confer clinical benefit. In 3-week cycles, patients received intratumoral MK-4621 0.4, 0.6, or 0.8 mg on days 1, 8, and 15 for 6 cycles (delivered via jetPEI®, Polyplus Transfection, Illkirch, France) plus intravenous pembrolizumab 200 mg on day 1 for 35 cycles. Treatment continued until disease progression or unacceptable toxicity. The primary objective was to establish a preliminary recommended phase 2 dose based on DLTs (cycle-1), AEs, and treatment discontinuations due to AEs; AEs were graded per NCI CTCAE v4.0. Tumor imaging was performed Q9W; response was assessed by the investigator.

Results As of May 14, 2020, 30 participants received therapy with MK-4621 0.4 (n=7), 0.6 (n=5), or 0.8 mg (n=18). Median time on therapy was 57 (range, 1-365) days. The most frequent tumor types were breast (20%) and melanoma (17%); 90% of patients received =2 prior lines of therapy. One patient in the 0.8-mg group experienced a DLT (grade 3 treatment-related pleural effusion), which resulted in treatment discontinuation; no other patient discontinued owing to AEs. Grade 3 treatment-related AEs occurred in 1 patient (14%) at the 0.4-mg dose (pyrexia), 1 patient (20%) at the 0.6-mg dose (hypertension), and 5 patients (28%) at the 0.8-mg dose (anemia [n=2], dyspnea/pleural effusion [n=1], lymphopenia [n=1], pyrexia [n=1]). No treatment-related grade 4/5 AEs occurred. Across dose levels, the most frequently occurring treatment-related AEs were pyrexia (63%), chills (37%), cytokine-release syndrome (20%), and nausea (20%). Efficacy outcomes are below (table 1). Significant changes in blood interferon-gamma inducible protein-10 and monocyte chemotactic protein-2 were observed at each dose level, consistent with the mechanism of action of MK-4621.

Abstract 794 Table 1 Efficacy outcomes

Table. Efficacy Outcomes

	MK-4621 0.4 mg + Pembrolizumab (n=7)	MK-4621 0.6 mg + Pembrolizumab (n=5)	MK-4621 0.8 mg + Pembrolizumab (n=18)
Best overall response, n (%)[a]			
CR	0	0	0
PR	0	0	2 (11)[b]
SD	2 (29)	1 (20)	4 (22)
PD	3 (43)	3 (60)	8 (44)
Unevaluable[c]	0	0	1 (6)
No assessment[d]	2 (29)	1 (20)	3 (17)
ORR, % (95% CI)[e]	0 (0–41)	0 (0–52)	11 (1–35)

[a]With confirmation based on investigator assessment per RECIST version 1.1.
[b]PR occurred in 1 patient with cervical cancer and 1 patient with lung cancer.
[c]Insufficient data for assessment of response.
[d]No postbaseline assessment of response.
[e]Defined as best overall response with confirmation based on investigator assessment per RECIST version 1.1. 95% CI based on the exact (Clopper-Pearson) method for binomial data.

Conclusions The combination of intratumoral MK-4621 plus intravenous pembrolizumab had a manageable safety profile. At the highest dose level, modest antitumor activity was observed in patients treated with combination therapy.

Trial Registration ClinicalTrials. gov identifier, NCT03739138

Ethics Approval An independent institutional review board or ethics committee approved the protocol at each study site, and the trial is being conducted in compliance with Good Clinical Practice guidelines and the Declaration of Helsinki.

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795 A MULTICENTER PHASE II TRIAL (SWOG S1609, COHORT 51) OF IPILIMUMAB 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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Trial Registration NCT02834013

Ethics Approval This study was approved by the NCI CIRB.

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