National Institute for Health and Care Excellence

Single Technology Appraisal (STA)

Pemigatinib for treating relapsed or refractory advanced cholangiocarcinoma with FGFR2 alterations

Response to consultee and commentator comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Response
Wording	Incyte Biosciences UK	Agree	Thank you for your comment. The remit of the scope has been updated to align with that provided by the Department of Health and Social Care for this appraisal.
	British Society of Gastroenterology	Yes I believe so.	Thank you for your comment. The remit of the scope has been updated to align with that provided by the Department of Health and Social Care for this appraisal.
Timing Issues	Incyte Biosciences UK	Currently there is no standard of care for cholangiocarcinoma (CCA) patients who have relapsed disease or are refractory after chemotherapy. Given the rapid progression seen with CCA, patients with FGFR2 rearrangements/fusions require a	Thank you for your comment. No action required.

Section	Consultee/ Commentator	Comments [sic]	Response
		treatment option like pemigatinib that could reduce or stabilise their disease.	
	British Society of Gastroenterology	Relatively urgent for a rare cancer as this is a cancer which is increasing in incidence and carries a high mortality	Thank you for your comment. No action required.
Additional comments on the draft remit	British Society of Gastroenterology	May we also consider its use as 1st line in patients with FGFR2 gene alterations, rather than only as 2nd or 3rd line	Thank you for your comment. NICE will appraise this technology within its marketing authorisation for relapsed or refractory cholangiocarcinoma.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Incyte Biosciences UK	Agree	Thank you for your comment. No action required.
	British Society of Gastroenterology	CCA should be divided into iCCA, pCCA, dCCA. What about peri-hilar CCA? What are OS estimates for current systemic Treatments?	Thank you for your comment. The background information has been updated to specify 3 types of CCA and does include information on overall survival estimates for people diagnosed with CCA. Please note that this this section is intended to provide a brief summary of the disease and is not designed to be exhaustive.
	AMMF – The Cholangiocarcinoma Charity	I think the background information on cholangiocarcinoma (CCA) is somewhat lacking in depth and accuracy. This is a	Thank you for your comment. The background information has been updated to specify 3 types of

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		poorly understood cancer, with very few treatment options, little in the way of robust data, and what there is can be confusing because of a lack of correct coding within the ICD system. Also, there are actually three types of CCA, not two. There is little robust data for the incidence, mortality and survival of those with CCA, and what there is is further confused by the fact there has been no code in the WHO ICD-10, and previous iterations, for what is believed to be the most commonly occurring type, hilar (perihilar) CCA. This has meant that hilar CCA could be diagnosed, but not correctly coded and recorded. With the advent of ICD-11, the three types are now coded separately as: 2C18.0 Hilar CCA 2C12.10 Intrahepatic CCA 2C15.0 Extrahepatic CCA: Adenocarcinoma of biliary tract, distal bile duct	CCA and the increasing incidence of CCA has been noted.

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		So, it would be more accurate to say there are three types, not two. The incidence of cholangiocarcinoma is known to be increasing but, because of confusion about disease classification, there seems to be little robust evidence to support this. However, over the last couple of years, AMMF has been undertaking a data project in partnership with PHE, and this has confirmed (as yet unpublished) that over a period of 17 years (2001 -2017) there has been an increase in CCA of 52%, whereas, in comparison, using Cancer Research UK data, the age-standardised incidence of all cancers (combined) has decreased by 6% over the same timeframe. Similarly, the mortality rate of CCA has also been shown to rise over the same period, whereas the mortality of all cancers has shown a marked decrease over the same timeframe.	
The technology/ intervention	Incyte Biosciences UK	Agree	Thank you for your comment. No action required.

