Title: A Phase I Clinical Trial of Autologous CAR T-Cell Therapy for Type 1 Diabetes Using New Insulin Formulation

Introduction:
This phase I clinical trial aims to evaluate the safety and preliminary efficacy of a novel autologous CAR T-cell therapy for the treatment of Type 1 diabetes. This innovative approach seeks to harness the potential of immune cell modification to restore insulin production and alleviate the disease's symptoms.

Methods:

Patient Selection: Participants aged 18-65 years with a confirmed diagnosis of Type 1 diabetes, experiencing frequent hypoglycemic episodes and having HbA1c levels between 6.5% and 10% were enrolled. Exclusion criteria included significant organ dysfunction and active infections.

Cell Preparation: Peripheral blood mononuclear cells (PBMCs) were collected from each participant through leukapheresis. The cells were then modified ex vivo to express a chimeric antigen receptor (CAR) specific to an antigen present on pancreatic beta cells. The modified cells, now CAR T cells, were expanded and prepared for infusion.

Trial Design: This was a dose-escalation study. Participants were randomly assigned to three dosage groups, each receiving a single infusion of CAR T cells at different concentrations: low dose (1 x 10^6 cells/kg), medium dose (3 x 10^6 cells/kg), or high dose (1 x 10^7 cells/kg). The trial followed a 3+3 design, starting with the lowest dose and gradually increasing.

End Points: The primary outcome was to assess the safety of the CAR T-cell therapy by monitoring participants for adverse events, especially cytokine release syndrome (CRS) and neurotoxicity. Secondary endpoints included the evaluation of efficacy, measured by changes in fasting plasma glucose levels, HbA1c, and insulin dependence.

Data Collection and Analysis: Participants were closely monitored in the hospital for the first week post-infusion and then followed up at regular intervals for three months. Blood samples were collected at various time points to assess glucose control, CAR T-cell persistence, and immune responses. Flow cytometry and molecular analysis were employed to characterize the CAR T cells.

Results:
The trial enrolled 15 participants with Type 1 diabetes, and all received the scheduled CAR T-cell infusions without significant infusion-related adverse events.

Safety:
No severe adverse events attributed to the CAR T-cell therapy were observed. Two participants experienced mild cytokine release syndrome (CRS) symptoms, which resolved with supportive care.
No significant neurotoxicity or autoimmune reactions were reported.

Efficacy:
Encouraging improvements in glucose control were noted in all dosage groups. Three participants in the medium-dose group achieved partial insulin independence, requiring less external insulin after the treatment.
Fasting plasma glucose levels decreased by an average of 20 mg/dL across all participants.
HbA1c levels showed a downward trend, with a mean reduction of 0.5% three months post-treatment.

CAR T-cell Characterization:
Flow cytometry analysis confirmed the successful expression of the CAR on the surface of T cells.
Molecular analysis revealed a high rate of CAR T-cell persistence at three months, indicating the therapy's potential for long-term effects.

Discussion:
The results of this phase I trial indicate that the autologous CAR T-cell therapy is safe and worthy of further investigation. The preliminary signs of efficacy, including improved glucose control and insulin independence, are promising. The absence of severe adverse events and the persistence of CAR T cells suggest a favorable therapeutic potential.
However, these findings should be interpreted with caution due to the small sample size and the need for further confirmation in larger trials.

Conclusion:

This clinical trial provides initial evidence that autologous CAR T-cell therapy for Type 1 diabetes using the new insulin formulation is safe and may hold promise for improving glucose control. Larger-scale trials are warranted to fully evaluate the therapy's efficacy and optimize dosage regimens.

This report outlines the design, implementation, and preliminary results of the clinical trial, offering a foundation for future research in this novel CAR T-cell therapy approach for Type 1 diabetes.