Inclusion Criteria:

Antigen expression at ≥1+ intensity in ≥ 10% of tumor cells by IHC

Criteria for inclusion:

- Engineered autologous specific peptide
- Evaluate the safety and tolerability of genetically engineered autologous specific peptide
- Recognize the MAGE-A4 restricted peptide:

  Melanoma

  MAGE-A4 SPEAR T-cells

STUDY DESIGN

- An open-label study of autologous genetically modified MAGE-A4-specific T cells in urothelial cancer (transitional cell cancer of the bladder, ureter or renal pelvis), melanoma, squamous cell carcinoma of the head and neck, ovarian cancer, NSCLC (squamous, adenosquamous, or large cell), esophageal (squamous and adenocarcinoma) or gastric cancer
- Subjects must screen positive for relevant HLA alleles and MAGE-A4 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 20 subjects across tumors
- If 1 out of 3 subjects experiences 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 for 3 days
- Subjects discontinue “interventional phase” at disease progression
- Long term follow up to 15 years post T cell infusion

STUDY OBJECTIVES & ENDPOINTS

Primary Objectives

- To evaluate the safety and tolerability of autologous genetically modified MAGE-A4 SPEAR T-cells in subjects with HLA-A*02 and MAGE-A4 positive inoperable locally advanced or metastatic tumors
- To evaluate the antitumor activity of MAGE-A4 SPEAR T-cells
- To explore potential mechanisms of response and resistance to MAGE-A4 SPEAR T-cells
- To evaluate germline polymorphisms in cytokine genes and their association with cytokine release syndrome (CRS)

Endpoints

- Adverse events, including serious adverse events
- Laboratory assessments
- Incidence of dose limiting toxicities (DLTs) and determination of optimally tolerated dose range
- Persistence of MAGE-A4 SPEAR T-cells
- Overall response rate, best overall response, time to response, duration of response, duration of stable disease, progression-free survival, overall survival
- Measurement of persistence, phenotype and functionality of MAGE-A4 SPEAR T-cells in the blood
- Measurement of changes in MAGE-A4 SPEAR T-cell subsets, immunosuppressive cell populations and clonal outgrowth of T cell populations in the blood
- Evaluation of the tumor microenvironment and measurement of immune cell markers and clonal outgrowth of T cell populations in tumor pre- and post-infusion
- Assess DNA for polymorphisms in cytokine genes including those previously associated with CRS

SITES & INVESTIGATORS

This study is open and currently enrolling

- MD Anderson Cancer Center, Houston, TX
- Sarah Cannon Research Institute, Nashville, TN
- Fox Chase Cancer Center, Philadelphia, PA
- Princess Margaret Cancer Centre, Toronto, ON, Canada
- Adaptimmune, Philadelphia, PA

For more information visit www.ClinicalTrials.gov or www.adaptimmune.com

Direct your questions to connie.erickson-miller@adaptimmune.com

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