

PRELIMINARY SAFETY, EFFICACY AND PHARMACOKINETIC RESULTS OF THE EP4 ANTAGONIST INV-1120 FROM A FIRST-IN-HUMAN STUDY IN SUBJECTS WITH ADVANCED SOLID TUMORS

<http://dx.doi.org/10.1136/jitc-2022-SITC2022.0597>

¹John Sarantopoulos, ²Amita Patnaik, ³Zhaopie Zeng, ³Johannes Nippgen, ³Yongkui Sun, ³Yi Zhu*. ¹Mays Cancer Center, San Antonio, TX, United States; ²South Texas Accelerated Research Therape, San Antonio, TX, United States; ³Shenzhen Ionova Life Science Co., Ltd, Shenzhen, China

Background INV-1120 is a highly selective, small-molecule antagonist of the E-type prostanoid receptor 4 (EP4) for prostaglandin E2 (PGE2), an immunosuppressive mediator of tumor immune microenvironment. Objectives of this first in human study were to assess safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), maximum tolerated dose (MTD) and recommended phase 2 dose of INV-1120.

Methods Dose-escalation was based on the traditional “3+3” dose-escalation design in sequential escalating dose cohorts (15, 30, 60, 100, 150, 200, 250, 300 mg). Dose limiting toxicity (DLT) evaluation period was 28 days. Efficacy evaluation was performed every 8 weeks by RECIST 1.1. Blood samples were collected for pharmacokinetic characterization of the treatment.

Results Twenty-four patients were enrolled and treated with single-agent INV-1120 in 6 dose cohorts (15 mg, n=3; 30 mg, n=3; 60 mg, n=6; 100 mg, n=3; 150mg, n=3; 200 mg, n=6). The median age is 58.0 with the range from 20 to 80. 10 patients are male and 14 are female. Tumor types include colorectal cancer (8), lung cancer (4), parotid adenocarcinoma (2), sarcoma (2) and others (8). 7 patients had received prior CPI therapy.

There were two DLTs, one at 60 mg (grade 2 duodenal ulcer) and one at 200 mg (grade 2 duodenitis).

At least 1 TEAE was reported in 24 patients (100%). The most common TEAEs (all grades) were diarrhea (6 subjects, 25.0%), nausea (6, 25.0%), anemia (6, 25.0%), and fatigue (5, 20.8%). Drug-related TEAEs occurred in 13 patients (54.2%) and grade ≥ 3 treatment related TEAEs occurred in one patient (4.2%). Five patients (20.8%) were discontinued or interrupted for treatment due to TEAEs, and two of them due to TEAEs that were unrelated to study drug treatment.

Twenty-one patients were evaluable for efficacy as of the cut-off date of May 30, 2022. Stable disease was observed in 9 of 21(42.9%) patients. Among the 9 patients with stable disease, 5 had treatment duration ≥ 18 weeks.

INV-1120 was rapidly absorbed across all doses, and time to maximum drug concentration was observed at ~ 2 hours postdose. The exposure of INV-1120 appeared to increase with dose from 15 mg to 100/150 mg and plateaued thereafter. There is no PD markers data available currently.

Conclusions Single agent INV-1120 was generally well tolerated and showed prolonged stable disease. Preclinical data showing the efficacy synergy when INV-1120 combining with anti PD-1 support phase Ib protocol amendment about INV-1120 in combination with anti PD-1, and the dose escalation of the combination study will explore INV 1120 at 60, 100 and 150mg QD.

Trial Registration Clinical trial registry number: NCT04443088.

Ethics Approval

Ethics statement: This study was approved by IntegReview IRB.