A MULTICENTER PHASE II TRIAL (SWOG S1609, COHORT 51) OF IPILIMUBAB AND NIVOLUMAB IN METASTATIC OR UNRESECTABLE ANGIOSARCOMA: A SUBSTUDY OF DUAL ANTI-CTLA-4 AND ANTI-PD-1 BLOCKADE IN RARE TUMORS (DART)

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Background Angiosarcoma is a rare cancer of endothelial cells that can be aggressive and carries a high mortality. A subset of angiosarcomas are characterized by high tumor mutational burden (TMB) and UV light exposure DNA mutational signature. Isolated case reports have suggested clinical efficacy of immune checkpoint blockade in angiosarcoma; no prospective studies of immune checkpoint inhibition in angiosarcoma have been reported. We report efficacy analysis results for patients with advanced or unresectable angiosarcoma treated with ipilimumab and nivolumab as a cohort of an ongoing phase II study for rare cancers (NCT02834013).

Methods This is a prospective, open-label, multicenter phase II clinical trial of ipilimumab (1mg/kg IV q6weeks) plus nivolumab (240mg IV q2weeks) for patients with metastatic or unresectable angiosarcoma. Primary endpoint is objective response rate as assessed by RECIST v1.1, including measurable cutaneous disease that can be followed by photography. Secondary endpoints include PFS, OS, stable disease at six months, and toxicity. A two-stage design is used with six patients in the first stage and an additional ten patients in the second stage.

Results At data cutoff, 16 patients with angiosarcoma were enrolled. Median age was 68 years (25-81 years). Median number of prior lines of therapy was 2 (0-5). 9 patients had cutaneous primary tumors of any cutaneous site, 7 had non-cutaneous primary tumors. ORR for all patients was 25% (4/16, table 1, figure 1). Subgroup analysis revealed that 60% (3/5) of patients with primary cutaneous tumors of the scalp or face had a confirmed objective response. 6-month PFS was 38%. 75% of patients experienced an adverse event (AE), and 25% experienced a grade 3-4 AE. 68.8% experienced an immune related AE (irAE), and 2 (12.5%) developed grade 3 or 4 irAEs. Grade 3-4 irAEs were ALT and AST increase and diarrhea. There were no grade 5 toxicities.

Conclusions The combination of ipilimumab and nivolumab was well tolerated and had an ORR of 25% in angiosarcoma regardless of primary site, with 3 of 5 patients with cutaneous tumors of the scalp or face responding. Ipilimumab and nivolumab warrant further investigation in angiosarcoma.

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Ethics Approval This study was approved by the NCI CIRB.

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