Initial Safety, Efficacy, and Product Attributes from the SURPASS Trial with ADP-A2M4CD8, a SPEAR T-Cell Therapy Incorporating an Affinity Optimized TCR Targeting MAGE-A4 and a CD8α Co-Receptor

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Background
• The ongoing SURPASS trial (NCT04044859) evaluates safety and efficacy of multiple generations of SPEAR T-Cell therapies targeting the MAGE-A4 tumor antigen.
• To increase the potency of SPEAR T-Cells, in前期increase was generally observed for infusion of cells expressing CD4+ T-cells, which resulted in a more homogeneous expansion of MAGE-A4+ tumor-infiltrating lymphocytes (TILs) across the entire tumor.
• This study describes the efficacy and safety of ADP-A2M4CD8 T-cells from patients with lung cancer.

Objectives
• To evaluate the anti-tumor activity of ADP-A2M4CD8 T-cells in patients with MAGE-A4+ cancers.
• To identify serum and tumor factors that influence response or toxicity.

Trial Design
• The ongoing SURPASS trial evaluates safety and efficacy of multiple generations of SPEAR T-Cell therapies targeting the MAGE-A4 tumor antigen.
• CD8α co-receptor is critical for SPEAR T-cell efficacy; CD4+ T-cells appear to play a key role in potentiating T-cell responses.

Results
• Median age, years (range): 63 (30–84)
• 56% male
• 36% (n = 53) had prior systemic therapy in the metastatic or unresectable locally advanced setting
• 10 (20%) had prior lymphodepletion with fludarabine 30 mg/m²/day for 4 days and cyclophosphamide 600 mg/m²/day for 2 days
• For patients treated with ADP-A2M4CD8 (range ~1–5.7 billion transduced cells), the most pronounced SPEAR T-cell induced increase was evident for serum IFNγ concentrations.

Key Eligibility Criteria
- Diagnosis of advanced gastroesophageal cancers, HNSCC, non-small cell lung cancer, advanced MRCLS, or synovial sarcoma
- Patient has experienced ≥2 prior systemic therapies
- Good performance status (Karnofsky 50–100)
- Evidence of measurable disease according to RECIST v1.1
- Age ≥18 and ≤75 years
- Written informed consent

Conclusions
• ADP-A2M4CD8 SPEAR T-cells have shown an acceptable safety profile and demonstrate clinical benefit in patients with MAGE-A4+ cancers. MAGE-A4+ tumors have had best overall response of SD or PR.

Abbreviations
SPEAR: Specific Peptide Enhanced Affinity Receptor
TCR: T-cell receptor
ADP: Autologous donor product
MP: Manufactured product
DL: Dose level
PR: Partial response
PD: Progression disease
SD: Stable disease
MAGE-A4: Melan-A/Mart-1 antigen
EGJ: Esophagogastric junction
HNSCC: Head and neck squamous cell carcinoma
MRCLS: Mesothelial-rich carcinosarcoma
SCC: Squamous cell carcinoma
EGJ: Esophagogastric junction
HNSCC: Head and neck squamous cell carcinoma
MRCLS: Mesothelial-rich carcinosarcoma
SCC: Squamous cell carcinoma

References
1. Ahmed Galal, John V. Heymach, Ahmed Galal, Samuel D. Saibil, Adrian Sacher, Francesca E. Brophy, Gareth Betts, Natalie Bath, Will Simpson, Tipping, Jessica Tuor, Raymond Luke, Trupti Trivedi, Quan Luo, Jean-Marc Navicki, Paula M. Fracasso, Karen Miter, Mark Dudley, Marcus O. Butler. The University of Texas MD Anderson Cancer Center, Houston, TX, USA; Duke Cancer Center, Durham, NC, USA; Washington University School of Medicine, St. Louis, MO, USA; Princess Margaret Cancer Centre, Toronto, Ontario, Canada; Adaptiveimmune, Abingdon, Oxfordshire, UK; and Philadelphia, PA, USA. Initial Safety, Efficacy, and Product Attributes from the SURPASS Trial with ADP-A2M4CD8, a SPEAR T-Cell Therapy Incorporating an Affinity Optimized TCR Targeting MAGE-A4 and a CD8α Co-Receptor. The 2020 ASCO Annual Meeting Virtual Program: Abstract 5504. 2020 Jun;58(suppl 1):5504. doi: 10.1200/JCO.2020.38.15_suppl.5504. Free full text available from ClinicalTrials.gov can be accessed by scanning the QR code here.