

**SPEAR-heading**

# **THE CANCER REVOLUTION**

Ad Rawcliffe, CEO, and Elliot Norry, CMO

**Building a cell therapy franchise:  
SURPASS Phase 1 trial data at ESMO  
September 13, 2021**



# Disclaimer

This presentation contains “forward-looking statements,” as that term is defined under the Private Securities Litigation Reform Act of 1995 (PSLRA), which statements may be identified by words such as “believe,” “may,” “will,” “estimate,” “continue,” “anticipate,” “intend,” “expect” and other words of similar meaning. These forward-looking statements involve certain risks and uncertainties. Such risks and uncertainties could cause our actual results to differ materially from those indicated by such forward-looking statements, and include, without limitation: the success, cost and timing of our product development activities and clinical trials; our ability to submit an IND and successfully advance our technology platform to improve the safety and effectiveness of our existing TCR therapeutic candidates; the rate and degree of market acceptance of T-cell therapy generally and of our TCR therapeutic candidates; government regulation and approval, including, but not limited to, the expected regulatory approval timelines for TCR therapeutic candidates; and our ability to protect our proprietary technology and enforce our intellectual property rights; amongst others. For a further description of the risks and uncertainties that could cause our actual results to differ materially from those expressed in these forward-looking statements, as well as risks relating to our business in general, we refer you to our Annual Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 9, 2021 and our other SEC filings.

We urge you to consider these factors carefully in evaluating the forward-looking statements herein and you are cautioned not to place undue reliance on such forward-looking statements, which are qualified in their entirety by this cautionary statement. The forward-looking statements contained in this presentation speak only as of the date the statements were made and we do not undertake any obligation to update such forward-looking statements to reflect subsequent events or circumstances.

We intend that all forward-looking statements be subject to the safe-harbor provisions of the PSLRA.

# Arming Cells. Against Cancer. For Good.

To transform the lives of people  
with cancer by designing and  
delivering cell therapies

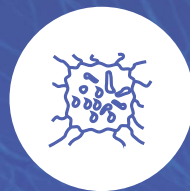


## 5-year core value drivers: our “2-2-5-2” plan



**Two**  
marketed  
SPEAR T-cell  
products targeting  
MAGE-A4

- Synovial sarcoma
- Esophageal and EGJ cancers



**Two**  
additional BLAs  
for SPEAR T-cell  
products

- Additional indications for MAGE-A4 targeted products
- ADP-A2AFP



**Five**  
autologous  
products in the  
clinic

- HiT
- Next-gen TILs
- New targets
- Broader HLA coverage



**Two**  
allogeneic  
products entering  
the clinic

- SPEAR T-cell product targeting MAGE-A4
- HiT mesothelin – partnered with Astellas

### Integrated Cell Therapy Capabilities

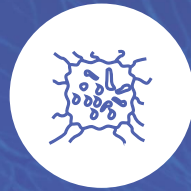
Research | Preclinical | Translational | Clinical | CMC | Regulatory | Commercial

# SURPASS is a signal finding trial with our next-generation SPEAR T-cells targeting MAGE-A4



**Two**  
marketed  
SPEAR T-cell  
products targeting  
MAGE-A4

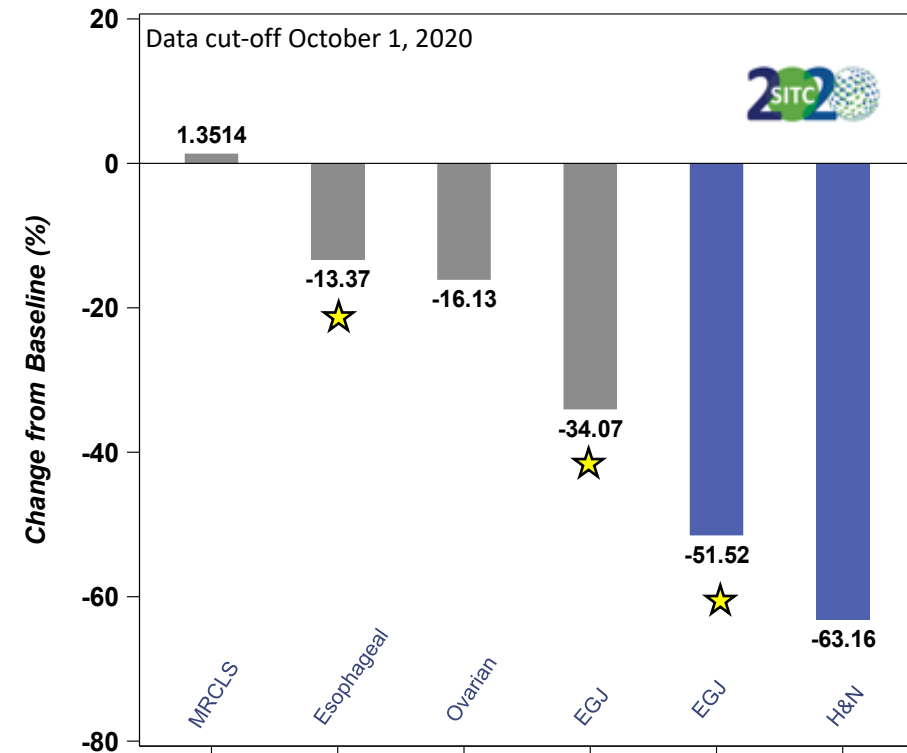
- Synovial sarcoma
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**Two**  
additional BLAs  
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- Additional indications for MAGE-A4 targeted products
- ADP-A2AFP

