

The Synovial Sarcoma Subset Analysis of the Multi-Histology Phase I Trial of ADP-A2M4 (MAGE-A4)

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Disclosure Information: Brian A. Van Tine (Presenter)

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- Research Grant: Merck; Tracon
- Advisory Board: Immune Design; Daiichi Sankyo
- Speaker: Adaptimmune

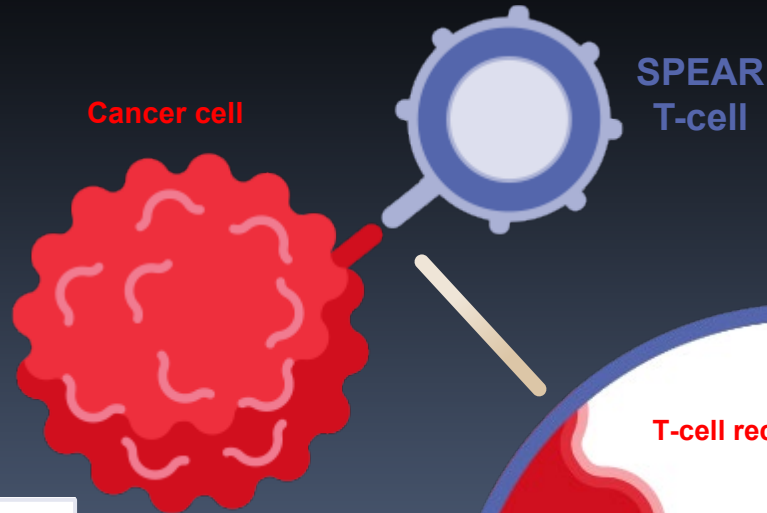
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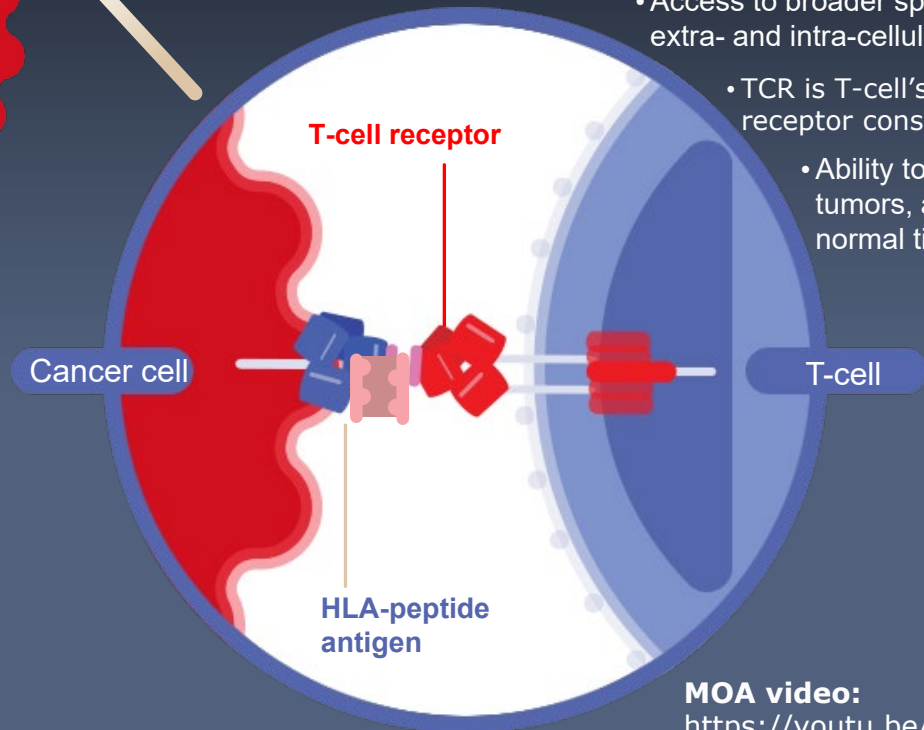
Background

