OUTCOMES OF PATIENTS WITH ADVANCED SYNOVIAL SARCOMA TREATED WITH AFAMITRESGENE AUTOLEUCEL ("AFAMI-CEL")

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Disclosure Information

Personal financial interests

- Consultant: Acuta Capital Partners, Advenchen, Bayer, Boxer Capital, Cytokinetics, Deciphera Pharmaceuticals, Daiichi Sankyo, EcoR1 Capital, Putnam, Salarius Pharmaceuticals, Aadi Biosciences, Race Oncology, Hinge Bio Inc., Kronos Bio Inc.
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- Data advisory boards: Aadi Bioscience, Advenchen, Agenus, Bayer US Medical Affairs Oncology, Boehringer Ingelheim, Curis, EcoR1 Capital, PTC Therapuetics, Regeneron

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Afami-cel for Synovial Sarcoma

Historical outcomes are poor for advanced synovial sarcoma

- Time to next treatment or death has a strong correlation with overall survival in metastatic sarcoma

Median overall survival at ≥ second line: <12 months[1]

Median TNT-D from the start of[2]:

Second line:	Third line:	Fourth line:
5.7 months	3.4 months	2.3 months

Afami-cel is an autologous TCR T-cell therapy for treatment of HLA-A*02–eligible patients with advanced synovial sarcoma whose tumors are positive for the cancer testis antigen, MAGE-A4

- In the Phase 2 SPEARHEAD-1 trial, afami-cel was efficacious in heavily pre-treated patients with synovial sarcoma (overall response rate: 38.6%[3])
  - Higher response rates were observed in patients with synovial sarcoma who were female, had higher MAGE-A4 expression, had lower disease burden at baseline, or did not require bridging therapy
  - Responses were durable (median of 11.6 months in synovial sarcoma)

1. Carroll C, et al. *Future Oncol*. 2022;18:3651–65. 2. Savina M, et al. *BMC Med*. 2017;15:78. 3. Van Tine B, et al. Presented at CTOS 2022.
afami-cel, afamitresgene autoleucel; HLA, human leukocyte antigen; MAGE-A4, melanoma-associated antigen A4; TCR, T-cell receptor; TNT-D, time to next treatment or death.

