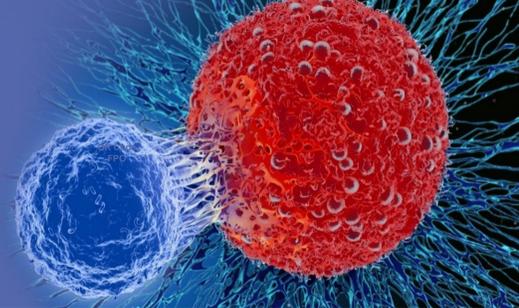


Enrollment of Pediatric Participants With MAGE-A4-Positive Solid Tumors in a Phase 1/2, Open-Label, Basket Trial of Afami-cel (“Afami-cel”)

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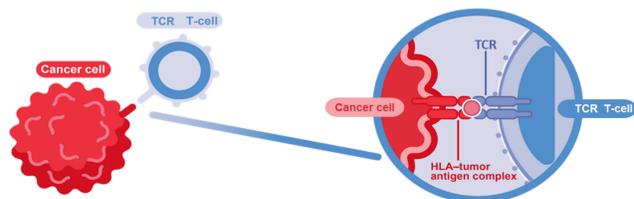
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Introduction

- Afamitresgene autoleucel (afami-cel; **Figure 1**) is an affinity-enhanced T-cell receptor (TCR) T-cell therapy genetically engineered to target melanoma-associated antigen A4 (MAGE-A4)-positive solid tumors in human leukocyte antigen (HLA) A*02-eligible patients¹
- The Phase 2 SPEARHEAD-1 (NCT04044768) trial evaluated afami-cel in adult participants with advanced/metastatic synovial sarcoma (SyS) or myxoid/round cell liposarcoma (MRCLS)
- SPEARHEAD-1 produced encouraging anti-tumor data (**Figure 2**) and an acceptable benefit-to-risk profile.² These findings are being used to support a Biologics License Application submission
- MAGE-A4 is also expressed in various rare solid tumors occurring in children and adolescents (**Table 1, Figure 3**)³
- These patients have limited treatment options in the recurrent or metastatic setting and may also potentially benefit from afami-cel
- Therefore, a Phase 1/2 clinical trial (**Figure 4**; SPEARHEAD-3; NCT05642455) is being initiated to more fully describe the prevalence of MAGE-A4 expression in relapsed/refractory solid tumors of pediatric, adolescent, and adult (up to age 21) patients, and to evaluate the safety and anti-tumor activity of afami-cel in this population

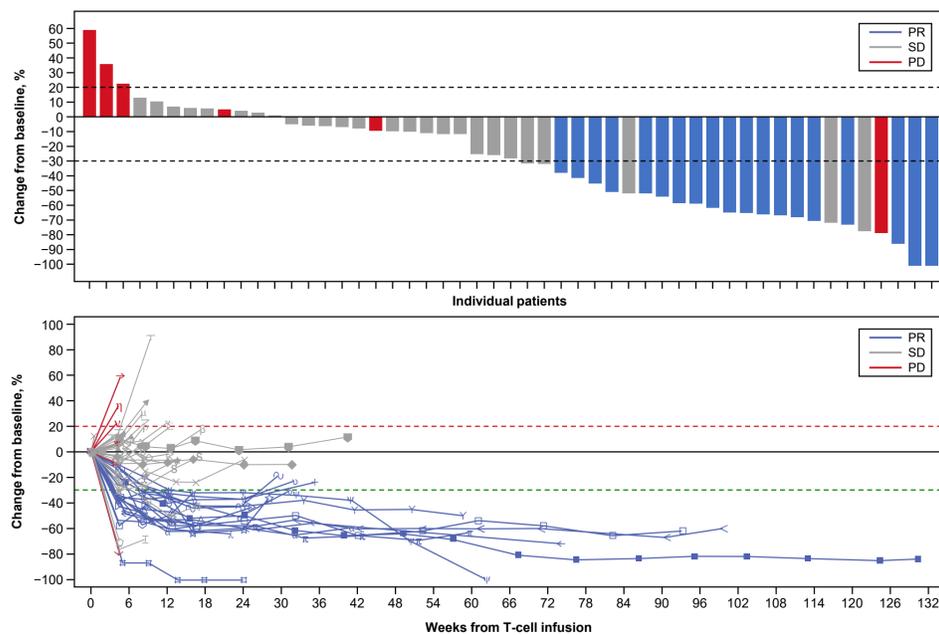
Figure 1. Afami-cel



afami-cel, afamitresgene autoleucel; HLA, human leukocyte antigen; TCR, T-cell receptor.

