BACKGROUND

• AGEN2003 is an individualized, fully synthetic neoantigen vaccine comprising computationally defined peptide immunogens complexed to recombinant heat shock protein (HSP) and administered with QS-21 Stimulon® adjuvant (Figure 1).

• HSPs efficiently deliver neoantigens to the correct immune cells to activate a robust, specific anti-cancer immune response with significantly less peptide.

• In animal models and clinical trials, vaccines employing HSP-peptide complexes mixed with QS-21 elicit antigen-specific CD8+ and CD4+ T-cell responses.

• This study evaluated single-agent treatment with AGEN2003 vaccine with QS-21 in patients with advanced cancer that is refractory to standard therapies in Phase 1 clinical trial (NCT02929977), as well as compassionate use access.

Figure 1. AGEN2003 Vaccine

METHODS

Study Objectives

• Primary objectives
  - To demonstrate the safety and tolerability of single-agent treatment with AGEN2003 with QS-21 in patients with advanced cancer that is refractory to standard therapies

• Exploratory objectives
  - Clinical: To evaluate overall survival (OS), progression-free survival (PFS), and objective response rate (ORR) per RECIST v1.1 from time of first administration in patients with advanced cancer receiving AGEN2003 with QS-21 treatment

Study Design

• This was a Phase 1a study evaluating single-agent treatment of AGEN2003 with QS-21 in 3 patients with advanced solid tumors that were refractory to standard-approved therapies, with 2 patients additionally treated under a similar protocol through compassionate use.

• An institutional review board at each participating site approved the study and, after signing an informed consent form, patients were treated with AGEN2003.

• The vaccine consisted of synthetically produced peptides (124 peptides, ~10 µg total) generally 27 amino acids in length, specific to each patient’s tumor, mixed with 240 µg Hsc70 and was administered subcutaneously with 50 µg QS-21 bi-weekly up to 1 year (Figure 2).

Figure 2. Study Design

• All patients allowed access to archival tumor tissue or allowed procurement of fresh tumor tissue (if an adequate archival sample was not available) for whole-exome sequencing.

• To evaluate presence of subject-specific, tumor neoantigen-specific T cells in circulation, IFN-γ ESIFlow assay was performed on peripheral blood mononuclear cells (PBMCs) stimulated with peptide pools containing predicted MHC I and MHC II epitopes (Figure 3).

Figure 3. Method of Determining Tumor Neoantigen-specific T Cells in Circulation

RESULTS

Patient P1 (Phase 1a Study)

• Demographics and baseline characteristics of Patient P1 (ID #189-002) are described in Table 1, and vaccine immunogenicity and immune contexture in tumor biopsy is depicted in Figure 4.

Figure 4. Vaccine Immunogenicity and immune contexture in Patient P1

Table 1. Demographics and Baseline Characteristics of Patient P1

Patient P2 (Phase 1a Study)

• Demographics and baseline characteristics of Patient P2 (ID #189-006) are described in Table 2, and vaccine immunogenicity and immune contexture in tumor biopsy is depicted in Figure 5.

Figure 5. Vaccine Immunogenicity and immune contexture in Patient P2

DISCUSSION

• AGEN2003 was well tolerated with no serious adverse events attributable to the vaccine.

• All patients described here had failed multiple lines of prior therapy and PBMC procurement was inadequate to detect immune response to certain neoantigens was either augmented or induced de novo.

• As of July 2018, 2 patients (both with a quantifiable immune response) remain alive. The vaccine described here has been subsequently modified and this new version, called AGEN2017, is the subject of an ongoing Phase 1a study (n=3; patients with solid tumors, completely resected yet at risk of relapse; NCT03673020), after which it will be combined in future trials with immunomodulatory antibodies including Ageron’s CTLA-4 antagonist AGEN1894 and our PD-1 antagonist AGEN2034.