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


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

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

1Steven O’Day*, 2Anthony El khouery, 3Chethan Ramamurthy, 4Andrea Bullock, 5Irina Sharipova, 6Seira, 7Haiyong Han, 8Lemik Ohanianian Managardi, 9Temiguiz Kaleta, 10Anna Wlodytk, 11Olesia Wiżyk, 12Waldo Ortuzar, 13Marek Arczukiewicz, 14Jennifer Buell, 15Dhan Chand, 16Michael Gordon, 17John Wayne Cancer Institute, Santa Monica, CA, USA; 18University of Southern California, Los Angeles, CA, USA; 19University of Texas at San Antonio, San Antonio, TX, USA; 20Beth Israel Deaconess Medical Center, Boston, MA, USA; 21Agenus, Lexington, MA, USA; 22Translational Genomics Research, Phoenix, AZ, USA; 23Translational Genomics Research Institute, Phoenix, AZ, USA; 24Honorealth, Scottsdale, AZ, USA

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 I 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) dose every 2 weeks. Dose-limiting toxicities were evaluated in the first 28 days of treatment. Neontigen 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 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

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0398

COSIBELIMAB, AN ANTI-PD-L1 ANTIBODY: PRELIMINARY SAFETY AND EFFICACY RESULTS FROM A GLOBAL, MULTICOHORT PHASE 1 CLINICAL TRIAL

1Dean Harris*, 2Daniel Brungs, 3Rahul Ludwah, 4Andrew Mant, 5Margaret McGrath, 6Andrea Tazbihkhzoo, 7Andrey Akopov, 8Natalia Fadeneva, 9Boris Kasparov, 10Nadezhda Kovalenko, 11Andrey Kozlov, 12Fedor Moiseenko, 13Vasily Oscheipkov, 14Piotr Koralewski, 15Dariusz Kowalski, 16Iwona Lugowska, 17Arumee Diepaphurunkul, 18Viree Srirungpon, 19James Oliviero, 20Philip Clingan, 21Christchurch Hospital, Christchurch, New Zealand; 22Southeastern Medical Day Care Centre, Wollongong, Australia; 23Princess Alexandra Hospital, Woolloongabba, Australia; 24Eastern Health, Box Hill, Australia; 25Greenlopes Private Hospital, Greenslopes, Australia; 26Pindara Private Hospital, Benowa, Australia; 27First St. Petersburg State Med Univ, Saint-Petersburg, Russian Federation; 28Chelyabinsk Reg Clinical Oncology Center, Chelyabinsk, Russian Federation; 29NMRC of Oncology n.a. N.N. Petrov, Saint-Petersburg, Russian Federation; 30Volgograd Reg Clinical Onc disp, Volgograd, Russian Federation; 31Novosibirsk Reg Clinical Onc disp, Novosibirsk, Russia; 32St. Petersburg Clin Res and Practical Ct, Saint-Petersburg, Russian Federation; 33Multidisciplinary Clin Med Ctr, Tyumen, Russian Federation; 34Zakład Specjalistyczny Ludwika Rydygier, Kraków, Poland; 35National Research Institute of Oncology, Warsaw, Poland; 36Mahanak Nakorn Chiang Mai Hospital, Chiang Mai, Thailand; 37Prince of Songkla University, Songkhla, Thailand; 38King Chulalongkorn Memorial Hospital, Bangkok, Thailand; 39Checkpoint Therapeutics, New York, NY, USA

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).