

# ADP-A2M4 (MAGE-A4) IN PATIENTS WITH SYNOVIAL SARCOMA

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# DISCLOSURE INFORMATION

Van Tine, Brian

## Personal financial interests

- Advisory Role/Consultant: Epizyme; CytRx; Janssen; Plexxicon
- Consultant, Advisory Role/Speaker, Research/Trial Support, Travel Support: Lilly
- Speaker Bureau: Caris
- Research Grant/Consulting/Ad Board: Pfizer
- Consultant: Bayer
- Research Grant: Merck; Tracon
- Advisory Board: Immune Design; Daiichi Sankyo
- Speaker: Adaptimmune

## Institutional financial interests

- Research Grant: Lilly; Merck
- Trial Support: Oncothreon; Gliknik; Celidex Therapeutics; ImClone Systems; Peregrine Pharmaceuticals; BIND Therapeutics; Regeneron Pharmaceuticals; MabVax Therapeutics; Millenium; AbbVie; Janssen Research Foundation; Jounce Therapeutics; EMD Serono; Puma Biotechnology; VentiRx Pharmaceuticals; Taiho Pharmaceuticals; Gilead Sciences; Incyte; Daiichi Pharmaceutical; Novartis; Pfizer; Acerta; Inventiv Health; Celgene; Sanofi; AstraZeneca; Merrimack Pharmaceuticals; Biothera Pharmaceuticals; Medimmune; Blueprint Medicines; Bristol-Myers Squibb; Enzychem Lifesciences Corporation; Eisai; Genentech; Corvus; Johnson & Johnson; Threshold Pharmaceuticals; Bayer; BeiGene; GlaxoSmithKline; Molecular Insight Pharmaceuticals; Gem Pharmaceuticals; Deciphera Pharmaceuticals; Forma Therapeutics, Bavarian Nordic; Hoffman-LaRoche; Caris Life Sciences; Morphotek; Soligenix; Eleison Pharmaceuticals; AADi; Immune Design; TRACON Pharmaceuticals; NanoCarrier; Advenchen Laboratories; Karyopharm Therapeutics; Hutchison MediPharma

This study (NCT03132922) is sponsored by Adaptimmune LLC

# BACKGROUND

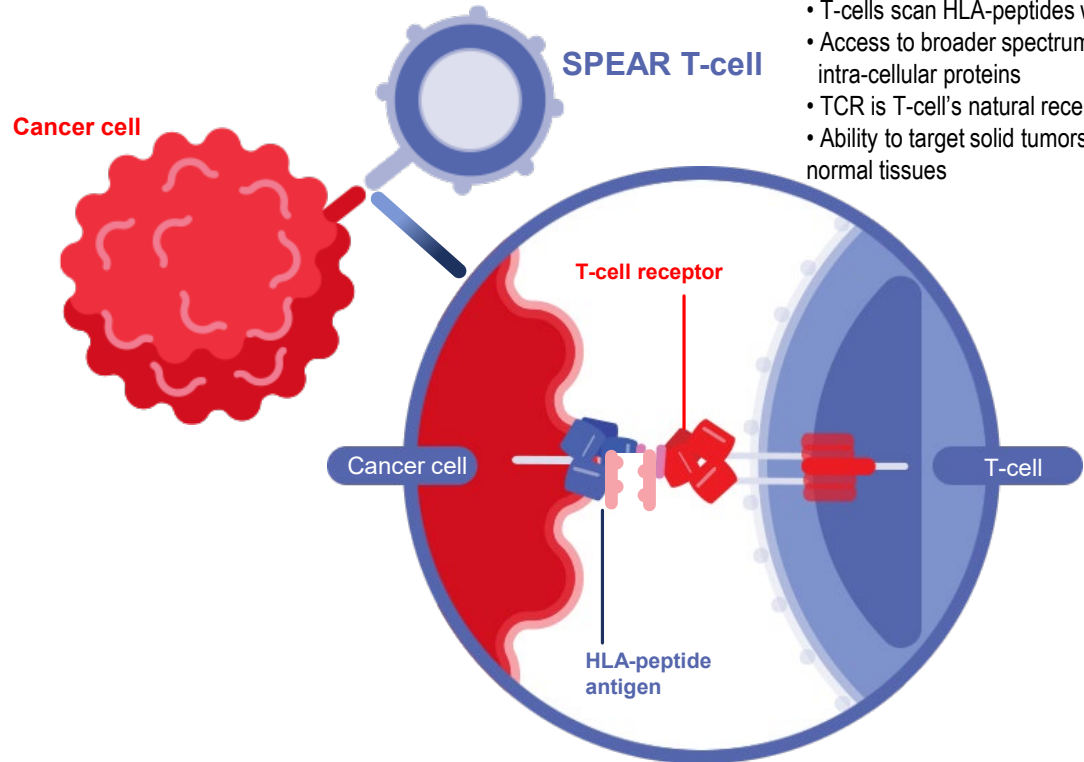
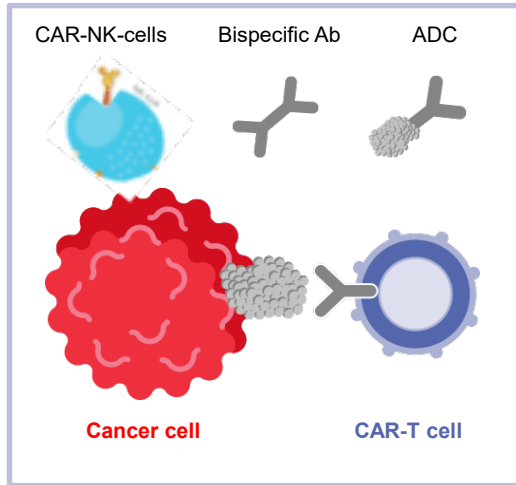
## Synovial Sarcoma and MAGE-A4 Expression

