**SPEARHEAD-1: Preliminary Translational Insights from a Phase 2 Trial of Afamitresgene Autooleucel (Formerly ADP-A2M4) in Patients with Advanced Synovial Sarcoma or Myxoid/Round Cell Liposarcoma**

**Introduction**

- Patients with advanced synovial sarcoma or myxoid/round cell liposarcoma (MRCLS) have a high unmet medical need for more effective therapies.
- MAGE-A4 is expressed in synovial sarcoma and MRCLS.
- Afamitresgene autoleucel (afami-cel; formerly ADP-A2M4) is an autologous CD4+ T-cell product engineered to target MAGE-A4.

**Methods**

- In the Phase 2, open-label SPEARHEAD-1 (NCT04044768) trial, 15 evaluable patients (13 synovial sarcoma, 2 MRCLS) were enrolled.
- Afamitresgene autoleucel (afami-cel) and (control) non-afami-cel T-cells were administered.
- Patients were treated with afami-cel as monotherapy or in conjunction with a PD-1 inhibitor.
- Clinical responses have been seen across the range of eligible screening patients, including those with PR, SD, and PD.

**Cytotoxicity**

- In vitro killing of MAGE-A4+ tumor cells by manufactured product (CD8+ SPEAR T-cells) was significantly greater compared to CD4+ control T-cells.
- Persistence

**Induction of Immune Response**

- Before and post-infusion patient serum samples were analysed for levels of 92 immuno-oncology markers.
- Afami-cel administration led to upregulation of a subset of peripheral markers consistent with IFN-gamma and IL-12 pathways (Figure 3A).

**Tumor Biopsies**

- Clinical responses have been seen across the range of eligible screening patients, including those with PR, SD, and PD.

**Conclusions**

- Afami-cel SPEAR T-cells successfully engendered in all patients and maintained high levels of persistence in the majority of patients followed for at least 6 months post-infusion.
- Afami-cel induced immune responses were associated with clinical responses.
- Clinical benefit seen across broad range of MAGE-A4 expression within sample.

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*Figure 1. A. Hematopoietic cells (CD45+CD3+) infiltrating tumor from a Phase 2 Trial of Afamitresgene Autoleucel SPEARHEAD-1: Preliminary Translational Insights. T-cell receptor (TCR)-based recognition was observed in a subset of peripheral markers consistent with IFN-gamma and IL-12 pathways (Figure 3A). B. Clinical responses have been seen across the range of eligible screening patients, including those with PR, SD, and PD. Patient indicated with an “X” was treated in the Phase 1 trial; Right, n=17 synovial sarcoma treated in SPEARHEAD-1. Patients are ordered in terms of Excel Scientific Solutions, which was contracted and compensated by Adaptimmune for these services.*