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23rd European Congress on Gynaecological Oncology
Oct 28-30, 2022 | Berlin, Germany

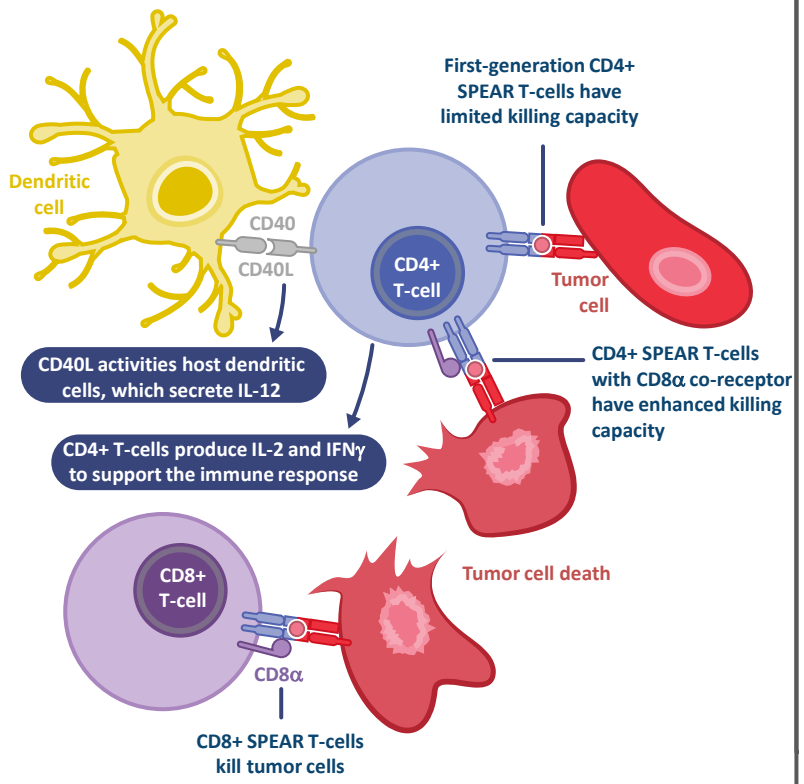
Preliminary Clinical Outcomes of ADP-A2M4CD8, a Next-Generation Autologous T-Cell Receptor T-Cell Therapy, in Patients With Advanced Epithelial Ovarian Cancer

