SAFETY AND EFFICACY OF THE SELECTIVE FGFR INHIBITOR DEBIO 1347 IN PHASE 1 STUDY PATIENTS WITH FGFR GENOMICALLY ACTIVATED ADVANCED BILIARY TRACT CANCER

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ABSTRACT #447

SUMMARY

• Biliary tract cancers (BTC) are aggressive tumours with limited treatment options and poor overall survival.
• Aberrant Fibroblast Growth Factor Receptor (FGFR) signalling has been implicated in BTC carcinogenesis.
• Debio 1347 is an orally available selective FGFR inhibitor with potent antitumor effect in preclinical model bearing FGFR alterations.1
• Debio 1347 showed encouraging clinical trial activity and manageable toxicity in treatable advanced BTC patients (CT130581) in a 2:1 ratio of BTLC:SD (n=20). Phase I study show safety profile (NCICTN91765597).
• Here we report preliminary results from the BTC patients of the dose escalation portion of this study.

METHODS

• This FIH study enrolled patients with advanced solid malignancies featuring defined activating alterations of FGFR2, 3 or 3 amplifications, exons deletions and translocations.
• Pharmacokinetics in BTC patients was comparable to that in patients with other solid malignancies (grey lines).

RESULTS

• Eight patients, all with cholangiocarcinoma (iCCA) and one with gallbladder cancer (GBC), were treated with Debio 1347 at doses between 60 and 150 mg orally daily in 28-day cycles (Table 1).
• All patients had hepatic dominant lesions, with 5-8 prior systemic lines of treatment (mostly 2 or 3 lines).
• The most common TAEs were hepatic/LFTs (9), nausea (5), dry mouth (5) and headaches (3). No Grade 3 related TAEs were reported except Grade 3 hyperphosphatemia (1).
• Asymptomatic regression was seen in an iCCA patient, whose tumor harbored FGFR3 mutation (details are shown). The decision of treatment was 7 weeks.
• The Intrahepatic Radiology Review updated this response to confirmed complete response (CR) (Fig. 2, Fig. 3).
• These additional iCCA patients (FGFR2/3 translocation/ROCK1) (Table 1), and one GBC patient (FGFR3) iCCA translocation had larger lesions regression >26% and stayed on treatment between 20-70 weeks (Fig. 1, Fig. 2).
• Overall disease control rate was 62.5%.
• Increase in photofusible levels, used as an indicator of target engagement, was observed in all patients (Fig. 5).
• Pharmacokinetics in BTC patients were comparable to that in patients with other solid malignancies (Fig. 4).

CONCLUSIONS

• All explored doses demonstrated sustained plasma exposure to Debio 1347 and target engagement.
• These results suggest that BTC patients with genenic events, translocations and mutations leading to activation of FGFR2/3, may benefit from treatment with Debio 1347.
• Further recruitment is ongoing in the expansion cohort of this trial focused on translocations only.