NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Atezolizumab with bevacizumab for untreated hepatocellular carcinoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of atezolizumab with bevacizumab within its marketing authorisation for untreated hepatocellular carcinoma.

Background

Hepatocellular carcinoma (HCC) is the most common form of liver cancer developing from the main liver cells, called hepatocytes. HCC accounts for up to 55% of primary liver cancer diagnoses in men and up to 28% of diagnoses in women in England.[1] Most people with HCC will have liver cirrhosis (scarring of the liver), which can develop following long periods of chronic liver disease. In 2017 there were a total of 4,975 registrations of newly diagnosed malignant neoplasm of liver and intrahepatic bile ducts. Based on the percentages of HCC diagnoses above, this is equal to 2,736 newly diagnosed cases of HCC in men and up to 1,393 in women in England.[2] The average age at diagnosis is 66 years.[3]

Treatment 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 trans arterial chemoembolisation (using doxorubicin or cisplatin) or selective internal radiation therapy, and external beam radiotherapy. People who do not respond to these therapies or have metastatic disease, are treated with sorafenib or lenvatinib in the first line setting. NICE technology appraisal guidance 474 recommends sorafenib as an option for treating advanced HCC only for people with Child-Pugh grade A liver impairment. NICE technology appraisal guidance 551 recommends lenvatinib as an option for untreated, advanced, unresectable HCC only for people with Child-Pugh grade A liver impairment and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. Some people may choose not to have systemic therapy, may not respond or may be intolerant to this therapy. These people with HCC are treated with best supportive care.

The technologies

Atezolizumab (Tecentriq; Roche) is a humanised, anti-programmed cell death ligand-1 (PD-L1) monoclonal antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. Atezolizumab, increases the ability of the immune system to attack the cancer cells and slows down disease progression and is administered by intravenous infusion.

Bevacizumab (Avastin, Roche) is a humanised immunoglobin (IgG10) monoclonal antibody that binds to vascular endothelial growth factor (VEGF) preventing tumour growth. Bevacizumab decreases tumour growth by stopping the development of tumour blood vessels and is administered via intravenous infusion.

Atezolizumab with bevacizumab does not currently have a marketing authorisation in the UK for treating hepatocellular carcinoma. It is being studied in a randomised open-label trial compared with sorafenib in adults with locally advanced or metastatic and/or unresectable hepatocellular carcinoma who have not had prior systemic therapy.

Intervention(s)	Atezolizumab with bevacizumab
Population(s)	Adults with locally advanced or metastatic and/or unresectable hepatocellular carcinoma who have had no previous systemic treatment
Comparators	• Sorafenib • Lenvatinib • Best supportive care (BSC)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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 or subsequent technologies will be taken into account.

Other considerations	If the evidence allows, the following subgroups will be considered. These include people who choose not to have systemic therapy with sorafenib or lenvatinib, may not respond or may be intolerant to these therapies. 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 and NICE Pathways	**Related Technology Appraisals:** Lenvatinib for untreated advanced hepatocellular carcinoma (2018) NICE Technology appraisal guidance 551. Sorafenib for treating advanced hepatocellular carcinoma (2017) NICE Technology appraisal guidance 474. **Appraisals in development (including suspended appraisals):** Nivolumab for untreated advanced hepatocellular carcinoma NICE technology appraisal guidance [ID1248]. Publication date to be confirmed Selective internal radiation therapies for treating hepatocellular carcinoma NICE technology appraisal guidance [ID1276]. Publication date to be confirmed **Related Interventional Procedures:** Irreversible electroporation for treating primary liver cancer (2013) NICE interventional procedures guidance 444. Microwave ablation of hepatocellular carcinoma (2007) NICE interventional procedures guidance 214. Laparoscopic liver resection (2005) NICE interventional procedures guidance135. Radiofrequency-assisted liver resection (2007) NICE interventional procedures guidance 211. Radiofrequency ablation of Hepatocellular carcinoma (2003) NICE interventional procedures guidance 2. Ex-vivo hepatic resection and reimplantation for liver cancer (2009) NICE interventional procedures guidance 298. Selective internal radiation therapy for primary hepatocellular carcinoma (2013) NICE interventional procedures guidance 460.

	Chemosaturation via percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic liver cancer (2014) NICE interventional procedures guidance 488. **Related NICE Pathways:** Liver cancers (2020) NICE pathway
Related National Policy	**NHS England:** The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) chapter 131 (page 357): Specialist services for complex liver, biliary and pancreatic diseases in adults. NHS England (2016) The use of stereotactic ablative radiotherapy (SABR) as a treatment option for patients with hepatocellular carcinoma or cholangiocarcinoma. Clinical commissioning policy. Reference: NHS England: 16022/P **Department of Health and Social Care:** Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy

References

1 National Cancer Registration and Analysis Service (2010) Trends in incidences in primary liver cancer subtypes. Accessed August 2019

2 Office for National Statistics ((2017) Cancer Registration Statistics, England Accessed August 2019

3 Patient (2015) Hepatocellular carcinoma. Accessed August 2019