A PHASE 1 STUDY EXPLORING THE SAFETY AND TOLERABILITY OF THE SMALL-MOLECULE PD-L1 INHIBITOR, INCB099280, IN PATIENTS WITH SELECT ADVANCED SOLID TUMORS

Hans Prenen, Thierry Lesimple, Marie Robert, Brant Delafontaine, Jean-Pascal Machiels, Tarek Meniawy, Eric Van Cutsem, Maria P. Kotecki, Sarina Piha-Paul, Michael Schweizer, Shirish Gadgeel, Louis Viviers, Jason Howe, Antoine Italiano, University Hospital Antwerp, Antwerp, Belgium; CLIP2 and ARPEGO Networks, Rennes, France; Unicancer Group ICO René Gauducheau Site, CLIP2 and ARPEGO Networks, Saint-Herblain, France; Drug Research Unit Ghent, UZ Ghent, Ghent, Belgium; Cliniques Universitaires Saint-Luc, UCLo, Brussels, Belgium; Linear Clinical Research and University, Nedlands, Western Australia, WA, Australia; University Hospitals Gasthuisberg, Leuven, Belgium; Institut Jules Bordet, Brussels, Belgium; University of Texas MD Anderson Cancer, Houston, TX, USA; University of Washington and Fred Hutchi, Seattle, WA, USA; Henry Ford Cancer Institute/Henry Ford Health, Detroit, MI, USA; Incyte Corporation, Wilmington, DE, USA; Early Phase Trials Unit, Institut Bergon, Bordeaux, France

Background INCB099280 is an orally administered, small-molecule inhibitor of programmed cell death ligand 1 (PD-L1). This is an ongoing, phase 1, open-label, multicenter study.

Methods Eligible patients are aged ≥18 years with advanced solid tumors and an Eastern Cooperative Oncology Group performance status of 0–1. Patients had disease progression after treatment with available therapies or were ineligible for or without access to standard treatment. The study is being conducted in two parts: in part 1, a Bayesian optimal interval design is being used to identify the maximum tolerated dose (MTD) of INCB099280; in part 2, two doses have been expanded for patients with various tumor types who were immunotherapy-naïve. The primary endpoints are (1) safety and tolerability as measured by monitoring frequency/severity of adverse events (AEs) and (2) determining a pharmacologically active dose and/or MTD. Anti-tumor activity is assessed using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.

Results As of April 22, 2022, 73 patients had received INCB099280 at total daily doses ranging from 100 to 800 mg. Among all patients, median (range) age was 62 (21–82) years, 60.3% were women, 57.5% were white, 43.8% had gastrointestinal malignancies, 56.2% had ≥2 prior lines of therapy, and 6.8% had prior exposure to an immune check-point inhibitor. 46 patients (63.0%) discontinued treatment, 38 of whom discontinued for disease progression. Treatment-emergent AEs (TEAEs) occurring in >20% of patients were decreased appetite, fatigue, nausea, anemia, diarrhea, asthenia, and vomiting. Serious TEAEs (SAEs) occurred in 21 patients (28.8%); SAEs occurring in >1 patient were pneumonia and sepsis (n=3 each) and anemia, dyspnea, and urinary tract infection (n=2 each). Grade ≥3 treatment-related TEAEs occurred in 5 patients (6.8%): asthenia, fatigue, elevated lipase, decreased appetite, hypophagia, and confusional state (n=1 each). One patient had a protocol-defined dose-limiting toxicity (DLT; 600-mg once-daily group; unable to receive ≥75% of the prescribed dose owing to vomiting). The 600-mg once-daily dose was expanded in 9 patients with no further DLTs. Several responses have been observed, and updated results will be presented.

Conclusions INCB099280 was generally well tolerated at total daily doses up to 800 mg. Unlikely with the first-generation oral PD-L1 inhibitor INCB086550, no dose-limiting immune-mediated peripheral neuropathy has occurred to date with INCB099280. Preliminary efficacy indicates anti-tumor activity.

Continued investigation and further development are warranted.

Trial Registration NCT04242199

Ethics Approval This study was reviewed and approved by the institutional review boards of the participating institutions. Approval numbers are: WIRB (USA), 20202491; University of Texas, MD Anderson Cancer Center (USA), 2020-0082; Alfred HREC (Australia), HREC/60995/Alfred-2020; Bellberry (Australia), HREC2020-05-463; EudraCT EC (Belgium), 2019-004967-35 (Ref#, 5407); EudraCT EC (France), 2019-004967-35 (FR EC, 20.10.09.40853). All patients provided written informed consent.