Phase 1/2 Study of CTLA-4 Inhibitor AGEN1884 + PD-1 Inhibitor AGEN2034 in Patients With Advanced/Refractory Solid Tumors, With Expansion Into Second-Line Cervical Cancer and Solid Tumors

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BACKGROUND

• In clinical trials, the combined inhibition of PD-1 and CTLA-4 pathways by blocking receptor-ligand interactions has resulted in clinical responses in several tumor types, including melanoma, breast cancer, renal cell carcinoma, and colorectal cancer. In addition, melanoma and non-small cell lung cancer. As a result, pembrolizumab (PD-1) or ipilimumab (CTLA-4) are currently under evaluation as monotherapy in phase II/III studies in subjects with advanced melanoma (NCT01272841 and NCT01680475, respectively).

• The phase 2 portion of this study evaluating AGEN1884 in combination with AGEN2034 in adults with second-line cervical cancer, and other advanced/metastatic solid tumors, is currently ongoing (NCT02939976 and NCT03719583, respectively).

• Antigen-specific T-cell activation is regulated by a balance of co-stimulatory and co-inhibitory signals, such as those mediated by inhibitory receptors such as programmed death-1 (PD-1) and programmed death-ligand 1 (PD-L1) from the PD-1 pathway, and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) from the CTLA-4 pathway.

• The binding of these receptors to their ligands results in impaired T-cell function. For these reasons, antibody blockade of PD-1 and CTLA-4 has been identified as a therapeutic modality to reinvigorate immune-targeted T-cell responses.

Figure 1. Overview of Pathways Affected by CTLA-4 and PD-1

METHODS

• In the phase 1 portion, which is still ongoing, preliminary results demonstrate that AGEN1884 (1 mg/kg q6w) + AGEN2034 (3 mg/kg q2w) is generally safe, well tolerated, and active in adults with metastatic melanoma and is currently being tested in multiple other indications.2-4

• There was 1 death not related to the study (66-year-old female with lung cancer treated with AGEN2034 and AGEN1884; pulmonary embolism, n=1).

• There were 3 patients who discontinued from the study treatment by the investigator.

• 3 patients experienced serious TEAEs considered related to study treatment.

• Serious TEAEs occurred in 5 patients: 3 receiving AGEN2034 1 mg/kg q2w + AGEN1884 1 mg/kg q6w and 2 receiving AGEN2034 3 mg/kg q2w + AGEN1884 1 mg/kg q6w. In these patients, serious TEAEs included disease progression (n=1), hypotension, n=1).

• The summary of overall response is presented in Table 4.

• The partial response was ongoing in 5 of the 7 patients with metastatic colorectal cancer. For patients with ≥60 days of treatment, stable disease was ongoing in 1 of their cohort (with breast cancer), and 1 patient had disease progression, respectively.

• The summary of best overall response is listed in Table 4.

DISCUSSION

• Three patients discontinued from the study treatment as determined by the investigator.

• The phase 2 portion of this study evaluating AGEN1884 in combination with AGEN2034 in adults with second-line cervical cancer, and other advanced/metastatic solid tumors, is currently ongoing (NCT02939976 and NCT03719583, respectively).

• The phase 2 recommended dose was determined as AGEN2034 3 mg/kg q2w + AGEN1884 1 mg/kg q6w.

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