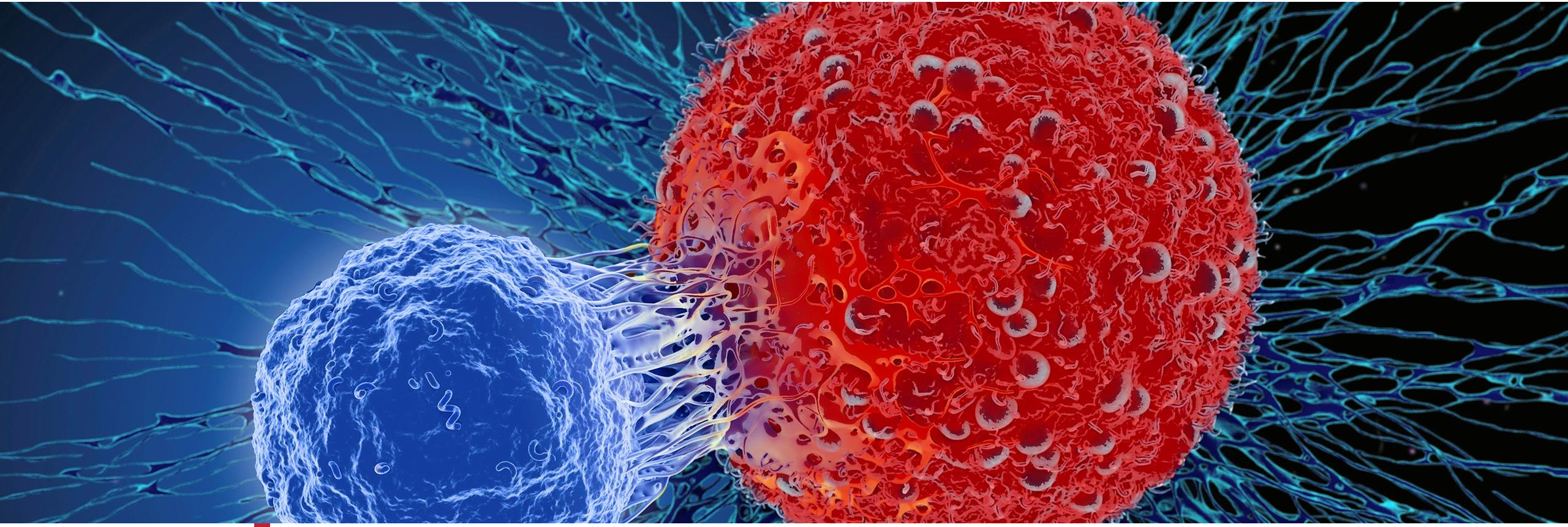
Adaptimmune

TRANSFORMING T CELL THERAPY



Administration of afamitresgene autoleucel (afami-cel), an autologous affinity enhanced T-cell receptor (TCR) therapy to be indicated for the treatment of advanced (unresectable/metastatic) synovial sarcoma (SyS) and myxoid round cell liposarcoma (MRCLS)

ICD-10 Coordination and Maintenance Committee Meeting March 8, 2022

Agenda

- Disease overview of synovial sarcoma (SyS) and myxoid round cell liposarcoma (MRCLS)
- Treatment paradigm shift with afami-cel T-cell receptor (TCR) therapy
- Review of manufacturing process and clinical data
- Conclusions

Soft tissue sarcomas (STS) are rare, unique, and clinically challenging

- Synovial sarcomas (SyS) represent a unique subset of STS and account for 5-10% of all STS cases[1]
- Estimated 1,000 patients/year are diagnosed in the United States[2]
- Frequent in adolescents and young adults (mean age of 39 years at diagnosis)[1]
- Both sexes affected equally[1]
- Most commonly present as soft tissue masses anywhere in the body. Vast majority in lower extremities, adjacent to the knee joint[1]
- Clinical manifestations are very heterogeneous[1]
- Cancer testis antigens (CTAs) highly expressed in SyS: MAGE-A4, NY-ESO-1, PRAME, SAGE[3]

- Liposarcomas account for 15-20% of all STS cases
  - 20-30% are of the myxoid or myxoid round cell liposarcoma (MRCLS) subtype[4]
- MRCLS arise preferentially in adolescents and younger adults[4]
- Characterized by a high rate of hematogenous metastases to extrapulmonary sites and/or recurrent tumors in up to 40% of patients[4]
- Local and/or distant failures typically take place within the first 5 years after diagnosis, but later events are not unusual[4]
- 10-year overall survival rates of approximately 70%[4]

