Poster CO117

Real-world treatment patterns and outcomes in unresectable advanced and metastatic biliary tract cancers (BTC): a literature review

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Objective

- This literature review aimed to identify treatment guidelines, and real-world treatment patterns and outcomes for unresectable advanced and metastatic BTC

Conclusions

- This review broadly assessed real-world treatment patterns and outcomes, unrestricted by treatment type or line, in unresectable advanced and metastatic BTC
- Current treatments for unresectable advanced and metastatic BTC have poor real-world survival (<12 months in most reports)
- Although GEMCIS was established as 1L SoC a decade ago, GEMCIS remains the most used 1L chemotherapy, highlighting the lack of innovation in the treatment landscape
- This research highlights that there is an urgent unmet need for novel treatments with improved outcomes in this aggressive indication
- Additional observational studies are needed to further understand the effectiveness of currently available treatments, and also newly available therapies such as durvalumab, ivosidenib and pemigatinib

Plain language summary

Why did we perform this research?

Bile duct cancers are rare and aggressive, and are usually diagnosed at a late stage (unresectable advanced or metastatic BTC) when patients cannot be cured.[1,2] With the treatments that are currently available, at least half of all patients diagnosed at this stage die less than 12 months after the start of their first treatment.[2] This study aimed to better understand what treatments patients receive in the real world, and how well these work.

How did we do this research?

We searched for treatment guidelines and studies publishing how well treatments for unresectable advanced or metastatic BTC work in the real world, using specific criteria to select relevant publications.

What did we find?

Real-world studies confirmed that most patients only live for under or around 12 months after starting treatment. The treatment most commonly used first after diagnosis has remained the same for over ten years.

What are the implications of this research?

Our research shows that there is an urgent need to find better treatments for patients with unresectable advanced or metastatic BTC. Since this review was conducted, new treatments have become available, so future real-world studies should be performed show how well these new treatments work in the real world.

Disclosures

This review was funded by AstraZeneca. V Peirce, L Qin, and S Johal are employees of and hold stock in AstraZeneca.

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Poster presented at ISPOR 2023 May 7–10 Boston, MA, USA

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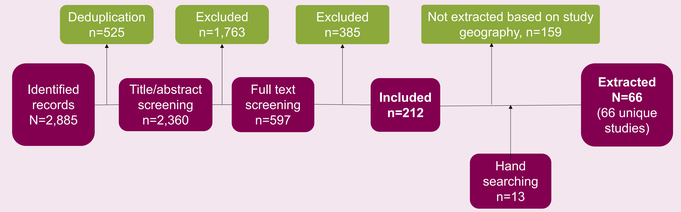
Introduction

- BTC are a group of rare and aggressive malignancies[1,2]
- Up to 80% of patients are diagnosed with unresectable or metastatic disease for which curative treatments are unavailable[3]
- Available treatments for unresectable advanced or metastatic BTC typically show poor median overall survival (mOS) of <12 months[4]
- Gemcitabine plus cisplatin (GEMCIS) has been the standard-of-care (SoC) first-line (1L) treatment for the past decade, however recently guidelines have been updated to include new treatments
- At second-line (2L) leucovorin calcium (folinic acid), fluorouracil, and oxaliplatin (FOLFOX) is SoC, with targeted treatments for tested mutations recommended for some patients in the most recent guidelines
- This literature review aimed to understand treatment guideline recommendations, and real-world treatment patterns and outcomes for unresectable advanced and metastatic BTC

Methods

- The review followed Centre for Research Dissemination guidelines for systematic reviews[5] for searching and screening, with a pragmatic approach to data extraction
- Databases (MEDLINE, Embase, Evidence-Based Medicine Reviews) were searched from 01.01.2000 to 11.25.2021, and supplemented by manual searching of health technology assessments, relevant congresses, guideline agencies and review reference lists (2019–2021)
- Eligible records were 1) treatment guidelines and 2) observational studies reporting treatment patterns or clinical/safety outcomes, in adults with unresectable advanced or metastatic BTC with no intervention restrictions
- Only multi-country studies and those performed in the UK, Germany, France, Australia, Canada, and South Korea were extracted, to restrict the broad search strategy while maintaining representation of a wide range of BTC incidences. Only the highest priority publications from South Korea were extracted
- Here we present treatment recommendations and the most commonly reported outcomes for 1L, 2L and palliative treatments (mOS, and median progression-free survival [mPFS] for 1L treatments)

