NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Durvalumab with gemcitabine and cisplatin for untreated unresectable or advanced biliary tract cancer ID4031

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of durvalumab with gemcitabine and cisplatin within its marketing authorisation for treating untreated unresectable or advanced biliary tract cancer.

Background

The biliary tract includes the organs and ducts that make and store bile. The liver and gallbladder are connected to the small bowel by a network of small tubes called ducts which carry bile.[1,2] Biliary tract cancer (BTC) includes bile duct cancer, gallbladder cancer and ampullary cancer. Cancer of the bile ducts is called cholangiocarcinoma and is classified depending on which part of the bile duct the cancer originates. The main types of cholangiocarcinoma include intrahepatic (affects bile ducts inside the liver), hilar or perihilar (affects bile ducts just outside the liver) and distal extrahepatic (affects the common bile duct outside the liver).[3,4]

The incidence rate of cholangiocarcinomas in England was 3.58 per 100,000 in 2013.[5] The mortality rate of cholangiocarcinomas reported in 2013 was 3.64 per 100,000 population in England.[5] Currently, there are no UK wide statistics available for bile duct cancer and gallbladder cancer survival by stage.

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.[6,7] People with unresectable tumours are offered palliative treatment. The treatments vary depending on Eastern Cooperative Oncology Group (ECOG) performance status (PS), molecular profiling and disease distribution.[8]

Chemotherapy is typically used in the first-line treatment of BTC that cannot be surgically removed.[4] People with unresectable BTC are typically offered chemotherapy with a combination of cisplatin and gemcitabine.[4] For some BTCs, oxaliplatin might be offered instead of cisplatin, especially if there are any concerns over kidney function.[9] Frailer people might be offered single-agent chemotherapy with gemcitabine, fluorouracil (5-FU) or capecitabine alone.[4] For disease that has progressed following first-line treatment, further chemotherapy is recommended. Radiotherapy in addition to chemotherapy may also be offered to some people to relieve symptoms.[7]

The technology

Durvalumab (Imfinzi, AstraZeneca) with gemcitabine and cisplatin does not currently have a marketing authorisation in the UK for untreated advanced biliary tract cancer. It has been studied in a clinical trial compared with placebo in adults with unresectable advanced or metastatic biliary tract cancers.

Intervention	Durvalumab with gemcitabine and cisplatin
Population	Adults with untreated, unresectable advanced or metastatic biliary tract cancer
Subgroups	If evidence allows, results by type of biliary tract cancer and level of PD-L1 expression will be considered

Comparators	Established clinical management without durvalumab including:
	• Gemcitabine with cisplatin
	• For people with poor kidney function:
	  ○ Gemcitabine with oxaliplatin
	• For frailer people:
	  ○ Gemcitabine alone
	  ○ Fluorouracil (5-FU) alone
	  ○ Capecitabine alone

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 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:** Pemigatinib for treating relapsed or refractory advanced cholangiocarcinoma with FGFR2 fusion or rearrangement (2021). NICE technology appraisal guidance 722. **Related appraisals in development:** Pembrolizumab with gemcitabine and cisplatin for untreated advanced biliary tract cancer NICE technology appraisal guidance [ID4034]. Publication date to be confirmed. Infigratinib for treating relapsed or refractory advanced cholangiocarcinoma with FGFR2 fusion or rearrangement NICE technology appraisal guidance [ID3992]. Publication date to be confirmed. **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. Chemosaturation via percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic liver cancer (2014) NICE interventional procedures guidance 488. 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
Related National Policy	NHS England (2020) The use of Stereotactic Ablative Radiotherapy (SABR) as a treatment option for patients with Hepatocellular carcinoma or Cholangiocarcinoma Clinical Commissioning Policy. The NHS Long Term Plan, 2019 NHS Long Term Plan NHS England (2019) Selective internal radiation therapy (SIRT) for the treatment of chemotherapy refractory or intolerant, unresectable primary Intrahepatic cholangiocarcinoma (all ages) Clinical Commissioning Policy. Reference 170112P NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105. Specialist cancer services (adults) Department of Health and Social Care (2016) NHS outcomes framework 2016 to 2017: Domain 1 NHS England (2016) Clinical Commissioning Policy: The use of Stereotactic Ablative Radiotherapy (SABR) as a treatment option for patients with Hepatocellular carcinoma or Cholangiocarcinoma (16022/P). NHS England (2013) Hepatobiliary and Pancreas (Adult) NHS Standard Contract. Reference A02/S/a.

Questions for consultation

What treatments are established clinical practice in the NHS for people with untreated advanced biliary tract cancer?

Where do you consider durvalumab with gemcitabine and cisplatin will fit into the existing care pathway for untreated advanced biliary tract cancer?

How relevant are the subgroups ‘type of biliary tract cancer’ and ‘level of PD-L1 expression’ in the scope? Are there any other subgroups of people in whom durvalumab with gemcitabine and cisplatin is expected to be more clinically effective and cost effective or other groups that should be examined separately?

How will people eligible for durvalumab be identified?

- Will implementation of additional testing be required to facilitate the use of this technology in NHS clinical practice?

Would durvalumab with gemcitabine and cisplatin be a candidate for managed access?

Do you consider that the use of durvalumab with gemcitabine and cisplatin 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 durvalumab with gemcitabine and cisplatin 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;

- 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. We welcome comments on the appropriateness of appraising this topic through this 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. National Health Services (NHS). What is bile duct cancer? - Bile duct cancer (cholangiocarcinoma). Accessed 6 October 2022.

2.Macmillan Cancer Support. Bile duct cancer (cholangiocarcinoma). Accessed 6 October 2022.

3. Cancer Research UK. What is bile duct cancer? Accessed 6 October 2022.

4. ESMO. Biliary tract cancer: a guide for patients. Accessed 6 October 2022.

5. Public Health England. National Cancer Intelligence Network Rare and less common cancers - Incidence and Mortality in England, 2010 to 2013. 2015. Accessed 6 October 2022.

6. Valle, Juan W., et al. "Biliary tract cancer." The Lancet 397.10272 (2021): 428-444.

7. BMJ Best Practice (Cholangiocarcinoma). Accessed 6 October 2022.

8. Lamarca, A., J. Edeline, and L. Goyal. "How I treat biliary tract cancer." ESMO open 7.1 (2022): 100378.

9. Valle, Juan W., et al. "Biliary cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up." Annals of Oncology 27 (2016): v28-v37.