Abstracts

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

Breeilyn Wilky1, Anthony El-Khouseniy2, Andrea Bullock3, Apostolia Tsimberidou4, Danuka Mahadevan5, Kim Margolin6, Jonathan Trent7, Bruno Bockorny8, Justin Moser9, Peter Hossen10, Marwan Fakih11, Benjamin Schlechter12, Jacob Thomas13, Ani Balmanoukian14, Rachel Sanborn15, Chassain Abou-Alfa16, Gary Schwartz17, Diana Hanna18, Waldo Ozturk Feliu19, Joseph Grossman20, Katherine Rosenthal21, James Godwin22, Laymin Patel23, Bonnie Bullock24, Justin Stebbing25, Bhupendra Rawal23, Hunter Cole26, Chloe Delepine27, Jacky Chow28, Ross Walker29, Chris MacDermaid30, Dhan Chand31, Bonnie Bullock32, Justin Stebbing33, Bhupendra Rawal34, Hunter Cole35, Chloe Delepine36, Jacky Chow37, Ross Walker38, Chris MacDermaid39, Dhan Chand40, Michael Gordon41, Heinz-Josef Lenz42, Steven O’Day43, University of Colorado Cancer Center, Aurora, CO, USA; 2University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA, USA; 3Beth Israel Deaconess Medical Center, Boston, MA, USA; 4The University of Texas MD Anderson Cancer Center, Houston, TX, USA; 5The University of Texas Health Sciences Center at San Antonio, San Antonio, TX, USA; 6Providence Saint John’s Cancer Institute, Santa Monica, CA, USA; 7Susan G. Komen Comprehensive Cancer Center, University of Miami, Miami, FL, USA; 8HononHealth Research and Innovation Institute, Scottsdale, AZ, USA; 9City of Hope Comprehensive Cancer Center, Duarte, CA, USA; 10Dana-Farber Cancer Institute, Boston, MA, USA; 11The Angeles Clinic and Research Institute, Los Angeles, CA, USA; 12Earle A. Chiles Research Institute, Providence Cancer Institute, Portland, OR, USA; 13Memorial Sloan Kettering Cancer Center, New York, NY, USA; 14Herbert Irving Comprehensive Cancer Center, Columbia University School of Medicine, New York, NY, USA; 15Agenus, Lexington, MA, USA; 16Agenus and Imperial College London, London, MA, USA; 17Agenus 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 quartiles of 12.1-105.7 days). 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).