Final Analysis from SPEARHEAD-1 Cohort 1 of Afamitresgene Autoleucel ("Afami-cel" [Formerly ADP-A2M4]) in Advanced Synovial Sarcoma and Myxoid/Round Cell Liposarcoma

Brian A. Van Tine,[1] Dejka M. Araujo,[2] Jean-Yves Blay,[3] Axel Le Cesne,[4] Kristen Ganjoo,[5] Claudia Maria Valverde Morales,[6] Albiruni Ryan Abdul Razak,[7] Scott Schuetze,[8] Michael J. Wagner,[9] Erin Van Winkle,[10] Cheryl McAlpine,[11] Jean-Marc Navenot,[10] Martin Isabelle,[11] Robyn Broad, PhD,[11] Revashnee Naidoo,[11] Ruoxi Wang,[11] Dzmitry Batrakou,[11] Thejo Annareddy,*[10] Swethajit Biswas,*[11] Dennis Williams,[10] Elliot Norry,[10] Sandra P. D'Angelo[12]

[1]**Washington University School of Medicine, St. Louis, MO, USA**; [2]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [3]Centre Léon Bérard, Lyon, France; [4]Institut Gustave Roussy-Gustave Roussy Cancer Center-DITEP, Villejuif Cedex, France; [5]Stanford Cancer Center, Palo Alto, CA, USA; [6]Vall D'Hebron University Hospital, Barcelona, Spain; [7]Princess Margaret Cancer Centre, Toronto, ON, Canada; [8]University of Michigan, Ann Arbor, MI, USA; [9]University of Washington/Fred Hutch/Seattle Cancer Care Alliance, Seattle, WA, USA; [10]Adaptimmune, Philadelphia, PA, USA; [11]Adaptimmune, Abingdon, Oxfordshire, UK; [12]Memorial Sloan Kettering Cancer Center, New York, NY, USA

*At the time the study was conducted

2022 ctos® ANNUAL MEETING

ctos
Bringing together the world's sarcoma specialists

Disclosure Information

Brian A. Van Tine, MD, PhD (presenter)

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: Oncothyreon; 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; Hoffmann-LaRoche; Caris Life Sciences; Morphotek; Soligenix; Eleison Pharmaceuticals; AADi; Immune Design; TRACON Pharmaceuticals; NanoCarrier; Advenchen Laboratories; Karyopharm Therapeutics; Hutchison MediPharma

Afamitresgene Autoleucel
“Afami-cel” (Formerly ADP-A2M4)

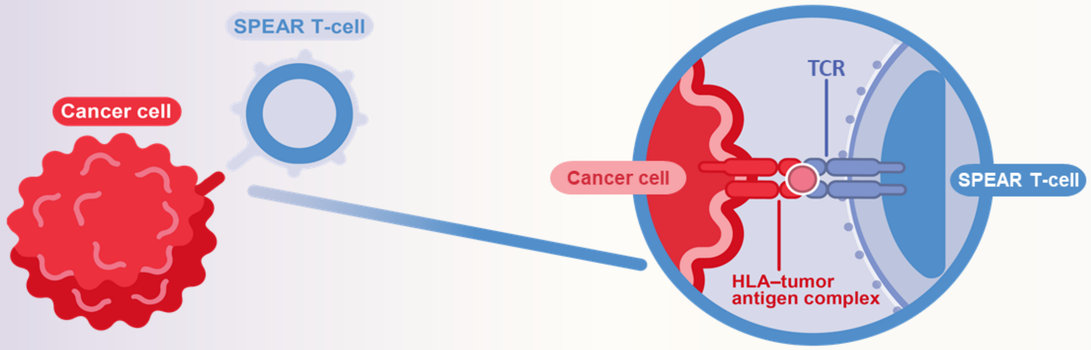
Background

- Patients with advanced synovial sarcoma or MRCLS have a high unmet medical need for more effective therapies
- MAGE-A4 is expressed in synovial sarcoma and MRCLS[1,2]

Afami-cel

- SPEAR T-cells target MAGE-A4+ tumors

SPEAR T-Cell Mechanism of Action



T-cell receptor-based recognition

- T-cells scan HLA peptides presented on diseased cells, including tumor cells
- TCRs targeting peptide antigens bind and activate the T-cell
- Natural TCRs can target both intra and extracellular antigens
- Using TCRs engineered to recognize and bind to specific cancer peptides, SPEAR T-cells can target solid tumors

HLA, human leukocyte antigen; MAGE-A4, melanoma-associated antigen A4; MRCLS, myxoid/round cell liposarcoma; SPEAR, specific peptide enhanced affinity receptor; TCR, T-cell receptor. 1. Iura K. Virchows Archiv 2017;471:383–392. 2. Wang T. et al. Cancer Res 2022;82(12_Supplement):LB001.