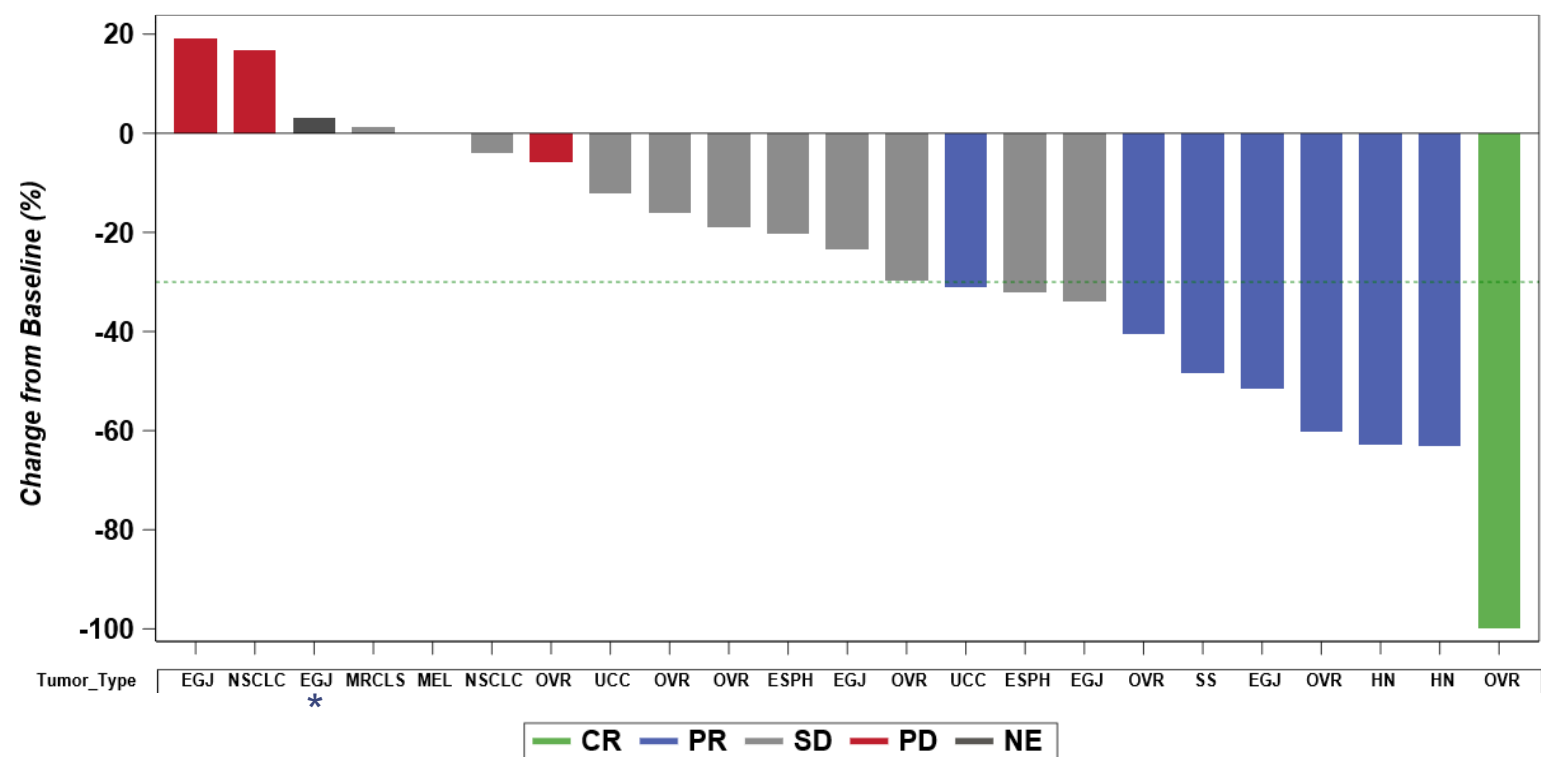
**SURPASS Trial BOR in 6 patients with multiple tumor indications**



**Decision to focus on lung, head and neck, bladder, and gastroesophageal cancers**

# Responses in 5 solid tumor types including a complete response in ovarian cancer

Initial efficacy is very promising with response rate of 36% (8/22\*) and 86% (19/22\*) disease control



Data supports next-gen hypothesis, MAGE-A4 target, and potential of SPEAR T-cells in multiple solid tumor indications for people with cancer

Data represent percent 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; Of 25 patients treated, 3 were not evaluable at the time of data cut-off: 2 patients (ovarian or esophageal cancers) did not have post-baseline scans; 1 patient (EGJ) had a post-baseline scan that did not meet the ≥4 weeks duration for stable disease; CR=complete response; PR=partial response; SD=stable disease; PD=progressive disease; NE=not evaluable; EGJ=esophagogastric junction cancer; NSCLC=non-small cell lung cancer; MRCLS=myxoid/round cell liposarcoma; OVR=ovarian cancer; ESPH=esophageal cancer; UCC=urothelial carcinoma or bladder cancer; SS=synovial sarcoma; HN=head and neck cancer

