SPEARHEAD-1: A PHASE 2 TRIAL OF AFAMITRESGENE AUTOLEUCEL (FORMERLY ADP-A2M4) IN PATIENTS WITH ADVANCED SYNOVIAL SARCOMA OR MYXOID/ROUND CELL LIPOSARCOMA

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DISCLOSURE INFORMATION
BRIAN A. VAN TINE (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

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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]

Afami-cel

- SPEAR T-cells target MAGE-A4+ tumors
- Compelling clinical responses have been observed in patients with synovial sarcoma and MRCLS, occurring across a wide range of MAGE-A4 expression and cell doses[2]

HLA = human leukocyte antigen; MAGE = Melanoma Antigen Gene; MRCLS = myxoid/round cell liposarcoma; SPEAR = Specific Peptide Enhanced Affinity Receptor

1. Iura K. Virchows Archiv 2017;471:383–392. 2. D'Angelo. Oral presentation: 2021 ASCO Annual Meeting

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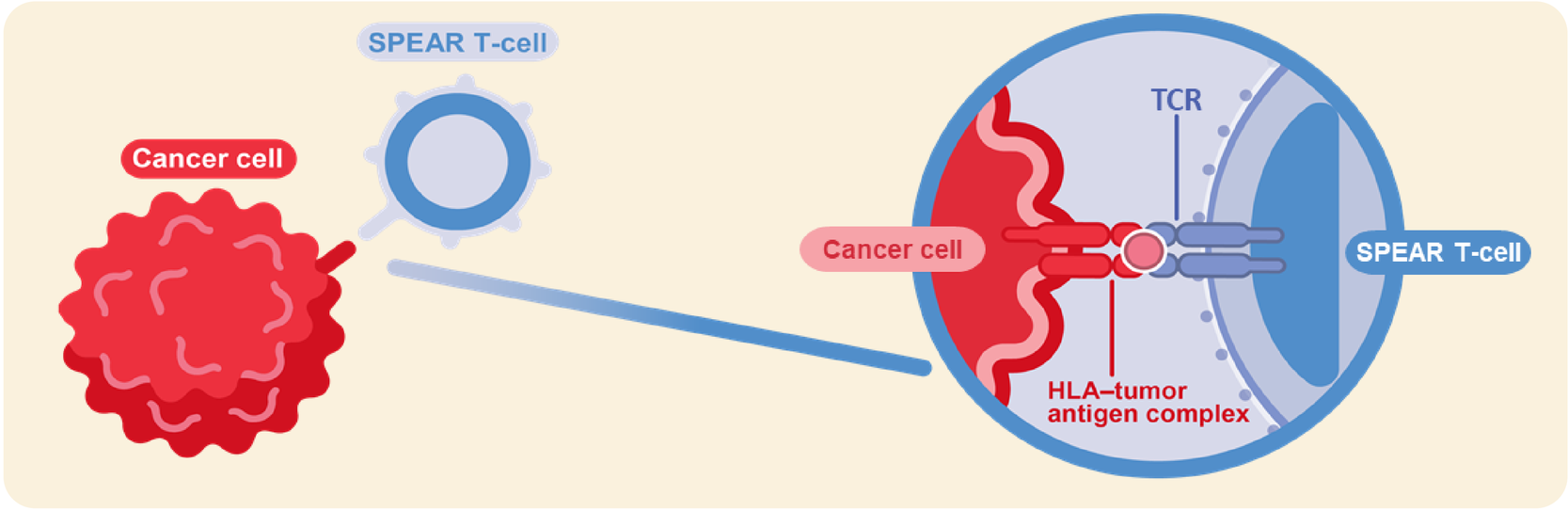
SPEAR T-CELL MECHANISM OF ACTION



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
- Using TCRs engineered to recognize and bind to specific cancer peptides, SPEAR T-cells can target solid tumors

TCR = T-cell receptor

SPEARHEAD-1 (NCT04044768)
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
- 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 endpoints

