NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Health Technology Evaluation

Zanidatamab with chemotherapy with or without tislelizumab for untreated HER2-positive unresectable advanced gastro-oesophageal adenocarcinoma ID6672

Draft Scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of zanidatamab and chemotherapy with or without tislelizumab for untreated HER2-positive unresectable advanced gastro-oesophageal adenocarcinoma.

Background

Stomach cancer is a malignant tumour arising from cells in the stomach. The most common types of stomach cancer are gastric or gastro-oesophageal junction adenocarcinoma. Gastroesophageal 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. Although these cancers occur in close to each other in the body, they are considered separate conditions.

Stomach cancer is more common in men than women, with approximately 3,476 cases diagnosed in men, and 1,978 cases in women in England in 2023.[1] Around half of all new cases of gastric cancer in the UK are diagnosed in people aged 75 years and over.[2]Over the past few years there has been an increase in incidence of tumours at the junction of the oesophagus and stomach.[1]

Initial symptoms of gastric or gastro-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. The 5-year survival for people diagnosed with stomach cancer between 2016 and 2020 was 23.9%.[4]

The aim of treatment in advanced or metastatic gastric or gastro-oesophageal junction adenocarcinoma is primarily palliative; to prevent progression, extend survival and relieve symptoms with minimal adverse effects.

For people who have untreated HER2-positive metastatic gastric or gastrooesophageal junction adenocarcinoma, that express high levels of HER2 as defined by a positive immunohistochemistry score of 3 (IHC3 positive), NICE technology appraisal 208 recommends trastuzumab in combination with cisplatin and capecitabine or fluorouracil.

NICE technology appraisal 191 recommends capecitabine in combination with a platinum-containing agent as an option for inoperable untreated advanced gastric cancer. Additional treatments are also available for the treatment of HER-negative cancers.

NICE clinical 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.

The technology

Zanidatamab (Ziihera, Jazz Pharmaceuticals) with chemotherapy with or without tislelizumab does not currently have a marketing authorisation for the treatment of advanced HER2-positive gastric or gastroesophageal with locally advanced or metastatic gastroesophageal adenocarcinoma. It is being studied in a clinical trial compared with trastuzumab and chemotherapy.

Zanidatamab has a marketing authorisation for the treatment of adults with unresectable locally advanced or metastatic HER2-positive (IHC3+) biliary tract cancer previously treated with at least one prior line of systemic therapy.

Intervention(s)	Zanidatamab with chemotherapy with or without tislelizumab
Population(s)	People with untreated, unresectable locally advanced or metastatic gastroesophageal adenocarcinoma
Subgroups	If the evidence allows, the following subgroups will be considered: • HER2 status by IHC score • ECOG performance status

Comparators	• Chemotherapy including:
	  ○ doublet treatment with fluorouracil or capecitabine in combination with cisplatin or oxaliplatin
	  ○ triplet treatment with fluorouracil or capecitabine in combination with cisplatin or oxaliplatin plus epirubicin
	• Trastuzumab with cisplatin plus capecitabine or fluorouracil

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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should 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	**Related technology appraisals:** Pembrolizumab with trastuzumab and chemotherapy for untreated locally advanced unresectable or metastatic HER2-positive gastric or gastro-oesophageal junction adenocarcinoma (2024). NICE technology appraisal TA983 Trastuzumab for the treatment of HER-2 positive metastatic gastric cancer (2010). NICE technology appraisal 208 Capecitabine for the treatment of advanced gastric cancer (2010). NICE technology appraisal 191 **Related NICE 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

Questions for consultation

Where do you consider zanidatamab will fit into the existing care pathway for untreated HER2-positive advanced gastro-oesophageal junction cancer?

Have all relevant comparators been included in the draft scope?

Which of the listed comparators would zanidatamab be most likely to displace if it were recommended?

Have all relevant subgroups been included in the draft scope?

Is the clinical trial evidence that could inform this evaluation generalisable to the NHS clinical practice population? If not, could you explain why?

Please select from the following, will zanidatamab be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would zanidatamab be a candidate for managed access?

Do you consider that the use of zanidatamab 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 zanidatamab 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 Highly Specialised Technologies Programme. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation

References

1. NHS Digital. Cancer Registration Statistics, England, 2023. Accessed: April 2026

2. Cancer Research UK. Stomach cancer incidence statistics. Accessed April 2026.

3. Cancer Research UK. Oesophageal cancer incidence statistics. Accessed April 2026

4. NHS England. Digital Cancer Survival in England, cancers diagnosed 2016 to 2020, followed up to 2021. Accessed April 2026.