2022 ctos® ANNUAL MEETING

Presented by:
Brian A. Van Tine, MD, PhD

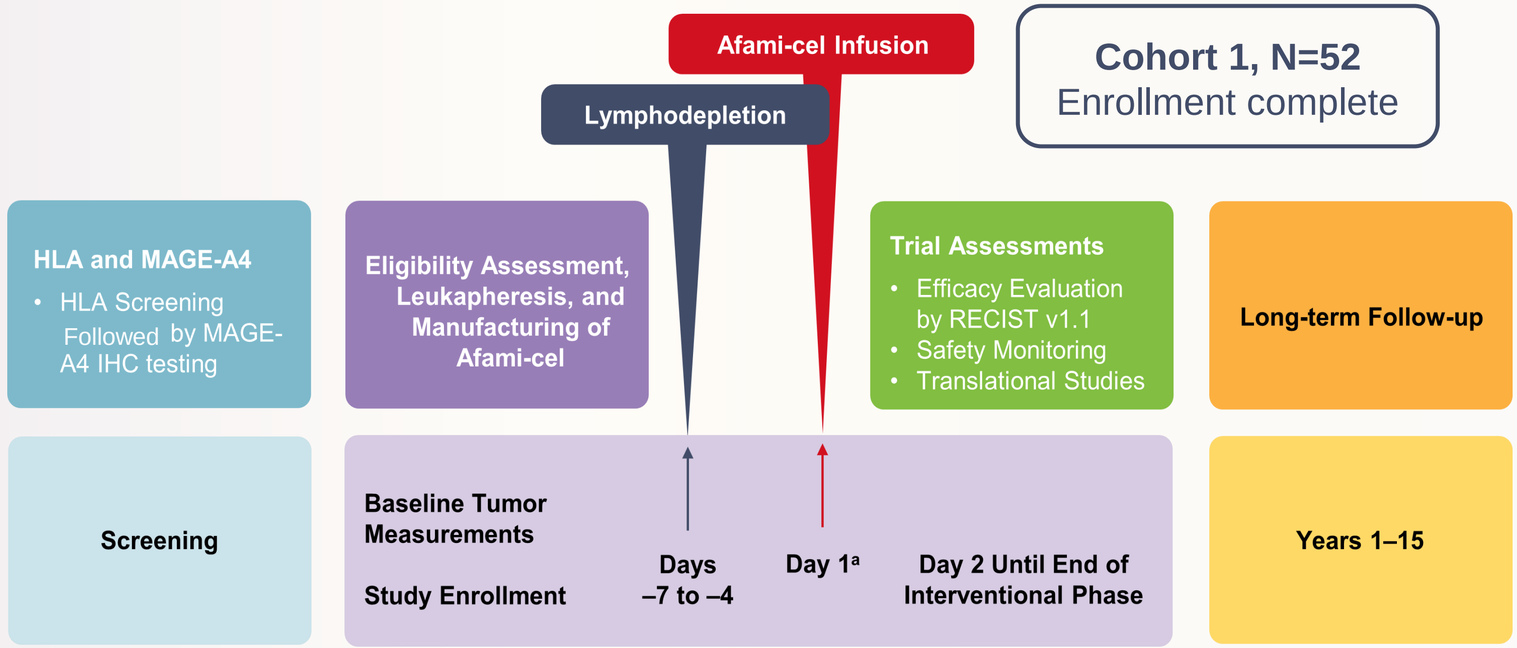
ctos
Bringing together the world’s sarcoma specialists

SPEARHEAD-1 (NCT04044768) Trial Design

Phase 2 Trial of Afami-cel in Patients with Advanced Synovial Sarcoma or MRCLS

Key eligibility criteria

- ECOG performance status 0 or 1
- HLA-A*02 positive
- Aged ≥16 and ≤75 years
- Tumor MAGE-A4 expression by immunohistochemistry
- Must have previously received either an anthracycline- or ifosfamide-containing regimen



Primary endpoint

ORR per RECIST v1.1 by independent review

Key secondary endpoints

- AEs and serious AEs
- AEs of special interest
- Duration of response
- Time to response
- Progression-free and overall survival

[a]Patient is hospitalized for T-cell infusion and discharged at the discretion of the investigator. AE, adverse event; ECOG, Eastern Cooperative Oncology Group; HLA, human leukocyte antigen; IHC, immunohistochemistry; MAGE-A4, melanoma-associated antigen A4; MRCLS, myxoid/round cell liposarcoma; ORR, overall response rate; RECIST, Response Evaluation Criteria in Solid Tumors.

2022 ctos® ANNUAL MEETING

Presented by:

Brian A. Van Tine, MD, PhD

ctos

Bringing together the world's sarcoma specialists

Cohort 1: Baseline Patient and Disease Characteristics

Characteristic, mITT	N=52
Sex, n (%)	
Male	28 (53.8)
Female	24 (46.2)
Age, years, median (range)	41.0 (19–73)
Race, n (%)	
White	45 (86.5)
Black or African American	2 (3.8)
Asian	3 (5.8)
Missing	2 (3.8)
Primary tumor type, n (%)	
Synovial sarcoma	44 (84.6)
MRCLS	8 (15.4)
Geographic region, n (%)	
North America	37 (71.2)
Europe/UK	15 (28.8)

Characteristic, mITT	N=52
MAGE-A4 expression, median H-score (range)	232.9 (112–300)
Baseline target tumor lesion(s) ≥10 cm, n (%)	27 (51.9)
ECOG performance status, n (%)	
0	27 (51.9)
1	24 (46.2)
2	1 (1.9)
Prior lines of systemic therapy, median (range)	3 (1–12)
Most common prior systemic therapy, n (%)	
Doxorubicin	49 (94.2)
Ifosfamide	48 (92.3)
Pazopanib	21 (40.4)
Received bridging therapy, n (%)	20 (38.5)
Pazopanib	11 (55)
Ifosfamide	3 (15)
Trabectedin	3 (15)
Other (doxorubicin, docetaxel, pegylated liposomal doxorubicin hydrochloride)	3 (15)

Data cut-off August 29, 2022. Cohort 1 data. H-score: 3 x percentage of strongly staining cells + 2 x percentage of moderately staining cells + percentage of weakly staining cells. ECOG, Eastern Cooperative Oncology Group; MAGE-A4, melanoma-associated antigen A4; mITT, modified intent-to-treat population; MRCLS, myxoid/round cell liposarcoma.