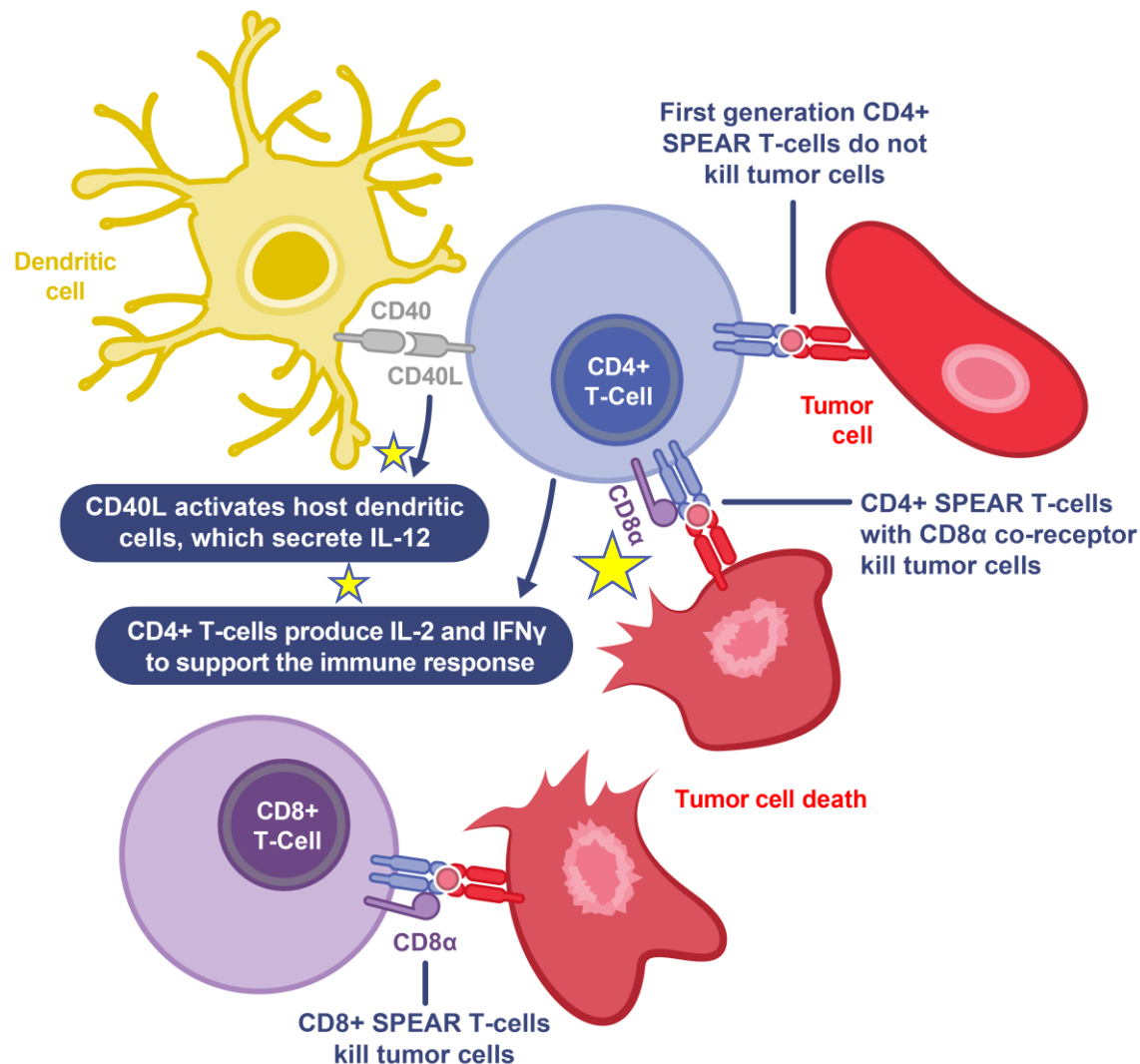


# Clinical and translational data substantiates next-gen hypothesis

Designing and delivering better T-cell therapies for people with cancer

★ *Enables helper T-cells to kill tumor cells*

★ *Engages the broader immune system*

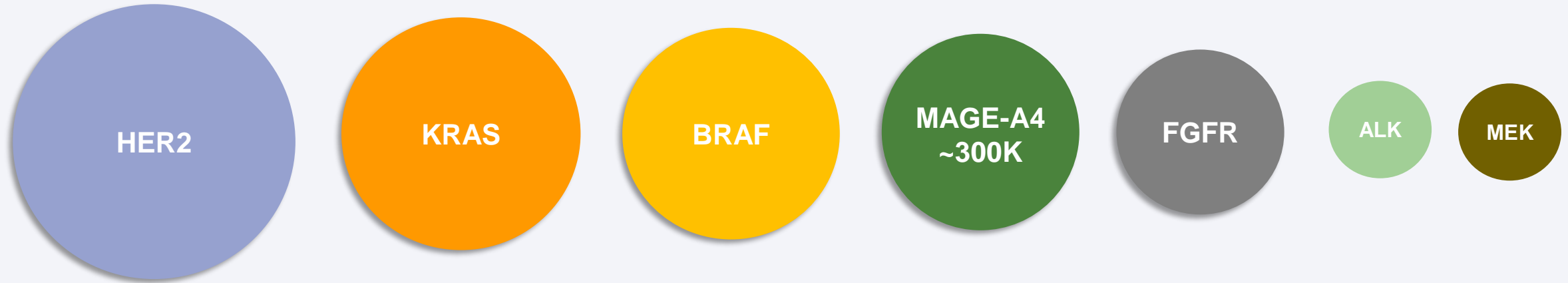


# MAGE-A4 is a validated and significant cancer target

Similar opportunity size to BRAF and FGFR



New cases per year in the US and EU











~95K MAGE-A4+ deaths per year



Of which ~39K deaths are HLA2+



# Responses in multiple solid tumor indications with ADP-A2M4CD8

Indication		Mortality US and EU*	MAGE-A4 Expression **	Potential MAGE-A4 +ve Patients	Potential MAGE-A4 +ve Patients Factored for HLA***
Synovial sarcoma	afami-cel SURPASS	1,804+	67 %	1,209	 496
MRCLS	afami-cel	2,000	34 %	680	 279
Gastroesophageal (esophageal, EGJ, and gastric)	SURPASS	101,080	17 %	17,184	 7,045
Head and neck	afami-cel SURPASS	44,500	18 %	8,010	 3,284
Urothelial	SURPASS	53,180	33 %	17,549	 7,195
NSCLC-Squamous	afami-cel	101,661	38 %	38,631	 15,839
Melanoma	afami-cel	19,750	16 %	3,160	 1,296
Ovarian	SURPASS	38,840	22 %	8,545	 3,503
				<b>Total MAGE-A4: 94,968</b>	<b>Total MAGE-A4 HLA A2: 38,937</b>

Significant potential for SPEAR T-cell franchise targeting MAGE-A4



## SURPASS Phase 1 trial update – ESMO 2021

“We are encouraged by these promising early data from the SURPASS trial. Having previously seen strong responses with afami-cel, this next-generation cell therapy appears safe and demonstrated antitumor activity for a majority of patients across many cancer indications.”

