AB052. P-20. Phase 2, open-label study of second-line M7824 treatment in patients with locally advanced or metastatic biliary tract cancer

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Background: Transforming growth factor β (TGF-β) signaling promotes tumor immunosuppression; its inhibition in the tumor microenvironment may enhance the response to anti-PD-L1 treatment. M7824 is an innovative first-in-class bifunctional fusion protein composed of 2 extracellular domains of TGF-βRII (a TGF-β "trap") fused to a human IgG1 mAb against PD-L1. Building upon encouraging efficacy observed in a phase 1 study, the present study will evaluate M7824 clinical benefit in patients with pretreated biliary tract cancer (BTC).

Methods: This multicenter, international trial is evaluating M7824 monotherapy in patients with locally advanced or metastatic (LA/M) BTC unselected for tumor PD-L1 expression who had disease progression after or were intolerant to first-line platinum-based therapy. Eligible patients must have histologically or cytologically confirmed LA/M intrahepatic cholangiocarcinoma (CCA), extrahepatic CCA, or gallbladder cancer. Patients must not have received prior immunotherapy, therapy with checkpoint inhibitors, or anti-TGF-β therapy. Patients will receive M7824 1,200 mg every 2 weeks intravenously up to 24 months or until confirmed disease progression, unacceptable toxicity, or trial withdrawal. The primary endpoint is confirmed objective response; key secondary endpoints include duration of response, progression-free survival, overall survival, and safety.

Results: This is a trial in progress; results are pending.

Conclusions: BTCs are a group of cancers with poor prognosis and few treatment options. For second-line therapy, no standard of care exists, and overall response rates (ORRs) with chemotherapy are <10%. M7824 has demonstrated promising preclinical activity as well as antitumor activity and a manageable safety profile in two phase 1 studies. In an expansion cohort of study NCT02699515 of 30 patients with pretreated advanced BTC, M7824 monotherapy demonstrated a 23.3% confirmed ORR by investigator assessment, with durable responses. The present study is, therefore, supported by preclinical and clinical evidence and will provide further insight of M7824 in BTC. Previously presented at the 2019 Cholangiocarcinoma Foundation Conference, Borad *et al.* Reused with permission.

Keywords: Bintrafusp alfa; M7824; transforming growth factor β (TGF-β); PD-L1; bifunctional; biliary tract cancer (BTC)

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