AHNS 11TH INTERNATIONAL CONFERENCE ON HEAD & NECK CANCER

Preliminary results of the Phase 1 SURPASS trial of ADP-A2M4CD8, a next-generation SPEAR T-cell therapy, in patients with head and neck cancer

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DISCLOSURES

Mateo Bover declares no conflicts of interest

- This study is sponsored by Adaptimmune
- All Adaptimmune co-authors are employees of, and/or may hold stock/options in, Adaptimmune
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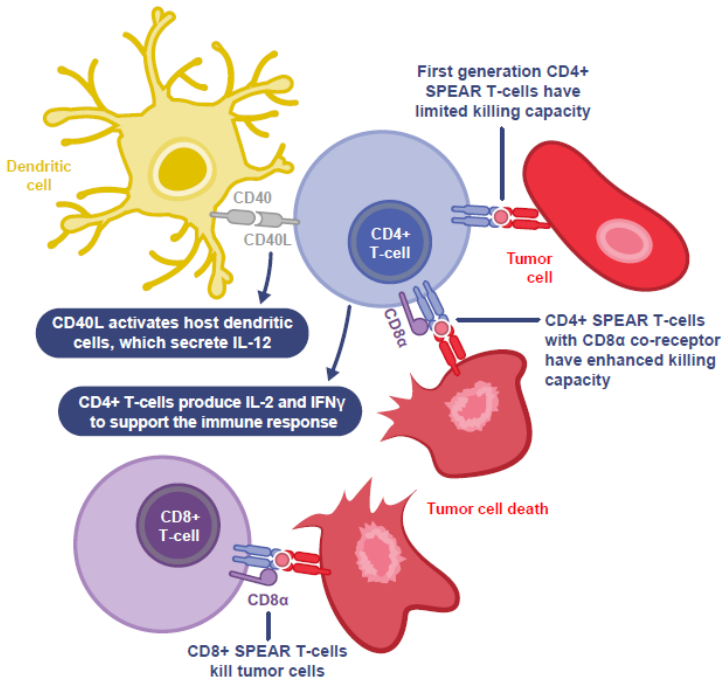
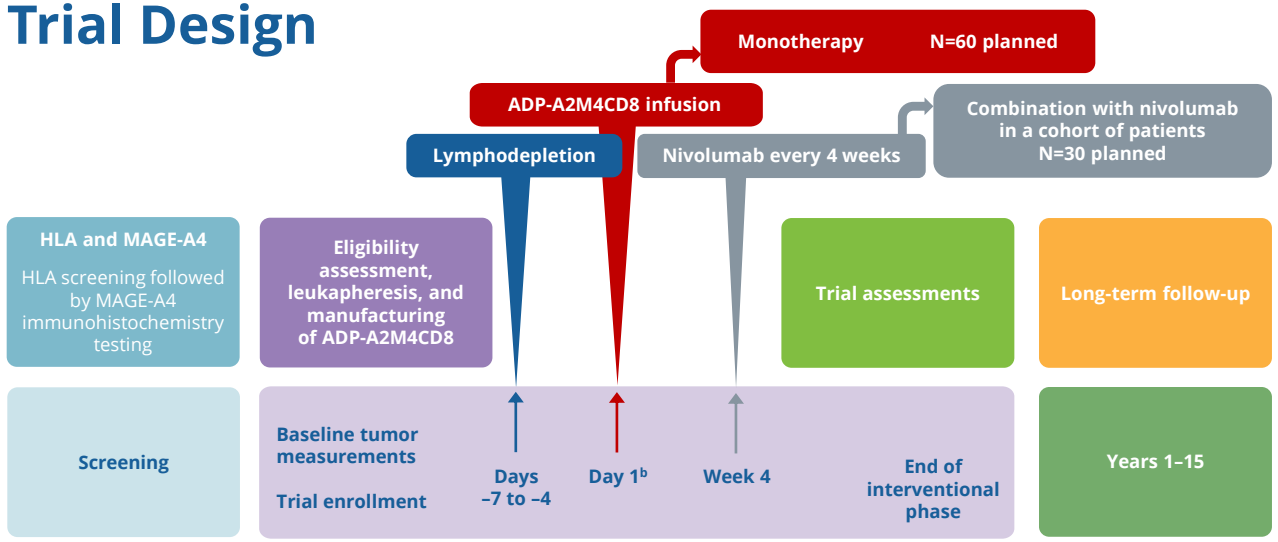
SURPASS, a Phase 1 trial of ADP-A2M4CD8 T-cell receptor T-cell therapy in patients with advanced solid tumors[a] expressing MAGE-A4