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

Safety and tolerability

- AEs and SAEs
- AEs of special interest

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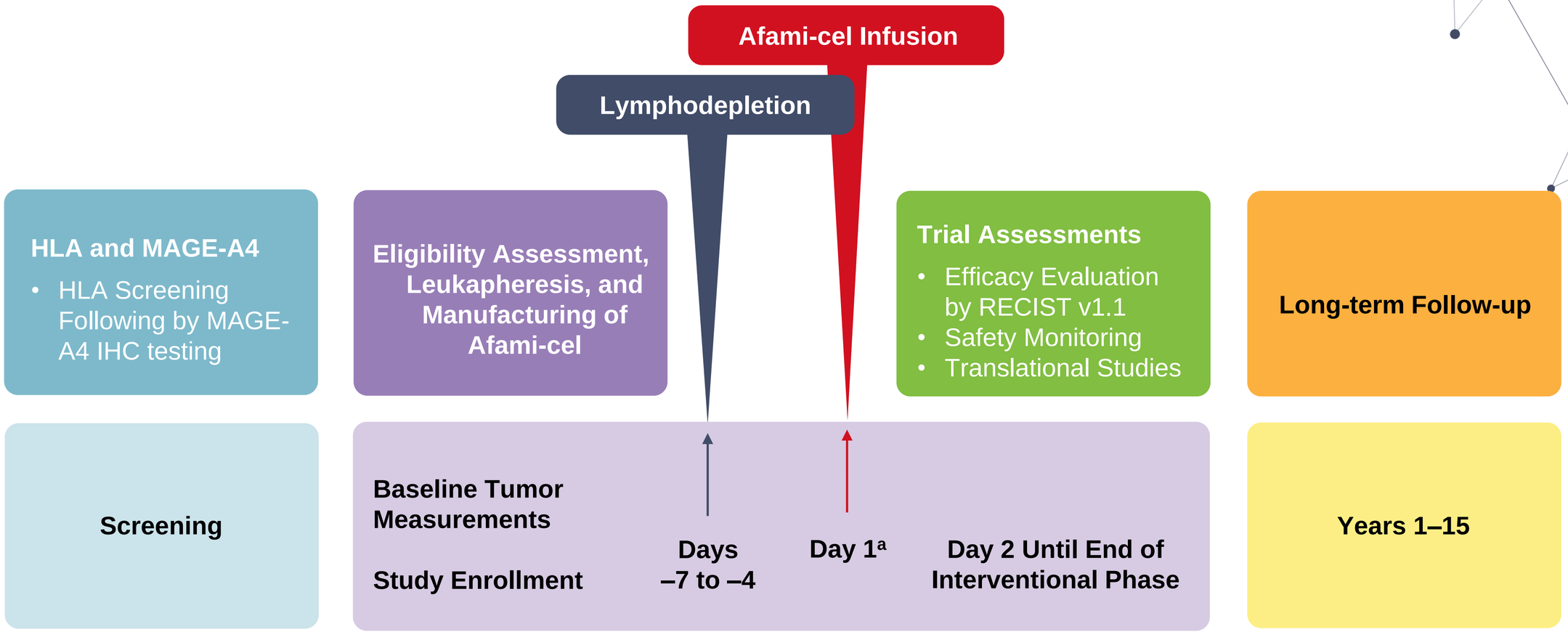
AE = adverse event; ECOG = Eastern Cooperative Oncology Group; ORR = overall response rate; RECIST = Response Evaluation Criteria in Solid Tumours

SPEARHEAD-1 TRIAL DESIGN



Approximately 90 patients are planned to be treated
- Cohort 1: 45 patients
- Cohort 2: 45 patients

IHC = immunohistochemistry;. [a]Patient is hospitalized for T-cell infusion and discharged at the discretion of the Investigator

DISPOSITION

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 infusion[a]	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

Data cut-off September 1, 2021

Cohort 1 data. mITT = modified intent to treat. [a]Reasons for discontinuation prior to T-cell infusion included disease progression, did not meet eligibility criteria, withdrawal of consent, or investigator decision

