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

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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 2 mg/kg every 6 weeks (Q6W), BOT 0.1-2 mg/kg Q6W+BAL 3 mg/kg every 2 weeks, or a fixed-dose of BOT 150 mg Q6W+BAL 450 mg 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 median follow-up 6.1 months).

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 2 mg/kg or 150 mg+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/after 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