Introduction

- ADP-A2M10 SPEAR T-cells are genetically engineered autologous T-cells that express a high-affinity, MAGE-A10-specific T-cell receptor (TCR) targeting MAGE-A10 tumor in the context of HELLA (Figure 1).
- NCT03989577 was an adaptive, dose-escalation trial utilizing a modified 3+3 design to evaluate the safety of ADP-A2M10 SPEAR T-cells (Table 1).
- One patient (T5) failed to progress (F) after T-cell infusion, but subsequently developed aplastic anemia and died. T-cell persistence in patient cohort 3 was assessed post-infusion of the third dose of ADP-A2M10 (Figure 2).

Trial Design

- ADP-A2M10 T-cells were infused at doses of 0.1, 0.3, 0.5, 1.0, and 1.5 × 10^6 transduced cells/µL. T-cells were expanded in vitro for 14 days in the UK prior to a second infusion with an expanded cell dose of 0.1 × 10^6–15 × 10^6 transduced cells/µL (Table 1).
- Patient persistence in larger cohorts was compared with baseline tumor measurements for the first infusion of ADP-A2M10; one report of cytokine release syndrome (CRS) (Grade 4) on Day 1–2, 1 grade 3 respiratory failure on Day 1–4 and cyclophosphamide 10 mg/kg on Day 1–3 is a severe adverse event.
- One patient (T5) had previously undergone cyclophosphamide 10 mg/kg from baseline measurements in the first infusion of ADP-A2M10 (Figure 4).
- ADP-A2M10 T-cells were detected in peripheral blood from patients at all dose levels.
- Peak ADP-A2M10 persistence appears to be dose dependent and trended higher in DLT phase 2 (Table 2).

Results

- A total of 1, 3, and 3 patients received 0.1, 0.3, and 0.5 × 10^6 transduced cells, respectively.
- One patient with PD, who subsequently developed aplastic anemia and died. T-cell persistence in patient cohort 3 was assessed post-infusion of the third dose of ADP-A2M10 (Figure 2).
- One patient (T5) failed to progress (F) after T-cell infusion, but subsequently developed aplastic anemia and died. T-cell persistence in patient cohort 3 was assessed post-infusion of the third dose of ADP-A2M10 (Figure 2).
- One patient (T5) had previously undergone cyclophosphamide 10 mg/kg from baseline measurements in the first infusion of ADP-A2M10 (Figure 4).
- ADP-A2M10 T-cells were detected in peripheral blood from patients at all dose levels.
- Peak ADP-A2M10 persistence appears to be dose dependent and trended higher in DLT phase 2 (Table 2).

Conclusions

- ADP-A2M10 SPEAR T-cells have shown acceptable safety and no evidence of toxicity related to off-target binding or autoreactivity.
- One patient developed aplastic anemia and died after receiving the highest lymphodepleting regimen followed by a second infusion of ADP-A2M10.
- Given the minimal anti-lumur activity and the discovery that MAGE-A10 expression frequently overlaps with MAGE-A4 expression, the official program has closed.

Key Eligibility Criteria

- Inclusion Criteria
  - Aged ≥18 years.  
  - Eastern Cooperative Oncology Group (ECOG) performance status of 0–1.  
  - Adequate organ function per institutional minimum.  
  - NSCLC stage IIIB or IV or recurrent disease.  
  - ECOG status 0–1 and adequate organ function.  
  - MAGE-A10 expression frequently overlaps with MAGE-A4 expression.  
  - MAGE-A10 is expressed in 10%–50% of NSCLC cancers.  
  - One patient had a PR, but subsequently developed aplastic anemia and died.

- Exclusion Criteria
  - A history of symptomatic CNS metastases must have received treatment prior to enrollment.  
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