- . Synovial sarcoma represents ~10% of all soft tissue sarcomas
- . Metastatic disease has poor prognosis
- . MAGE-A4 is highly expressed in synovial sarcoma patients
  - . 2017 study<sup>1</sup> showed that 82% of synovial sarcoma tumor samples expressed MAGE-A4 by immunohistochemistry
- . ADP-A2M4 SPEAR T-cells are autologous CD4<sup>+</sup> and CD8<sup>+</sup> T-cells genetically engineered to express an affinity-enhanced T-cell receptor (TCR) that recognizes the HLA-A2-restricted peptide MAGE-A4<sub>230-239</sub> (GVYDGREHTV)

# BACKGROUND

## ADP-A2M4 SPEAR (Specific Peptide Enhanced Affinity Receptor) T-cells

For most approaches, access to extracellular proteins only



### TCR-based recognition

More options for targeting cancers by enhancing the natural immune system:

- T-cells scan HLA-peptides with TCRs
- Access to broader spectrum of extra- and intra-cellular proteins
- TCR is T-cell's natural receptor construct
- Ability to target solid tumors as opposed to normal tissues

# OBJECTIVES

- Phase 1 Dose Escalation, Multi-Tumor Study to Assess the Safety, Tolerability and Antitumor Activity of ADP-A2M4 in HLA-A2<sup>+</sup> Subjects with MAGE-A4<sup>+</sup> Tumors
- This presentation focuses on data from patients with synovial sarcoma

