NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Trastuzumab deruxtecan for treating HER2-low metastatic or unresectable breast cancer after chemotherapy

Draft scope

Draft remit/evaluation objective

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

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. The cancer is said to be metastatic if it has spread beyond the breast and nearby lymph nodes to other organs in the body such as the bones, liver and lungs. 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. HER2-positive breast cancer is defined as tumours with an immunohistochemistry (IHC) score of 3+ for HER2 staining or IHC score of 2+ with HER2 gene amplification by in situ hybridisation assay. HER2-negative has been re-classified into HER2-low which refers to tumours with an IHC score of 1+ or 2+ without HER2 gene amplification, while HER2-negative refer to tumours with an IHC score of 0, no staining.[1]

In 2019 in England, 48,387 people were diagnosed with breast cancer.[2] About 50% to 55% of all primary breast cancers are HER2-low.[3] About 4% of people with breast cancer in England in 2019 had stage IV (metastatic) breast cancer when they were diagnosed.[4] The 1-year survival rate for people diagnosed at stage IV in England is 66%.[5] Around 35% of people with early or locally advanced disease will progress to metastatic breast cancer in the 10 years following diagnosis.[6]

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

There are currently no recommended treatments for HER2-low metastatic or unresectable breast cancer. NICE clinical guideline 81 (CG81) recommends systemic sequential therapy for most patients with advanced breast cancer having chemotherapy. Where anthracyclines are not suitable (because they are contraindicated or because of prior anthracycline treatment) the sequencing should follow: single-agent docetaxel as a first-line treatment, single-agent vinorelbine or capecitabine as second line treatment, and single-agent capecitabine or vinorelbine (whichever was not used as second line treatment) as third line treatment. In addition, NICE technology appraisal 423 recommends eribulin as an option for treating locally advanced or metastatic breast cancer when it has progressed after at least two chemotherapy regimens.

The technology

Trastuzumab deruxtecan (Enhertu, Daiichi-Sankyo) is an antibody-drug conjugate that has 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-low unresectable or metastatic breast cancer after chemotherapy. It has been compared with chemotherapy comprising capecitabine, eribulin, gemcitabine, paclitaxel or nab-paclitaxel in a clinical trial in people with HER2-low, unresectable or metastatic breast cancer previously treated with chemotherapy.

Trastuzumab deruxtecan as monotherapy is indicated for the treatment of people with unresectable or metastatic HER2-positive breast cancer who have received one or more prior anti-HER2-based regimens.

Intervention(s)	Trastuzumab deruxtecan
Population(s)	People with HER2-low, unresectable or metastatic breast cancer previously treated with chemotherapy
Comparators	For people who have had 1 line of chemotherapy for metastatic disease: • capecitabine • vinorelbine For people who have had 2 or more lines of chemotherapy for metastatic disease: • eribulin
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. 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** Alpelisib with fulvestrant for treating hormone receptor-positive, HER2-negative, PIK3CA-mutated advanced breast cancer (2022). NICE technology appraisal guidance 816. Review date TBC. Abemaciclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy (2021). NICE technology appraisal guidance 725. Review date 2024. Ribociclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy (2021). NICE technology appraisal guidance 687. Review date 2024. Abemaciclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer (2019). NICE technology appraisal guidance 563. Review date 2022. Ribociclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer (2017). NICE technology appraisal guidance 496. Review date TBC. Palbociclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer (2017). NICE technology appraisal guidance 495. Review date TBC.

	Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens (2016). NICE technology appraisal guidance 423. Review date TBC. **Related appraisals in development** Taselisib for previously treated ER-positive, HER2-negative, PIK3CA-positive breast cancer in postmenopausal women. NICE technology appraisal guidance [ID1401]. Publication date to be confirmed. Talazoparib for treating BRCA 1 or 2 mutated advanced breast cancer after prior chemotherapy. NICE technology appraisal guidance [ID1342]. Publication date to be confirmed. **Related Guidelines** Advanced breast cancer: diagnosis and treatment (2009; updated 2017). NICE guideline 81. Review date TBC. Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer (2013; updated 2019). NICE guidance 164. Review date TBC. Improving outcomes in breast cancer (2002; checked 2014). NICE cancer service guideline CSG1. Review date TBC. **Related Quality Standards** Breast cancer (2011; updated 2016) NICE quality standard 12.
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

Are taxanes relevant comparators for people with HER2-low metastatic or unresectable breast cancer after chemotherapy?

Where do you consider trastuzumab deruxtecan will fit into the treatment pathway for HER2-low metastatic or unresectable breast cancer?

Would trastuzumab deruxtecan be a candidate for managed access?

Do you consider that the use of trastuzumab deruxtecan 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 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.

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/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Marchiò C, Annaratone L, Marques A, et al. (2021) Evolving concepts in HER2 evaluation in breast cancer: Heterogeneity, HER2-low carcinomas and beyond. Semin Cancer Biol. 2021 Jul;72:123-135.

2. NHS Digital (2022) Cancer registration statistics, England, 2019. Accessed October 2022.

3. Gampenrieder SP, Rinnerthaler G, Tinchon C, et al. (2021) Landscape of HER2-low metastatic breast cancer (MBC): results from the Austrian AGMT_MBC-Registry. Breast Cancer Res 23, 112.

4. Cancer Research UK (2022) Early diagnosis data hub. Accessed October 2022.

5. Cancer Research UK (2022) Breast cancer survival statistics. Accessed October 2022.

6. Dewis R and Gribbin J (2009) Breast cancer: diagnosis and treatment, an assessment of need. Cardiff: National Collaborating Centre for Cancer. Accessed October 2022.