- T cells scan HLA-peptide complexes presented on the surface of cells, including tumor cells
- TCRs targeting tumor peptide antigens bind and activate the T cell
- TCRs can target both intra- and extracellular antigens
- Using TCRs engineered to recognize and bind to specific peptides from MAGE-A4, afami-cel can target, infiltrate, and kill solid tumors

Figure 2. Anti-tumor data from the Phase 2 SPEARHEAD-1 trial of afami-cel in adult patients with advanced SyS or MRCLS



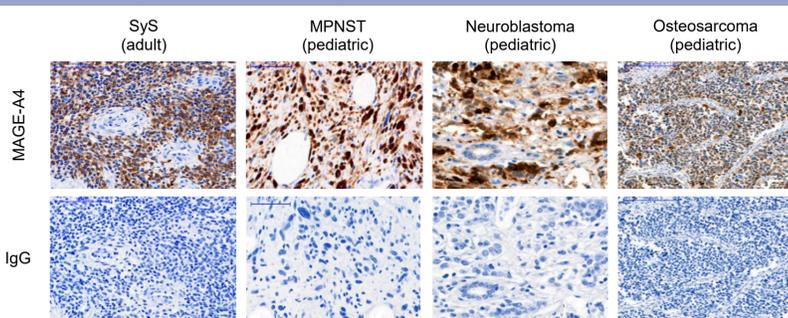
Data cut-off August 29, 2022. Cohort 1 data. Data represent percent changes from baseline in sum of diameters (SLD for non-nodal lesions and short axis for nodal lesions) in target lesions through progression or prior to surgical resection. afami-cel, afamitresgene autoleucel; MRCLS, myxoid/round cell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

Table 1. MAGE-A4 prevalence in certain pediatric cancers

Tumor types, % (n/N)	Pediatric (TMA)	Mixed pediatric/adult (TMA)	Adult (tissue blocks)
SyS	33 (5/15) ^a	–	6 (20/30)
MPNST	6 (3/53)	–	–
Neuroblastoma	13 (4/29)	20 (11/54)	–
Osteosarcoma	–	14 (18/133)	–

MAGE-A4 expression was determined by Adaptimmune using a MAGE-A4 immunohistochemistry clinical trial assay with a diagnostic cutoff of $\geq 30\%$ tumor cells stained at $\geq 2+$ intensities. The MAGE-A4 prevalence was determined by the MAGE-A4 IHC clinical trial assay using commercially procured or third-party-provided TMAs or tissue blocks. ^aMAGE-A4 prevalence in pediatric synovial sarcoma was determined by a different MAGE-A4 IHC assay using the same antibody clone and same diagnostic cutoff ($\geq 30\%$, $\geq 2+$) as the clinical trial assay. MPNST, malignant peripheral nerve sheath tumor; SyS, synovial sarcoma; TMA, tissue microarray.

Figure 3. Representative MAGE-A4 expression as determined by an immunohistochemistry clinical trial assay

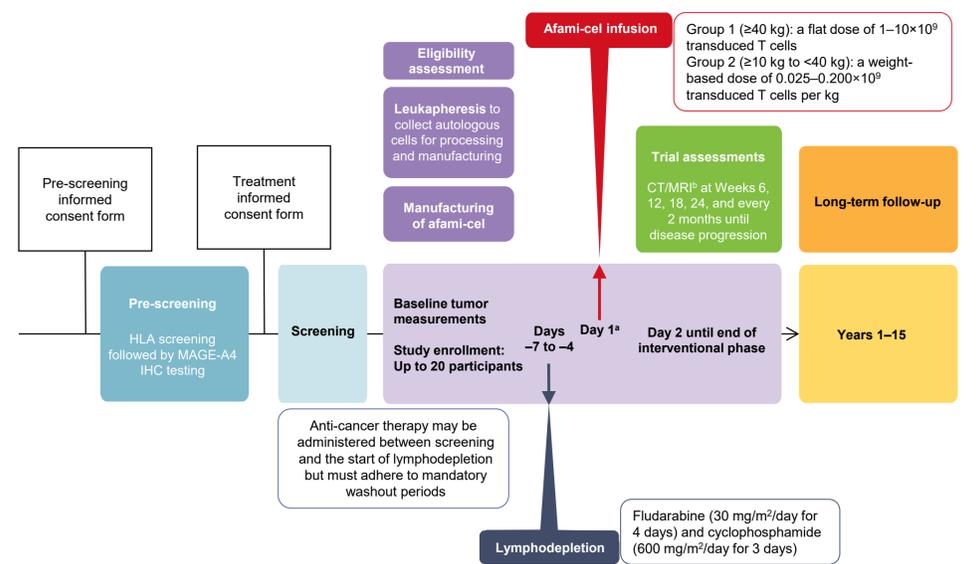


IgG, immunoglobulin G; MAGE-A4, melanoma-associated antigen A4; MPNST, malignant peripheral nerve sheath tumor; SyS, synovial sarcoma.

