Supplementary Table 2: Summary of currently unreported, ongoing phase II and phase III trials with use of PD-1/PD-L1 inhibitors in the management of patients with biliary tract cancer

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| **Palliative Intent – First line** | | | | | | | |
| **NCT number** | **Phase** | **Country (no. of centres)** | **Recruitment ongoing\*** | **PD-1/PDL-1 inhibitor** | **BTC cancers included** | **Investigational Arms** | **Primary outcome measures** |
| NCT04677504 | II | International (52) | No | Atezolizumab | Advanced IHC, EHC, GBC | Arm 1:  Atezolizumab (1200mg) 3 weekly + bevacizumab (15mg/kg) 3 weekly +  Gemcitabine (1000mg/m2) day 1 and day 8, 3 weekly + Cisplatin (25mg/m2) day 1 and day 8, 3 weekly  Arm 2:  Atezolizumab (1200mg) 3 weekly + Placebo 3 weekly + Gemcitabine (1000mg/m2) day 1 and day 8, 3 weekly + Cisplatin (25mg/m2) day 1 and day 8, 3 weekly | Progression free survival |
| **Palliative Intent – Second line and beyond** | | | | | | | |
| NCT04976634 | II | International (13) | Yes | Pembrolizumab | Advanced and metastatic solid tumours\*\* including BTC (IHC, EHC and GBC) | Pembrolizumab (400mg) 6 weekly + Belzutifan (120mg) once a day + Lenvatinib (20mg) once a day | Objective response rate and safety (number of participants who experience at least one dose-limiting toxicity,  number of participants who experience at least one adverse event, number of participants who discontinue study treatment due to an adverse event) |
| NCT04727996 | II | Republic of Korea (1) | Yes | Tislelizumab | Unresectable or recurrent IHC, EHC, GBC and Ampulla of Vater Cancer | Tislelizumab (200mg) 3 weekly + Sitravatinib (120 mg) once a day | Disease control rate |
| NCT04298021 | II | Republic of Korea (1) | Yes | Durvalumab | Advanced IHC, EHC, GBC and Ampulla of Vater Cancer | Arm 1:  Durvalumab (1500mg) 4 weekly + ceralasertib (240mg) twice a day on day 15 to day 28  Arm 2:  Olaparib (300mg) twice a day on day 1 to day 28 + ceralasertib (160mg) four times a day on day 1 to day 7 | Disease control rate |
| NCT03991832 | II | Canada (1) | Yes | Durvalumab | IDH-mutated solid tumours† including IDH-mutated BTC (IHC) | Durvalumab (1500mg) 4 weekly + Olaparib (300mg) twice a day | Overall response rate and overall disease control rate |

Key:

BTC = Biliary tract cancer, IHC = Intrahepatic cholangiocarcinoma, EHC = Extrahepatic cholangiocarcinoma, GBC = Gallbladder cancer, IDH = Isocitrate dehydrogenase

\* Information from <https://clinicaltrials.gov>, updated on 30th June 2022

\*\* Other advanced and metastatic solid tumours included were hepatocellular carcinoma, colorectal cancer, pancreatic ductal adenocarcinoma, endometrial cancer and oesophageal cancer

† The study involved three cohorts of patients: Cohort A: IDH-mutated gliomas, Cohort B: IDH-mutated cholangiocarcinoma, Cohort C: Other IDH-mutated solid tumour