Case Reports: Correlates of Response Following Adoptive Transfer of ADP-A2M4, Affinity-Enhanced T-Cells Targeting MAGE-A4 in Synovial Sarcoma

Svetlana Fayngerts1, Zohar Wolkhinsky1, Shravani Shitole1, Joana Serna2, Rebecca Dryer-Minney1, Ruoxi Wang1, Jean-Marc Navenot1, Olga Ochkur1, Gareth Betts1, Natalie Bath1, Ein Van Winckle1, Tom Holdich1, Malin Lygren1, Rafael Amador1, Marcus Butler2, David Hong2, Alex Topping2, Samik Basu2, Indu Ramachandran3

1Adaptimmune, Philadelphia, PA, USA; 2Princess Margaret Cancer Centre, Toronto, ON, Canada; 3MD Anderson Cancer Center, Houston, TX, USA

*Former employee of Adaptimmune

Introduction

- ADP-A2M4 is a genetically engineered chimeric affinity-enhanced T-cell receptor-modified T-cell product directed towards a MAGE-A4 peptide expressed on the surface of HLA-A*02+ tumor cells
- ADP-A2M4 is currently being tested in a phase I/IIa dose escalation trial (NCT03132922) for patients with advanced MAGE-A4+ synovial sarcoma
- Clinical responses with ADP-A2M4 have been reported in patients with advanced MAGE-A4+ synovial sarcoma

Figure 1. Best overall response in 12 patients with post-baseline assessments.

Figure 2. High persistence of transduced ADP-A2M4 T-cells in a responder.

Figure 3. Intratumoral infiltration of SPEAR T-cells post-infusion without loss of antigen expression in a responder.

Figure 4. Good induction of IFNγ and IL-15 observed in a responder.

Figure 5. The infusion of SPEAR T-cells and post-infusion SPEAR T-cells isolated from the tumor adjacent fluid from a responder and a non-responder.

Results

- In the first 12 patients (1048) in the ADP-A2M4 treatment arm: IFNγ and IL-15 expression were observed in a responder (12440) and a non-responder (12391)
- Intra-tumoral infiltration and activity may represent a mechanism of resistance
- PD-L1 upregulation in response to SPEAR T-cell tumor infiltration and activity may represent a mechanism of resistance
- High persistence (by vector copies/µg DNA) in a responder (12440); lower levels in a non-responder (12391)
- Persistence of transduced ADP-A2M4 T-cells was measured by qPCR of the lentiviral vector PSI sequence in genomic DNA extracted from PBMCs collected at the indicated visits

Conclusions

- High expression levels of IFNγ and IL-15 in the post-infusion samples
- Good infiltration of tumor sites, as inferred from the pre- and post-infusion samples
- Induction of IFNγ and IL-15 in response to SPEAR T-cell tumor infiltration and activity may represent a mechanism of resistance
- We continue to analyze biomarkers in the 10 additional synovial sarcoma patients who have been treated

Acknowledgments and Disclosures


References

2. As reported in November 2019. Princess Margaret Cancer Centre, Toronto, ON, Canada.