Figure 1. PRISMA flow diagram



Results and interpretation

- 66 relevant records were extracted (Fig 1): 16 treatment guidelines and 50 observational studies. Most studies (n=20) were conducted in South Korea
- Among 50 observational studies, 25 (50%) and 11 (22%) reported 1L- and 2L treatment outcomes, respectively; 22 (44%) reported outcomes for treatment lines described as 'palliative'

1L treatment patterns and outcomes

- Chemotherapy was the most recommended 1L treatment in guidelines. GEMCIS was recommended as SoC, with alternative chemotherapies suggested for patients who are not fit enough to receive GEMCIS
- In line with guidelines, 23/25 1L studies reported on chemotherapy and GEMCIS was the most common chemotherapy (10/23 studies). Other 1L chemotherapies were also reported on frequently, including other gemcitabine-based and fluoropyrimidine-based regimens
- GEMCIS treatment exposure was described using various units in 6/10 studies, with 3/6 reporting median cycles (range 3.5-5 cycles)
- Although mOS showed fairly wide ranges within and across treatment types, mOS with 1L chemotherapy was generally poor, being less than 12 months in most studies (16/23; range 4.7–22.3 months; Fig 2A). No treatment type seemed to notably improve mOS over other treatments
- mPFS was reported by 10 studies. Like mOS, mPFS outcomes showed wide ranges (Fig 2B) and no treatment type seemed to notably improve mPFS over other treatments
- mPFS was typically high in studies that also reported high mOS. These studies generally had small samples or selected specific patient populations (e.g. higher performance status, or patients who had already responded well to treatment)

2L treatment patterns and outcomes

- Beyond 1L, guidelines disagreed on the utility of additional lines of chemotherapy due uncertainty in the survival benefits. Guidelines suggested a wide range of locoregional modalities and other treatments such as stenting and drainage
- 2L treatment patterns seemed misaligned to guideline recommendations, as almost all 2L studies (10/11) described outcomes for chemotherapy, most commonly for fluoropyrimidine (FP) based regimens (5/10 studies)
- Consistent with 1L, mOS with 2L chemotherapy was poor, being <12 months in 5/10 studies (range 4.9–21.5 months; Fig 3). The apparent overlap between 1L and 2L mOS may be explained, to an extent, by inherent selection by 2L studies of patients fit enough to receive 2L therapy
- 2L mOS also showed wide ranges, with no treatments clearly superior to others. Again, studies achieving comparatively high mOS included small or specific patient populations
- No studies reported on targeted 2L treatments included in the latest guidelines

Palliative treatment patterns and outcomes

- Because the treatment intent for unresectable BTC is not curative, all management may be considered palliative. 22 studies described 'palliative' treatments without specifying treatment line
- Consistent with 1L and 2L, mOS for 'palliative' treatments was poor, being <12 months in 9/18 studies reporting mOS (Fig 4)
- Again no treatments were clearly superior to others. Outcomes showed fairly wide ranges within and across treatment types, with high mOS typically in studies with small or specific patient populations

Strengths and limitations

- This review was conducted using a systematic search and screening approach, including a broad range of databases and publication years
- Limitations include the geographically-limited sample, as well as reporting imprecision across studies for resectability status and for treatment line definitions

Abbreviations

1L, first line; 2L, second line; BTC, biliary tract cancers; CCA, cholangiocarcinomas; eCCA, extrahepatic cholangiocarcinomas, FOLFORINOX, fluorouracil, leucovorin, oxaliplatin and irinotecan; FP, fluoropyrimidine; GBC, gallbladder carcinoma; gem, gemcitabine; GEMCARB, gemcitabine and carboplatin; GEMCIS, gemcitabine and cisplatin; GEMOX, gemcitabine and oxaliplatin; iCCA, intrahepatic cholangiocarcinoma; mPFS, median progression-free survival; mOS, median overall survival; OS, overall survival; PDL1, programmed death ligand 1; PFS, progression-free survival; XP, capecitabine-cisplatin.

