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Oncology Executive Summary/ Manuscript Brief

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Objective: In this Phase 2 clinical trial, the researchers set out to confirm the efficacy and safety of the anti-CD19 CAR-T treatment Tisagenlecleucel in children and young adults with CD19+, relapsed or refractory B-cell acute lymphoblastic leukemia (ALL).

Key Findings:

- By harvesting a patient's own T-cells and utilizing a viral vector, the researchers successfully engineered the modified T-cell with a chimeric antigen receptor (CAR) against the B-cell protein CD19.
- These engineered T-cells were then infused in the patient, in a CAR-T treatment called Tisagenlecleucel.
- The therapy achieved an overall remission rate of 81% among 75 patients with at least 3 months of follow-up after a single infusion, surpassing the null hypothesis (remission rate of ≤20%).
- The remissions were durable, with a 6-month relapse-free survival rate of 80%.
- Cytokine release syndrome occurred in 88% of patients.
    - It was effectively managed with supportive measures and anticytokine therapy.
- Neurological events were noted in 40% of patients and were managed with supportive care.
    - e.g. confusion, delirium, agitation, tremor, and sedation

Clinical Implications:

- Tisagenlecleucel is a highly effective treatment for children and young adults with CD19+, relapsed or refractory B-cell acute lymphoblastic leukemia (ALL).
- More promising research could lead to updating the current American Society of Hematology (ASH) guidelines for management of relapsed/refractory acute lymphoblastic leukemia in adolescents and young adults, which currently prioritizes treatments such as blinatumomab and/or inotuzumab.[2]
    - The guideline panel cited lack of head-to-head studies between CAR-T and these existing therapies.
- It requires monitoring for the onset of cytokine release syndrome.
    - This is a serious, but predictable complication, that is treated straightforwardly.
- It requires monitoring for neurological events.

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Limitations:

- The single-cohort design means the study included no control arm (placebo or active-control).
    - Without a control arm, it is difficult to assert causation.
- The study excluded patients that had already failed anti-CD19 therapy or any prior gene therapy.
    - The patient population was potentially less refractory than the broader relapsed/refractory clinical setting, which may limit the generalizability of these findings.
- The sample size of 75 in the final sample appears low. The authors justify the sufficient power of the study based on a null hypothesis of ≤20% remission rate, as against an alternative hypothesis of 45+% remission rate, but without an explanation of where these cutoff values came from, they seem arbitrary and possibly self-serving.

References

1. Maude SL, Laetsch TW, Buechner J, et al. Tisagenlecleucel in children and young adults with B-cell lymphoblastic leukemia. *N Engl J Med*. 2018;378(5):439-448. doi:10.1056/nejmoa1709866.

2. O'Dwyer KM, Winestone LE, Cheung MC, et al. ASH 2026 guidelines for management of relapsed/refractory disease in adolescents and young adults with ALL. *Blood Adv.* Published online February 11, 2026. doi:10.1182/bloodadvances.2021006479.