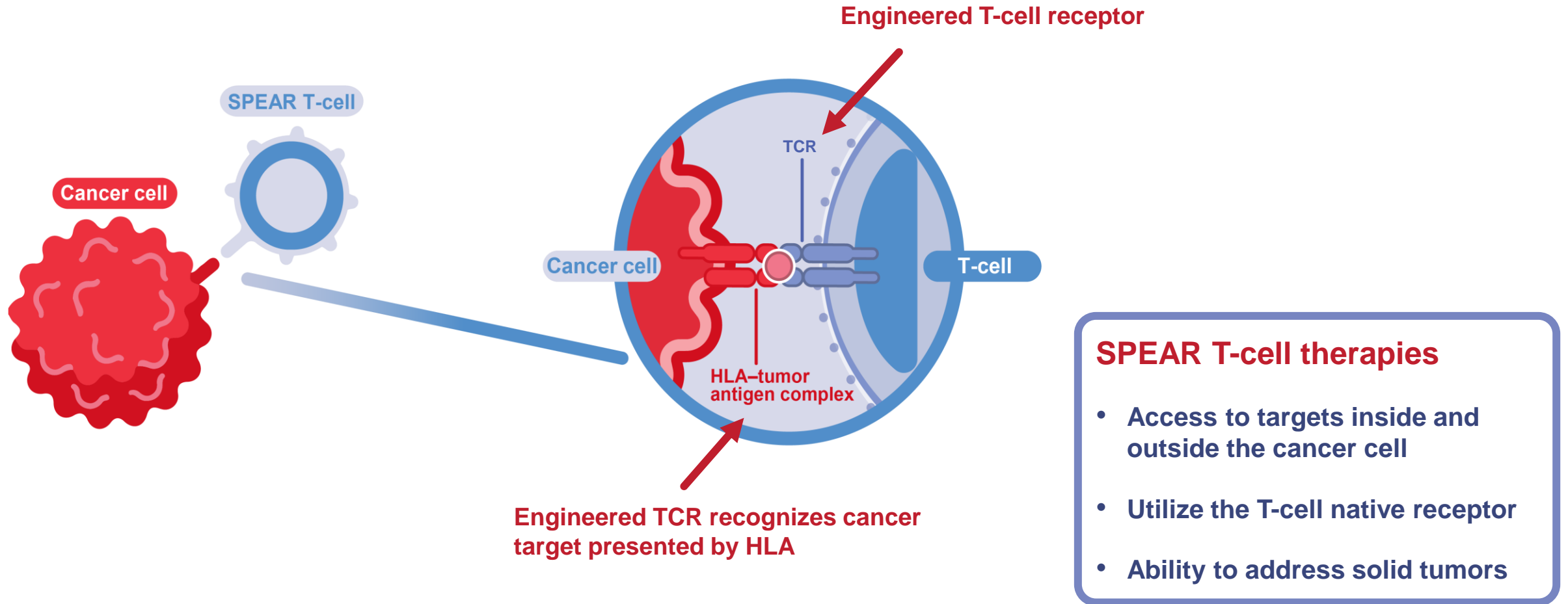
Dr. David Hong  
Principal Investigator, SURPASS trial  
Professor, Deputy Chairman in the Department of Investigational  
Cancer Therapeutics (Phase I Program) at The University of  
Texas MD Anderson Cancer Center





# T-cell receptor (TCR) therapies are critical when addressing solid tumors

Adaptimmune is uniquely positioned to address MAGE-A4 expressing solid tumors



HLA = human leukocyte antigen; SPEAR = Specific Peptide Enhanced Affinity Receptor; TCR = T-cell receptor

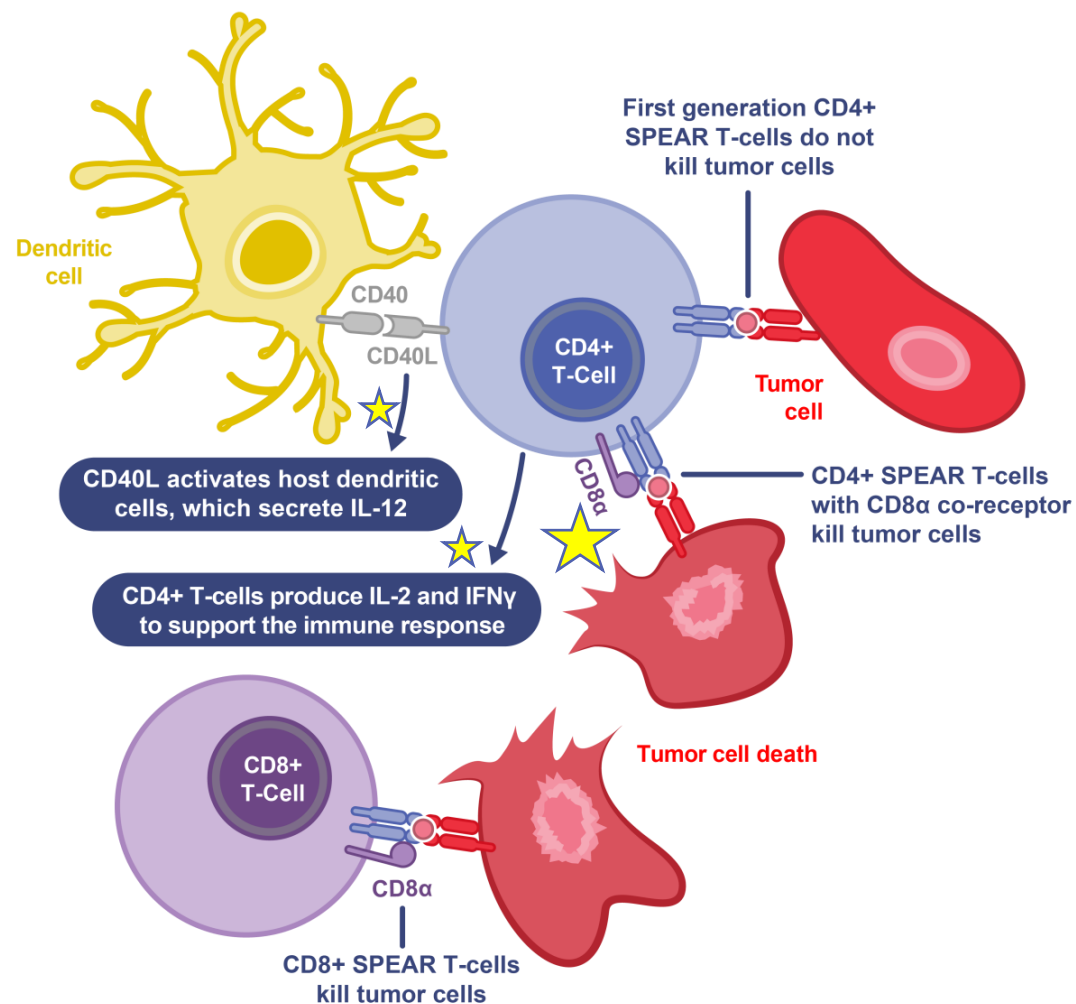
# Next-generation T-cell therapy ADP-A2M4CD8 designed to be a more potent product

