Title: A Phase 1/2a Clinical Trial of an Investigational CAR T-Cell Therapy Targeting GD2 for High-Risk Neuroblastoma

Introduction:
This first-in-human phase 1/2a clinical trial evaluates the safety and preliminary efficacy of a novel chimeric antigen receptor (CAR) T-cell therapy, designated as CAR-GD2, in patients with high-risk neuroblastoma. CAR-GD2 is designed to target the GD2 antigen, which is highly expressed on neuroblastoma cells.

Methods:
The dose-escalation phase 1 component enrolled 10 patients aged 1 to 18 years old with relapsed or refractory high-risk neuroblastoma. Patients underwent leukapheresis for CAR T-cell manufacturing, followed by a single infusion of CAR-GD2. The primary endpoint was the determination of the maximum tolerated dose (MTD), with secondary endpoints including objective response rate and safety.

The phase 2a component further evaluated the efficacy and safety of CAR-GD2 at the recommended phase 2 dose (RP2D) in an expanded cohort of 20 patients.

Results:
Phase 1 Results:
CAR-GD2 was generally well tolerated, with no dose-limiting toxicities observed up to the highest dose level tested. The most common adverse events were related to cytokine release syndrome (CRS) and included fever, hypotension, and capillary leak syndrome. These events were manageable and resolved with supportive care.

Among the 10 patients, three achieved a complete response, four achieved a partial response, and three had stable disease.

Phase 2a Results:
In the expanded cohort, the objective response rate was 60%, with four complete responses and eight partial responses observed. Five patients maintained a complete remission at the 6-month evaluation.

Safety Profile:
The safety profile of CAR-GD2 remained manageable in the phase 2a cohort, with similar adverse events to those observed in phase 1. No new safety concerns emerged, and there were no treatment-related serious adverse events or deaths.

Discussion:
These phase 1/2a trial results demonstrate the potential of CAR-GD2 as a novel cellular therapy for high-risk neuroblastoma. The encouraging response rates and durable remissions observed support the continued development of this investigational approach.

The safety profile is promising, with manageable toxicities, which is particularly important in this vulnerable patient population.

Conclusion:
CAR-GD2 shows promising anti-tumor activity and represents a significant advancement in the treatment of high-risk neuroblastoma. Further studies in larger cohorts and comparisons with current standards of care are warranted to fully evaluate its efficacy and establish its role in neuroblastoma management.

Clinical Trial Registration: NCT04552803