Background Integrin beta-6 plays a role in tumor pathogenesis and invasiveness, and is correlated with poor outcomes in several cancers, making it a therapeutic target of interest. SGN-B6A is an investigational vedotin ADC comprised of an integrin beta-6-directed monoclonal antibody conjugated to monomethyl auristatin E (MMAE) via a protease-cleavable linker. SGN-B6A elicits antitumor activity through MMAE-mediated cytotoxicity, bystander effect, and immunogenic cell death. Herein, we present the first clinical data in Part A (dose escalation) of a Phase 1 clinical trial evaluating SGN-B6A.

Methods SGNB6A-001 (NCT04389632) is a Phase 1, open-label, multicenter dose-escalation/expansion study evaluating the safety, pharmacokinetics, and antitumor activity of SGN-B6A (confirmed objective response per Response Evaluation Criteria in Solid Tumors v1.1) in adults with advanced solid tumors.

Part A is enrolling patients with histologically or cytologically confirmed metastatic or unresectable solid tumors, relapsed or refractory disease or intolerance to standard-of-care therapies. Data for continuous weekly dosing (Days 1, 8, and 15 in a 21-day cycle [Q1W]) and intermittent dosing (Days 1 and 8 in a 21-day cycle [2Q3W]) are presented in this abstract.

Results As of 10 May 2022, 30 patients in Q1W (0.8, 1.0, and 1.2 mg/kg) and 18 patients in 2Q3W (1.2 or 1.25 mg/kg) received SGN-B6A. Baseline demographics are outlined in Table 1. In Q1W, 1 dose limiting toxicity (DLT) of stomatitis (5.9%) was reported at the 1.2 mg/kg dose level (n=17; Table 2). The most common treatment-related adverse events (TRAEs) in Q1W across all doses (n=30) were fatigue (26.7%), peripheral sensory neuropathy (23.3%), alopecia (20%) and decreased appetite (20%). The most common Grade 3 TRAE was fatigue (10%); alopecia and peripheral sensory neuropathy (16.7% each), and the most common Grade ≥ 3 TRAEs were diarrhea, hyperglycemia, and neutropenia (11.1%).

Objective responses were observed in Q1W and 2Q3W in several tumor types including non-small cell lung, head and neck squamous cell, esophageal, and cutaneous squamous cell cancer, starting at 1.2 mg/kg. Detailed efficacy results will be presented.

Conclusions SGN-B6A at both dosing schedules demonstrated an acceptable safety profile, with more favorable tolerability at 2Q3W (table 2). Preliminary antitumor activity has been observed starting at 1.2 mg/kg. Enrollment in Part B (dose expansion) is ongoing.

Trial Registration NCT04389632

REFERENCES
1. Li F, Zhang Y, Shi F, Zhang L, Yan J, Sun Q, She J. Expression of Integrin β6 and HAX-1 Correlates with Aggressive Features and Poor Prognosis in Esophageal Squamous Cell Carcinoma. Cancer Management and Research. 2020;12:9599-9608

Ethics Approval The trial is being conducted in compliance with the Declaration of Helsinki and International Conference on Harmonization Guidelines for Good Clinical Practice. All patients, or their legal representatives, provided informed consent. All participating sites have been approved by a corresponding institutional review board or independent ethical committee per the participating institution.