Addition of CD8 $\alpha$  co-receptor alongside MAGE-A4 targeted T-cell receptor intended to increase antitumor immune response

***ADP-A2M4CD8 is designed to be a more potent product***

***ADP-A2M4CD8 expresses the same MAGE-A4 targeted TCR as afami-cel along with a CD8 $\alpha$  co-receptor***

***CD4+ helper T-cells can now kill tumor cells and still provide help to engage the broader immune system to fight cancer***



# SURPASS: A Phase 1 trial with a next-generation T-cell therapy in multiple solid tumors

## Key eligibility and endpoints

### KEY ELIGIBILITY CRITERIA

- Advanced gastric, esophageal, esophagogastric junction (EGJ), bladder, lung, head and neck, and ovarian cancers
- ECOG 0 or 1
- Aged  $\geq 18$  and  $< 75$  years
- HLA-A\*02 positive
- MAGE-A4 expression:  $\geq 30\%$  of tumor cells that are  $\geq 2+$  by immunohistochemistry
- Measurable disease per RECIST v1.1



### SAFETY AND TOLERABILITY

- Adverse Events (AEs)
- AEs of Special Interest



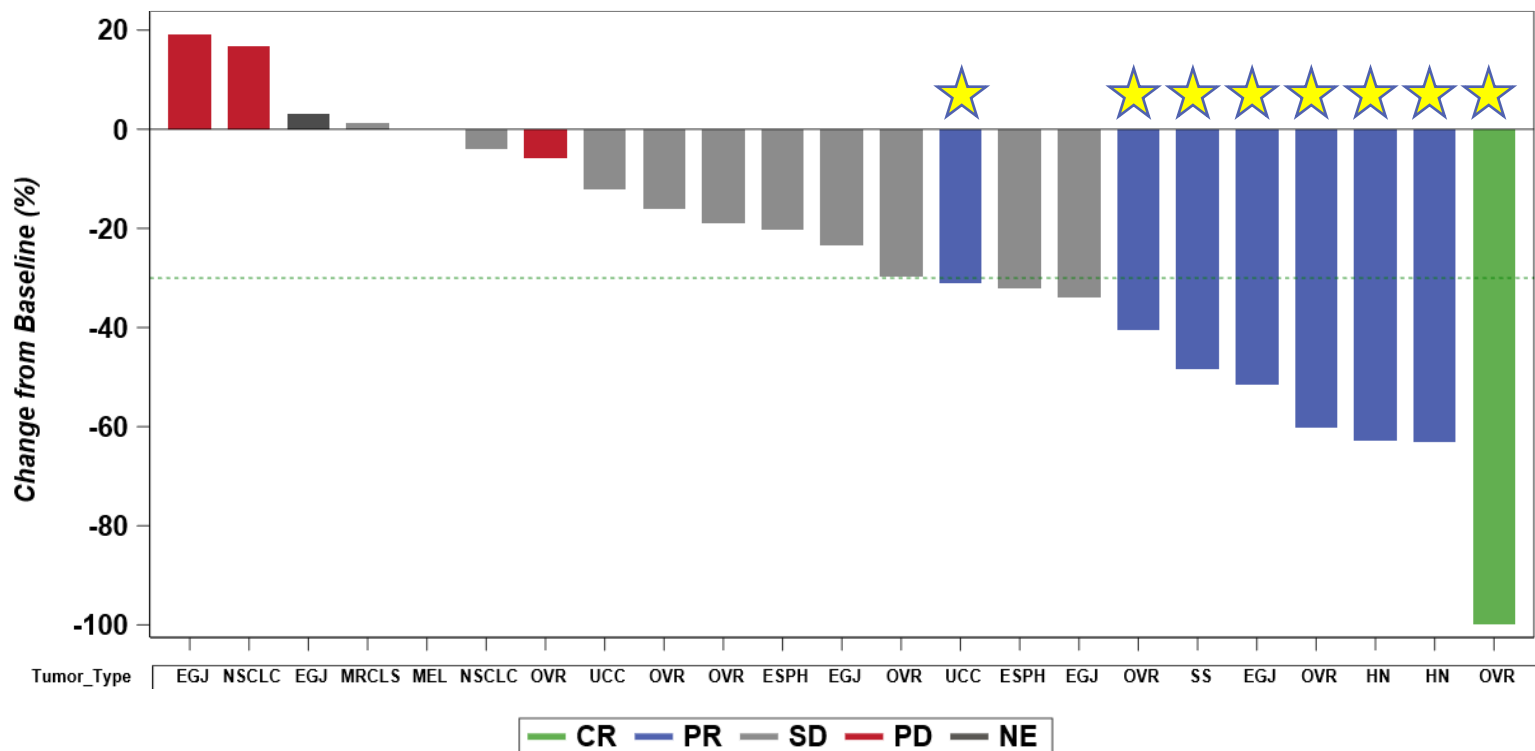
### EFFICACY

- Responses per RECIST v1.1
- Duration of response
- Time to response
- Progression-free and overall survival