## Primary

- Evaluate safety and tolerability of ADP-A2M4 T-cell therapy

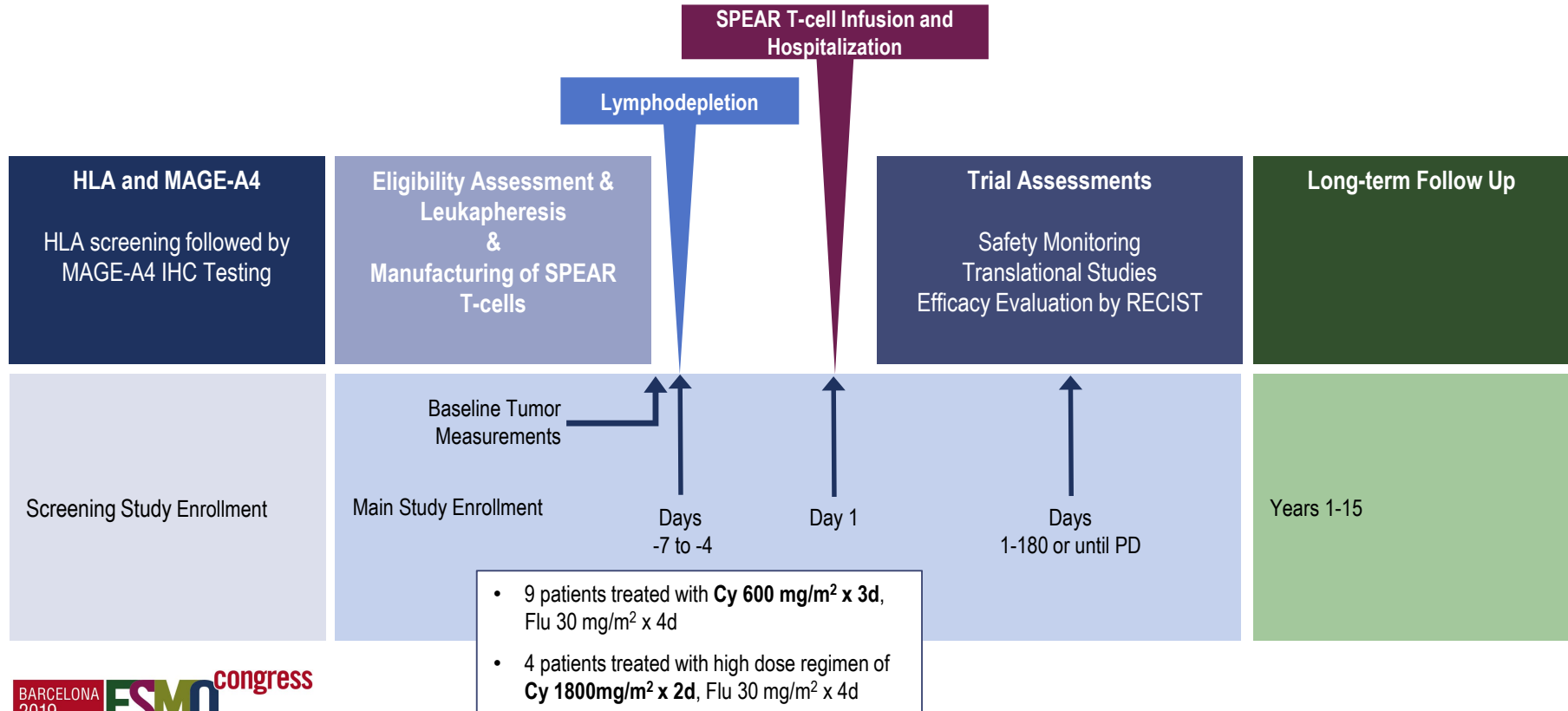
## Secondary

- Evaluate the anti-tumor activity of ADP-A2M4 T-cells
- Evaluate potential therapy-related delayed AEs for 15 years post-infusion

## Exploratory

- Evaluate the persistence, phenotype and functionality of transduced and non-transduced T-cells
- Characterize the tumor and serum factors that may influence response or resistance to ADP-A2M4 therapy

# METHODS: STUDY DESIGN



# PATIENT CHARACTERISTICS

| N=13*                             |             |  |
|-----------------------------------|-------------|--|
| Sex                               | Male: 8     | Female: 5                                    |
| Age                               | Median: 53  | Range: 31 - 76<br><i>Two patients &gt;70</i> |
| Race                              | White: 11   | Asian: 2                                     |
| ECOG status                       | ECOG 0 = 7  | ECOG 1 = 6                                   |
| Prior lines of systemic therapies | Median: 2   | Range: 1 - 5                                 |
| Cell dose x 10 <sup>9</sup>       | Median: 9.7 | Range: 3.41 - 9.98                           |

\*13<sup>th</sup> treated patient did not have post-baseline assessment at time of data cut off.

