ELSEVIER

Blood 142 (2023) 1022–1023

The 65th ASH Annual Meeting Abstracts

ORAL ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: EARLY PHASE AND INVESTIGATIONAL THERAPIES

Updated Results of a Phase I Open-Label Single-Arm Study of Dual Targeting BCMA and CD19 Fastcar-T Cells (GC012F) As First-Line Therapy for Transplant-Eligible Newly Diagnosed High-Risk Multiple Myeloma

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Background
High-risk (HR) newly-diagnosed multiple myeloma (NDMM) has poor outcomes with standard first-line therapies, even in transplant-eligible (TE) patients (pts). A CAR-T therapy with high efficacy and manageable safety profile would be a potential solution to this significant unmet need. GC012F is an autologous B cell maturation antigen (BCMA) and CD19 dual-targeting CAR-T cells therapy developed on the novel FasTCAR-T enabling next-day manufacturing platform [J Clin Oncol 41, 2023 (suppl; abstr 8005)]. The phase I single-arm study has been conducted in frontline setting for TE high-risk NDMM pts to characterize the safety and feasibility of GC012F CAR-T cell therapy (NCT04935580). The data was presented at ASH 2022 for initial 13 pts (Blood (2022) 140 (Supplement 1): 889-890.). Here we present updated data with longer follow up and 9 additional pts treated (total N=22) in this study.

Methods
This is a single arm, open-label phase I investigator-initiated study (NCT04935580). TE NDMM pts, aged between 18-70, and with one or more of the following features were considered eligible for the study: R-ISS-II or-III; del17p, t (4;14), t (14;16), or 1q21amp $\geq$ 4 copies; extramedullary disease (EM); IgD or IgE subtype; LDH > the upper limit of normal; or any of the high-risk definition of mSMART3.0.
As of the data cutoff date, 22 evaluable pts (median age 59, range 43-69) are reported here. The median time from diagnosis to infusion was 100 days (range 63-152). All patients had one or more high-risk features including 91% R-ISS stage II or III, 55% with EM, 32% 1q21$\geq$4 copies, and 9% IgD type. Of the 22 pts, 21 pts received 2 cycles induction therapy of bortezomib, lenalidomide and dexamethasone (VRd), and one patient received 1 cycle bortezomib, epirubicin, and dexamethasone (PAD) and 1 cycle VRd prior to the infusion. GC012F was administered as a single infusion at 3 doses levels (DL) of $1x10^5$/kg (n=1), $2x10^5$/kg (n=4), or $3x10^5$/kg (n=17), after a standard 3-day lymphodepletion consisting of cyclophosphamide and fludarabine
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Results
As of June 9 th, 2023 data cutoff, 22 patients were enrolled and evaluable for safety and efficacy. Median follow-up was 13.6 months (range 2.1-23.9 months). Overall response rate (ORR) was 100% and stringent complete response (sCR) rate was 95.5%. All treated pts (100%) across all dose levels achieved minimal residual disease (MRD) negativity assessed by Euroflow (sensitivity of 10^{-6}). All evaluable pts achieved MRD negativity at Month 1, and maintained MRD- at landmark analysis of Month 6 and Month 12. Median duration of response (DOR) and progression-free survival (PFS) were not reached. Only 6 pts (27%) experience low-grade cytokine release syndrome (CRS), including 23% grade 1 (n=5) and 4% grade 2 (n=1). No treatment-related grade $\geq$3 CRS, nor ICANS of any grade, and nor deaths occurred in the study. Robust CAR T-cell expansion was observed in all pts; the median peak expansion (Cmax) was 62,131 (range: 8,754-331,159) copies /μg DNA with a median Tmax of 10 days (range 9-14 d).

Conclusion
Consistent with the previous RRMM cohort treated with GC012F, initial data from this phase I study demonstrated that BCMA-CD19 dual-targeting FasTCAR-T GC012F resulted in deep and durable response in transplant-eligible newly-diagnosed high-risk pts with a very favorable safety profile. All three dose groups achieved 100% MRD negativity and 100% ORR and sCR. The promising preliminary results achieved with GC012F demonstrate potential of CAR-T therapy in newly-diagnosed MM pts. Further research with larger patient population and longer follow-up shall bring the hope to this unmet medical need.

Disclosures No relevant conflicts of interest to declare.

Figure 1:

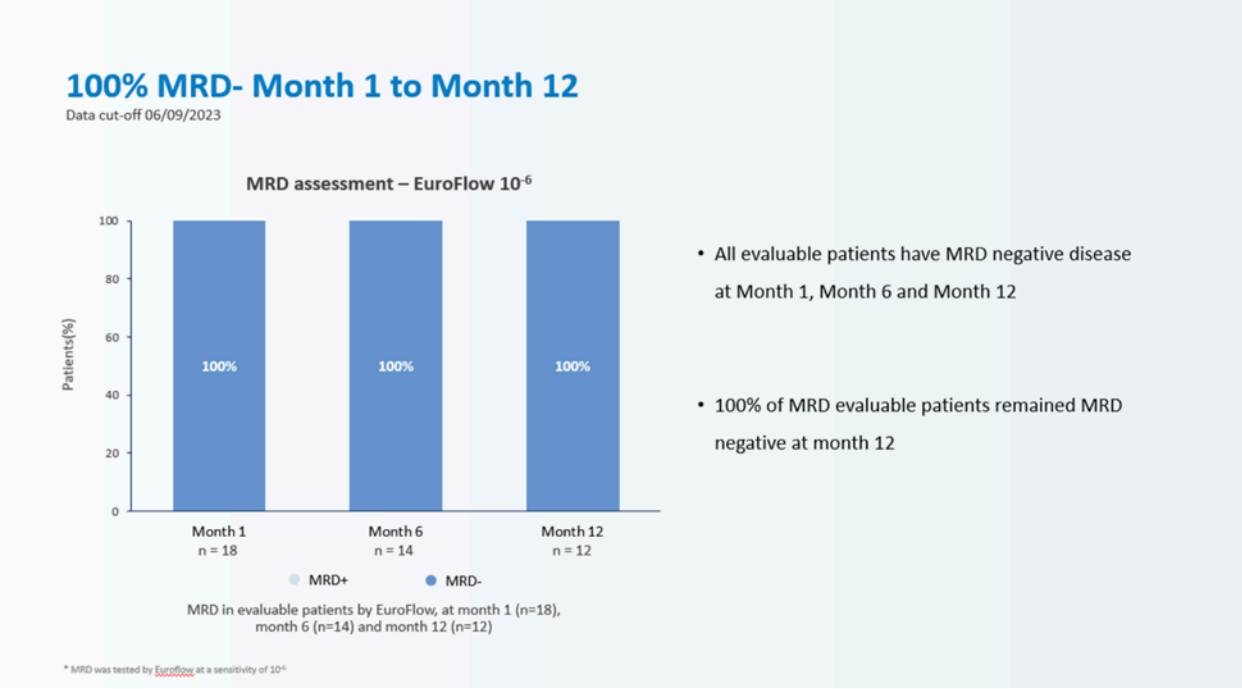

Figure 1

https://doi.org/10.1182/blood-2023-174841