1. Gazendam AM, et al. Curr Oncol. 2021; 28(3):1909-1920. 2. Sultan I, Rodriguez-Galindo C, Saab R, Yasir S, Casanova M, Ferrari A Cancer. 2009 Aug 1; 115(15):3537-47. 3. Mitchell G, Pollack SM, Wagner MJ. Journal for Immunotherapy of Cancer 2021;9:e002072. 4. Chowdhry V, Goldberg S, DeLaney TF, et al. Sarcoma. 2018;2018:8029157. Published 2018 Nov 1. doi:10.1155/2018/8029157

There is significant unmet need in the treatment of patients with advanced STS

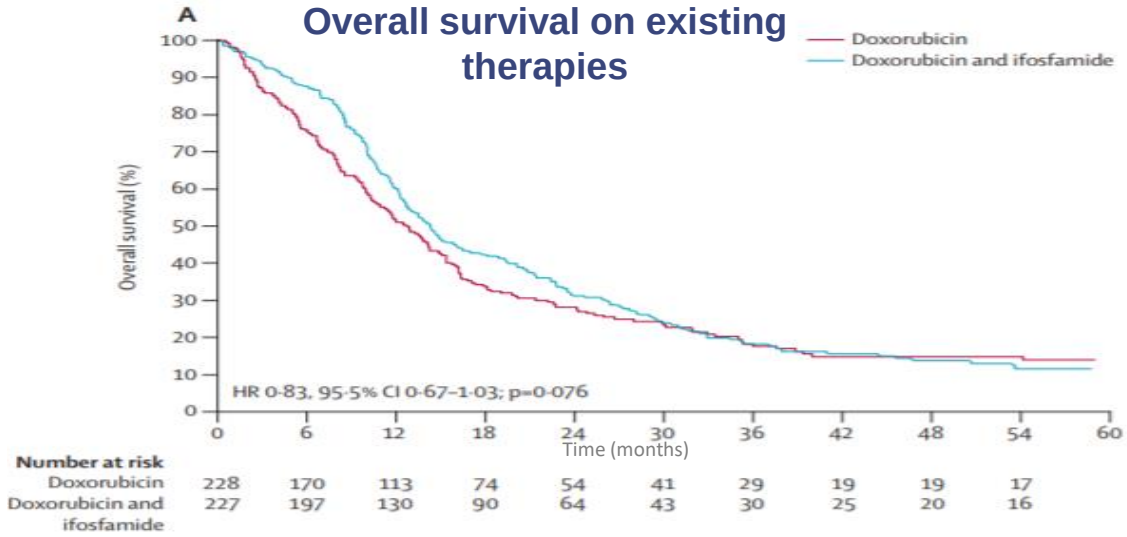
No consensus on standard of care after progression with 1st line therapy

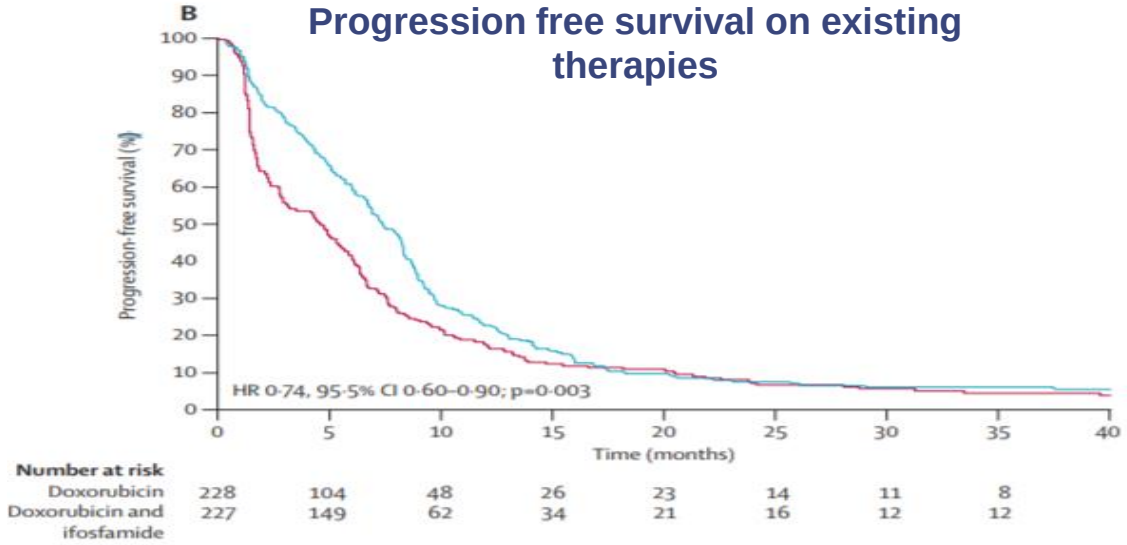
Limited efficacy with 2nd line therapies
(Overall response rates [ORRs] of ~15% or lower)