# SAFETY: ADVERSE EVENTS ≥ GRADE 3

| Preferred Term                 | Grade ≥3<br>N (%) |
|--------------------------------|-------------------|
| Leukopenia                     | 12 (92.3%)        |
| Lymphopenia                    | 12 (92.3%)        |
| Neutropenia                    | 10 (76.9%)        |
| Anemia                         | 5 (38.5%)         |
| Thrombocytopenia               | 5 (38.5%)         |
| Hypophosphatemia               | 5 (38.5%)         |
| Rash                           | 3 (23.1%)         |
| Febrile neutropenia            | 3 (23.1%)         |
| CRS                            | 2 (15.4%)         |
| Hyponatremia                   | 2 (15.4%)         |
| Acute kidney injury            | 1 (7.7%)          |
| Acute left ventricular failure | 1 (7.7%)          |
| Anal abscess                   | 1 (7.7%)          |

| Preferred Term              | Grade ≥3<br>N (%) |
|-----------------------------|-------------------|
| Aplastic anemia             | 1 (7.7%)          |
| Arrhythmia                  | 1 (7.7%)          |
| Decreased appetite          | 1 (7.7%)          |
| Endocarditis staphylococcal | 1 (7.7%)          |
| Hypermagnesemia             | 1 (7.7%)          |
| Hypocalcemia                | 1 (7.7%)          |
| Hypotension                 | 1 (7.7%)          |
| Influenza like illness      | 1 (7.7%)          |
| Pancytopenia                | 1 (7.7%)          |
| Pleural effusion            | 1 (7.7%)          |
| Sciatica                    | 1 (7.7%)          |
| Sepsis                      | 1 (7.7%)          |
| Troponin increased          | 1 (7.7%)          |



# ADVERSE EVENT OF INTEREST

## Aplastic Anemia (AA)

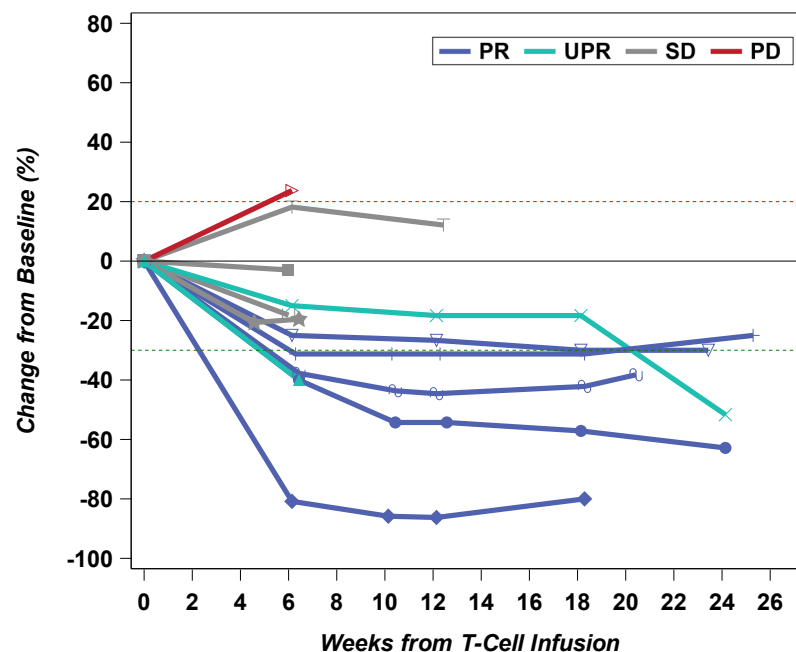
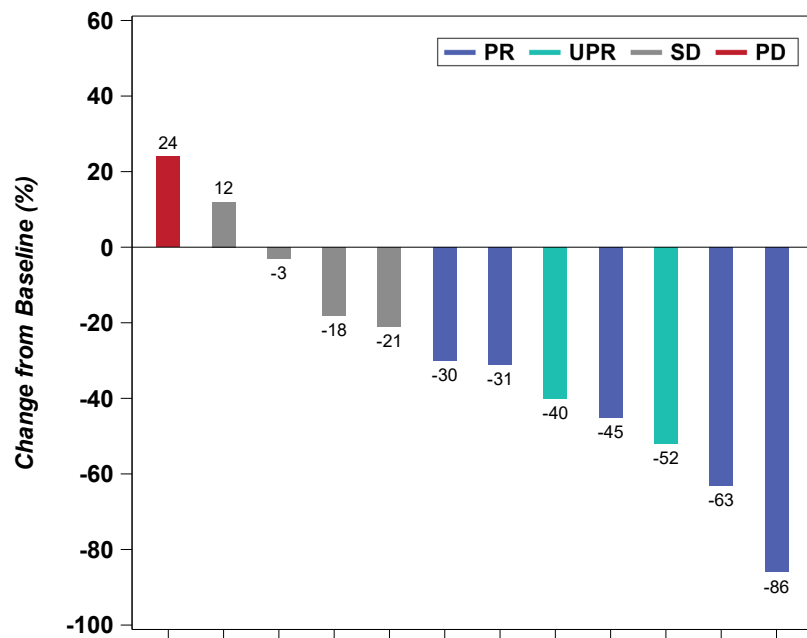
- . AA has been reported in other cell therapies using a high dose lymphodepletion regimen<sup>1</sup>
- . Three cases of fatal aplastic anemia reported in trials with three different TCRs using a lymphodepletion regimen of Flu 30 mg/m<sup>2</sup> x 4d, Cy 1800mg/m<sup>2</sup> x 2d
  - . 76-year-old patient with synovial sarcoma treated with ADP-A2M4 (MAGE-A4)
  - . 73-year-old patient with synovial sarcoma treated with NY-ESO-1 TCR<sup>1</sup>
  - . 66-year-old patient with NSCLC treated with ADP-A2M10 (MAGE-A10, NCT02989064)
- . All cases were reported to regulatory agencies
- . RT-PCR did not detect MAGE antigens in the bone marrow

