NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Atezolizumab with bevacizumab for adjuvant treatment of resected or ablated hepatocellular carcinoma at high risk of recurrence

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of atezolizumab plus bevacizumab within its marketing authorisation for adjuvant treatment of resected or ablated hepatocellular carcinoma (HCC) at high risk of recurrence.

Background

In the UK, around 3,600 people are diagnosed with HCC each year. It is the third most common cancer worldwide, but rare in the UK. Around 4 times as many men get it as women.[1] HCC develops from the main liver cells, called hepatocytes, and is usually related to liver cirrhosis (scarring of the liver), which can develop after long periods of chronic liver disease. The average age at diagnosis is 66 years.[2]

Treatment depends on the location and stage of the cancer, and how well the liver function is preserved. Treatment options include surgery, ablation, systemic chemotherapy, transarterial chemoembolisation and selective internal radiation therapy. Some people may be able to have a liver transplant.[2]

Although resection and ablation can cure hepatocellular cancer, rates of recurrence are high. There is no established adjuvant treatment option in the NHS for HCC after resection or ablation.[3] The risk of recurrence is related to the size of the resected tumour, the number of tumours, whether there was vascular invasion, a higher alpha fetoprotein (AFP) level, the cause of the disease, and cirrhotic background (tissue changes that can lead to cancer).[3]

The technology

Atezolizumab (Tecentriq), bevacizumab (Avastin).

Atezolizumab with bevacizumab does not currently have a marketing authorisation in the UK for adjuvant treatment of HCC at high risk of recurrence after complete surgical resection or ablation. The combination has been studied in a clinical trial compared with active surveillance as adjuvant treatment of HCC at high risk of recurrence after surgical resection or ablation.

Atezolizumab with bevacizumab does have a marketing authorisation in the UK for treating advanced or unresectable HCC that has not had previous systemic treatment.

Intervention(s)	Atezolizumab with bevacizumab
Population(s)	People who have HCC at high risk of recurrence after complete surgical resection or ablation

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Comparators	Established clinical management without atezolizumab with bevacizumab
Outcomes	The outcome measures to be considered include: • recurrence-free survival • overall survival • time to recurrence • time to extrahepatic spread or macrovascular invasion • time to stopping treatment • 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 in development:** Pembrolizumab for adjuvant treatment of hepatocellular carcinoma [ID3994] Publication date to be confirmed Durvalumab for adjuvant treatment of hepatocellular carcinoma at high risk of recurrence after curative liver resection or ablation TS ID 11797 Publication date to be confirmed **Related interventional procedures:** Microwave ablation for treating liver metastases (2016) NICE interventional procedures guidance 553

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	Irreversible electroporation for treating liver metastases (2013) NICE interventional procedures guidance 445 Cryotherapy for the treatment of liver metastases (2010) NICE interventional procedures guidance 369 Radiofrequency ablation for colorectal liver metastases (2009) NICE interventional procedures guidance 327 Ex-vivo hepatic resection and reimplantation for liver cancer (2009) NICE interventional procedures guidance 298 Microwave ablation of hepatocellular carcinoma (2007) NICE interventional procedures guidance 214 Radiofrequency-assisted liver resection (2007) NICE interventional procedures guidance 211 Laparoscopic liver resection (2005) NICE interventional procedures guidance 135 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) NHS manual for prescribed specialist services (updated March 2023) chapter 105 Specialist cancer services (adults) and chapter 131 Specialist services for complex liver, biliary and pancreatic diseases in adults

Questions for consultation

Are there any subgroups of people in whom atezolizumab with bevacizumab is expected to be more clinically effective and cost effective? Are there other groups that should be examined separately?

Are any treatments considered to be established clinical practice in the NHS for adjuvant treatment of resected or ablated HCC at high risk of recurrence?

How is a high risk of recurrence assessed in people who have had resection or ablation treatment for their HCC? Is AFP level routinely tested in HCC? Would any other diagnostic tests not routinely used in HCC be needed to test risk of recurrence?

Where do you consider atezolizumab with bevacizumab will fit into the existing care pathway for resected or ablated HCC at high risk of recurrence?

Would atezolizumab with bevacizumab be a candidate for managed access?

Do you consider that the use of atezolizumab with bevacizumab can result in any potential substantial health-related benefits that are unlikely to be included in the quality-adjusted life year (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

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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 atezolizumab with bevacizumab 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. (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. Liver Cancer UK (2022) HCC liver cancer. Accessed November 2023
2. Patient (2023) Primary liver cancer. Accessed November 2023
3. Hack SP, Spahn J, Chen M et al. (2020) IMbrave 050: a phase III trial of atezolizumab plus bevacizumab in high-risk hepatocellular carcinoma after curative resection or ablation. Future Oncology 16(15):975–89

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