Identifying MAGE-A4–Positive Tumors for SPEAR T-Cell Therapies in HLA-A’02–Eligible Patients

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Footnotes and abbreviations used in text
- 1T-cells can harbor HLA alleles present on dominant cells, including tumor cells.
- 2Tumors targeting peptide antigen load and active for the T-cell.
- 3Tumors targeting large tumor antigen and/or antigen.
- 4Using TCRs engineered to recognize and bind to specific cancer peptides, SPEAR T-cells can target solid tumors.
- 5Here we present data from a multinational, multicenter, screening study (NCT03887880) that prospectively evaluated HLA subtypes and MAGE-A4 profiles to determine eligibility; eligible to ethics in clinical trials assessing the safety and efficacy of SPEAR T-cell therapy targeting MAGE-A4.
- 6HLA-A’02–eligible patients with metastatic solid cancers.
- 7The screening study protocol follows a two-step testing process: HLA typing via a high resolution (4-digit, 8-sequence) base assay.
- 8Blood samples were used as the source of DNA.
- 9A Sanger sequencing-based typing assay was used at the lab (American Red Cross, Philadelphia, PA).
- 10We abstract reported eligibility results based on HLA criteria used at the time of testing; and those criteria were subsequently amended.
- 11Here we present results based on the patients who satisfied the amended HLA criteria listed above.
- 12MAGE-A4 positivity in tumor samples is defined as a histofluorescence intensity (HFI) score of 1 or greater.
- 13Histofluorescence intensity is determined by immunohistochemical (IHC) staining on 5-μm sections of formalin-fixed, paraffin-embedded tissue; 33 patients had a median of 10% MAGE-A4+ tumor cells.
- 14The percentage of patients eligible based on the expression of at least 1% of three or more) was: 110 %, not expressing), and MAGE-A4+ rate was 11.6% of Hispanic or Latino patients, 19.9% of Black or African American patients, and 57.2% of Asian patients.

HLA

- The data from the National Memeoriter Program show that the percentage of individuals expressing different common HLA-A2 alleles greatly among racial and ethnic backgrounds.12

- A*02:01 P generally the most prevalent allele, but its frequency is higher in White populations and lower in Asian and Black or African American populations.11

- A total of 897 patients had their HLA-A types accurately determined; among them, 2729 (45%) were either not screened or showed no positive results.

- Eligibility rates were different between races and ethnicities (Table 1).

Figure 1. Sanger-Powered Enriched Affinity Receptor T-Cells (SPEAR T-Cells).

Table 1. HLA Screening, Eligibility, Race, and Ethnicity

<table>
<thead>
<tr>
<th>Race/Ethnicity</th>
<th>Screening (%)</th>
<th>Eligible (%)</th>
<th>Summed (%)</th>
<th>Eligible (%)</th>
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<tbody>
<tr>
<td>White, not Hispanic</td>
<td>4646/220</td>
<td>2177</td>
<td>30.3</td>
<td>61.4</td>
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<tr>
<td>White, Hispanic</td>
<td>298/94</td>
<td>95</td>
<td>10.1</td>
<td>15.9</td>
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<td>African American</td>
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<td>77</td>
<td>1.2</td>
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<td>Black or African American</td>
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<tr>
<td>Asian</td>
<td>64/16</td>
<td>11</td>
<td>0.3</td>
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Figure 2. Distribution of HLA-As by Race and Ethnicity

- In the 273 HLA-A02+ eligible patients, 1543 had tumor samples evaluated by MAGE-A4 across sites in the US, Canada, and Spain among these, 321 patients were MAGE-A4+.

- MAGE-A4+ tumor expression was collected across 4 tumors for analysis.

- Overall, MAGE-A4+ rate remained stable within 6 years of tissue archival (Figure 3). The effect of storage time beyond 4 years on MAGE-A4 detection could not be assessed due to limited sample availability.

- In some indications (e.g., non-small cell lung cancer (NSCLC), MAGE-A4+ rate and expression level were higher in squamous cell carcinoma (SCC) compared to adenocarcinoma.

- Overall, MAGE-A4 expression level (P score) was higher in squamous cell carcinoma (SCC) and non-small cell lung cancer (NSCLC) tumors than in melanoma. MAGE-A4 expression level (P score) was also higher in squamous cell carcinoma samples.

- In both esophageal cancer and NSCLC, MAGE-A4+ rate was higher in squamous cell carcinoma samples, compared with adenocarcinoma samples. MAGE-A4 expression level (P score) was also higher in squamous cell carcinoma samples (Figure 4).

Figure 3. Effect of Archived Tissue, Paraffin Embedded Tumor Sample Time on MAGE-A4 Positivity Across Cancer Types

Figure 4. MAGE-A4 Positivity and Expression by Cancer Type

References


Acknowledgments and Disclosures

This study (NCT03887880) was sponsored by Adaptimmune. All authors provided by the study sponsors. LM001: American Association for Cancer Research (AACR), April 8–13, 2022; Hybrid, New Orleans, LA, USA