NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab in combination for untreated, locally advanced or metastatic, triple negative breast cancer ID1546

Draft scope

Draft remit/appraisal objective

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

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. The cancer is said to be 'advanced' if it has spread to other parts of the body such as the bones, liver, and lungs (metastatic cancer), or if it has grown directly into nearby tissues and cannot be completely removed by surgery.

Over 45,900 people were diagnosed with breast cancer in England in 2016, and there were approximately 9,554 deaths from breast cancer in 2016.[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 people who are not suitable for anthracyclines (because they are 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.

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 for untreated, locally advanced or metastatic, triple negative breast cancer. It has been studied in a clinical trial with chemotherapy (nab-paclitaxel, paclitaxel, or gemcitabine/carboplatin) and compared with placebo with chemotherapy in adults with untreated, locally advanced or metastatic, triple negative breast cancer.

Intervention(s)	Pembrolizumab (with chemotherapy)
Population(s)	People with locally advanced or metastatic, triple negative breast cancer who have not received prior chemotherapy for metastatic disease
Comparators	• Anthracycline based chemotherapy • Single agent taxane chemotherapy regimens (docetaxel and 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.

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: Gemcitabine for the treatment of metastatic breast cancer (2007) NICE technology appraisal guidance 116. Guidance on static list. Appraisals in development: Atezolizumab for untreated, locally advanced or metastatic, triple negative, PD-L1 positive breast cancer proposed NICE technology appraisal [ID1522] 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.

Questions for consultation

Have all relevant comparators for pembrolizumab been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for untreated locally advanced or metastatic, triple negative breast cancer?

- What is the standard chemotherapy for untreated advanced triple negative breast cancer?

Are the outcomes listed appropriate?

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

- If the evidence allows should the clinical and cost-effectiveness of pembrolizumab be considered separately for people with and without the PD-L1 biomarker?

Where do you consider pembrolizumab will fit into the existing NICE pathway, 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 pembrolizumab 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 pembrolizumab 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 pembrolizumab 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 (2018) Cancer registration statistics, England, 2016. Accessed October 2018.

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

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.