Caution should be used with high-dose lymphodepletion in heavily pretreated older patients; protocols have been amended

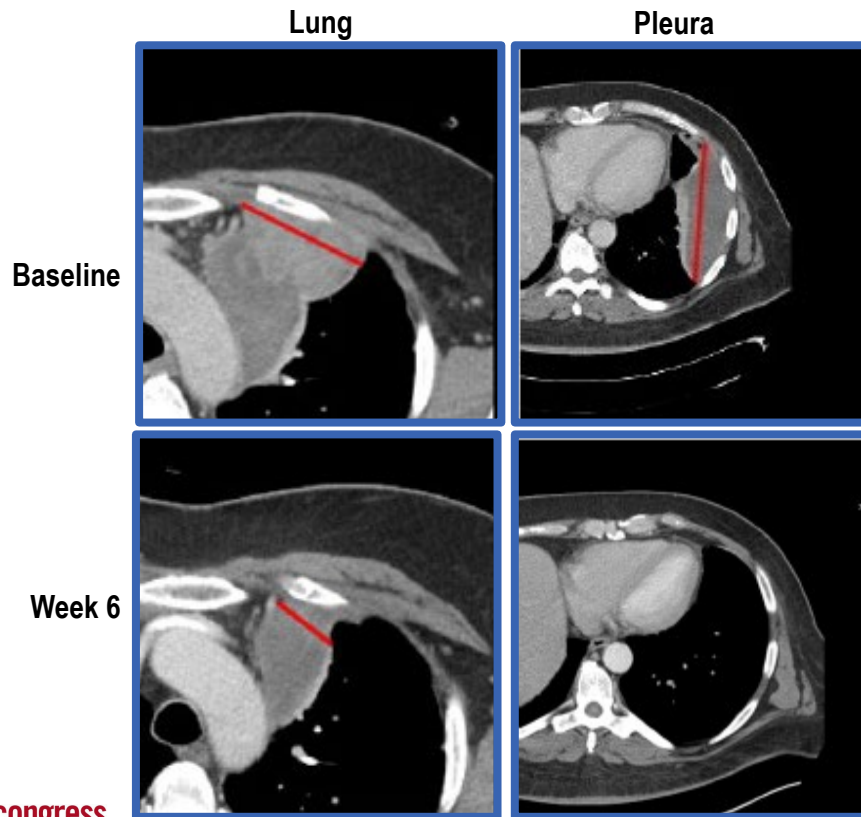
- Moderate lymphodepletion regimen: Flu 30 mg/m<sup>2</sup> x 4d, Cy 600 mg/m<sup>2</sup> x 3d
- Patients must be ≤75 years old