Presented by:
Brian A. Van Tine, MD, PhD

Responses per RECIST v1.1 by Independent and Investigator Reviews

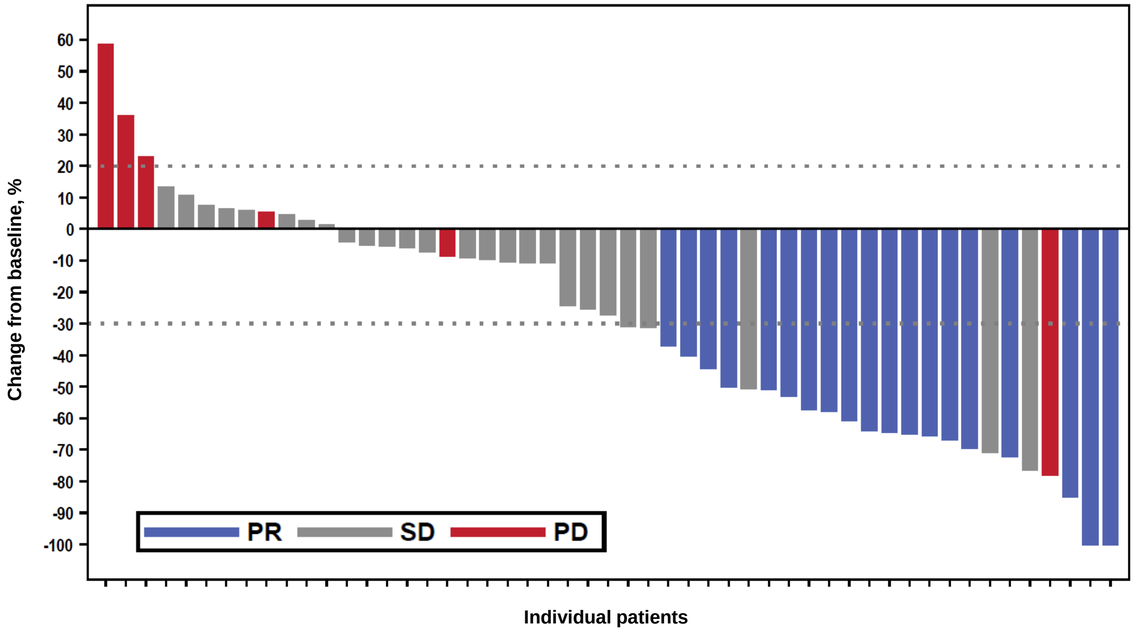
	Independent review N=52	Investigator review N=52
Complete response, n (%)	0 (0)	2 (3.8)
Partial response, n (%)	19 (36.5)	17 (32.7)
Stable disease, n (%)	27 (51.9)	25 (48.1)
Progressive disease, n (%)	6 (11.5)	8 (15.4)
Overall response rate, % (95% CI)	**36.5 (23.62–51.04)**	**36.5 (23.62–51.04)**
Synovial sarcoma, n=44	38.6 (24.36–54.50)	40.9 (26.34–56.75)
MRCLS, n=8	25.0 (3.19–65.09)	12.5 (0.32–52.65)

- High level of concordance between independent and investigator reviews
- Primary endpoint uses independent review, which is shown going forward

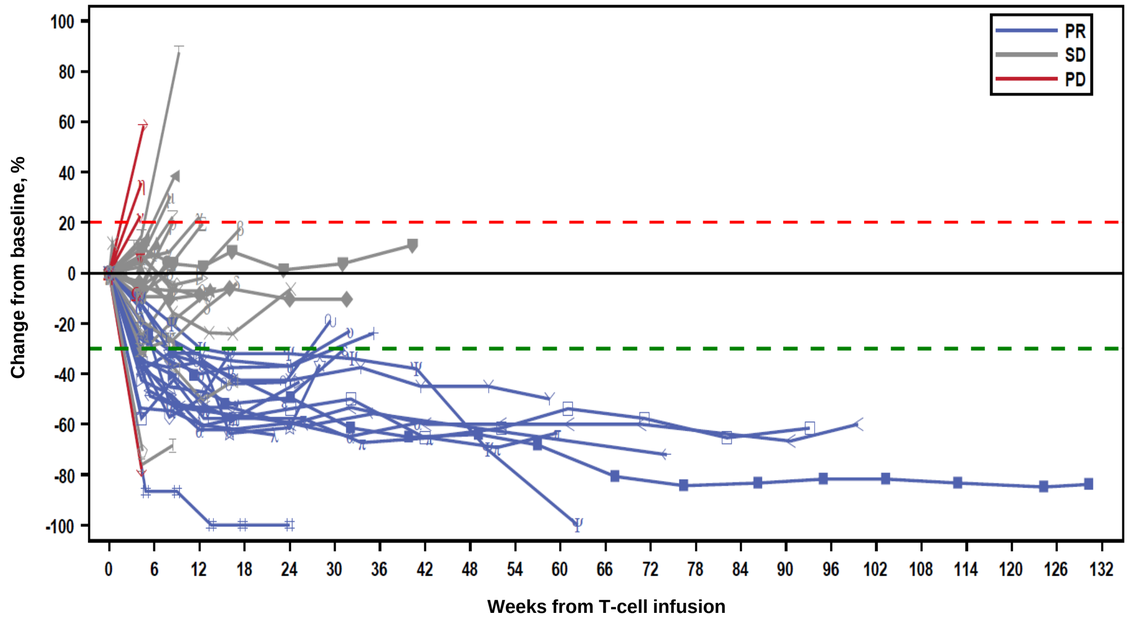
Data cut-off August 29, 2022. Cohort 1 data. Overall response rate = complete responses + partial responses. MRCLS, myxoid/round cell liposarcoma; RECIST, Response Evaluation Criteria in Solid Tumors.

