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 therapy.

**Results**

142 patients (98 combination, 44 monotherapy [13 crossover]) were evaluated 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-L1 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).