Figure 4. SPEARHEAD-3 (NCT05642455) trial design

Key eligibility criteria

Inclusion criteria	Exclusion criteria
Age 2–21 years	Active autoimmune or immune-mediated disease
Body weight ≥ 10 kg	Known CNS metastases
Histologically confirmed diagnosis of relapsed/refractory case of any one of: SyS, MPNST, high-risk neuroblastoma, or osteosarcoma	HLA-A*02:05 in either allele; or any A*02 with same protein sequence as HLA-A*02:05
Must have previously received a systemic chemotherapy	
Measurable disease according to RECIST v1.1 (or INRC, 2017, neuroblastoma patients only)	
Express at least one HLA-A*02 inclusion allele	
Tumor shows MAGE-A4 expression confirmed by central laboratory	
Performance status: ECOG 0–1 or Lansky Score ≥ 80	



Key endpoints

Primary endpoints: Safety	Secondary endpoints
Incidence of dose-limiting toxicities	Anti-tumor activity: overall response rate, ^c time to response, duration of response, best overall response, progression-free survival, overall survival
AEs, including serious adverse events	Peak persistence and other pharmacokinetic parameters of afami-cel cells
Incidence, severity, and duration of the AEs of special interest	Development and validation of an in vitro diagnostic assay
Replication competent lentivirus	
T-cell clonality and insertional oncogenesis	

^aPatient is hospitalized for ≥ 24 hours following T-cell infusion and discharged at the discretion of the investigator.

^bINRC assessments for patients with neuroblastoma.

^cPer RECIST v1.1 (or INRC, 2017, in neuroblastoma patients only).

AE, adverse event; afami-cel, afamitresgene autoleucel; CNS, central nervous system; CT, computerized tomography; ECOG, Eastern Cooperative Oncology Group; HLA, human leukocyte antigen; IHC, immunohistochemistry; INRC, International Neuroblastoma Response Criteria; MAGE-A4, melanoma-associated antigen A4; MPNST, malignant peripheral nerve sheath tumor; MRI, magnetic resonance imaging; RECIST, Response Evaluation Criteria in Solid Tumors; SyS, synovial sarcoma.

Table 2. Study sites and investigators

Site name	Investigator name
Washington University/St. Louis Children's Hospital	Amy Armstrong
MSK Kids	Tara O'Donohue
Cincinnati Children's Hospital Medical Center	Brian Turpin
Dana-Farber Cancer Institute/Boston Children's	Natalie Collins
Stanford/Lucile Packard Children's Hospital	Sneha Ramakrishna
Children's Hospital Colorado	Vanessa Fabrizio
University of Wisconsin, American Family Children's Hospital	Christian Capitini
UT Southwestern/Children's Health Dallas	Matt Campbell
Seattle Children's Hospital	Mark Fluchel
Duke Cancer Center	Kris Mahadeo
National Institutes of Health	John Glod
Children's Hospital of Philadelphia	Theodore Laetsch

Conclusions

- This SPEARHEAD-3 basket trial investigating the safety and efficacy of afami-cel in HLA-A*02-eligible patients aged 2–21 years with MAGE-A4-positive advanced solid tumors was opened in August 2023 and will enroll participants at the United States sites listed in **Table 2**

References

- Hong DS, et al. *Nat Med*. 2023;29:104.
- Van Tine BA, et al. Oral presented at CTOS 2022; Vancouver, BC, Canada.
- Biswal S, et al. *Clin Cancer Res*. 2022;28(18 suppl):A023.

Footnotes and Abbreviations Used in Text

Afami-cel; afamitresgene autoleucel; HLA, human leukocyte antigen; MAGE-A4, melanoma-associated antigen A4; MRCLS, myxoid/round cell liposarcoma; SyS, synovial sarcoma; TCR, T-cell receptor.

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