Presented by:
Brian A. Van Tine, MD, PhD

Change From Baseline in Target Lesion SLD Colored by Best Overall Responses



Change From Baseline in Target Lesion SLD Over Time Colored by Best Overall Responses



Median time to response

- 4.9 weeks (range: 4.1–12.1)

Median duration of response

- Synovial sarcoma: 50.3 weeks (range: 11.7–122.0+)
- MRCLS: 18.2 weeks (range: 12.4–24.0)

8 responses ongoing as of the data cut-off

Data cut-off August 29, 2022. Cohort 1 data. Data represent percent changes from baseline in sum of diameters (SLD for non-nodal lesions and short axis for nodal lesions) in target lesions through progression or prior to surgical resection
MRCLS, myxoid/round cell liposarcoma; PD, progressive disease; PR, partial response; SLD, sum of longest diameters; SD, stable disease.

Presented by:
Brian A. Van Tine, MD, PhD

Treatment Emergent Serious Adverse Events and Adverse Events of Special Interest

Treatment emergent SAE in ≥3% of patients, preferred term	N=52, n (%)	
	Any causality	Related to T-cell infusion
Any	26 (50.0)	13 (25.0)
Cytokine release syndrome	5 (9.6)	5 (9.6)
Pleural effusion	3 (5.8)	1 (1.9)
Abdominal pain	2 (3.8)	0 (0)
Back pain	2 (3.8)	0 (0)
Deep vein thrombosis	2 (3.8)	1 (1.9)
Empyema	2 (3.8)	1 (1.9)
Pulmonary embolism	2 (3.8)	1 (1.9)
Pyrexia	2 (3.8)	2 (3.8)
Spinal cord compression	2 (3.8)	0 (0)
Tumor pain	2 (3.8)	0 (0)