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

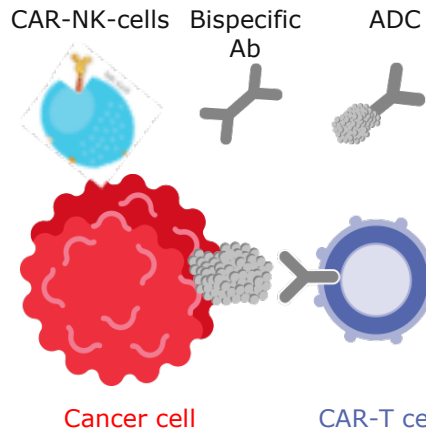


TCR-based recognition

- 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 scan natural receptor construct
 - Ability to target solid tumors, as opposed to normal tissues



For most approaches, access to extracellular proteins only



MOA video:

<https://youtu.be/zdI8IGXoQd0>

Objectives

- Phase 1 Dose Escalation, Multi-Tumor Study to Assess the Safety, Tolerability and Antitumor Activity of ADP-A2M4 in HLA-A2⁺ Subjects with MAGE-A4⁺ Tumors (NCT03132922)
- This presentation focuses on data from patients with synovial sarcoma

Primary

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

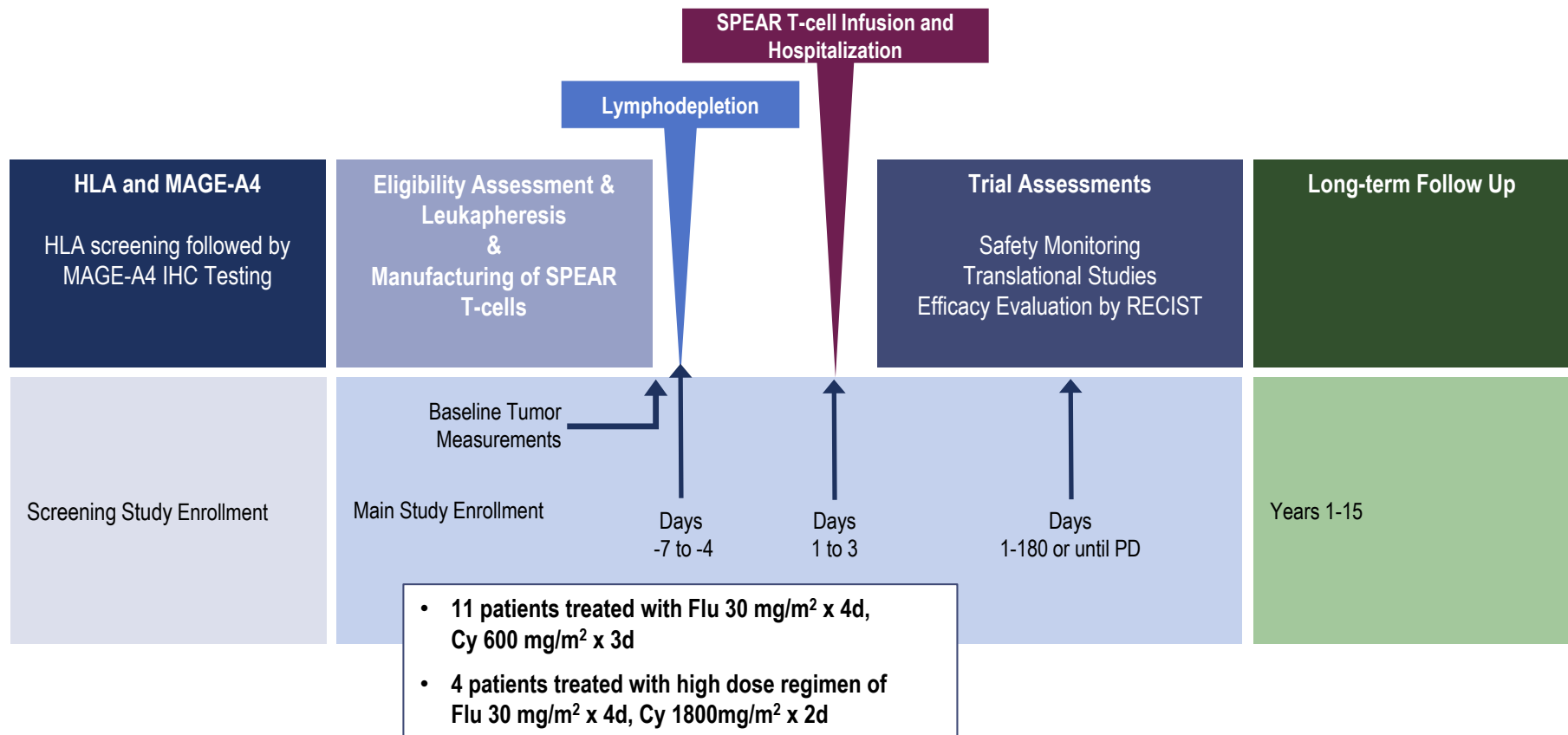
Secondary

- Evaluate the antitumor 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

Characteristic	N=15
Sex, n (%)	
Male	9 (60.0)
Female	6 (40.0)
Median age (range), years	49 (31, 76)
Race, n (%)	
White	13 (86.7)
Asian	2 (13.3)
ECOG performance status, n (%)	
0	9 (60.0)
1	6 (40.0)
Prior lines of systemic therapy, median (range)	2.5 (1, 6)
Most common prior systemic therapies, n (%)	
Ifosfamide/Anthracycline (concurrent)	9 (60.0)
Ifosfamide/Anthracycline or Anthracycline/Ifosfamide (sequential)	3 (20.0)
Ifosfamide only	3 (20.0)
Pazopanib	7 (46.7)
MAGE-A4 expression % of tumor cells 2 ⁺ /3 ⁺ by IHC, median (range)	94.3 (8.3, 100)
Cell dose x 10 ⁹ , median (range)	8.9 (3.41, 9.98)