Date: Thursday Oct 27, 2022; 2:50 PM – 3:50 PM
Name: Dr. Kathleen Moore

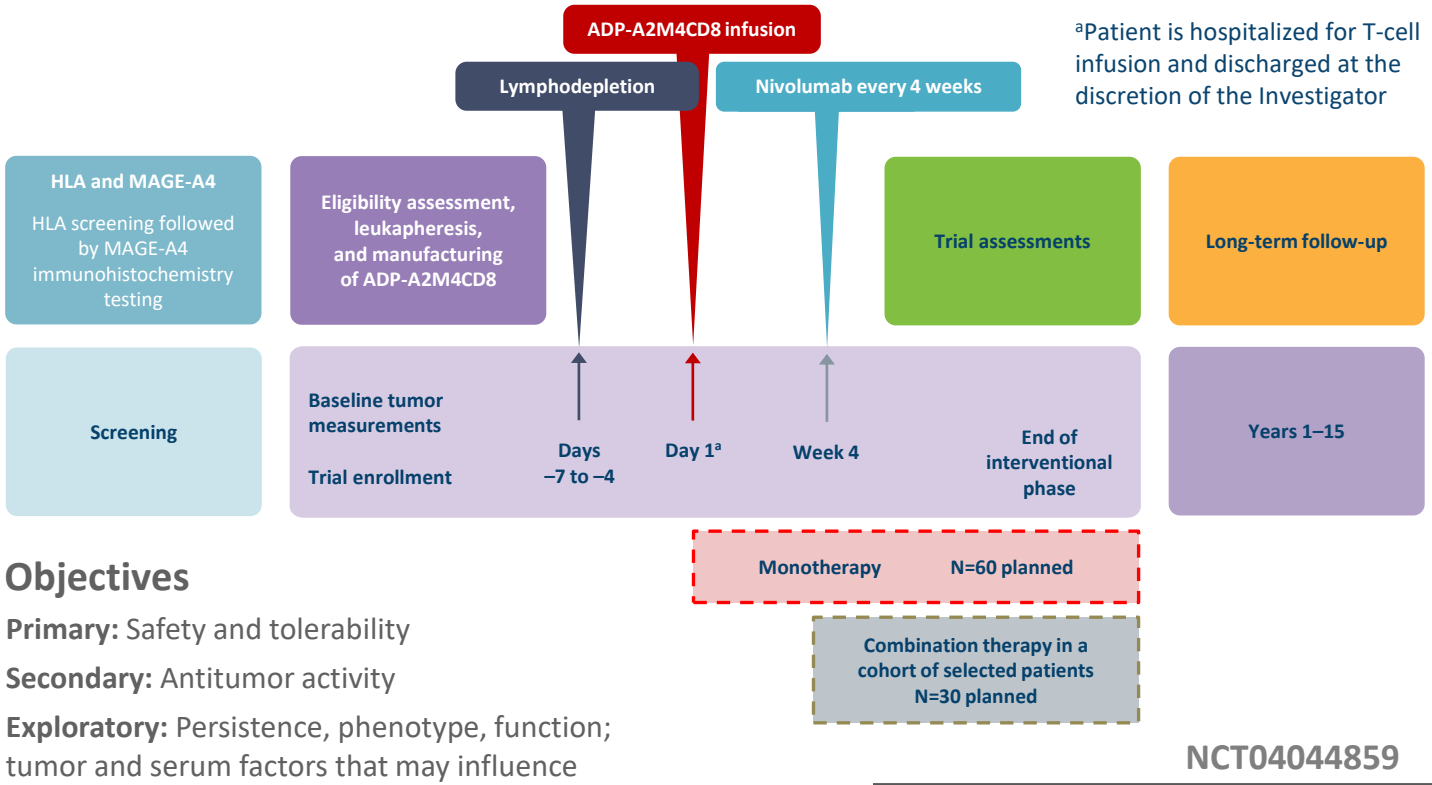
Declaration of Interests

The Phase 1 SURPASS Trial Evaluates ADP-A2M4CD8 Next-Generation SPEAR T-Cell Therapy in Selected Solid Tumors

Designed to increase potency by expressing a CD8α co-receptor



SURPASS trial design



Objectives

Primary: Safety and tolerability

Secondary: Antitumor activity

Exploratory: Persistence, phenotype, function; tumor and serum factors that may influence response or resistance

NCT04044859

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

Baseline Patient and Disease Characteristics

Eligibility in ovarian cancer based on HLA and MAGE-A4 inclusion criteria from the screening protocol (NCT02636855) as of November 19, 2021[1]

- HLA eligible: 49%
- MAGE-A4 positive: 24%

Baseline patient and disease characteristics

	N=14
Median age, years (range)	59 (40, 75)
H-score,[a] median (range)	237.5 (95, 300)
Transduced T-cells × 10^9, median (range)	3.17 (1.14, 9.95)
ECOG performance status, n (%)	
0	6 (42.9)
1	8 (57.1)
No. of prior lines of therapy, median (range)	4 (2, 8)

- Most patients were high-grade serous (79%; 11/14)
  - Others were clear cell (n=2) and low-grade serous (n=1)
- Most patients had a platinum-free interval of <6 months
- All patients were previously treated with bevacizumab, and most patients (64%) received a prior PARP inhibitor

Data cut-off August 1, 2022. 1. Wang T, et al. *Cancer Res.* 2022;82(12 suppl):LB001. [a]H-score: 1×(% of 1+ cells) + 2×(% of 2+ cells) + 3×(% of 3+ cells). ECOG, Eastern Cooperative Oncology Group; HLA, human leukocyte antigen; MAGE-A4, melanoma-associated antigen A4; PARP, poly adenosine diphosphate-ribose polymerase

Safety (All Tumor Indications)

Adverse events related to T-cell infusion in ≥10% of patients[a]

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

Serious adverse events and those related to T-cell infusion in ≥5% of patients[a]

Preferred term	N=44, n (%)	
	SAE	Related SAE
Any SAE	27 (61.4)	21 (47.7)
CRS	14 (31.8)	14 (31.8)
Hypoxia	3 (6.8)	3 (6.8)
ICANS	3 (6.8)	3 (6.8)
Pyrexia	3 (6.8)	2 (4.5)

