SUBCUTANEOUS NEMVALEUKIN ALFA IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS WITH REFRACTORY SOLID TUMORS (ARTISTRY-2)

1Omid Hamidi*, 2Sarina A Piha-Paul, 3Stephen V Liu, 4Ralph Boccia, 5Justin A Call, 6Trisha M Wise-Draiper, 7Angela Tatiana Alisar, 8Anthony J Olszanski, 9John Wrangle, 10Anthony F Shields, 11Aranzazu Manzano, 12Emiliano Calvo, 13Shwetha Asha, 14Yangchun Du, 15Carlos Mayo, 16Leah Rider, 17Marc S Ernstoff. 1The Angeles Clinic and Research Institute, A Cedars-Sinai Affiliate, Los Angeles, CA, USA; 2Department of Investigational Cancer Therapeutics, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA; 3Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC, USA; 4The Center for Cancer and Blood Disorders, Bethesda, MD, USA; 5Utah Cancer Specialists, West Valley City, UT, USA; 6Division of Hematology-Oncology, University of Cincinnati Cancer Center, Cincinnati, OH, USA; 7Atlantic Health System, Atlantic Medical Group, Morristown, NJ, USA; 8Department of Hematology/Oncology, Fox Chase Cancer Center, Philadelphia, PA, USA; 9Holdings Cancer Center, Medical University of South Carolina, Charleston, SC, USA; 10Department of Oncology, Karmanos Cancer Center, Wayne State University, Detroit, MI, USA; 11UTEC Hospital Clínico San Carlos, Madrid, Spain; 12START Madrid-COCC, Centro Integral Oncológico Clara Campal, Madrid, Spain; 13Alkermes, Inc., Waltham, MA, USA; 14Department of Medicine, Roswell Park Comprehensive Cancer Center, Buffalo, NY, USA

Background Ncemvaleukin alfa (ncemvaleukin, ALKS 4230) is a novel, engineered cytokine that selectively binds to the intermediate-affinity interleukin-2 receptor to preferentially activate antitumor CD8+ T cells and natural killer cells, with minimal expansion of immunosuppressive regulatory T cells. The first-in-human study, ARTISTRY-1, demonstrated antitumor activity with intravenous (IV) nemvaleukin (6 μg/kg on days 1–5 per 21-day cycle) monotherapy and nemvaleukin + pembrolizumab, with manageable safety in heavily pretreated adults with advanced solid tumors.1 ARTISTRY-2 (NCT03861793) is a phase 1/2 study evaluating the safety, antitumor activity, and pharmacokinetics/pharmacodynamics of subcutaneous (SC) nemvaleukin + pembrolizumab in patients with advanced solid tumors.

Methods In ARTISTRY-2, the recommended phase 2 dose (RP2D) of SC nemvaleukin was identified as 3 mg every 7 days (Q7D).2 In phase 2, SC nemvaleukin + pembrolizumab was administered in the following cohorts: non-small-cell lung cancer (NSCLC), squamous cell carcinoma of the head and neck (SCCHN), gastric and gastroesophageal junction cancer (G/GJE), and ovarian cancer. Cohorts 1 (OC1) and 2 (OC2). OC2 cohort included definition of platinum resistance, number of prior lines of therapy and requirement for prior treatment with bevacizumab, reflecting baseline characteristics associated with higher likelihood of clinical benefit. Investigator-assessed antitumor activity (RECIST v1.1) and safety are reported as of April 21, 2023.

Results In phase 2, 59 patients (11 NSCLC, 10 SCCHN, 13 G/GJE, 17 OC1, 8 OC2) received SC nemvaleukin + pembrolizumab. Antitumor activity was observed, including 2 partial responses (PRs) in OC (ORR 15.4% [OC1, 2/13]) and 1 PR in NSCLC (ORR 10% [NSCLC, 1/10]); responders were checkpoint inhibitor-naïve. The most frequent treatment-related adverse events (TRAEs) of any grade (>40%) included pyrexia (50.8%) and injection-site reactions (45.8%), and of grade 3/4 (>5%) were fatigue (6.8%), lymphocyte count decreased (6.8%), and lymphopenia (5.1%). A total of 7 patients (11.9%) discontinued the study due to TRAEs. There was 1 treatment-related grade 5 event of pneumonitis (NSCLC cohort). The safety profile of SC nemvaleukin + pembrolizumab was consistent with that reported for IV dosing, except for injection-site reactions.

Conclusions SC nemvaleukin 3 mg Q7D with pembrolizumab was generally well tolerated and demonstrated antitumor activity in patients with refractory solid tumors. Although antitumor activity was observed, the robustness of this activity was less than that observed with the daily ×5 IV dosing; therefore, a less frequent IV dosing schedule of nemvaleukin is being explored in ARTISTRY-3 (NCT04592653).

Acknowledgements The authors would like to thank all the patients who are participating in this study and their families. The study is sponsored by Alkermes, Inc. Medical writing and editorial support was provided by Parexel International and funded by Alkermes, Inc.

Trial Registration Clinicaltrials.gov NCT03861793

REFERENCES


Ethics Approval The study protocol and its amendments, patient informed consent form, and all relevant documents were approved by an institutional review board or local ethics committee. This study is being conducted according to Declaration of Helsinki and all applicable guidelines from the International Council on Harmonisation (ICH) E6 Good Clinical Practice, US Code of Federal Conduct, and state, local and federal laws. All patients are required to provide written informed consent to participate.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0724