

Lapatinib for breast cancer (for use in women with previously treated advanced or metastatic breast cancer)

Appraisal consultation document response

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Joint submission from:

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We are disappointed that the Appraisal Committee is unable to recommend Lapatinib (in combination with capecitabine) for the routine treatment of women with advanced or metastatic breast cancer whose tumours overexpress HER2. However, we acknowledge that there needs to be further robust evidence and welcome the committee's proposal for research comparing lapatinib plus capecitabine with trastuzumab-containing regimens and other chemotherapy regimens used in the advanced or metastatic setting after progression with trastuzumab. We also welcome the call for further research to have a particular emphasis on identifying potential subgroups who may particularly benefit from lapatinib.

i) Do you consider that all of the relevant evidence has been taken into account?

As noted in the Appraisal Consultation Document, we acknowledge that there are issues surrounding insufficient evidence and uncertainties in the data, in particular with regards to the comparators.

We welcome consideration of the patient perspective on acceptance of side effects by people at this stage of disease and would like to see more qualitative evidence regarding patient perspective taken into account for outcome measures.

We would like to see further consideration of the advantages lapatinib could provide in terms of its administration. Patients with metastatic breast cancer commonly have limited treatment options and lapatinib is particularly advantageous as it is administered orally as a tablet. This treatment therefore offers significant benefits to patients' quality of life and does not result in additional hospital visits that may occur with alternative treatment regimens, providing the patient with valuable extra time to spend with friends and family. Administration by tablet form also reduces NHS costs of treatment provision as well as patient costs associated with attending hospital such as parking, travel, time off work and child care. Although non-NHS/PSS costs are not within the perspective the Secretary of State gives to NICE, we believe that these are important factors for the Appraisal Committee to consider.

ii) Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence, and that the preliminary views on the resource impact and implications for the NHS are appropriate?

We share the Appraisal Committee's concern about the pooling of estimates from non-RCT and observational studies. However, there is evidence to show that lapatinib would be an effective treatment option for some patients with metastatic breast cancer as there was a statistically significant improvement in the time to progression and the progression-free survival when compared with capecitabine monotherapy.¹

Evidence suggests that the potential side effects of lapatinib can be controlled resulting in a relatively high quality of life without a reduction in clinical effectiveness.² For people with metastatic breast cancer the importance of this should not be underestimated. Furthermore, as noted in the Appraisal

¹ Section 3.3, p. 6, Appraisal Consultation Document

Evidence from GlaxoSmithKline Clinical Study Report EGF100151: A phase III randomised, open-label, multicenter study comparing GW572016 and capecitabine (Xeloda) versus capecitabine in women with refractory advanced or metastatic breast cancer (03 April 2006 data cut-off)

² Section 4.4, pp. 12-13, Appraisal Consultation Document

Consultation Document, people at this stage of disease are often willing to accept side effects in order to have the benefits of treatment.

We acknowledge that the evidence to support the clinical effectiveness of lapatinib for patients with (or at a high risk of developing) brain metastases is currently unclear. We welcome the EMEA request to have lapatinib-containing therapy further investigated as a beneficial treatment for this sub-group, as patients who develop brain metastases often experience a negative impact on their quality of life.

iii) Do you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS?

It is disappointing to note that the committee is not able to recommend lapatinib (in combination with capecitabine) for the routine treatment of women with advanced or metastatic breast cancer whose tumours overexpress HER2. As patient organisations, we would like to emphasise how important it is to offer patients greater treatment choice.

We support NICE's recommendation that further work needs to be done to clarify the optimum treatment for those whose disease has progressed following treatment on anthracyclines, taxanes and trastuzumab. Lapatinib (with capecitabine) could be an alternative as it targets both the Erb1 and Erb2 receptors. However, to inform what should be regarded as a standard treatment pathway there needs to be evidence comparing this with trastuzumab-containing regimens and other chemotherapy regimens so that clear guidance can be given to clinicians to eliminate the variation that currently exists.

We also welcome the recommendation that in this further research emphasis should be placed on identifying potential subgroups (such as those with brain metastases) who could particularly benefit from this treatment.

We also note that research is being carried out to improve the methods of accurately detecting those patients who will benefit from HER2 (Erb2) receptor targeted treatments. These cancers are often more aggressive and the prognosis for these patients is typically poor. Targeted treatments for these cancers are needed to ensure that we improve the quality of life and survival for this group of patients.

iv) Are there any equality related issues that need special consideration that are not covered in the ACD?

The recent NICE Citizens Council report into QALYs and the severity of illness recommends that NICE and its advisory bodies should take the severity of a disease into account when making decisions.³ We would like to see, in the

³ 'Report on NICE Citizens Council meeting - Quality Adjusted Life Years (QALYs) and the severity of illness, 31 Jan-2 Feb 2008' <http://www.nice.org.uk/media/2C3/31/CCRReportOnQALYsAndSeverity.pdf>

'consideration of the evidence' section, whether the Appraisal Committee was persuaded in this instance to take the severity of this condition into consideration alongside the cost and clinical effectiveness evidence.