Lack of success in development since the 1980s:
Several trials have been investigating the addition of other chemotherapeutic drugs to doxorubicin to improve overall survival (OS)

Doxorubicin plus ifosfamide (1st line metastatic)

- Nearly doubled ORR (27% vs 14%) and significantly prolonged progression-free survival (PFS) in the combination arm (7.4 vs 4.6 months)
- However, OS (14.3 vs 12.8 months) was not statistically significant and the combination showed far more toxicity than doxorubicin alone





The Lancet Oncology 2014 15415-423DOI: (10.1016/S1470-2045(14)70063-4)

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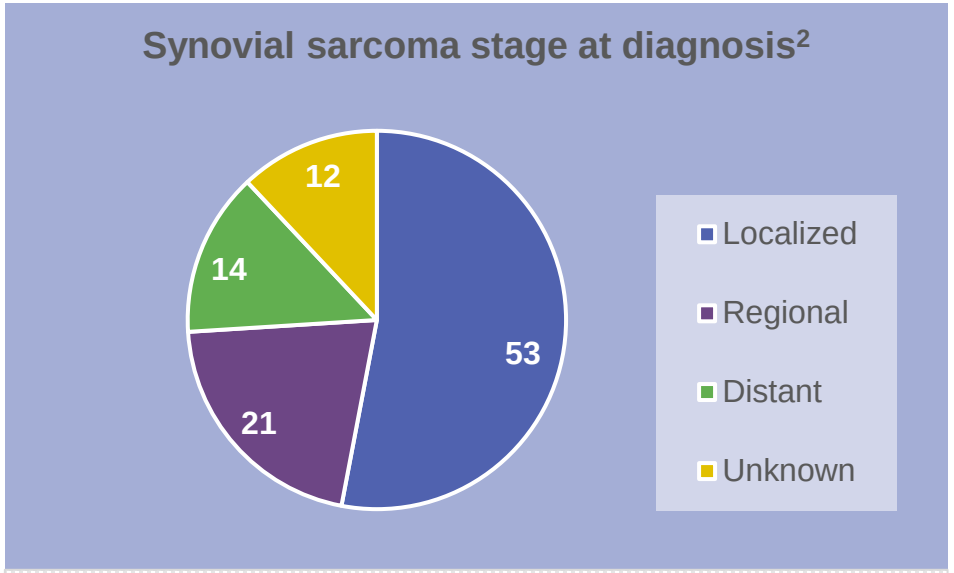
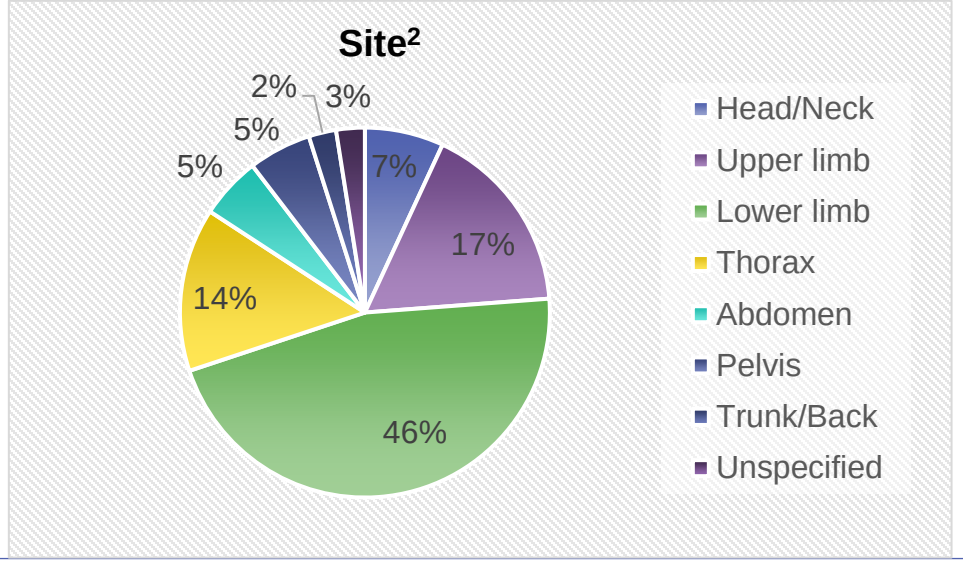
Poor prognosis in SyS: late local recurrence, distant metastases, and highly unpredictable tumor behavior[1]

