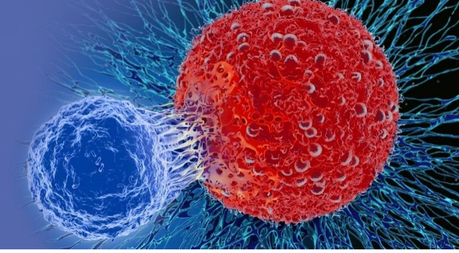
# SURPASS-2 Trial Design: A Phase 2, Open-Label Study of ADP-A2M4CD8 SPEAR T-Cells in Advanced Esophageal or Esophagogastric Junction Cancers

David S. Hong,[1] Shadia Ibrahim Jalal,[2] Elena Elimova,[3] Jaffer A. Ajani,[1] Mariela A. Blum Murphy,[1] Andres Cervantes,[4] T.R. Jeffry Evans,[5] Haeseong Park,[6] Quan Lin,[7] Paul Noto,[7] Michael Shnaidman,[7] Daniel Campbell,[7] Marisa Rosenberg,[7] Francine Elizabeth Brophy,[7] Hassan Danesi,[7] Joseph Chao,[8] David H. Ilson[9]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX; [2]Indiana University, Simon Cancer Center, Indianapolis, IN; [3]Princess Margaret Cancer Centre, Toronto, ON, Canada; [4]Biomedical Research Institute INCLIVA, University of Valencia, Valencia, Spain; [5]University of Glasgow, Beatson West of Scotland Cancer Centre, Glasgow, UK; [6]Washington University School of Medicine, St. Louis, MO; [7]Adaptimmune, Philadelphia, PA; [8]City of Hope National Medical Center, Duarte, CA; [9]Memorial Sloan Kettering Cancer Center, New York, NY

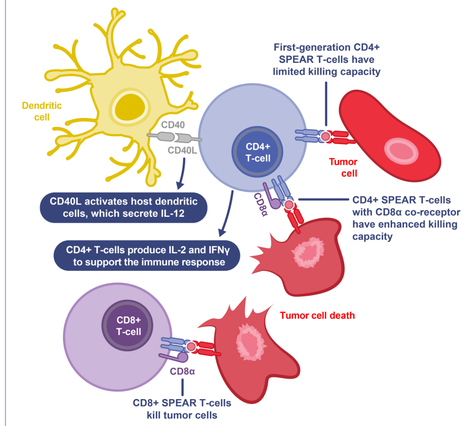
SURPASS-2 on ClinicalTrials.gov can be accessed by scanning the QR code



## Introduction

- ADP-A2M4CD8 is an autologous specific peptide enhanced affinity receptor (SPEAR) mixed CD4+ and CD8+ T-cell product that expresses an engineered T-cell receptor (TCR) designed to target the melanoma-associated antigen A4 (MAGE-A4) protein in human leukocyte antigen A*02 (HLA-A*02)-positive patients
- These SPEAR T-cells also express wild-type CD8α co-receptors, designed to provide additional functionality to CD4+ T-cells[1] (**Figure 1**)
- MAGE-A4 expression has been described in several solid tumors, including esophageal and esophagogastric junction (EGJ) cancers[2] (**Figure 2**)

**Figure 1**. ADP-A2M4CD8 Next-Generation SPEAR T-Cells

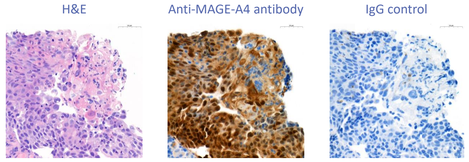



- SPEAR T-cells are a mix of CD4+ and CD8+ T-cells engineered with a TCR recognizing an intracellular tumor antigen in an HLA-restricted fashion
- ADP-A2M4CD8 are next-generation SPEAR T-cells targeting MAGE-A4 with a CD8α co-receptor introduced into T-cells alongside the TCR
- The co-expression of CD8α adds CD8+ killer cell capability to CD4+ helper cells, while also maintaining/enhancing their helper cell capabilities
- The enhanced TCR interaction results in a more potent response because the ADP-A2M4CD8 next-generation CD4+ SPEAR T-cells can now both kill tumor cells as well as engage the broader immune system including dendritic cell activation

