Enhancement of TCR-engineered T-cells Targeting MAGE-A4 Antigen by Co-expression of CD8α and Inhibition of AKT Signaling during ex vivo T-cell Expansion

Emily M. Schmidt1, Katerina Mandilovich1, Natalie Bath1, Gareth Betts1, William Spinner1, Kathryn Sun1, Ian Donaldson1, Cheryl McAlpine1, Ray Luke1, Jean-Marc Navenot1, Joseph P. Sanderson1, Phil Bassett1, Chris Evans1, Karen Miller1, Quan Lin2, Mark Dudley3, Alex Tipping1

1Adaptimmune, Oxfordshire, United Kingdom; 2Adaptimmune, Philadelphia, PA

Abstract

Introduction

A thymus-specific positive selection drives the development of T-cells with an expanded repertoire of receptors capable of recognizing pathogen-derived antigens. However, the expansion process can be limited by various factors, including the activation of the AKT pathway. In this study, we aimed to enhance the functional response of T-cells targeting the MAGE-A4 antigen by co-expressing CD8α and inhibiting AKT signaling.

Methods

SPEAR T-cells were generated from patients with advanced cancer and expanded ex vivo using CD8α expression and AKT inhibition. The effects of CD8α expression and AKT inhibition on T-cell attributes and in vivo efficacy were evaluated.

Results

CD8α expression and AKT inhibition enhanced T-cell attributes, including an increased proliferative potential and cytotoxicity. In vivo, AKT inhibition resulted in increased persistence of T-cells in peripheral blood.

Conclusions

The combination of CD8α expression and AKT inhibition represents a promising approach for enhancing the functional response of T-cells targeting MAGE-A4.

Acknowledgments and Disclosures

This study was supported by the National Cancer Institute (NCI) and was conducted as part of an investigator-sponsored trial (NCT04044859). The authors declare no conflicts of interest.

References


Table 1. Patients treated with ADP-A2M4CD8 SPEAR T-cells as of the data cutoff (August 2, 2021)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=25</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, n (%), male</td>
<td>13 (52.0)</td>
<td></td>
</tr>
</tbody>
</table>
| **Adaptimmune, Oxfordshire, United Kingdom; 2Adaptimmune, Philadelphia, PA**

**E-poster 373: Society for Immunotherapy of Cancer (SITC)** 10–14 November 2021

Presenter contact information: Alex.Tipping@adaptimmune.com

**Adaptimmune, Oxfordshire, United Kingdom; 2Adaptimmune, Philadelphia, PA**

**Adaptimmune, Oxfordshire, United Kingdom; 2Adaptimmune, Philadelphia, PA**

**Adaptimmune, Oxfordshire, United Kingdom; 2Adaptimmune, Philadelphia, PA**

**Adaptimmune, Oxfordshire, United Kingdom; 2Adaptimmune, Philadelphia, PA**