Biomarker Correlates of Clinical Outcomes From a Global Phase 1b Study of JNJ-90014496, CD20/CD19 Bispecific Chimeric Antigen Receptor-T cell Therapy for Patients with Large B-cell Lymphoma

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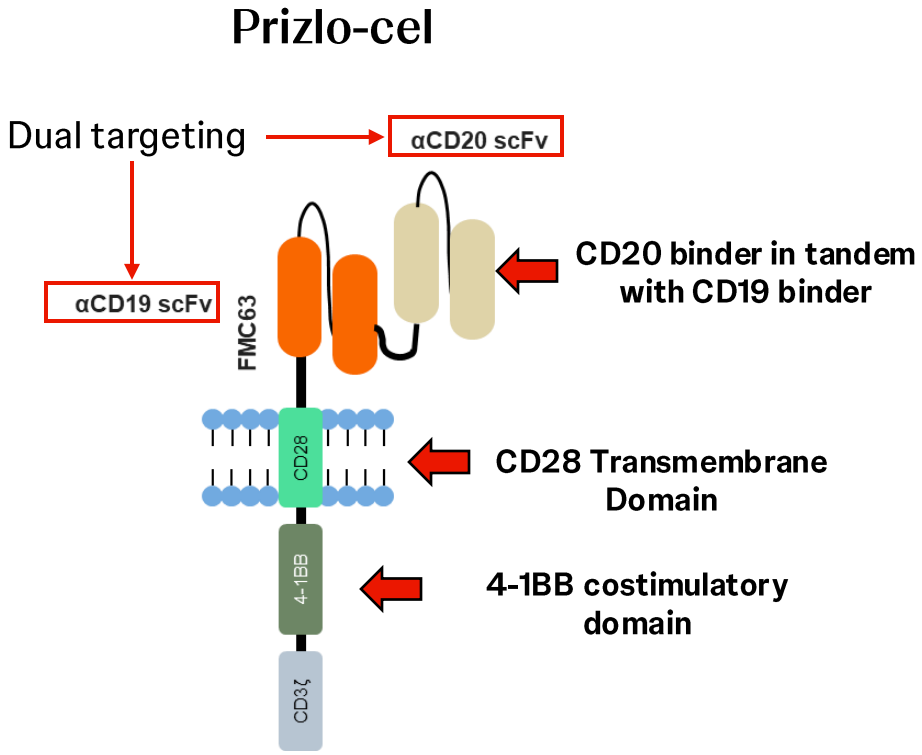
Presented by M Suraneni at American Society of Hematology; December 7, 2025; Orlando, FL

Prizlo-cel (*Prize-lo cel*; JNJ-90014496) is a Dual Antigen Targeting CD20/CD19 CAR T with an Optimized CAR Design

- CD19 CAR-T have demonstrated curative potential in R/R LBCL,[1] yet >50% of patients still relapse, in part due to CD19 tumor antigen escape[2-4]
- Dual targeting of CD20 and CD19 may prevent relapses driven by antigen loss and address the challenge of tumor heterogeneity[1,5,6]
- **Prizlo-cel targets two clinically validated antigens with an optimized CAR design and a differentiated CD20 binder[7]:**
  - CD20 binder targets membrane-proximal epitope on B cells spanning both CD20 loops, enabling tight binding to the cell membrane



Prizlo-cel's optimized design with a differentiated CD20 binder may improve synapse formation and T cell activation leading to enhanced clinical outcomes

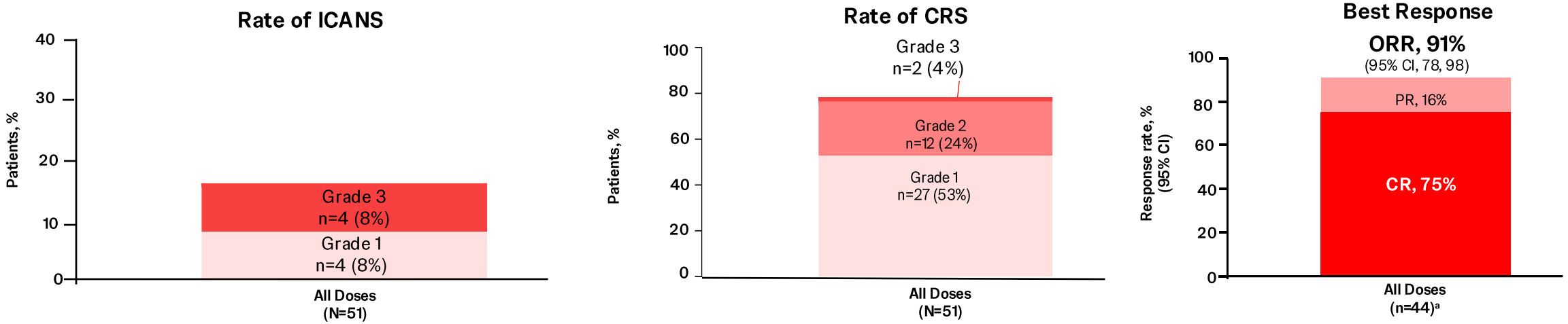
CAR, chimeric antigen receptor; CD, cluster of differentiation; R/R, relapsed/refractory.

