153O 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

C. Yoo[1], D-Y. Oh[2], H.J. Choi[3], M. Kudo[4], M. Ueno[5], S. Kondo[6], L-T. Chen[7], M. Osada[8], C. Helwig[9], I. Dussault[10], M. Ikeda[11]

[1]Medical Oncology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea, [2]Medical Oncology, Seoul National University Hospital, Seoul, Republic of Korea, [3]Medical Oncology, Yonsei Cancer Center, Seoul, Republic of Korea, [4]Department of Gastroenterology and Hepatology, Kindai University, Osaka, Japan, [5]Department of Gastroenterology, Hepatobiliary and Pancreatic Medical Oncology Division, Kanagawa Cancer Center, Yokohama, Japan, [6]Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center, Tokyo, Japan, [7]Internal Medicine, National Cheng Kung University Hospital, National Institute of Cancer Research, Tainan, Taiwan, [8]Medical Oncology, Merck Serono, Tokyo, Japan, [9]Biostatistics, Merck KGaA, Darmstadt, Germany, [10]Clinical Biomarkers, Immuno-Oncology, EMD Serono, Billerica, MA, USA, [11]Department of Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital East, Kashiwa, Japan

Background: BTCs are a group of cancers with poor prognosis and few treatment options, encompassing intrahepatic (IHCC) and extrahepatic (EHCC) cholangiocarcinomas, gallbladder carcinoma (GC), and ampullary carcinoma (AC). For 2L chemotherapy, no standard of care exists, and overall response rates (ORRs) are <10%. M7824 is an innovative first-in-class bifunctional fusion protein composed of 2 extracellular domains of TGF-β receptor II (a TGF-β "trap") fused to a human IgG1 mAb

against PD-L1. We report the safety and efficacy of M7824 in Asian patients (pts) with pretreated BTC.

Methods: Pts who progressed after ≥1 line of chemotherapy receive M7824 1200 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 wk median follow-up, 30 pts received M7824 for a median of 8.9 (range, 2.0–57.6) wk; 5 pts were on active treatment. Treatment-related adverse events (TRAEs) occurred in 60% of pts; most common were maculopapular rash and pyrexia (13.3% each), as well as lipase increase and rash (10.0% each). 10 pts (33.3%) experienced grade ≥3 TRAEs, including 3 grade 5 (1 septic shock [bacteremia, unknown etiology; 249 and 14 days after first and last dose, resp.], 2 due to interstitial lung disease [ILD; 1 on treatment post 3 doses, 1 after 6 mo of initial ILD diagnosis and last dose). Objective responses were observed in 7 pts (ORR, 23.3%; IHCC, 4/10 pts; EHCC, 1/7 pts; GC, 2/12 pts; AC, 0/1 pts), with 1 durable complete response (5.6+ mo) and 4/6 partial responses (PRs) ongoing at data cutoff (0.7+, 2.8, 3.9+, 5.5+, 5.6, and 6.9+ mo). 1 additional pt with GC had an ongoing PR for 7.6+ mo after initial pseudoprogression.

Conclusions: M7824 monotherapy has an acceptable safety profile and promising efficacy in Asian pts with pretreated BTC, with durable responses in 8/30 pts (27%; includes 1 pt with pseudoprogression) across BTC subtypes, including responses in pts with IHCC, EHCC, and GC (ORRs, 40%, 14%, and 17%, resp.).

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