Safety: Adverse Events Occurring in >25% of Patients

Term	Any grade, n (%)	Grade ≥ 3, n (%)
Leukopenia	14 (93.3)	14 (93.3)
Lymphopenia	14 (93.3)	14 (93.3)
Neutropenia	13 (87.7)	12 (80.0)
CRS	12 (80.0)	2 (13.3)
Fatigue	11 (73.3)	0 (0.0)
Pyrexia	10 (66.7)	0 (0.0)
Nausea	9 (60.0)	0 (0.0)
Thrombocytopenia	9 (60.0)	6 (40.0)
Anemia	8 (53.3)	7 (46.7)
Diarrhea	8 (53.3)	1 (6.7)
Sinus tachycardia/Tachycardia	7 (46.7)	1 (6.7)
Hypophosphatemia	6 (40.0)	5 (33.3)
Vomiting	6 (40.0)	0 (0.0)
Arthralgia	5 (33.3)	1 (6.7)
Decreased appetite	5 (33.3)	1 (6.7)
Dizziness	5 (33.3)	0 (0.0)
Dyspnea	5 (33.3)	0 (0.0)
Febrile neutropenia	5 (33.3)	5 (33.3)
Hypotension	5 (33.3)	1 (6.7)
Rash	5 (33.3)	3 (20.0)
ALT increased	5 (33.3)	0 (0.0)
Headache	4 (26.7)	0 (0.0)
Tumor pain	4 (26.7)	0 (0.0)

Data cut off 23-Oct 2019

Adverse Event of Interest

Aplastic Anemia (AA)

- AA has been reported in other cell therapies using a high-dose lymphodepletion regimen¹
- Three cases of fatal aplastic anemia reported in trials with three different TCRs using a lymphodepletion regimen of Flu 30 mg/m² x 4d, Cy 1800 mg/m² 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 TCR¹
 - 66-year-old patient with NSCLC treated with ADP-A2M10 (MAGE-A10, NCT02989064) (*AA cases reported at ESMO 2019*²)
- All cases were reported to regulatory agencies
- RT-PCR did not detect MAGE antigens in the bone marrow

Patients who were affected received a higher lymphodepleting regimen and were elderly; protocols have been amended