1. Zhang Y, et al. *Chin. Med. J. 2023*;136(3):269-279. 2. Shuster SJ, et al. *N Engl J Med*. 2019;380(1):45-56. 3. Neelapu SS, et al. N *Engl J Med*. 2017;377(26):2531-44. 4. Abramson JS, et al. *Lancet*. 2020;396(10254):839-52. 5. Plaks V, et al. *Blood*. 2021;138(12):1081-85. 6. Yang N, et al. *J Transl Med*. 2024;22(1):274. 7. Yu W, et al. *Blood*. 2025;145(14):1526-1535.

Prizlo-cel Global Phase 1b: Dual CD20/CD19 Targeting Prizlo-cel Shows Deep Responses and a Favorable Safety Profile in R/R LBCL

Global phase 1b study in patients with R/R CAR-T naïve LBCL (NCT05421663) was previously presented[1]

- Fewer grade 3 ICANS and CRS were observed across all the doses tested
- No prophylactic treatment for CRS or ICANS
- High CR rates were achieved at all doses and irrespective of number of prior lines of therapy



Correlative analysis of biomarker data to clinical outcomes for 51[c] patients from this prizlo-cel Phase 1b study are presented here

Clinical Data cutoff: 21 April 2025.

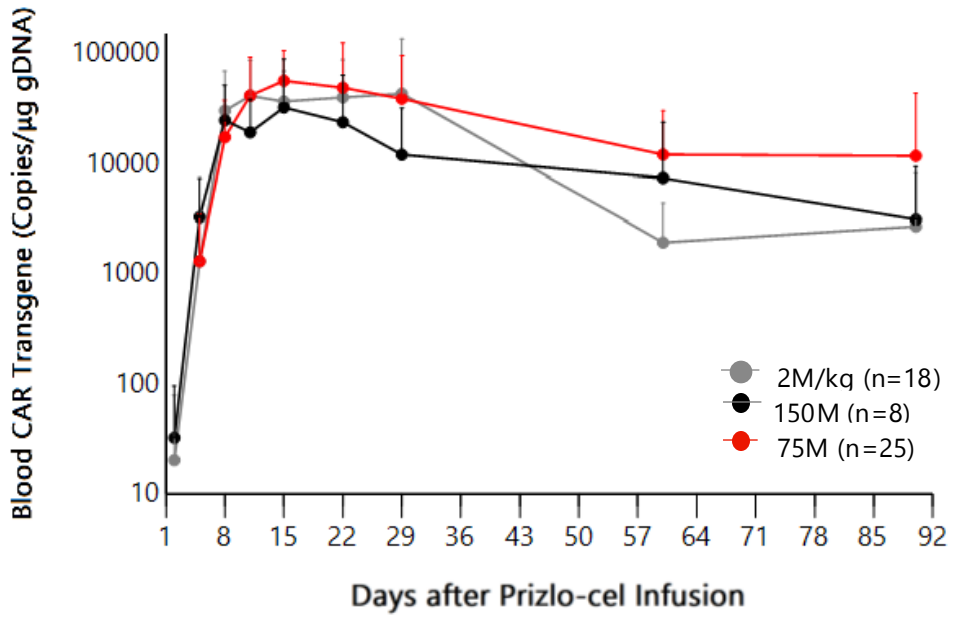
[a]Three patients were not included in the efficacy analysis (2 patients achieved CR to bridging therapy and 1 patient was ongoing without any disease evaluations). [b]Seven patients were not included in the efficacy analysis (6 patients achieved CR to bridging therapy and 1 patient was ongoing without any disease evaluations). [c]In some cases, biomarker data was not available for all 51 patients

CR, complete response; CRS, cytokine releasing syndrome; GR, grade; ICANS, immune effector cell-associated neurotoxicity syndrome; M, million; ORR, objective response rate; R/R, relapsed/refractory.

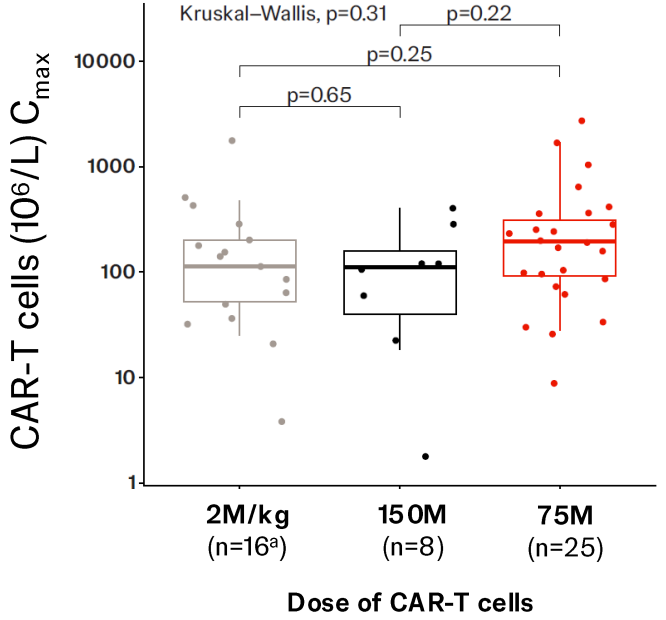
1. Patel K, et al. European Hematology Association; June 12-15, 2025; Milan Italy.