- T-cell receptor T-cell therapy modified with additional CD8α co-receptor to treat human leukocyte antigen (HLA) A*02–eligible patients with tumors expressing melanoma-associated antigen A4 (MAGE-A4)



Trial Design



NCT04044859

Primary objective

- Evaluate the safety and tolerability of ADP-A2M4CD8

Secondary objectives

- Evaluate the antitumor activity of ADP-A2M4CD8

Exploratory objectives

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

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

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[a]Advanced endometrial, esophageal, esophagogastric junction, gastric, head and neck, melanoma, non-small cell lung, ovarian, or urothelial cancers. [b]Patient is hospitalized for T-cell infusion for ≥72 hours and discharged at the discretion of the Investigator

Patient characteristics and disposition

Characteristic	Overall monotherapy, N=43	Head and neck cancer, n=4
Female, n (%)	21 (49)	2 (50)
Median age, y (range)	60 (31–75)	59.5 (43–70)
H score,[a] median (range)	250 (95–300)	287.5 (140–300)
Transduced T cells × 10^9, median (range)	4.57 (0.95–9.95)	5.46 (4.6–6.5)
ECOG performance status, n (%) 0 1	 13 (30) 30 (70)	 1 (25) 3 (75)
Number of prior systemic therapies, median (range)	3 (1–8)	3 (1–5)
Median baseline tumor sum of lesion diameter, mm (range)	79 (10–341)	69 (19–164)
Patients who received systemic bridging therapy, n (%)	23 (54)	2 (50) → Paclitaxel and cetuximab, and tipifarnib

- The overall ADP-A2M4CD8 monotherapy population also included patients with esophageal, esophagogastric junction, gastric, melanoma, non-small cell lung, ovarian, synovial sarcoma, myxoid/round cell liposarcoma, and urothelial cancers
- Prior therapies in patients with head and neck cancer included:
  - One line: 5-fluorouracil (5fu), carboplatin, pembrolizumab; three lines: cisplatin, carboplatin, paclitaxel, pembrolizumab, cetuximab, panitumumab; three lines: 5fu, carboplatin, cetuximab, nivolumab, taxane, cetuximab; five lines: cisplatin, 5fu, paclitaxel, cetuximab, carboplatin, nivolumab, CX-2029
- Three of the four head and neck patients were screened for human papillomavirus; all were negative

5fu, 5-fluorouracil; ECOG, Eastern Cooperative Oncology Group

Data cutoff Nov 23, 2022. [a]H score: 1 ×(% of 1+ cells) + 2 ×(% of 2+ cells) + 3 ×(% of 3+ cells)

Safety

Adverse events of any grade related to T-cell infusion in ≥15% of patients	Overall monotherapy, N=43
Any event, n (%)	40 (93)
Cytokine release syndrome	32 (74)
Neutropenia	13 (30)
Anemia	9 (21)
Fatigue	9 (21)
Pyrexia	8 (19)
Rash	7 (16)
Thrombocytopenia	7 (16)

- Two Grade 5 (fatal) events occurred in the overall population:
  - Cytokine release syndrome and pancytopenia, both deemed related

