NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab in combination for untreated, locally recurrent inoperable or metastatic, triple negative breast cancer [ID1546]

Final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for treating untreated, locally recurrent inoperable or metastatic, triple negative breast cancer.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. Locally recurrent cancer is cancer that has come back after an initial treatment, at or near the same place as the original tumour. Inoperable cancer is cancer that cannot be completely removed by surgery. Metastatic cancer is cancer that has spread to other parts of the body such as the bones, liver, and lungs.

In 2017, there were over 46,100 people diagnosed with breast cancer in England, and there were approximately 9,502 deaths from breast cancer.[1,2] The 5-year survival rate for people with metastatic breast cancer in England is 15%.[3] Approximately 16% of people with invasive breast cancers have locally advanced or metastatic disease when they are diagnosed,[4] and around 35% of people with early or locally advanced disease will progress to metastatic breast cancer.[5]

Around 15% of breast cancers (approximately 7500 cases a year in England and Wales) are triple negative breast cancers whereby the cancer cells test negative for oestrogen and progesterone receptors (hormone receptor negative cancer) and human epidermal growth factor receptor 2 (HER2-negative cancer). It is diagnosed more frequently in younger people and people with BRCA1 mutations (a gene on chromosome 17 that normally helps to suppress cell growth, which is an inherited gene mutation that may increase the risk of breast cancer). Triple negative breast cancer can be particularly aggressive, is more likely to recur than other breast cancers, and is associated with poorer survival.[6]

Chemotherapy is the main treatment for advanced triple negative breast cancer. CG81 recommends single-agent docetaxel as a first-line treatment for advanced breast cancer not suitable for anthracyclines (because it is contraindicated or because of prior anthracycline treatment). It considers combination chemotherapy for people for whom a greater probability of response is important and who understand and are likely to tolerate the additional toxicity. TA639 recommends atezolizumab with nab-paclitaxel for

treating triple-negative, unresectable, locally advanced or metastatic breast cancer in adults whose tumours express PD-L1 at a level of 1% or more and who have not had previous chemotherapy for metastatic disease.

The technology

Pembrolizumab (Keytruda, Merck Sharp & Dohme) is a humanised, anti-programmed cell death 1 (PD-1) antibody involved in the blockade of immune suppression and the subsequent reactivation of anergic T-cells. It is administered intravenously.

Pembrolizumab does not currently have a marketing authorisation in the UK as part of a combination therapy regimen for untreated, locally recurrent inoperable or metastatic triple-negative breast cancer. It has been studied in a clinical trial with chemotherapy (nab-paclitaxel, paclitaxel, or gemcitabine and carboplatin) and compared with placebo with chemotherapy in adults with previously

Intervention(s)	Pembrolizumab (with nab-paclitaxel, paclitaxel, or gemcitabine and carboplatin)
Population(s)	People with previously untreated locally recurrent inoperable or metastatic, triple negative breast cancer
Comparators	• Anthracycline based chemotherapy • Single agent taxane chemotherapy regimens (docetaxel or paclitaxel) For people whose tumours have PD-L1 expression ≥1% • Atezolizumab in combination with nab-paclitaxel
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • 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 be taken into account. If appropriate, the economic modelling should include the costs associated with diagnostic testing for PD-L1 in people with triple negative breast cancer who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 5.9 of the Guide to the Methods of Technology Appraisals'.
Other considerations	If the evidence allows subgroups by degree of PD-L1 expression will be considered. 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, triple-negative, advanced breast cancer (2020) NICE technology guidance 639. Next review: 2023. Gemcitabine for the treatment of metastatic breast cancer (2007) NICE technology appraisal guidance 116. Guidance on static list. Appraisals in development: Atezolizumab with paclitaxel for untreated unresectable advanced triple-negative breast cancer [ID2705] Expected publication date: November 2021 Related Guidelines: Advanced breast cancer: diagnosis and treatment: diagnosis and treatment (2009, updated 2017) NICE

	guideline CG81 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, Manual for prescribed specialised services 2017/18: 105 – Specialist cancer services (adults) Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2, 4 and 5.

References

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

2 Cancer research UK (2019) Breast cancer mortality statistics. Accessed April 2020.

3 Cancer Research UK (2014) Breast cancer survival statistics. Accessed October 2018.

4 Cancer Research UK (2014) Breast cancer incidence statistics. Accessed October 2018.

5 Dewis R and Gribbin J (2009) Breast cancer: diagnosis and treatment, an assessment of need. Cardiff: National Collaborating Centre for Cancer. Accessed October 2018.

6 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.