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

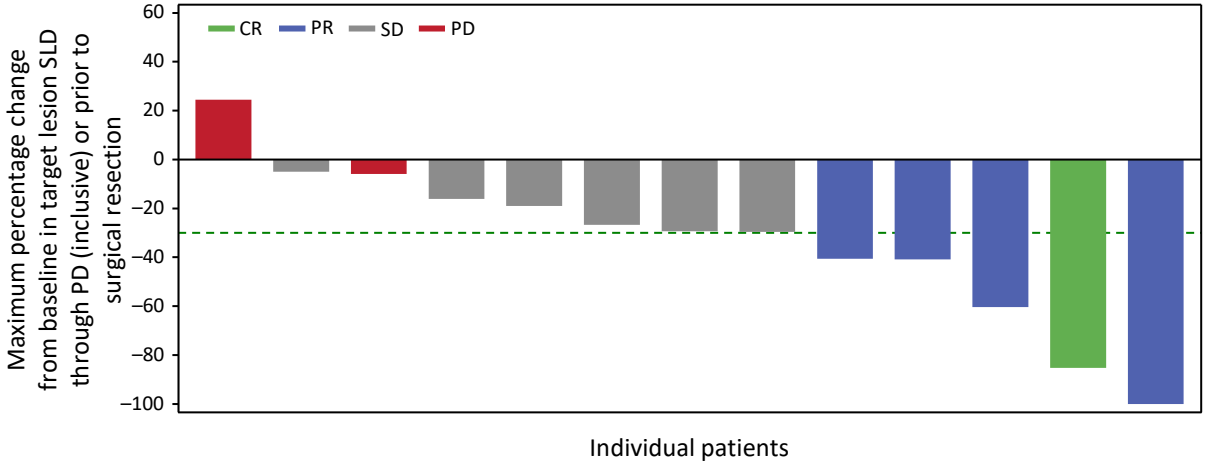
- 71-year-old man with adenocarcinoma of esophagus
- History of chronic anemia
- Developed new lesions in liver
- Cause of death: bone marrow failure

Events were consistent in the ovarian subgroup

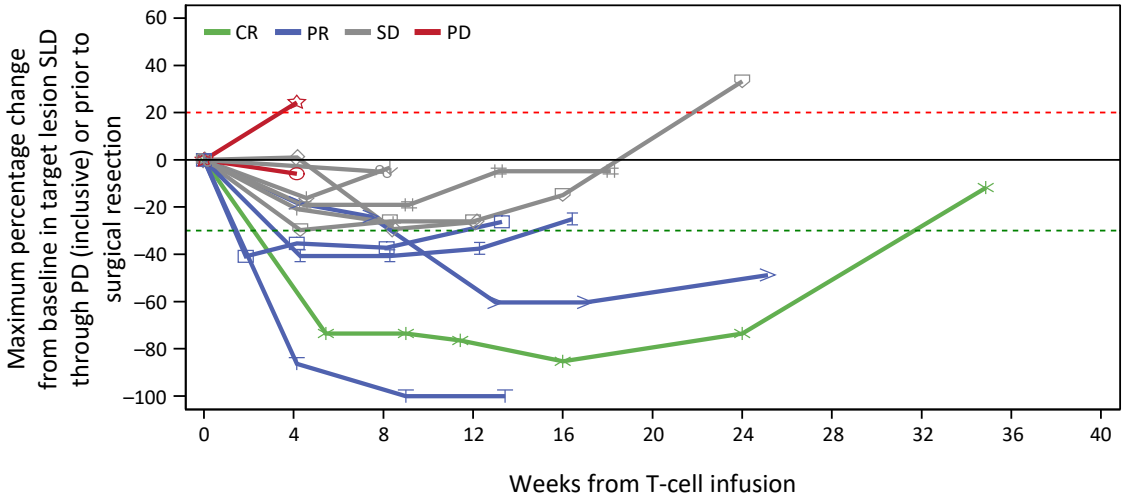
Data cut-off August 1, 2022. [a]Modified intent-to-treat population. AE, adverse event; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; RBC, red blood cell; SAE, serious adverse event; WBC, white blood cell