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

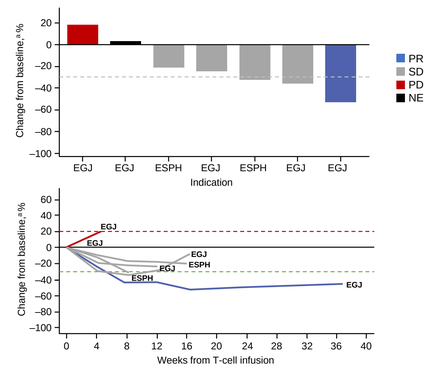
- In the ongoing Phase 1 SURPASS study (NCT04044859) of ADP-A2M4CD8 in patients with different tumor types, most adverse events (AEs) have been consistent with those typically experienced by patients undergoing chemotherapy and/or adoptive T-cell therapies[1]
- As of August 2, 2021, among evaluable patients in the Phase 1 SURPASS trial with esophageal or EGJ cancers, best overall responses were 1 partial response, 4 stable disease, and 1 progressive disease; 5 out of 7 experienced decreases in target lesions[1] (**Figure 3**)

**Figure 2.** MAGE-A4 Expression in 1 Patient With Esophagogastric Junction Cancer Screened in the SURPASS-2 Study




Magnification: 40×. H&E, haematoxylin and eosin; IgG, immunoglobulin G; MAGE-A4, melanoma-associated antigen A4

**Figure 3.** Data Related to Esophageal and Esophagogastric Junction Cancers from the Phase 1 SURPASS Trial (ESMO 2021)[1] Confirm the Potential of the Phase 2 SURPASS-2 Trial

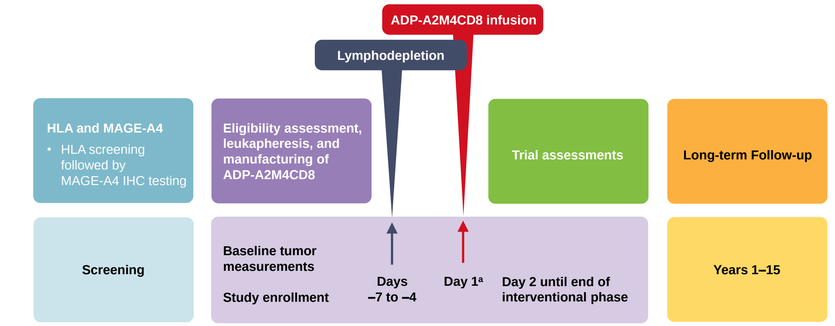



[a]Data represent percentage changes from baseline in sum of diameters (sum of the long diameters for non-nodal lesions and short axis for nodal lesions) in target lesions through progression or prior to surgical resection; responses evaluated by RECIST v1.1 per investigator assessment. Data cut-off August 2, 2021. EGJ, esophagogastric junction; ESPH, esophageal; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; NE, not evaluable

## SURPASS-2 Trial Details

- SURPASS-2 (NCT04752358) is a Phase 2, open-label, single-arm trial to assess efficacy and safety of ADP-A2M4CD8 SPEAR T-cells in HLA-A*02-positive patients with advanced esophageal or EGJ cancers that express MAGE-A4 antigen (**Figure 4**)
- A total of 45 patients between the ages of 18 and 75 years old, inclusive, (**Table 1**) will be treated across sites in North America and Europe
- The primary endpoint is overall response rate, and key secondary endpoints include AEs, serious AEs, and AEs of special interest (**Table 2**)
- Collected T-cells will be transduced with a self-inactivating lentiviral vector expressing the high affinity MAGE-A4-specific TCR and the CD8α co-receptor (**Figure 5**)
- Lymphodepleting chemotherapy, consisting of intravenous (IV) cyclophosphamide 600 mg/m$^2$/day for 3 days and IV fludarabine 30 mg/m$^2$/day for 4 days, will be given approximately 1 week prior to treatment with ADP-A2M4CD8
- ADP-A2M4CD8 dose will range between 1 × $10^9$ to 10 × $10^9$ transduced cells administered by a single IV infusion