Prizlo-cel Global Phase 1b: Comparable CAR-T Cell Expansion and Persistence Across All Doses Tested

Mean (+SD) CAR-T transgene levels over time



C_{max} of CAR-T cell levels by dose



- Comparable peripheral CAR-T levels were observed across all doses tested

[a]Two patients were not included in the analysis due to lack of available samples for testing.
CAR, chimeric antigen receptor; C_{max}, maximum concentration; M, million; t_{max}, time at maximum observed concentration.

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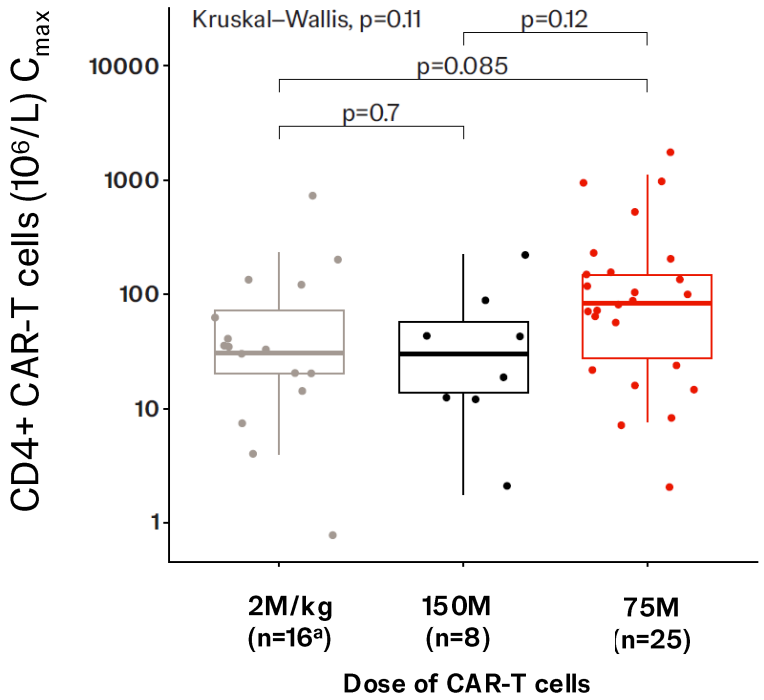
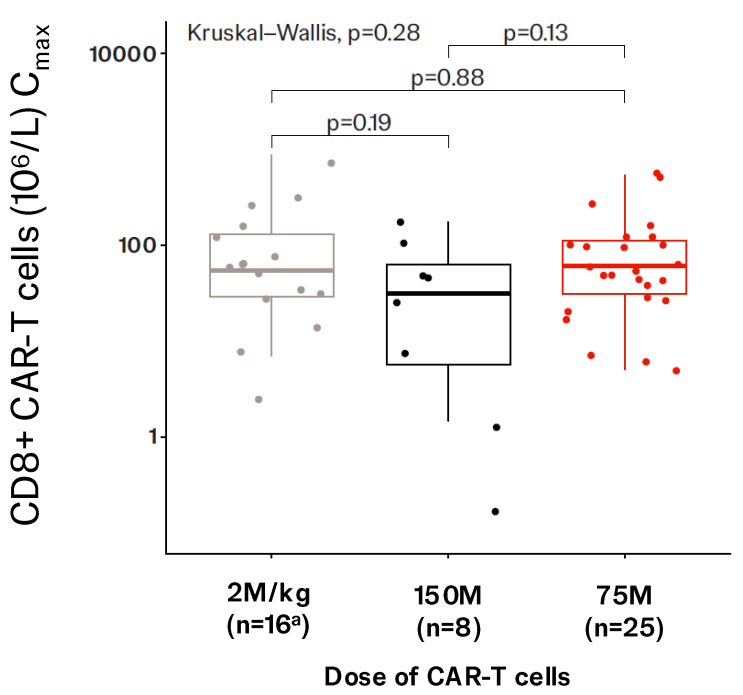
Prizlo-cel Global Phase 1b: Comparable CD4+ and CD8+ CAR-T Cells at Peak Expansion Across All Doses Tested

