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TITLE: DURABLE RESPONSES IN PATIENTS WITH SYNOVIAL SARCOMA IN THE PHASE I TRIAL OF ADP-A2M4 (MAGE-A4)

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ABSTRACT BODY:

Objective: This trial (NCT03132922) evaluated safety, tolerability, and antitumor activity of ADP-A2M4, genetically engineered autologous specific peptide enhanced affinity receptor (SPEAR) T-cells directed towards a MAGE-A4 peptide in patients (pts) with multiple solid tumor malignancies. Herein, follow-up data from pts with advanced synovial sarcoma is presented (n=16). The main portion of this trial is closed for enrollment, a low-dose radiation sub-study remains open.

Methods: This Phase I dose-escalation, expansion trial evaluated HLA-A*02 positive (excluding *02:05) pts with advanced cancers expressing MAGE-A4. Autologous T-cells were isolated, transduced with a lentiviral vector containing the MAGE-A4^{c1032} TCR, and expanded. Prior to infusion, pts received lymphodepletion with cyclophosphamide and fludarabine. Cohorts 1, 2, 3, and Expansion were to receive transduced cell doses of up to: 0.12×10^9, 1.2×10^9, 6×10^9, and 10×10^9, respectively. Disease was assessed per RECIST v1.1 by CT/MRI at wks 6, 12, 18, and 24, and every 3 months for 2 years, then every 6 months or until disease progression.

Results: As of Apr 2020, 16 pts with advanced synovial sarcoma were treated in either Cohort 3 or Expansion with a median transduced cell dose of 8.86×10^9 (range: 3.41 to 9.97×10^9). Median age was 49.0 yrs (range: 31 to 76) and median H-score of MAGE-A4 expression was 248.5 (range: 60.4 to 300). All pts received prior chemotherapy (median 2.5 regimens, range 1 to 6). Most common (>30%) AEs ≥Grade 3 were lymphopenia, leukopenia, neutropenia, anemia, thrombocytopenia, hypophosphatemia, and febrile neutropenia. Cytokine release syndrome (any grade) was reported in 13 pts (81%); the majority was Grade 1 or 2 (11 pts). One pt with synovial sarcoma had a Grade 5 SAE, (76-yr-old female; aplastic anemia) leading to modification of the lymphodepletion regimen and eligibility criteria. The Overall Response Rate was 44% and the Best Overall Response was PR (7), SD (7), PD (1), and pending (1). Responses were durable (median duration approximately 28 wks (range: 12 to 54^+ wks [PR at 54 wks ongoing]). Median OS had not been reached. SPEAR T-cells were detectable in peripheral blood and tumor tissue, and responded to antigen in vitro. Increases in T-cell infiltration, MHCI, and PD-L1 expression were observed in post-infusion tumor biopsies of some responding pts. Higher MAGE-A4 levels were associated with greater tumor reduction.

Conclusion: ADP-A2M4 induced clinical responses in pts with synovial sarcoma and had an acceptable safety profile. Transduced T-cells persist in vivo and remain functional. Analyses to determine factors that may influence response remain ongoing. These data support the ongoing SPEARHEAD-1 trial (NCT04044768).

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