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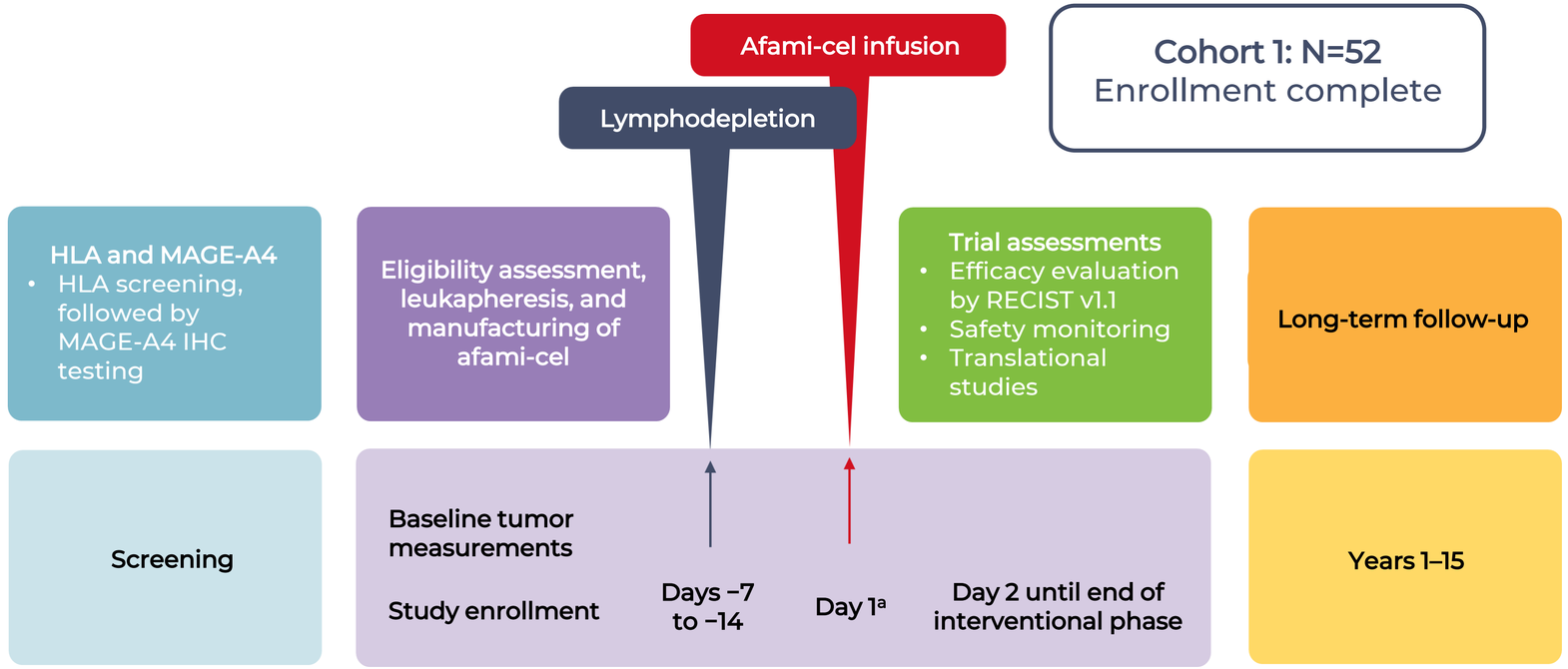
SPEARHEAD-1 (NCT04044768) Trial Design

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

Key eligibility criteria

- ECOG performance status of 0 or 1
- HLA-A*02 positive
- Aged ≥16 and ≤75 years
- Tumor MAGE-A4 expression by IHC
- 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; afami-cel, afamitresgene autoleucel; 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.

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Baseline Characteristics

Patients with synovial sarcoma in Cohort 1

	Synovial sarcoma (n=44)
Age at consent, years, median (range)	40.5 (19–73)
Female, n (%)	22 (50.0)
Race, n (%)	
Asian	3 (6.8)
Black or African American	2 (4.5)
White	39 (88.6)
Ethnicity	
Hispanic or Latino	2 (4.5)
Not Hispanic or Latino	38 (86.4)
Not reported	4 (9.1)
Geographic region, n (%)	
Europe/United Kingdom	13 (29.6)
North America	31 (70.5)
Number of lines of prior systemic therapy, median (range)	3 (1–12)
ECOG performance status, n (%)	
0	23 (52.3)
1[a]	21 (47.7)
Baseline target tumor lesion sum of longest diameter ≥100 mm, n (%)	21 (47.7)
MAGE-A4 expression H score at pre-screening, median (range)[b]	256.5 (133–300)

- 36.4% patients (16/44) received bridging therapy
  - The bridging therapies administered were:
    - Pazopanib (11 patients)
    - Ifosfamide (three patients)
    - Trabectedin (one patient)
    - Doxorubicin (one patient)
- Median time on bridging therapy
  - Pazopanib: 41 days
  - Chemotherapy: two cycles

Data cut-off: August 30, 2023. [a]Baseline ECOG performance status for one patient was recorded as 2 due to a transcription error but was subsequently confirmed as 1. [b]H score is derived by (3 x percentage of strongly staining cells) + (2 x percentage of moderately staining cells) + percentage of weakly staining cells, giving a range of 0–300. ECOG, Eastern Cooperative Oncology Group; MAGE-A4, melanoma-associated antigen A4.

