

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

Catenacci D, Rha S, Bang YJ, Wainberg Z, Chao J, Lee KW, Korn WM, Kim Y, Song E, Chiu C, Yen C, Berlin J, Kim J, Sikorski R, Collins H, Clark L, Inamdar S, Zhang C, Lee J.

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+ \geq 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 \geq 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.