NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Sorafenib for advanced hepatocellular carcinoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of sorafenib, within its licensed indication, for the first line systemic treatment of advanced hepatocellular carcinoma.

Background

Hepatocellular carcinoma is the most common type of primary liver cancer. Hepatocellular carcinomas usually occur in the context of cirrhosis (scarring of the liver), which can be caused by viral hepatitis, primarily hepatitis B and C, alcohol abuse, hemochromatosis, certain autoimmune diseases of the liver, and other diseases that result in chronic inflammation of the liver. However, 25% of patients with hepatocellular carcinoma have no history or risk factors for cirrhosis. The risk of developing hepatocellular carcinoma is higher in men than in women and the average age of diagnosis in the United Kingdom is 66 years.

More than 2,000 new cases of hepatocellular carcinoma are diagnosed in England and Wales per year. However, it is thought that the incidence will increase in the next few years mainly as a result of the increasing prevalence of hepatitis B and C virus infections.

The stage of hepatocellular carcinoma is usually reported using the tumour, metastasis and node (TMN) classification. This is based on the extent of the primary tumour (T), whether lymph nodes are affected (N) and whether metastases are present (M). A Child-Pugh score can also be assigned to hepatocellular carcinoma which can be used to predict the prognosis and strength of required treatment. The score uses five clinical measures of liver disease, and classifies liver disease into Child-Pugh A, B and C class; people with Child-Pugh class A have the best prognosis.

Untreated hepatocellular carcinoma has a median survival of 4 to 6 months from the time of diagnosis. The extent of hepatic dysfunction limits treatment options. The only potentially curative treatment for hepatocellular carcinoma is surgery, which implies hepatic resection or liver transplantation, but only a small proportion of patients will be eligible for either of these treatments. In such cases, clinical management may include percutaneous ablation, radiofrequency ablation, chemoembolisation, and systemic therapy with drugs such as doxorubicin, cisplatin and fluorouracil, tamoxifen, interferon or other biological agents.

The technology

Sorafenib (Nexavar, Bayer) is a multikinase inhibitor that inhibits the development of tumour blood vessels and tumour cell proliferation. It has dual action, inhibiting the raf cascade, and the human vascular endothelial growth factor/platelet derived growth factor receptors on tumour cells, vascular endothelial cells and pericytes.

Sorafenib has a marketing authorisation for the treatment of hepatocellular carcinoma. The registration trial for sorafenib included people with advanced hepatocellular carcinoma with no previous systemic therapy whose tumour was unsuitable for or have progressed after surgical or locoregional therapies. Participants in the registration trial also had to meet the following criteria: a life expectancy of at least 12 weeks; an ECOG performance status of 0, 1, or 2; histologically or cytologically documented hepatocellular carcinoma; at least one measurable tumour that was not previously treated with local therapy; and Child Pugh A liver function status.

Intervention(s)	Sorafenib
Population(s)	Adults with advanced hepatocellular carcinoma whose disease is unsuitable for local or loco-regional curative therapy or has progressed after those types of therapy
Standard comparators	Standard care which may include doxorubicin, cisplatin or biological agents, depending on performance status and disease severity
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • time to symptomatic progression • tumour response • health-related quality of life • adverse effects of treatment

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 time horizon for the economic evaluation should be sufficiently long so as to incorporate all the important costs and benefits related to this condition. Where evidence allows, any likely dose-adjustment during treatment should be taken account of. Costs will be considered from an NHS and Personal Social Services perspective
Other considerations	If evidence permits, the appraisal will seek to identify subgroups of individuals for whom sorafenib may be particularly clinically and cost effective, for example by age, performance status or degree of underlying cirrhosis. Guidance will only be issued in accordance with the marketing authorisation
Related NICE recommendations	Related Interventional Procedures Guidance: Interventional Procedure Guidance No. 2, Jul 2003, 'Radiofrequency ablation for hepatocellular carcinoma' Interventional Procedure Guidance No. 135, Jul 2005, 'Laparoscopic liver resection for solitary liver metastasis from colorectal cancer, hepatocellular carcinoma, and for benign liver tumours or cysts' Interventional Procedure Guidance No. 211, Feb 2007, 'Radiofrequency-assisted liver resection for primary or secondary liver cancer' Interventional Procedure Guidance No. 214, Mar 2007, 'Microwave ablation of hepatocellular carcinoma'