Antitumor Activity per RECIST v1.1 by Investigator Review and SPEAR T-Cell Persistence Over Time (Patients with Ovarian Cancer)

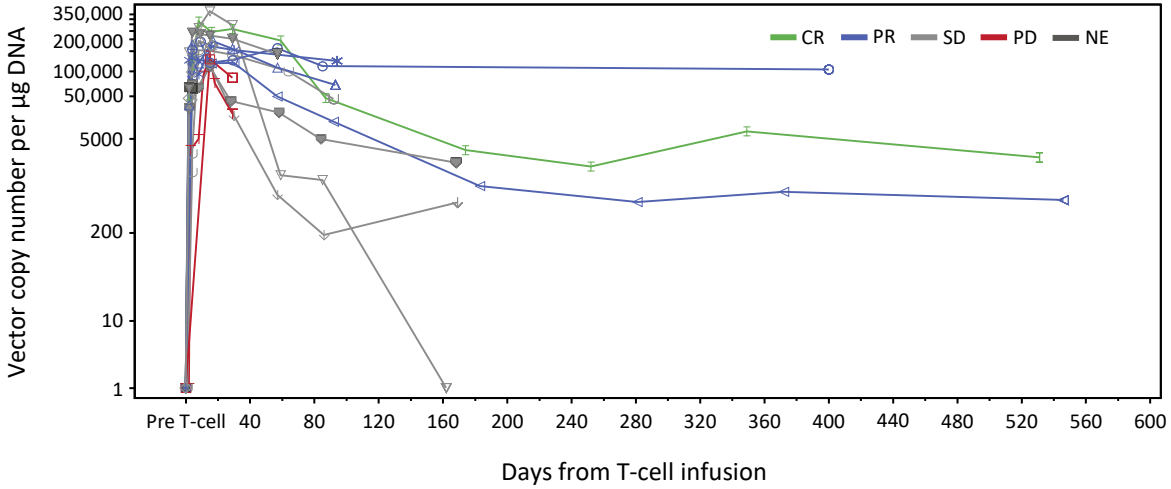
Change from baseline in target lesion SLD colored by best overall response



Change from baseline in target lesion SLD over time colored by best overall response



ADP-A2M4CD8 SPEAR T-cell persistence



Overall response rate

- 36% (5 of 14 patients)*

Disease control rate[a]

- 79% (11 of 14 patients)*

Duration of response (range)[b]

- 9+ to 30 weeks

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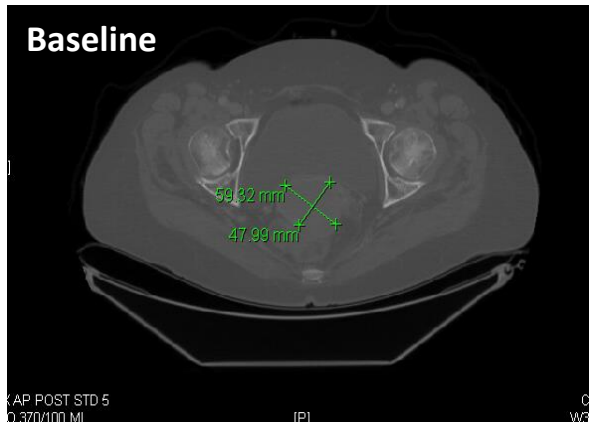
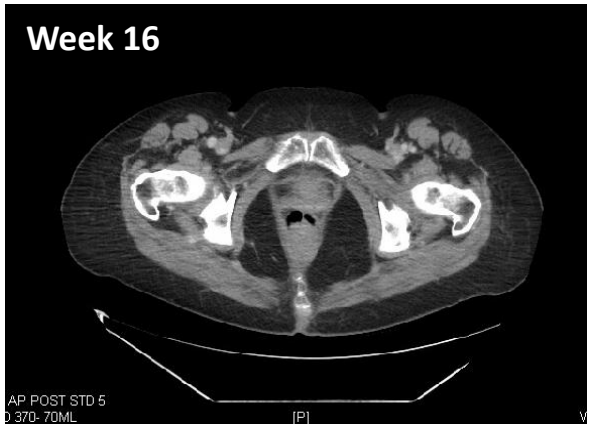
Data cut-off August 1, 2022. [a](CR+PR+SD)/N. [b]Median duration of response was not reached due to the limited number of responders. CR, complete response; NE, not evaluable; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease; SLD, sum of longest diameters; SPEAR, specific peptide enhanced affinity receptor * 1 pt was evaluable but died prior to first scan

