Supplementary Table 1: Summary of up-to-date, reported phase II trials with the use of PD-1/PD-L1 inhibitors in the management of patients with biliary tract cancer

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| **Neo-adjuvant Intent** | | | | | | | | |
| **Identification number**  **Author & Year of Publication** | **Country**  **(no. of centres)** | **PD-1/PDL-1 inhibitor** | **BTC cancers included** | **PS** | **No. of patients** | **Investigational Arms** | **Primary outcome measure** | **Median overall survival (months)** |
| ChiCTR2100044476  Qiyi Zhang et al. 2021  [33] | China (1) | Pembrolizumab, tislelizumab, sintilimab, camrelizumab, toripalimab | Unresectable IHC, EHC, GBC | 0-1 | 38 | Pembrolizumab (200mg),  or tislelizumab (200mg),  or sintilimab (200mg),  or camrelizumab (200 mg),  or toripalimab (240 mg),  3-weekly  AND  Lenvatinib (body weight ≥60 kg = 12 mg; <60 kg = 8 mg) once a day | Objective response rate: 42.1% | 17.7 |
| **Palliative Intent – First line** | | | | | | | | |
| **Identification number**  **Author & Year of Publication (reference)** | **Country**  **(no. of centres)** | **PD-1/PDL-1 inhibitor** | **BTC cancers included** | **PS** | **No. of patients** | **Investigational Arms** | **Primary outcome measure** | **Median overall survival (months)** |
| NCT03046862  Do-Youn Oh et al.  2022  [43] | Republic of Korea (1) | Durvalumab | Unresectable or recurrent IHC, ECH, GBC, ampulla of Vater cancer | 0-1 | 128 | Arm 1:  Gemcitabine (100mg/m2) day 1 and day 8, 3 weekly  AND  Cisplatin (25mg/m2) day 1 and day 8, 3 weekly for 1 cycle  AND  Durvalumab (1.12g) 3 weekly + Tremelimumab (75mg) 3 weekly from cycle 2  Arm 2:  Durvalumab (1.12g) 3 weekly  AND  Tremelimumab (75mg) 3 weekly  AND  Gemcitabine (100mg/m2) day 1 and day 8, 3 weekly  AND  Cisplatin (25mg/m2) day 1 and day 8, 3 weekly  Arm 3:  Durvalumab (1.12g) 3 weekly  AND  Gemcitabine (100mg/m2) day 1 and day 8, 3 weekly  AND  Cisplatin (25mg/m2) day 1 and day 8, 3 weekly | Response rate:  66% of patients achieved an objective response  Arm 1:  Response rate = 50%  Complete response = 7%  Partial response = 43%    Arm 2:  Response rate = 70%  Complete response = 2%  Partial response = 68%  Arm 3:  Response rate = 72%  Complete response = 6%  Partial response = 66% | Information not available |
| NCT03796429  Wei Lei et al. 2021  [35] | China (1) | Toripalimab | Advanced ICH, ECH, GBC | 0-1 | 50 | Toripalimab (240mg) 3 weekly  AND  Gemcitabine (1000mg/m2) on day 1 and day 8 every 3 weeks  AND  S1 (40-60mg) twice a day for 14 days every 3 weeks | Progression free survival: 7.0 months  Overall survival: 16.0 months | 16.0 |
| NCT03486678  Xiaofeng Chen et al.  2020  [36] | China (1) | Camrelizumab | Advanced ICH, EHC, GBC | 0-1 | 38 | Camrelizumab (3mg/kg) day 1 and 15  AND  Gemcitabine (800 mg/m2) day 1 and 15  AND  Oxaliplatin (85mg/m2) day 2 and 16 | Progression free survival: 6.1 months | 11.8 |
| NCT03311789  Kaichao Feng et al. 2020  [37] | China (1) | Nivolumab | Advanced, unresectable or metastatic IHC, EHC, GBC | 0-2 | 32 | Nivolumab (3mg/kg) 3 weekly  AND  Gemcitabine (1000mg/m2) on day 1 and 15, 3 weekly  AND  Cisplatin (75mg/m2) on day 1, 3 weekly | Objective response rate: 55.6% | 8.5 |
| NCT03101566  Vaibhav Sahai et al. 2020  [38] | USA (6) | Nivolumab | Advanced unresectable IHC, EHC, GBC | 0-1 | 71 | Arm 1: Nivolumab (360mg) 3 weekly  AND  Gemcitabine (1000mg/m2) on day 1 and 8, 3 weekly  AND  Cisplatin (25mg/m2) on day 1 and 8, 3 weekly  for 6 months  THEN  Nivolumab (240mg) 2 weekly  Arm 2: Nivolumab (240mg) 2 weekly  AND  Ipilimumab (1mg/kg) 6 weekly | Progression free survival at 6 months:  Arm 1: Progression free survival = 70%  Arm 2: Progression free survival = 18.6% | Information not available |
