Nursing Considerations For the Use of MAGE-A4-Targeted SPEAR T-Cells in Patients With Synovial Sarcoma

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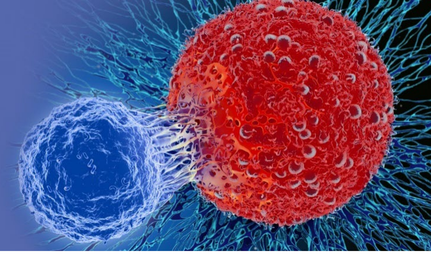
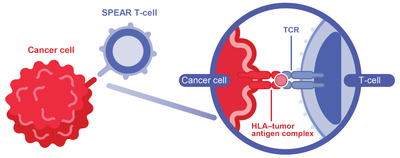


Introduction

- Sarcomas are rare malignant tumors, representing ~1% of all cancers in adults worldwide and ~2% of cancer-related mortality[1,2]
- Synovial sarcoma represents 5% of all soft tissue sarcoma, and one-third of the diagnoses occur in patients aged <30 years[3]
- Effective treatment options for patients with advanced relapsed synovial sarcoma are limited, creating an unmet need for patients with advanced disease who have progressed after first-line therapy
- Afamitresgene autoleucel (formerly ADP-A2M4), a SPEAR T-cell therapy directed toward HLA-A*02-restricted MAGE-A4 peptides, is being evaluated in clinical trials to investigate safety and anti-tumor activity in patients with synovial sarcoma (**Figure 1**)

Figure 1. T-Cells Are Engineered to Enhance the Affinity of the T-Cell Receptors So They Can Recognize Cancer Proteins, and As a Result Can Detect and Fight Cancer Within Patients



TCR-based recognition

More options for targeting cancers by enhancing the natural immune system

- T-cells scan HLA-tumor antigen complexes with TCRs
- Access to a broader spectrum of extra- and intra-cellular proteins
- TCR is the T-cell's natural receptor construct
- Ability to address solid tumors

Objectives

- Patient considerations are highlighted with the intent to enhance nursing care and patient experience related to the administration of this investigational product in the synovial sarcoma population
- Patients with multiple tumor types were treated in the trial, including data presented here from patients with advanced synovial sarcoma (n=16) (**Table 1**)

Table 1. Patient Characteristics

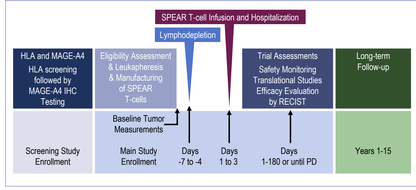
Characteristic	N=16
Sex, n (%)	
Male	10 (62.5)
Female	6 (37.5)
Median age, years (range)	49.0 (31–76)
Race, n (%)	
White	14 (87.5)
Asian	2 (12.5)
ECOG performance status, n (%)	
0	10 (62.5)
1	6 (37.5)
Median MAGE-A4 expression by H-score (range)[a]	249 (60–300)
Prior lines systemic therapy, median (range)	2.5 (1–6)
Most common systemic therapies	
Ifosfamide	16 (100.0)
Anthracycline (doxorubicin or epirubicin)	13 (81.2)
Pazopanib	7 (43.8)
Cell dose × 10^9, median (range)	9.28 (3.4–10)

[a]H score is a method of assessing immunohistochemistry results. H-score is assigned using the following formula: [1 × (% cells 1+) + 2 × (% cells 2+) + 3 × (% cells 3+)]. The final score ranges from 0 to 300

Trial Design

- This Phase I dose-escalation, expansion trial evaluated HLA-A*02 positive (excluding *02:05) patients with multi-tumor types expressing MAGE-A4 (**Figure 2**)
- Patients could receive cell doses between 0.12 × 10^9 and 10 × 10^9 transduced cells
- Disease was assessed per RECIST v1.1 by CT/MRI every 6 weeks up to month 24 and every 3 months thereafter until disease progression
- Prior to infusion, patients received lymphodepletion with cyclophosphamide and fludarabine

Figure 2. Trial Design



Safety Results

- In general, patients have tolerated the treatment well with an acceptable safety profile
- Most AEs were consistent with those typically experienced by patients with cancer undergoing cytotoxic chemotherapy or immunotherapy (**Table 2**)

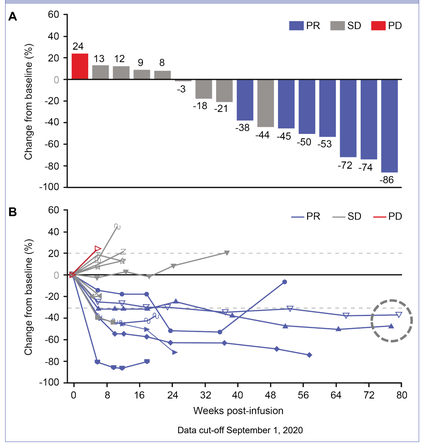
Table 2. Incidence of AEs Related to T-Cell Infusion

