**Supplementary Table S4. Summary of Included Single-Group Observational Studies of 2L Treatments for Advanced BTC**

| **Author, year** | **Study period** | **N** | **1L chemo** | **Drug** | **ORR, %** | **Median OS, months** | **Median PFS, months** | **6-month OS, %** | **6-month PFS, %** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Brungs 2017 | 2008-2011 | 25 | GEM-PLT,  MIX (5FU), GEM,  MIX (TAX-based) | Mixed (FLUOR±/  GEM±PLT/  nabPAC) | NR | NR | 3.2 | NR | NR |
| Caparica 2019 | 2007-2017 | 12 | GEM-PLT | FOLFIRI | NR | 5 | 1.7 | NR | NR |
| Dang 2019 | 2014-2016 | 29 | GEM+PLT | FOLFOX4 | 31 | NR | 2.53 | NR | NR |
| Dodagoudar 2016 | 2010-2014 | 66 | GEM+PLT | FOLFOX4 | 24.24 | 7.5 | 3.9 | NR | NR |
| Inoue 2020 | 2009-2019 | 83 | CIS-GEM | Mono Tx (S1) | 3.2 | 6 | NR | NR | NR |
| Jung 2017 | 2005-2016 | 40 | GEM,  GEM-CIS, GEMOX,  GEM-IRI | Combo Tx (CAP+CIS) | 10 | 6.3 | 2.3 | NR | NR |
| Kameda 2013 | 2010-2013 | 20 | GEM, GEM-S1 based | Combo Tx (GEM+CIS) | 15 | 13.7 | 6.5 | NR | NR |
| Kang 2014 | 2003- 2012 | 50 | GEM-PLT, FLUOR+CIS, GEM, EPI+CIS+LV+URA/TEG, EPI+CIS+5FU | Mixed (FLUOR±PLT/  GEM±PLT) | 6.3 | 5.5 | 1.9 | NR | NR |
| Katayose 2012 | 2005-2007 | 11 | GEM | Mono Tx (S1) | 9.1 | 15 | NR | NR | NR |
| Kobayashi 2012 | 2007-2011 | 51 | GEM, GEM+CIS | Mono Tx (S1) | 4 | 6 | 2.3 | NR | NR |
| Lowery 2019 | 2010- 2015 | 198 | GEM+PLT, FUDR, Other | Mixed (FLUOR±/GEM±/  FUDR/Other[NS]) | NR | 11 | NR | NR | NR |
| Mizrahi 2020  *Related publication: Mizrahi 2019* | 2007-2017 | 50 | NR | FOLFIRI | NR | 7.7 | 2.4 | NR | NR |
| Moretto 2013 | 2001-2009 | 6 | FOLFOX, GEM, GEMOX, GEM+5-FU | FOLFIRI | 0 | NR | NR | NR | NR |
| Okano 2018 | 2009- 2015 | 45 | GEM, GEM-based | Mixed (GEM±/S1±/TKIs) | 0 | 8.3 | 3 | NR | NR |
| Park 2009 | 2004-2007 | 22 | NR | Mono Tx (S1) | 10 | NR | NR | NR | NR |
| Sasaki 2009 | 2005-2008 | 16 | GEM | Mono Tx (S1) | 18.8 | 8 | NR | NR | NR |
| Sasaki 2013 | 2008- 2012 | 60 | GEM, GEM-S1 | Combo Tx (GEM+CIS) | 1.7 | 6.7 | NR | NR | NR |
| Sebbagh 2016 | 2004- 2013 | 52 | NR | Mixed (FLUOR±) | NR | 8.4 | 3.2 |  | 25.7 |
| Shin 2020 | 2014-2018 | 40 | GEM+CIS | Combo Tx (CAP+CIS) | 12.5 | 7 | 2.8 | NR | NR |
| Singh 2016 | 2012- 2014 | 22 | NR | Mixed (FLUOR±/DOCE) | 9 | NR | NR | NR | NR |
| Sirohi2015 | 2012- 2013 | 75 | NR | Mixed (CAP±/non-CAP±/Unknown) | 16 | NR | NR | NR | NR |
| Taghizadeh 2020 | 2016-2019 | 6 | GEM-CIS, GEM+nabPAC | FOLFIRI | 66.7 | NR | NR | NR | NR |
| Takahara 2018 | 2000-2016 | 139 | GEM, GEM-CIS, GEM-S1, MIX (GEM-based),  S1, FOLFIRINOX | Mixed (GEM+CIS/GEM/S1) | 4 | 7.7 | 2.8 | NR | NR |
| Walter 2013 | 1991- 2011 | 96 | GEM, 5FU-GEM, GEM-PLT, 5FU, other | Mixed (FLUOR±/GEM±/TGT/Other [NS]) | 9 | 7.5 | 2.8 | 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).