Figure 2. Outcomes of 1L treatments

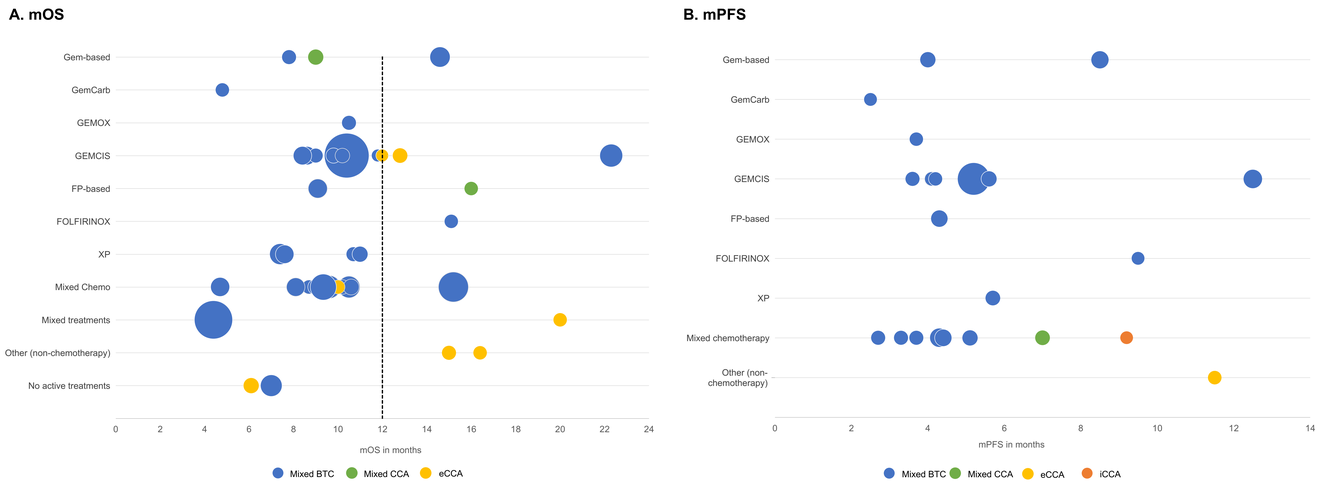


Figure 3. mOS for 2L treatments

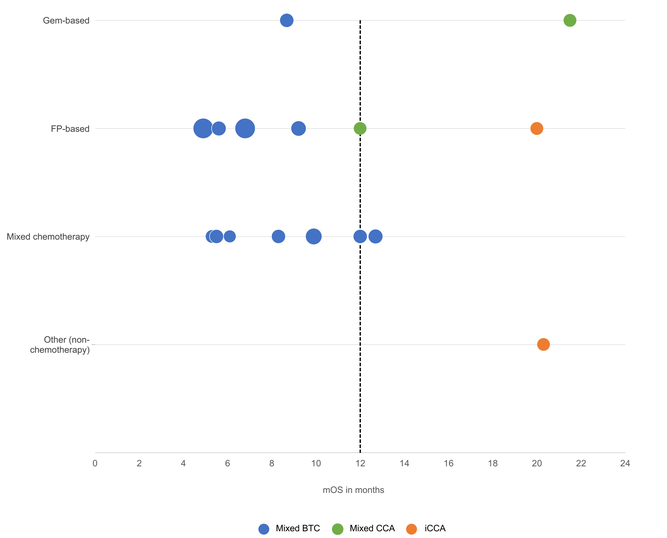
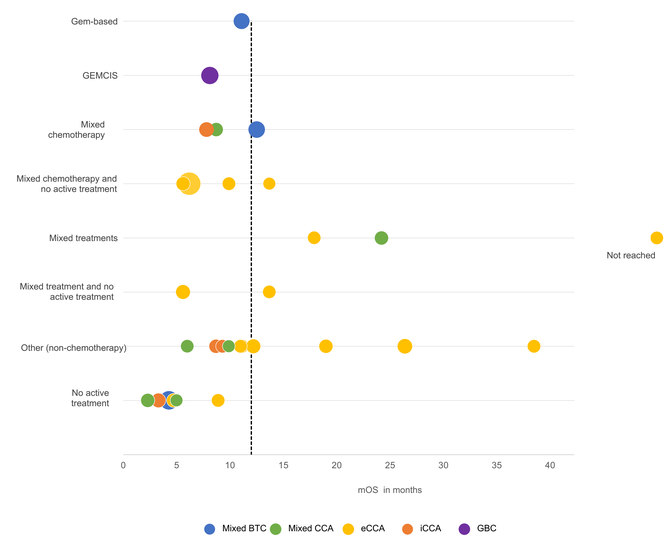


Figure 4. mOS for palliative treatments



Note: Marker sizes are proportional to the number of study participants in each study.