770 SAFETY, EFFICACY, AND PHARMACOKINETIC RESULTS FROM A PHASE I FIRST-IN-HUMAN STUDY OF ABBV-151 WITH OR WITHOUT ANTI-PD1 MAB (BUDIGALIMAB) IN PATIENTS WITH LOCALLY ADVANCED OR METASTATIC SOLID TUMORS

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Background Glycoprotein-A repetitions predominant (GARP) is expressed on regulatory T-cells and modulates release of active transforming growth factor β1 (TGFβ1), an immunosuppressive cytokine. ABBV-151 is a first-in-class monoclonal antibody (mAb) that binds to the GARP-TGFβ1 complex, blocking the release of active TGFβ1. Preclinical data demonstrate that blocking GARP-TGFβ1 and programmed cell death protein-1 (PD-1) improves antitumor efficacy compared with anti–PD-1 alone. Combining ABBV-151 with the anti–PD-1 mAb budigalimab may enable increased antitumor efficacy by reducing the immunosuppressive effects of TGFβ1. Herein, we report preliminary safety, efficacy, and pharmacokinetic (PK) results from a first-in-human, phase 1 study (NCT03821935) assessing ABBV-151 ± budigalimab in adult patients (≥18 years) with locally advanced/metastatic solid tumors. Results from the all-comer dose escalation (ESC) phase and two cohorts from the dose expansion (EXP) phase are available: anti-PD-1/PD-ligand (L)1 naïve hepatocellular carcinoma (HCC) and anti-PD-1/PD-L1 relapsed/refractory urothelial cancer (UC).

Methods ESC patients must be refractory/intolerant to existing effective therapies; EXP cohorts have tumor-specific eligibility requirements. The primary ESC endpoint is the recommended phase II dose of ABBV-151 ± budigalimab. The primary EXP endpoint is preliminary efficacy of ABBV-151 + budigalimab, assessed by objective response rate per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.

Results As of June 2022, 157 patients have been enrolled, 57 in ESC (23 ABBV-151 monotherapy; 34 combination therapy) and 100 in EXP (including 36 UC; 12 HCC). As of January 2022, safety data were available for 129 patients. Any-grade adverse events (AEs) were reported in 119/129 (92%) patients. Most commonly: fatigue (28%), pruritus (27%), and nausea (22%). Grade 3-4 AEs occurred in 66/129 (51%) patients, with drug-related grade 3-4 AEs in 18/129 (14%) patients. ABBV-151 showed dose proportional PK. No antitumor responses were reported for the ABBV-151 monotherapy ESC cohorts. In the combination ESC cohorts, there were 4 confirmed responses, 1 unconfirmed response, and 4 patients had stable disease (SD) ≥6 months. In the anti-PD-1/PD-L1 relapsed/refractory UC EXP cohort, there were 5 confirmed responses, 1 unconfirmed response, and 5 patients had a best response of SD. In the anti-PD-1/PD-L1 naïve HCC EXP cohort, there were 5 confirmed responses, including one response per immune RECIST, and 3 patients had a best response of SD.

Conclusions ABBV-151 ± budigalimab showed a manageable safety profile in patients with advanced solid tumors. Preliminary efficacy results demonstrate durable antitumor activity with ABBV-151 + budigalimab, including in anti-PD-1 relapsed/refractory UC and in anti-PD-1 naïve HCC.

Acknowledgements AbbVie and the authors thank all the trial investigators and the patients who participated in this clinical trial. Medical writing support was provided by Rebecca L. Crepeau, PhD, from Aptitude Health, Atlanta, GA, USA and funded by AbbVie.

Trial Registration NCT03821935

Ethics Approval The study was approved by the Advarra Ethics Board, under the license number IRB00000971.

http://dx.doi.org/10.1136/jitc-2022-SITC2022.0770