Immune Monitoring of CD34+ Placental Cell Derived Natural Killer Cell Therapy (PNK-007) in Phase I Study of Multiple Myeloma

INTRODUCTION

Natural Killer (NK) cells are innate immune cells which play an important role in host immune surveillance against pathogen infection and cell transformation. Multiple studies adaptively transferring NK cells in clinical settings have demonstrated the potential of NK cells to induce remissions for hematological indications with a consistent safety profile.

Celularity has developed a novel proprietary GMP platform that enables the scalable production of an off-the-shelf, allogeneic NK cell therapy. Using this technology platform, Celularity developed PNK-007, a Placental Hematopoietic Stem Cells Derived Natural Killer cell therapy.

PNK-007 shows cytotoxic activity against various cancer cell lines and has been evaluated in a Phase I study for the treatment of relapsed/refractory acute myeloid leukemia and in multiple myeloma patients undergoing autologous stem cell transplant (ASCT). Here, we present translational data from multiple myeloma monitoring minimal residual disease (MRD) using EuroFlow validated assays for 5 years. We characterize immune reconstitution and immune correlates associated with the clinical protocol and PNK-007 administration.

RESULTS

- Among 15 patients treated, 11 patients measured MRD+ at post-induction baseline. 7 of those 11 patients converted MRD+ to MRD- over the 1 year follow-up period. The remaining 4 patients tested MRD- for the duration of the study, 2 of those patients were relapse/refractory myeloma at enrollment.
- PNK-007 infusion at day 7 and day 14 post-ASCT did not interfere with bone marrow engraftment and immune reconstitution.
- Serum analysis demonstrated absence of allo-HLA antibodies in all subjects.
- PNK-007 cell persistence was not detectable by flow cytometry in patients at day +7 post-PNK-007, the earliest post-infusion timepoint measured.
- mIL-2 administration did not significantly affect reconstitution of patients’ NK cells. However, mIL-2 stimulated shedding of soluble IL-2 receptor in the serum, indicative of a negative feedback loop. mIL-2 also significantly enhanced transient levels of T° relative to patients not receiving mIL-2.
- Patients CD4 and CD8 T cell populations showed inhibited effect response 7-14 days post-PNK-007 dosing, potentially in response to mIL-2, and increased numbers of T°. At all measured timepoints up to day 90 post-ASCT, T cells were not significantly different in response to PNK/Alondium stimulation with minimal levels of IL-4 and IL-17.

Discussion

Translational data from this Phase I study of PNK-007 established that dosing up to 3x10^5 cells/kg at 14 or 1x10^5 cells/kg at 7 days post-transplant did not impair engraftment or immune reconstitution. EuroFlow MRD assessment of the bone marrow shown conversion of 7 of 11 patients from MRD+ to MRD- over the course of 1 year. The administration of IL-2 in this clinical study did not appear to benefit NK cell reconstitution but instead stimulated soluble IL-2Rα antagonism and increased systemic levels of T°. Hoping potential disadvantages of mIL-2 administration in this setting. Our results support the feasibility of PNK-007 in the MM + ASCT setting and will help inform the design of future clinical trials.

For a clinical summary associated with this clinical trial, please visit www.mdpi.com/2673-7384/4/6/4457.