Updated Safety and Efficacy From SURPASS

The Phase I Trial Results of ADP-A2M4CD8, a Next-Generation Autologous T-Cell Receptor T-Cell Therapy, in Previously Treated Patients With Unresectable or Metastatic Tumors

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On behalf of the study team

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Declaration of Interests
Dr. David S. Hong (last 36 months)

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**Other ownership interests:** Molecular Match (Advisor), OncoResponse (Founder, Advisor), Telperian (Founder, Advisor)
ADP-A2M4CD8 Next-Generation SPEAR T-Cell Therapy

Designed to increase potency by expressing a CD8α co-receptor

- Specific peptide enhanced affinity receptor (SPEAR) T-cell therapy modified with addition of a CD8α co-receptor to treat human leukocyte antigen (HLA) A*02–eligible patients with unresectable or metastatic tumors expressing melanoma-associated antigen A4 (MAGE-A4)
- To increase the potency of CD4+ T-cells, a CD8α co-receptor was genetically engineered alongside the T-cell receptor (TCR)
- This is intended to increase TCR binding avidity and enhance the polyfunctional response of engineered CD4+ T-cells against MAGE-A4+ tumors

HLA, human leukocyte antigen; IFNγ, interferon gamma; IL, interleukin; MAGE-A4, melanoma associated antigen A4; SPEAR, specific peptide enhanced affinity receptor; TCR, T-cell receptor

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**Objectives**

**Primary**
- Evaluate the safety and tolerability of ADP-A2M4CD8

**Secondary**
- Evaluate the antitumor activity of ADP-A2M4CD8

**Exploratory**
- Persistence, phenotype, function of transduced and non-transduced T-cells
- Tumor and serum factors that may influence response or resistance

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**Screening**

- HLA and MAGE-A4
  - HLA screening followed by MAGE-A4 immunohistochemistry testing

**Monotherapy**

- N = 60 planned

**Combination therapy in a cohort of selected patients**

- N = 30 planned

**Trial assessments**

- Baseline tumor measurements
- Eligibility assessment, leukapheresis, and manufacturing of ADP-A2M4CD8
- Lymphodepletion
- Nivolumab every 4 weeks
- ADP-A2M4CD8 infusion
- Trial enrollment
- Days -7 to -4
- Day 1
- Week 4
- End of interventional phase
- Years 1–15

**Long-term follow-up**

- Patient is hospitalized for T-cell infusion and discharged at the discretion of the Investigator

**Dr. David S. Hong**
## Patient Characteristics

**Heavily pre-treated patients in multiple solid tumor indications**

**Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=44</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>23 (52.3)</td>
</tr>
<tr>
<td>Median age, y (range)</td>
<td>59.0 (31, 75)</td>
</tr>
<tr>
<td>H-score, a median (range)</td>
<td>250.0 (95, 300)</td>
</tr>
<tr>
<td>Transduced T-cells x 10⁹, median (range)</td>
<td>4.64 (0.95, 9.95)</td>
</tr>
<tr>
<td>ECOG performance status, n (%)</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>13 (29.5)</td>
</tr>
<tr>
<td>1</td>
<td>31 (70.5)</td>
</tr>
<tr>
<td>Target tumor ≥5 cm, n (%)</td>
<td>29 (65.9)</td>
</tr>
<tr>
<td># of prior systemic therapies, median (range)</td>
<td>3 (1, 8)</td>
</tr>
<tr>
<td>Patients who received systemic bridging therapy, n (%)</td>
<td>23 (52.3)</td>
</tr>
</tbody>
</table>

**Tumor type**

<table>
<thead>
<tr>
<th>Tumor type</th>
<th>N=44; n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovarian</td>
<td>14 (31.8)</td>
</tr>
<tr>
<td>Esophagogastric junction, esophageal, gastric</td>
<td>13 (29.5)</td>
</tr>
<tr>
<td>Urothelial</td>
<td>7 (15.9)</td>
</tr>
<tr>
<td>Head and neck</td>
<td>4 (9.1)</td>
</tr>
<tr>
<td>Non-small cell lung cancer (NSCLC)</td>
<td>2 (4.5)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>2 (4.5)</td>
</tr>
<tr>
<td>Synovial sarcoma</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td>Myxoid/round cell liposarcoma (MRCLS)</td>
<td>1 (2.3)</td>
</tr>
</tbody>
</table>

*aH-score: 1 ×(% of 1+ cells) + 2 ×(% of 2+ cells) + 3 ×(% of 3+ cells)*

Data cut off Aug 1, 2022.

ECOG, Eastern Cooperative Oncology Group

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Safety

Adverse events (AEs) related to T-cell infusion in ≥10% of patients

<table>
<thead>
<tr>
<th>Preferred term</th>
<th>N=44; n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>40 (90.9)</td>
</tr>
<tr>
<td>CRS</td>
<td>32 (72.7)</td>
</tr>
<tr>
<td>Neutropenia/neutrophil count decreased</td>
<td>13 (29.5)</td>
</tr>
<tr>
<td>Anemia/RBC decreased</td>
<td>10 (22.7)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>10 (22.7)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>9 (20.5)</td>
</tr>
<tr>
<td>Leukopenia/WBC decreased</td>
<td>7 (15.9)</td>
</tr>
<tr>
<td>Rash</td>
<td>7 (15.9)</td>
</tr>
<tr>
<td>Thrombocytopenia/platelet count decreased</td>
<td>7 (15.9)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>6 (13.6)</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>6 (13.6)</td>
</tr>
<tr>
<td>ICANS</td>
<td>6 (13.6)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>6 (13.6)</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>5 (11.4)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>5 (11.4)</td>
</tr>
<tr>
<td>Sinus tachycardia/tachycardia</td>
<td>5 (11.4)</td>
</tr>
</tbody>
</table>

