Enrollment of Pediatric and Adolescent Patients with MAGE-A4+ Advanced Synovial Sarcoma into Cohort 2 of SPEARHEAD-1: A Phase 2 Trial of Afamitresgene Autoleucel ("Afami-cel" formerly ADP-A2M4)

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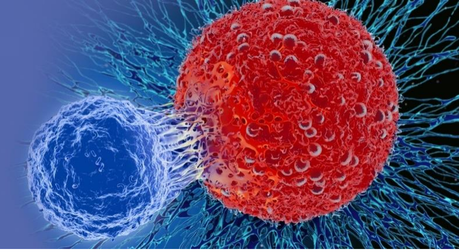
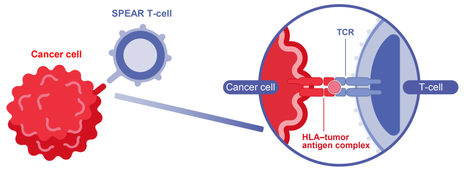


Introduction

- Afamitresgene autoleucel ("afami-cel" formerly ADP-A2M4) is an autologous, specific peptide enhanced affinity receptor (SPEAR) T-cell therapy (**Figure 1**) targeting solid tumors expressing melanoma-associated antigen A4 (MAGE-A4) in human leukocyte antigen (HLA) A*02-eligible patients.

Figure 1. Specific Peptide Enhanced Affinity Receptor T-Cells



- 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.
- Scan QR code to find out more about HLA and MAGE-A4.

HLA, human leukocyte antigen; SPEAR, specific peptide enhanced affinity receptor; TCR, T-cell receptor.

- Safety and efficacy of afami-cel is being evaluated in the Phase 2 SPEARHEAD-1 trial (NCT04044768) in patients with advanced synovial sarcoma or myxoid/round cell liposarcoma.
- Preliminary data from Cohort 1 of SPEARHEAD-1 (data cut-off September 1, 2021)[1] showed that, based on an overall response rate of 34% by independent review, the trial will meet its primary endpoint in the final analysis. These data further validate the potential of afami-cel to address an unmet medical need and will be used to support Adaptimmune's Biologics License Application submission in 2022.

Cohort 1[1]

47 patients (**39** with synovial sarcoma)

16–75 years old

26 centers across North America and Europe

34.0% overall response rate per independent review (**35.9%** in synovial sarcoma)

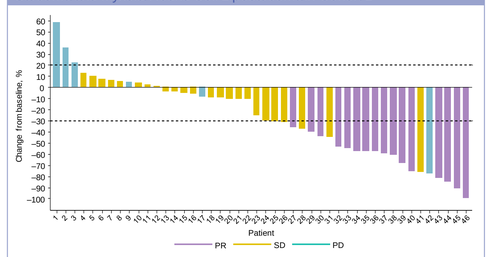
Favorable benefit to risk profile (mainly **low-grade** cytokine release syndrome and **tolerable or reversible** hematologic toxicities)

Recruitment is closed

Rationale for SPEARHEAD-1 Cohort 2 Development

- Synovial sarcoma is the most common malignant nonrhabdomyosarcoma soft-tissue sarcoma in children and adolescents.[2]
- Few treatment options are available, especially for those who experience disease progression after first-line therapy.[3]
- High unmet need for new pediatric therapeutics to treat advanced synovial sarcoma in the second-line setting.
- Patients aged ≥16 years with advanced synovial sarcoma, post first-line systemic therapy, showed an overall response rate (ORR) of 35.9% in Cohort 1 of SPEARHEAD-1 (**Figure 2**).
- ORR of afami-cel was higher than those historically reported for pazopanib and trabectedin in the second-line metastatic setting.[4]

Figure 2. Responses per RECIST v1.1 by Independent Review in Synovial Sarcoma and Myxoid/Round Cell Liposarcoma in Cohort 1[1]



- ORR = 34% (95% CI: 20.86–49.31)
- 16/47 responders: 14 synovial sarcoma, 2 MRCLS

MRCLS, myxoid round cell liposarcoma; ORR, overall response rate; PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease.
Data cut-off September 1, 2021.

- Given the high unmet need and positive results of Cohort 1, Cohort 2 has opened and will include children and adolescents with synovial sarcoma for treatment with afami-cel.
- Up to 45 patients with synovial sarcoma, post first-line chemotherapy, will be treated in Cohort 2 of SPEARHEAD-1 to enable a pooled analysis of ORR in >90 patients across Cohorts 1 and 2.