- In a long term follow up study[1]:
  - **47% local recurrence**
    - average time = 4.1 years (range 0.5-14.9 years, interquartile range [IQR] 1.0-7.2 years)
  - **47% metastases**
    - average time = 5.9 years (range 0.5-16.3 years, IQR 2.4-8.1 years)
- Metastases: lungs, lymph nodes, and bone[1]
- Survival Rates[1]:
  - 5 years = 74.2% (±6%)
  - 10 years= 61.2% (±6%)
  - 15 years = 46.5% (±7%)





1. Krieg AH, et al. *Ann Oncol*. 2011;22(2):458-67. 2. Aytekin MN, et al. J Orthoped Surg. 2020;28(2):2020

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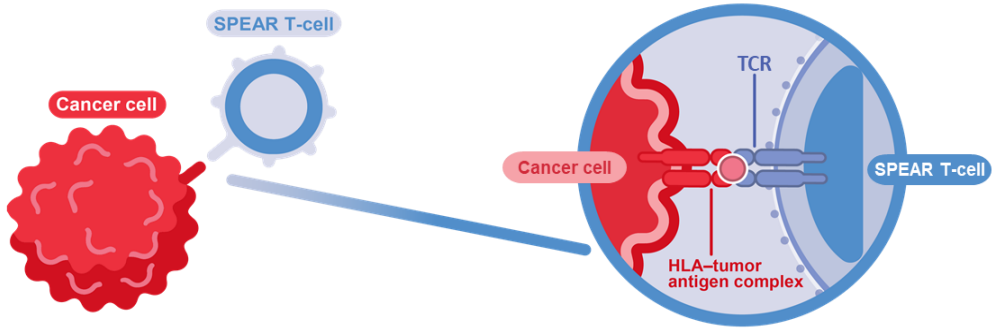
Afami-cel is a unique, personalized cancer treatment belonging to a new class of T-cell therapies



- T-Cell receptor (TCR) 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 through the HLA-peptide complex presented on the cell surface
  - Using TCRs engineered to recognize and bind to specific cancer peptides, SPEAR T-cells can target solid tumors
- Afamitresgene autoleucel (afami-cel) is a first-in-class, autologous affinity enhanced TCR T-cell therapy that recognizes the HLA-A/MAGE-A4 complex in tumor cells. Afami-cel is in a Phase 2 clinical trial for the treatment of patients with advanced (unresectable/metastatic) SyS or MRCLS that progressed on or after previous lines of treatment
- Afami-cel has received Orphan Drug Designation (ODD) and Regenerative Medicine Advanced Therapy (RMAT) designation from the FDA as a treatment for patients with HLA-A*02 and MAGE-A4 expression in synovial sarcoma
- If FDA approved, afami-cel will be used to treat a subset of patients in the approved indications who are HLA-A*02 positive and whose tumors express MAGE-A4

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The manufacturing process for afami-cel is similar to that of CAR-T therapies

APHERESIS COLLECTION TO CRYOPRESERVATION

- Fresh apheresis collection at local hospital
- Pack in insulated shipper with temperature control and tracking
- Courier to central manufacturing facility
- Wash cells in automated device
- Cryopreservation in controlled-rate freezer and store <-130°C

CELL MANUFACTURING SYSTEM

- Removal of beads in CTS™ DynaMag™
- *Ex vivo* expansion (static gas-permeable bags + Xuri™ W25 Wave Bioreactor)
- Lentiviral transduction
- Positive selection of T-cells using CD3/28 beads in gas-permeable bags and CTS™ DynaMag™
- Wash cells in automated device using closed single-use disposable system
- Thaw cryopreserved apheresis in automated device

QUALITY CONTROL

- Harvest of cells in automated device
- Formulate dose in infusible cryomedia and cryopreserve in controlled-rate freezer; store at below – (negative) 130°C
- Release testing at analytical labs

SHIPPING

- Once release criteria are met, courier to designated infusion center (temperature control + tracking)

SITE STORAGE

- Infusion center receives manufactured product and stores at below – (negative) 130°C prior to start of lymphodepletion

INFUSION

- Thaw cells in automated device for direct infusion at local hospital

Source: https://www.adaptimmune.com/technology/manufacturing

SPEARHEAD-1 (NCT04044768)

