NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Nivolumab for adjuvant treatment of oesophageal or gastro-oesophageal junction cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for adjuvant treatment of resected oesophageal or gastro-oesophageal junction cancer.

Background

Oesophageal cancer is a malignant tumour arising from cells lining the oesophagus (gullet), which is the muscular tube through which food passes from the throat to the stomach. The two main types of oesophageal cancer are squamous cell carcinoma and adenocarcinoma. Cancers in the upper or middle part of the oesophagus are usually squamous cell carcinomas. Cancers in the lower oesophagus are usually adenocarcinomas. This includes those in the junction where the oesophagus joins the stomach[1]. 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[2].

There were an estimated 7,569 new diagnoses of oesophageal cancer in England in 2017[3]. It is more common in men than women, with approximately 19 new cases for every 100,000 males and 8 for every 100,000 females. Around 41% of all new cases in the UK, from 2015-2017, were diagnosed in people aged 75 and over[3]. 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, oesophageal cancer is often diagnosed at a late stage, with around 70-80% diagnosed at stage 3 (locally advanced) or 4 (metastatic) and 20-30% diagnosed at an early stage (stage 1 or 2)[3].

Surgery with chemotherapy or chemoradiotherapy can be used to treat early oesophageal and gastro-oesophageal junction cancer. NICE clinical guideline (NG83) recommends that patients with localised oesophageal and gastro-oesophageal junctional adenocarcinoma may receive chemotherapy before or before and after surgery, or chemoradiotherapy before surgery. For patients with squamous cell carcinoma of the oesophagus, NICE clinical guideline (NG83) recommends radical chemoradiotherapy alone or chemoradiotherapy before surgery. The most common chemotherapy agents include fluorouracil, capecitabine, cisplatin, epirubicin and docetaxel[4]. In advanced oesophageal or gastro-oesophageal junction cancer, the main aim of treatment is primarily palliative; to prevent progression, extend survival and relieve symptoms with minimal adverse effects.

The technology

Nivolumab (Opdivo, Bristol-Myers Squibb) is a human 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 adjuvant treatment of oesophageal cancer in the UK. It is being studied in a clinical trial versus placebo in people with resected oesophageal or gastro-oesophageal junction cancer who have previously had treatment with chemoradiotherapy followed by surgery.

Intervention(s)	Nivolumab
Population(s)	Adults with resected oesophageal or gastro-oesophageal junction cancer
Comparators	• Routine surveillance
Outcomes	The outcome measures to be considered include: • overall survival • disease-free survival • 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.
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	Appraisals in development: Pembrolizumab with chemotherapy and surgery for treating resectable gastric or gastro-oesophageal junction cancer. Proposed NICE technology appraisal [ID2696]. Publication date to be confirmed.

	Related Guidelines: Oesophago-gastric cancer: assessment and management in adults (2018). NICE guideline NG83. Review date: to be confirmed Related Interventional Procedures: Minimally invasive oesophagectomy (2011) NICE interventional procedures guidance 407 Photodynamic therapy for early stage oesophageal cancer (2006) NICE interventional procedures guidance 200 Related Quality Standards: Oesophago-gastric cancer (2018) NICE quality standard 176 Related NICE Pathways: Oesophageal and gastric cancer (2020) NICE pathway.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View' NHS England (2019) Proton Beam Therapy for Oesophageal Cancer in Adults (1874) NHS England (2019) Clinical Commissioning Policy: 18F-fluorodeoxyglucose (FDG) positron emission tomography-computed-tomography (PET CT) as part of radical radiotherapy treatment planning for oesophageal cancer (all ages) Ref: NHS England: 170115P NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 105, Specialist Cancer services (adults) Department of Health (2016) NHS Outcomes Framework 2016-2017. Domains 1 and 2.

References

1. Macmillan Cancer Support. Oesophageal Cancer. Available from: http://www.macmillan.org.uk/information-and-support/oesophageal-gullet-cancer/understanding-cancer/types-oesophageal-cancer.html 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. Oesophageal Cancer Incidence Statistics. 2017. Available from: http://www.cancerresearchuk.org/health-professional/cancer-

statistics/statistics-by-cancer-type/oesophageal-cancer/incidence#heading-Zero Accessed September 2020

4. Cancer Research UK. Oesophageal cancer – chemotherapy treatment. Available from: https://about-cancer.cancerresearchuk.org/about-cancer/oesophageal-cancer/treatment/chemotherapy/chemotherapy-treatment Accessed September 2020