



## Health Technology Appraisal

### Lapatinib and trastuzumab in combination with an aromatase inhibitor for the first-line treatment of metastatic hormone receptor positive breast cancer which over-expresses HER2

#### Joint response submitted by:

Breast Cancer Care  
Breakthrough Breast Cancer  
Breast Cancer Campaign  
Macmillan Cancer Support

#### Benefits

Women with metastatic breast cancer are aware of the newer biological treatments and are frustrated with the slow process by which they can be made available in clinical practice. Therefore, Breast Cancer Care, Breakthrough Breast Cancer, Breast Cancer Campaign and Macmillan welcome this appraisal process.

Metastatic breast cancer is not curable and therefore it is essential that effective treatment options to extend progression free survival and/or overall survival are made available to this patient group as quickly as possible.

There has been more awareness of possible interactions or cross talk between HER2 receptors and hormone receptors which may be a primary contributor to the development of resistance to hormone therapy. The following clinical trials have shown efficacy when combining hormone and biological therapies:

- EGF30008 trial - Lapatinib and letrozole overall response rate (ORR) 28% compared to 15% letrozole alone. Lapatinib plus letrozole also showed a statistically significant improvement in progression free survival (PFS) and clinical benefit (responsive or stable disease  $\geq$  6 months) when compared to letrozole plus a placebo.<sup>1</sup>

<sup>1</sup> Johnston S, Pippen J Jr, Pivot X, Lichinitser M, Sadeghi S, Dieras V, Gomez HL, Romieu G, Manikhas A, Kennedy MJ, Press MF, Maltzman J, Florance A, O'Rourke L, Oliva C, Stein S, Pegram M. (2009) 'Lapatinib combined with letrozole versus letrozole and placebo as first-line



- TAnDEM study- Patients receiving Herceptin and Arimidex showed significant improvements in PFS compared to patients receiving Arimidex alone, 4.8 months compared to 2.4 months respectively.<sup>2</sup>
- eLEcTRA trial- Results showed that letrozole plus trastuzumab is superior to letrozole monotherapy.<sup>3</sup>

The possible health benefits and improved clinical outcomes of these treatments outweigh the experience of possible side effects. The opinion of Breast Cancer Care, Macmillan Cancer Support, Breakthrough Breast Cancer and Breast Cancer Campaign is that while the side effects may be difficult for some women, generally they are manageable and do not impact significantly on quality of life. From women using services at Breast Cancer Care there are some discussions about these treatments and side effects via our specialist online, telephone and face to face events. Many women are aware of the cardiac problems of trastuzumab and the side effects of aromatase inhibitors are also a common area of discussion, in particular the arthralgia type symptoms. As lapatinib is a newer drug we find women who have received it to be in a minority but the side effects appear tolerable in comparison to chemotherapy.

Any side effects appear to be outweighed by women's desire to have access to the newer biological therapies, which potentially can increase their progression free survival. It is worth bearing in mind that this treatment would be used under strict clinical supervision which would enable side effects to be managed and treatment to be stopped should they become intolerable.

The treatment combination of lapatinib plus an aromatase inhibitor is also advantageous as it is administered orally. 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

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therapy for postmenopausal hormone receptor-positive metastatic breast cancer.' *Journal of Clinical Oncology*, 27(33): 5538-46.

<sup>2</sup> Kaufman B, Mackey JR, Clemens MR, Bapsy PP, Vaid A, Wardley A, Tjulandin S, Jahn M, Lehle M, Feyereislova A, Révil C, Jones A. (2009) 'Trastuzumab plus anastrozole versus anastrozole alone for the treatment of postmenopausal women with human epidermal growth factor receptor 2-positive, hormone receptor-positive metastatic breast cancer: results from the randomized phase III TAnDEM study.' *Journal of Clinical Oncology*, 27(33): 5529-37.

<sup>3</sup> Huober J, Fasching P, Paepke S, Kubista E, Barsoum M, Wallwiener D. and Harbeck N (2009) 'Letrozole in combination with trastuzumab is superior to letrozole monotherapy as first line treatment in patients with hormone-receptor-positive, HER2- positive metastatic breast cancer (MBC) – results of the eLEcTRA trial.' *Cancer Research* 69 (Meeting Abstract Supplement) 4094.



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.

### **Concerns**

Although this appraisal is welcomed, we are concerned that under the present system unless the research shows a high increase in terms of months of survival, this appraisal may result in a similar situation to previous biological therapies resulting in women only being able to access these drugs via private means, extended access or via the top-up system. Metastatic breast cancer patients who are both hormone receptor positive and HER2 positive already have very limited treatment options. We would like to emphasise the importance of options for effective treatments and therefore our concern at the possibility of neither lapatinib nor trastuzumab being made available in combination with an aromatase inhibitor in this setting.

We would welcome treatments for metastatic breast cancer (when clinically appropriate) to be available as NHS treatments and not restricted to women based on their ability to pay privately in order to reduce variation within this patient population regarding access to the most effective treatments.

We welcome patient access schemes as we recognise that they allow access to medicines that would otherwise be unavailable under the standard NICE appraisal process. In relation to the Tykerb Patient Access Programme (lapatinib for the treatment of women with previously treated advanced or metastatic breast cancer) however, clinicians have expressed concern about the operation of the scheme, such as the time necessary to make submissions to Primary Care Trusts and the tight restrictions on licensed use. It is important to ensure that any additional administrative requirements that may arise are minimised so that potential burdens on the NHS and clinicians are kept to a minimum. We hope that the establishment of the Patient Access Liaison Unit (PASLU) at NICE to support the Department of Health, will continue to work in engaging the NHS in developing improved capacity to manage operational patient access schemes.