Phase 2 trial of afami-cel in patients with advanced SyS or MRCLS

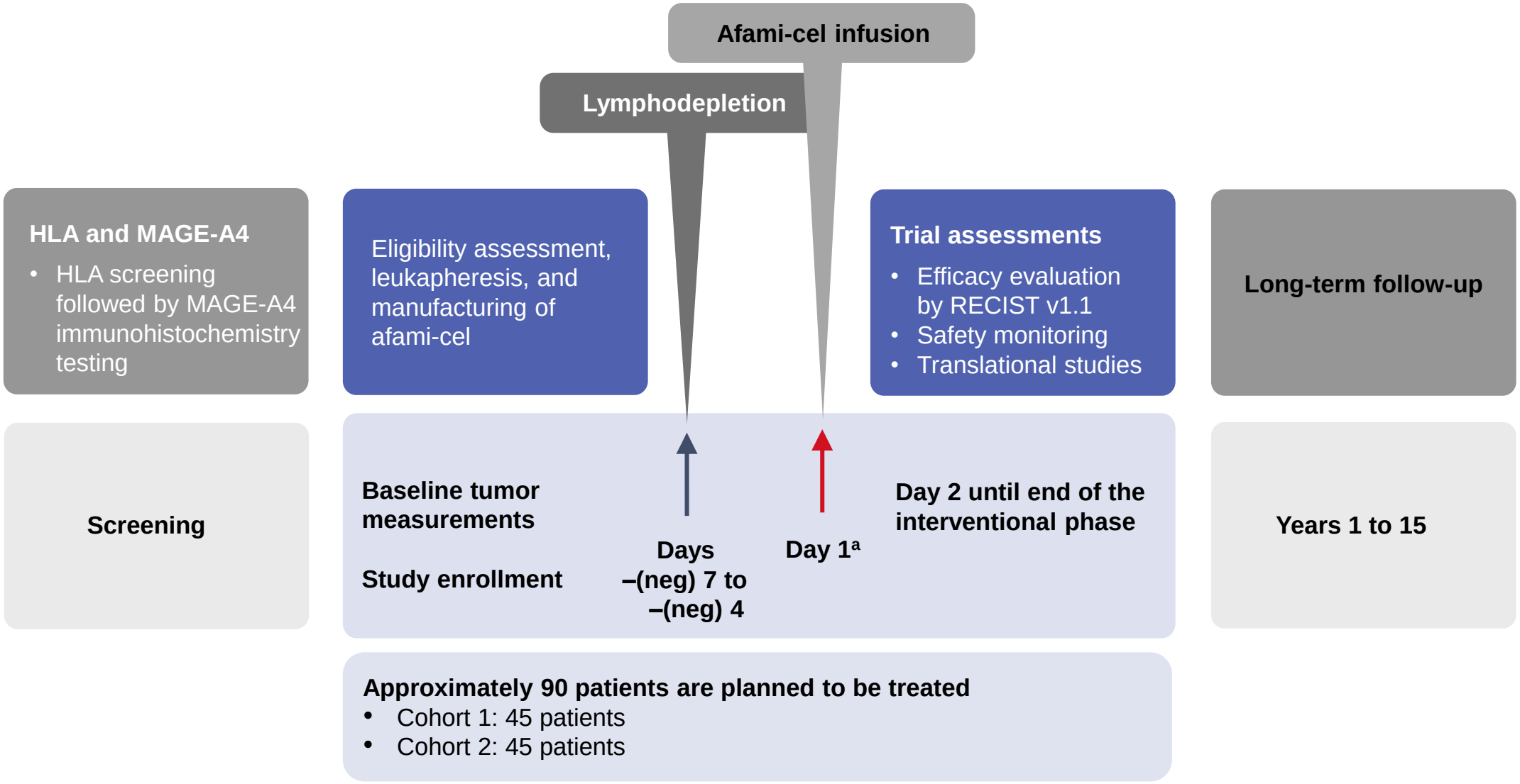
Key eligibility criteria

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

Efficacy: primary endpoint	• ORR per RECIST v1.1 by independent review
Efficacy: key secondary endpoint	• Duration of response • Time to response • Progression-free and overall survival
Safety and tolerability	• Adverse events (AEs) and serious adverse events (SAEs) • AEs of special interest

ECOG= Eastern Cooperative Oncology Group performance scale
https://clinicaltrials.gov/ct2/show/NCT04044768

SPEARHEAD-1 study trial design



[a] Patient is hospitalized for T-cell infusion and discharged at the discretion of the investigator

Source: Van Tine, B., D'Angelo, S., Attia, S., et al. (2021, November 10-13). SPEARHEAD-1: A phase 2 trial of afamitresgene autoleucel (formerly ADP-A2M4) in patients with advanced synovial sarcoma or myxoid/round cell liposarcoma [Conference presentation abstract 1080870]. 2021 Connective Tissue Oncology Society (CTOS) Virtual Annual Meeting.