CD4+ CAR-T cell expansion

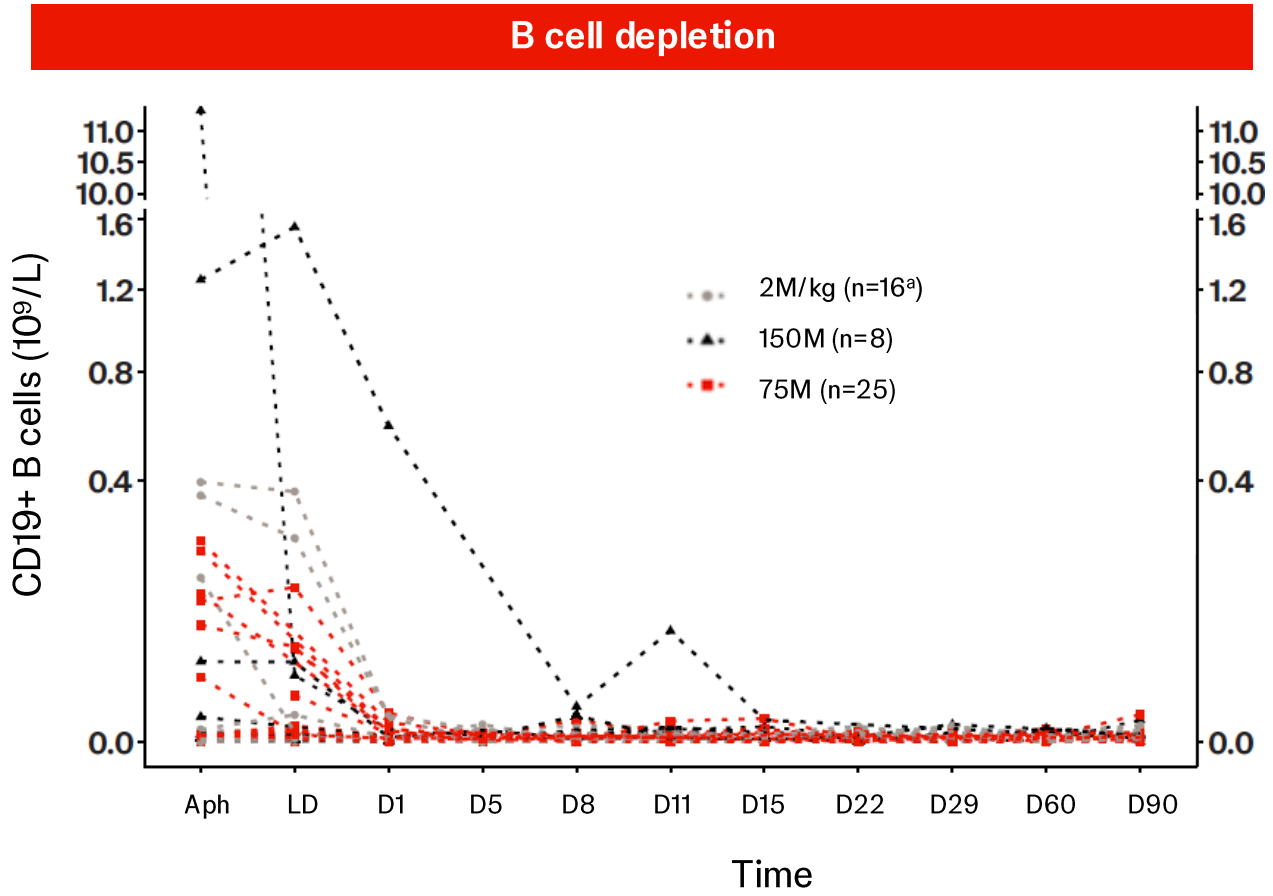


CD8+ CAR-T cell expansion



[a]Two patients were not included in the analysis due to lack of available samples for testing.
CAR, chimeric antigen receptor; C_{max}, maximum concentration; M, million; t_{max}, time at maximum observed concentration.

