NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Atezolizumab with chemotherapy for neoadjuvant treatment of resectable early or locally advanced invasive triple-negative breast cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of atezolizumab within its marketing authorisation for neoadjuvant treatment of resectable early or locally advanced invasive triple-negative breast cancer.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. It is described as invasive when the cancer cells have grown through the lining of the ducts into the surrounding tissue. Breast cancer is described as 'early' if it is restricted to the breast, or the breast and nearby lymph nodes, and has not spread to other parts of the body (clinical stages 1 and 2). It is described as 'locally advanced' if the cancer is in a large part of the breast (more than 5 cm) but has not spread to other parts of the body (clinical stage 3), and described as 'advanced' if it has spread to other parts of the body and cannot be completely removed by surgery (clinical stage 4).

Over 46,100 people were diagnosed with breast cancer in England in 2017[1] and there were approximately 9,500 deaths from breast cancer in England in the same year.[2] Around 15% of breast cancers are triple-negative breast cancers whereby the cancer cells test negative for oestrogen receptors and progesterone receptors (hormone-receptor-negative cancer) and human epidermal growth factor receptor 2 (HER2-negative cancer)[3].

Triple-negative breast cancer is associated with poor prognosis with high risk of relapse and short progression-free survival (PFS) and overall survival (OS). As many as 50% of patients diagnosed with stage 1 to 3 triple-negative breast cancer experience disease recurrence, and 37% die in the first 5 years after surgery[4]. Depending on the stage of its diagnosis, triple-negative breast cancer can be particularly aggressive, is more likely to recur than other subtypes of breast cancer and is associated with poorer survival. It is diagnosed more frequently in younger women, and it is more frequent amongst women with BRCA1 mutations (a gene on chromosome 17 that normally helps to supress cell growth, which is an inherited gene mutation that may increase the risk of breast cancer)[5].

NICE guideline 101 (NG101) recommends neoadjuvant chemotherapy for people with oestrogen receptor-negative invasive breast cancer as an option to reduce tumour size before surgery. It further recommends consideration of adding a platinum to an anthracycline-containing neoadjuvant chemotherapy regimen for triple-negative invasive breast cancer. Standard chemotherapy options used for neoadjuvant treatment of triple-negative breast cancer include doxorubicin, epirubicin, docetaxel and paclitaxel.

The technology

Atezolizumab (Tecentriq, Roche) is a humanised, anti-programmed cell death ligand-1 (PD-L1) monoclonal antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is delivered by intravenous infusion.

Atezolizumab does not currently have a marketing authorisation in the UK for neoadjuvant treatment of resectable early or locally advanced invasive triple-negative breast cancer. It has been studied in a clinical trial as neoadjuvant treatment in combination with chemotherapy (nab-paclitaxel followed by doxorubicin and cyclophosphamide), compared with chemotherapy and placebo, in adults with previously untreated early or locally advanced triple-negative breast cancer.

Intervention(s)	Neoadjuvant atezolizumab in combination with chemotherapy
Population(s)	Adults with resectable early or locally advanced triple-negative invasive breast cancer
Comparators	Standard neoadjuvant chemotherapy without atezolizumab
Outcomes	The outcome measures to be considered include: • overall survival • disease free survival • surgical outcomes • 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 taken into account. The availability of any managed access arrangement for the intervention 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.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Atezolizumab with nab-paclitaxel for treating PD L1-positive, locally advanced or metastatic, triple-negative breast cancer (2020). NICE Technology Appraisal 639. Review date 2023. Appraisals in development (including suspended appraisals) Pembrolizumab in combination for untreated, locally advanced or metastatic, triple negative breast cancer. NICE technology appraisals guidance [ID1546]. Publication expected April 2021. Pembrolizumab in combination with chemotherapy for neoadjuvant treatment of triple negative breast cancer. NICE technology appraisals guidance [ID1500]. Publication date to be confirmed. Related Guidelines: Early and locally advanced breast cancer: diagnosis and management (2018). NICE guideline 101. Review date to be confirmed. Related Quality Standards: Breast cancer (2011). NICE quality standard 12. Related NICE Pathways: Early and locally advanced breast cancer (2019) 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) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 3 to 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Is the population defined in the scope appropriate?

What proportion of people with early or locally advanced invasive triple-negative breast cancer are given a neoadjuvant chemotherapy regimen that contains both a platinum agent and an anthracycline?

Are the outcomes listed appropriate?

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

Where do you consider atezolizumab will fit into the existing NICE pathway, Early and locally advanced breast cancer?

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 atezolizumab 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 atezolizumab 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 atezolizumab 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).

References

1 Office for National Statistics (2019) Cancer registration statistics, England, 2017. Accessed September 2020.

2 Cancer research UK (2018) Breast cancer mortality statistics. Accessed September 2020.

3 The Institute of Cancer Research (2016) Promising drug target for aggressive 'triple negative' breast cancers identified. Accessed September 2020.

4 Costa RLB and Gradishar WJ. Triple-negative breast cancer: current practice and future directions. Journal of Oncology Practice 13, no. 5 (May 1 2017) 301-303.

5 Couch FJ, Hart SN, Sharma P et al. Inherited mutations in 17 breast cancer susceptibility genes among a large triple-negative breast cancer cohort unselected for family history of breast cancer. Journal of Clinical Oncology 2015;33(4):304-311