The SPEARHEAD-1 Trial of Afamitresgene Autoleucel ("Afami-cel" [Formerly ADP-A2M4]): Analysis of Overall Survival in Advanced Synovial Sarcoma

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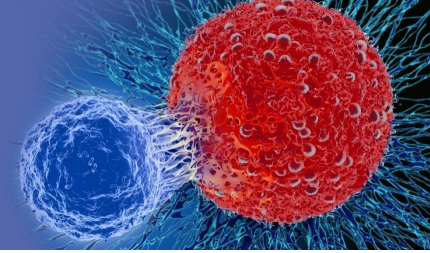


Introduction

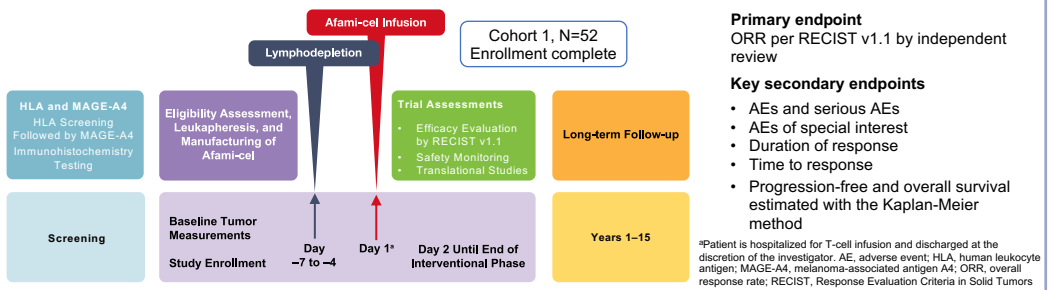
- Afami-cel is an autologous T-cell receptor (TCR) T-cell therapy engineered to target melanoma-associated antigen A4 (MAGE-A4) in human leukocyte antigen (HLA) A*02–eligible patients (pts) with advanced solid tumors
- Synovial sarcoma is a rare and aggressive tumor representing 5-10% of soft tissue sarcomas
- Outcomes are poor in the metastatic setting, with a 5-year overall survival (OS) of 15%,[1] and median OS (mOS) in real-world studies ranging from 9.6 to 16 months from the start of second-line therapy and ≤8 months from the start of third-line therapy[2-4]
- SPEARHEAD-1 (NCT04044768, **Figure 1**) is an ongoing, Phase 2, open-label trial to evaluate the efficacy and safety of afami-cel in pretreated pts with advanced/metastatic synovial sarcoma (Cohorts 1 and 2) or myxoid/round cell liposarcoma (Cohort 1)
- As of August 29, 2022, the 44 pts with synovial sarcoma who received afami-cel in Cohort 1 (**Table 1**) showed an overall response rate (ORR) by independent review per RECIST v1.1 of 38.6%, with a median (range) time to response of 4.9 weeks (4.1–12.1)[5]
- Responses were seen across all subgroups; higher response rates were observed in pts who were female, had higher MAGE-A4 expression, had lower disease burden at baseline, or did not require bridging therapy
- The safety profile included cytokine release syndrome and reversible hematologic toxicities, with no grade 5 events[5]
- Here, we report updated interim mOS data in pts with advanced synovial sarcoma in Cohort 1

Table 1. Baseline characteristics of patients who received afami-cel in Cohort 1 of the SPEARHEAD-1 Trial

Characteristic	Synovial sarcoma (N=44)
Sex, n (%)	
Male	22 (50.0)
Female	22 (50.0)
Age at consent, years, median (range)	40.5 (19–73)
Race, n (%)	
Asian	3 (6.8)
Black or African American	2 (4.5)
White	39 (88.6)
H score of MAGE-A4 expression at pre-screening, median (range)	257.3 (132–300)
ECOG at baseline, n (%)	
0	23 (52.3)
1	20 (45.5)
2	1 (2.3)
Bridging therapy, yes, n (%)	16 (36.4)
Transduced cells received, range	2.68–9.99 × 10^9
Prior lines of systemic therapy, median (range)	3 (1–12)
Baseline sum of lesion diameter ≥100 mm by independent review, n (%)	21 (47.7)
HLA-A*02:01P expression, n (%)	42 (95.5)[a]

[a]Of the remaining two pts, one (2.3%) each expressed HLA-A*02:02P and :06P
H score is derived by (3 × percentage of strongly staining cells) + (2 × 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

Figure 1. SPEARHEAD-1 trial design



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 estimated with the Kaplan-Meier method

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

Methods

- Pts received intravenous infusion of afami-cel after lymphodepletion chemotherapy consisting of fludarabine 30 mg/m^2 × 4 days and cyclophosphamide 600 mg/m^2 × 3 days