Prizlo-cel Global Phase 1b: Comparable B Cell Depletion Across All Doses Tested

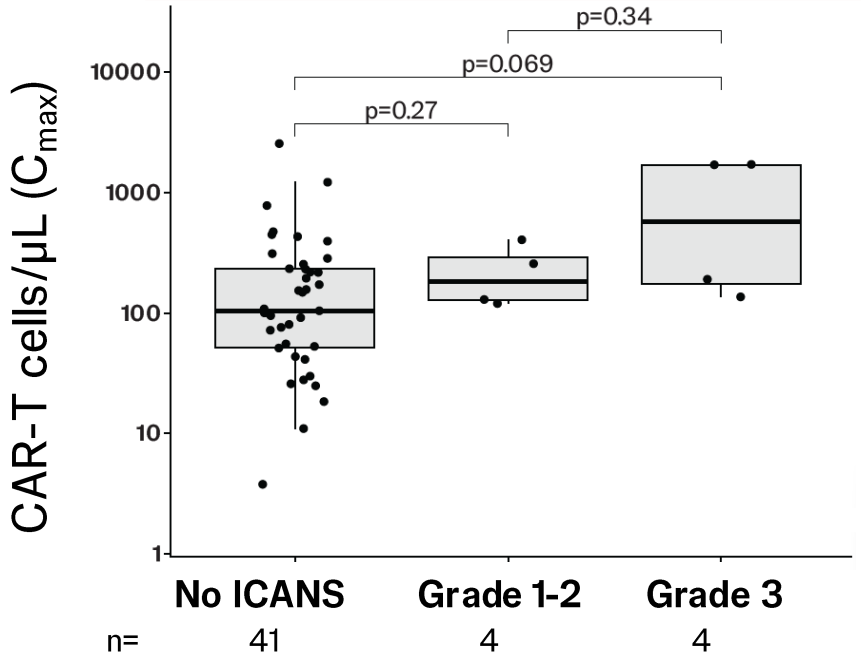


- Median B cell depletion was observed at ~Day 5 across all doses

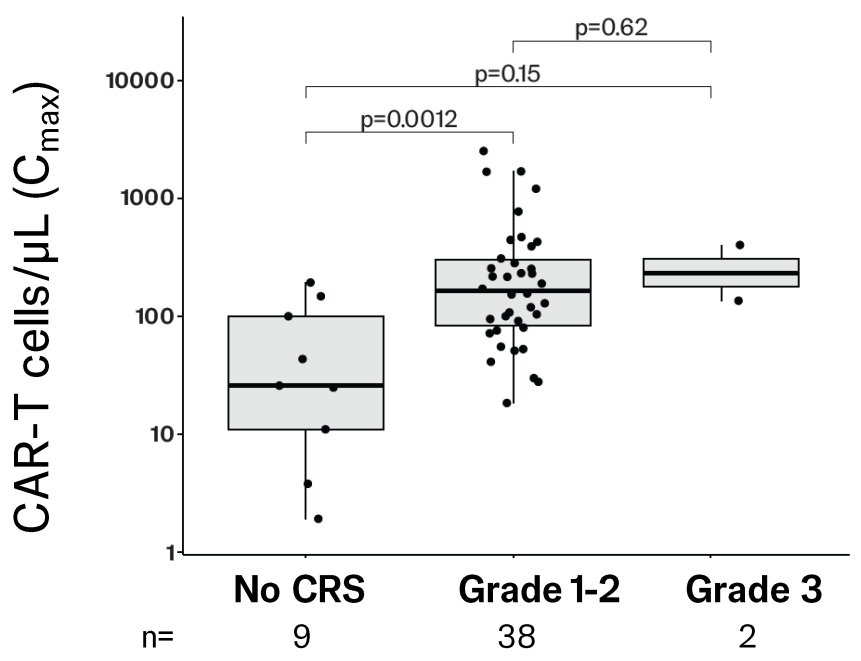
[a]Two patients were not included in the analysis due to lack of available samples for testing.
Aph, aphesis; D, day; LD, lymphodepletion; M, million.

Prizlo-cel Global Phase 1b: Few Grade 3 ICANS and CRS Events Observed with Comparable CAR-T Expansion

CAR-T cell levels by ICANS Grade



CAR-T cell levels by CRS Grade



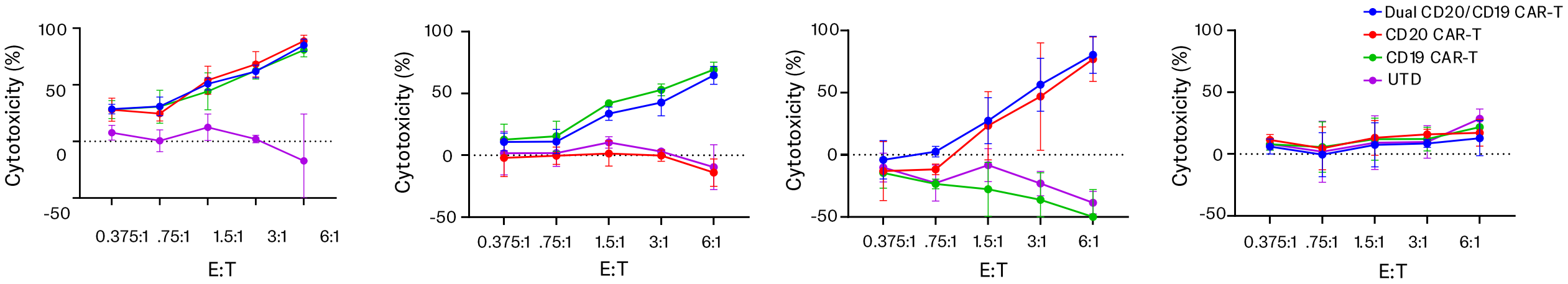
Prizlo-cel has a manageable safety profile even in the absence of prophylactic steroids

Two patients were not included in the analysis due to lack of available samples. From the two patients with missing data, one patient had no ICANS and Grade 1 CRS and one patient had no ICANS or CRS.
CAR, chimeric antigen receptor; C_{max}, maximum concentration; CRS, cytokine releasing syndrome; ICANS, immune-effector cell-associated neurotoxicity syndrome.

Prizlo-cel Global Phase 1b: Dual Targeting CD20/CD19 CAR-T Consistently Demonstrates *In Vitro* Cytotoxicity in Cell Lines Expressing either CD20, CD19 or Both

- A research grade CD20/CD19 dual targeting CAR-T using the prizlo-cel construct was used in *in vitro* cytotoxicity experiments

