AB053. P-21. M7824 (MSB0011359C), a bifunctional fusion protein targeting transforming growth factor β (TGF-β) and PD-L1, in Asian patients with pretreated biliary tract cancer (BTC): efficacy by BTC subtype

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Background: Biliary tract cancers (BTCs) are a group of cancers with poor prognosis and few treatment options. For 2L chemotherapy, no standard-of-care therapy exists, and overall response rates ORRs) are <10%. M7824 is an innovative first-in-class bifunctional fusion protein composed of 2 extracellular domains of transforming growth factor (TGF)-βRII (a TGF-β "trap") fused to a human IgG1 mAb against PD-L1. We report the safety and efficacy of M7824 in Asian patients with pretreated BTC.

Methods: Patients with BTC [including intrahepatic (IHCC) and extrahepatic (EHCC) cholangiocarcinomas, gallbladder carcinoma (GC), and ampullary carcinoma (AC)] who progressed after ≥1 line of chemotherapy received M7824 1,200 mg q2w until disease progression, unacceptable toxicity, or trial withdrawal in this expansion cohort of the ongoing phase 1, open-label trial NCT02699515. The primary objective is safety/tolerability; secondary objectives include best overall response per RECIST v1.1.

Results: At 39 weeks median follow-up, 30 patients received M7824 for a median of 8.9 (range, 2.0–57.6) weeks; 5 patients were on active treatment. Treatment-related adverse events (TRAEs) occurred in 60% of patients; most common were maculopapular rash and pyrexia (13.3% each), as well as lipase increase and rash (10.0% each). Ten patients (33.3%) experienced grade ≥3 TRAEs, including 3 of grade 5 [1 septic shock (bacteremia, unknown etiology; 249 and 14 days after first and last dose, respectively), 2 interstitial lung disease (ILD) AEs (1 on treatment post 3 doses, 1 occurring 6 months after initial ILD diagnosis and last dose)]. Objective responses were observed in 7 patients (ORR, 23.3%; IHCC, 4/10 patients; EHCC, 1/7 patients; GC, 2/12 patients; AC, 0/1 patients), with 1 durable CR (5.6+ months) and 4/6 PRs ongoing at data cutoff (0.7+, 2.8, 3.9+, 5.5+, 5.6, 6.9+ months). One additional patient with GC had an ongoing PR for 7.6+ months after initial pseudoprogression.

Conclusions: M7824 monotherapy has an acceptable safety profile and promising efficacy in Asian patients with pretreated BTC, with durable responses in 8/30 patients (27%; includes 1 patient with pseudoprogression) across BTC subtypes, including responses in patients with IHCC, EHCC, and GC (ORRs, 40%, 14%, and 17%, respectively). Previously presented at ESMO Asia 2018, FPN 153O, Yoo *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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