Cohort 2

- Diagnosis of advanced, inoperable synovial sarcoma
- HLA-A*02 and tumor MAGE-A4 positive
- **Aged ≥10 years and ≤75 years**
- **Weighs ≥40 kg**
- Measurable disease per RECIST v1.1
- **ECOG performance status of 0 or 1 for patients aged ≥16 years old, and Lansky score ≥80% for patient's aged ≥10 to <16 years old**
- At least one prior line of systemic chemotherapy
- Prior lentivirus-containing cell therapy permissible if no detectable systemic persistence

AGES 10+

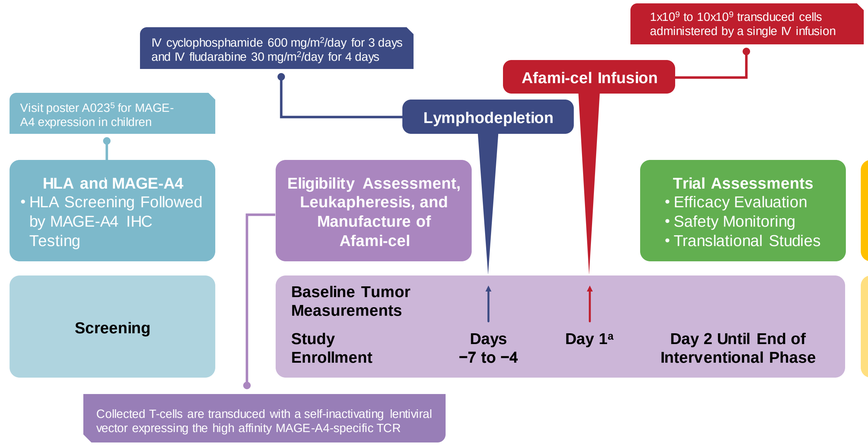
- No active autoimmune disease
- No symptomatic central nervous system metastases

ECOG, Eastern Cooperative Oncology Group; HLA, human leukocyte antigen; MAGE-A4, melanoma-associated antigen A4. RECIST, Response Evaluation Criteria in Solid Tumors.

SPEARHEAD-1 Cohort 2 Trial Design

- Cohort 2 trial design mirrors that of Cohort 1 (**Figure 3**).
- HLA and MAGE-A4 screening in Cohort 2 is conducted at a central laboratory using the same method as Cohort 1.
- All patients undergo apheresis, and their isolated T-cells are then transduced with the MAGE-A4^{c1032} TCR using a lentivirus vector, followed by ex vivo expansion (**Figure 4**).
- Enrollment in Cohort 2 of SPEARHEAD-1 is now open, including 7 pediatric sites across the USA and France (**Figure 5**).

Figure 3. SPEARHEAD-1 Cohort 2 Trial Design



Primary endpoint: efficacy

- ORR per RECIST v1.1 by independent review

Additional efficacy endpoints

- Duration of response
- Time to response
- Progression-free and overall survival

Secondary endpoint: safety

- AEs and SAEs
- AEs of special interest: cytokine release syndrome, immune effector cell-associated neurotoxicity syndrome, and prolonged cytopenia

Additional safety endpoints

- Replication competent lentivirus
- T-cell clonality and insertional oncogenesis

[a]Patient is hospitalized for T-cell infusion and discharged at the discretion of the investigator.
AE, adverse event; HLA, human leukocyte antigen; IHC, immunohistochemistry; IV, intravenous; MAGE-A4, melanoma-associated antigen A4; ORR, overall response rate; RECIST, Response Evaluation Criteria in Solid Tumors. SAE, serious AE; TCR, T-cell receptor.

Figure 4. Patient Cell Journey

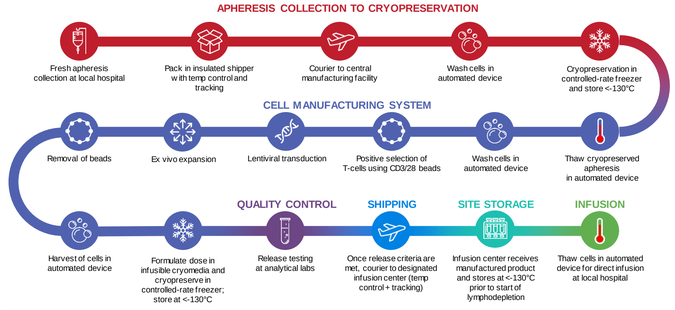
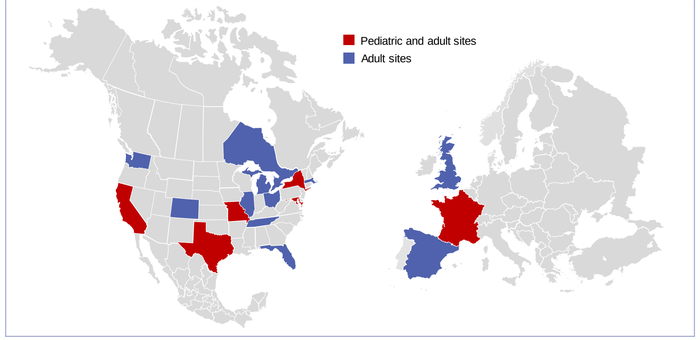


Figure 5. Locations of SPEARHEAD-1 Cohort 2 Trial Sites Across North America and Europe



A038: American Association for Cancer Research (AACR) Special Conference: Sarcomas, May 9-12, 2022; Hybrid, Montreal, QC, Canada

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Abbreviations used in text

HLA, human leukocyte antigen; MAGE-A4, melanoma-associated antigen A4; ORR, overall response rate; SPEAR, specific peptide enhanced affinity receptor; TCR, T-cell receptor.