NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab with platinum-based chemotherapy for untreated advanced oesophageal or gastroesophageal junction cancer

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab with platinum-based chemotherapy within its marketing authorisation for unresectable locally advanced or metastatic oesophageal cancer or gastroesophageal junction adenocarcinoma that has not been previously treated.

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.[1] Gastroesophageal junction cancer can develop directly at the gastroesophageal junction (where the stomach joins the oesophagus). It can also spread from the oesophagus across the gastroesophageal junction or from the stomach across the gastroesophageal junction.[2] The two main types of oesophageal cancer are squamous cell carcinoma and adenocarcinoma. In the upper and middle part of the oesophagus, cancers tend to be squamous cell carcinomas, which develop from cells that make up the inner lining of the oesophagus. Cancers in the lower part (including gastroesophageal junction cancer) tend to adenocarcinomas, which usually develop in gland cells.[1] The most common symptoms are difficulty swallowing, food regurgitation, nausea or vomiting, unexplained weight loss and persistent indigestion or cough.[3]

Oesophageal cancer is more common in men than women. In 2017, there were 2,289 new diagnoses in women and 5,280 in men (a total of 7,569 new cases) in England.[4] The risk of developing oesophageal cancer increases with age. Around 40% of all new cases in UK are diagnosed in people aged over 75.[5] Because of the nature of symptoms, oesophageal cancer is often diagnosed at an advanced stage. On average 70-80% are diagnosed at stage 3 (locally advanced) or 4 (metastatic).[6] For adults diagnosed between 2013 and 2017 in England, the 1-year survival rate for people with oesophageal cancer is around 47% and 5-year survival rate is 17%.[7]

The aim of treatment in advanced or metastatic oesophageal cancer or gastroesophageal junction adenocarcinoma is primarily palliative. NICE clinical guideline (NG83) 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.

The technology

Pembrolizumab (Keytruda, MSD) is a humanised monoclonal antibody that targets and blocks a receptor on the surface of lymphocytes known as PD-1. The PD-1

receptor is part of the immune checkpoint pathway and blocking its activity may promote an anti-tumour immune response. It is administered intravenously.

Pembrolizumab does not currently have a marketing authorisation in the UK for untreated advanced oesophageal cancer or gastroesophageal junction cancer. It has been studied in a randomised clinical trial, in combination with cisplatin and fluorouracil versus cisplatin plus fluorouracil in people with previously untreated locally advanced unresectable, or metastatic oesophageal or gastroesophageal junction cancer.

Intervention(s)	Pembrolizumab with platinum-based chemotherapy
Population(s)	Adults with untreated, unresectable locally advanced or metastatic oesophageal cancer or gastroesophageal junction adenocarcinoma
Comparators	Platinum-based chemotherapy without pembrolizumab, such as: • doublet treatment with fluorouracil or capecitabine plus cisplatin or oxaliplatin • triplet treatment with fluorouracil or capecitabine plus cisplatin or oxaliplatin epirubicin
Outcomes	The outcome measures to be considered include: • overall survival • progression-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 patient access schemes for the intervention or comparator technologies will be taken into account.

Other considerations	If the evidence allows, consideration will be given to subgroups based on cancer histology and biological markers (PD-L1 or HER2). If appropriate, the appraisal should include consideration of the costs and implications of additional testing for biological markers, but will not make recommendations on specific diagnostic tests or devices. 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:** None **Appraisals in development (including suspended appraisals):** Nivolumab with cisplatin and fluorouracil for untreated advanced oesophageal squamous cell carcinoma. [ID2712] Proposed NICE technology appraisal guidance. Publication date to be confirmed. Pembrolizumab with trastuzumab and chemotherapy for untreated HER2-positive advanced gastric or gastro-oesophageal junction cancer [ID3742] Proposed NICE technology appraisal guidance. Publication date to be confirmed. Pembrolizumab for gastric or gastroesophageal junction adenocarcinoma [ID1305] Proposed NICE technology appraisal guidance. Publication date to be confirmed. Nivolumab in combination with chemotherapy for untreated advanced gastric, gastro-oesophageal junction or oesophageal adenocarcinoma [ID1465] Proposed NICE technology appraisal guidance. Publication expected October 2021. **Related Guidelines:** Oesophago-gastric cancer: assessment and management in adults (2018). NICE guideline 83 Review date: not published. **Related Interventional Procedures:** Endoscopic submucosal dissection of oesophageal dysplasia and neoplasia (2010) NICE interventional procedures guidance 355 Palliative photodynamic therapy for advanced oesophageal cancer (2007) NICE interventional procedures guidance 206 **Related Quality Standards:**

	Oesophago-gastric cancer (2018) NICE quality standard 176 **Related NICE Pathways:** Oesophageal and gastric cancer (last updated 2018) 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 2A Department of Health (2014) The national cancer strategy: 4th annual report Chapters 4 and 5 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2, 4 and 5 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1. Macmillan cancer support (2020) Signs and symptoms of oesophageal cancer. Accessed April 2020
2. Cancer Research UK (2018) About gastro oesophageal junction cancer. Accessed November 2020
3. Macmillan cancer support (2020) What is oesophageal cancer? Accessed April 2020
4. Office for National Statistics (2019) Cancer registration statistics, England, 2017. Accessed April 2020.
5. Cancer Research UK (2019) Oesophageal cancer incidence statistics. Accessed April 2020.
6. NCRAS (2019) Stage breakdown by CCG 2017. Accessed April 2020.
7. Office for National Statistics (2019) Cancer survival in England - adults diagnosed Accessed April 2020.