

A phase I/II study evaluating the safety and efficacy of ivermectin in combination with balstilimab in patients with metastatic triple negative breast cancer.

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Background: Despite recent FDA approval of immune checkpoint inhibitor (ICI) and antibody–drug conjugates (ADCs), therapeutic options for metastatic triple negative breast cancer (mTNBC) remain limited. Preclinical data showed that ivermectin induces robust T cell infiltration into breast tumors and turning “cold” tumors “hot” in mouse model of TNBC. Balstilimab is a fully humanized IgG4 anti-PD-1 agent with proven safety and efficacy in metastatic cervical cancer. The current phase I/II trial is designed to test the safety and efficacy of the combination of ivermectin and balstilimab in patients with mTNBC. **Methods:** Key eligibility criteria include patients with unresectable or metastatic TNBC; progressed on 1–2 prior chemotherapies including an ICI-containing regimen; ECOG 0–1; RECIST 1.1 measurable disease. Eligible patients receive balstilimab 450 mg, IV, on Day 1 and ivermectin (30, 45 or 60 mg po daily), PO, Days 1–3, 8–10, 15–17 of each 21 days cycle till disease progression or intolerance. The primary objective of the phase 1 portion of the study is to determine the recommended phase 2 dose of ivermectin in combination with balstilimab using NCI-CTCAE v5.0. The primary objective of the phase II portion of the study is to determine the efficacy of the combination using the objective response rate (ORR). Secondary objectives are progression free survival (PFS), overall survival (OS), clinical benefit rate (CBR), and patients' quality of life (QOL) by EORTC QLQ-C30. **Results:** This study has accrual 9 patients to-date. Median age was 52 years (IQR 47–56, range 38–68), 4 (44.4%) were non-Hispanic white, 3 (33.3%) were Hispanic, and 2 were other (22.2%). Median lines of metastatic chemo or targeted therapy prior to the start of trial registration was 5 (IQR 2–5, range 1–7). Dose level 1 and 2 were completed with only 1 serious adverse event (AE) attributed to disease related anemia. All grades treatment related AEs are: 2 maculo-papular rash (grade 1), 1 patient each for anemia (grade 3), diarrhea (grade 1), dysgeusia (grade 1), generalized muscle weakness (grade 1), hypothyroidism (grade 2), and vomiting (grade 1). The initial ECOG value was 0 among 8 patients and 1 patient had ECOG of 1. Six (66.7%) patients had prior immune checkpoint inhibitors, 6 (66.7%) had positive tumor PD-L1 expression. The study will continue to accrual of dose level 3. Of 8 evaluable patients, 1 had SD, 6 had PD, and 1 had PR. The median PFS was 2.5 month (95% CI 66 – Not reached). The 4-month clinical benefit rate was 37.5% (95% CI 15.3%–91.7%). OS is too early to be assessed. **Conclusions:** The combination of ivermectin and balstilimab is safe and well tolerated. Encouraging CBR was observed in this heavily pretreated population, which warranted continued investigation. Clinical trial information: NCT05318469. Research Sponsor: None.