Background PRO1160 is a novel antibody-drug conjugate (ADC) directed to CD70, an antigen mediating immuno-suppression that is overexpressed in multiple solid tumors and hematologic malignancies, with limited distribution in normal tissues. PRO1160 comprises (1) a human monoclonal antibody specific for CD70, (2) a protease-cleavable proprietary hydrophilic linker, and (3) exatecan, a topoisomerase 1 inhibitor. Comprehensive prior work demonstrated that the hydrophilic linker confers excellent physicochemical properties and pharmacokinetics (PK) across a range of payload mechanisms and is superior to conventional linkers on these critical parameters for ADCs. In addition, exatecan is broadly active in many tumor types, is membrane permeable, and is not a substrate of multidrug resistance pumps, thus likely lending strong bystander effects and durable treatment responses. PRO1160 is highly potent in cell-derived xenograft models of renal cell carcinoma (RCC), non-Hodgkin lymphoma (NHL), and nasopharyngeal carcinoma (NPC). PRO1160 also demonstrates marked antitumor activity in patient-derived xenograft models of diverse tumor sites, histologies, molecular subtypes, target expression levels, and Epstein Barr Virus status. PRO1160 is stable in circulation and displays PK characteristics indistinguishable from the parent antibody in rats. In a GLP toxicity study in cynomolgus monkeys, the primary PRO1160-related toxicity resided in the thymus and bone marrow, was consistent with exatecan toxicities, and was reversible.

Methods PRO1160-001 is an ongoing, open-label Phase 1/2 study to evaluate the safety, tolerability, PK, and antitumor activity of PRO1160 in patients with metastatic RCC, metastatic or relapsed NPC, or advanced relapsed/refractory NHL.

Patients must have measurable disease per the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 or the Lugano Classification for NHL. Patients must also have previously received therapies known to confer clinical benefit unless considered ineligible, refused by the patient, or not available in the region.

PRO1160 is given by intravenous infusion on Day 1 of a 21-day cycle and treatment may continue until disease progression, unacceptable toxicity, or other reason for discontinuation. The primary objectives are to evaluate the safety and tolerability of PRO1160 and to identify the maximum tolerated dose, if reached, and recommended phase 2 dose (RP2D).

This study consists of 2 parts, Part A: dose-escalation and dose-level expansion, and Part B: 3 tumor-specific expansion cohorts (metastatic RCC, metastatic or relapsed NPC, and advanced relapsed/refractory NHL) treated at the RP2D. PK, immunogenicity, and antitumor activity will also be evaluated. The study is currently enrolling at sites in the US, with future enrollment in China planned (Clinicaltrials.gov: NCT05721222).

Trial Registration Clinicaltrials.gov NCT05721222

Ethics Approval The study obtained ethics approval (WCG Institutional Review Board; ID 20230476) and participants gave informed consent prior to taking part.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0718