CAR T

A Clinical Response



Thank You