# ADP-A2M4 SPEAR T-CELLS INDUCE CLINICAL RESPONSES

Best overall response in 12 patients\* with post-baseline assessments



# SIGNIFICANT TUMOR REDUCTION



## 86% decrease in RECIST 1.1 and significant symptom improvement

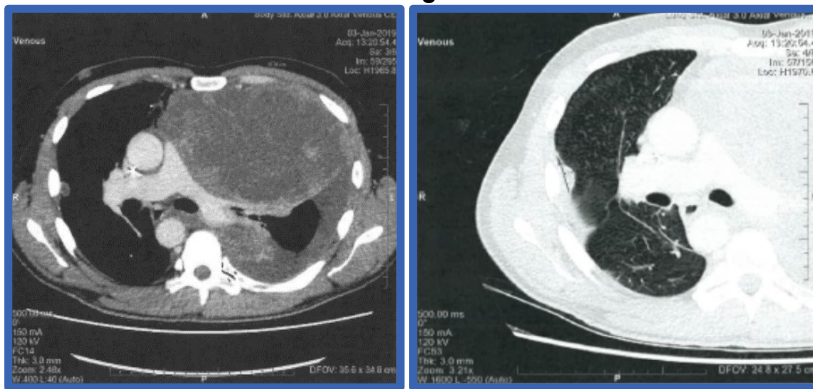
- 53-year-old male
- Longstanding history of synovial sarcoma
  - Treated with surgery, radiotherapy, and multiple chemotherapy regimens
- High MAGE-A4 expression in tumor
  - Baseline SLD\* 24 cm
- $9.87 \times 10^9$  SPEAR T-cells
- Did well post-infusion
  - Grade 1 CRS and cytopenias
- Baseline scans:
  - Extensive disease in the lung and pleura-based tumor masses
- Week 6 scans:
  - One large pleura-based lesion disappeared and others reduced via RECIST 1.1 criteria