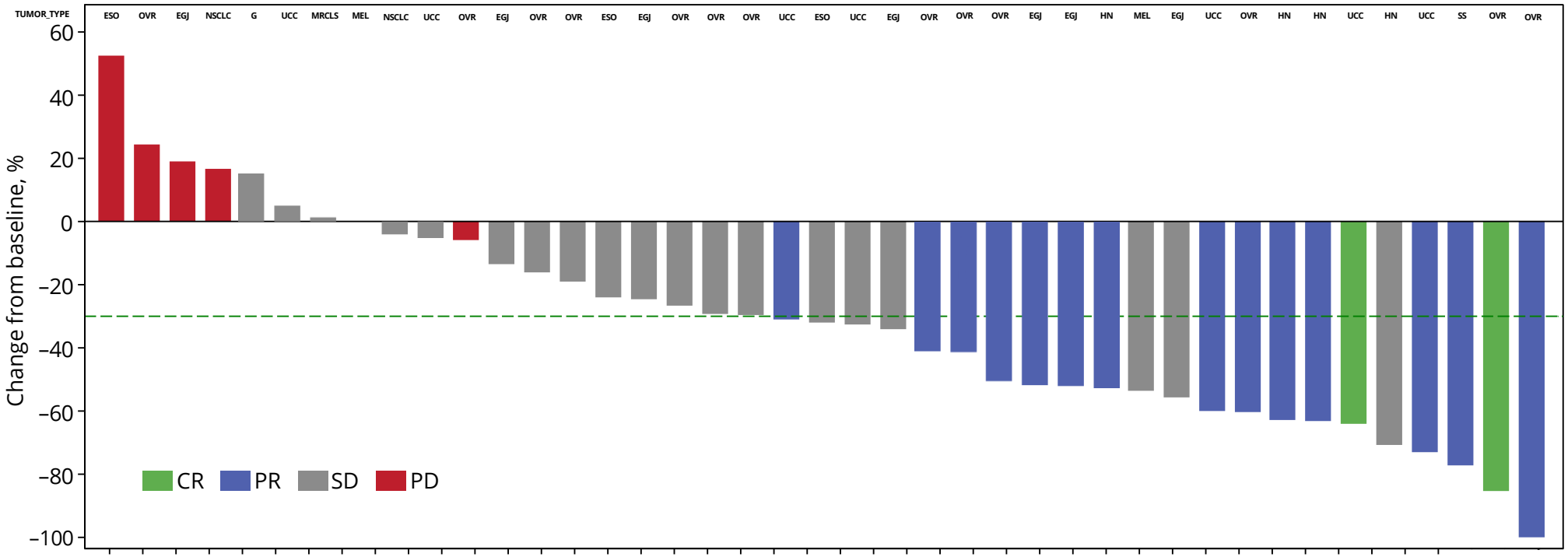
Serious adverse events related to T-cell infusion in ≥5% of patients	Overall monotherapy, N=43
Any event, n (%)	21 (49)
Cytokine release syndrome	14 (33)
Immune effector cell–associated neurotoxicity syndrome	3 (7)
Hypoxia	3 (7)

- In the four patients with head and neck cancer:
  - There were no Grade 5 events
  - One had a serious adverse event of Grade 3 pleural effusion, deemed unrelated
  - Two experienced cytokine release syndrome (Grades 2 and 4); both recovered
  - None experienced immune effector cell–associated neurotoxicity syndrome

Efficacy in the overall monotherapy population

- Overall response rate per RECIST v1.1 in the monotherapy population: 16/43 (37%)
- Median duration (range) of response: 19.1 (7.4–81.0) weeks

Maximum Percentage Change in Sum of Diameters Through PD (Inclusive) or Prior to Surgical Resection

