NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Heath Technology Appraisal

Veliparib in combination for treating BRCA-positive, HER2-negative breast advanced cancer ID1404

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of veliparib within its marketing authorisation for treating BRCA-positive, human epidermal growth factor 2 (HER2)-negative, breast advanced 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.

Some people have gene mutations that may increase the risk of breast cancer. Mutated inherited genes that increase the risk of breast cancer include BRCA 1 and 2. About 12% of women in the general population will develop breast cancer at some point during their lives. In contrast, 72% of women who inherit the BRCA 1 mutation and around 69% of women who inherit the BRCA 2 mutation will develop breast cancer by the age of 80 years.[1]

In 2016, there were approximately 45,960 new diagnoses of breast cancer in England.[2] It is estimated that approximately 75-85% of women with breast cancer will have HER2-negative tumours.[3] Approximately 13% of women with breast cancer have advanced disease when they are diagnosed,[4] and around 35% of people with early or locally advanced disease will progress to metastatic breast cancer.[5]

Current treatments for advanced breast cancer aim to relieve symptoms, prolong survival and maintain a good quality of life with minimal adverse events. Treatment depends on whether the cancer cells have HER2 and hormone positive receptors, the extent of the disease, and previous treatments.

NICE clinical guideline 81 recommends sequential therapy for the majority of patients with advanced breast cancer who have decided to be treated with chemotherapy. Single agent docetaxel is first-line treatment for people who are not suitable for anthracyclines (because they are contraindicated or because of prior anthracycline treatment either in the adjuvant or metastatic setting). Combination chemotherapy is considered for people for whom a greater probability of response is important and who understand and are likely to tolerate the additional toxicity. Bevacizumab is not recommended for first-line treatment of metastatic breast cancer (NICE technology appraisals 263 and 214).

Single agent vinorelbine or capecitabine is second-line treatment, and single agent capecitabine or vinorelbine (whichever was not used as second-line treatment) is then used as third-line treatment. NICE technology appraisal 423 recommends eribulin for advanced breast cancer after 2 or more chemotherapy regimens. Eribulin

is not recommended for advanced breast cancer after 1 chemotherapy regimen (NICE technology appraisal 515).

The technology

Veliparib (ABT-888, AbbVie) is a poly adenosine diphosphate-ribose polymerase (PARP) inhibitor. It acts by blocking PARP-1 and PARP-2 which are enzymes involved in the repair of damaged DNA. It is administered orally.

Veliparib does not currently have a marketing authorisation in the UK for BRCA-positive, HER2-negativeadvanced breast cancer. It has been studied in a clinical trial in combination with carboplatin and paclitaxel and compared with placebo in combination with carboplatin and paclitaxel in people with BRCA-positive, HER2-negative advanced breast cancer who received up to two chemotherapy regimens (including up to one platinum therapy in any setting) for advanced disease (including neo/adjuvant chemotherapy if received in the past 6 months). The trial did not include people whose disease has progressed or recurred within 12 months of completing platinum therapy.

Intervention(s)	Veliparib in combination with carboplatin and paclitaxel
Population(s)	People with BRCA-positive, HER-2 negative advanced breast cancer
Comparators	First-line chemotherapy regimens • anthracyclines based chemotherapy (for example fluorouracil with epirubicin and cyclophosphamide [FEC]) • docetaxel monotherapy • paclitaxel monotherapy • combination therapy (for example docetaxel in combination with capecitabine) Second-line chemotherapy regimens • single agent vinorelbine or capecitabine Third-line chemotherapy regimens • single agent capecitabine or vinorelbine (whichever was not used as second-line treatment) • 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 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: Eribulin for treating locally advanced or metastatic breast cancer after one prior chemotherapy regimen (2018) NICE technology appraisal guidance 515. Next review: 2021. Eribulin for treating locally advanced or metastatic breast cancer after 2 or more chemotherapy regimens (2016) NICE technology appraisal guidance 423. Next review: 2019. Bevacizumab in combination with capecitabine for the first-line treatment of metastatic breast cancer (2012) NICE technology appraisal guidance 263. Placed on the static list (2015). Bevacizumab in combination with a taxane for the first-line treatment of metastatic breast cancer (2011) NICE technology appraisal guidance 214. Placed on the static list (2013). Gemcitabine for the treatment of metastatic breast cancer (2007) NICE technology appraisal guidance 116 Placed on the static list (2010). Appraisals in development Olaparib for treating BRCA 1 or 2 mutated metastatic breast cancer after prior chemotherapy [ID1382] Expected publication in July 2020. Talazoparib for treating BRCA 1 or 2 mutated advanced breast cancer after prior chemotherapy [ID1342] Publication

	date to be confirmed. Related Public Health Guidance/Guidelines: Tumour profiling tests to guide adjuvant chemotherapy decisions in people with breast cancer (2018) NICE Diagnostic guidance 34. Next review December 2021. Advanced breast cancer: diagnosis and treatment (2009, updated 2017). NICE guideline CG81. Surveillance check in January 2018. Familial breast cancer: Classification and care of people at risk of familial breast cancer and management of breast cancer and related risks in people with a family history of breast cancer (2013, updated 2017). NICE guideline 164. Surveillance check in January 2018. Related Quality Standards: Breast cancer (2011, updated 2016). NICE quality standard 12. Related NICE Pathways: Advanced breast cancer (2019) NICE Pathway Familial breast cancer (2019) NICE Pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England NHS manual for prescribed specialist services 2018/2019 (2018) 105. Specialist cancer services (adults) Department of Health, NHS Outcomes Framework 2016-2017 (2016) Domains 1 and 2

Questions for consultation

Have all relevant comparators for veliparib in combination with carboplatin and paclitaxel been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for BRCA-positive, HER2-negative advanced breast cancer?
- Should carboplatin with paclitaxel be considered as a relevant comparator for veliparib in combination with carboplatin and paclitaxel?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom veliparib in combination with carboplatin and paclitaxel 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 veliparib be considered separately for people with positive and negative hormone receptor status?

- If the evidence allows, should the clinical and cost-effectiveness of veliparib be considered separately for people who are platinum therapy naive, and those who have previously received platinum therapy?

Where do you consider veliparib in combination with carboplatin and paclitaxel 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 the treatments 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 veliparib 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 veliparib 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 National Cancer Institute (2018). BRCA1 and BRCA2: Cancer risk and genetic testing. Accessed April 2018.

2 Office for National Statistics (2016) Cancer registration statistics, England, 2016. Accessed August 2019.

3 Macmillan. Information and support: HER-2 positive breast cancer. Accessed August 2019.

4 Cancer Research UK (2014) Breast cancer incidence statistics. Accessed August 2019.

6 Dewis R and Gribbin J (2009) Breast cancer: diagnosis and treatment, an assessment of need. Cardiff: National Collaborating Centre for Cancer. Accessed August 2019.