**Figure 4.** SURPASS-2 Study Design




[a]Patient is hospitalized for T-cell infusion and discharged at the discretion of the Investigator. HLA, human leukocyte antigen; IHC, immunohistochemistry; MAGE-A4, melanoma-associated antigen A4; SPEAR, specific peptide enhanced affinity receptor

**Table 1.** Key Eligibility Criteria

| Inclusion criteria |
|---|
| Diagnosis of advanced esophageal or EGJ cancers |
| HLA-A*02 and MAGE-A4 positive |
| Aged ≥18 years and ≤75 years |
| Measurable disease per RECIST v1.1 |
| ECOG performance status of 0 or 1 |
| Has received a maximum of two prior lines of combination or single agent systemic treatment for advanced or metastatic disease before treatment with ADP-A2M4CD8 as the next therapy |
| **Exclusion criteria** |
| Active auto immune or immune-mediated disease |
| Leptomeningeal disease, carcinomatous meningitis, or symptomatic CNS metastases |

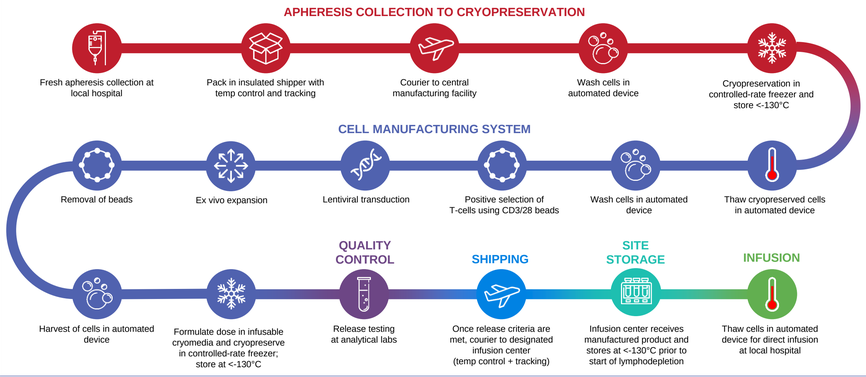
CNS, central nervous system; ECOG, Eastern Cooperative Oncology Group; EGJ, esophagogastric junction; HLA-A*02, human leukocyte antigen A*02; MAGE-A4, melanoma-associated antigen A4; RECIST, Response Evaluation Criteria in Solid Tumors

**Table 2.** Key Endpoints

| Primary endpoint |
|---|
| Overall response rate per RECIST v1.1 by an IRAC |
| **Secondary endpoints** |
| AEs and serious AEs |
| AEs of special interest |
| Replication-competent lentivirus |
| T-cell clonality and insertional oncogenesis |
| BOR per RECIST v1.1 by the IRAC, and by investigator radiological assessment |
| PFS per RECIST v1.1 by the IRAC, and by investigator radiological assessment |
| Overall survival |
| **Exploratory endpoint** |
| Patient-reported outcomes using EQ-5D-3L |

AE, adverse event; BOR, best overall response; PFS, progression-free survival; IRAC, independent radiological assessment committee; RECIST, Response Evaluation Criteria in Solid Tumors

