NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal (STA)

Pertuzumab in combination with trastuzumab and docetaxel for the treatment of HER2 positive metastatic or locally recurrent unresectable breast cancer

Thank you for agreeing to give us your views on the technology and the way it should be used in the NHS.

Patients and patient advocates can provide a unique perspective on the technology, which is not typically available from the published literature.

To help you give your views, we have provided a template. The questions are there as prompts to guide you. You do not have to answer every question. Please do not exceed the 8-page limit.

About you

Your name:

Name of your organisation: Breakthrough Breast Cancer

Are you (tick all that apply):

- a patient with the condition for which NICE is considering this technology?
- a carer of a patient with the condition for which NICE is considering this technology?
- **an employee of a patient organisation that represents patients with the condition for which NICE is considering the technology? If so, give your position in the organisation where appropriate (e.g. policy officer, trustee, member, etc)**
- other? (please specify)

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What do patients and/or carers consider to be the advantages and disadvantages of the technology for the condition?

1. Advantages

(a) Please list the specific aspect(s) of the condition that you expect the technology to help with. For each aspect you list please describe, if possible, what difference you expect the technology to make.

This review considers the use of pertuzumab in combination with trastuzumab and docetaxel for the treatment of patients with HER2 positive breast cancer that has advanced or locally recurred. This is a first line indication. Typical treatment for these women would be trastuzumab and docetaxel.

HER2 positive breast cancer is so called due to the presence of the HER2 receptor on the surface of the cancer cells. It is these receptors that are targeted by trastuzumab. However, it is possible for HER2 positive cancer cells to evade destruction by trastuzumab. They do this by forming pairs with other receptors that are members of the HER family and it is these resulting dimers which can ultimately lead to tumour growth and survival. Pertuzumab is able to limit tumour growth and promote cancer cell destruction by blocking the pairing of HER2 family proteins.

The CLEOPATRA trial, that compares trastuzumab plus docetaxel with or without the addition of pertuzumab, demonstrates the latter is effective at limiting tumour progression to a greater extent than is observed for trastuzumab and docetaxel alone. Specifically, it was found that patients who received pertuzumab had a 6.1 month progression free survival benefit compared to patients who received only trastuzumab and docetaxel (18.5 months vs 12.4 months).[1]

It's also expected that treatment with pertuzumab will lead patients to have longer overall survival. Currently, precise data on survival is not available. However, survival findings presented thus far have been positive and it's been reported that pertuzumab reduces risk of death by 34%.[2] When considering patients who received pertuzumab versus patients who did not the following survival data has been reported:[2]
Patients alive after 1 year: 94% vs 89%
Patients alive after 2 years: 81% vs 69%
Patients alive after 3 years: 66% vs 50%

(b) Please list any short-term and/or long-term benefits that patients expect to gain from using the technology. These might include the effect of the technology on:

[1] Baselga *et al*., New England Journal of Medicine. 2012
[2] Swain *et al*. San Antonio Breast Cancer Symposium 2012. Poster P5-18-26

- the course and/or outcome of the condition
- physical symptoms
- pain
- level of disability
- mental health
- quality of life (lifestyle, work, social functioning etc.)
- other quality of life issues not listed above
- other people (for example family, friends, employers)
- other issues not listed above

As described above pertuzumab in combination with trastuzumab and docetaxel can offer patients enhanced progression-free survival compared to treatment with trastuzumab and docetaxel alone. We know patients who have locally recurrent or metastatic breast cancer, for which there is no cure, value treatments that can help them control their cancer and stop it progressing. This can give them a more positive outlook on their treatment regimen and the course of their illness.

Certainly delayed time to disease progression, if associated with few severe side effects of treatment, allows patients with metastatic breast cancer to continue with some aspects of their normal daily life and delays the associated debilitating symptoms and emotional distress that progression may bring.

Specifically, recent data from the CLEOPATRA study showed patients who received pertuzumab had less incidence of constipation and peripheral oedema than those who received trastuzumab and docetaxel alone. The number of patients who experienced these events are as follows (patients who received pertuzumab vs patients who did not):[2]
constipation -101 patients (24.8%) vs 122 patients (30.8%)
peripheral oedema - 63 patients (15.4%) vs 101 patients (25.5%)

2. Disadvantages

Please list any problems with or concerns you have about the technology. Disadvantages might include:

- aspects of the condition that the technology cannot help with or might make worse
- difficulties in taking or using the technology
- side effects (please describe which side effects patients might be willing to accept or tolerate and which would be difficult to accept or tolerate)
- impact on others (for example family, friends, employers)
- financial impact on the patient and/or thier family (for example cost of travel needed to access the technology, or the cost of paying a carer)

In the CLEOPATRA study there were some treatment-related side effects that are more prevalent for patients who received pertuzumab than those who did not. These included febrile neutropenia, diarrhoea, rash and mucosal inflammation. The number of patients on

the CLEOPATRA study who experienced these events are as follows (patients who received pertuzumab vs patients who did not):[2]
febrile neutropenia – 56 patients (13.7%) vs 30 patients (7.6%)
diarrhoea – 278 patients (68.1%) vs 191 patients (48.2%)
rash – 149 (36.5%) vs 95 (24%)
mucosal inflammation - 112 patients (27.5) vs 79 patients (19.9)

What is important to note is that in the CLEOPATRA study most events of febrile neutropenia, diarrhoea and rash occurred only during the period when treatment involved docetaxel. Furthermore, the longer treatment progressed the less likely these adverse events were to occur.