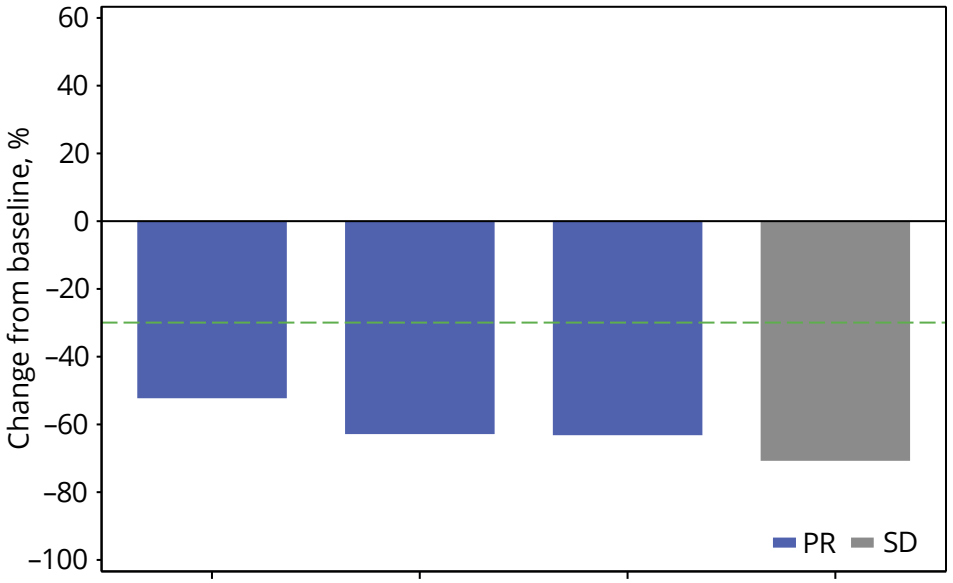


CR, complete response; EGJ, esophagogastric junction cancer; ESO, esophageal cancer; G, gastric cancer; HN, head and neck cancer; MEL, melanoma; mITT, modified intention-to-treat; MRCLS, myxoid cell liposarcoma; NSCLC, non-small cell lung cancer; OVR, ovarian cancer; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SS, synovial sarcoma; UCC, urothelial carcinoma

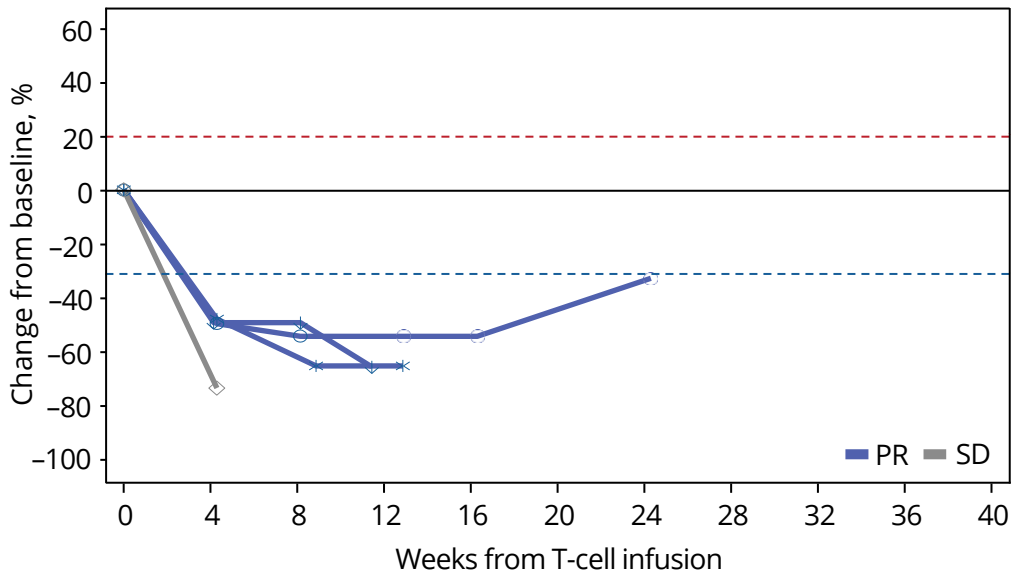
Efficacy in patients with head and neck cancer

- Best overall response rate per RECIST v1.1 by the investigator's review: 75% (3 PR and 1 SD)
- Median (range) duration of response: 8.7 (7.4–20.1) weeks