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BASELINE CHARACTERISTICS

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

RESPONSES PER RECIST V1.1 BY INDEPENDENT AND INVESTIGATOR REVIEWS

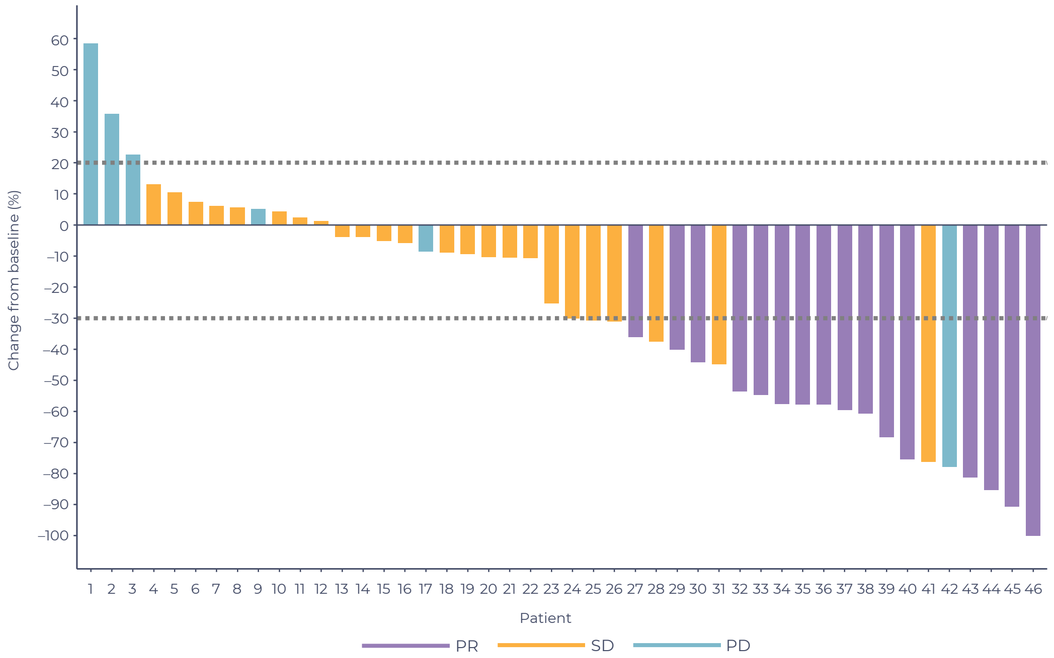
	Independent review N=47, n (%)	Investigator review N=50, n (%)
Complete response	0 (0.0)	2 (4.0)
Partial response	16 (34.0)	15 (30.0)
Stable disease	24 (51.1)	25 (50.0)
Progressive disease	6 (12.8)	8 (16.0)
Not evaluable	1 (2.1)	0 (0.0)
Overall response rate [95% CI]	**16 (34.0) [20.86, 49.31]**	**17 (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

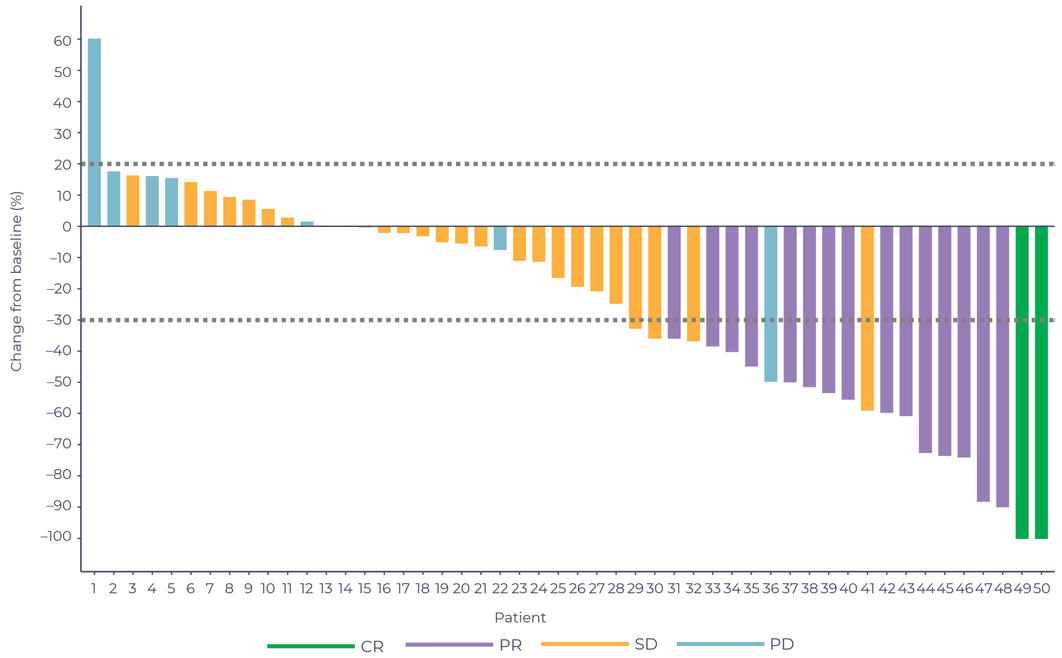
Cohort 1 data. CR = complete response; PR = partial response; SD = stable disease. Three patient scans were pending review by Independent review at the time of the data cut-off

BEST OVERALL RESPONSES PER RECIST V1.1 BY INDEPENDENT AND INVESTIGATOR REVIEWS

Independent review



Investigator review



Data cut-off September 1, 2021

Cohort 1 data. PD, progressive 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