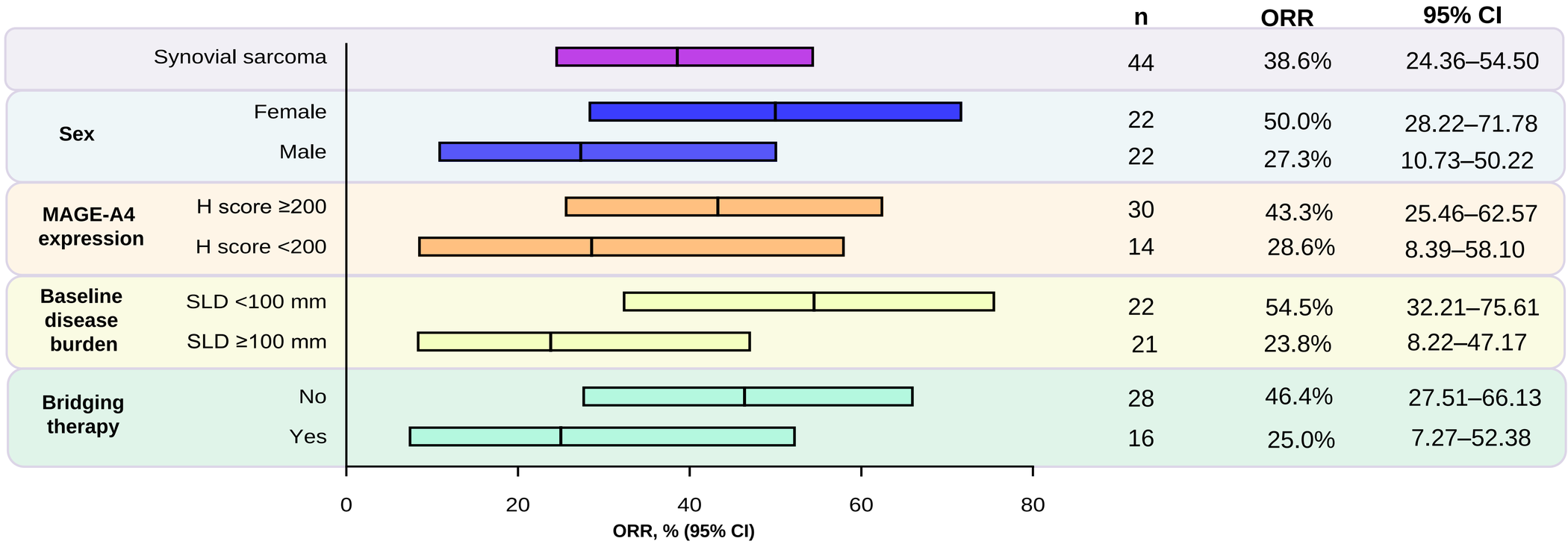
There were no Grade 5 events

Adverse events of special interest	N=52
Cytokine release syndrome	
Any grade, n (%)	37 (71.2)
Grade ≥3, n (%)	1 (1.9)
Time to onset, days, median (range)	2 (1–23)
Time to resolution, days, median (range)	3 (1–14)
Tocilizumab use, n (%)	19 (36.5)
Grade ≥3 cytopenia at any time after lymphodepletion	
Lymphopenia	50 (96.2)
Neutropenia	44 (84.6)
Leukopenia	42 (80.8)
Anemia	16 (30.8)
Thrombocytopenia	10 (19.2)
Grade ≥3 cytopenia at Week 4 post-infusion	
Any, n (%)	10 (19.2)
Neutropenia, n (%)	5 (9.6)
Anemia, n (%)	4 (7.7)
Thrombocytopenia, n (%)	3 (5.8)
Immune effector cell-associated neurotoxicity syndrome	
Any grade, n (%)	1 (1.9)
Grade ≥3, n (%)	0 (0)

Data cut-off August 29, 2022. Cohort 1 data. SAE, serious adverse event.

Presented by:
Brian A. Van Tine, MD, PhD

Overall Response Rate in Subgroups of Patients with Synovial Sarcoma

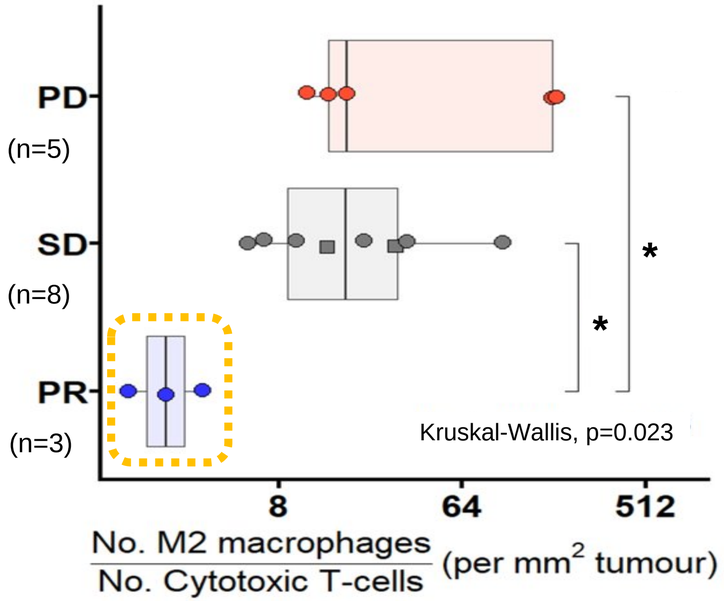


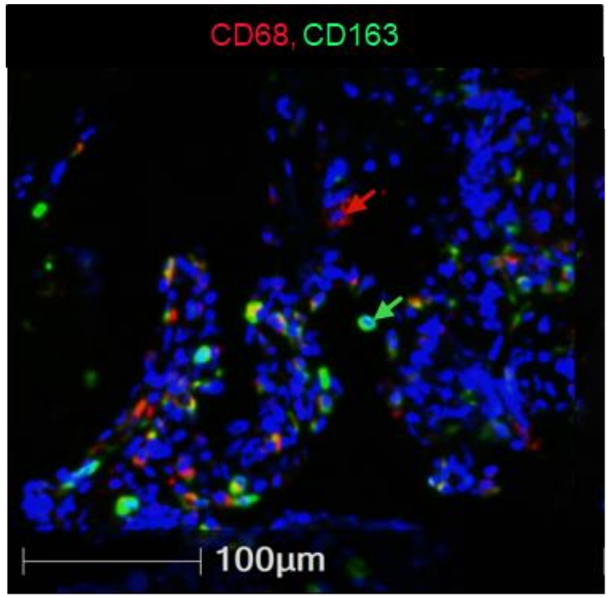
Responses were similar among patients stratified by age, number of prior lines of systemic therapy, transduced cell dose, and cytokine release syndrome

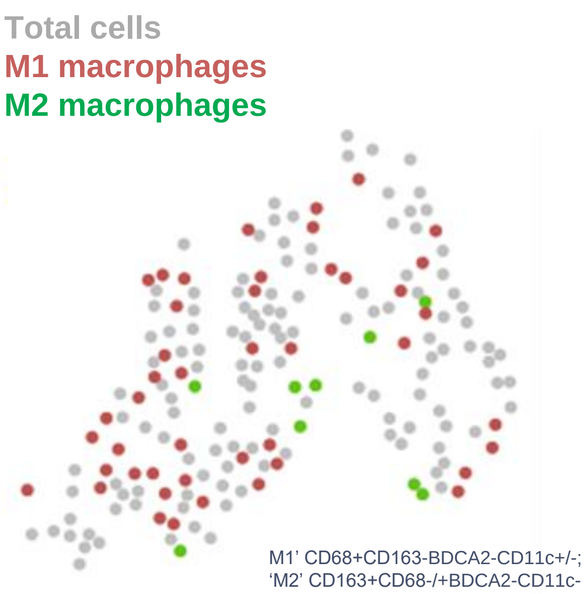
Data cut-off August 29, 2022. Cohort 1 data. Overall response rate = complete responses + partial responses. Error bars show upper and lower 95% CIs based on exact Clopper-Pearson (exact binomial) method. MAGE-A4, melanoma-associated antigen A4; ORR, overall response rate; SLD, sum of longest diameters.

