

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Final scope

**Final remit/evaluation objective**

To appraise the clinical and cost effectiveness of trastuzumab deruxtecan within its marketing authorisation for treating HER2-low unresectable or metastatic 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 status is defined according to the immunohistochemistry (IHC) and in situ hybridisation (ISH) criteria. HER2-positive breast cancer is defined as tumours with an IHC score of 3+ for HER2 staining or IHC score of 2+ with HER2 gene amplification by ISH assay. The introduction of HER2-low re-defined the classification of HER2-negative into: HER2-low which refers to tumours with an IHC score of 1+ or 2+ without HER2 gene amplification, and HER2-negative which refers to tumours with an IHC score of 0, no staining.<sup>1</sup>

In 2019 in England, 48,387 people were diagnosed with breast cancer.<sup>2</sup> About 50% to 55% of all primary breast cancers are HER2-low.<sup>3</sup> About 4% of people with breast cancer in England in 2019 had stage IV (metastatic) breast cancer when they were diagnosed.<sup>4</sup> The 1-year survival rate for people diagnosed at stage IV in England is 66%.<sup>5</sup>

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 unresectable or metastatic 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. [NICE technology appraisal 116](#) recommends gemcitabine with paclitaxel for treating metastatic breast cancer only when docetaxel monotherapy or docetaxel plus capecitabine are also considered appropriate. [NICE technology appraisal 423](#)

Final scope for the evaluation of trastuzumab deruxtecan for treating HER2-low unresectable or metastatic breast cancer after chemotherapy

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recommends eribulin as an option for treating locally advanced or metastatic breast cancer when it has progressed after at least 2 chemotherapy regimens. [NICE technology appraisal 819](#) recommends sacituzumab govitecan as an option for treating unresectable, triple-negative locally advanced or metastatic breast cancer after 2 or more systemic therapies, at least 1 of which was for advanced disease.

**The technology**

Trastuzumab deruxtecan (Enhertu, Daiichi-Sankyo) 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 adults with unresectable or metastatic HER2-positive breast cancer who have received one or more prior anti-HER2-based regimens.

<b>Intervention(s)</b>	Trastuzumab deruxtecan
<b>Population(s)</b>	Adults with HER2-low, unresectable or metastatic breast cancer previously treated with chemotherapy
<b>Comparators</b>	<p>Established clinical management without trastuzumab deruxtecan, including:</p> <ul style="list-style-type: none"> <li>• anthracyclines</li> <li>• capecitabine</li> <li>• platinum therapies</li> <li>• taxanes</li> <li>• vinorelbine</li> </ul> <p>For people who have had 2 or more lines of chemotherapy for metastatic disease:</p> <ul style="list-style-type: none"> <li>• eribulin</li> </ul> <p>For people whose disease is hormone receptor negative:</p> <ul style="list-style-type: none"> <li>• sacituzumab govitecan</li> </ul>

<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• progression free survival</li> <li>• overall survival</li> <li>• response rate</li> <li>• duration of response</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p>
<b>Other considerations</b>	<p>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.</p>
<b>Related NICE recommendations</b>	<p><b>Related Technology Appraisals</b></p> <p><a href="#">Sacituzumab govitecan for treating unresectable triple-negative advanced breast cancer after 2 or more therapies</a> (2022). NICE technology appraisal guidance 819. Review date TBC.</p> <p><a href="#">Alpelisib with fulvestrant for treating hormone receptor-positive, HER2-negative, PIK3CA-mutated advanced breast cancer</a> (2022). NICE technology appraisal guidance 816. Review date TBC.</p> <p><a href="#">Abemaciclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy</a> (2021). NICE technology appraisal guidance 725. Review date 2024.</p> <p><a href="#">Ribociclib with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after</a></p>

	<p><a href="#">endocrine therapy</a> (2021). NICE technology appraisal guidance 687. Review date 2024.</p> <p><a href="#">Abemaciclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer</a> (2019). NICE technology appraisal guidance 563. Review date 2022.</p> <p><a href="#">Ribociclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer</a> (2017). NICE technology appraisal guidance 496. Review date TBC.</p> <p><a href="#">Palbociclib with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer</a> (2017). NICE technology appraisal guidance 495. Review date TBC.</p> <p><a href="#">Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens</a> (2016). NICE technology appraisal guidance 423. Review date TBC.</p> <p><a href="#">Gemcitabine for the treatment of metastatic breast cancer</a> (2007). NICE technology appraisal guidance 116. Static list.</p> <p><b>Related appraisals in development</b></p> <p><a href="#">Taselisib for previously treated ER-positive, HER2-negative, PIK3CA-positive breast cancer in postmenopausal women</a>. NICE technology appraisal guidance [ID1401]. Publication date to be confirmed.</p> <p><a href="#">Talazoparib for treating BRCA 1 or 2 mutated advanced breast cancer after prior chemotherapy</a>. NICE technology appraisal guidance [ID1342]. Publication date to be confirmed.</p> <p><b>Related Guidelines</b></p> <p><a href="#">Advanced breast cancer: diagnosis and treatment</a> (2009; updated 2017). NICE guideline 81. Review date TBC.</p> <p><a href="#">Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer</a> (2013; updated 2019). NICE guidance 164. Review date TBC.</p> <p><a href="#">Improving outcomes in breast cancer</a> (2002; checked 2014). NICE cancer service guideline CSG1. Review date TBC.</p> <p><b>Related Quality Standards</b></p> <p><a href="#">Breast cancer</a> (2011; updated 2016) NICE quality standard 12.</p>
<b>Related National Policy</b>	<p>The NHS Long Term Plan, 2019. <a href="#">NHS Long Term Plan</a></p> <p>NHS England (2018/2019) <a href="#">NHS manual for prescribed specialist services (2018/2019)</a></p>

### 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.