NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pembrolizumab for previously treated metastatic triple negative breast cancer

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of pembrolizumab within its marketing authorisation for previously treated metastatic triple negative breast.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. 'Locally advanced' cancer describes tumours that are larger than 5 cm in size, or have grown into the skin or muscle of the chest or nearby lymph nodes. Metastatic breast cancer describes disease that has spread to another part of the body, such as the bones, liver, or lungs.

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 8000 cases a year in England and Wales) are triple negative breast cancers whereby the cancer cells test negative for oestrogen receptors, progesterone receptors and human epidermal growth factor receptor 2. 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, women with BRCA1 mutations (a gene on chromosome 17 that normally helps to suppress cell growth).[6]

The role of current treatments for metastatic breast cancer is to palliate symptoms, prolong survival and maintain a good quality of life with minimal adverse events. Triple negative breast cancers are difficult to treat because the tumours do not respond to targeted therapies. Chemotherapy is the main treatment for triple negative breast cancer. NICE clinical guideline 81 (CG81) recommends that systemic sequential therapy is offered to the majority of patients with advanced breast cancer who have decided to be treated with chemotherapy. Combination chemotherapy should be considered to treat patients with advanced breast cancer for whom a greater probability of response is important and who understand and are likely to tolerate the additional toxicity.

NICE clinical guideline 81 (CG81) recommends anthracycline-based regimens as the initial treatment, followed by sequential lines of treatment with docetaxel first line followed by capecitabine and vinorelbine as second or third line. Technology appraisal 423 recommends eribulin as an option for treating locally advanced or metastatic breast cancer in adults, only when it has progressed after at least 2 chemotherapy regimens (which may include an anthracycline or a taxane, and capecitabine). Gemcitabine monotherapy and is also used in clinical practice in the UK.

Pembrolizumab is expected to be used in second or third line of treatment.

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 metastatic triple negative breast cancer. It has been studied in clinical trials, compared with capecitabine, eribulin, gemcitabine and vinorelbine in adults with metastatic triple negative breast cancer who have received one or two prior systemic treatments.

Intervention(s)	Pembrolizumab
Population(s)	People with metastatic triple negative breast cancer who have received either one or two prior systematic treatments for metastatic cancer
Comparators	• Docetaxel (if not been used in the first line setting) • Capecitabine • Vinorelbine • Gemcitabine • Eribulin
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 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 Technology Appraisals: • Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens (2016) NICE technology appraisal guidance 423. Review date December 2019 • Eribulin for treating locally advanced or metastatic breast cancer after one prior chemotherapy regimen (2018) Ongoing NICE Technology appraisal. Publication date to be confirmed. Related Guidelines: • 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 • Advanced breast cancer: diagnosis and treatment: diagnosis and treatment (2009, updated 2017) NICE guideline CG81 Guidelines in development • Tumour profiling tests to guide adjuvant chemotherapy decisions in people with breast cancer (update of DG10) NICE diagnostics guidance. Publication expected February 2018

	Related Quality Standards: • Breast cancer (2011, updated 2016) NICE quality standard QS12 Related NICE Pathways: • Advanced breast cancer (2015) NICE pathway • Familial breast cancer (2015) 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

Have all relevant comparators for pembrolizumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for triple negative breast cancer?

Would combination therapies be given for treating triple negative breast cancer at this stage and if so, which?

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, Managing 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 Office for National Statistics (2018) Cancer registration statistics, England, 2016. Accessed January 2018.

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

3 Cancer Research UK (2014) Breast cancer survival statistics. Accessed November 2017.

4 Cancer Research UK (2014) Breast cancer incidence statistics. Accessed November 2017.

5 Dewis R and Gribbin J (2009) Breast cancer: diagnosis and treatment, an assessment of need. Cardiff: National Collaborating Centre for Cancer. Accessed November 2017.

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

