with CD3ζ followed by CD19-CAR containing NKp30 as a co-stimulatory domain, aiming to enhance cytotoxic activity against malignant B cells. **Material and methods:** (i) Construction of lentiviral vectors encoding CD19-NKp30-CAR and CD3ζ, separately; (ii) production of lentiviral particles carrying CD3ζ through transfection of HEK-293T cells; (iii) transduction of NK-92 cells via spinoculation. **Results:** CD19-NKp30-CAR construct was assembled by cloning the domains followed by and ligation using Gibson assembly. The construct was validated by restriction enzyme digestion and PCR amplification of the CAR transgene. This construct will be used to transduce NK-92 cells that were previously modified with CD3ζ via lentiviral transduction. Lentiviral vectors encoding CD3ζ were produced by transfection of HEK-293T cells, associated with helper plasmids, resulting in a titer of $1.335 \times 10^8$ TU/mL. Transduction of NK-92 cells reached 17.4% of CD3ζ-positive cells detected by flow cytometry on day three post-transduction. These modified cells were enriched via cell sorting. **Discussions and conclusion:** NK-92 cells can be engineered to the stable expression of CD3ζ, enabling further modification with CD19-NKp30-CAR, thereby enhancing cytotoxic activity against B cells malignancies.

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## EFFICACY AND SAFETY OF BELUMOSUDIL VERSUS BEST AVAILABLE THERAPY FOR THE TREATMENT OF CHRONIC GRAFT-VERSUS-HOST DISEASE IN THE US POPULATION

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**Introduction:** To date, no clinical studies have undertaken a head-to-head evaluation of the efficacy and safety of belumosudil vs best available therapy (BAT) for the treatment of relapsed/steroid-refractory chronic graft-versus-host disease (cGVHD) as lines of therapy (LOTs) 3–6. **Aim:** This non-interventional study was designed to estimate the efficacy and safety of belumosudil vs BAT in treating cGVHD patients aged ≥ 12 years who had failed 2–5 prior LOTs via emulation of a target trial. **Material and methods:** Data were collected from patient medical records across 8 sites in the United States (US) between March 1, 2015 and March 27, 2024. Adjusted comparative analysis of cGVHD treatment outcomes following belumosudil vs BAT was performed at the LOT level, with a standardized LOT algorithm applied across all sites. The primary study estimate was defined as the causal ratio of overall response rate (ORR), calculated as the ratio of average overall response (OR) for belumosudil vs BAT at LOTs 3–6 after 6 months of follow-up from the time of LOT initiation. OR was defined as complete (CR) or partial response (PR) of cGVHD based on the 2014 National Institutes of Health consensus criteria, physician-assessed CR or PR, or steroid dose taper of ≥ 50% without disease progression. Death, relapse, and initiation of a new LOT were categorized as failure to respond. The secondary study estimate was the difference in failure-free survival (FFS) between belumosudil and BAT at LOTs 3–6 after 1 year of follow-up. Targeted maximum likelihood estimation, an advanced methodology for causal inference with real-world data, was used to generate all study estimates while adjusting for biases common in non-interventional studies and accounting for correlations among multiple LOTs from the same patient. Adverse events (AEs), including those leading to hospitalization and/or death, observed in were descriptively summarized for belumosudil vs BAT LOTs 3–6 using unadjusted counts and rates per 100 LOT-years. **Results:** A total of 196 patients met all eligibility criteria. Of these, 113 were treated with belumosudil and 83 were not, resulting in 358 LOTs (113 belumosudil, 245 BAT). Baseline characteristics were generally well-balanced across belumosudil and BAT LOTs. The estimated 6-month ORR was 38.7% for belumosudil vs 26.8% for BAT. The 6-month ORR ratio between groups was 1.44 (95% confidence interval [CI]: 1.04, ∞; $p = 0.03$), corresponding to a 44% improvement with belumosudil over BAT. The estimated 1-year FFS was 61.2% for belumosudil vs 47.8% for BAT, resulting in a 1-year FFS difference of 13.5% (95% CI: 1.5%, 100.0%; $p = 0.03$). The AE rate per 100 LOT-years was 41.2% for belumosudil and 51.6% for BAT LOTs 3-6. Belumosudil LOTs had a lower AE rate per 100 LOT-years in 69% of the AE categories. **Discussion and conclusion:** This study demonstrated that belumosudil has superior efficacy compared with BAT in real-world patients with relapsed/steroid-refractory cGVHD. The safety profile of belumosudil-treated patients was consistent with its previously established clinical profile.

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## EFFICACY OF CAR-T THERAPY FOR REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: A SYSTEMATIC REVIEW AND METANALYSIS

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