A FIRST-IN-HUMAN TRIAL OF AN INTEGRIN BETA-6 TARGETED ANTIBODY-DRUG CONJUGATE (ADC), SGN-B6A, IN PATIENTS WITH ADVANCED SOLID TUMORS: INTERIM RESULTS OF A PHASE 1 STUDY (SGNB6A-001)

1Antoine Hollebecque*, 2Juanita Lopez, 3Sarina Pha-Raul, 4Abhin Dowlati, 5Anna Patnaik, 6Vladimir Galvao, 7Bruno Bukovsky, 8Kartik Sehgal, 9Edward Kingsley, 10Rachel Sanborn, 11Solange Peters, 12Yan Sun, 13Gabriela Patlaja-Vrana, 14Natanya Nazarenko, 15Emiliano Calvo, 16Institut Gustave Roussy, Villejuif, France; 17The Royal Marsden Hospital (Surrey), London, UK; 18The University of Texas, Houston, TX, USA; 19Case Western Reserve University, Cleveland, OH, USA; 20START San Antonio, San Antonio, TX, USA; 21Vall d’Hebron Institute of Oncology, Barcelona, Spain; 22Beth Israel Deaconess Medical Center, Boston, MA, USA; 23Dana-Farber Cancer Institute, Boston, MA, USA; 24Comprehensive Cancer Centers of Nevada, Las Vegas, NV, USA; 25Earle A. Chiles Research Institute, Portland, OR, USA; 26Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; 27Seagen Inc., Bothell, WA, USA; 28START Madrid-COCC, Madrid, Spain

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.1,2 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.3 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 reported across all dose groups was neutropenia (10%).

In 2Q3W (n=18), two patients experienced DLTs (diabetes, neuropenia, and rash maculo-papular [5.6%]). The most common TRAEs were alopecia, diarrhea, and peripheral sensory neuropathy (16.7% each), and the most common Grade ≥ 3 TRAEs were diabetes, hyperglycemia, and neuropenia (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, Shang Y, Shi F, Zhang L, Yan J, Sun Q, She J. Expression of Integrin b6 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.

Abstract 731 Table 1. Baseline demographics Summary of baseline demographics of all patients treated in Q1W and 2Q3W

Abstract 731 Table 2. Adverse events and dose limiting toxicities Summary of the most common treatment-related adverse events (all grades) and dose limiting toxicities for all patients treated in Q1W and 2Q3W


A762 J Immunother Cancer 2022;10(Suppl 2):A1–A1595