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Authors: Marcus O. Butler[1], Melissa L. Johnson[2], Kunle Odunsi[3], Francine E. Brophy[4], Trupti Trivedi[4], Quan Lin[4], Mark Dudley[4], Rebecca Dryer-Minnerly[4], Jean-Marc Navenot[4], Paula M. Fracasso[4], Elliot Norry[4], David S. Hong[5]

Affiliations: [1]Princess Margaret Cancer Centre, Toronto, ON, CA; [2] Sarah Cannon Research Institute / Tennessee Oncology, Nashville, TN, USA; [3]Roswell Park Comprehensive Cancer Center, Buffalo, NY,USA; [4]Adaptimmune, Philadelphia, PA, USA; [5]MD Anderson Cancer Center, Houston, TX, USA

Title: Initial Safety with a Novel Next-Generation ADP-A2M4CD8 SPEAR T-cell Construct Incorporating a CD8α Co-receptor

Background: The ongoing SURPASS trial (NCT04044859) evaluates safety and tolerability of next-generation genetically engineered autologous ADP-A2M4CD8 SPEAR T-cells directed against a MAGE-A4 peptide expressed on HLA-A*02 tumors. The next-generation ADP-A2M4CD8 SPEAR T-cells co-express the CD8α co-receptor with the engineered MAGE-A4^{c1032} T-cell receptor (TCR). In preclinical studies, ADP-A2M4CD8 demonstrated increased cytotoxicity compared to the first-generation ADP-A2M4 TCR (AACR Abstract 2019).

Methods: This first-in-human dose-escalation trial evaluates safety and efficacy of ADP-A2M4CD8 using a modified 3+3 design. Patients (pts) must be HLA-A*02 positive with advanced cancers expressing the MAGE-A4 protein. Eligible pts undergo apheresis, T-cells are isolated, transduced with a lentiviral vector containing the MAGE-A4^{c1032} TCR along with the CD8α co-receptor, and expanded. Prior to ADP-A2M4CD8 infusion, patients receive a lymphodepletion regimen of fludarabine 30 mg/m^2/day for 4 days and cyclophosphamide 600 mg/ m^2/day for 3 days. The initial dose selected for ADP-A2M4CD8 is 0.8-1.2 × 10^9 transduced cells, escalated to 1.2-3 × 10^9, and then 3-6 × 10^9 transduced cells. Expansion cohort allows for doses 1.0-10 × 10^9.

Results: As of 3 February 2020, 2 pts (1 male with gastro-esophageal junction cancer; 1 female with ovarian cancer) were treated in Cohort 1. There was a marked elevation in serum IFN-γ within 1 week following T-cell infusion in the first pt treated, which was accompanied by detectable levels of transduced cells in peripheral blood peaking 2 weeks post-infusion.

Neither pt had DLTs, encephalopathy, neurotoxicity, or other SAEs at the time of data cut-off. One pt experienced G1 CRS. Data will be updated at the time of the congress.

Conclusions: ADP-A2M4CD8 SPEAR T-cells show no evidence of toxicity related to off-target binding or alloreactivity in the first evaluable patient. Importantly, the first evaluable patient has had a confirmed partial response with a tolerable safety profile in the presence of T-cell activation and clinical activity. This trial is ongoing, and updated data will be presented.