**Supplementary Table S1. Summary of Included RCTs of 2L Treatments for Advanced BTC**

| **Trial** | **N** | **1L chemo** | **Drug** | **Arm, n** | **ORR, %** | **Median OS, months** | **Median PFS, months** | **6-month OS, %** | **6-month PFS, %** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Cereda 2016 (NCT01530503) | 57 | GEM and PLAT analogs | Arm 1: CAP  Arm 2: CAP-MMC | Arm 1: 28  Arm 2: 29 | Arm 1: 0  Arm 2: 3 | Arm 1: 9.5  Arm 2: 8.1 | Arm 1: 2.1  Arm 2: 2.3 | NR | Arm 1: 8  Arm 2: 10 |
| Javle 2020a (TreeTopp/ NCT03093870) | 127 | GEM+CIS,  GEM+OTHER | Arm 1: CAP-VAR  Arm 2: CAP-PBO | Arm 1: 64  Arm 2: 63 | Arm 1: 9.4  Arm 2: 4.8 | Arm 1: 7.8  Arm 2: 7.5 | Arm 1: 2.83  Arm 2: 2.79 | NR | NR |
| Kim 2020 (SWOG 1310/ NCT02042443) | 44 | GEM, PLAT | Arm 1: TRAM  Arm 2: MIX  (5FU-LV/CAP) | Arm 1: 24  Arm 2: 20 | Arm 1: 8  Arm 2: 10 | Arm 1: 4.3  Arm 2: 6.6 | Arm 1: 1.4  Arm 2: 3.3 | NR | NR |
| Lamarca 2019 (ABC06/ NCT01926236) | 162 | GEM+CIS | Arm 1: ASC  Arm 2: ASC-mFOLFOX | Arm 1: 81  Arm 2: 81 | Arm 1: NR  Arm 2: 5 | Arm 1: 5.3  Arm 2: 6.2 | Arm 1: NR  Arm 2: 4 | Arm 1: 35.5  Arm 2: 50.6 | NR |
| Won Kim 2020 (NCT03464968) | 114 | GEM+CIS | Arm 1: mFOLFOX  Arm 2: mFOLFIRI | Arm 1: 57  Arm 2: 57 | Arm 1: 5.9  Arm 2: 4.0 | Arm 1: 6.3  Arm 2: 5.7 | Arm 1: 2.8  Arm 2: 2.1 | Arm 1: 54.2  Arm 2: 43.6 | NR |
| Zheng 2018 (NCT02558959) | 60 | GEM+CIS | Arm 1: XELIRI  Arm 2: IRI | Arm 1: 30  Arm 2: 30 | Arm 1: 13.3  Arm 2: 6.7 | Arm 1: 10.1  Arm 2: 7.3 | Arm 1: 3.7  Arm 2: 2.4 | NR | NR |

1L, first-line; 2L, second-line; BTC, biliary tract cancer; chemo, chemotherapy; NR, not reported; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; RCT, randomized controlled trial. See also *Treatment abbreviations* section.

“-“ or “+” indicates that combination treatment was received (eg, CAP-PBO, capecitabine plus placebo, CAP+CIS, capecitabine plus cisplatin). “±” indicates that a treatment was received either in combination with the next listed treatment or as a monotherapy (eg, FLUOR±PLT, fluoropyrimidine with or without a platinum). “/” indicates that either treatment listed was received (eg, GEM+CIS/S1, gemcitabine plus cisplatin *or* S1).