# Initial efficacy is promising with response rate of 36% (8/22\*) and 86% (19/22\*) disease control

Best overall response by RECIST v1.1

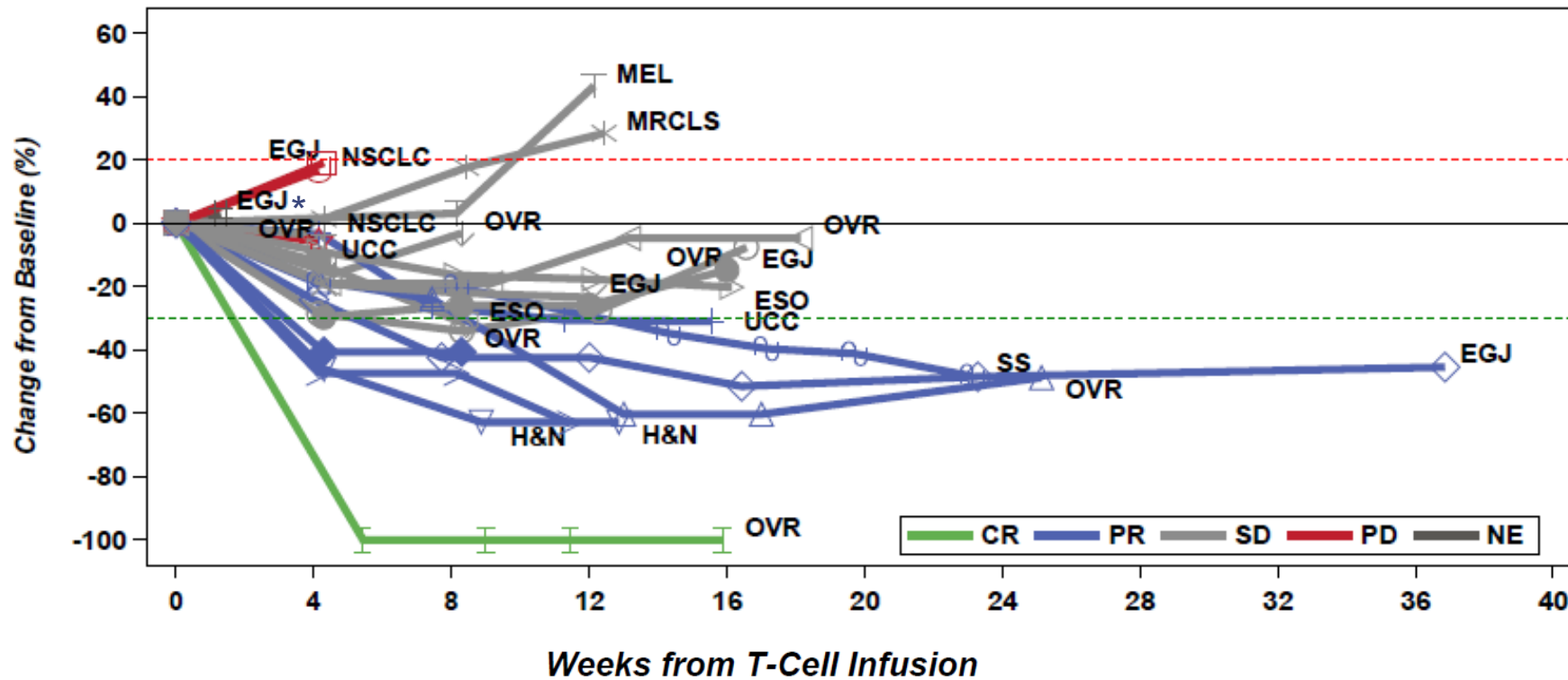


- Overall response rate of 36% (8/22\*) with majority of patients experiencing antitumor activity
- A complete response in a patient with ovarian cancer – and partial responses in ovarian (2), head and neck (2), EGJ, bladder, and synovial sarcoma cancers

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# Initial durability encouraging and will continue to evolve

Several patients receiving clinical benefit for 24 weeks or more post-infusion



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- Some patients experience continued reductions in tumors over several months post-infusion
- Median duration of response not reached