Maximum Percentage Change in Sum of Diameter



Change from Baseline in Sum of Diameters in Target Lesions

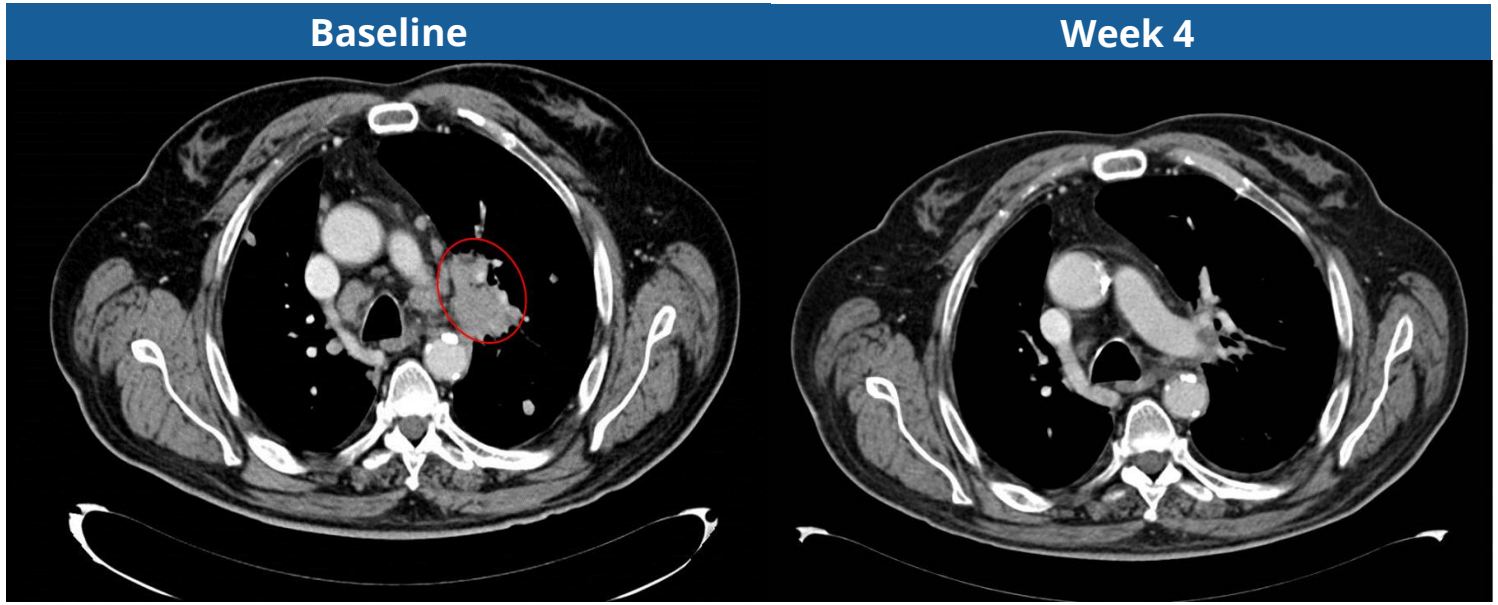


PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease

Data cut off Nov 23, 2022. The patient with SD had a >30% decrease in sum of the lesion diameters, but at only one timepoint, hence SD per RECIST v1.1