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Safety

Treatment-emergent adverse events in ≥25% of patients with synovial sarcoma in Cohort 1, regardless of causation

	Synovial sarcoma (n=44)	
Event, n (%)	Any grade	Grade ≥3
Any treatment-emergent adverse event	44 (100.0)	44 (100.0)
Lymphopenia	43 (97.7)	43 (97.7)
Neutropenia	40 (90.9)	39 (88.6)
Leukopenia	38 (86.4)	37 (84.1)
Cytokine release syndrome	33 (75.0)	1 (2.3)
Nausea	29 (65.9)	1 (2.3)
Anemia	18 (40.9)	13 (29.5)
Vomiting	16 (36.4)	0
Constipation	15 (34.1)	0
Fatigue	15 (34.1)	0
Thrombocytopenia	15 (34.1)	8 (18.2)
Pyrexia	14 (31.8)	2 (4.5)
Hypophosphatemia	12 (27.3)	1 (2.3)
Dyspnea	12 (27.3)	2 (4.5)
Abdominal pain	11 (25.0)	2 (4.5)

- Patients received afami-cel doses of 2.68–9.99x10^9 transduced cells
- There were no Grade 5 adverse events
- Cytokine release syndrome was common:
  - Primarily Grade 1 (23/44; 52.3%)
  - Median time to onset of 2 days (range: 1–5)
  - Median time to resolution of 3 days (range: 1–14)
- One patient experienced immune effector cell–associated neurotoxicity syndrome (Grade 1), which lasted <24hr

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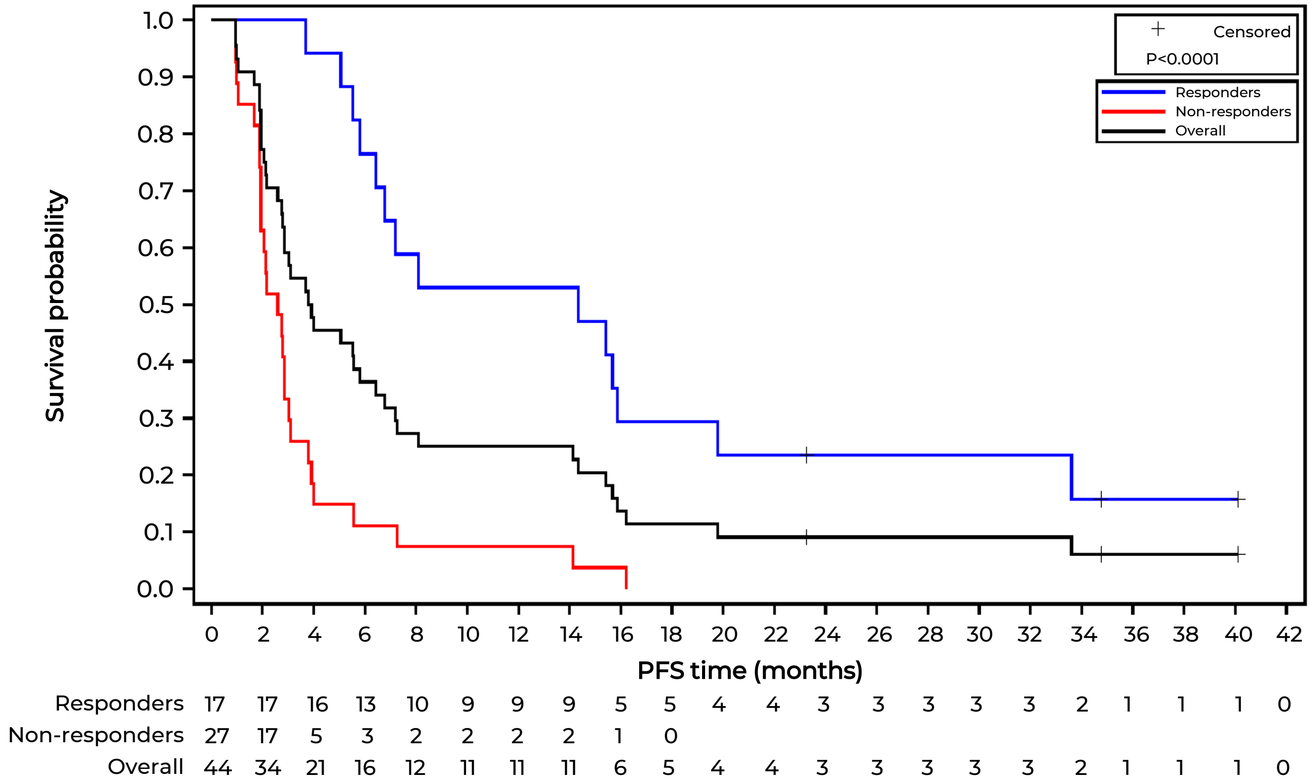
Data cut-off: August 29, 2022. afami-cel, afamitresgene autoleucel.