Raji | **Raji CD20 KO** | **Raji CD19 KO** | **Raji CD20/CD19 KO**

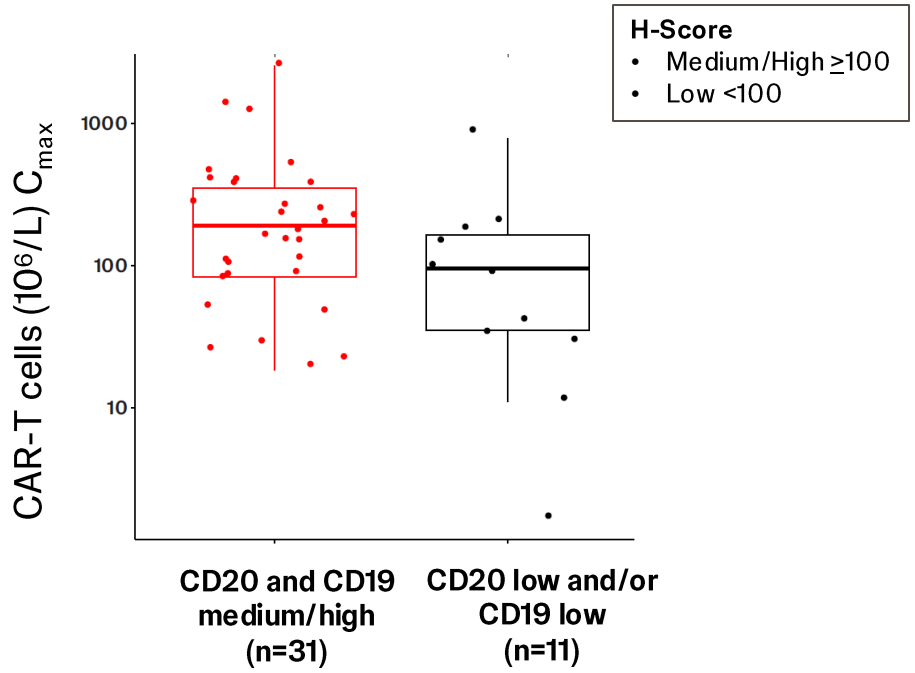


Dual targeting CD20/CD19 CAR-T demonstrated *in vitro* cytotoxicity in all isogenic cell lines compared to single antigen targeting CAR-Ts

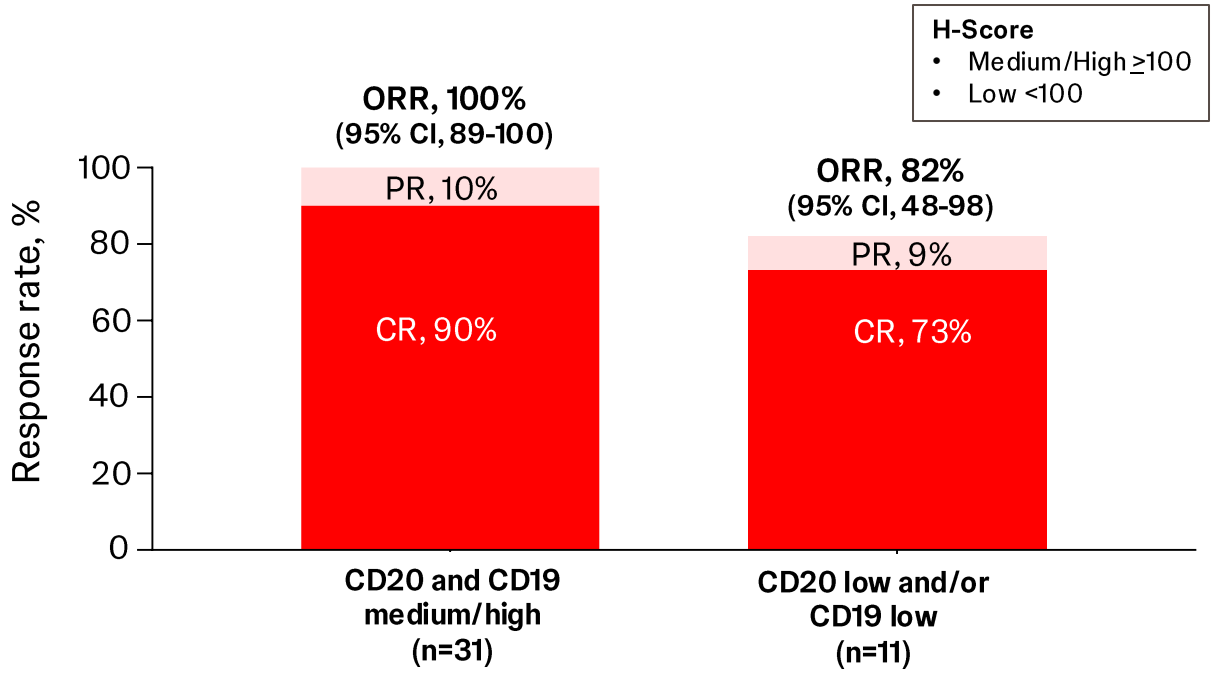
Experiments were run in triplicate.
CAR, chimeric antigen receptor; E:T, effector cell to target cell; UTD, Untransduced.

Prizlo-cel Global Phase 1b: CAR-T Cell Expansion and High CR Rates are Observed Across a Range of CD20 and CD19 Antigen Expression Levels

CAR-T expansion by CD20 and CD19 antigen levels



CR rates by CD20 and CD19 antigen levels



CAR-T cell expansion and depth of response remain high in patients with low expression of either antigen, suggesting effective dual antigen targeting of CD20 and CD19

CD20 and CD19 expression was analyzed in 42 patients with baseline samples available with sufficient tumor tissue for immunohistochemistry testing and were defined as medium/high (H-score ≥ 100) and low (H-score < 100).
Tumor samples from 42 patients showed high levels of baseline CD20 expression (H-score >200 in 79% of patients), but variable CD19 expression by IHC (median [interquartile range] 190 [168 to 220]). Using an H-score cutoff of 100, 16% patients had low or heterogenous expression levels of target antigen: 9% had low levels of either CD20 or CD19 expression and 7% showed low levels of both target antigens.
CAR, chimeric antigen receptor; C_{max}, maximum concentration; CR, complete response; ORR, objective response rate; PR, partial response.

