NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Zolbetuximab with chemotherapy for untreated claudin 18.2 positive HER2 negative unresectable advanced gastric or gastro-oesophageal junction adenocarcinoma ID5123

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of zolbetuximab with chemotherapy within its marketing authorisation for untreated claudin 18.2 positive HER2 negative unresectable advanced gastric or gastro-oesophageal junction adenocarcinoma.

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. Oesophageal cancer is a malignant tumour arising from cells lining the oesophagus. The most common histological subtype of gastric, gastro-oesophageal junction and oesophageal cancer is adenocarcinoma. Claudin 18 variant 2 is a protein found in the glands lining the inside of the stomach, where it helps the gastric cells to stick to each other. In people with gastric or gastro-oesophageal junction cancer, claudin 18.2 is much more widespread and is thought to be involved in the survival and spread of the cancer cells.

Gastric cancer is more common in men than women, with 3,405 cases diagnosed in men, and 1,810 cases in women in England on average per year from 2016 to 2018[1]. Around half of all new cases of gastric cancer in the UK are diagnosed in people aged 75 years and over. Oesophageal cancer is also more common in men than women, with 5,349 cases diagnosed in men, and 2,332 cases in women in England on average per year from 2016 to 2018[2]. Around 41% of all new cases of oesophageal cancer in the UK are diagnosed in people aged 75 and over[2].

Initial symptoms of gastric or oesophageal 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 and oesophageal cancer are often diagnosed at an advanced stage. The 5-year survival for people diagnosed with stomach cancer and oesophageal cancer between 2013 and 2017 was 21.6% and 17% respectively[3].

The aim of treatment in advanced or metastatic gastric, gastro-oesophageal junction cancer or oesophageal adenocarcinoma 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 guideline 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.

NICE technology appraisal 737 recommends pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy as an option for untreated locally advanced unresectable or metastatic carcinoma of the oesophagus or HER2-negative gastrooesophageal junction adenocarcinoma in adults whose tumours express PD-L1 with a combined positive score (CPS) of 10 or more. NICE technology appraisal 857 recommends nivolumab with platinum- and fluoropyrimidine-based chemotherapy as an option for untreated HER2-negative, advanced or metastatic gastric, gastrooesophageal junction or oesophageal adenocarcinoma in adults whose tumours express PD-L1 with a CPS of 5 or more.

The technology

Zolbetuximab (Claudiximab, Astellas Pharma) with chemotherapy does not currently have a marketing authorisation in the UK for untreated claudin 18.2 positive HER2 negative unresectable advanced gastric or gastro-oesophageal junction adenocarcinoma. It has been studied in clinical trials in people with untreated claudin 18.2 positive HER2 negative unresectable advanced gastric or gastro-oesophageal junction adenocarcinoma.

Intervention(s)	Zolbetuximab with chemotherapy
Population(s)	People with untreated claudin 18.2 positive HER2 negative unresectable advanced gastric or gastro-oesophageal junction adenocarcinoma
Subgroups	If the evidence allows, the following subgroups will be considered: • Subgroups by tumour location

Comparators	• Chemotherapy alone, which includes doublet treatment with fluorouracil or capecitabine plus cisplatin or oxaliplatin
	• Pembrolizumab with chemotherapy (subject to NICE evaluation)
	• For people whose tumours express PD-L1:
	  ○ pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy (with CPS of 10 or more and for gastro-oesophageal junction adenocarcinoma only)
	  ○ nivolumab with platinum- and fluoropyrimidine-based chemotherapy (with CPS of 5 or more)

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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The use of zolbetuximab is conditional on the presence of claudin 18.2. The economic modelling should include the costs associated with diagnostic testing for claudin 18.2 in people with gastric or gastro-oesophageal junction adenocarcinoma who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
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	**Related Technology Appraisals:** Nivolumab with platinum- and fluoropyrimidine-based chemotherapy for untreated HER2-negative advanced gastric, gastro-oesophageal junction or oesophageal adenocarcinoma (2023). NICE technology appraisals guidance 857. Pembrolizumab with platinum-based chemotherapy for untreated advanced oesophageal cancer (2021). NICE technology appraisals guidance 737. Capecitabine for the treatment of advanced gastric cancer (2010). NICE technology appraisal 191. **Related appraisals in development:** Pembrolizumab with chemotherapy for treating HER2-negative advanced gastric or gastro-oesophageal junction adenocarcinoma. NICE technology appraisals guidance [ID4030]. Publication expected May 2024. **Related Guidelines:** Oesophago-gastric cancer: assessment and management in adults (2018). NICE guideline 83. Last reviewed August 2022. **Related Interventional Procedures:** Laparoscopic gastrectomy for cancer (2008). NICE interventional procedures guidance 269. **Related Quality Standards:** Oesophago-gastric cancer (2018) NICE quality standard 176.
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)

Questions for consultation

Where do you consider zolbetuximab with chemotherapy will fit into the existing care pathway for untreated HER2-negative advanced gastric or gastro-oesophageal junction cancer?

Would zolbetuximab with chemotherapy be a candidate for managed access?

Are the biomarker tests to establish the correct diagnosis of claudin 18.2 positive standard practice in the NHS?

Do you consider that the use of zolbetuximab and chemotherapy can result in any potential 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 committee to take account of these benefits.

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 zolbetuximab 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).

References

1. Cancer Research UK. Stomach cancer incidence statistics. Accessed November 2023

2. Cancer Research UK. Oesophageal cancer incidence statistics. Accessed November 2023.

3. Office for National Statistics (2019). Cancer survival in England - adults diagnosed. Accessed November 2023.