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POSTER ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

CD27-Armored BCMA-CAR T Cell (CBG-002) Therapy for Relapsed and Refractory Multiple Myeloma: A Phase I Clinical Trial

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Introduction:
Several BCMA CAR T-cell products have been approved for relapsed or refractory multiple myeloma (RRMM), but long-term response has not been established. There is growing interest in the use of next-generation CAR T-cell therapy in RRMM. CBG002 is an armored BCMA CAR T-cell product engineered to constitutively express CD27, which binds CD70 to promote T-cell proliferation and differentiation. In vitro, CBG-002 cells exhibited enhanced proliferation, greater cytotoxicity and a higher proportion of memory T cells compared to control BCMA-CAR T cells; in animal models, CBG-002 infusion also resulted in improved tumor control and prolonged survival in MM xenograft mice. Based on the preclinical data, we conducted a phase I clinical trial to evaluate its safety and efficacy in patients with RRMM.

Methods:
This is a single-arm, open-label, phase I study (NCT04706936). Key eligibility criteria were RRMM patients who had received at least 3 prior regimens, including a proteasome inhibitor and an immunomodulatory drug; the percentage of BCMA expression ≥50% on myeloma cells, detected by either flow cytometry and immunohistochemistry. Patients received 3 days of fludarabine (30 mg/m ^{2}) and cyclophosphamide (300 mg/m ^{2}) followed by a single dose of CBG-002 infusion. The dose-escalation study follows a "3+3" design with 1×10^6/kg, 2×10^6/kg and 3×10^6/kg CAR-T cell cohorts. The primary endpoint was safety, including grade 3 or 4 treatment-emergent adverse events (TEAEs) and dose-limiting toxicities (DLTs); The secondary endpoints were overall response rate (ORR), duration of response (DOR), progression-free survival (PFS) and overall survival (OS).

Results:
As of June 25, 2023, 12 patients were enrolled and 1 patient was later excluded due to <50% BCMA expression. Among the evaluable 11 patients, there were 9 males and 2 females; median age was 52 years (range 36-66), 5/11 (45.5%) patients had high-risk cytogenetics including complex karyotype, t(4;14),1q21 amplification and del(17p), 4 (36.4%) had extramedullary disease (EMD). The median number of prior treatments was 5 (range 3-7); 7/11 pts were triple-agent exposed and refractory; 5/11 underwent ASCT. The most common TEAEs were neutropenia (G3/4 63.6%), thrombocytopenia (G3/4 36.4%) and anemia (G3/4 45.5%). Nine patients developed G1/2 CRS, which resolved spontaneously except for 2 patients who required steroids and tocilizumab, and no patients developed G3/4 CRS or ICANS. The median time to onset of CRS was 7 days (range 5-21) and the median duration was 6 days (range 5-8). At a median follow-up of 9 months, the ORR was 81.8%, including sCR/CR of 63.6%, VGPR 9.1% and PR 9.1%. After infusion, 8 pts were MRD negative in bone marrow by flow cytometry at day 28, 5 pts continued at month 3. The median OS was 14 months and the OS rate was 100%. The median PFS was 9 months and the PFS rate was 60%. The CBG-002 kinetics paralleled peripheral blood sCD27 levels with a median time to peak of 15 days (range 7-14). The fold increase in sCD27 levels was significantly higher in responders (12.1, range 1.2-83.8) than in non-responders (1.68, range 0.81-9.45).

Conclusions:
In this phase I study, CBG-002, a CD27-armored BCMA-CAR T therapy has demonstrated remarkable safety and clinical activity in RRMM patients.

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