AB046. P-14. TREETOPP: a phase 2/3 study of varlitinib plus capecitabine versus placebo plus capecitabine as second-line treatment in patients with advanced or metastatic biliary tract cancers (BTCs)

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Background: Biliary tract cancers (BTCs) are rare and have a poor prognosis. These cancers are often diagnosed at advanced stage with limited treatment options and poor overall survival (OS). Overexpression of epidermal growth factor receptor (EGFR), HER2, HER3, and HER4 vary from 23–57%, 4–13%, 12–23% and 59–60% of BTCs, respectively. Varlitinib is a small molecular tyrosine kinase inhibitor of EGFR, HER2 and HER4 with potent antitumor effect in preclinical BTC models. Varlitinib also demonstrated tumor shrinkage responses and durable disease stabilization in BTC patients in phase IB study.

Methods: A randomized, double-blind, placebo-controlled phase 2 (Part 1)/3 (Part 2) study to compare the efficacy of varlitinib (300 mg BID, every day) versus placebo, when combined with capecitabine (1,000 mg/m^2, BID for 14 days). The primary endpoints of Part 1 are objective response rate (ORR) and progression-free survival (PFS) and for Part 2 is OS. Eligible patients include those with confirmed advanced or metastatic 2nd line BTC, including intrahepatic or extrahepatic cholangiocarcinoma, gallbladder cancer and carcinoma of ampulla of Vater. Patients must have failed gemcitabine-contained 1st line systemic treatment. The target sample size is 482 patients, and enrollment has started on May 24, 2017. Safety data will be listed and summarized. Co-primary endpoints of Part 1 will be analyzed using data from an Independent Central Review of radiological data. A Hochberg procedure will be used to control the familywise type I error rate for Part 1 at the 10% level (one-sided). For Part 2, the primary endpoint, OS, will be tested at the two-sided 5% significance level.

Trial registration: Clinical trial information: NCT03093870

Keywords: Varlitinib; pan-Her inhibitor; biliary tract cancer

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