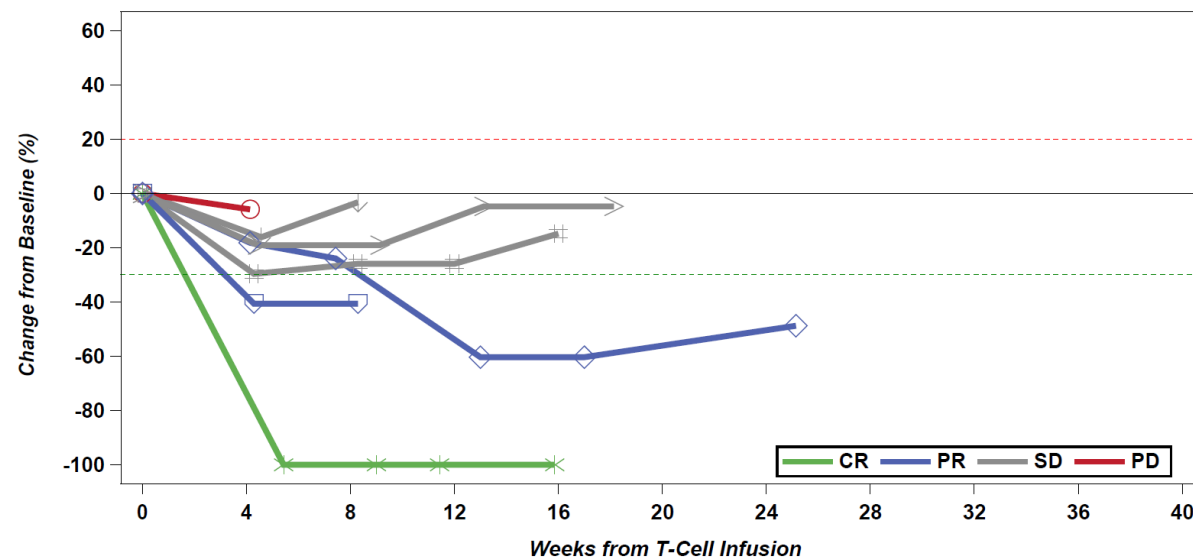
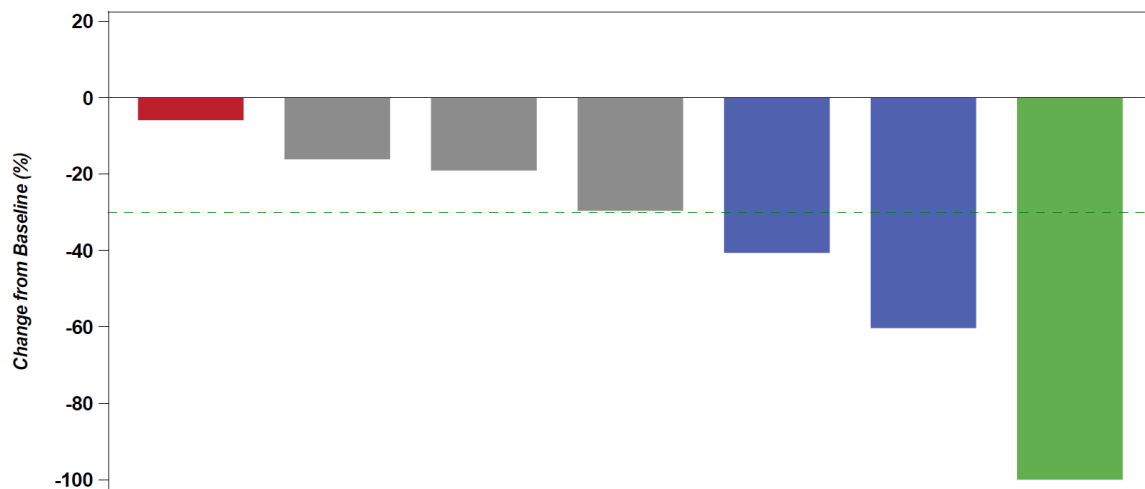
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# Reductions in target lesions in all evaluable patients with ovarian cancer

Out of 7 evaluable patients - one complete response, 2 partial responses, and 3 stable diseases



Data from patients with ovarian cancer



CR PR SD PD

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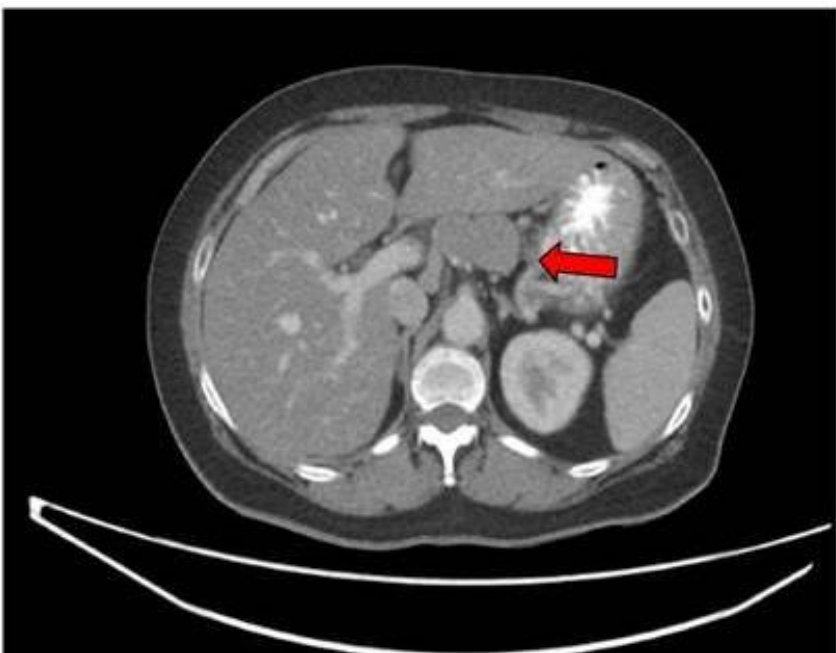
**SURPASS trial focused on enrolling patients with lung, head and neck, bladder, gastroesophageal, and ovarian cancers**



