NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Trastuzumab deruxtecan for treating HER2-positive unresectable or metastatic breast cancer after trastuzumab and a taxane [ID3909]

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of trastuzumab deruxtecan within its marketing authorisation for HER2-positive unresectable or metastatic breast cancer after trastuzumab and a taxane.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. Metastatic breast cancer is when the cancer has spread beyond the breast and nearby lymph nodes to other organs in the body. Unresectable means that the cancer cannot be removed by surgery. Human epidermal growth factor receptor 2 (HER2) is a receptor for a growth factor which occurs naturally in the body. When human epidermal growth factor attaches itself to HER2 receptors on breast cancer cells, it can stimulate the cells to divide and grow. Some breast cancer cells have more HER2 receptors than others. In this case, the tumour is described as being HER2-positive.

In 2017, there were 46,109 new diagnoses of breast cancer in England.[1] There were approximately 3,900 cases of breast cancer in stage IV in the UK in 2018 according to the National Cancer Registration and Analysis Service.[2] In 2017 in England, there were 10,219 deaths from breast cancer.[3] It is estimated that approximately 15-20% of women with breast cancer will have HER2-positive tumours.[4]

Current treatments for advanced breast cancer aim to relieve symptoms, prolong survival and maintain a good quality of life with few adverse events. Treatment depends on whether the cancer cells have particular receptors (hormone receptor status or HER2 status), the extent of the disease and previous treatments.

For people with HER2-positive unresectable or metastatic breast cancer who have not had previous anti-HER2 treatment or chemotherapy for their metastatic disease, NICE technology appraisal guidance 509 recommends pertuzumab with trastuzumab and docetaxel as first line treatment. NICE technology appraisal guidance 34 recommends trastuzumab with paclitaxel as an option for people with tumours expressing HER2 who have not received chemotherapy for metastatic breast cancer and in whom anthracycline is not appropriate. For disease that has progressed after trastuzumab and a taxane, NICE technology appraisal guidance 458 recommends trastuzumab emtansine as an option for treating HER2-positive unresectable, locally advanced or metastatic breast cancer.

The technology

Trastuzumab deruxtecan (Enhertu, Daiichi-Sankyo) is an antibody-drug conjugate which consists of a HER2 antibody with the same amino acid sequence as trastuzumab linked to a chemotherapy agent. It binds to a specific target HER2

expressed on cancer cells and delivers a cytotoxic agent to the cancer cells to kill them. It is administered intravenously.

Trastuzumab deruxtecan does not currently have a marketing authorisation in the UK for treating HER2-positive unresectable or metastatic breast cancer after trastuzumab or a taxane. It has been compared with trastuzumab emtansine in a clinical trial in people with HER2-positive, unresectable or metastatic breast cancer previously treated with trastuzumab and taxane.

Trastuzumab deruxtecan as monotherapy is indicated for the treatment of adult patients with unresectable or metastatic HER2-positive breast cancer who have received two or more prior anti-HER2-based therapies.

Intervention(s)	Trastuzumab deruxtecan
Population(s)	People with HER2-positive unresectable or metastatic breast cancer who have received trastuzumab and a taxane
Comparators	Trastuzumab emtansine
Outcomes	The outcome measures to be considered include: • progression free survival • overall survival • response rate • duration of response • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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. The availability and cost of biosimilar and generic products should be taken into account.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Pertuzumab with trastuzumab and docetaxel for treating HER2-positive breast cancer (2018) NICE technology appraisal guidance 509. Trastuzumab emtansine for treating HER2-positive advanced breast cancer after trastuzumab and a taxane (2017) NICE technology appraisal guidance 458. Guidance on the use of trastuzumab for the treatment of advanced breast cancer (2002) NICE technology appraisal guidance 34 Terminated appraisals None. Appraisals in development (including suspended appraisals) None. Related Guidelines: 'Advanced breast cancer: diagnosis and treatment (2009) NICE guideline CG81 last updated August 2017 Related Quality Standards: Breast cancer (2011, updated 2016) NICE quality standard QS12 Related NICE Pathways: Advanced breast cancer (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) Specialist cancer services (adults) Chapter 105 NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year

	Forward View' Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. Department of Health, Improving Outcomes: A Strategy for Cancer, fourth annual report, Dec 2014

Questions for consultation

Have all relevant comparators for trastuzumab deruxtecan been included in the scope? Which treatments are considered to be established clinical practice in the NHS for HER2-positive unresectable or metastatic breast cancer after trastuzumab and a taxane?

Would trastuzumab deruxtecan be used as an alternative to trastuzumab emtansine?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom trastuzumab deruxtecan is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider trastuzumab deruxtecan will fit into the existing NICE pathway, Advanced breast cancer (2018)?

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 trastuzumab deruxtecan 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 trastuzumab deruxtecan 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 trastuzumab deruxtecan 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Office for National Statistics. Cancer registration statistics, England 2017. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancerregistrationstatisticscancerregistrationstatisticsengland Accessed October 2021

2. National Cancer Registration and Analysis Service (NCRAS). Stage breakdown by CCG 2016. London: Public Health England, 2018. Available from: http://www.ncin.org.uk/view?rid=3604 Accessed October 2021

3. Office for National Statistics. Death Registrations Summary Statistics, England and Wales, 2017. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarri

ages/deaths/datasets/deathregistrationssummarytablesenglandandwalesreferencetables Accessed October 2021

4. Macmillan Cancer Support Receptors for HER2. Available from https://www.macmillan.org.uk/cancer-information-and-support/breast-cancer/receptors-for-breast-cancer Accessed October 2021