A Phase 1/2a Study to Evaluate the Safety, Tolerability, Immunogenicity, and Anti-tumor Activity of GEN-009 Adjuvanted Neoantigen Vaccine in Adult Patients with Selected Solid Tumors

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Background

• GEN-009 is a personal adjuvanted neoantigen vaccine being developed for the treatment of patients with solid tumors.
• Genocea’s proprietary Antigen Lead Acquisition System (ATLAS™) is used to prioritize tumor neoantigens that will be synthesized into peptides for inclusion in GEN-009.
• ATLAS uses a patient’s peripheral blood T cells and antigen presenting cells to screen for every patient-specific immunogenic tumor mutation.
• The ATLAS neoantigen selection is based on a cytokine read-out.
• Neoantigens prioritized by ATLAS contain an epitope that is recognized by the patient’s T cells and capable of eliciting patient-specific stimulatory CD4+ or CD8+ T cell responses.
• Unlike in silico models, ATLAS is also able to identify inhibitory neoantigens that will be excluded from a patient’s vaccine (see Poster #166).
• GEN-009-101 is a first-in-human, multicenter phase 1/2a study being conducted in 3 parts enrolling patients with melanoma, non-small cell lung cancer (NSCLC), squamous cell carcinoma of the head and neck (SCCHM), urothelial carcinoma (UC) and renal cancer (RC, in Parts B and C only).
• The GEN-009 vaccine consists of 4 to 20 synthetic long peptides (SLPs) administered with the adjuvant Hitolin (gly-DICl). The SLPs will be divided into 4 pools administered subcutaneously, one pool per limb.

Screening Period

Decision Points (DP)
• DP #1: Decision to proceed with vaccine manufacture. Requires identification of a suitable number and quality of neoantigens and patient meets eligibility criteria.
• DP #2: Successful manufacture of GEN-009 peptides. Patient continues to meet eligibility criteria.

Sample Collection and Vaccination Schedule

Vaccination schedule: Day 1, Day 22, Day 43 with booster vaccinations after week 12 and week 24.
• An alternative schedule will be evaluated if above schedule is safe but does not provide adequate immunogenicity.

Sample Size

• Part A: 9 patients will enroll on Schedule 1. Additional patients will enroll to ensure there are 6 DLT-evaluable patients. If alternative schedule is evaluated, 6 DLT-evaluable patients will also be required.
• Part B: 15 patients in each of the 5 disease-specific cohorts.
• Part C: Up to 40 patients. An interim analysis will be performed for futility after approximately 15 patients have been evaluated.

Summary

• GEN-009-101 is a first-in-human, multicenter phase 1/2a study evaluating the safety and antitumor activity in patients with melanoma, NSCLC, SCCHN, urothelial carcinoma and renal cell cancer treated with GEN-009, a personalized adjuvanted peptide vaccine. GEN-009 is currently enrolling patients in Part A.
• Neoantigens for inclusion in GEN-009 are selected using Genocea’s proprietary ATLAS technology.
• ATLAS prioritizes potential neoantigens based on each patient’s CD4+ and CD8+ T cell responses to all potential neoantigens independent of HLA type.
• GEN-009-101 is evaluating GEN-009 as monotherapy and in combination with nivolumab.
• Safety and immunogenicity data from Part A are expected in 1H 2019.

Key Inclusion Criteria

• Age ≥18 years with histologically confirmed diagnosis of 1 of the following tumor types:
  • Melanoma (cutaneous)
  • NSCLC
  • SCC/NH (oral, oropharyngeal, hypopharyngeal, or laryngeal)
  • Urothelial carcinoma of the bladder, ureter, urethra, or renal pelvis that has predominantly transitional cell/urothelial features on histologic testing
  • Renal cell carcinoma with a clear cell component (Parts B and C only)
• Adequate tumor tissue for NGS.
• ECOG 0 or 1.
• Adequate hematologic, liver and kidney function.

Part A Specific Criteria

• Completed or will complete treatment with curative intent and has NED.

Part B Specific Criteria

• Receiving or will initiate full-dose nivolumab in accordance with USPI for the eligible tumor types and received ≥75% of planned dose prior to Day 1 vaccination.
• Disease assessment prior to starting nivolumab, prior to DP#1 and prior to DP#2.
• Measurable disease AND must have PR or SD at DP#1.

Part C Specific Criteria

• Has received prior standard therapy including 1 prior PD-1/PD-L1 containing regimen.
• Measurable disease.

Objectives

• Determine safety and immunogenicity (Parts A, B, C).
• Determine schedule for further evaluation (Part A).
• Evaluate antitumor activity in combination with nivolumab (Part B) or as monotherapy (Part C).
• Evaluate additional cellular responses (Parts A, B, C).
• Evaluate polyfunctional T cell responses by ICS
• Evaluate tumor infiltrating T cells (Parts B, C).

Study Assessments

• Safety: Safety measurements include evaluation of adverse events (AE), serious AEs and AESI
• Efficacy: Efficacy will be evaluated using RECIST 1.1
  • Part A: Tumor response rate*. Duration of response, Progression-free survival
  • Part B: Objective response rate, Duration of response, Progression-free survival
  • Part C: Objective response rate, Duration of response, Progression-free survival

Immunogenicity

Blood will be collected to evaluate cellular immune responses to vaccination:
• IFN-γ/GrB Fluorospot assay to assess CD4+ and CD8+ T cell response to each individual SLP (ex vivo and in vitro stimulated)
• CD4+ and CD8+ polyfunctional T cell responses by ICS
• Immunophenotyping of PBMC cell populations by flow cytometry
Tumor biopsies will also be collected and assessed (Parts B and C), including RNA sequencing and immunofluorescence to evaluate tumor microenvironment and infiltrating cells.

Acknowledgements

We would like to thank the patients who consented to participate in this study and their families.