778 BOTENSILIMAB, A NOVEL INNATE/ADAPTIVE IMMUNE ACTIVATOR, PLUS OR MINUS BALSTILIMAB (ANTI-PD-1) IN "COLD" AND I-O REFRACTORY METASTATIC SOLID TUMORS

[1]Breelyn Wilky*, [2]Anthony El-Khoueiry, [3]Andrea Bullock, [4]Apostolia Tsimberidou, [5]Daruka Mahadevan, [6]Kim Margolin, [7]Jonathan Trent, [3]Bruno Bockorny, [8]Justin Moser, [7]Peter Hosein, [9]Marwan Fakih, [10]Benjamin Schlecter, [2]Jacob Thomas, [11]Ani Balmanoukian, [12]Rachel Sanborn, [13]Ghassan Abou-Alfa, [14]Gary Schwartz, [2]Diana Hanna, [15]Waldo Ortuzar Feliu, [15]Joseph Grossman, [15]Katherine Rosenthal, [15]James Godwin, [15]Jaymin Patel, [15]Bonnie Bullock, [16]Justin Stebbing, [15]Bhupendra Rawal, [15]Hunter Cole, [15]Chloe Delepine, [15]Jacky Chow, [15]Ross Walker, [15]Chris MacDermaid, [15]Dhan Chand, [8]Michael Gordon, [2]Heinz-Josef Lenz, [17]Steven O'Day. *[1]University of Colorado Cancer Center, Aurora, CO, USA; [2]University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA, USA; [3]Beth Israel Deaconess Medical Center, Boston, MA, USA; [4]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [5]The University of Texas Health Sciences Center at San Antonio, San Antonio, TX, USA; [6]Providence Saint John's Cancer Institute, Santa Monica, CA, USA; [7]Sylvester Comprehensive Cancer Center, University of Miami, Miami, FL, USA; [8]HonorHealth Research and Innovation Institute, Scottsdale, AZ, USA; [9]City of Hope Comprehensive Cancer Center, Duarte, CA, USA; [10]Dana-Farber Cancer Institute, Boston, MA, USA; [11]The Angeles Clinic and Research Institute, Los Angeles, CA, USA; [12]Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR, USA; [13]Memorial Sloan Kettering Cancer Center, New York, NY, USA; [14]Herbert Irving Comprehensive Cancer Center, Columbia University School of Medicine, New York, NY, USA; [15]Agenus, Lexington, MA, USA; [16]Agenus and Imperial College London, Lexington, MA, USA; [17]Agenus and Providence Saint John's Cancer Institute*, Lexington, MA, USA*

Background Botensilimab (BOT) promotes optimized T cell priming, activation and memory formation by strengthening antigen presenting cell/T cell co-engagement. As an Fc-enhanced next-generation anti-CTLA-4 antibody, BOT also promotes intratumoral Treg depletion and reduces complement fixation. We present results from patients with metastatic solid tumors treated with BOT±balstilimab (BAL; anti-PD-1) in an expanded phase IA/B study; NCT03860272.

Methods Patients received either BOT monotherapy at 0.1-3 mg/kg every 3 weeks (Q3W), BOT monotherapy 1 or 2mg/kg every 6 weeks (Q6W), BOT 0.1-2mg/kg Q6W+BAL 3 mg/kg every 2 weeks, or a fixed-dose of BOT 150mg Q6W+BAL 450mg Q3W. Unconfirmed responses are included. Of the 44 BOT monotherapy patients, 13 crossed over to combination.

Results 142 patients (98 combination, 44 monotherapy [13 crossover]) were evaluable for efficacy/safety (treated as of April 7, 2022 with ≥1 Q6W tumor-imaging assessment). Patients had immunologically cold and/or immunotherapy resistant tumors and were heavily pretreated: 61% received ≥3 prior lines of therapy including 34% prior immunotherapy. Median follow-up was 6.1 months.

Disease-specific combination therapy cohorts are being expanded with BOT at 1 or 2mg/kg or 150mg+BAL (including 4 crossover patients): (1) microsatellite stable (MSS) colorectal cancer (n=44, ORR 25%), (2) platinum resistant ovarian cancer (n=18, ORR 28%), (3) sarcoma (n=12, ORR 42%, and (4) PD-(L)1 relapsed/refractory non-small cell lung cancer (n=3, ORR 67%).

The ORR was 22% (22/98; 3 CR/19 PR) with median duration of response [DOR] not reached (range,1.4+ to 19.5 + months) in all combination patients (BAL+BOT 0.1-2 mg/kg or 150 mg); 13/22 responses are ongoing. In addition, 15% (2/13) monotherapy patients achieved PR after crossing over to combination therapy. The ORR was 11% (5/44; 1 CR/4 PR) in all monotherapy patients (BOT 0.1-3 mg/kg). Responses were independent of PD-L1 expression and tumor mutation burden. Further evaluation of biomarkers is ongoing including paired biopsies (before/during treatment).

Grade 1/2, 3 or 4 treatment-related adverse events (TRAE) occurred in 88%, 29%, 2% respectively. Diarrhea/colitis (19%) was the only grade 3/4 TRAE occurring in ≥5% of patients. There were no cases of hypophysitis or myocarditis. Pneumonitis occurred in 4 patients (3%). Two patients had grade 5 TRAEs (enterocolitis, colonic perforation).

Conclusions BOT±BAL demonstrates remarkable activity in heavily pretreated patients with solid tumors historically unresponsive to immunotherapy. The safety profile is consistent with the mechanism of action of BOT. Randomized studies in MSS CRC, pancreatic cancer, and melanoma are planned to open this year.

Trial Registration NCT03860272

http://dx.doi.org/10.1136/jitc-2022-SITC2022.0778