Biomarker correlates of response in patients with advanced Myxoid/Round Cell Liposarcoma (MRCLS) treated with NY-ESO-1 TCR T cells (Letegetrene aluloecue)

Poster No. 391

Introduction

- This is an open-label phase II trial of NY-ESO-1 TCR T cell therapy (Letegetrene aluloecue) in patients with advanced MRCLS on trial 2021-049.
- The primary endpoint is complete regression of measurable disease (CRMD) at 28 days post infusion (C28d).
- Secondary endpoints include partial regression of measurable disease (PRMD), tumor shrinkage (TS), and overall survival (OS).
- The study was conducted at 9 centers across 8 countries (Australia, Canada, Germany, India, Japan, Spain, USA, and the UK).
- The recruitment phase of this study was completed in December 2020.

Methods

- Patients received LDR-B (Cohort 2) vs. LDR-A (Cohort 1) to induce lymphodepletion and high peak cell expansion.
- The peak expansion was significantly associated with weight-normalized lymphocyte count data at infusion for 4 patients across both trials.
- The lymphodepletion regimen (LDR-B) utilized optimized doses of anti-CD19/CD20 (LDR-B) prior to infusion.
- Complete lymphodepletion at infusion (0–50% depletion, median 0%, range 0%–0%)

Results

- Association of decreased lymphocyte and monocyte counts at the time of infusion with response.
- Five out of 6 responders with available laboratory data exhibited reduced lymphocyte depletion at infusion (p=0.0182), with AUC0–28d demonstrating tumor volume reduction (p=0.0569) (Figure 5A). (Adj. R2=0.606)
- LDR-B-induced strong depletion of lymphocytes at the time of infusion (p=0.0182) versus LDR-A (Figure 4B). (Adj. R2=0.606)
- TNFα production of monocytes did not show any association with response (Figure 4B).
- Responders showed robust lymphocyte depletion at the time of infusion (p=0.0182) (Figure 1A) and was trended towards higher peak cell expansion (Cmax) versus LDR-A (Table 1).

Conclusions

- Differential expression of cytokines in responders vs. non-responders (LDR-B cohort).
- Several cytokines such as granulocyte-macrophage colony-stimulating factor (GM-CSF), IL-12, receptor agonist (RA), interferon-gamma (IFN-γ), IL-7, and tumor necrosis factor (TNF) were upregulated in the first week following lymphodepletion in responders when compared with non-responders (Figure 6A).
- In LDR-A cohort, responders showed elevated production of IL-15, IL-15, IL-12, IL-7, IL-6, and IL-10, and a week of one-time infusion (Figure 6B).

Disclosures