**Supplementary Table S2. Summary of Included Single-Arm Trials of 2L Treatments for Advanced BTC**

| **Trial** | **N** | **1L chemo** | **Drug** | **ORR, %** | **Median OS, months** | **Median PFS, months** | **6-month OS, %** | **6-month PFS, %** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Ahn 2015 (NCT01425879) | 8 | MIX (GEM-based) | MK2206 | 0 | 3.5 | 1.7 | – | – |
| Belkouz 2020 (NCT02456714) | 30 | GEM+CIS | FOLFIRINOX | 10 | 10.7 | 6.2 | 66.7 | – |
| Buzzoni 2014 (EudraCT 2008-007152-94) | 39 | GEMOX, Other (NS) | EVER | 5.1 | 7.7 | 3.2 | 56.4 | 28.2 |
| He 2014 | 37 | GEM+CIS | FOLFOX4 | 21.6 | 6.9 | – | – | – |
| Hwang 2015 (NCT01127555) | 30 | GEM+CIS, GEM | mFOLFOX3 | 7.1 | 4.4 | 1.6 | – | – |
| Kim 2017 | 30 | GEM, GEM+CIS, GEMOX | SPI1620-DOCE | 10.3 | 4.87 | 2.6 | – | – |
| Kim 2019 (NCT02350686) | 50 | GEM+CIS | XELOX | 14 | 7.5 | 3.5 | – | – |
| Kobayashi 2017 (UMIN000005918) | 41 | GEM, GEM+CIS | GEM-S1 | 9.8 | 7 | 2.6 | – | – |
| Larsen 2018 | 50 | CAP+GEMOX, CAP+CET+GEMOX,  GEM+CIS | BEV-GEM-IRI-CAP | 6 | 6.4 | 3.6 | – | – |
| Lim 2012 | 33 | GEM, GEM+CIS, GEMOX, GEM+ERL, 5FU-based | iFAM | 6.5 | 5.6 | 2.2 | – | – |
| Matsuyama 2018 (UMIN000007571) | 27 | GEM+S1 | GEM-CIS | 4% | 6.5 | – | – | – |
| Oh 2011 | 32 | FLUOR | GEM | 6.9 | 4.1 |  | – | – |
| Roth 2011 (EudraCT 2005-003166-42) | 9 | GEM-based, FLUOR-based | IMAT | 0 | 4.9 | NR | NR | NR |
| Sasaki 2012 (UMIN000001614) | 22 | GEM mono | S1 | 22.7 | 13.5 | NR | NR | 38 |
| Suzuki 2013 (UMIN000000919) | 40 | GEM, GEM+CIS | S1 | 7.5 | 6.8 | 2.5 | NR | NR |
| Won Kim 2019a (NCT02773459) | 25 | GEM-based | BIN-CAP | 20 | 7.8 | 4.4 | NR | NR |
| Won Kim 2019b (NCT02115542) | 39 | GEM-based, FLUOR-based | REG | 9.4 | 7.9 | 2.8 | 52 | NR |
| Yi 2020 | 11 | Non-PLT chemotherapy | APT-GEMOX | 36.4 | NR | NR | NR | NR |
| Yi 2012 (NCT01082809) | 56 | GEM, GEM+PLT, FLUOR+PLT | SUN | 8.9 | 4.8 | NR | NR | NR |
| Zhao 2020 (ChiCTR1900022003) | 9 | GEM+CIS | ANL-CED | 25 | Not reached | Not reached | 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).