S186 UPDATED RESULTS OF A MULTICENTER FIRST-IN-HUMAN STUDY OF BCMA/CD19 DUAL-TARGETING FAST CAR-T GC012F FOR PATIENTS WITH RELAPSED/REFRACTORY MULTIPLE MYELOMA (RRMM)

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Background:
GC012F is a B cell maturation antigen (BCMA) and CD19 dual-targeting CAR-T developed on the novel FasT CAR-T platform enabling 22-36h manufacturing designed to improve depth of response and overall efficacy. Data was presented at ASCO and EHA 2021 for initial 19 pts. Here we present updated data for study (NCT04236011; NCT04182581) with longer follow up and 9 additional pts treated (total n=28) in 3 different dose levels.

Aims:
The study aims to assess safety and preliminary efficacy for FAST-CAR GC012F in RRMM patients.

Methods:
From October 2019 to November 2021, 28 heavily pretreated RRMM pts (age 27-76) with a median of 5 prior lines (range 2-9) were treated on this single-arm, open label, multicenter Investigator Initiated Trial receiving a single infusion of GC012F. 89.3% (25/28) were high risk (HR- mSMART), 8 pts had EM disease, 3 had never achieved a CR including after transplant, 1 pts presented with plasma cell leukemia, 24/28 pts were refractory to last therapy, 3 pts primary refractory. 9/28 pts had received prior anti-CD38, 27/28 pts prior IMiDs. 26/28 pts were refractory to PI, 26/28 pts to IMiDs. After lymphodepletion over 2-3 days (30 mg/m2/d, 300mg/ m2/d Flu/Cy) GC012F was administered as single infusion at 3 dose levels: 1x105/kg (DL1) n=2, 2x105/kg (DL2) n=10 and 3x105/kg (DL3) n=16.

Results:

As of Jan 26th 2022 cut-off, 28 pts - median follow-up (f/u) 6.3 mths (1.8-29.9) - had been evaluated for response. Overall response rate (ORR) in DL1 was 100% (2/2)- DL 2 -80% (8/10) DL 3 -93.8% (15/16) with 27 pts MRD negative by flow cytometry (sensitivity 10-4-10-6). 100% of MRD assessable pts (27/27) achieved MRD negativity. One patient out of 28 could not get assessed. At d28, 21/24 assessable patients were MRD negative (81.5%), 4/28 pts could not get d28 MRD assessment f/u due to COVID-19 restrictions however were assessed at a later timepoint. To date best response is MRD- sCR in 21/28 patients (75.0%) across all dose levels. Some pts after short f/u show responses that are still deepening. Cytokine Release Syndrome (CRS) was mostly low grade: gr 0 n=3 (10.7%), gr 1-2 n=23 (82.1%), gr 3 n=2 (7.1%) – no gr 4/5 CRS and no ICANs were observed (Graded by ASBMT criteria). Median duration of CRS was 3 d (1-8 d). PK results showed no difference amongst dose levels DL1 to DL3. Overall, CAR-T median Tmax was 10 d (range 8-14 d), median peak copy number (Cmax) was 97009 (16,011-374,346) copies /ug DNA with long duration of persistence of up to d793 (data cut-off). CAR-T geometric mean AUC0-28 for DL1, DL2 and DL3 were 468863, 631540 and 581620 copies/ug DNA×day, respectively. Pts continue to be monitored for safety and efficacy including DOR.

Conclusion:

BCMA-CD19 dual FasT CAR-T GC012F continues to provide deep and durable responses with a favorable safety profile in additional RRMM pts across all dose levels demonstrating a very high MRD negativity rate including in pts refractory to anti-CD38, PI and IMIDs. Based on these promising results GC012F is being studied in earlier lines of therapy as well as additional indications.