Progression-Free Survival

- Median PFS overall was 3.8 months (95% CI: 2.8–6.4)
- In the 17 patients with synovial sarcoma who had a RECIST response, median PFS was 14.3 months and 24-month PFS probability was 20%



	Overall	Responder	Non-responder
PFS, months, median (95% CI)	3.8 (2.8–6.4)	14.3 (5.8–19.8)	2.6 (1.9–3.0)
PFS probabilities (95% CI)			
12-month	0.3 (0.14–0.38)	0.5 (0.28–0.73)	0.1 (0.01–0.21)
24-month	0.1 (0.03–0.20)	0.2 (0.07–0.45)	0.0 (0.00–0.00)

Data cut-off: August 30, 2023. Response assessment was by RECIST v1.1 by independent review. PFS, progression-free survival; RECIST, Response Evaluation Criteria in Solid Tumors.

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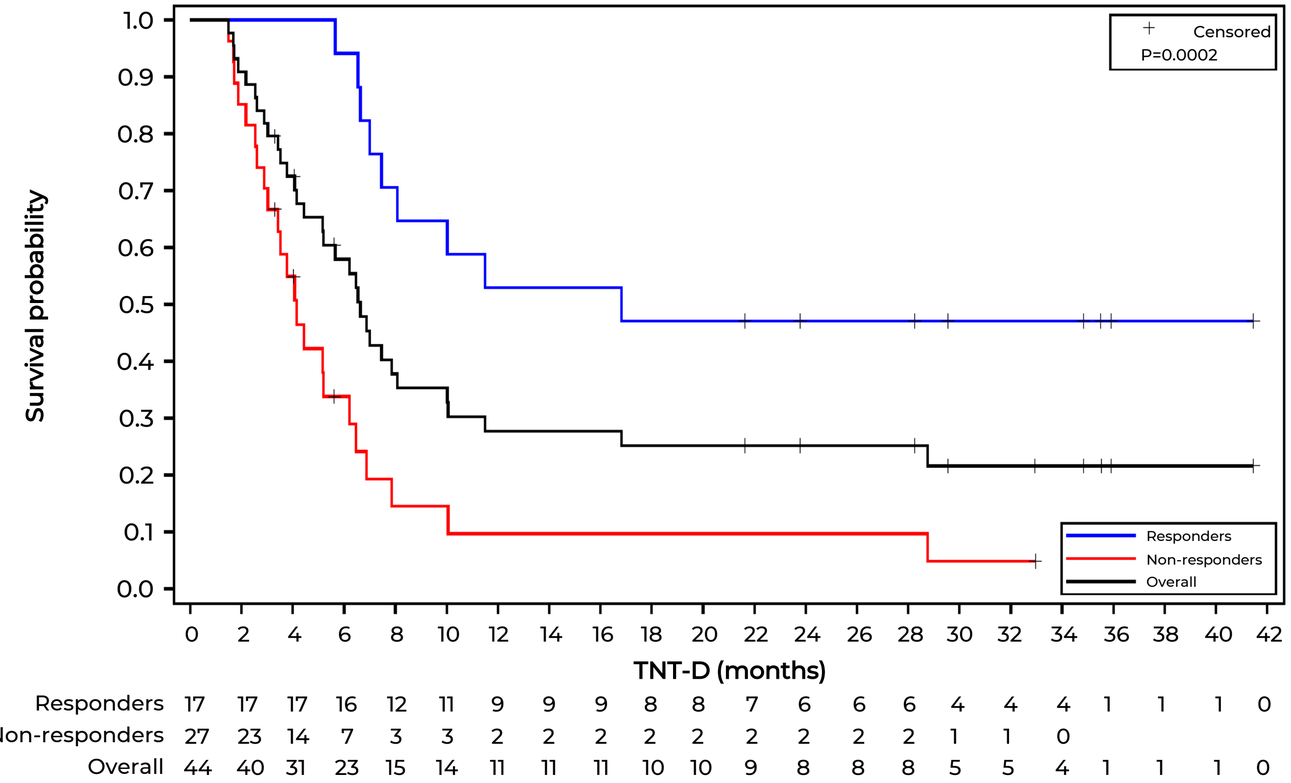
Time to Next Treatment or Death

