Initial Safety Assessment of MAGE-A4 Specific Peptide Enhanced Affinity Receptor (SPEAR) T-Cells

David S Hong,1 Marcus Butler,2 Melissa Johnson,3 Kunle Odunsi,4 Anthony J Olszanski,5 Brian A Van Thone,1 Karen Chagin,1 Maliyi Iyengar,1 Jean-Marc Navenot,6 Elliot Hong,3 Erin Van Winkle,3 Rafael Amado1

1MD Anderson Cancer Center, Houston, TX, USA; 2Princess Margaret Cancer Centre, Toronto, Ontario, Canada; 3San Diego Research Institute, Nithville, TN, USA; 4Thomson Park Conference Center, Center New York, NY, USA; 5Flour Cancer Center, Philadelphia, PA, USA; 6Washington University, St Louis, MO, USA; 7Adaptimmune,yclonimum, C starter, UK, and Philadelphia, PA, USA

Abstract

Background

MAGE-A4 is a tumour antigen that is expressed in high frequency in many human cancers. The generation of specific T-cells recognizing MAGE-A4 has been described utilizing T-cell receptors (TCR) and chimeric antigen receptors (CAR) strategies. Here, we describe the development of tumor-specific affinity receptor (SPEAR) T-cells recognizing MAGE-A4.

Methods

Study Design

Healthy donors were selected and screened for T-cell isolation and transduction. T-cells were transduced with a lentiviral vector which delivered a recombinant MAGE-A4 specific T-cell receptor (MAGE-A4 SPEAR T-cells). Upon transduction, cells were optimized for T-cell persistence and function.

Results

T-cell IgG, H&E, and IHC staining is shown in Figure 1. MAGE-A4 SPEAR T-cells were robustly generated and expanded with greater than 95% purity and 10^8 cells/mL at 4 days post transduction. The expression of MAGE-A4 on the surface of T-cells by flow cytometry is shown in Figure 2. MAGE-A4 expression was 20% 1+, 40% 2+, 10% 3+.

Conclusions

MAGE-A4 SPEAR T-cells could be generated in healthy donors and expanded significantly in vitro. MAGE-A4 SPEAR T-cells may provide a novel approach to targeted immunotherapy for patients whose tumours express MAGE-A4.

Acknowledgements

This work was supported by the Princess Margaret Cancer Centre, Roswell Park Cancer Center, and The University of British Columbia.

Disclosure

The authors of this poster meet all the criteria for authorship suggested by the International Committee of Medical Journal Editors. No competing financial interests exist.

References


Figure 1. Immunohistochemistry of MAGE-A+ tumor sections. MAGE-A+ tumors showing high density of MAGE-A4 SPEAR T-cells are shown in Figure 1. H&E, and IHC staining is shown in Figure 1. MAGE-A4 SPEAR T-cells were robustly generated and expanded with greater than 95% purity and 10^8 cells/mL at 4 days post transduction. MAGE-A4 expression was 20% 1+, 40% 2+, 10% 3+.

Figure 2. Expression of MAGE-A4 on the surface of T-cells by flow cytometry. MAGE-A4 expression was 20% 1+, 40% 2+, 10% 3+.

Figure 3. Enzyme-linked immunosorbent assay (ELISA) results for the patient dosed on 2 July 2018. MAGE-A4 SPEAR T-cell levels were measured in the blood (Table 1). The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level. The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level.

Figure 4. Enzyme-linked immunosorbent assay (ELISA) results for the patient dosed on 2 July 2018. MAGE-A4 SPEAR T-cell levels were measured in the blood (Table 1). The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level. The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level.

Figure 5. Flow cytometry analysis of T-cell persistence over time. MAGE-A4 SPEAR T-cells expand in number for at least 2 weeks after infusion. The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level. The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level.

Figure 6. Flow cytometry analysis of T-cell persistence over time. MAGE-A4 SPEAR T-cells expand in number for at least 2 weeks after infusion. The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level. The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level.

Figure 7. Flow cytometry analysis of T-cell persistence over time. MAGE-A4 SPEAR T-cells expand in number for at least 2 weeks after infusion. The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level. The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level.

Figure 8. Flow cytometry analysis of T-cell persistence over time. MAGE-A4 SPEAR T-cells expand in number for at least 2 weeks after infusion. The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level. The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level.

Figure 9. Flow cytometry analysis of T-cell persistence over time. MAGE-A4 SPEAR T-cells expand in number for at least 2 weeks after infusion. The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level. The most frequent AEs and treatment-related AEs are consistent with the expansion and persistence of MAGE-A4 SPEAR T-cells at the 0.1 × 10^6 dose level.