NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab for previously treated gastric or gastro-oesophageal junction cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for previously treated 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]. It is more common in men than women, with approximately 4,600 cases diagnosed in men, and 2,500 cases in women in 2013[2]. Around half of all new cases of stomach cancer are diagnosed in people aged over 75 years[2]. Initial symptoms of disease are vague and are similar to other stomach conditions but advanced stages of cancer 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, stomach cancer is often diagnosed at an advanced stage, with around 14% diagnosed at stage 3 (locally advanced), and 80% diagnosed at stage 4 (metastatic)[3].

Once the stage of the cancer has been established the main treatment option, if appropriate, is surgical resection of the tumour with or without adjunctive chemotherapy; these include cisplatin, capecitabine, 5FU (fluorouracil) and FOLFOX (folinic acid, fluorouracil and oxaliplatin). Radiotherapy may be used palliatively with or without chemotherapy. At advanced stages of the cancer surgery may not be an option at first but may potentially be operable after chemotherapy has down-staged the tumour. The aim of treatment in advanced 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 a first line option for advanced cancer. Other options include combination regimens, such as epirubicin with a platinum-containing agent and capecitabine or 5FU, docetaxel and irinotecan, FOLFIRI (irinotecan and 5FU), and if people are HER2-positive; then NICE technology appraisal 208 recommends trastuzumab in combination with cisplatin and capecitabine or 5FU. There is no standard treatment for previously treated advanced disease. People may be treated with taxane (docetaxel or paclitaxel) monotherapy or combination therapy once again at second line, but beyond second line there is no evidence on the effective use of these agents. NICE technology appraisal 378

does not recommend ramucirumab for treating advanced gastric cancer or gastro-oesophageal junction adenocarcinoma previously treated with chemotherapy.

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb) is a monoclonal antibody that targets 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. Nivolumab is administered intravenously.

Nivolumab does not currently have a marketing authorisation for gastric or gastro-oesophageal junction cancer in the UK. It is being studied in a clinical trial against placebo in people with unresectable advanced or recurrent gastric cancer that is refractory to standard therapy or in whom standard therapy is not tolerated.

Intervention(s)	Nivolumab
Population(s)	Adults with previously treated advanced or recurrent gastric or gastro-oesophageal junction cancer
Comparators	Chemotherapy including but not limited to: • docetaxel or paclitaxel monotherapy • best supportive care (including but not limited to antiemetics, blood transfusions, oesophageal stents, palliative radiotherapy and palliative surgery)
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.
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 Technology Appraisals:** Technology Appraisal No 378, Jan 2016. 'Ramucirumab for treating advanced gastric cancer or gastro–oesophageal junction adenocarcinoma previously treated with chemotherapy'. Review date proposed Jan 2019. Technology Appraisal No 208, Jul 2010, 'Trastuzumab for the treatment of HER2-positive metastatic gastric cancer'. Guidance on static list. Technology Appraisal No 191, Jul 2010, 'Capecitabine for the treatment of advanced gastric cancer'. Guidance on static list. **Related NICE Pathways:** NICE Pathway: Gastrointestinal Cancers, Pathway created: Nov 2013.
Related National Policy	**NHS England** NHS England (2016) Manual for prescribed specialised services 2016/17 Chapter 105: specialist cancer services (adults). NHS England (2016) Clinical Commissioning Policy: Robotic assisted surgery for oesophago-gastric cancers NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Oesophageal and Gastric (adult) **National Service Frameworks** Cancer **Other policies** Department of Health (2016) NHS outcomes framework 2016 to 2017 Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020

	Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy

Questions for consultation

Where would nivolumab fit in the treatment pathway for previously treated gastric cancer?

Have all relevant comparators for nivolumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for advanced or recurrent gastric or gastro-oesophageal cancer? Should irinotecan-based regimens be included?

How should best supportive care be defined as a comparator for previously treated gastric or gastro-oesophageal 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 groups that should be examined separately?

Where do you consider nivolumab 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 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.

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. Types of stomach cancer (2016). Cancer Research UK. Accessed December 2016

2. Stomach cancer statistics. Cancer Research UK. Accessed December 2016.

3. Survival statistics for stomach cancer. Cancer Research UK. Accessed December 2016.