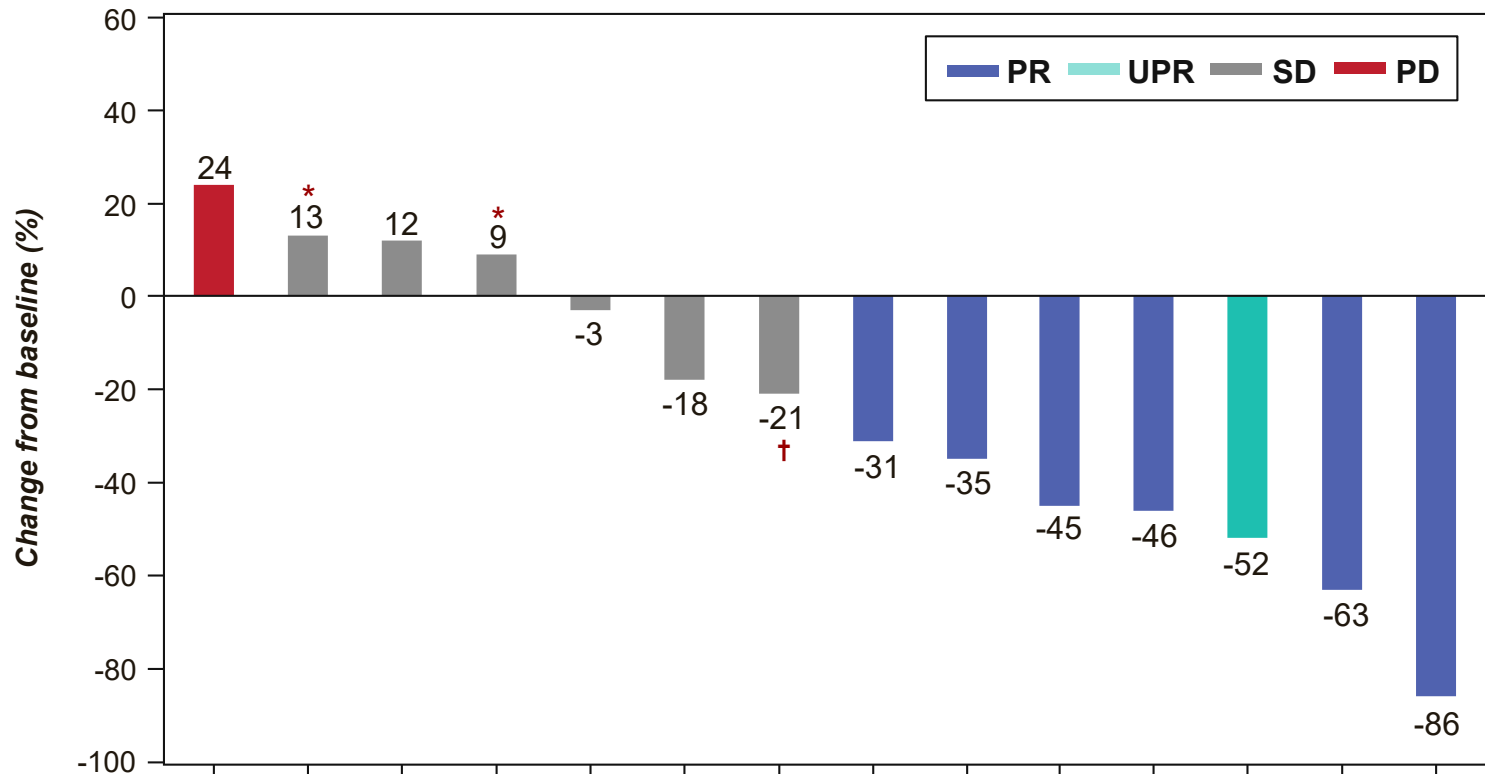
- Lower lymphodepletion regimen: Flu 30 mg/m² x 4d, Cy 600 mg/m² x 3d
- Patients must be ≤75 years old