Presented by:
Brian A. Van Tine, MD, PhD

Afami-cel Responders Show Shift in Tumour Microenvironment Balance from Immuno-suppressive to Pro-immune







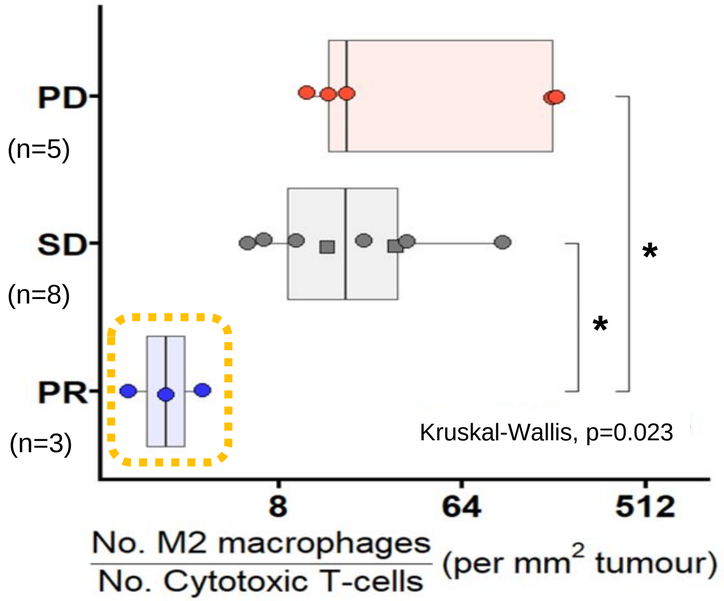
Better RECIST v1.1 responses associated with:

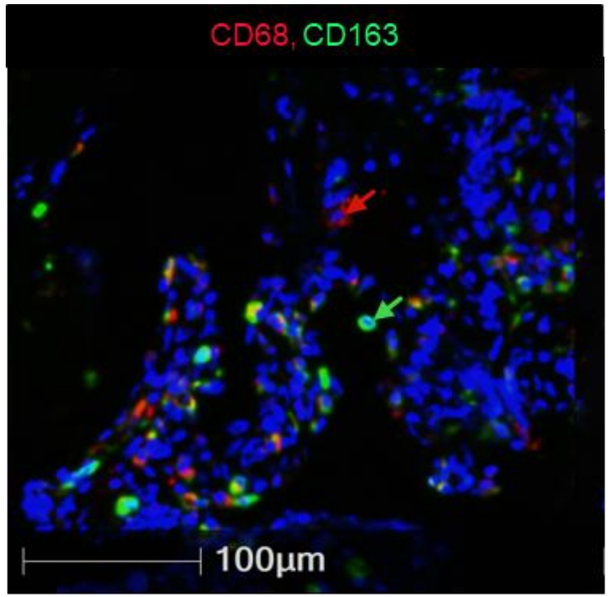
- Lower M2 immuno-suppressor macrophage to cytotoxic T-cell ratio after afami-cel infusion
- Greater M1 pro-immune macrophages at baseline and increases post-infusion (data not shown)

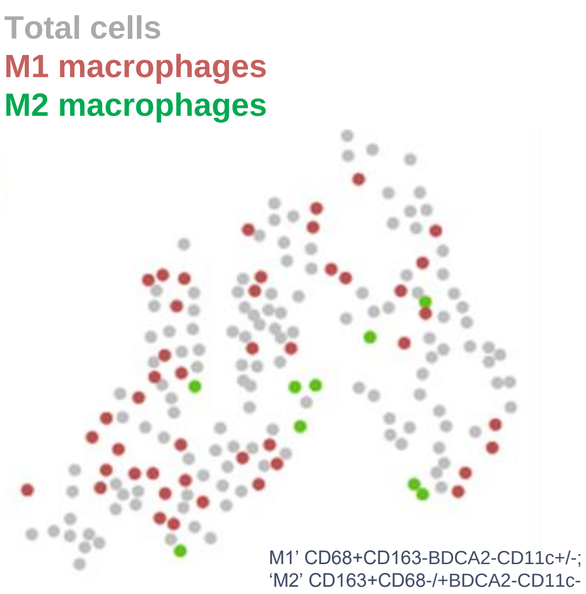
Data cut-off August 29, 2022. Cohort 1 data. PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

Presented by:
Brian A. Van Tine, MD, PhD

Afami-cel Responders Show Shift in Tumour Microenvironment Balance from Immuno-suppressive to Pro-immune







