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


http://dx.doi.org/10.1136/jitc-2020-SITC2020.0397

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**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 FcγRIIIA. 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 chemotherapy respectively. Notably, responders expressed either the low or high affinity FcγRIIIA. 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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**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 cell-based assays or in PD-1 refractory syngeneic tumor-bearing mouse models (B16F10 or KPC pancreatic tumor). Efficacy was evaluated as monotherapy, or in combination with anti-PD-1, focal radiation or chemotherapy. In an ongoing phase 1 study, AGEN1181 is administered intravenously once every 3- or 6-weeks as monotherapy (0.1–4 mg/kg), or every 6-weeks (1–4 mg/kg) in combination with balstilimab (3 mg/kg) dosed every 2 weeks. Dose-limiting toxicities were evaluated in the first 28 days of treatment. Neontantigen burden was assessed from pre-treatment tumor biopsy, as available, by next-generation sequencing. Fcγ receptor genotyping was assessed by real-time PCR. Immunophenotyping of peripheral blood mononuclear cells collected pre- and post-treatment were analyzed by flow cytometry.

**RESULTS** 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).

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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 metasta-
static 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 cosibeli-
mb 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%) experi-
enced ≥1 treatment-emergent adverse event (AE), 42 (37%) experi-
enced 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 53% (95% con-
fidence 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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400 COUPLEDCAR TM TECHNOLOGY FOR TREATING THYROID CANCER

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Background Chimeric antigen receptor modified T cells (CAR
T) have demonstrated remarkable clinical efficacy in the treat-
ment of B cell malignancies and multiple myeloma. Significant
challenges restrict their application across solid tumors due to
multiple obstacles, including the lack of robust in vivo CAR-T
cell expansion and persistence, the immunosuppressive tumor
microenvironment, and tumor escape due to heterogeneous
tumor cell composition with a potential loss of the targeted
tumor antigen. To address these difficulties, we generated CAR
tumor cell composition with a potential loss of the targeted
microenvironment, and tumor escape due to heterogeneous
cell expansion and persistence, the immunosuppressive tumor
multiple obstacles, including the lack of robust in vivo CAR-T
treatment of thyroid cancer patients according to an IRB approved protocol.

We treated two patients using anti-TSHR CoupledCAR T cells
and observed the rapid expansion of CAR T cells and
enhanced the killing of tumor cells. One patient’s best
response was complete remission, and the other was near
complete remission. Patient Profile: Patient 1 Male, 64Y, Papil-
lary Thyroid Carcinoma. In May 2017, Thyroid cancer was
diagnosed, bilateral total thyroidectomy, and right cervical
lymph node functional dissection were performed in Jun
2018, followed by iodine 131 isotope therapy. In December
2018, bilateral multiple cervical lymph nodes were enlarged,
especially on the right side. In February 2019, right neck lym-
phadenectomy was performed. Patient 2 Female, 60Y, Thyroid
Carcinoma. In Aug 2013, a ‘double lobectomy of the thyroid
gland’ was performed. From Oct 2013 to Jan 2014, she
received iodine 131 isotope therapy. In Sep 2014, she
was diagnosed with iodine - resistant thyroid cancer. From Sep to
Jan 2016, 5 cycles of chemotherapy were performed. In Jun
2016, she enrolled in the Anlotinib experimental group. In
Mar 2019, multiple metastases in both lungs and multiple
enlarged lymph nodes in the mediastinum were observed.
Observations and Results: Patient 1: One month after infusion
(M1), the patient was evaluated as PR: lymph node metastasis
became undetectable and the size of the thoracic paratracheal
nodule decreased significantly. Three months after
infusion (M3), the patient was evaluated as CR, and the
tumor tissue was substantially smaller than M1. Patient 2: M1,
the patient was evaluated as PR (Partial Response): the tumor
volume in the right lower lobe of the lung was reduced by
approximately 67.51% (decreased from 65*55 mm to 42*39
mm). Three months after infusion (M3), compared with that
before, the tumor volume was reduced by approximately
73.54% and SUV max value decreased from 14.9 to 2.8,
therefore, the patient was evaluated as nCR (near complete
remission).

Conclusions We show that TSHR is a good target for treating
thyroid cancer, and our anti-TSHR CoupledCAR T cells are
safe and effective for treating thyroid cancer. Recruitment
is ongoing to evaluate the safety and efficacy of our Coupled-
CAR T cells. Further, since our CoupledCAR® technology is a

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Abstracts