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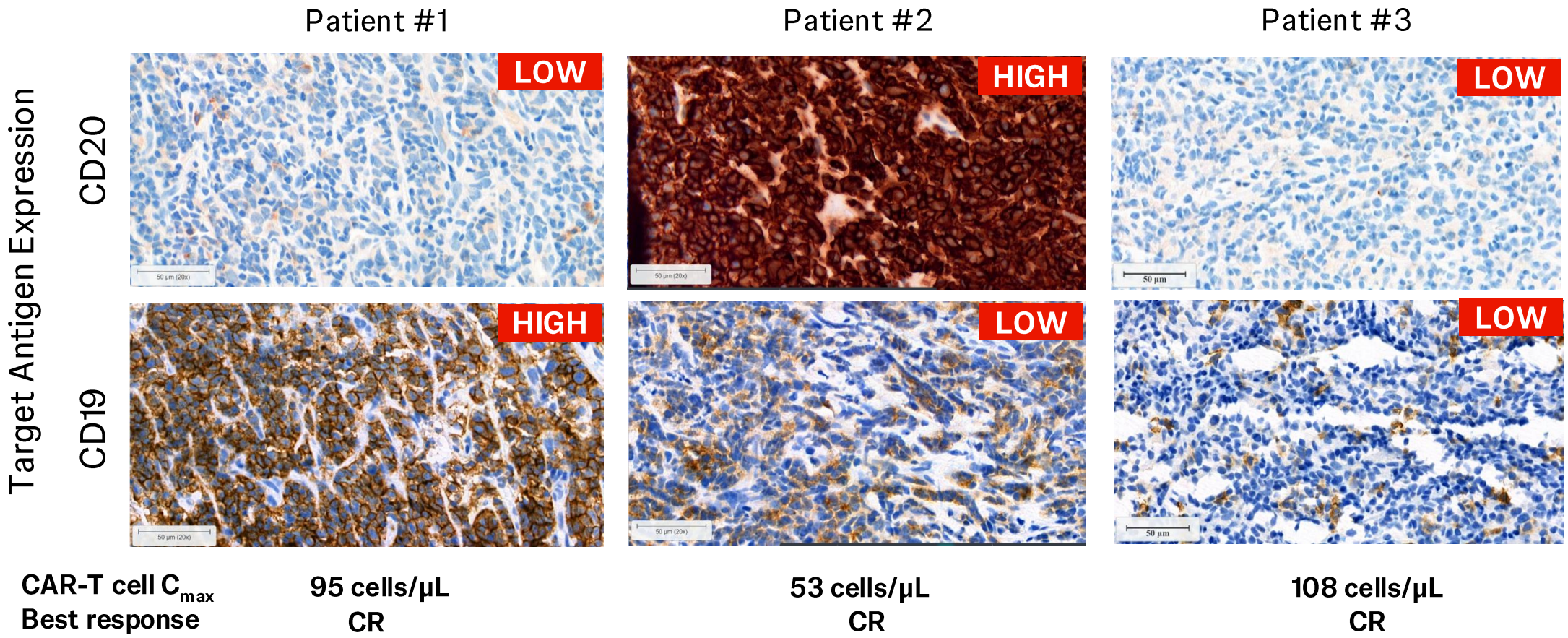
Prizlo-cel Global Phase 1b: High CAR-T Cell Expansion and Complete Responses Were Seen Even in Patients with Low Antigen Expression Levels

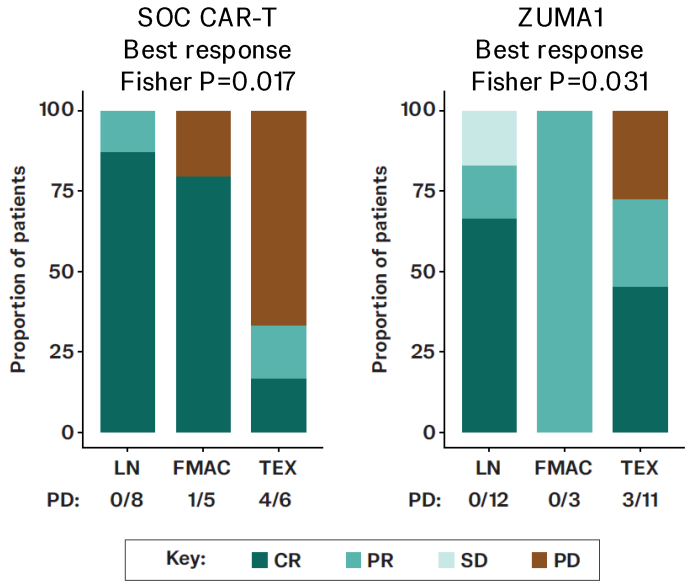


CD20 and CD19 expression was analyzed in baseline tumor samples using immunohistochemistry and defined as medium/high (H-score ≥ 100) and low (H-score < 100).
CAR, chimeric antigen receptor; C_{max}, maximum concentration; CR, complete response.

