

treatment-related AEs were fever/pyrexia (Grade 1: n=3; Grade 2: n=8) and injection site reactions (Grade 1: n=1; Grade 2: n=9). Preliminary estimate of median plasma half-life for AMV564 after SC injection was >48 hours, with dose-related increases in peak plasma concentration (C_{max}). Tumor responses were evaluable in 9 patients; 1 patient had not reached their first assessment and 1 patient was not efficacy evaluable due to a non-treatment-related AE resulting in study discontinuation. Single-agent activity has been observed including a complete response by RECISTv1.1 criteria in 1 patient with ovarian cancer refractory to all standard therapies and anti-PD-1 therapy, and stable disease in 4 additional patients.

Conclusions AMV564 has been well tolerated across multiple dose levels, with good plasma exposure and evidence of anti-tumor activity when administered subcutaneously. Single-agent anti-tumor activity was observed in an ovarian cancer patient.

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Trial Registration NCT04128423

Ethics Approval The study was approved by the Institutional Review Board at each center where the study is being conducted.

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PHASE 1/2 STUDY OF SUBCUTANEOUSLY ADMINISTERED ALKS 4230, A NOVEL ENGINEERED CYTOKINE, AS MONOTHERAPY AND IN COMBINATION WITH PEMBROLIZUMAB, IN PATIENTS WITH ADVANCED SOLID TUMORS: ARTISTRY-2

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Background ALKS 4230 is a novel engineered cytokine designed to selectively bind and activate the intermediate affinity IL-2 receptor. Intravenous (IV) dosing of ALKS 4230 has shown encouraging efficacy and acceptable tolerability, as monotherapy and in combination with pembrolizumab, in patients with advanced solid tumors (ARTISTRY-1, NCT02799095). Subcutaneous (SC) dosing may be preferable to IV in certain clinical situations.

Methods ARTISTRY-2 (NCT03861793) is an ongoing phase 1/2 study of SC ALKS 4230 ± pembrolizumab. In phase 1, cohort-specific doses of SC ALKS 4230 are administered on either an every-7-day (q7d) or every-21-day (q21d) schedule

Abstract 373 Table 1 Most common (≥20%) TRAEs overall and by dose schedule (by investigator assessment)

	q7d				q21d			q7d + q21d Overall (N = 38)
	0.3 mg (n = 7)	0.6 mg (n = 3)	1 mg (n = 7)	3 mg (n = 7)	1 mg (n = 4)	3 mg (n = 4)	10 mg (n = 6)	
Patients with ≥1 ALKS 4320-related TRAEs, n (%) ^a	7 (100)	2 (66.7)	7 (100)	5 (71.4)	4 (100)	4 (100)	3 (50)	32 (84.2)
Injection site reactions ^b , n (%)	6 (85.7)	1 (33.3)	3 (42.9)	4 (57.1)	4 (100)	3 (75)	2 (33.3)	23 (60.5)
Pyrexia, n (%)	4 (57.1)	0	2 (28.6)	4 (57.1)	0	3 (75)	2 (33.3)	15 (39.5)
Lymphopenia, n (%)	1 (14.3)	0	4 (57.1)	3 (42.9)	2 (50.0)	1 (25.0)	2 (33.3)	13 (34.2)
Chills, n (%)	3 (42.9)	0	1 (14.3)	3 (42.9)	0	3 (75.0)	2 (33.3)	12 (31.6)
Fatigue, n (%)	4 (57.1)	0	1 (14.3)	2 (28.6)	1 (25.0)	1 (25.0)	1 (16.7)	10 (26.3)
Nausea, n (%)	4 (57.1)	0	0	1 (14.3)	0	2 (50)	2 (33.3)	9 (23.7)

^aData as of July 24, 2020.

^bInjection site reactions include erythema, reaction, pruritus, pain, swelling, irritation, inflammation, and warmth at the injection site; all were grade 1 or 2 in severity.

during a 6-week lead-in period, followed by combination with IV pembrolizumab 200 mg q21d. Each patient assigned to a given cohort receives ALKS 4230 at a single dose level and on a schedule of either q7d or q21d. Safety, tolerability, dose-limiting toxicities (DLTs), and pharmacokinetics/pharmacodynamics from dose escalation, as of 7/24/2020 are reported in this abstract.

Results 38 patients have been treated with ALKS 4230 across 7 assigned cohorts, with SC doses ranging from 0.3 mg to 10 mg (median age, 61.5 [28–82] years; median number of prior therapies 4 [0–17]; 45% were previously treated with immunotherapy). 25 patients completed monotherapy and initiated combination therapy. Median duration of treatment was 64.5 (1–506) days. Systemic exposure to ALKS 4230 increased with increasing dose, resulting in a dose dependent increase in circulating natural killer and CD8+ T cells, without significant impact on regulatory T cells. Overall, adverse events (AEs), regardless of causality, occurred in 33 (86.8%) patients. Treatment-related AEs (TRAEs; investigator assessed) occurred in 32 (84.2%) patients, and the most common TRAEs are presented in table 1. One patient experienced a serious TRAE, a grade 3 tumor flare manifesting as colonic obstruction. The maximum tolerated dose as well as recommended phase 2 dose for SC administration has not yet been determined.

Conclusions ALKS 4230 is a promising investigational agent for the treatment of advanced solid tumors. The SC safety profile is consistent with the known and anticipated pharmacologic effects of ALKS 4230. Consistent with IV dosing, SC administration of ALKS 4230 q7d or q21d maintained the desired immune responses as demonstrated by pharmacodynamic outcomes. Potentially lower rates of fever and chills observed, relative to IV dosing, are presumed to be consistent with lower peak concentrations achieved so far via the SC route. The study, including dose escalation, is ongoing.

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Ethics Approval This study was approved by Ethics and Institutional Review Boards (IRBs) at all study sites; IRB reference numbers 20182543 (Western IRB), 00006731 (Roswell Park Comprehensive Cancer Center), STUDY00000056 (Georgetown University, MedStar Health Research Institute).

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