- 20 patients started additional systemic therapy post progression
- After a single afami-cel infusion, the 24-month probability of being alive and additional systemic treatment free was 30% overall



	Overall	Responder	Non-responder
TNT-D, months, median (95% CI)	6.6 (4.44–8.08)	16.8 (7.00–NE)	4.1 (2.89–6.21)
TNT-D probabilities (95% CI)			
12-month	0.3 (0.15–0.42)	0.5 (0.28–0.73)	0.1 (0.02–0.26)
24-month	0.3 (0.13–0.39)	0.5 (0.23–0.68)	0.1 (0.02–0.26)

Data cut-off: August 30, 2023. Response assessment was by RECIST v1.1 by independent review. afami-cel, afamitresgene autoleucel; NE, not estimable; RECIST, Response Evaluation Criteria in Solid Tumors; TNT-D, time to next treatment or death.

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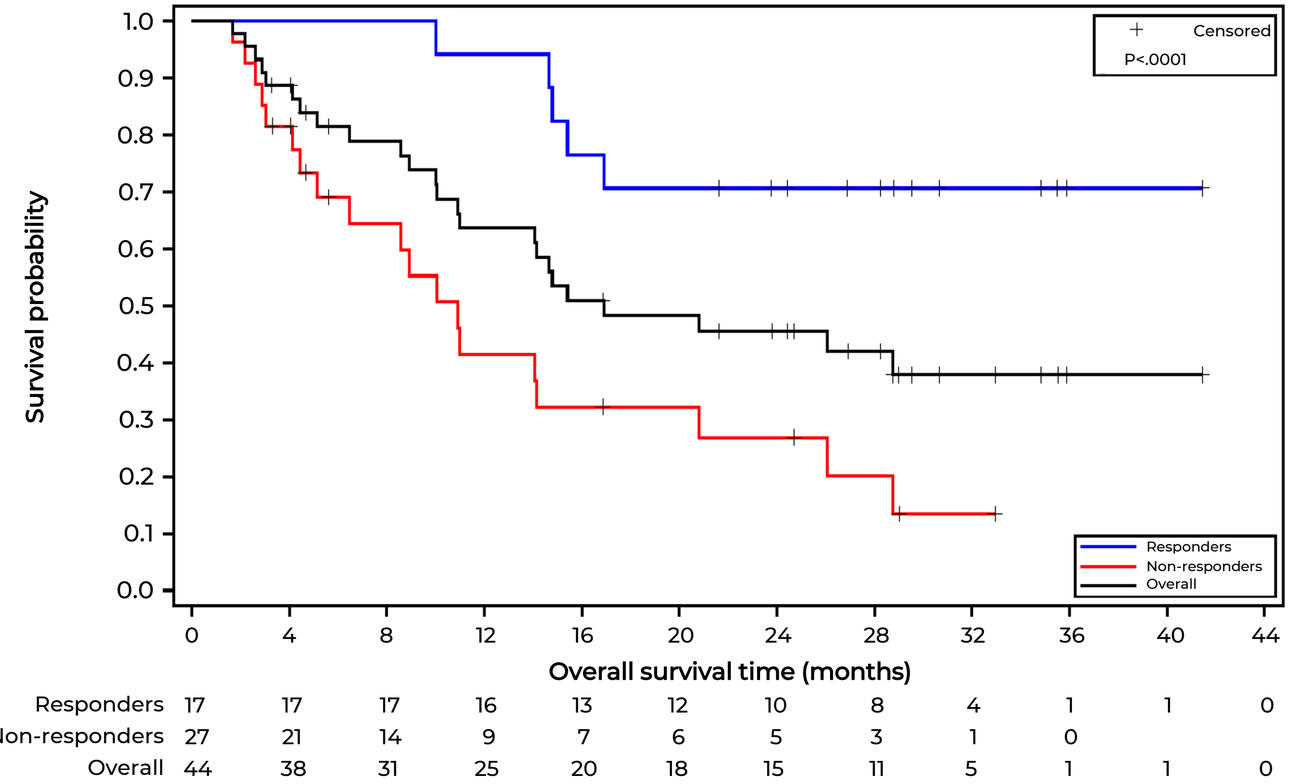
Overall Survival

