AB065. P-36. Debio 1347 in patients with cholangiocarcinoma harboring an *FGFR* gene alteration: preliminary results

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Background: Cholangiocarcinoma (CCA), an aggressive epithelial neoplasm of biliary tract, presents limited treatment options and poor overall survival. Aberrant fibroblast growth factor receptor (FGFR) signaling has been implicated in CCA carcinogenesis especially in intrahepatic cholangiocarcinoma (iCCA). Debio 1347 is an orally available selective FGFRi with potent antitumor effect in preclinical models of cancer bearing FGFR alterations. Debio 1347 showed encouraging preliminary clinical activity and manageable treatment-emergent adverse events (TEAE) in its first-in-human (FIH) Ph1 study (NCT1948297). Here we report results from the patients with CCA patients enrolled.

Methods: This FIH study enrolled patients with advanced solid malignancies harboring activating alterations of FGFR 1, 2, or 3. Patients received Debio 1347 at doses between 60 and 150 mg orally daily in 28-day cycles.

Results: Among 9 patients with CCA enrolled (as of November 20), all had iCCA, 5 patients had an FGFR2 translocation (56%), and one each had an FGFR1 translocation, FGFR2 mutation, FGFR2 activating deletion, and an FGFR3 mutation. The median number of lines of prior systemic therapy was 2 (range, 1–3). The most common TEAEs were hyperphosphatemia, nail changes, nausea, dry mouth and stomatitis. No grade ≥3 related TEAE were reported except grade 3 hyperphosphatemia (33%). Partial responses were observed in 2/9 (22%) patients, one with an FGFR2 translocation and one with an FGFR2 activating deletion; 4/9 (44%) patients had stable disease, and all had FGFR2 translocations. The median time on treatment was 24 weeks (range, 4–57 weeks).

Conclusions: These results demonstrate that patients with cholangiocarcinoma with activating alterations in FGFR may benefit from treatment with Debio 1347. The phase II FUZE trial of Debio 1347 for patients with advanced solid tumors harboring FGFR fusions will include a cohort for patients with cholangiocarcinoma.

Keywords: Debio 1347; fibroblast growth factor receptor inhibitor (FGFR inhibitor); FGFR fusions; cholangiocarcinoma

Cite this abstract as: Ng MC, Goyal L, Bang YJ, Oh DY, Chao TY, Cleary JM, Voss MH, Meric-Bernstam F, Iyer G, Heist RS, Ishii N, Kirpicheva Y, Pokorska-Bocci A, Vaslin A, Hu Y, Zanna C, Hyman D, Flaherty K. Debio 1347 in patients with cholangiocarcinoma harboring an *FGFR* gene alteration: preliminary results. HepatoBiliary Surg Nutr 2019;8(Suppl 1):AB065. doi: 10.21037/hbsn.2019.AB065