Updated survival analysis

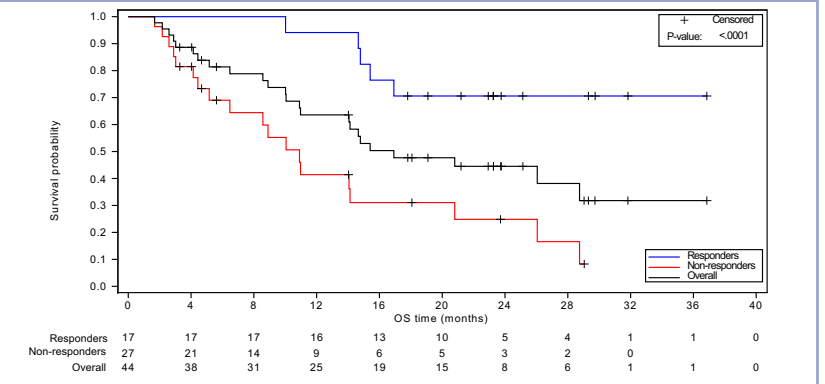
- An interim analysis was performed on March 29, 2023, when the median (range) follow-up time was 27.8 (16–38) months
- Median duration of response by independent review in the 17 pts with a response was 11.6 months (95% CI: 4.44–not estimable)
- Median progression-free survival was 3.8 months (95% CI: 2.8–6.4) and 4.1 months (95% CI: 2.8–6.9) by independent and investigator review, respectively
- Twenty-one pts received additional therapy during long-term follow-up (systemic therapy, n=20; radiation, n=8; other, n=4)
- mOS was 16.9 months (**Table 2**) with 45% of pts censored at the data cut-off
- The 12-month OS probability was 60% and 24-month probability was 40%
- OS was significantly longer in the 17 pts who had a RECIST v1.1 response by independent review (**Table 2, Figure 2**): the mOS was not reached, the 12-month OS probability was 90%, and 24-month probability was 70%
- **Figure 3** illustrates the variety of responses in pts with synovial sarcoma

Table 2. OS in pts with synovial sarcoma overall, and in responders vs non-responders by independent review

	Overall (N=44)	Responders (n=17)	Non-responders (n=27)
OS probabilities (95% CI)			
6 months	0.8 (0.66–0.90)	1.0 (1.0–1.0)	0.7 (0.47–0.83)
12 months	0.6 (0.47–0.76)	0.9 (0.65–0.99)	0.4 (0.22–0.60)
24 months	0.4 (0.29–0.59)	0.7 (0.43–0.87)	0.2 (0.09–0.45)
mOS, months (95% CI)	16.9 (10.91–not estimable)	Not reached (15.41–not estimable)	10.9 (5.16–20.80)

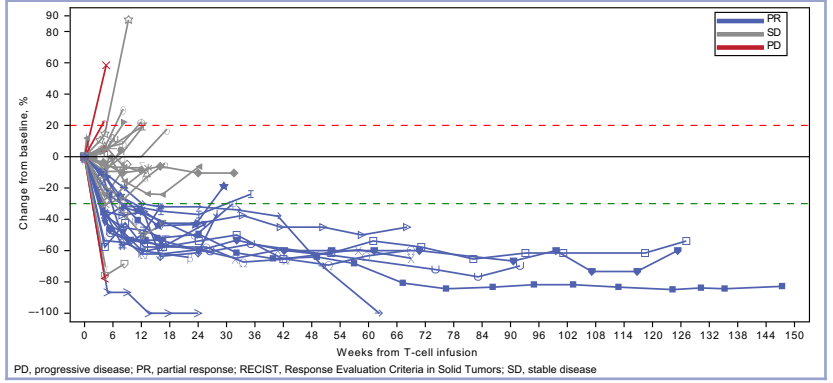
CI, confidence interval; OS, overall survival; mOS, median overall survival

Figure 2. OS for responders vs non-responders by RECIST v1.1 by independent review



OS, overall survival; RECIST, Response Evaluation Criteria in Solid Tumors

Figure 3. Change in sum of lesion diameter in target lesion from baseline using RECIST v1.1 by independent review



PD, progressive disease; PR, partial response; RECIST, Response Evaluation Criteria in Solid Tumors; SD, stable disease

Conclusions

- Pts with advanced synovial sarcoma treated in SPEARHEAD-1 were heavily pre-treated
- Afami-cel treatment resulted in durable responses in HLA-A*02-eligible pts with MAGE-A4–expressing synovial sarcoma
- Pts with advanced synovial sarcoma treated with afami-cel had meaningful survival, especially those pts with a RECIST response

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Footnotes and Abbreviations Used in Text
CI, confidence interval; HLA, human leukocyte antigen; MAGE-A4, melanoma-associated antigen A4; mOS, median overall survival; ORR, overall response rate; OS, overall survival; pts, patients; RECIST, Response Evaluation Criteria in Solid Tumors; TCR, T-cell receptor

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Data cut-off
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March 29, 2023