

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab in combination with chemotherapy for untreated advanced gastric or gastro-oesophageal junction cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab in combination with chemotherapy within its marketing authorisation for untreated advanced gastric or gastro-oesophageal junction cancer.

Background

Gastric cancer is a malignant tumour arising from cells in the stomach. The most common type of stomach cancer is gastric or gastro-oesophageal junction. The most common histological subtype of gastric or gastro-oesophageal junction cancer is adenocarcinoma which affects about 95% of people with the disease¹. Gastro-oesophageal junction (GOJ) cancer describes cancers where the centre of the tumour is less than 5cm above or below where the oesophagus meets the stomach².

Stomach cancer is more common in men than women, with approximately 3,378 cases diagnosed in men, and 1,764 cases in women in England in 2017³. Around half of all new cases of gastric cancer in the UK are diagnosed in people aged 75 years and over³. 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, vomiting blood, blood in the stool or black stool. Because of the nature of symptoms, gastric cancer is often diagnosed at an advanced stage, with around 17% diagnosed at stage 3 (locally advanced), and 34% diagnosed at stage 4 (metastatic) in England in 2014³. The 5-year survival for people diagnosed with stomach cancer between 2013 and 2017 was 21.6%⁴.

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 gastroesophageal 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. NICE clinical guideline (NG 83) recommends chemotherapy combination regimens for people who have a performance status 0 to 2 and

no significant comorbidities. Chemotherapy regimens 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.

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb) is a humanised monoclonal antibody that targets and blocks a receptor on the surface of lymphocytes known as PD-1. This receptor is part of the immune checkpoint pathway, and blocking its activity may promote an anti-tumour immune response. It is administered intravenously.

Nivolumab in combination with chemotherapy does not have a marketing authorisation in the UK for locally advanced or metastatic gastric or gastro-oesophageal junction cancer. It is being studied in a clinical trial which randomised patients into three treatment arms; nivolumab in combination with chemotherapy, nivolumab in combination with ipilimumab and chemotherapy only. The trial enrolled adults with untreated locally advanced or metastatic gastric or gastro-oesophageal junction cancer.

Intervention	Nivolumab in combination with chemotherapy
Population	Adults with untreated locally advanced or metastatic gastric or gastro-oesophageal junction cancer
Comparators	<ul style="list-style-type: none"> • Chemotherapy without nivolumab, such as: <ul style="list-style-type: none"> ○ Doublet treatment with fluorouracil or capecitabine plus cisplatin or oxaliplatin ○ Triplet treatment with fluorouracil or capecitabine plus cisplatin or oxaliplatin plus epirubicin • For people with HER2-positive gastric or gastro-oesophageal junction cancer <ul style="list-style-type: none"> ○ Trastuzumab with cisplatin plus capecitabine or fluorouracil

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • adverse effects of treatment • health-related quality of life.
Economic analysis	<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>
Other considerations	<p>If evidence allows subgroups by HER2 status will be considered.</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>
Related NICE recommendations and NICE Pathways	<p><u>Related Technology Appraisals:</u></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><u>Appraisals in development:</u></p> <p>‘Pertuzumab for untreated metastatic HER2-positive gastric or gastro-oesophageal junction cancer’ NICE technology appraisals guidance [ID1096] Publication date to be confirmed.</p> <p>‘Pembrolizumab for untreated metastatic gastric or</p>

	<p>gastro-oesophageal junction cancer' NICE technology appraisals guidance [ID1305] Publication date to be confirmed.</p> <p>Related Guidelines:</p> <p>'Oesophago-gastric cancer: assessment and management in adults' (2018). NICE guideline 83 Review date January 2020.</p> <p>Related Interventional Procedures:</p> <p>'Laparoscopic gastrectomy for cancer' (2008). NICE interventional procedures guidance 269.</p> <p>Related Quality Standards:</p> <p>Oesophago-gastric cancer NICE quality standard. Publication expected December 2018.</p> <p>Related NICE Pathways:</p> <p>Gastrointestinal cancers (2016) NICE Pathway</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View'</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 105, Specialist Cancer services (adults)</p> <p>Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domain 1.</p>

Questions for consultation

Have all relevant comparators for nivolumab been included in the scope?
Should trastuzumab be included as a comparator?

Which treatments are considered established clinical practice in the NHS for untreated locally advanced or metastatic gastric or gastro-oesophageal junction cancer?

Are the outcomes listed appropriate?

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

Are gastro-oesophageal junction cancer and oesophageal adenocarcinoma expected to respond similarly to treatment?

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Issue Date: October 2020

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Where do you consider nivolumab will fit into the existing [oesophageal and gastric cancer NICE pathway](#)?

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 nivolumab 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 nivolumab 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 nivolumab 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 September 2020.
2. Cancer Research UK. About gastro oesophageal junction cancer. 2018. Available from: <https://www.cancerresearchuk.org/about->

[cancer/gastro-oesophageal-junction-cancer/about](#) Accessed September 2020

3. Cancer Research UK [Stomach cancer incidence statistics](#). Accessed September 2020.
4. Office for National Statistics (2019). [Cancer survival in England - adults diagnosed](#). Accessed September 2020.