¹ Mackall et al, *J Clin Oncol* 2016

² Van Tine et al, *ESMO* 2019

ADP-A2M4 SPEAR T-Cells Induce Clinical Responses

Best overall response in 14 patients with post-baseline assessments

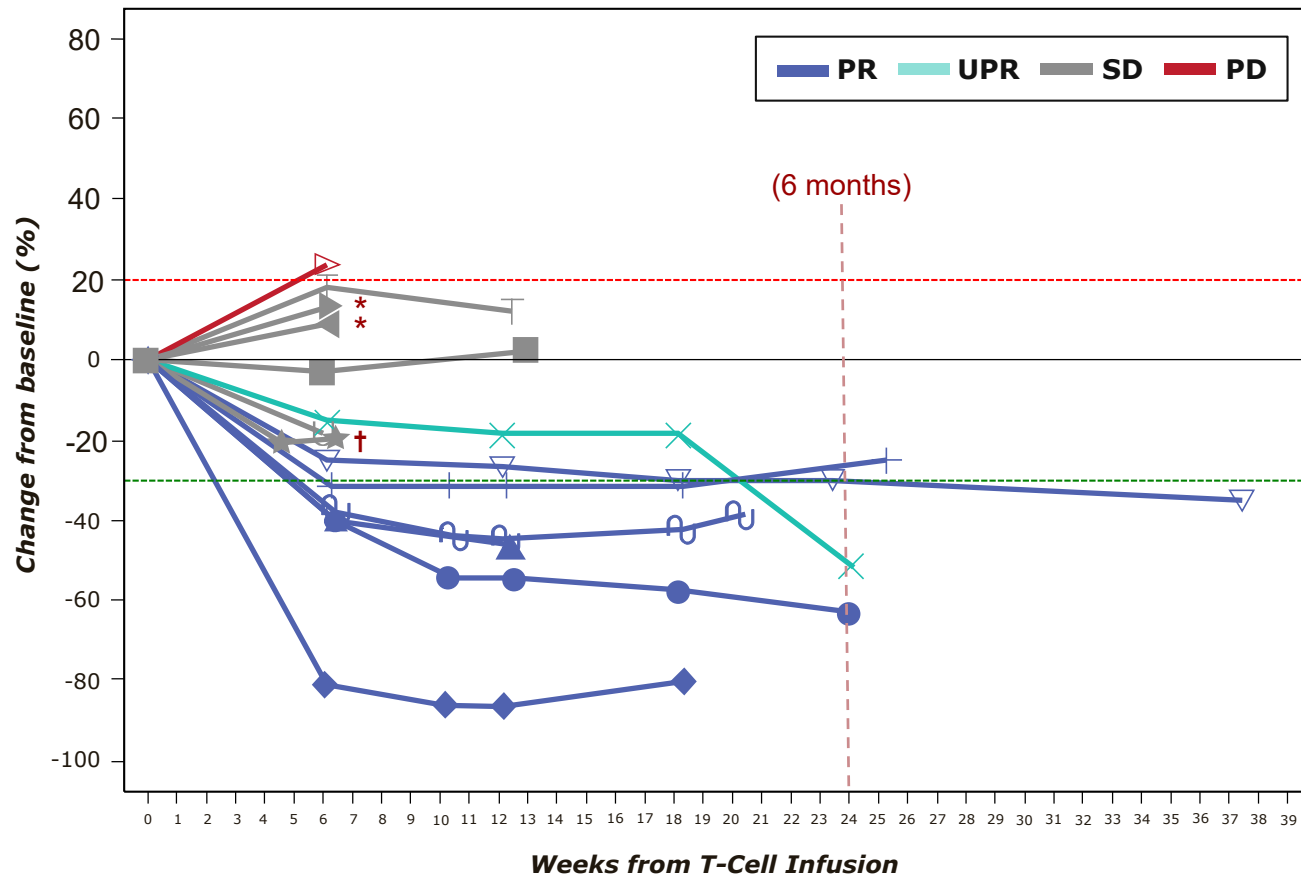


*2 patients had single scans †Patient with aplastic anemia

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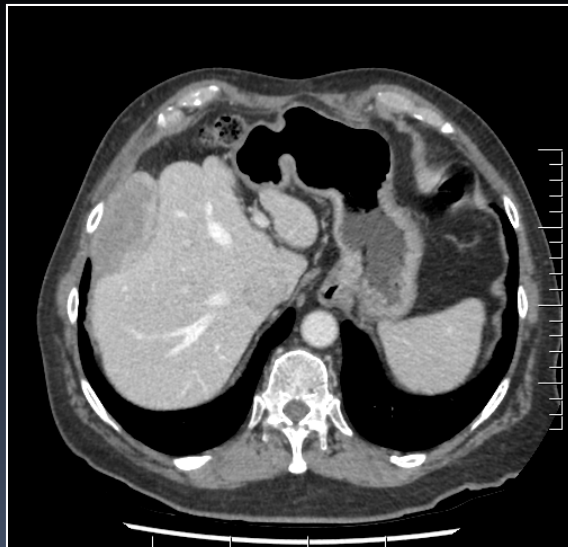
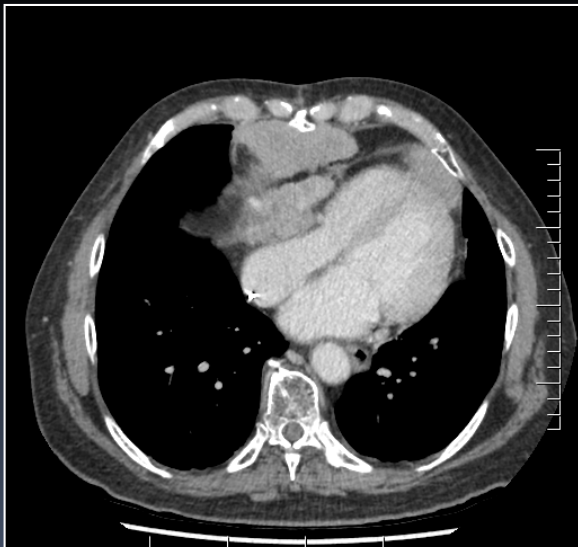


