NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pemigatinib for treating relapsed or refractory advanced cholangiocarcinoma with FGFR2 alterations

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pemigatinib within its marketing authorisation for treating cholangiocarcinoma.

Background

Cholangiocarcinoma is cancer of the bile duct. It mainly affects people aged over 65. Most people already have advanced cholangiocarcinoma when they are diagnosed because early disease is often asymptomatic. When symptoms occur, they include jaundice, weight loss, pain, sickness and fever.

Cholangiocarcinoma can be classified into 3 subtypes, depending on which part of the bile duct the cancer starts in. Intrahepatic cholangiocarcinoma (between 10-20% of cases) starts in the bile ducts inside the liver, peri-hilar cholangiocarcinoma starts just outside the liver (where the left and right hepatic ducts meet) and distal cholangiocarcinoma starts in the bile ducts near the bowel[1,2]. The overall incidence of cholangiocarcinoma is increasing with currently around 2,430 people diagnosed each year in the UK, although it is not always clear which subtype the cancer is[3]. Alterations of fibroblast growth factor receptors (FGFRs) are found in approximately 10-15% of intrahepatic cholangiocarcinoma and less commonly in other types of cholangiocarcinoma[4]. These receptors play a role in the growth and spread of the cancer cells. Of people diagnosed with cholangiocarcinoma in England in 2012, 28.5% of men and 24.6% of women survived for 1 year or more. Of people diagnosed in England in 2008, 6.6% of men and 4.4% of women survived for 5 years or more[5].

Surgery is currently the only curative treatment for cholangiocarcinoma. When surgery is not an option, people may receive chemotherapy or stent insertion. The most commonly used first chemotherapy regimen for cholangiocarcinoma is gemcitabine and cisplatin. Other chemotherapy treatments that may be used are capecitabine, fluorouracil and oxaliplatin. For disease with a poor performance status, gemcitabine monotherapy may be used. There is no established second chemotherapy regimen[6].

The technology

Pemigatinib (Pemazyre, Incyte) is a protein kinase inhibitor. It blocks protein kinases that are part of FGFRs. Blocking FGFRs is expected to reduce the growth and spread of the cancer. It is administered orally.

Pemigatinib does not currently have a marketing authorisation in the UK for treating relapsed or refractory advanced cholangiocarcinoma. It has been studied in clinical trials in people with advanced or surgically unresectable cholangiocarcinoma with and without FGFR2 alterations, whose disease has progressed after at least 1 prior systemic therapy.

Intervention(s)	Pemigatinib
Population(s)	People with advanced cholangiocarcinoma with FGFR2 fusion or rearrangement that is relapsed or refractory after at least 1 prior systemic therapy.
Comparators	• Chemotherapy • Best supportive care (including stent insertion)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • 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. 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 use of pemigatinib is conditional on the presence of FGF/FGFR gene alteration. The economic modelling should include the costs associated with diagnostic testing for the FGF/FGFR gene alteration in people with relapsed or refractory advanced cholangiocarcinoma who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals.
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 and NICE Pathways	**Related Interventional Procedures:** Selective internal radiation therapy for unresectable primary intrahepatic cholangiocarcinoma (2018) Interventional procedures guidance IPG630 Photodynamic therapy for bile duct cancer (2005) Interventional procedures guidance IPG134

	Endoscopic bipolar radiofrequency ablation for treating biliary obstruction caused by cholangiocarcinoma or pancreatic adenocarcinoma Interventional procedures guidance in development. Expected publication date: TBC **Related NICE Pathways:** Liver cancers (2020) NICE Pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domain 1. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1 Khan, SA, Tavolari, S, Brandi, G. Cholangiocarcinoma: Epidemiology and risk factors. Liver Int. 2019; 39(Suppl. 1): 19– 31. https://doi.org/10.1111/liv.14095

2 Cancer Research UK Types of bile duct cancer [accessed June 2020]

3 Cancer Research UK What is bile duct cancer? [accessed May 2020]

4 Apurva J et al, Cholangiocarcinoma With FGFR Genetic Aberrations: A Unique Clinical Phenotype. JCO Precision Oncology 2018 DOI: 10.1200/PO.17.00080

5 Public Health England Age-standardised incidence rates, one- and five-year survival, all patients diagnosed with upper gastrointestinal cancers, England [accessed May 2020]

6 Valle JW, Borbath I, Khan SA et al on behalf of the ESMO Guidelines Committee (2016) Biliary cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 27(5): v28-v37

