Background Botensilimab (BOT) promotes optimized T cell priming, activation and memory formation by strengthening antigen presenting cell/T cell co-engagement. As an Fc-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 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).

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 metastatic colorectal cancer, pancreatic cancer, and melanoma are planned to open this year.

Trial Registration NCT03860272


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).