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Disposition and baseline characteristics

Patients enrolled and underwent leukapheresis, n (%)	Overall, N=59
Patients received T-cell infusion (mITT)	50 (84.7)
Pending T-cell infusion	1 (1.7)
Discontinued prior to T-cell infusiona	8 (13.6)

Cohort 1
- Enrollment is complete
- Data used for primary efficacy analysis

Cohort 2
- Currently recruiting
- Data will strengthen the efficacy and safety database and aid in descriptive subgroup analyses

Characteristic, mITT	N=50
Sex, n (%)	
Male	27 (54)
Female	23 (46)
Age, years, median (range)	41 (19, 73)
Race, n (%)	
White	43 (86)
Black or African American	2 (4)
Asian	3 (6)
Missing	2 (4)
Geographic region, n (%)	
North America	37 (74)
Europe/UK	13 (26)

Characteristic, mITT	N=50
Primary tumor type, n (%)	
Synovial sarcoma	42 (84)
MRCLS	8 (16)
MAGE-A4 expression, H-score, median (range)	230.6 (112, 300)
Synovial sarcoma	256.2 (132, 300)
MRCLS	179.5 (112, 230)
ECOG performance status, n (%)	
0	28 (56)
1	22 (44)
Prior lines of systemic therapy, median (range)	3 (1, 12)
Cell dose x 10^9, median (range)	8.5 (2.7, 10.0)

Data cut-off September 1, 2021. Cohort 1 data. H-score derived: 3 x percentage of strongly staining cells + 2 x percentage of moderately staining cells + percentage of weakly staining cells

Source: Van Tine, B., D'Angelo, S., Attia, S., et al. (2021, November 10-13). SPEARHEAD-1: A phase 2 trial of afamitresgene autoleucel (formerly ADP-A2M4) in patients with advanced synovial sarcoma or myxoid/round cell liposarcoma [Conference presentation abstract 1080870]. 2021 CTOS Virtual Annual Meeting

Responses per RECIST V1.1 by independent and investigator reviews

	Independent review N=47, n (%)	Investigator review N=50, n (%)
Complete response	0 (0.0)	2 (4.0)
Partial response	16 (34.0)	15 (30.0)
Stable disease	24 (51.1)	25 (50.0)
Progressive disease	6 (12.8)	8 (16.0)
Not evaluable	1 (2.1)	0 (0.0)
Overall response rate [95% CI]	**16 (34.0) [20.86, 49.31]**	**17 (34.0) [21.21, 48.77]**
Synovial sarcoma	14 (35.9)	16 (38.1)
MRCLS	2 (25.0)	1 (12.5)
Disease control rate (CR+PR+SD)	40 (85.1)	42 (84.0)

Data cut-off September 1, 2021. SD
Cohort 1 data. CR = complete response; PR = partial response; = stable disease. Three patient scans were pending review by independent review at the time of the data cut-off