Confirmed partial response in a patient with Stage IV head and neck cancer

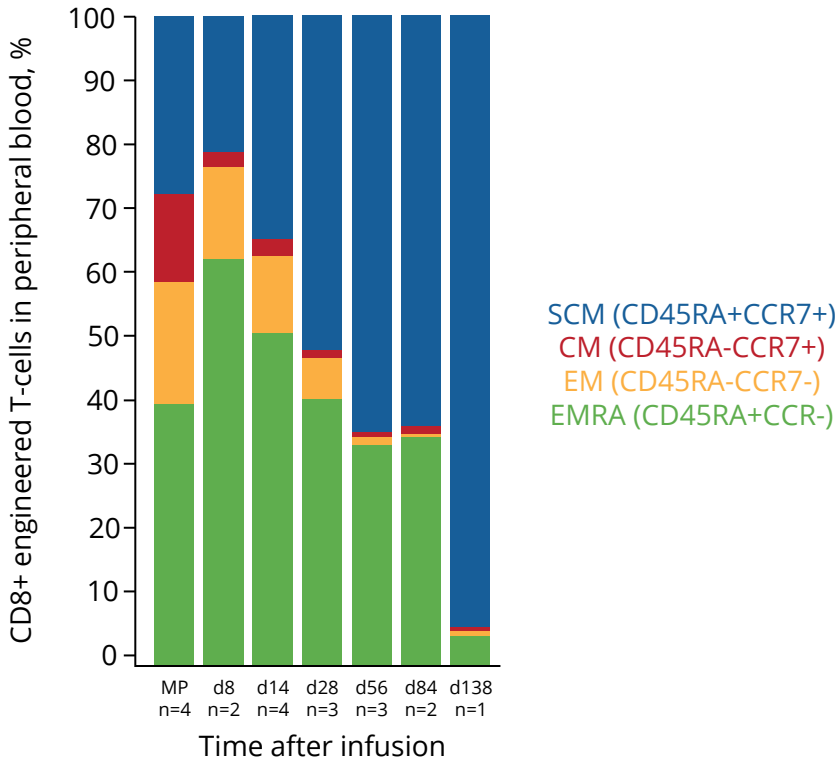
- 69-year-old White man with Stage IV squamous cell carcinoma head and neck cancer
- MAGE-A4 expression in tumor cells: 85% 3+,10% 2+, 5% 1+
- Baseline sum of the lesion diameters: 111 mm (5 target lesions)
- Prior systemic therapies: platinum-based therapy, nivolumab, taxane/cetuximab
- Patient was treated with 5 billion transduced T cells
- Confirmed response was initially reported at Week 4 and durable to Week 24



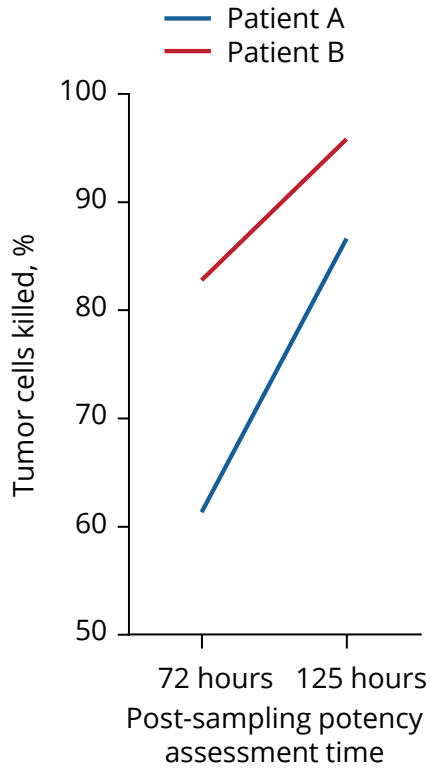
Hilar mass

Translational

- T cells that persist in the peripheral blood of patients with head and neck cancer adopt a stem cell memory phenotype



- At the time of clinical progression in two patients with data available, T cells retained the capacity to kill tumor cells in vitro



CM, central memory; EM, effector memory; EMRA, effector memory cells re-expressing CD45RA; MP, manufactured product; SCM, stem cell memory

Conclusions

- Encouraging efficacy with ADP-A2M4CD8 monotherapy in patients with advanced, previously treated, MAGE-A4+ head and neck cancer
- Toxicity in the overall population included cytokine release syndrome, immune cell–associated neurotoxicity syndrome, and prolonged cytopenia after lymphodepletion and T-cell infusion
  - Two of the patients with head and neck cancer experienced cytokine release syndrome (Grades 2 and 4, both recovered)
- The results with ADP-A2M4C8 monotherapy support expansion into earlier lines of therapy and combinations with anti–programmed cell death protein 1 checkpoint inhibitors
  - Additional cohorts in combination with nivolumab or pembrolizumab have been initiated in the SURPASS Phase 1 trial (ClinicalTrials.gov NCT04044859)