Updated antitumor activity and safety of FPA144, an ADCC-enhanced, FGFR2b isoform-specific monoclonal antibody, in patients with FGFR2b+ gastric cancer

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Background: FGFR2b-overexpressing gastric cancer is characterized by poor prognosis. FPA144, a humanized monoclonal IgG1 antibody that specifically binds to and blocks FGFR2b, has been engineered for enhanced antibody-dependent cell-mediated cytotoxicity (ADCC). FPA144-001 is a two-part Phase 1 study of FPA144 monotherapy in patients with advanced solid tumors, including gastric and gastroesophageal cancers (GEJ cancers).

Methods: Part 1A was a 3+3 design to assess safety and PK and to establish a recommended dose (RD) of FPA144. Patients with gastric cancer were enrolled in Part 1B to assess PK in gastric cancer. Part 2 includes 4 cohorts of gastric cancer patients with either high, moderate, low or no FGFR2b overexpression based on a centralized immunohistochemistry (IHC) assay. Here, we describe results of gastric cancer patients that highly overexpress FGFR2b (FGFR2b+ High) enrolled in Parts 1 and 2 of the study.

Results: As of October 28, 2016, 18 FGFR2b+ High (IHC 3+ ≥10% tumor membrane staining) patients were enrolled in the study. 12 of these patients received the RD of 15 mg/kg every 2 weeks. Enrolled patients received a median of 3 prior treatment regimens. Fatigue (22.2%, none ≥ gr 3) and infusion reaction (16.7%, 5.6% gr 3) were the most common treatment-related AEs. Treatment-related SAEs were reported in 2 patients: Grade 2 ulcerative keratitis and Grade 3 infusion reaction. There were 5 PRs, 4 confirmed and 1 unconfirmed. Disease control (PR+SD) was 55.6%, including a confirmed ORR of 22% with median DOR of 15.4 weeks. ctDNA analysis of a responding patient revealed baseline elevated FGFR2 gene copy (165 copies in the blood, mutation allele burden 66%) that decreased after monotherapy (nadir 75 copies, mutation allele burden 38.5%) corresponding with clinical response, serum tumor markers and near complete response on PET imaging.

Conclusions:

The demonstration of activity and an acceptable safety profile supports further development of FPA144 in patients with FGFR2b+ tumors. *FGFR2* gene amplification detected in ctDNA may provide a non-invasive diagnostic test for patient selection. Updated data will be presented. NCT02318329.