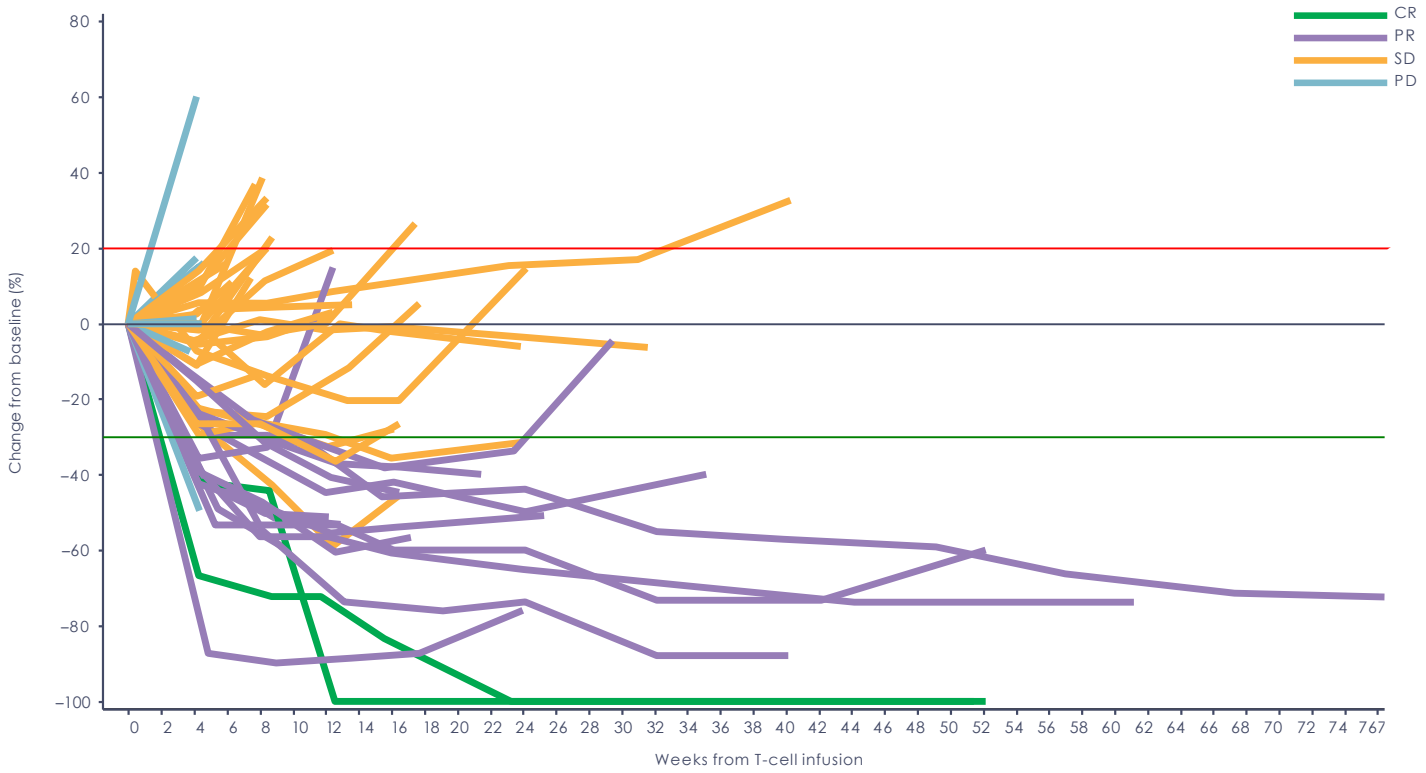
Source: Van Tine, B., D'Angelo, S., Attia, S., et al. (2021, November 10-13). SPEARHEAD-1: A phase 2 trial of afamitresgene autoleucel (formerly ADP-A2M4) in patients with advanced synovial sarcoma or myxoid/round cell liposarcoma [Conference presentation abstract 1080870]. 2021 CTOS Virtual Annual Meeting

Best overall responses per RECIST V1.1 by independent and investigator reviews

Data cut-off September 1, 2021. Cohort 1 data. CR = complete response; PD = progressive disease; PR = partial response; SD = stable disease. 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. Three patient scans were pending review by independent review at the time of the data cut-off

Source: Van Tine, B., D'Angelo, S., Attia, S., et al. (2021, November 10-13). SPEARHEAD-1: A phase 2 trial of afamitresgene autoleucel (formerly ADP-A2M4) in patients with advanced synovial sarcoma or myxoid/round cell liposarcoma [Conference presentation abstract 1080870]. 2021 CTOS Virtual Annual Meeting

Duration of response per RECIST V1.1 by investigator review



- Median time to response: 4.9 weeks (range, weeks: 4.1, 12.0)
- Median duration of response: not reached (range, weeks: 4.3+, 65.3+)

Data cut-off September 1, 2021 Cohort 1 data. 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. Follow-up by independent review was immature as of the data cut-off and is not presented. "+" denotes ongoing response at time of data cut-off

Source: Van Tine, B., D'Angelo, S., Attia, S., et al. (2021, November 10-13). SPEARHEAD-1: A phase 2 trial of afamitresgene autoleucel (formerly ADP-A2M4) in patients with advanced synovial sarcoma or myxoid/round cell liposarcoma [Conference presentation abstract 1080870]. 2021 CTOS Virtual Annual Meeting

Treatment emergent adverse events in ≥ 20% of patients

TEAE preferred term mITT, n (%)	N=50	
	Any grade	≥ Grade 3
Any	50 (100)	50 (100)
Lymphocyte count decreased	47 (94)	47 (94)
Neutrophil count decreased	43 (86)	40 (80)
White blood cell count decreased	42 (84)	40 (80)
Cytokine release syndrome	33 (66)	1 (2)
Nausea	31 (62)	0 (0)
Anemia	20 (40)	11 (22)
Constipation	17 (34)	0 (0)

TEAE preferred term mITT, n (%)	N=50	
	Any grade	≥ Grade 3
Fatigue	17 (34)	0 (0)
Pyrexia	17 (34)	1 (2)
Thrombocytopenia	16 (32)	8 (16)
Back pain	13 (26)	4 (8)
Decreased appetite	13 (26)	0 (0)
Vomiting	13 (26)	0 (0)
Abdominal pain	12 (24)	2 (4)
Dyspnea	10 (20)	2 (4)
Sinus tachycardia	10 (20)	0 (0)