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	British Society of Gastroenterology	What % of cases (iCCA, pCCA, dCCA) have FGFR alterations and does this vary by region/ethnicity?	Thank you for your comment. The background section has been updated to include information on the incidence of FGFR alterations based on type of CCA. Epidemiological factors will be considered as part of the appraisal.
Population	Incyte Biosciences UK	Agree	Thank you for your comment.
	British Society of Gastroenterology	Could/should we also consider its use as 1st line in patients with FGFR2 gene alterations, rather than only as 2nd or 3rd line	Thank you for your comment. NICE will appraise this technology within its marketing authorisation for relapsed or refractory cholangiocarcinoma.
Comparators	Incyte Biosciences UK	Disagree. Radiotherapy and Radioembolisation are not routinely commissioned on the NHS for the treatment of patients with CCA – this feedback was provided to Incyte by UK clinicians. The related Interventional procedure guidance listed in the draft scope (IPG630, IPG134) do not explicitly recommend use of the procedures - advising that current evidence is insufficient and may be used in the context of research.	Thank you for your comment. After the scoping teleconference, it was considered that these treatments are not routinely commissioned in the NHS, and they were removed as comparators.

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	British Society of Gastroenterology	Yes	Thank you for your comment. No action required.
Outcomes	Incyte Biosciences UK	Include: Duration of response Disease control rate	Thank you for your comment. After the scoping teleconference, it was considered that these outcomes would not be necessary to evaluate the clinical and cost-effectiveness of the technology.
	British Society of Gastroenterology	Yes	Thank you for your comment. No action required.
Economic analysis	Incyte Biosciences UK	The model will use a lifetime time horizon	Thank you for your comment. No action required.
	British Society of Gastroenterology	Clinically, increments in overall survival in this group of patients is measured in week/months rather than years	Thank you for your comment. No action required.
Equality and Diversity	Incyte Biosciences UK	No additional comment.	Thank you for your comment. No action required.
Other considerations	AMMF – The Cholangiocarcinoma Charity	There is very little in the treatment armoury for CCA patients. This new treatment presents the first opportunity for an effective 2nd line therapy for a small number of them.	Thank you for your comment. No action required.
Innovation	Incyte Biosciences UK	Currently there is no standard of care for CCA patients who have relapsed disease or are refractory after chemotherapy. Given the rapid progression seen with CCA, patients with FGFR2	Thank you for your comments. The company will have the opportunity to expand on the innovative potential of this technology in its submission and this will be considered by the appraisal committee

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		rearrangements/fusions require a treatment option like pemigatinib that could reduce or stabilise their disease. Historically systemic chemotherapies in second line treatment have limited efficacy and can result in significant toxicity. As a result a significant minority of patients who are not fit enough for chemotherapy receive palliative care only. Pemigatinib as an oral treatment demonstrates efficacy in patients with previously treated, locally advanced or metastatic CCA with FGFR2 rearrangements/fusions. In the phase 2 FIGHT-202 study the ORR was 35.5% (95% CI, 26.50%–45.35%) and the median DOR was 7.49 months (95% CI, 5.65–14.49 months). median OS 21.06 months (95% CI, 14.82 months–not estimable [NE]; not mature at data cutoff) and median PFS was 6.93 months (95% CI, 6.18–9.59 months). Less than 9% of patients (N=146) discontinued treatment due to adverse events during the study.	
	British Society of Gastroenterology	Yes: innovative and potentially quite significant for a sub-group of patients with this cancer	Thank you for your comments. The company will have the opportunity to expand on the innovative potential of this technology in its submission and this will be considered by the appraisal committee

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Additional comments on the draft scope	AMMF – The Cholangiocarcinoma Charity	The related interventional procedures listed against “Related NICE recommendations and NICE Pathways” are not available to CCA patient. SIRT was not approved after having been available for some time under the CtE process. It is currently listed as being available under clinical trial conditions, but the only trial, SIRCCA has now closed to recruitment. Photodynamic therapy (PDT) is not used following the negative outcome of the PHOTOSTENT-02 trial some years ago. And the”Endoscopic bipolar radiofrequency ablation” would seem to be in development.	Thank you for your comment. It was considered that these treatments are not routinely commissioned in the NHS and radiotherapy and radioembolisation were removed as comparators, however the related interventional guidance will remain in the scope.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope:

N/A