Clinical Trials Complete

**A PHASE II BASKET TRIAL OF DUAL ANTI-CTLA-4 AND ANTI-PD-1 BLOCKADE IN RARE TUMORS (DART SWOG 1609 COHORT 47) IN PATIENTS WITH GESTATIONAL TROPHOBLASTIC DISEASE**

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**Background** Immune checkpoint blockade has improved outcomes across tumor types; little is known about the efficacy of these agents in rare tumors. We report the results of the gestational trophoblastic disease (GTD) cohort of SWOG S1609 dual anti-CTLA-4 and anti-PD-1 blockade in rare tumors (DART).

**Methods** We performed a prospective, open-label, multicenter phase II clinical trial of ipilimumab plus nivolumab across multiple rare tumor cohorts, with the GTD cohort reported here. Eligible patients had progressed following at least one line of standard systemic therapy. All participants received nivolumab 240 mg i.v. every 2 weeks and ipilimumab 1 mg/kg i.v. every 6 weeks on a continuous schedule. The primary endpoint was overall response rate (ORR; complete response (CR) and partial response (PR)) by quantitative serum β-hCG; secondary endpoints included progression-free survival (PFS), overall survival (OS), stable disease >6 months, and toxicity.

**Results** Four eligible patients were enrolled and received therapy. The median number of prior lines of therapy was 2.5 (range 2-4). The median follow-up duration was 11 months. Three of the four patients had a response to therapy [ORR = 75% (CR, 25%, n=1; PR, 50%, n=2) (table 1)], including patients with: malignant gestational trophoblastic neoplasm (n=1, CR, PFS 11+ months), gestational choriocarcinoma (n=1, PR, PFS 10+ months), and choriocarcinoma (n=1, PR, PFS 6+ months). One patient with epithelioid trophoblastic tumor had progression as the best response to therapy. The 6-month PFS was 75% (95% CI 43-100%); all 4 patients were alive at the last follow-up. There were two treatment-related adverse events (TRAEs) of grade 3-4 toxicity: arthralgia and colitis (each observed once), both were immune-related; there were no grade 5 events. No patients discontinued treatment due to TRAEs.

**Conclusions** Ipilimumab plus nivolumab is well tolerated and demonstrated a 75% ORR in patients with GTD

**Acknowledgements** This study was funded by NIH/NCI grants U10CA180888, U01CA180819; and in part by Bristol-Myers Squibb Company.

**Trial Registration** ClinicalTrials.gov Identifier, NCT03498378

**Ethics Approval** This study was conducted in accordance with the Declaration of Helsinki ethical principles, Good Clinical Practices, principles of informed consent, and requirements of public registration of clinical trials (ClinicalTrials.gov Identifier, NCT03498378). The protocol and all amendments were approved by SWOG, the NCI, the NCI central institutional review board (CIRB), and the regulatory committees at the participating institutions. Written informed consent was obtained from each subject at enrollment.