

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Trifluridine–tipiracil for treating metastatic gastric or gastro-oesophageal junction cancer after 2 or more therapies

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of trifluridine–tipiracil within its marketing authorisation for previously treated metastatic gastric or gastro-oesophageal junction cancer.

Background

Stomach cancer is a malignant tumour arising from cells in the stomach. The most common type of stomach cancer is gastric or gastro-oesophageal junction adenocarcinoma, which affects about 95% of people with the disease.¹ Stomach cancer is more common in men than women, with approximately 3,500 cases diagnosed in men, and 1,900 cases in women in England in 2015.² Around half of all new cases of gastric cancer in the UK are diagnosed in people aged 75 years and over.² Initial symptoms of disease are vague and are similar to other stomach conditions but symptoms of advanced stages may include a lack of appetite and subsequent weight loss, fluid in the abdomen and blood in the stool. Because of the nature of symptoms, gastric cancer is often diagnosed at an advanced stage, with around 18% diagnosed at stage 3 (locally advanced), and 38% diagnosed at stage 4 (metastatic) in England in 2016.³

Over the past few years there has been a rapid increase in incidence of tumours at the junction of the oesophagus and stomach. These tend to come from changes in the lining of the oesophagus in turn leading to adenocarcinoma of the lowest part of the oesophagus, which goes across the gastro-oesophageal junction.

The aim of treatment in advanced or metastatic gastric or gastro-oesophageal junction cancer is primarily palliative; to prevent progression, extend survival and relieve symptoms with minimal adverse effects. NICE technology appraisal [191](#) recommends capecitabine in combination with a platinum-containing agent as an option for inoperable untreated advanced gastric cancer. Chemotherapy combination regimens used in untreated oesophago-gastric cancer include doublet treatment with fluorouracil or capecitabine in combination with cisplatin or oxaliplatin or triplet treatment with fluorouracil or capecitabine in combination with cisplatin or oxaliplatin plus epirubicin. For people who have untreated HER2-positive metastatic gastric or gastro-oesophageal junction cancer, NICE technology appraisal [208](#) recommends trastuzumab in combination with cisplatin and capecitabine or fluorouracil.

There is no standard treatment for previously treated advanced or metastatic disease. Best supportive care is commonly used at this stage. Taxane (docetaxel or paclitaxel) monotherapy may be an option or combination therapy may be given once again. NICE technology appraisal [378](#) does not recommend ramucirumab for treating advanced gastric cancer or gastro-oesophageal junction adenocarcinoma previously treated with chemotherapy.

The technology

Trifluridine-tipiracil hydrochloride (Lonsurf, Servier Laboratories) comprises of anucleoside analogue, trifluridine, and the thymidine phosphorylase inhibitor, tipiracil hydrochloride. The nucleoside analogue is incorporated into the DNA of tumour cells and inhibits tumour growth, whereas the thymidine phosphorylase inhibitor slows the breakdown of trifluridine to prolong its action. It is administered orally.

Trifluridine-tipiracil hydrochloride does not currently have a marketing authorisation in the UK for treating gastric or gastro-oesophageal junction cancer. It has been studied in randomised controlled trials, compared with placebo, for treating metastatic gastric or gastro-oesophageal junction cancer in adults for who have not responded to or were unable to tolerate 2 or more prior therapies.

Intervention(s)	Trifluridine–tipiracil hydrochloride
Population(s)	Adults with metastatic gastric or gastro-oesophageal junction cancer, who have had 2 or more previous therapies
Comparators	<ul style="list-style-type: none"> • Chemotherapy (such as docetaxel or paclitaxel monotherapy or combination chemotherapy) • Best supportive care (including but not limited to antiemetics, blood transfusions, oesophageal stents, palliative radiotherapy and palliative surgery).
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • duration of response • adverse effects of treatment • health-related quality of life.

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p>
<p>Other considerations</p>	<p>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.</p>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>Ramucirumab for treating advanced gastric cancer or gastro-oesophageal junction adenocarcinoma previously treated with chemotherapy (2016). NICE technology appraisal guidance 378. Review date January 2019.</p> <p>Capecitabine for the treatment of advanced gastric cancer (2010). NICE technology appraisal 191. No review date.</p> <p>Trastuzumab for the treatment of HER2-positive metastatic gastric cancer (2010) NICE technology appraisal 208. No review date.</p> <p>Appraisals in development (including suspended appraisals)</p> <p>Avelumab for treating gastric or gastro-oesophageal junction cancer after 2 therapies. NICE technology appraisal guidance [ID1289]. Suspended.</p> <p>Nivolumab for treating gastric or gastro-oesophageal junction cancer after 2 or more therapies. [ID1118] NICE technology appraisal guidance. Suspended.</p> <p>Pembrolizumab for previously treated oesophageal or gastro-oesophageal junction cancer [ID1357] NICE technology appraisal guidance. Publication expected:</p>

	<p>TBC</p> <p>Pembrolizumab for previously treated metastatic gastric or gastro-oesophageal junction cancer [ID1168] NICE technology appraisal guidance. Publication expected: TBC</p> <p>Related Guidelines:</p> <p>Oesophago-gastric cancer: assessment and management in adults (2018) NICE guideline 83</p> <p>Related Quality Standards:</p> <p>Oesophago-gastric cancer (2018) NICE quality standard 176</p> <p>Related NICE Pathways:</p> <p>Gastrointestinal cancers (2018) NICE pathway</p>
<p>Related National Policy</p>	<p>NHS England</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105: specialist cancer services (adults).</p> <p>NHS England (2013) Oesophageal and Gastric (adult). 2013/14 NHS Standard Contract for Cancer.</p> <p>NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Chemotherapy (adult). 2013/14 NHS Standard Contract for Cancer.</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2, 4, 5</p>

Questions for consultation

Have all relevant comparators for trifluridine–tipiracil been included in the scope? Which treatments are considered to be established clinical practice in the NHS for metastatic gastric or gastro-oesophageal junction cancer after 2 or more prior therapies?

How should best supportive care be defined?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom trifluridine–tipiracil is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider trifluridine–tipiracil will fit into the existing NICE pathway, [gastrointestinal cancers](#)?

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 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 trifluridine–tipiracil 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.

Do you consider trifluridine–tipiracil to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of trifluridine–tipiracil can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at <http://www.nice.org.uk/article/pmg19/chapter/1-Introduction>).

References

- 1 Macmillan Cancer Support [Types of stomach cancer](#). Accessed November 2018.
- 2 Cancer Research UK [Stomach cancer incidence statistics](#). Accessed November 2018.
- 3 National Cancer Registration and Analysis Service [Stage Breakdown by CCG 2016](#). Accessed November 2018.