(PF1235) PHASE 1 STUDY OF SL0349, A BISPECIFIC NANOBODY BASED BCMA/GPRC5D CAR-T, IN RELAPSED OR REFRACTORY MULTIPLE MYELOMA

Topic: 26. Gene therapy, cellular immunotherapy and vaccination - Clinical

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Background

BCMA CAR-T have emerged as breakthrough treatments for patients with relapsed/refractory multiple myeloma (RRMM). However, the development of drug resistance remains inevitable, leaving patients with limited later-line options. SL0349 is a bispecific nanobody-based chimeric antigen receptor T cell (CAR-T) product targeting both BCMA and GPRC5D, engineered with VHH binders and an optimized structure. This dual-targeting strategy aims to overcome antigen escape due to mutation or downregulation of either target. This article reports preliminary data from a currently active phase 1 study (NCT07003568), evaluating the safety and efficacy of this therapeutic approach.

Aims

This study aimed to evaluate the safety and preliminary efficacy of SL0349 in heavily pretreated patients with RRMM.

Methods

This open label, single dose, exploratory phase I study was initiated on June 1, 2025, and was carried out at Shanghai Liquan Hospital (Shanghai, China). Eligible patients aged 18 to 75 years had a diagnosis of RRMM. Patients were administered SL0349 at dose of 1.0×10^6 cells/kg. The primary objective was to assess safety, defined by adverse events and laboratory abnormalities, as well as the efficacy evaluation was designated as the secondary objective. Analyses of safety and efficacy were done in all patients who received SL0349 according to the protocol.

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Results

As of February 19, 2026, a total of 18 patients were infused with anti-BCMA/GPRC5D bispecific CAR T cells. The median age was 58.0 years old (Range 36-70). 8 were male and 10 were female patients, with 12 (66.7%) were Caucasian and 6 (33.3%) were Asian respectively. The median number of prior lines of therapy was 3 (range: 2-9). 13 patients (72.2%) were previously treated with stem-cell transplantation (SCT). 9 patients (50.0%) presented with extramedullary disease (EMD), of which 2 patients had central nerves system involvements. Among 12 patients with available cytogenetic assessment, 8 (66.7%) patients were diagnosed with high-risk cytogenetic profile.

The most common grade 3 or worse adverse events were hematologic toxicities in 94.44% (17/18) patients. Cytokine release syndrome occurred in 94.44% (17/18) patients, of which all cases were grade 1-2. Grade 1 immune effector cell-associated neurotoxicity syndrome occurred in 16.67% (3/18) patients. Off-target toxicities potentially related to GPRC5D expression in keratinized tissues were observed, including grade 1 nail changes (11.1%), grade 1 rash (11.1%). No cerebellar toxicities and grade 3 or above organ toxicities were observed.

The overall response rate was 100%, with CR (CR+sCR) rate of 83.3% (15/18). The measurable residual disease negativity rate was achieved in 100% (14/14) among available patients assessed by bone marrow flow cytometry. For patients with EMD, 66.67% (6/9) achieved sCR and 33.33% (3/9) achieved PR. Of the 13 patients previously treated with SCT, 76.92% (10/13) achieved sCR. The median time to response was 17 days (IQR 15-24) post-infusion.

The SL0349 CAR transgene concentrations (mean maximum concentration [C_{max}]=535071 copies/μg DNA) showed maximum peripheral expansion at a median of 13.5 (range: 10-21) days.

Summary/Conclusion

This analysis of the phase 1 study establishes a positive risk–benefit profile for a single low-dose infusion of SL0349, yielding early, deep responses in heavily pretreated RRMM patients, particularly for patients with high-risk cytogenetic features and/or EMD lesions.

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