Patients are often willing to accept negative side-effects as part of their treatment so long as they know what to expect and have been given all the necessary information before they begin treatment.[3] Certainly, when negative side-effects are associated with gains in progression-free survival or overall survival many patients are willing to accept these adverse effects.

3. Are there differences in opinion between patients about the usefulness or otherwise of this technology? If so, please describe them.

As highlighted above patients will differ in their willingness to accept risks associated with different treatment regimens. It is therefore very important that all patients are made aware and fully understand the possible risks and benefits of a treatment before making a decision about their treatment options.

4. Are there any groups of patients who might benefit **more** from the technology than others? Are there any groups of patients who might benefit **less** from the technology than others?

Not all breast cancer patients will benefit from this treatment because, as described above, it is only appropriate for the treatment of patients with HER2 positive category of the disease.

[3] Baselga *et al*. ASCO. Abstract 597

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This appraisal considers pertuzumab use as a first line treatment for metastatic disease. Studies on the efficacy of this drug in the adjuvant and neoadjuvant setting are currently ongoing.

Comparing the technology with alternative available treatments or technologies

NICE is interested in your views on how the technology compares with existing treatments for this condition in the UK.

(i) Please list any current standard practice (alternatives if any) used in the UK.

There is only one drug that specifically targets HER2 positive breast cancer and that is trastuzumab (Herceptin). This is given with chemotherapy, typically docetaxel.

(ii) If you think that the new technology has any **advantages** for patients over other current standard practice, please describe them. Advantages might include:
- improvement of the condition overall
- improvement in certain aspects of the condition
- ease of use (for example tablets rather than injection)
- where the technology has to be used (for example at home rather than in hospital)
- side effects (please describe nature and number of problems, frequency, duration, severity etc)

As described above, pertuzumab in combination with trastuzumab and docetaxel gives patients longer progression free survival.

(iii) If you think that the new technology has any **disadvantages** for patients compared with current standard practice, please describe them. Disadvantages might include:
- worsening of the condition overall

- worsening of specific aspects of the condition
- difficulty in use (for example injection rather than tablets)
- where the technology has to be used (for example in hospital rather than at home)
- side effects (for example nature or number of problems, how often, for how long, how severe).

Some adverse events are higher in patients who receive pertuzumab than those who do not. However, these are short-lived. These are described in more detail above.

Research evidence on patient or carer views of the technology

If you are familiar with the evidence base for the technology, please comment on whether patients' experience of using the technology as part of their routine NHS care reflects that observed under clinical trial conditions.

We are unaware of patients first-hand views and experiences of this technology.

Are there any adverse effects that were not apparent in the clinical trials but have come to light since, during routine NHS care?

Not that we are aware.

Are you aware of any research carried out on patient or carer views of the condition or existing treatments that is relevant to an appraisal of this technology? If yes, please provide references to the relevant studies.

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None that we are aware of.

Availability of this technology to patients in the NHS

What key differences, if any, would it make to patients and/or carers if this technology was made available on the NHS?

There is no cure for metastatic breast cancer. It is therefore vital a range of treatment options are made available that can allow patients to control or halt the progression of their disease and enhance survival.

It has been shown pertuzumab in combination with trastuzumab and docetaxel can enhance progression free survival by just over 6 months. This is a convincing and important finding as there is no other comparative treatment regimen that would elicit such a positive response. It would make a huge difference for patients to have access to this drug as we know the ability to control their disease is something of key importance to breast cancer patients and their loved ones. Furthermore, survival data for this drug has so far been positive. If it is shown this drug gives significant benefits in overall survival it is essential NHS patients have access this treatment option.

What implications would it have for patients and/or carers if the technology was **not** made available to patients on the NHS?

Given the high level of efficacy and relatively low toxicity of this treatment regimen we would be very disappointed if pertuzumab was not made available to NHS patients.

This drug represents one of the most positive advancements in the treatment of advanced HER2 positive breast cancer in recent years. If NICE fail to approve this drug it will deny patients access to a treatment with proven benefits. It would be deeply concerning if this were to be the case as it would indicate an uncertain future for the access patients have to breast cancer drugs.

Guidance for this drug is likely to be made available at the end of the year. If the committee decide against the approval of this technology it will most likely be too late for many patients to able to access it via the Cancer Drugs Fund (given that the Cancer Drugs Fund is

due to end at the end of March 2014). This could result in many patients, who are already in the end stages of their lives, being denied a treatment that has the potential to keep them alive for a significant extra number of months. We strongly hope the Committee is able to work with manufacturer and other stakeholders to approve this technology which could give patients extra time to spend with their families and loved ones, something of great importance to all concerned.

Are there groups of patients that have difficulties using the technology?

Equality

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 this appraisal:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/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 lead to recommendations that 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.

N/A

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Other Issues
Please consider here any other issues you would like the Appraisal Committee to consider when appraising this technology.

N/A