NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Durvalumab with tremelimumab for untreated advanced or unresectable hepatocellular carcinoma ID2725

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of durvalumab with tremelimumab within its marketing authorisation for untreated advanced or unresectable hepatocellular carcinoma in adults.

Background

Hepatocellular carcinoma (HCC) is the most common form of liver cancer in England, accounting for 65% of primary liver cancer diagnoses in men and 34% of diagnoses in women in 2021.[1] It is commonly associated with liver cirrhosis (scarring of the liver), which can be caused by viral infections such as hepatitis B or C, excessive alcohol intake, or other diseases that result in chronic inflammation of the liver.[1] There were a total of 3,021 new diagnoses of HCC in England in 2021. Of these, 2,362 were in men and 659 in women.[1]

The most common staging systems are the Barcelona Clinic Liver Cancer (BCLC) system and the Child–Pugh assessment of liver impairment. Other systems are the Eastern Cooperative Oncology Group [ECOG] score for tumour characteristics and performance status and the albumin-bilirubin (ALBI) grade system for assessing liver function. The stage at which HCC is detected has a significant impact on survival; people with advanced HCC have a poorer prognosis than people with early stage HCC.

Treatment for HCC depends on the location and stage of the cancer, and how well the liver function is preserved. For people with more advanced disease, treatment is palliative rather than curative. Treatment options include interventional procedures such as transarterial chemoembolisation (using doxorubicin or cisplatin) or selective internal radiation therapy (SIRT), and external beam radiotherapy. For unresectable advanced HCC only in adults with Child-Pugh grade A liver impairment and when conventional transarterial therapies are inappropriate, NICE technology appraisal guidance 688 recommends SIR-Spheres and TheraSphere.

For people whose condition does not respond to these therapies or who have metastatic disease, first-line systemic treatment options include:

- sorafenib as an option for treating advanced HCC only for people with Child-Pugh grade A liver impairment (NICE technology appraisal guidance 474)
- lenvatinib as an option for untreated, advanced, unresectable HCC in adults with Child-Pugh grade A liver impairment and an ECOG performance status of 0 or 1 (NICE technology appraisal guidance 551)
- atezolizumab plus bevacizumab as an option for treating advanced or unresectable HCC in adults who have not had previous systemic treatment

and only if they have Child-Pugh grade A liver impairment and an ECOG performance status of 0 or 1 NICE technology appraisal guidance 666).

Best supportive care is offered to people who choose not to have or cannot have systemic therapy or if their disease does not respond to systemic therapy.

The technology

Durvalumab (Imfinzi, AstraZeneca) in combination with tremelimumab is indicated for the first line treatment of adults with advanced or unresectable hepatocellular carcinoma.

Intervention(s)	Durvalumab plus tremelimumab
Population(s)	People with advanced or unresectable hepatocellular carcinoma
Comparators	• Atezolizumab with bevacizumab • Lenvatinib • Sorafenib • Selective internal radiation therapies (SIRT) including SIR-Spheres and TheraSphere • QuerumSphere (subject to ongoing NICE appraisal) • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • time-to-progression • response rates • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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:** Selective internal radiation therapies for treating hepatocellular carcinoma (2021) NICE technology appraisal guidance 688. Atezolizumab with bevacizumab for treating advanced or unresectable hepatocellular carcinoma (2020) NICE technology appraisal guidance 666. Lenvatinib for untreated advanced hepatocellular carcinoma (2018) NICE technology appraisal guidance 551. Sorafenib for treating advanced hepatocellular carcinoma (2017) NICE technology appraisal guidance 474. **Related technology appraisals in development:** Selective internal radiation therapy with QuiremSpheres for treating unresectable advanced hepatocellular carcinoma (Partial review of TA688) NICE technology appraisal guidance [ID6376] Publication expected June 2024. **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 treating primary liver cancer (2019) NICE interventional procedures guidance 664. Selective internal radiation therapy for primary hepatocellular carcinoma (2013) NICE interventional procedures guidance 460. Microwave ablation of hepatocellular carcinoma (2007) NICE interventional procedures guidance 214. Radiofrequency ablation of hepatocellular carcinoma (2003) NICE interventional procedures guidance 2.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan. NHS England (2023) Manual for prescribed specialist services (2023/2024) Chapter 105: Specialist cancer services (adults); Chapter 131: Specialist services for complex liver, biliary and pancreatic diseases in adults. NHS England. 2013/14 NHS Standard Contract for Hepatobiliary and pancreas (adult) A02/S/a. NHS England. 2013/14 NHS Standard Contract for cancer: chemotherapy (adults). Department of Health and Social Care (2016) NHS outcomes framework 2016 to 2017. NHS Digital (2022) NHS Outcomes Framework England, March 2022 Annual Publication.

Questions for consultation

Are selective internal radiation therapies and best supportive care relevant comparators? If relevant, how should best supportive care be defined?

Where do you consider durvalumab with tremelimumab will fit into the existing care pathway for advanced or unresectable hepatocellular carcinoma?

Would durvalumab with tremelimumab be a candidate for managed access?

Do you consider that the use of durvalumab with tremelimumab 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 tremelimumab are 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. (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. NHS Digital (2023) Cancer Registrations Statistics, England 2021- First release, counts only. Accessed April 2024.