Background: Biliary tract cancers (BTC) are often diagnosed at an advanced stage, with standard gemcitabine plus cisplatin combination chemotherapy providing limited benefit. The phase 2, multicohort KEYNOTE-158 study (NCT02628867) evaluated antitumor activity and safety of pembrolizumab (pembro), an anti–PD-1 antibody in patients (pts) with advanced BTC.

Methods: Pts aged ≥18 y with histologically/cytologically confirmed unresectable or metastatic BTC and prior progression/intolerance on standard therapy were enrolled if they had measurable disease per RECIST v1.1, ECOG PS ≤ 1, and tumor sample for evaluation of PD-L1 (PD-L1 IHC 22C3 pharmDx assay [Agilent Technologies]) and other biomarkers. Pts received pembro 200 mg Q3W for up to 2 y or until disease progression or unacceptable AEs. The primary endpoint was ORR; DOR, PFS, OS and safety were secondary endpoints. Response was assessed every 9 wks in year 1, then every 12 wks (RECIST v1.1, independent central review), DOR, PFS, and OS were evaluated using the Kaplan-Meier method. AE severity was graded per NCI CTCAE v4.0.

Results: At data cutoff (Jan 15, 2018), 104 pts with BTC (49% male; median age, 63 y [range, 34–84]); ≥2 prior therapies, 52%) were enrolled (median follow-up, 9.3 mo [range, 0.6–33.6]). ORR was 5.8% (95% CI, 2.1–12.1; 6 PR, 0 CR); 17 pts (16%) had SD. Median DOR was not reached (range, 6.2–15.7+ mo); 2 pts had DOR >15 mo. ORR was 6.6% (95% CI, 1.8–15.9) and 2.9% (95% CI, 0.1–15.3) among those with PD-L1 CPS ≥1 (n = 41) and CPS <1 (n = 34), respectively. Median PFS was 2.0 mo (95% CI, 1.9–2.1) and median OS was 9.1 mo (95% CI, 5.6–10.4). Median PFS was 1.9 mo (95% CI, 1.8–2.0) vs 2.1 mo (95% CI, 1.9–2.6) and median OS was 7.2 mo (95% CI, 5.3–11.0) vs 9.6 mo (95% CI, 5.4–12.8) among pts with PD-L1 CPS ≥1 vs < 1, respectively. 99 pts (including all responders) were evaluated for MSI status; none were MSI-H. Overall, 55% of pts had treatment-related AEs (most commonly fatigue [14%], rash [12%], pruritus [9%]); 13% had grade 3–5 AEs, and 16% had immune-mediated AEs. Treatment-related AEs led to discontinuation in 6 pts.

Conclusions: Pembro shows durable antitumor activity in a subset of pts with advanced BTC regardless of PD-L1 CPS and had manageable toxicity.

Clinical trial identification: NCT02628867.

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