A Phase I Single Arm, Open Label Clinical Trial Evaluating Safety of MAGE-A10<sup>c796</sup>T in Subjects with Advanced or Metastatic Head and Neck, Melanoma or Urothelial Tumors (NCT02989064)

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**ABSTRACT**

**Background**

MAGE-A10 is a cancer/testis antigen that has been detected by immunohistochemistry (IHC) in 42, 26 and 17% of urothelial, melanoma and head and neck tumors, respectively. This study will evaluate the safety and antitumor activity of genetically engineered affinity enhanced autologous MAGE-A10<sup>c796</sup>T cells directed towards a MAGE-A10 peptide expressed on tumors in the context of HLA *A02:01 and/or *A02:06.

**Methods**

This first-in-human T cell dose escalation study utilizes a modified 3+3 design to evaluate safety, including dose limiting toxicities (DLT). Secondary objectives include anti-tumor activity (overall response, duration of response, time to response, PFS, OS) and translational research assessments. Patients are screened under a separate protocol (NCT02636855). Those who are HLA*A02:01 and/or *A02:06 positive and have inoperable or metastatic (advanced) urothelial cancer, melanoma, or squamous cell head and neck tumors with MAGE-A10 expression and meet all other entry criteria are eligible for treatment. Patients must have received standard of care therapies and have progressive disease.

**STUDY DESIGN**

- An open-label study of autologous genetically modified MAGE-A10 specific T cells in head and neck, melanoma, or urothelial tumors
- Subjects must screen for relevant HLA alleles and MAGE-A10 antigen expression
- Eligible subjects will undergo leukapheresis and their T cells will be isolated, genetically engineered and expanded ex vivo
- This dose escalation study utilizes a modified 3+3 design (see table below)
- Expansion at optimal dose range up to 10 subjects across tumors
- If 1 or more subjects experience a DLT, expansion of additional 3 subjects will occur in that dose group
- Lymphodepletion is with fludarabine at 30 mg/m2 and cyclophosphamide at 600 mg/m2/day, on days -7, -6, and -5.
- Post-transplant immune profile for association with treatment outcome

**KEY ELIGIBILITY CRITERIA**

**Inclusion Criteria**

- Inoperable or metastatic (advanced) urothelial cancer
- Has received a platinum containing regimen in the adjuvant or metastatic setting or is ineligible for, or has refused platinum as part of the prior chemotherapy regimen; may have received prior immunotherapy
- Advanced melanoma
- Has received a PD-1 and/or CTLA-4 inhibitor
- Has received BRAF inhibitor or the combination of BRAF and MEK inhibitors for BRAF-V600 mutant melanoma
- Advanced squamous cell head and neck cancer
- May have received a platinum containing chemotherapy for treatment of primary tumor in adjuvant or metastatic setting or refused such treatment. May have received prior immunotherapy
- HLA*A02:01 and/or *A02:06 and MAGE-A10 positive
- ≥ 18 years of age
- Anticipated life expectancy >3 months
- ECOG performance status 0-1
- Adequate organ function

**Exclusion Criteria**

- Previous anti-cancer therapy toxicity must have recovered to ≤ Grade 1 (except for non-clinically significant toxicities).
- Subjects with Grade 2 toxicities that are deemed stable or irreversible can be enrolled
- History of chronic or recurrent severe autoimmune or immune mediated disease requiring steroids or other immunosuppressive treatments
- Major surgery within 4 weeks prior to lymphodepletion (must be fully recovered from any surgical related toxicities)
- Other active malignancy within 3 years
- Active brain or leptomeningeal metastases
- ECG showing clinically significant abnormality at screening
- Active infection with HIV, HBV, HCV or HTLV

**STUDY OBJECTIVES & ENDPOINTS**

**Primary**

- To evaluate the safety and tolerability of autologous genetically modified MAGE-A10<sup>c796</sup>T cells
- To evaluate the anti-tumor activity of autologous genetically modified T cells
- To understand mechanisms of resistance to MAGE-A10<sup>c796</sup>T
- To evaluate antigen spreading as a mechanism of response

**Secondary**

- Adverse events (AE), including serious adverse events
- Laboratory and cardiac assessments
- Persistence of MAGE-A10<sup>c796</sup>T
- Correlate circulating cytokines with CRS
- Overall response rate, best overall response, time to response, duration of response, duration of stable disease, progression-free survival, overall survival
- Associate persistence, phenotype and functionality of MAGE-A10<sup>c796</sup>T in with response
- To evaluate and compare the pre- and post-T cell infusion profile of immunosuppressive cell populations in the blood versus tumor and compare to treatment response
- To investigate the immune contexture of each subjects’ tumor with treatment response
- To determine MAGE-A10 expression in tumor post-therapy
- To assess antigen spreading and enhancement of the endogenous anti-tumor response following T cell infusion

**STUDY STATUS**

This study is currently active and enrolling; as of May 18, 2017, 4 subjects have been enrolled

**ANTIGEN EXPRESSION**

Example of immunohistochemistry staining of melanoma tissue for the MAGE-A10 antigen

**SITES & INVESTIGATORS**

MD Anderson Cancer Center, Houston, TX
Princess Margaret Cancer Centre, Toronto, ON, Canada
Massachusetts General Hospital, Boston, MA
Sarah Cannon Research Institute, Nashville, TN

For more information visit [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov) or [www.adaptimmune.com](http://www.adaptimmune.com)

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