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Significant Tumor Reduction

Baseline



Week 12



46% reduction by RECIST 1.1.

- 67-year-old male
- 4-yr history of disease
- Treated with surgery and radiotherapy
- Recurrence in the pericardium treated with debulking and ifosfamide
- High MAGE-A4 expression
- SLD* was 155 mm
- 9.95×10^9 SPEAR T-cells
- Baseline scans
 - Disease in the pericardium and liver
- Post-infusion
- Grade 2 CRS and cytopenias
- Week 12 scans
 - Reduction in target tumor lesions

(*SLD = Sum of the Longest Diameter of the target lesions)

Significant Tumor Reduction

Lung

Pleura

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
- 9.87×10^9 SPEAR T-cells
- Baseline scans
 - Extensive disease in the lung and pleura-based tumor masses
- Post-infusion
 - Grade 1 CRS and cytopenias
- Week 6 scans
 - One large pleura-based lesion disappeared and others reduced via RECIST 1.1 criteria

(*SLD = Sum of the Longest Diameter of the target lesions)

Reduction in Bulky Tumor

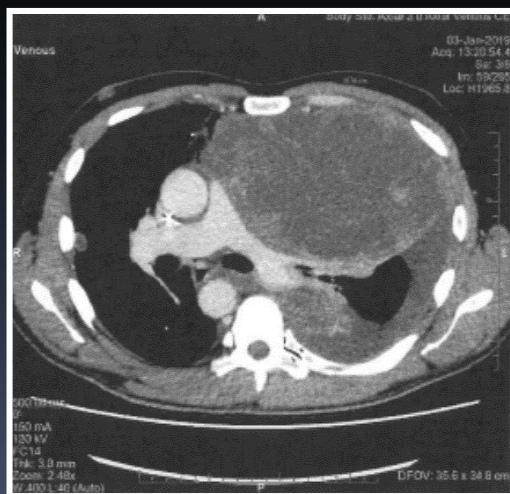
Lung

44% decrease by RECIST 1.1 and shortness of breath resolved

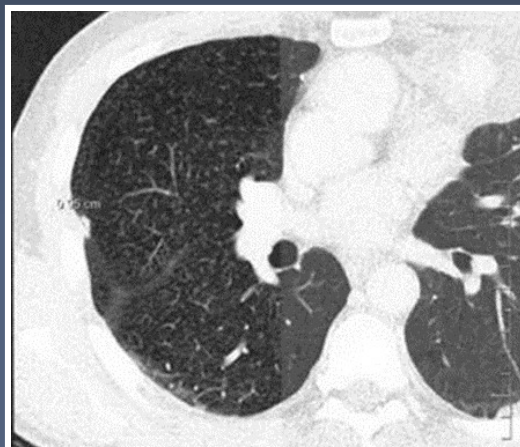
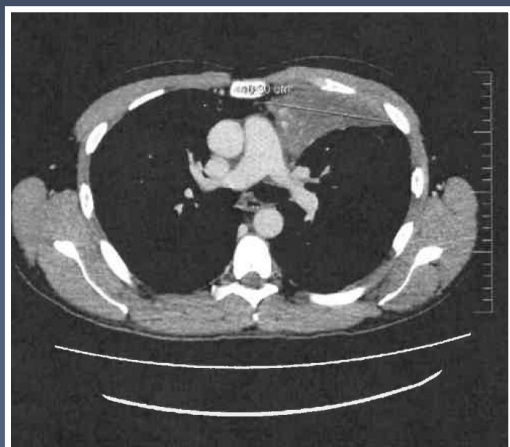
- 42-year-old male
- Diagnosed age 25 years
 - Recently developed metastatic disease
- Moderate MAGE-A4 expression
 - Baseline SLD* 20 cm
- 9.95×10^9 SPEAR T-cells
- Baseline symptoms and scans
 - Shortness of breath due to accumulation of fluid in pleural space
 - Tumor (left lung) displacing major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