\*Sum of the Longest Diameter of the target lesions

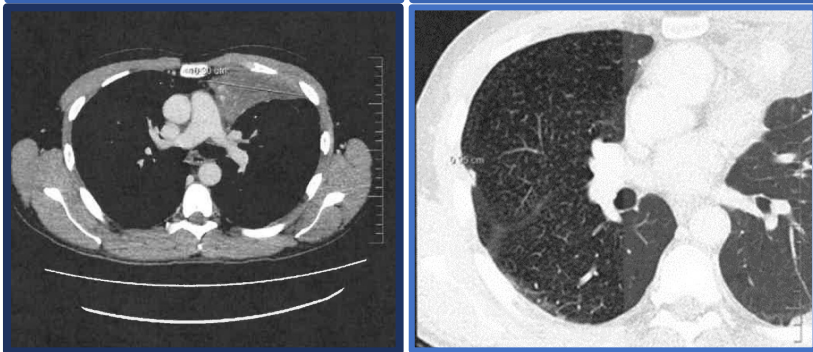
# REDUCTION IN BULKY TUMOR

## Lung

Baseline



Week 12

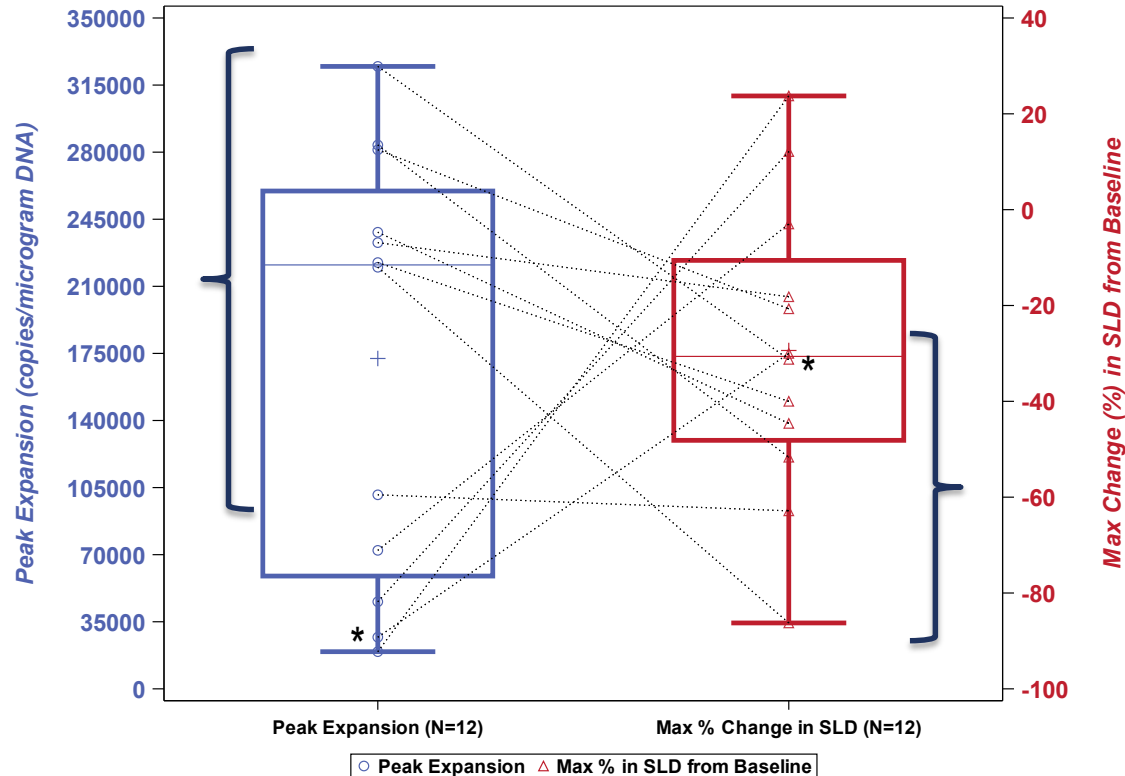


**44% decrease by RECIST 1.1 and shortness of breath resolved**

- 42-year-old male
- Diagnosed age 25
  - Recently developed metastatic disease
- Moderate MAGE-A4 expression
  - Baseline SLD 20 cm
- $9.95 \times 10^9$  SPEAR T-cells
- Did well post-infusion
  - Grade 2 CRS and cytopenias
- At baseline
  - Shortness of breath due to accumulation of fluid in pleural space
  - Tumor (left lung) displacing major blood vessels and compressing right lung
- Week 12 scans:
  - Tumor decreased and non-target lesion disappeared
  - Patient lung expanded; shortness of breath resolved

# TRANSDUCE T-CELLS PEAK EXPANSION

Higher peak expansion associated with decrease in tumor size from baseline



# CONCLUSIONS

- . ADP-A2M4 SPEAR T-cells induced clinical responses by RECIST 1.1 in 7/12 and clinical benefit rate in 11/12 assessed patients with synovial sarcoma
  - . Additional follow up needed to determine durability of responses
- . Most adverse events consistent with those typically experienced by cancer patients undergoing cytotoxic chemotherapy and/or cancer immunotherapy
  - . CRS was common in the treated patient population
- . Higher peak expansion is associated with decreases in tumor size from baseline
- . The ADP-A2M4 Phase 2 SPEARHEAD-1 Trial in synovial sarcoma and myxoid/round cell liposarcoma is now enrolling in North America, and soon in Europe (NCT04044768)

# ACKNOWLEDGMENTS

We thank the patients and their caregivers for taking part in this trial.

We thank the investigators and their teams who participated in this work.