Exploratory Study of Anti-BCMA–CD19 CAR-T Cell Therapy in Relapsed or Refractory IgG4-Related Disease

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In accordance with the clinical study protocol and the Good Clinical Practice (GCP) guidelines of the People's Republic of China, the study will be conducted to ensure proper implementation, recording, and reporting of data. The reliability of all study-related data and the appropriateness of data handling will be ensured. Quality control will be implemented at each stage of data processing, and all study-related data will be handled and analyzed by qualified biostatisticians.

10.1 Analysis Populations

The following six analysis populations will be defined in this study:

Full Analysis Set (FAS): includes all subjects who receive BCMA-CD19 CAR-T cell infusion.

1. Safety Analysis Set: includes subjects who receive BCMA-CD19 CAR-T infusion and have post-infusion safety assessments.
2. Pharmacokinetic (PK) Analysis Set: includes subjects who receive BCMA-CD19 CAR-T infusion, have at least one post-baseline PK assessment, and are not affected by protocol deviations impacting PK concentration analysis.
3. Pharmacodynamic (PD) Analysis Set: includes subjects who receive BCMA-CD19 CAR-T infusion, have at least one post-baseline PD assessment, and are not affected by protocol deviations impacting PD analysis.
4. Efficacy-Evaluable Set: includes subjects with baseline and at least one post-baseline efficacy evaluation.
5. Immune Microenvironment (IME) Analysis Set: includes subjects with baseline and at least one post-baseline immune microenvironment evaluation.

All analysis set definitions will be finalized at the data review meeting.

10.2 Statistical Methods

10.2.1 Subject Disposition

The subject disposition will summarize screening and enrollment status, including reasons for screening failure. For enrolled subjects, analysis will summarize enrollment and study completion. Reasons for withdrawal will be documented and summarized.

10.2.2 General Statistical Analysis

Statistical analyses will be performed using SAS version 9.4 or higher (or other validated software). Continuous variables will be summarized with counts, means, standard deviations, medians,

minima, and maxima. Categorical or ordinal variables will be summarized with counts and percentages. Baseline is defined as the last valid measurement prior to infusion. Details of statistical analysis will be specified in a separate statistical analysis plan.

10.2.3 Protocol Deviations

Protocol deviations will be graded as "minor" or "major" and finalized at the data review meeting. Major deviations will be summarized with counts and percentages.

10.2.4 Demographic and Baseline Characteristics

The FAS will be used to summarize demographics and baseline characteristics, including medical history, disease history, and baseline disease characteristics. Continuous variables will be summarized with descriptive statistics; categorical or ordinal variables with counts and percentages.

10.2.5 Concomitant Medications and Therapies

Concomitant medications will be coded using the WHO Drug dictionary; non-drug therapies will be coded using MedDRA. Use of concomitant medications and non-drug therapies will be summarized.

10.2.6 Safety and Tolerability Analyses

Safety analysis will be performed in the Safety Analysis Set. All adverse events will be coded using MedDRA, summarized by system organ class (SOC) and preferred term (PT), and presented with counts and percentages. Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) will be graded per ASTCT 2018 criteria. Laboratory abnormalities will be graded per CTCAE v5.0. Electrocardiogram findings will be compared with baseline.

10.2.7 Efficacy Analyses

The FAS will be used for analysis of primary and secondary efficacy endpoints. Endpoint-specific hypotheses and statistical methods (e.g., change from baseline analyses at prespecified time points) will follow the predefined statistical analysis plan.

10.2.8 Pharmacokinetic Analysis

The PK Analysis Set will be used to perform descriptive statistics of PK parameters and concentrations at different time points, reporting means, standard deviations, medians, minima, maxima, geometric means, and coefficients of variation.

10.2.9 Pharmacodynamic Analysis

The PD Analysis Set will be used for descriptive statistics of cytokine levels and other PD biomarkers at different time points, reporting means, standard deviations, medians, minima, maxima, geometric means, and coefficients of variation.

10.2.10 Immune Microenvironment Analysis

The IME Analysis Set will be used to analyze the composition, spatial distribution, and gene expression characteristics of immune microenvironment cell types (including immune cells, stromal cells, and epithelial cells), combined with cell-cell interaction analyses to report abundance, spatial localization, and dynamic changes.