AEs of special interest

Cytokine release syndrome (CRS)
- Overall, 32 patients (72.7%) experienced CRS
- 6 patients (14%) experienced Grade ≥3 CRS
- Time to onset, days, median (range): 3 (1,9)
- Time to resolution, days, median (range): 5 (1,15)
- Anti-IL6 therapy for CRS: 27 patients (61%)

Prolonged cytopenia
- 11 patients (25%) experienced Grade ≥3 cytopenia at Week 4 post-infusion

Immune effector cell-associated neurotoxicity syndrome (ICANS)
- 3 patients (6.8%) experienced a related SAE of ICANS
- 2 patients (5%) experienced Grade ≥3 ICANS

Data cut off Aug 1, 2022.
AE, adverse event; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; IL6, interleukin 6; RBC, red blood cell; SAE, serious AE; WBC, white blood cell

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### Safety

Serious AEs (SAEs) and SAEs related to T-cell infusion in ≥5% of patients

<table>
<thead>
<tr>
<th>Preferred term</th>
<th>SAE, N=44; n (%)</th>
<th>Related SAE, N=44; n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any SAE</td>
<td>27 (61.4)</td>
<td>21 (47.7)</td>
</tr>
<tr>
<td>CRS</td>
<td>14 (31.8)</td>
<td>14 (31.8)</td>
</tr>
<tr>
<td>Hypoxia</td>
<td>3 (6.8)</td>
<td>3 (6.8)</td>
</tr>
<tr>
<td>ICANS</td>
<td>3 (6.8)</td>
<td>3 (6.8)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>3 (6.8)</td>
<td>2 (4.5)</td>
</tr>
</tbody>
</table>

There were 2 related Grade 5 (fatal) SAEs:

- **CRS**
  - 60-year-old with ovarian cancer
  - Large tumor burden in lungs and previous lung radiotherapy
  - Cause of death: pneumonia and CRS

- **Pancytopenia**
  - 71-year-old man with adenocarcinoma of esophagus
  - History of chronic anemia
  - Developed new lesions in liver
  - Cause of death: bone marrow failure

Data cut off Aug 1, 2022. 

AE, adverse event; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; MAGE-A4, melanoma associated antigen A4; SAE, serious AE.
Efficacy

Antitumor activity in multiple tumor types per RECIST v1.1 by investigator review

Overall confirmed response rate of 28% (n=12) and additional 5% (n=2) with unconfirmed responses awaiting confirmatory scans

- Median duration of response 12 weeks (range 7 to 65+ weeks)
- Disease control rate of 81%
- Confirmed clinical responses in ovarian, esophagogastric junction, urothelial, head and neck, and synovial sarcoma cancers

Evaluable population (N=43)
Data cut off Aug 1, 2022.
CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; RECIST, response evaluation criteria in solid tumors; uPR, unconfirmed PR; SD, stable disease

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Efficacy
Antitumor activity in multiple tumor types per RECIST v1.1 by investigator review

Ovarian

Head and neck

Esophagogastric junction, esophageal, and gastric

Urothelial

Data cut off Aug 1, 2022.
CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; RECIST, response evaluation criteria in solid tumors; uPR, unconfirmed PR; SD, stable disease

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Confirmed Response in a Patient With Stage IV Head and Neck Cancer

- 69-year-old White man with stage IV SCC head and neck cancer
- MAGE-A4 expression in tumor cells: 85% 3+, 10% 2+, 5% 1+
- Baseline SLD: 111 mm (5 target lesions)
- Prior systemic therapies: platinum-based therapy, nivolumab, taxane/cetuximab
- Patient was treated with 5 billion transduced T-cells
- Confirmed response was initially reported at Week 4

Data cut off Aug 1, 2022.
MAGE-A4, melanoma associated antigen A4; SCC, squamous cell carcinoma; SLD, sum of lesion diameters
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Translational Data

Clear evidence of stem cell memory engraftment; activation markers associated with longer duration of response
Conclusions

- Encouraging efficacy with ADP-A2M4CD8 monotherapy in patients with advanced disease across multiple MAGE-A4+ solid tumor indications
- Toxicity included CRS, ICANS, and prolonged cytopenia after lymphodepletion and T-cell infusion
- ADP-A2M4CD8 continues to show an acceptable benefit-to-risk profile in multiple MAGE-A4+ unresectable or metastatic tumors
- The efficacy and safety results with ADP-A2M4CD8 monotherapy support expansion into combination therapy with an anti-PD1 checkpoint inhibitor
  - An additional treatment cohort with nivolumab has been initiated in the SURPASS Phase 1 trial
- Encouraging data signals in multiple tumor types, with Phase 2 studies for esophageal and esophageal gastric junction (SURPASS-2) and ovarian (SURPASS-3) cancers initiated or planned
Acknowledgements


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- For further questions please contact: dshong@mdanderson.org