INTRODUCTION

- Autologous stem cell transplant (ASCT) improves minimal residual disease (MRD) negativity and prolongs progression-free survival in patients with newly diagnosed multiple myeloma.
- Multiple myeloma natural killer (NK) cells are dysfunctional, negatively impacting outcomes.
- BHV-1100 is an antibody recruiting molecule (ARM) that binds to CD38 target cell antigen and recruits NK cells for antibody-dependent cellular cytotoxicity (ADCC) without inducing fratricide.
- Cytokine-induced memory-like (CIML) NK cells effectively treat myeloid disorders.
- We designed a first-in-human study of autologous CIML NK cells coated ex vivo with BHV-1100 for MRD+ patients with newly diagnosed multiple myeloma undergoing ASCT.

METHODS

- In the ongoing phase 1 study (NCT04634435), eligible patients had previously received ASCT and autologous stem cell transplant.
- The study schematic (Figure 1) shows an overview of ASCT with BHV-1100.

PATIENTS AND TREATMENT

- Data from first 5 enrolled patients are presented; median follow-up was 191 days.
- CIML NK cells were manufactured with a 100% success rate and infused at target dose of 5-10 x 10^6 cells/kg body weight 24 hours after melphalan 200 mg/m².
- Patients received 3.9-6.0 x 10^8 kg body weight stem cells.
- Engraftment based on recovery of neutrophil count occurred on days 12-14.
- Aside from anticipated infusion reactions, no severe or unexpected adverse events were noted.
- Longer follow-up is required to assess safety and efficacy.

IN VIVO RESULTS

NK Expansion and Persistence

- There was a 3.5-fold expansion of NK cells in the peripheral blood from day 7 (from 11.1% to 41%) to day 28 that persisted until day 60 (25% total peripheral blood mononuclear cells (PBMC) (Figure 2).
- Most expanded NK cells were CD56dim, CD16+, killer cell immunoglobulin-like receptor KIR+, and CD57+ (Figure 3).
- CD57 and KIR expression increased over time from day 7 to day 60 (Figure 3C, D).
- Regulatory T cells increased by day 7 (3% vs 15% total PBMC) and returned to baseline after day 14, most likely reflecting the effect of IL-2 treatment.

Figure 2. ARMored NK Cells Expand After Infusion

CORRELATIVE IN VITRO RESULTS

Functional capacity of ARMed CIML NK cells

- BHV-1100 ARMored CIML NK cells were stable for up to 24 hours at 4°C.
- The BHV-1100 ARMored CIML NK cells had a higher killing capacity towards MOLP8 multiple myeloma cell lines compared with untreated CIML NK cells at baseline (Figure 4A).
- 90.8% vs 61% target cell death at both 4 hours and 24 hours (2:1 ratio).
- ARM0210 CIML NK cells showed increased CD107a expression (26% vs 14.9%) and IFNγ production (53% vs 37%) compared with untreated CIML NK cells at 24 hours (Figure 4B).

Figure 4. ARMed NK Cells Have Enhanced Activity Against Multiple Myeloma cell lines

KEY POINTS

- BHV-1100 is an antibody-recruiting molecule (ARM) that binds to CD38 target cell antigen and recruits NK cells for ADCC.
- Autologous, BHV-1100 ARM0210 CIML NK cells have enhanced anti-multiple myeloma activity in vitro and expand and persist in vivo, peaking at 28 days after infusion
- In a first-in-human study in patients with multiple myeloma undergoing ASCT, no severe or unexpected adverse events were noted with BHV-1100 ARM0210 CIML NK cells; longer follow-up is required.
- BHV-1100 ARM0210 CIML NK cells represent an innovative approach to boost autologous cancer immunosurveillance in the context of ASCT for multiple myeloma.

REFERENCES


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