NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Zanidatamab for treating HER2-positive advanced biliary tract cancer after 1 or more systemic treatments [ID6388]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of zanidatamab within its marketing authorisation for treating HER2-positive advanced biliary tract cancer after 1 or more systemic treatments.

Background

The biliary tract consists of the organs and ducts that make, store and transport bile in the digestive system. Biliary tract cancer (BTC) includes bile duct cancer (cholangiocarcinoma), gallbladder cancer and ampullary cancer.[1] Cholangiocarcinoma can be further classified into three subtypes depending on which part of the bile duct the cancer originates – this may be inside the liver (intrahepatic) or outside the liver (extrahepatic). Intrahepatic cholangiocarcinoma (iCCA) starts in the bile ducts inside the liver. Peri-hilar and distal cholangiocarcinoma are both extrahepatic - peri-hilar cholangiocarcinoma starts just outside the liver (where the left and right hepatic ducts meet) and distal cholangiocarcinoma starts in the bile ducts near the bowel.[2]

In England in 2021, around 2,800 people were diagnosed with cholangiocarcinoma, 1,100 people were diagnosed with gallbladder cancer and 500 people were diagnosed with ampullary cancer.[3] In 2019, there were 2,754 deaths from cholangiocarcinoma in England.[4] Most people in England are diagnosed at stage 3 or 4. Diagnosis at later stages is associated with poorer survival outcomes.[5] Human epidermal growth factor receptor 2 (HER2) is a receptor for a growth factor which occurs naturally in the body. When human epidermal growth factor attaches itself to HER2 receptors on cancer cells it can stimulate the cells to divide and grow. High levels of HER2 expression are found in 4-16% of biliary tract cancers[6] – these are known as HER2-positive cancers.

Surgery remains the curative intent treatment option leading to long-term survival for people diagnosed with resectable BTC. Most people with BTCs are diagnosed with unresectable locally advanced or metastatic disease. Chemotherapy is typically used in the first-line treatment of BTC that cannot be surgically removed. People with unresectable or advanced BTC are typically offered chemotherapy with a combination of cisplatin and gemcitabine. For some BTCs, oxaliplatin might be offered instead of cisplatin, especially if there are any concerns over kidney function. Frailer people might be offered single-agent chemotherapy with gemcitabine, fluorouracil (5-FU) or capecitabine alone.[7] Recently, NICE has recommended durvalumab with gemcitabine and cisplatin (see NICE technology appraisal guidance 944) as an option for treating locally advanced, unresectable, or metastatic biliary tract cancer in adults, which may be preferred for people who are suitable for this treatment.

For disease that has progressed following first-line treatment, people may be offered further chemotherapy with folinic acid, fluorouracil and oxaliplatin (FOLFOX). Radiotherapy in addition to chemotherapy may also be offered to some people to relieve symptoms. NICE technology appraisal guidance 722 and NICE technology appraisal guidance 1005 recommend pemegatinib and futibatinib respectively for treating advanced cholangiocarcinoma with FGFR2 fusion or rearrangement after systemic therapy in adults. NICE technology appraisal guidance 944 recommends ivosidenib for treating locally advanced or metastatic cholangiocarcinoma with an IDH1 R132 mutation in adults after 1 or more systemic treatments. There are no treatments currently recommended by NICE specifically for HER2-positive biliary tract cancer after 1 or more systemic treatments.

The technology

Zanidatamab (brand name unknown) does not currently have a marketing authorisation in the UK for treating HER2-positive advanced biliary tract cancer after 1 or more systemic treatments. It has been studied in a single arm clinical trial in HER2-positive locally advanced or metastatic biliary tract cancer in adults that had received at least one prior gemcitabine-containing systemic chemotherapy.

Intervention(s)	Zanidatamab
Population(s)	Adults with unresectable HER2-positive advanced biliary tract cancer previously treated with at least one prior line of systemic therapy.'
Subgroups	If evidence allows, results by type of biliary tract cancer
Comparators	Established clinical management without zanidatamab, which may include: • Folinic acid, fluorouracil and oxaliplatin (FOLFOX) • Best supportive care (including active symptom control)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates (including overall response rates) • time to treatment discontinuation • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The use of zanidatamab is conditional on being HER2-positive. The economic modelling should include the costs associated with diagnostic testing for HER2-positive status in people with advanced biliary tract cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals:** Futibatinib for previously treated advanced cholangiocarcinoma with FGFR2 fusion or rearrangement (2024). NICE technology appraisal guidance 1005. Ivosidenib for treating advanced cholangiocarcinoma with an IDH1 R132 mutation after 1 or more systemic treatments (2024). NICE technology appraisal guidance 948. Durvalumab with gemcitabine and cisplatin for treating unresectable or advanced biliary tract cancer (2024). NICE technology appraisal guidance 944. Pemigatinib for treating relapsed or refractory advanced cholangiocarcinoma with FGFR2 fusion or rearrangement (2021). NICE technology appraisal guidance 722. **Related interventional procedures:** Melphalan chemosaturation with percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic

	cancer in the liver (2021) NICE interventional procedures guidance 691. Irreversible electroporation for primary liver cancer (2019) NICE interventional procedures guidance 664. Selective internal radiation therapy for unresectable primary intrahepatic cholangiocarcinoma (2018) NICE interventional procedures guidance 630. Endoscopic bipolar radiofrequency ablation for treating biliary obstruction caused by cancer (2018) NICE interventional procedures guidance 614. Cryotherapy for the treatment of liver metastases (2010) NICE interventional procedures guidance 369 Photodynamic therapy for bile duct cancer (2005) NICE interventional procedures guidance 134. Endoscopic bipolar radiofrequency ablation for treating biliary obstruction caused by cholangiocarcinoma or pancreatic adenocarcinoma NICE interventional procedures guidance. Publication date to be confirmed.

References

1. AMMF (2023). What is cholangiocarcinoma? Accessed April 2025.

2. Cancer Research UK (2024). What is bile duct cancer? Accessed April 2025.

3. NHS Digital (2023) Cancer registration statistics, 2021. Accessed April 2025.

4. AMMF (2023) Introduction to Cholangiocarcinoma. Accessed April 2025.

5. Jose S, Zalin-Miller A, Knott C, et al (2023) Cohort study to assess geographical variation in cholangiocarcinoma treatment in England. World Journal of Gastrointestinal Oncology. 15(12):2077.

6. ESMO. Biliary tract cancer: a guide for patients. April February 2025.

7. BMJ Best Practice. Cholangiocarcinoma. April February 2025.