

Biliary tract cancers: addressing healthcare disparities and improving access to innovative treatments in Europe

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The incidence of biliary tract cancers (BTCs), particularly intrahepatic cholangiocarcinoma (iCCA), is increasing globally.¹ This trend is especially notable among younger individuals in Europe and imposes a significant socio-economic burden on society.^{1,2} Most patients with BTC are diagnosed at an advanced stage or have comorbidities, making them ineligible for curative-intent surgery and associated with shorter survival.³ However, recent advances in BTC treatments, such as combining immune checkpoint inhibitors (ICIs) with standard-of-care chemotherapy (i.e., cisplatin plus gemcitabine) and the use of molecularly-targeted drugs, along with the development of intra-arterial therapies for some liver-limited or -predominant iCCA cases, have led to improved outcomes while maintaining BTC patients' quality of life.^{4,5}

Despite these advances, significant gaps remain in equitable care delivery and access to novel therapies for BTC patients. In this issue of *The Lancet Regional Health – Europe*, Rimassa and colleagues^{6,7} offer an update on newly available treatment options and a comprehensive overview of the disparities in BTC care pathways across Europe.

The first article “Mapping the landscape of biliary tract cancer in Europe: challenges and controversies”⁶ emphasizes disparities in access to diagnostic tools, multidisciplinary care, and treatment options across Europe, particularly in socio-economically disadvantaged regions and Eastern European countries.⁸ These inequalities often result in delayed diagnosis and

treatment, considerably worsening patient outcomes. To address these challenges, the authors propose several key recommendations: (i) enhancing early diagnoses and reducing delays through increased awareness among healthcare professionals, particularly secondary care physicians, as well as health authorities and the public; (ii) promoting more coordinated multidisciplinary team (MDT) discussion across institutions and countries in Europe, and ensuring the case presentation and discussion of patients with BTC in molecular tumor boards (MTBs), which integrate expertise from both basic and medical scientists; (iii) leveraging the pivotal role of patient advocacy groups to advance these efforts. Of note, organizations such as the American Cholangiocarcinoma Foundation, AMMF–The Cholangiocarcinoma Charity in the UK, and in more recent years the Italian APIC, the Spanish ATUVIBI, the Thai CCA Foundation, and the Frenchs ACABi scientific and Espoir Voies Biliaires patient's association, along with Digestive Cancers Europe (DiCE, non-specific to BTC) at the European level, are making significant contributions to these efforts. However, it is noteworthy that many countries still lack dedicated advocacy groups for BTC. Furthermore, the article also stresses the urgent need to develop biomarkers and to enhance the potential of artificial intelligence (AI) in facilitating early diagnosis and personalized decision-making for BTC patients is an area of active investigation.

The second article “New systemic treatment paradigms in advanced biliary tract cancer and variations in patient access across Europe”⁷ discusses the significant progress in BTC treatment strategies over the past decade, including the increased access to ICIs and targeted therapies such as Fibroblast Growth Factor Receptor (FGFR) inhibitors (e.g., pemigatinib, futibatinib) and mutant Isocitrate Dehydrogenase 1 (IDH1) inhibitors (e.g., ivosidenib) for patients with *FGFR2* fusions or *IDH1* mutations, respectively. However,



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the implementation of these advanced therapies in routine clinical practice remains inconsistent across Europe, with disparities not only between countries but also within regions and centers within a given country—Spain, for example. The authors conducted an international survey of 47 European physicians, revealing that first-line standard-of-care chemo-immunotherapy (with cisplatin plus gemcitabine chemotherapy backbone) is broadly available, with over 80% of institutions providing access to ICIs such as durvalumab and/or pembrolizumab. Nonetheless, access to targeted therapies such as FGFR and mutant IDH1 inhibitors remains limited.

Furthermore, molecular testing by next-generation sequencing (NGS) is recommended for all patients who could benefit from targeted treatment (i.e., virtually all advanced BTC patients with ECOG PS ≤ 2 , with about 40% of them harbouring targetable alterations), as per the European Society for Medical Oncology (ESMO) Precision Medicine Working Group.⁹ However, access to NGS is still limited due to cost and logistic barriers. The misalignment between the approval of drugs by international regulatory bodies and the authorization and reimbursement of the associated biomarker tests at the national level further complicates its use.¹⁰ Ongoing European collaborative projects, such as the Precision-BTC-Network CA22125, supported by the European Cooperation in Science and Technology Action (COST), and the European Network for the Study of Cholangiocarcinoma (ENSCCA), aim to address these disparities and improve the current situation. Notably, clinical trials such as the ongoing SAFIR ABC-10 trial (NCT05615818) in UK, France, and Belgium, which compares targeted therapy as maintenance treatment after four cycles of standard-of-care chemo-immunotherapy versus the continuation of chemo-immunotherapy in patients with druggable alterations, will help to explore further the potential of the precision medicine in BTCs earlier in the treatment algorithm. Finally, the article also highlights challenges such as limited tissue availability for molecular analysis and socio-economic disparities in access to liquid biopsy and clinical trials, which remain significant barriers to improving treatment outcomes.

In conclusion, international collaboration is essential to harmonize care pathways, improve treatment access, and streamline approval processes. This is the driving philosophy behind collaborative initiatives, such as the COST Actions and the ENSCCA, which bring together multiple stakeholders to tackle these challenges. These significant issues must be addressed through a comprehensive, holistic approach while recognizing the need for tailored solutions that reflect each country's unique healthcare systems and circumstances.

Contributors

Anthony Turpin contributed with conceptualization, investigation, methodology, resources, visualization, project administration, writing

the original draft, reviewing and editing. Tian V Tian, Alice Boilève and Cindy Neuzillet contributed with investigation, validation, writing the original draft, reviewing and editing.

Declaration of interests

Anthony Turpin has received personal fees from Servier, Viatris, Incyte Bioscience, BMS, and Merck, as well as grants and personal fees from AstraZeneca and MSD outside the submitted work.

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