Data cut-off September 1, 2021

Cohort 1 data. TEAE = treatment-emergent adverse event. Grouped terms: lymphocyte count decreased/lymphopenia, neutrophil count decreased/ neutropenia, white blood cell count decreased/leukopenia, anemia/red blood cell count decreased, thrombocytopenia/platelet count decreased, sinus tachycardia/tachycardia

Source: Van Tine, B., D'Angelo, S., Attia, S., et al. (2021, November 10-13). SPEARHEAD-1: A phase 2 trial of afamitresgene autoleucel (formerly ADP-A2M4) in patients with advanced synovial sarcoma or myxoid/round cell liposarcoma [Conference presentation abstract 1080870]. 2021 CTOS Virtual Annual Meeting

Treatment emergent serious adverse events and adverse events of special interest

Treatment emergent SAE ≥ 3% preferred term, n (%)	N=50	
	Any causality	Related to T-cell infusion
Any	22 (44)	12 (24)
Cytokine release syndrome	3 (6)	3 (6)
Pleural effusion	3 (6)	1 (2)
Abdominal pain	2 (4)	0 (0)
Back pain	2 (4)	0 (0)
Deep vein thrombosis	2 (4)	1 (2)
Empyema	2 (4)	1 (2)
Pulmonary embolism	2 (4)	1 (2)
Pyrexia	2 (4)	2 (4)
Spinal cord compression	2 (4)	0 (0)
Tumor pain	2 (4)	0 (0)

AEs of special interest	N=50
Cytokine release syndrome	
Any grade, n (%)	33 (66)
≥ Grade 3, n (%)	1 (2)
Time to onset, days, median (range)	3 (1, 23)
Time to resolution, days, median (range)	3 (1, 14)
Tocilizumab use, n (%)	15 (30)
Grade ≥ 3 cytopenia at week 4 post-infusion	
Any, n (%)	8 (16)
Neutropenia, n (%)	4 (8)
Anemia, n (%)	3 (6)
Thrombocytopenia, n (%)	2 (4)
Immune effector cell-associated neurotoxicity syndrome	
Any grade, n (%)	1 (2)
≥ Grade 3, n (%)	0 (0)

Data cut-off September 1, 2021
Cohort 1 data. Two patients had grade 5 events (both unrelated to T-cell therapy): worsening neoplasm malignant (1) and acute respiratory failure (1)

Source: Van Tine, B., D'Angelo, S., Attia, S., et al. (2021, November 10-13). SPEARHEAD-1: A phase 2 trial of afamitresgene autoleucel (formerly ADP-A2M4) in patients with advanced synovial sarcoma or myxoid/round cell liposarcoma [Conference presentation abstract 1080870]. 2021 CTOS Virtual Annual Meeting

Inpatient administration of afami-cel

- Inpatient administration is considered mandatory for post infusion safety monitoring especially for potential immunological adverse events, such as cytokine release syndrome, which is a common adverse event for autologous cell therapies
  - Once admitted to the hospital, the patient receives between 1 to 10 billion transduced T-cells (afami-cel dose range) as a single intravenous infusion administered through a central or peripheral vein
  - Administration of afami-cel is similar to that of CAR T and TIL therapies
- Information regarding afami-cel and its associated administration procedure will be documented in the medical record and identifiable from multiple perspectives (e.g., Medication Administration Record [MAR], physician orders, pharmacy notes, treatment summary, progress notes, etc.)

Conclusions

- Afami-cel has received Orphan Drug Designation (ODD) and Regenerative Medicine Advanced Therapy (RMAT) designation from the FDA as a treatment for patients with HLA-A*02 and MAGE-A4 expression in synovial sarcoma
- Data from SPEARHEAD-1 demonstrate afami-cel is efficacious in heavily pre-treated patients
  - Overall response rate was 34%
  - Durability of responses is encouraging
- The benefit-risk profile of afami-cel has been acceptable, with mainly low-grade cytokine release syndrome and reversible hematologic toxicities
- SPEARHEAD-1 is ongoing
  - Cohort 1 has completed enrollment and will be used to support Adaptimmune's Biologics License Application (BLA) submission in 2022
  - Enrollment in Cohort 2 of this study is ongoing
- No current ICD-10-PCS codes describe the administration of afami-cel. New ICD-10-PCS codes are needed to identify afami-cel use in the inpatient setting