## Complete response (CR) ongoing at 6 months in a patient with Grade 3 serous ovarian cancer

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Baseline 12 Jan 2021



First reassessment 30 March 2021

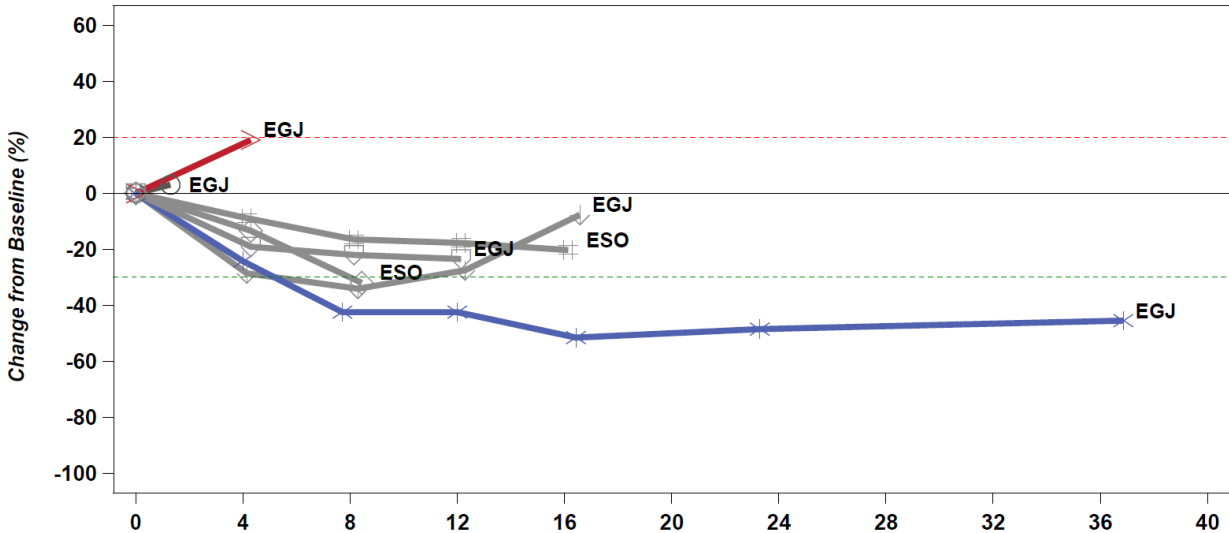
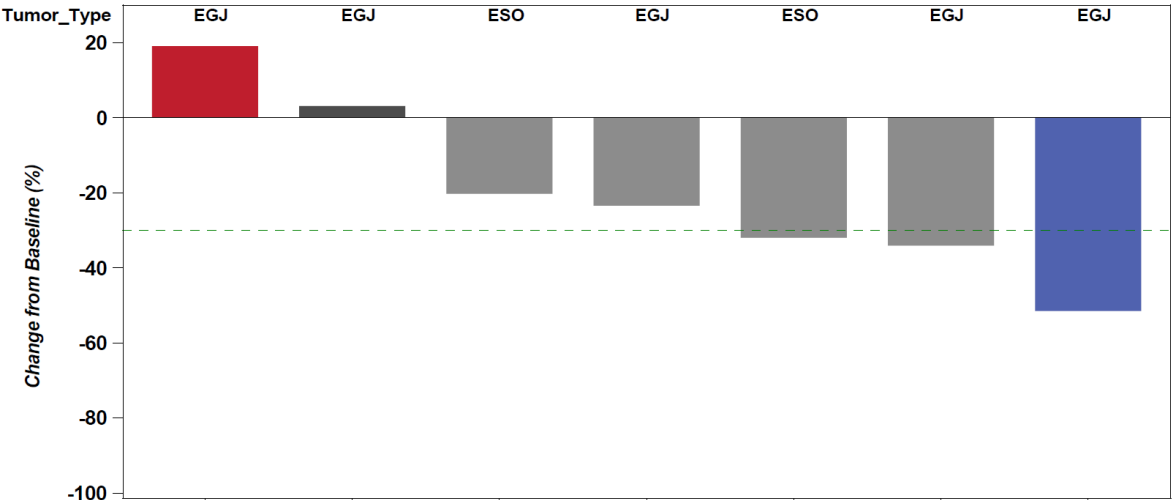


- Platinum resistant\* patient treated with 3.24 billion ADP-A2M4CD8 SPEAR T-cells in the Expansion Group
- Adverse events were consistent with those of patients undergoing cytotoxic cancer therapy, with one related SAE (Grade 1, fever) resolved within 1 week

# Data in esophageal and EGJ cancers confirm potential of Phase 2 SURPASS-2 trial



Data from patients with esophagogastric junction (EGJ) or esophageal cancers



PR SD PD NE

Data represent percent 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

Phase 2 SURPASS-2 trial for patients with EGJ or esophageal cancers has initiated

# Translational data substantiate increased potency of next-generation ADP-A2M4CD8 product

Analyses comparing first- and next-generation MAGE-A4 targeted T-cell therapy



- Addition of CD8 $\alpha$  to next-gen product results in greater tumor cell killing by CD4+ SPEAR T-cells *in vitro*
  - As shown by data from patient manufactured products used in Phase 1 afami-cel trial (first-gen) and the SURPASS trial
- Additional data shows that next-gen ADP-A2M4CD8 engages the broader immune system
  - Post-infusion increases in a subset of the 22 measured serum cytokines
  - Statistically significant increase in serum IL-12 with the next-generation product indicative of dendritic cell engagement (i.e., a broader immune response)

***Enables helper T-cells to kill tumor cells***

***Engages the broader immune system***

## Safety: acceptable safety profile of next-generation ADP-A2M4CD8 product

Adverse events related to T-cell infusion in  $\geq 10\%$  of patients; SAEs in  $>1$  patient



- Most adverse events were consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy and/or adoptive cell therapy
- Out of 25 patients treated as of data cut off
  - 18 (72%) experienced CRS of any grade related to the T-cell therapy, with 4 grade  $\geq 3$  (16%)
  - 4 (16%) experienced immune effector cell-associated neurotoxicity syndrome (ICANS) related to T-cell therapy of any grade with 2 grade  $\geq 3$  (8%)
  - There were 8 (32%) CRS and 3 (12%) ICANs SAEs related to T-cell therapy
  - One patient experienced a fatal SAE of pancytopenia

***To date, safety profile of ADP-A2M4CD8 has been acceptable***



# Data supports next-gen hypothesis and potential of ADP-A2M4CD8 for people with cancer

- ADP-A2M4D8 is efficacious and generally well-tolerated in heavily pre-treated patients across a broad range of tumor indications
  - Responses in 5 solid tumor indications
    - › Overall response rate of 36%
    - › A complete response in a patient with ovarian cancer, which remains ongoing
    - › Most patients experienced tumor reduction
  - Initial durability data is encouraging
  - To date, safety profile of ADP-A2M4CD8 has been acceptable
- Data demonstrate that ADP-A2M4CD8 does what it was designed to do
  - Produce a more potent antitumor response and better CD4 helper function
- SURPASS trial is enrolling eligible patients with gastroesophageal, head and neck, lung, bladder, and ovarian cancers
- Phase 2 SURPASS-2 trial has initiated for people with esophageal and EGJ cancers



***Poster available on September 16, 2021 on ESMO website***



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