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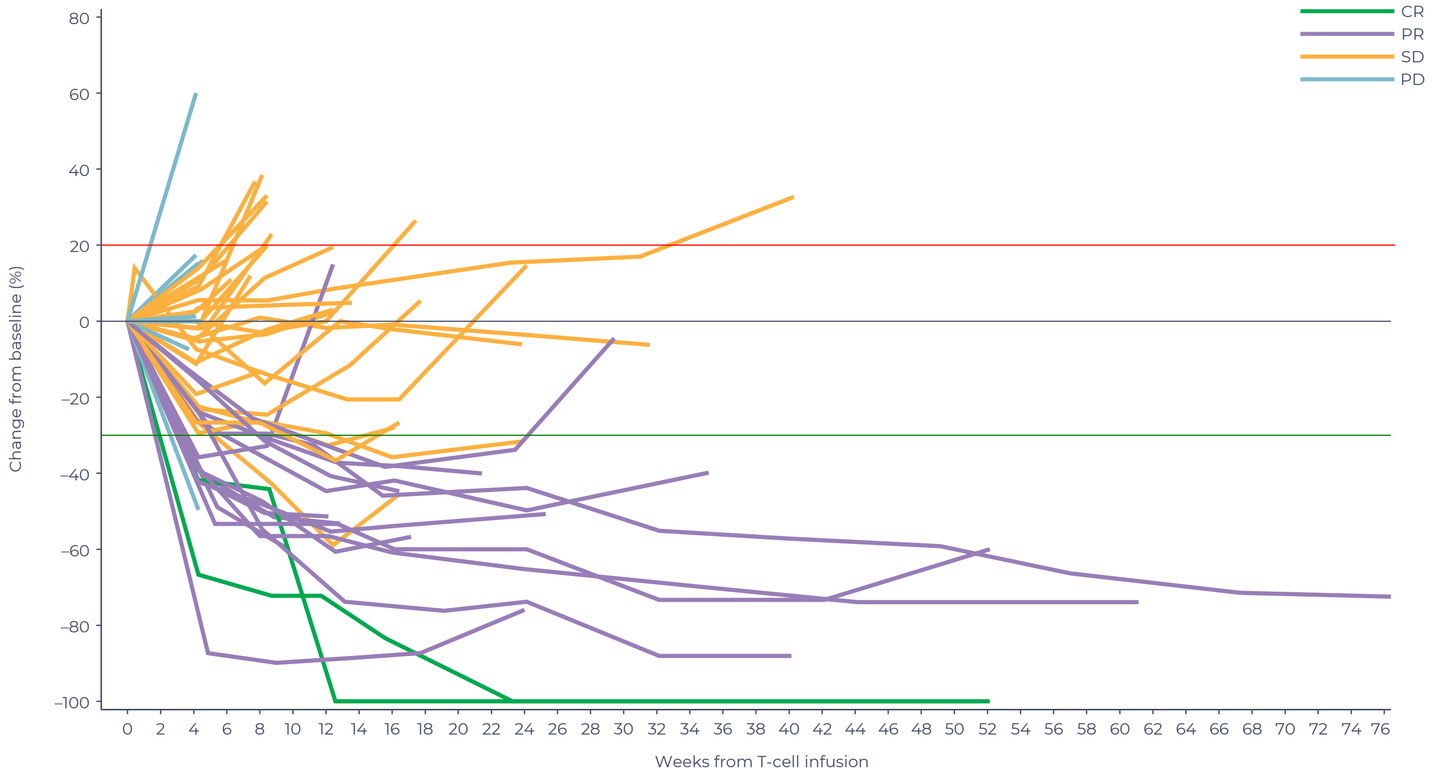
DURATION OF RESPONSE PER RECIST V1.1 BY INVESTIGATOR REVIEW



- 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

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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

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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

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Cohort 1 data. Two patients had Grade 5 events (both unrelated to T-cell therapy): worsening neoplasm malignant (1) and acute respiratory failure (1)

CONCLUSIONS

- Data 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 favorable, with mainly low-grade cytokine release syndrome and tolerable/reversible hematologic toxicities
- SPEARHEAD-1 is ongoing
  - Cohort 1 has completed enrolment and will be used to support Adaptimmune's Biologics License Application submission next year
  - Enrollment in Cohort 2 of this study is ongoing
- Please visit our SPEARHEAD-1 poster (#P146) for details on the translational data providing insight into these clinical findings

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- We thank the **investigators** and their **teams** who participated
- For further questions, please contact: bvantine@wustl.edu