**Initial Safety Assessment of MAGE-A10 Specific Peptide Enhanced Affinity Receptor (SPEAR) T-cells in Two Clinical Trials**

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**Abstract**

MAGE-A10 is a highly immunogenic cancer antigen expressed in 10%–50% of melanoma, breast, lung, and other solid tumors. Previous clinical trials of MAGE-A10 TCR and TCR-T cells demonstrated MB-1-specific TCR expression in 30%–50% of CD8+ T cells and tumor regression in a few melanoma patients.

**Introduction**

MAGE-A10 is a highly immunogenic cancer antigen expressed in 10%–50% of melanoma, breast, lung, and other solid tumors. Previous clinical trials of MAGE-A10 TCR and TCR-T cells demonstrated MB-1-specific TCR expression in 30%–50% of CD8+ T cells and tumor regression in a few melanoma patients.

**Methods**

**Patients**

Patients of 20 years and older with measurable disseminated NSCLC or disseminated melanoma and HLA*02 with >=1 MAGE-A10-specific CD8+ TCR-positive peripheral blood T-cells were eligible for enrollment. T-cells detected MAGE-A10-specific TCRs in 10% of CD8+ T cells.

**Randomization**

Eligible patients were randomized in a 1:1 ratio to receive MAGE-A10-SPEAR T-cells in two phases: Study 1 (NSCLC, n=3 patients) and Study 2 (melanoma, n=283 patients) (Figure 1).

**Study 1**

Patients received lymphodepleting chemotherapy followed by T-cell infusion on Days -7, -6, and -5. The dose escalation was based on the T-cell infusion schedule (Table 1).

**Study 2**

Patients received prophylactic anti-tumor vaccine therapy for 1 week before T-cell infusion and 1 week after the last T-cell infusion. All stained tissue samples were evaluated and scored by a pathologist.

**Conclusions**

The most frequent AEs were consistent with those associated with prior TCR-T cell therapy. The trials are currently accruing for Group 2. The results are available at ClinicalTrials.gov (NCT02989064 and NCT02592577).

**Acknowledgements**

The authors of this poster meet all the criteria for authorship suggested by the International Committee of Medical Journal Editors. The authors received no financial or other support in preparation of this poster.

**Disclosures**

MB: honoraria from BMS, Merck, Novartis, and Roche; consulting/advisory role for Adaptimmune, BMS, EMD Serono, GSK, Immunocore, Immunovaccine, Merck, Mirati Therapeutics, Neovia, Novartis, Pfizer, and Takeda; consulting/advisory role for Baxter, Bayer, Genentech, Guidepoint Global, Dynavax, EMD Serono, G1 Therapeutics, Genentech-Roche, Genmab, Hengrui Therapeutics, Janssen, Lilly, Lycera, Merck, Mirati, Molecular Template, Novartis, Pfizer, and Takeda; consulting/advisory role for Bayer, Genentech, Inivata, NeoHealth, Nektar, and Pfizer

**Figure 1**

**Figure 1. Consort diagrams of enrollment by therapy and group.**

- **A.** Representative MAGE-A10 nucleotide/peptide (NCP) vaccine in NSCLC.
- **B.** MAGE-A10 expression is elevated across several cancer indications.

**Figure 2**

**Figure 2. Cytokine expression levels following SPEAR T-cell therapy.**

- **A.** Data from MAGE-A10 TCR studies are consistent with previous studies of NY-ESO-1 studies.
- **B.** The trials are currently accruing for Group 2.

**Figure 3**

**Figure 3. Study 2 results.**

- **A.** Results of Study 2: Patients who received MAGE-A10 SPEAR T-cells with CY and FLU had higher cytokine levels than patients who received CY and FLU only.
- **B.** The trials are currently accruing for Group 2.