AB062. P-33. Efficacy and safety of varlitinib, a reversible pan-HER tyrosine kinase inhibitor, in combination with platinum-based regimens in biliary tract cancers: a pooled analysis from three phase 1 studies

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Background: Varlitinib is a nanomolar inhibitor of EGFR, HER2, and HER4 and has shown potent anti-tumor activity as monotherapy in preclinical BTC models. During phase (Ph) 1 development, significant tumor shrinkage was observed in biliary tract cancer (BTC) patients (pts). Tissue microarray analysis has revealed that ~70% of BTC pts exhibit HER overexpression, suggesting varlitinib could be beneficial in BTC.

Methods: Data from BTC pts were pooled from 3 Ph1 trials of varlitinib (dosed 200–500 mg BID) in combination with cisplatin and 5-FU/capecitabine (cape) (study 002); oxaliplatin and 5-FU/cape (study 002SG); cisplatin and gemcitabine (study 007). The depth of tumor response, disease control rate (DCR), and treatment-related adverse events (TRAEs) were analysed.

Results: As of 12 June 2018, 43 pts were recruited: 12 (27.9%); 10 (23.3%) and 21 (48.8%) from study 002; 002SG and 007 respectively. Studies 002SG and 007 were still ongoing at data cut-off. Twenty (46.5%) pts were male and the median age was 62 years (range, 42–82 years). Most tumors were cholangiocarcinoma (74.4%), followed by gallbladder cancer (16.3%) and carcinoma of the ampulla of Vater (9.3%). Fourteen (32.6%) pts had received ≥1 prior lines of treatment. Of the 37 pts evaluable for efficacy (those with measurable disease and received ≥1 dose of treatment), partial responses were observed in 10 (27.0%) pts and stable disease in 16 (43.2%) pts, with a DCR of 70.3%. The median depth of tumor response was –10.8% (range, –87.1% to 49.5%). Of 43 pts, the most frequent (≥30%) TRAE (any grade) were fatigue (37%), decreased appetite (34%), and nausea (32%) and the most common grade ≥3 TRAE were hyperbilirubinemia (12%), increased AST (9%), and neutropenia (9%). The median PFS data is not matured and will be provided if evaluable at the time of presentation.

Conclusions: Varlitinib with platinum-based chemotherapy has a promising efficacy and safety profile in BTC. A Ph2/3 randomised study of varlitinib and cape in 2nd line BTC and a Ph1b/2 study of varlitinib with platinum-based chemotherapy in 1st line BTC are ongoing.

Keywords: Varlitinib; pan-HER inhibitor; biliary tract cancer (BTC)

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