N=16; n (%)	Any grade	≥Grade 3
Patients with any AEs	16 (100)	16 (100)
Lymphopenia/lymphocyte count decreased	16 (100)	16 (100)
Cytokine release syndrome	14 (88)	2 (13)
Leukopenia/WBCs decreased	14 (88)	14 (88)
Neutropenia/neutrophil count decreased	14 (88)	13 (81)
Fatigue	11 (69)	0
Nausea	10 (63)	0
Pyrexia	10 (63)	0
Thrombocytopenia/platelet count decreased	10 (63)	7 (44)
Anemia/RBCs decreased	9 (56)	7 (44)
Diarrhea	8 (50)	0
Hypophosphatemia	8 (50)	7 (44)
Sinus tachycardia/tachycardia	7 (44)	0
Vomiting	7 (44)	0
Arthralgia	5 (31)	0
Decreased appetite	5 (31)	1 (6)
Dizziness	5 (31)	0
Dyspnea	5 (31)	0
Hypotension	5 (31)	1 (6)
Rash	5 (31)	3 (19)
Alanine aminotransferase increased	4 (25)	0
Cough	4 (25)	0
Headache	4 (25)	0
Musculoskeletal pain	4 (25)	0
Pruritus	4 (25)	0
Tumor pain	4 (25)	0

Efficacy Results

- Confirmed responses in 44% of patients with synovial sarcoma who received afamitresgene autoleucel, and a disease control rate of 94% (**Figure 3A**)
- Responses were durable, with a median duration of response of 28 weeks (range, 12–72+ weeks) (**Figure 3B**)
- Responses were superior to rates observed with available second-line therapies in synovial sarcoma[4-6]

Figure 3. Durable Responses in Synovial Sarcoma



Afamitresgene Autoleucel Administration Considerations

- Nurses play a key role in the safe administration of treatment and should understand specialized considerations (**Table 3**)
- It is imperative for nurses to educate patients and caregivers on identifying signs of CRS and neurotoxicity and prolonged cytopenias
  - AEs are most likely to occur within the first month following T-cell infusion, but may occur at later time points
- Nurses should be informed about the treatment algorithms for these AEs (**Table 3**)

Table 3. Afamitresgene Autoleucel Administration and Toxicity Considerations

Status	Strategy
Lymphodepletion	
Lymphodepletion with fludarabine (30 mg/m² for 4 days) and cyclophosphamide (≤ 600 mg/m² for 3 days)	• IV hydration • Mesna • G-CSF • Anti-microbial and anti-fungal prophylaxis
Infusion	
Hospitalization	• Staff treating trial patients should be experienced in acute post-transplant care and the management of associated toxicities
Pre T-cell infusion	• Weight • Pre-medicate with antihistamines and acetaminophen • Thawing of T-cells • Tocilizumab stocked in pharmacy
T-cell infusion	• Patient should be hospitalized • Administer by gravity over 15–30 min • Infusion over 45 min from thaw; if adverse reaction occurs, then reduce rate of infusion, and administer acetominophen, non-steroidal anti-emetic, IV fluids, and supplemental oxygen
Toxicity	
Cytokine release syndrome	• Gr 1: supportive care (IV fluids, maintain hydration and blood pressure); assess for infection and treat • Gr 2: supportive care; monitor organ function; administer O_2 and anti-IL6 therapy • Gr 3–4: anti-IL6 therapy, ICU management. **Note:** Administer anti-IL6 therapy at any time if clinically indicated (i.e., intervention beyond supportive measures, symptoms persisting ≥ 24 hours, patient with comorbidities or older age)
Encephalopathy	• Supportive care; ≥ 24 hours: anti-IL6 therapy, neuro consultation/EEG/neuroimaging
Prolonged cytopenias	• Bone marrow biopsy • Increase CBC frequency • G-CSF • Immunosuppressives/anti-microbial prophylaxis

Conclusions

Future Research:

- Afamitresgene autoleucel induced clinical and durable responses in patients with synovial sarcoma and had an acceptable safety profile in the Phase 1 trial
- Based on these data, an open-label Phase 2 trial (SPEARHEAD-1) to evaluate the efficacy, safety, and tolerability of afamitresgene autoleucel in 45 patients with advanced synovial sarcoma and myxoid/round cell liposarcoma is ongoing (ClinicalTrials.gov Identifier: NCT04044768)

Implications for Nursing:

- Nurses play a key role when caring for synovial sarcoma patients receiving afamitresgene autoleucel SPEAR T-cell therapy
- An understanding of clinical trial data will prepare nurses to provide evidence-based education on associated risks/benefits
- Clinical practice with the synovial sarcoma population can be enhanced when nurses are equipped with knowledge associated with the administration of this novel therapy

Abbreviations

AE, adverse event; CBC, complete blood count; CRS, cytokine release syndrome; CT, computed tomography; ECOG, Eastern Cooperative Oncology Group; EEG, electroencephalogram; G-CSF, granulocyte colony-stimulating factor; HLA, human leukocyte antigen; IHC, immunohistochemistry; IL6, interleukin 6; IV, intravenous; MRI, magnetic resonance imaging; PD, progressive disease; PR, partial response; RBC, red blood cell; SD, stable disease; SPEAR, specific peptide enhanced affinity receptor; WBC, white blood cell

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To view the mechanisms of action of SPEAR T-cells, please click here