Case Studies of 2 Responding Patients with Ovarian Cancer

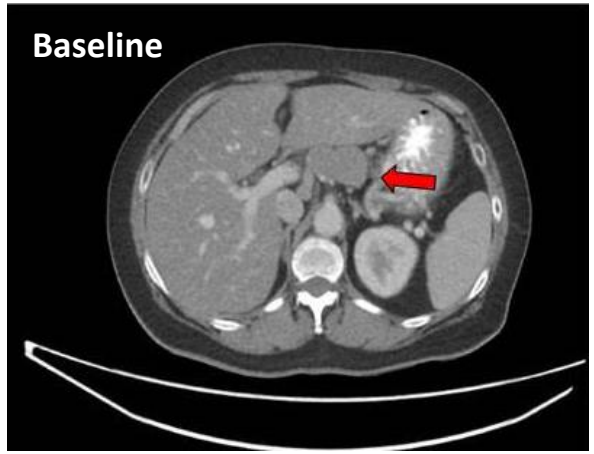
Stage III platinum-resistant high-grade serous ovarian cancer (BRAC1/2)

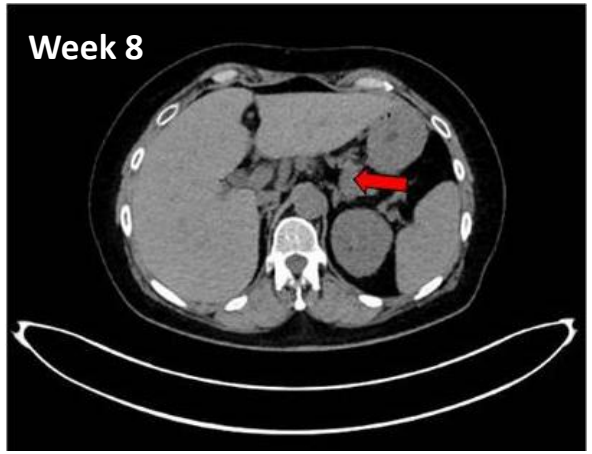




- **Baseline:** Low MAGE-A4 expression (25% tumor cells with 3+ staining); prior history of multiple surgeries and systemic therapies
- **Dose:** 6.6 billion ADP-A2M4CD8 cells
- **Response:** PR at Week 4 and confirmed at Week 8
- **Safety:** One related SAE (Grade 1, CRS) resolved within 1 week. Ten days later, 3 related SAEs (Grade 2, hypoxia; Grade 2, dyspnea; Grade 3, rash); all resolved
- **Data cut-off August 1, 2022**

Grade 3 serous ovarian cancer (pT3bN1)





- **Baseline:** High MAGE-A4 expression with 95% tumor cells with 3+ staining; prior history of multiple surgeries and systemic therapies
- **Dose:** 3.24 billion ADP-A2M4CD8 cells
- **Response:** CR at Week 4 and confirmed at Week 8
- **Safety:** One related SAE (Grade 1, pyrexia/fever) resolved within 1 week
- **Data cut-off August 2, 2021**

CR, complete response; CRS, cytokine release syndrome; MAGE-A4, melanoma-associated antigen A4; PD, progressive disease; SAE, serious adverse event

Conclusions

- Encouraging anti-tumor activity with ADP-A2M4CD8 monotherapy in patients with advanced MAGE-A4+ ovarian cancer
- Toxicity included CRS, ICANS, and prolonged cytopenia after lymphodepletion and T-cell infusion
- ADP-A2M4CD8 monotherapy continues to show an acceptable benefit-to-risk profile; mechanism of action supports expansion into combination therapy with an anti-PD1 checkpoint inhibitor
  - An additional treatment cohort with nivolumab has been initiated in the Phase 1 SURPASS trial
- Results support initiation of a planned Phase 2 study for ovarian cancer (SURPASS-3)

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome

Patients and their caregivers for taking part in this trial

Investigators and their teams who participated in this work

THANK YOU!