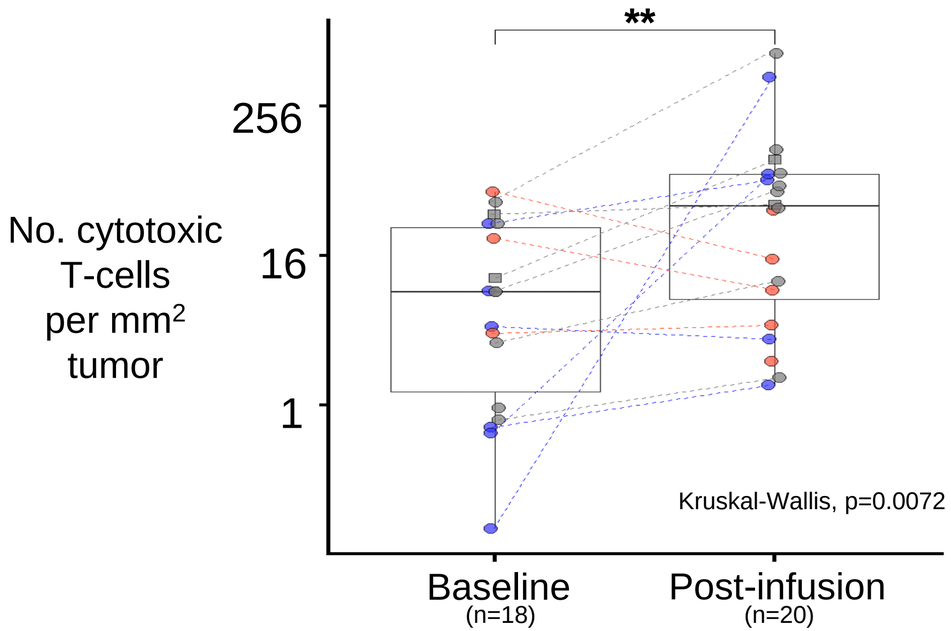
Better RECIST v1.1 responses associated with:

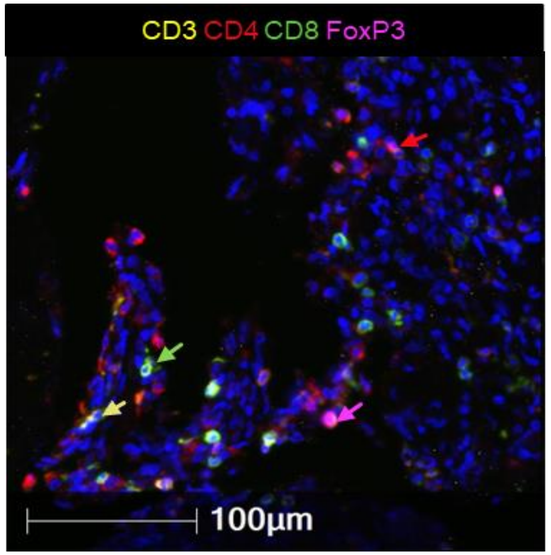
- Lower M2 immuno-suppressor macrophage to cytotoxic T-cell ratio after afami-cel infusion
- Greater M1 pro-immune macrophages at baseline and increases post-infusion (data not shown)

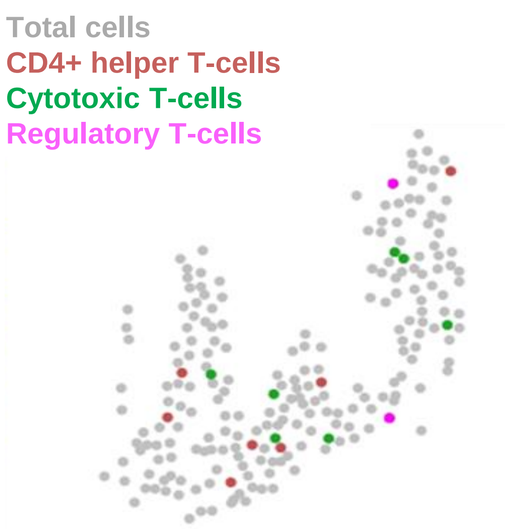
Data cut-off August 29, 2022. Cohort 1 data. PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.

