Appendix B

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

Draft scope

Draft 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. Intrahepatic cholangiocarcinoma (iCCA) starts in the bile ducts inside the liver, 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] Currently, there are no UK wide statistics available for bile duct cancer and gallbladder cancer survival by stage. 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.[5] NICE technology appraisal guidance 944 recommends durvalumab for gemcitabine and cisplatin as an option for treating locally advanced, unresectable, or metastatic biliary tract cancer in adults.

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 has recommended pemegatinib (TA722) and futibatinib (TA1005) for treating advanced cholangiocarcinoma with FGFR2 fusion or

rearrangement after systemic therapy in adults. NICE has also recommended ivosidenib (TA948) 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 previously treated HER2-positive advanced biliary tract cancer
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
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.

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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 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.

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	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.

Questions for consultation

Where do you consider zanidatamab will fit into the existing care pathway for HER2-positive advanced biliary tract cancer?

Have all relevant subgroups been included?

Have all relevant comparators been included?

Would futibatinib and ivosidenib be considered relevant comparators? Is it possible that people with FGFR fusion or rearrangement or people with a IDH1 R132 mutation would also be HER2 positive?

Please select from the following, will zanidatamab be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would zanidatamab be a candidate for managed access?

Do you consider that the use of zanidatamab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which zanidatamab will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

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- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

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

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

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

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

5. ESMO. Biliary tract cancer: a guide for patients. Accessed February 2025.

6. BMJ Best Practice. Cholangiocarcinoma. Accessed February 2025.

7. Ostwal V, Mandavkar S, Bhargava P et al (2024) Trastuzumab plus gemcitabine-cisplatin for treatment-naïve human epidermal growth factor receptor 2–positive biliary tract adenocarcinoma: A multicenter, open-label, phase II study (TAB). Journal of Clinical Oncology. 1;42(7):800-7.