NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab in combination with chemotherapy for neoadjuvant treatment of triple negative breast cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for the neoadjuvant treatment of triple negative breast cancer.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast.

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] Around 15% of breast cancers (approximately 7500 cases a year in England[3]) are triple negative breast cancers whereby the cancer cells test negative for oestrogen receptors (ER-), progesterone receptors (PR-) and human epidermal growth factor receptor 2 (HER2-).

Triple negative breast cancer is associated with poor diagnosis with high risk of relapse and short progression-free survival (PFS) and overall survival (OS). As many as 50% of patients diagnosed with early-stage TNBC (stages I-III) 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 suppress cell growth, which is an inherited gene mutation that may increase the risk of breast cancer).[5]

Chemotherapy is the main treatment for triple negative breast cancer. NICE guideline 101 (NG81) recommends neoadjuvant chemotherapy that contains both a platinum and an anthracycline is offered for people with triple-negative invasive breast cancer.

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 the neoadjuvant treatment of triple negative breast cancer. It has been studied in a clinical trial in people with newly diagnosed, locally advanced triple negative breast cancer, in combination with chemotherapy in the neoadjuvant setting. It was compared with placebo plus chemotherapy. Within the same clinical trial it was also studied in the adjuvant setting alone, compared with placebo.

Intervention	Neoadjuvant pembrolizumab in combination with chemotherapy
Population	Adults with previously untreated triple negative breast cancer
Comparators	Standard neoadjuvant chemotherapy without pembrolizumab
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 patient access schemes for the intervention or comparator 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 Guidelines: • Early and locally advanced breast cancer: diagnosis and management (2018) NICE clinical guideline NG101 • Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer. (2013, updated 2017) NICE clinical guideline CG164 Related Quality Standards: • Breast cancer (2011, updated 2016) NICE quality standard QS12 Related NICE Pathways: • Early and locally advanced breast cancer NICE pathway • Familial breast cancer NICE pathway http://pathways.nice.org.uk/
Related National Policy	NHS England, Manual for prescribed specialised services 2017/18: 105 – Specialist cancer services (adults) Department of Health, Improving Outcomes: A Strategy for Cancer, fourth annual report, Dec 2014 Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 2, 4 and 5.

Questions for consultation

Is the population defined in the scope appropriate?
What patient population would be normally considered eligible for neoadjuvant therapy in triple negative breast cancer?

Which treatments are considered to be established clinical practice in the NHS for neoadjuvant treatment of triple negative breast cancer?

What neoadjuvant chemotherapies are given when treating 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?

Where do you consider pembrolizumab 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 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 September 2018.

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

3 The Institute of Cancer Research (2016) Promising drug target for aggressive 'triple negative' breast cancers identified. Accessed September 2018.

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