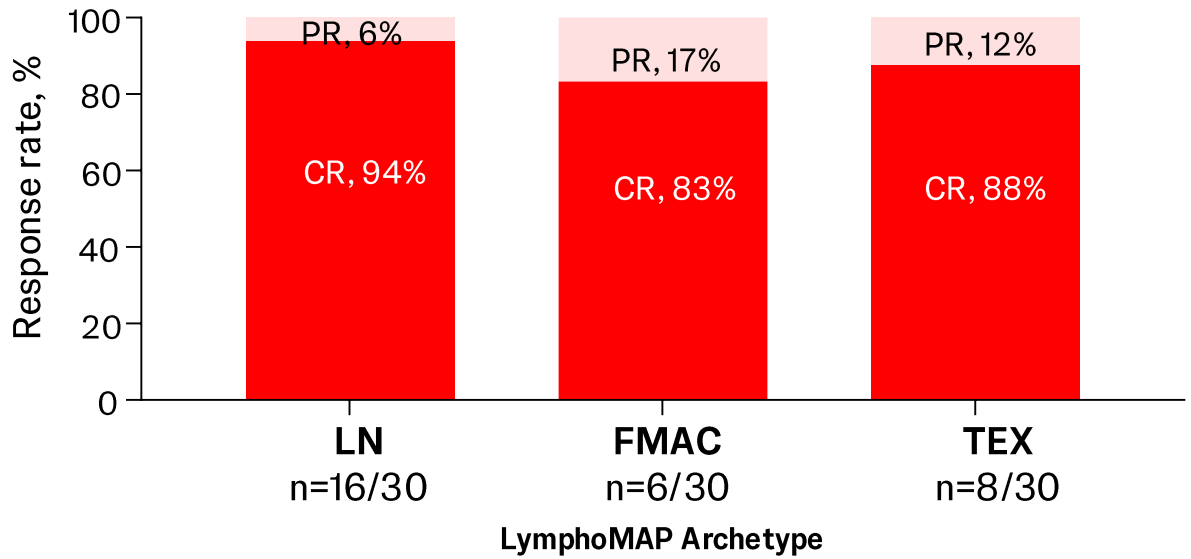
Prizlo-cel Global Phase 1b: High CR Rates Across All Three LymphoMAP TME Archetypes

- MD Anderson recently characterized 3 Lymphoma Microenvironment Archetype Profiles (LymphoMAPs) that may predict clinical response to CD19 CAR-T: LN, FMAC and TEX[1]
  - LN associated with better efficacy; FMAC and TEX associated with worse efficacy

CD19 CAR-T: Best response by LymphoMAP archetypes[1]



Prizlo-cel: Best Response by LymphoMAP archetypes



Prizlo-cel CR rate was consistently high (>80%) across all LymphoMAP archetypes, potentially differentiating prizlo-cel from SOC CD19 CAR T

LymphoMAP data was available for 30 patients across doses: 2M/kg (n=12), 150M (n=5), and 75M (n=13).
LN: lymph node architectural cell types with naive and memory T cells; FMAC a sparsity of T cells and high frequency of cancer-associated fibroblasts and tumor-associated macrophages; TEX: activated macrophages and exhausted CD8+ T cells.
CAR, chimeric antigen receptor; CR, complete response; FMAC, fibroblast/macrophage; LN, lymph node; PD, progressive disease; PR, partial response; SD, stable disease; SOC, standard of care; TEX, T exhausted.

1. Li X, et al. *Cancer Cell*. 2025;43(7):1347-64.

Prizlo-cel Global Phase 1b: Correlative Analysis Conclusions

- With an optimized CAR design, prizlo-cel shows a favorable safety profile and high CR rates in CAR-T–naïve patients with R/R LBCL[1]
- Potent CAR-T cell expansion and peripheral B cell depletion drive strong efficacy across all doses tested
- High CR rates were observed across a range of CD20 and/or CD19 antigen expression levels
- High CR rates were observed even in immunosuppressive TME archetypes,[2] when compared to approved CD19 CAR-Ts

Prizlo-cel, a dual targeting CAR-T with a differentiated CD20 binder coupled with CD19 binder, may overcome limitations of single-antigen targeting CAR-T cells, with a potential to improve clinical outcomes

CAR, chimeric antigen receptor; CR, complete response; R/R, relapsed/refractory; TME, tumor microenvironment.

1. Patel K, et al. European Hematology Association; June 12-15, 2025; Milan Italy. 2 . Li X, et al. *Cancer Cell*. 2025;43(7):1347-64.

Acknowledgments

- We thank the patients who participated in the study, their families, and the investigators and clinical research staff from the study centers

- We thank Gourav Choudhary, PhD, for designing and executing the in vitro analysis. We also thank Pallavi Daggumati for her support with biomarker operations.

- Editorial support was provided by Jennifer Venzie, PhD (SystemOne) and funded by Johnson & Johnson

- This study was sponsored by Johnson & Johnson

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