| **Palliative Intent – Second line and beyond** | | | | | | | | |
| **Identification number**  **Author & Year of Publication (reference)** | **Country (no. of centres)** | **PD-1/PDL-1 inhibitor** | **BTC cancers included** | **PS** | **No. of patients** | **Investigational Arms** | **Primary outcome measure** | **Median overall survival (months)** |
| NCT02703714  Robin Kate Kelly et al. 2022  [39] | USA (1) | Pembrolizumab | Advanced IHC, EHC, GBC | 0-1 | 42 | Pembrolizumab (200mg) 3 weekly AND  Sargramostim (GM-CSF) (250 micrograms) day 1-14 of cycle 1-2 or 2-3 | Progression free survival: 63 days  Overall survival: 93 days | 3.1 |
| NCT04306367  Chao Yin et al. 2022  [40] | USA (1) | Pembrolizumab | Advanced IHC, EHC, GBC | 0-1 | 12 | Pembrolizumab (200mg) 3 weekly AND  Olaparib (300mg) twice a day | Response rate: Partial response = 1 patient  Stable disease = 4 patients  Progressive disease = 7 patients\* | Information not available |
| NCT04679038  J Xie et al.  2022  [30] | China (16) | SHR-1701\* | Metastatic or locally advanced solid tumours\*\* including BTC (IHC, EHC, GBC) | 0-1 | 9 | SHI-1701† (30mg) 3 weekly  AND  Famitinib (20mg) once a day | Objective response rate: 13% | Information not available |
| NCT03797326  Luis Villanueva et al. 2021  [31] | International (88) | Pembrolizumab | Advanced solid tumours†† including BTC (IHC, EHC, GBC) | 0-1 | 31 | Pembrolizumab (200mg) 3 weekly AND  Lenvatinib (20mg) once a day for 21 days | Objective response rate: 10%  Partial response = 10%  Stable disease = 58% | 8.6 |
| NCT03201458  Mark Yarchoan et al. 2021  [41] | USA (41) | Atezolizumab | Metastatic or unresectable IHC, EHC, GBC | 0-1 | 77 | Arm 1: Atezolizumab on day 1 and 15 of 28 day cycle  Arm 2: Atezolizumab on day 1 and 8 of 28 day cycle  AND  Cobimetinib once a day for 21 days of a 28 day cycle | Progression free survival:  Arm 1:  Progression free survival = 1.87 months  Arm 2:  Progression free survival = 3.65 months | Information not available |
| NCT02829918  Richard D Kim et al.  2020  [42] | USA (3) | Nivolumab | Unresectable, locally advanced or metastatic IHC, EHC, GBC | 0-1 | 54 | Nivolumab (240mg) 2 weekly for 16 weeks  THEN  Nivolumab (480mg) 4 weekly | Objective response rate:  Investigator-assessed objective response rate = 22%  Independent review objective response rate = 11% | 14.24 |
| NCT02923934  Oliver Klein et al.  2020  [32] | Australia (5) | Nivolumab | Advanced rare cancers§§ including BTC (IHC, EHC, GBC) | 1 | 39 | Nivolumab (3 mg/kg) 3 weekly  AND  Ipilimumab (1 mg/kg) 3 weekly for 4 doses  THEN  Nivolumab (3mg/kg) 2 weekly | Disease control rate: 44% | 5.7 |
| NCT02054806  Sarina A Piha-Paul et al. 2020  [22] | International (26) | Pembrolizumab | Advanced solid tumours§ including BTC (ICH, ECH, GBC) | 0-1 | 104 | Pembrolizumab (200mg) 3 weekly | Objective response rate: 5.8% | 7.4 |

Key:

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

\* Interim results

\*\* Other metastatic or locally advanced solid tumours included were pancreatic, renal cell and hepatocellular carcinoma

† SHR-1701 is a bifunctional fusion protein targeting PD-L1 and transforming growth factor ß receptor II

†† Other advanced solid tumours included were triple negative breast cancer, ovarian cancer, gastric cancer, colorectal cancer, glioblastoma, biliary tract cancers, pancreatic cancer

§ Other advanced solid tumours included were anal, neuroendocrine, carcinoid, endometrial, cervical, vulval, SCLC, mesothelioma, thyroid, salivary gland, parotid gland, colorectal

§§ Other advanced rare cancers included were upper gastrointestinal, neuroendocrine and rare gynaecological tumours