NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab with chemotherapy and surgery for treating resectable gastric or gastro-oesophageal junction cancer.

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab with chemotherapy and surgery within its marketing authorisation for treatment of resectable 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. Gastro-oesophageal junction cancer describes cancers where the centre of the tumour is less than 5cm above or below where the oesophagus meets the stomach[1]. The most common histological subtype of gastric cancer is adenocarcinoma, which account for 95% of stomach cancers[2,].

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 2017[3]. Around half of all new cases of gastric cancer in the UK are diagnosed in people aged 75 years and over[3].

Initial symptoms of gastric cancer 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 cancers are often diagnosed at an advanced stage. In England in 2014 70% of patients with a known stage were diagnosed at an advanced stage (stage 3 or 4) and 30% were diagnosed at an early stage (stage 1 or 2)[3]. The 5-year survival for people diagnosed with stomach cancer between 2013 and 2017 was 21.6%[4].

Treatment for gastric or gastro-oesophageal junction cancer will depend on several factors such as the site of the cancer, how far the cancer has grown or spread and the persons overall health and fitness. For some palliative management will be most appropriate, when surgery is appropriate for people with gastric and gastro-oesophageal junction cancer NICE clinical guideline (NG83) recommends chemotherapy is offered before and after surgery.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised, anti-programmed cell death 1 (PD-1) antibody involved in the blockade of immune

suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

Pembrolizumab with chemotherapy and surgery does not currently have a marketing authorisation in the UK for treating resectable gastric or gastro-oesophageal junction cancer. It is being studied in a clinical trial compared with placebo plus chemotherapy as neoadjuvant/adjuvant treatment for localised gastric or gastroesophageal junction adenocarcinoma.

Intervention(s)	Neoadjuvant/adjuvant pembrolizumab with chemotherapy
Population(s)	People with resectable gastric or gastro-oesophageal junction cancer
Comparators	Standard neoadjuvant/adjuvant chemotherapy without pembrolizumab
Outcomes	The outcome measures to be considered include: • overall survival • disease-free survival • response rate • 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 availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account'.
Other considerations	If evidence allows subgroups by PD-L1 status will be considered. 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	Appraisals in development: Nivolumab for adjuvant treatment of oesophageal or gastro-oesophageal junction cancer. Proposed NICE technology appraisal [ID1676]. Publication date to be confirmed. Related Guidelines: 'Oesophago-gastric cancer: assessment and management in adults' (2018). NICE guideline 83 Review date January 2020. Related Interventional Procedures: 'Laparoscopic gastrectomy for cancer' (2008). NICE interventional procedures guidance 269. Related Quality Standards: Oesophago-gastric cancer NICE quality standard. Publication expected December 2018. Related NICE Pathways: Gastrointestinal cancers (2020) NICE Pathway Oesophageal and gastric cancer (2021) NICE Pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 105, Specialist Cancer services (adults) 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 NHS England (2016) Clinical Commissioning Policy: Robotic assisted surgery for oesophago-gastric cancers. Ref: NHS England: 16006/P NHS England (2013) 2013/14 NHS standard contract for cancer: oesophageal and gastric (adult). Reference: B11/S/a. NHS England (2019) Implementing a timed oesophago-gastric cancer diagnostic pathway: a handbook for local health and care systems

Questions for consultation

Have all relevant comparators for pembrolizumab with chemotherapy and surgery been included in the scope?

What is the usual chemotherapy regimen used in clinical practice in the NHS in the neoadjuvant/adjuvant setting for gastric or gastro-oesophageal junction cancer?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom pembrolizumab with chemotherapy and surgery is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider pembrolizumab with chemotherapy and surgery 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 pembrolizumab with chemotherapy and surgery 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 pembrolizumab with chemotherapy and surgery 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 pembrolizumab with chemotherapy and surgery 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. Cancer Research UK. About gastro oesophageal junction cancer. 2018. Accessed March 2021

2. Macmillan Cancer Support Types of stomach cancer 2019. Accessed March 2021.

3. Cancer Research UK Stomach cancer incidence statistics. Accessed March 2021.

4. Office for National Statistics (2019). Cancer survival in England - adults diagnosed. Accessed March 2021.