(*SLD = Sum of the Longest Diameter of the target lesions)

Baseline

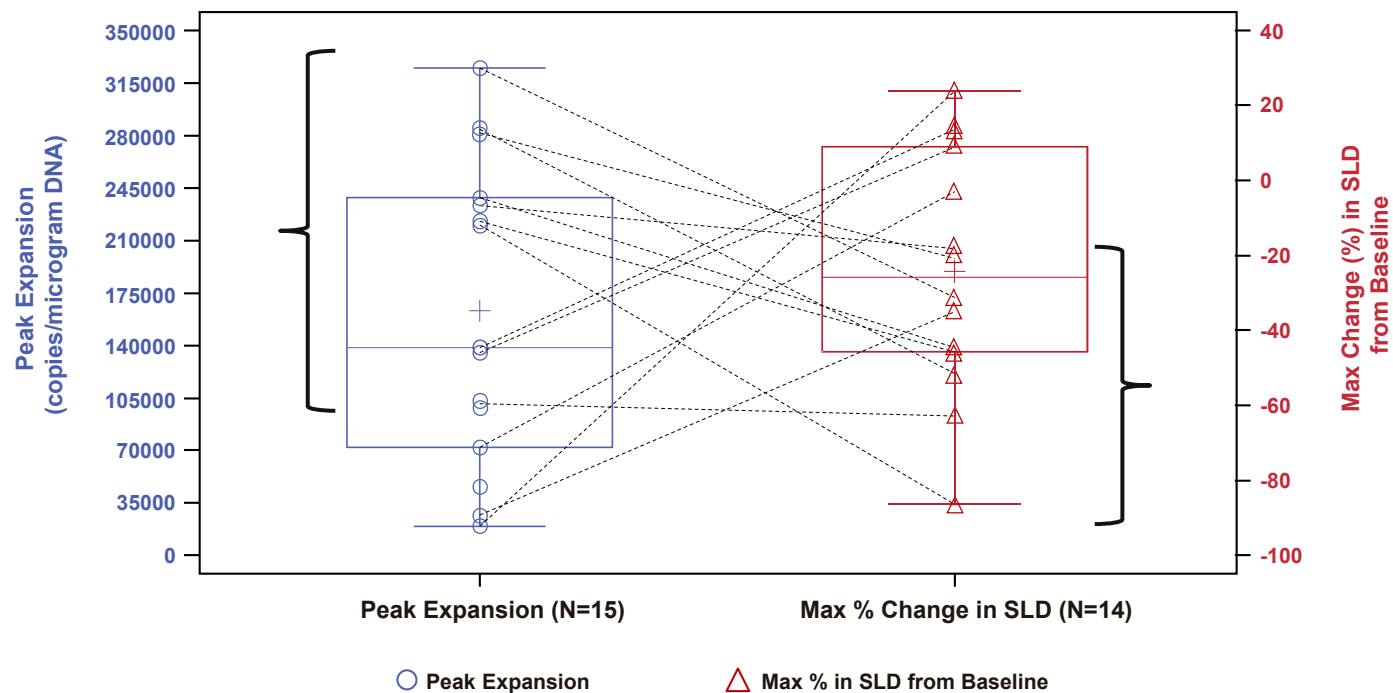


Week 12



Transduced T-Cells Peak Expansion

Higher peak expansion associated with decrease in tumor size from baseline



Data cut off 23-Oct 2019

Conclusions

- ADP-A2M4 SPEAR T-cells induced clinical responses by RECIST 1.1 in 7/14 and disease control in 13/14 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)

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