immunotherapeutic agents with concomitant biopsy procedures to date are associated with a high technical success rate & favorable safety profile.

Acknowledgements Joshua Hein, Mara Castaneda, Jyotsna Pera, Yunfang Jiang, Shuang Liu, Holly Liu and Anna Lui

Trial Registration N/A

Ethics Approval The study was approved by Institution’s Ethics Board, approval number 2020-0536: A retrospective study to determine the safety, feasibility and technical challenges of real-time image guidance for intra-tumor injection and biopsy across multiple solid tumors.

Consent 2020-0536 Waiver of Informed Consent

REFERENCE


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AGEN1181, AN FC ENGINEERED ANTI-CTLA-4 ANTIBODY, DEMONSTRATES CLINICAL ACTIVITY, ALONE OR IN COMBINATION WITH BALSTILIMAB (ANTI-PD-1), AND BROADENS THE THERAPEUTIC POTENTIAL OF CTLA-4 THERAPY

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Background Immune checkpoint therapies targeting CTLA-4, alone, or in combination with anti-PD-1 have shown durable responses in cancer patients. However, responses are limited to a small subset of patients in the most common immunogenic cancers. Here we describe, a novel anti-CTLA-4 antibody, AGEN1181, with enhanced FcγR-dependent functionality that harnesses a novel mechanism of action to promote superior T cell activation and anti-cancer immunity. Concordant with preclinical findings, we report preliminary safety, pharmacodynamic and efficacy data from a phase 1 study of AGEN1181 (NCT03860272), alone or in combination with balstilimab (anti-PD-1 antibody) in a range of immunogenic and non-immunogenic tumors.

Methods The functional activity of AGEN1181 or AGEN1181-like mouse surrogate were assessed in primary tumor models. AGEN1181-like mouse surrogate were assessed in primary tumor models. The functional activity of AGEN1181 or AGEN1181-like mouse surrogate were assessed in primary tumor models. The functional activity of AGEN1181 or AGEN1181-like mouse surrogate were assessed in primary tumor models.

Results Preclinically, AGEN1181 demonstrated superior T cell activation than a standard IgG1 anti-CTLA-4 analogue in donors expressing either the low or high affinity FcγRIIA. In poorly immunogenic tumor-bearing mouse models, AGEN1181-like surrogate demonstrated robust tumor control in combination with anti-PD-1 and focal radiation or chemotherapy. As of August 25th, 2020, we observed a clinical benefit rate of 63–53% at 6 and 12 weeks respectively among evaluable treated patients. We observed two durable responses in patients with endometrial cancer that were BRCA-, microsatellite stable and PD-L1 negative. These patients progressed on prior PD-1 therapy or chemoradiation respectively. Notably, responders expressed either the low or high affinity FcγRIIA. AGEN1181 showed potent dose-dependent increases in peripheral CD4+Ki67+, CD4+ICOS+ and CD4+HLA-DR+ T-cells. Treatment was well tolerated through the highest dose tested. Grade 3 or greater immune-related adverse events occurred in 28.5% patients and were consistent with CTLA-4 therapies.

Conclusions AGEN1181 is designed to expand the benefit of anti-CTLA-4 therapy to a broader patient population. AGEN1181, alone or in combination with balstilimab, demonstrates clinical activity in heavily pretreated patients.

Trial Registration NCT03860272

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COSIBELIMAB, AN ANTI-PD-1 ANTIBODY: PRELIMINARY SAFETY AND EFFICACY RESULTS FROM A GLOBAL, MULTICOHORT PHASE 1 CLINICAL TRIAL

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Background Cosibelimab is a high affinity, fully-human IgG1 monoclonal antibody that directly binds to programmed death ligand-1 (PD-L1) and blocks its interaction with the programmed death receptor-1 (PD-1) and B7.1 receptors to restore an anti-tumor immune response. Cosibelimab has the additional benefit of a functional Fc domain capable of inducing antibody-dependent cellular cytotoxicity and complement-dependent cytotoxicity against tumor cells. Study CK-301–101 is a global, multicenter, multicohort trial that is enrolling patients (pts) with select advanced cancers, including pivotal cohorts of pts with metastatic and locally advanced cutaneous squamous cell carcinoma (cSCC) and a cohort of pts with previously untreated advanced non-small cell lung cancer (NSCLC).
Methods

Eligible pts were aged ≥18 years with an Eastern Cooperative Oncology Group performance status of 0–1. The cSCC cohorts enrolled pts with histologically confirmed metastatic or locally advanced cSCC not amenable to local therapy. The NSCLC cohort enrolled previously untreated NSCLC pts with advanced disease and a PD-L1 tumor proportion score of at least 50%. Pts received a fixed dose of 800 mg cosibelimab administered intravenously every two weeks. Anti-tumor activity was assessed by Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 and were conducted every 8 weeks for the initial 32 weeks on study, and every 12 weeks thereafter.

Results

As of August 2020, 114 pts (73M/41F, median age 66 years) with diverse tumor types have been enrolled and treated with cosibelimab. Among these pts, 103 (90%) experienced ≥1 treatment-emergent adverse event (AE), 42 (37%) experienced a grade ≥3 AE, and 6 (5%) experienced a grade ≥3 drug-related AE. The most common AEs were fatigue (25%), anemia (21%), rash (18%) and nausea (16%) and the most common drug-related AEs were fatigue (15%) and rash (14%). In 42 cSCC pts evaluable for response, ORR based on investigator assessment of tumor response was 55% (95% confidence interval [CI]: 39, 70), including 5 (12%) complete responses, with 20/23 (87%) responses ongoing and 10 responses ≥6 months in duration as of data cutoff. In 23 NSCLC pts evaluable for response, ORR based on investigator assessment was 44% (95% CI: 24, 65), with 5/11 (45%) responses ongoing and 10 responses ≥6 months in duration.

Conclusions

Cosibelimab has a predictable and manageable safety profile and demonstrated robust clinical activity in cSCC and NSCLC pts, including durable complete and partial responses. Updated results will be presented.

Trial Registration

NCT03212404

Ethics Approval

The study was approved by an appropriate ethics committee for each participating institution. Informed consent was obtained for all subjects.

Consent

Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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