- Median OS was 16.9 months (95% CI: 10.9–NE), with 45.5% of patients censored at the data cut-off
- Estimated OS probability in the 17 patients with synovial sarcoma who had a RECIST response was 90% at 12 months and 70% at 24 months



	Overall	Responder	Non-responder
OS, months, median (95% CI)	16.9 (10.9–NE)	Not reached (15.4–NE)	10.9 (5.2–20.8)
OS probabilities (95% CI)			
12-month	0.6 (0.47–0.76)	0.9 (0.65–0.99)	0.4 (0.22–0.60)
24-month	0.5 (0.30–0.60)	0.7 (0.43–0.87)	0.3 (0.11–0.46)

Median follow-up time was 32.8 months.

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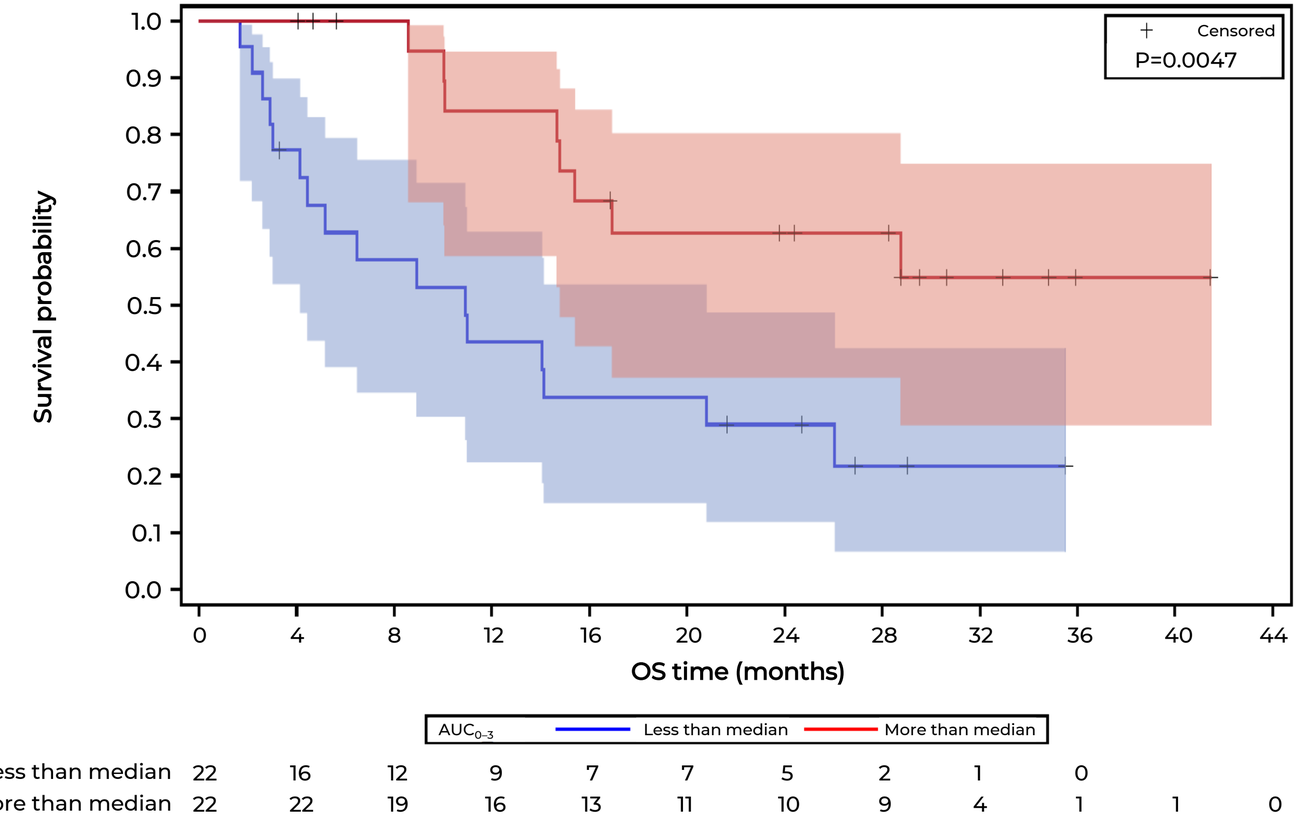
Data cut-off: August 30, 2023. NE, not estimable; OS, overall survival; RECIST, Response Evaluation Criteria in Solid Tumors.

Exposure-Response Relationship With OS

- Higher afami-cel cellular persistence ($AUC_{0–3}$) was associated with longer OS
- Median OS was not reached in patients with afami-cel exposure above the median



	$AUC_{0–3}$	
	Above the median	Below the median
OS, months, median (95% CI)	Not reached (14.78–NE)	10.9 (4.14–20.80)

- Exposure here is measured with $AUC_{0–3}$:
  - Area under the concentration-time curve for afami-cel (measured by vector copies/µg DNA) over the first 3 months post infusion

Data cut-off: August 30, 2023. afami-cel, afamitresgene autoleucel; AUC, area under the concentration-time curve; NE, not estimable; OS, overall survival.

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Conclusions

- Patients with advanced synovial sarcoma treated with afami-cel in SPEARHEAD-1 were heavily pre-treated
- Encouraging treatment-free intervals after a single afami-cel infusion in advanced synovial sarcoma
  - 24-month probability of being alive without additional systemic therapy was 30%
  - Median time to next treatment of 6.6 months after a median of three prior lines of therapy compares favorably with historical rates of 3.4 months[1]
- Promising OS, especially in those patients with a RECIST response
  - Median OS was 16.9 months overall
  - In patients with a RECIST response, median OS was not reached and survival probability at 24 months was 70%
- An exposure-response relationship was observed between afami-cel cellular persistence and OS
- SPEARHEAD-1 is ongoing
  - Additional access to afami-cel is ongoing in Cohort 3
- Rolling BLA submission for afami-cel has initiated and planned to complete this year

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1. Savina M, et al. *BMC Med*. 2017;15:78. afami-cel, afamitresgene autoleucel; OS, overall survival; RECIST, Response Evaluation Criteria in Solid Tumors; TNT-D, time to next treatment or death.

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