

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Durvalumab with tremelimumab for untreated advanced or unresectable hepatocellular carcinoma [ID2725]

Final scope

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 system is the Barcelona Clinic Liver Cancer (BCLC) system. The Child–Pugh assessment of liver impairment and Eastern Cooperative Oncology Group [ECOG] performance score are used to assign BCLC stage. 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.²

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 bland embolisation, transarterial chemoembolisation (using doxorubicin or cisplatin) or selective internal radiation therapy (SIRT), and external beam radiotherapy.² 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.

Systemic therapy can be given if the condition is refractory to locoregional therapy or when these therapies are not suitable because of the extent of cancer within the liver or metastatic disease. NICE recommends the following first-line systemic treatment options:

- sorafenib for treating advanced HCC only for people with Child-Pugh grade A liver impairment ([NICE technology appraisal guidance 474](#))
- lenvatinib 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 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 has a marketing authorisation 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	<ul style="list-style-type: none"> • Atezolizumab with bevacizumab • Lenvatinib • Sorafenib • Selective internal radiation therapies (SIRT) including SIR-Spheres and TheraSphere • QuirumSpheres (subject to ongoing NICE appraisal) • Best supportive care
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • time-to-progression • response rates • adverse effects of treatment • health-related quality of life.

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p>
<p>Other considerations</p>	<p>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.</p>
<p>Related NICE recommendations</p>	<p>Related technology appraisals:</p> <p>Selective internal radiation therapies for treating hepatocellular carcinoma (2021) NICE technology appraisal guidance 688.</p> <p>Atezolizumab with bevacizumab for treating advanced or unresectable hepatocellular carcinoma (2020) NICE technology appraisal guidance 666.</p> <p>Lenvatinib for untreated advanced hepatocellular carcinoma (2018) NICE technology appraisal guidance 551.</p> <p>Sorafenib for treating advanced hepatocellular carcinoma (2017) NICE technology appraisal guidance 474.</p> <p>Related technology appraisals in development:</p> <p>Selective internal radiation therapy with QuiremSpheres for treating unresectable advanced hepatocellular carcinoma (Partial review of TA688) NICE technology appraisal guidance [ID6376] Publication expected July 2024.</p> <p>Related interventional procedures:</p> <p>Melphalan chemosaturation with percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic</p>

	<p>cancer in the liver (2021) NICE interventional procedures guidance 691.</p> <p>Irreversible electroporation for treating primary liver cancer (2019) NICE interventional procedures guidance 664.</p> <p>Selective internal radiation therapy for primary hepatocellular carcinoma (2013) NICE interventional procedures guidance 460.</p> <p>Microwave ablation of hepatocellular carcinoma (2007) NICE interventional procedures guidance 214.</p> <p>Radiofrequency ablation of hepatocellular carcinoma (2003) NICE interventional procedures guidance 2.</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan (2019) NHS Long Term Plan.</p> <p>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.</p> <p>NHS England. 2013/14 NHS Standard Contract for Hepatobiliary and pancreas (adult) A02/S/a.</p> <p>NHS England. 2013/14 NHS Standard Contract for cancer: chemotherapy (adults).</p> <p>Department of Health and Social Care (2016) NHS outcomes framework 2016 to 2017.</p> <p>NHS Digital (2022) NHS Outcomes Framework England, March 2022 Annual Publication.</p>

References

1. NHS Digital (2023) [Cancer Registrations Statistics, England 2021- First release, counts only](#). Accessed June 2024.
2. Suddle A, Reeves H, Hubner R et al. (2024) [British Society of Gastroenterology guidelines for the management of hepatocellular carcinoma in adults](#). Gut published online first doi: 10.1136/gutjnl-2023-331695. Accessed June 2024.