**Figure 5.** Patient Cell Journey




## Study Sites and Investigators

| Site name | Investigator name | Region |
|---|---|---|
| The Montreal General Hospital – McGill University Health Centre – Cedars Cancer Centre | Alcindor, Jean Joseph Thierry | Canada |
| University Health Network[a] | Elimove, Elena | Canada |
| University of Oklahoma Health Sciences Center[a] – Stephenson Cancer Center | Asch, Adam, S | United States |
| The University of Chicago Medicine | Olsen, Daniel | United States |
| City of Hope National Medical Center | Chao, Joseph | United States |
| Froedtert Hospital and Medical College of Wisconsin[a] | George, Ben | United States |
| University of Texas – MD Anderson Cancer Center[a] | Hong, David, S | United States |
| Indiana University – Simon Cancer Center | Jalal, Shadia | United States |
| Northwestern Medical Faculty Foundation | Kalyan, Aparna | United States |
| Massachusetts General Hospital[a] | Klempner, Samuel | United States |
| Memorial Sloan Kettering Cancer Center[a] | Ku, Geoffrey, Y | United States |
| Providence Health & Services – Providence Cancer Center Oncology and Hematology Care Clinic | Leidner, Rom, S | United States |
| Mayo Clinic Jacksonville | Mahipal, Amit | United States |
| University of Kansas Clinical Research Center | Saeed, Anwaar, M | United States |
| The University of Texas Southwestern Medical Center | Sanjeevaiah, Aravind Raj | United States |
| Mayo Clinic Rochester | Starr, Jason | United States |
| University of Wisconsin Carbone Cancer Center | Uboha, Natalya, V | United States |
| Duke University Medical Center[a] | Uronis, Hope | United States |
| Washington University School of Medicine[a] | Van Tine, Brian, A | United States |
| Centre Leon-Berard – Centre de Recherche en Cancerologie Lyon-Est | Coutzac Bergougnan, Clelia | France |
| Centre Eugene Marquis | Edeline, Julien | France |
| Institut Gustave Roussy | Hollebecque, Antoine | France |
| Hopital Huriez | Turpin, Anthony | France |
| Hospital Universitari Vall d'Hebron | Diez Garcia, Marc | Spain |
| Hospital Clinico Universitario de Valencia – INCLIVA Biomedical Research Institute[a] | Fleitas Kanonnikoff, Tania | Spain |
| Grupo Hospital de Madrid – Hospital Universitario Madrid Sanchinarro[a] | Garcia Morillo, Marcial | Spain |
| Hospital Universitario 12 de Octubre[a] | Gomez Martin, Carlos Jesus | Spain |
| Hospital Universitario Virgen del Rocio[a] | Limon Miron, Maria Luisa | Spain |
| Hospital Universitario Fundacion Jimenez Diaz[a] | Moreno Garcia, Victor | Spain |
| Clinica Universidad de Navarra[a] | Ponz Sarvise, Mariano | Spain |
| Beatson West of Scotland Cancer Centre | Evans, Thomas Ronald Jeffry | United Kingdom |
| The Christie – The Christie NHS Foundation Trust | Pillai, Manon | United Kingdom |
| Guy's Hospital – Guy's and St Thomas NHS Foundation Trust | Sarker, Debashis | United Kingdom |
| University College Hospital | Shiu, Kai-Keen, K | United Kingdom |

[a]Sites involved in the Phase 1 SURPASS and Phase 2 SURPASS-2 studies. NHS, National Health Services

## Recruitment

- As of December 1, 2021: 34 sites have been selected and 4 sites have been activated
- 18 patients have been pre-screened
  - 4 patients are undergoing the pre-screening process to determine eligibility
  - 13 patients have completed pre-screening and are HLA ineligible
  - 1 patient is HLA eligible and MAGE-A4 positive
- Recruitment is ongoing

### Acknowledgments and Disclosures

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### Abbreviations used in text

AE, adverse event; EGJ, esophagogastric junction; HLA, human leukocyte antigen; IV, intravenous; MAGE-A4, melanoma-associated antigen A4; SPEAR, specific peptide enhanced affinity receptor; TCR, T-cell receptor

### References

1. Hong et al. Safety and efficacy from the SURPASS trial with ADP-A2M4CD8, a SPEAR T-cell therapy incorporating a CD8α co-receptor and an affinity optimized TCR targeting MAGE-A4. Poster (540P) presented at: ESMO 2021; Virtual
2. Ishihara et al. *BMC Cancer*. 2020;20:606