NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Nivolumab with ipilimumab for untreated advanced or unresectable hepatocellular carcinoma

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of nivolumab with ipilimumab within its marketing authorisation for advanced or unresectable hepatocellular carcinoma that has not been treated with systemic therapy.

Background

Hepatocellular carcinoma (HCC) develops from the main liver cells, known as hepatocytes. It is more common in people with liver cirrhosis. Cirrhosis is scarring of the liver, which can be caused by hepatitis B or C, or long-term alcohol use. It is also more common in people with non-alcoholic fatty liver disease (also known as metabolic dysfunction-associated steatotic liver disease).

HCC is the most common type of primary liver cancer, accounting for around 85% of cases.[1] In England around 3,000 people are diagnosed each year in England.[2] HCC affects around 4 times as many men than women.[2] The average age at diagnosis in the UK is 66.[3]

HCC can be classified using the Child–Pugh scoring system, which grades liver damage from grade A, the least severe, to grade C, the most severe. The Barcelona Clinic Liver Cancer (BCLC) system combines tumour characteristics with the Child-Pugh score and performance status (measured on the Eastern Cooperative Oncology Group [ECOG] scale) to classify patients into 5 stages (0, A, B, C and D), which can be used to determine prognosis and define treatment options.

Treatment for HCC depends on the location, stage of the cancer and how well the liver is working. People diagnosed with advanced HCC have a poorer prognosis than people with early-stage disease. For people with intermediate stage disease, treatment options include interventional procedures such as transarterial bland embolisation, transarterial chemoembolisation (using doxorubicin or cisplatin) and selective internal radiation therapy (SIRT). 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 or 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 in the liver or metastatic disease. NICE recommends the following first-line systemic treatment options:

- durvalumab with tremelimumab (NICE technology appraisal guidance 1090)
- atezolizumab with bevacizumab when people have Child–Pugh grade A liver impairment and an ECOG performance status of 0 or 1 (NICE technology appraisal guidance 666)

- lenvatinib when people have Child–Pugh grade A liver impairment and an ECOG performance status of 0 or 1 (NICE technology appraisal guidance 551)
- sorafenib for people with Child-Pugh grade A liver impairment (NICE technology appraisal guidance 474).

If standard therapies are unsuccessful, people with HCC are offered best supportive care.

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb Pharmaceuticals) with ipilimumab (Yervoy, Bristol-Myers Squibb Pharmaceuticals) has a marketing authorisation for the first-line treatment of unresectable or advanced hepatocellular carcinoma.

Intervention(s)	Nivolumab with ipilimumab
Population(s)	Adults with advanced or unresectable hepatocellular carcinoma that has not been treated with systemic therapy
Comparators	• Durvalumab with tremelimumab • Atezolizumab with bevacizumab • Lenvatinib • Sorafenib
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.

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:** Durvalumab with tremelimumab for untreated advanced or unresectable hepatocellular carcinoma NICE technology appraisal guidance (2025) NICE technology appraisal guidance 1090 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 interventional procedures:** Image-guided percutaneous laser ablation for primary and secondary liver tumours (2024) Interventional procedures guidance 788 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 quality standards:** Liver disease (2017) NICE quality standard 152

References

1. NHS England (2024) Hepatocellular carcinoma surveillance: minimum standards [accessed October 2025]

2. Liver Cancer UK Statistics about liver cancer [accessed October 2025]

3. Patient (2023) Primary liver cancer [accessed October 2025]