Presented by:
Brian A. Van Tine, MD, PhD

Afami-cel Provokes Cytotoxic T-cell Tumor Infiltrate







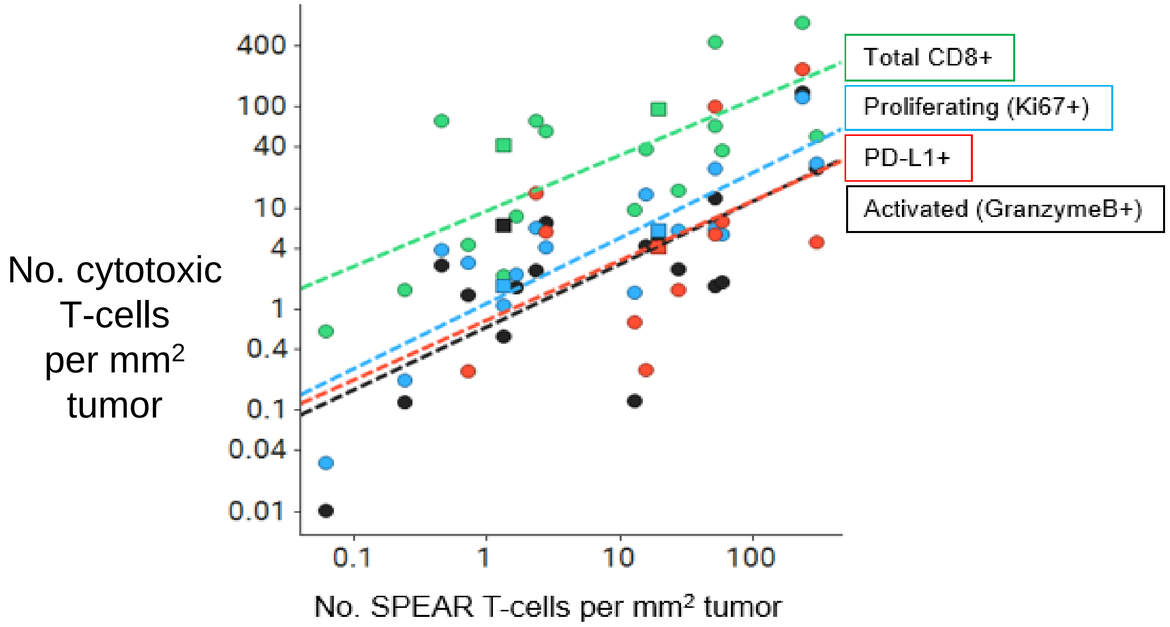
T-cells: 'Cytotoxic' CD3+CD8+; 'Helper' CD3+CD4+; 'Regulatory' CD3+CD4+FoxP3+

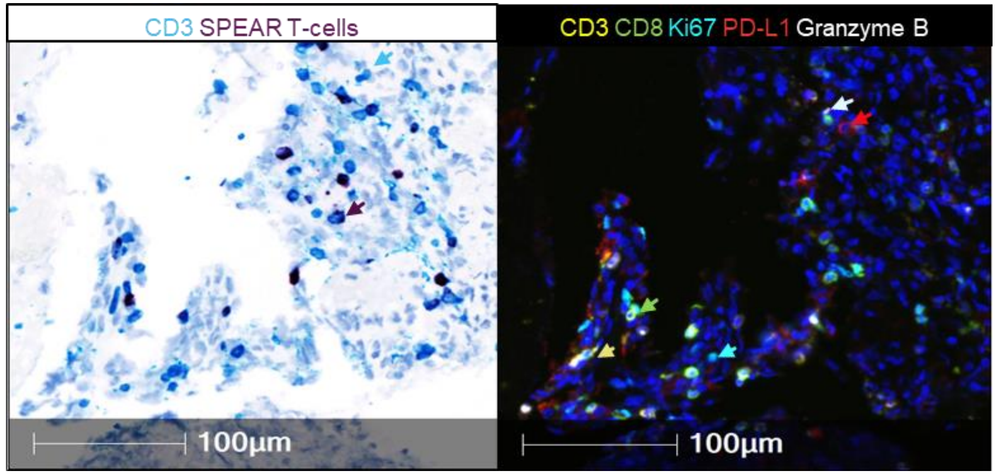
Significantly greater number of cytotoxic T-cells detected in tumor biopsies after afami-cel infusion

Data cut-off August 29, 2022. Cohort 1 data.

Presented by:
Brian A. Van Tine, MD, PhD

Intratumoral Afami-cel Mechanistically Drives Infiltration of Activated and Proliferative Cytotoxic T-cells





Spearman correlation with no. SPEAR-T cells (n=21):Total CD8+ R=0.51, p=0.0189; Proliferating R=0.6, p=0.00369; PD-L1+ R=0.56, p=0.0077; Activated R=0.4, p=0.070

- Higher afami-cel infiltration is associated with increased activated and proliferative cytotoxic T-cells in the tumor microenvironment
- Trend for greater tumoral afami-cel infiltration with greater peripheral exposure (data not shown)

Data cut-off August 29, 2022. Cohort 1 data. SPEAR, specific peptide enhanced affinity receptor.

Presented by:
Brian A. Van Tine, MD, PhD

Conclusions

- Afami-cel is efficacious in heavily pre-treated patients with synovial sarcoma and MRCLS
  - Overall response rate in synovial sarcoma is 38.6%
  - Responses are durable: median of 50.3 weeks in synovial sarcoma
- Safety profile included cytokine release syndrome and reversible hematologic toxicities
- Responses were observed across all subpopulations
  - Higher response rates were observed in patients who are female, had higher MAGE-A4 expression, had lower disease burden at baseline, or did not require bridging therapy
- Translational data show that afami-cel mechanistically drives tumoral infiltration of activated and proliferative cytotoxic T-cells, shifting balance from immuno-suppressive to pro-immune
- SPEARHEAD-1 is ongoing
  - Cohort 1 has completed treatment and will be used to support Adaptimmune's Biologics License Application submission
  - Additional access to afami-cel is ongoing in Cohort 2

Presented by:
Brian A. Van Tine, MD, PhD

Acknowledgements

- We thank the **patients** and their **caregivers** for taking part in this trial
- We thank the **investigators** and their **teams** who participated
- For further questions, please contact: bvantine@wustl.edu

Presented by:

Brian A. Van Tine, MD, PhD