Lapatinib or trastuzumab in combination with an aromatase inhibitor for the first-line treatment of metastatic hormone-receptor-positive breast cancer that overexpresses HER2

GlaxoSmithKline welcomes the opportunity to respond to the post-appeal Appraisal Consultation Document (ACD) for lapatinib and trastuzumab in combination with an aromatase inhibitor (NICE 2012).

Our comments on the ACD are structured below in response to the specific questions posed by NICE.

1. **Has all of the relevant evidence been taken into account?**
   GlaxoSmithKline considers that the ACD does take into account the relevant evidence.

2. **Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?**

As previously highlighted in our response to the Assessment Report and the first ACD, (NICE 2011a, NICE 2011b) GlaxoSmithKline (GSK) disagrees with the approach to the economic modelling taken by the Assessment Group, which we believe has an impact on the interpretation of the clinical and cost effectiveness evidence reported in this second ACD.

2.1. Clinical evidence and cost effectiveness

The clinical evidence suggests that lapatinib plus an aromatase inhibitor and trastuzumab plus an aromatase inhibitor are of comparable efficacy and this is acknowledged in section 4.3.3 of the ACD which states:

"The Committee noted that the curves showing the percentages of people alive without progression for the treatment arms were similar to each other between the trials. It understood from clinical specialists that this would be expected in clinical practice (that is, that there would be no difference in the clinical effectiveness of lapatinib and trastuzumab)."

When evaluated on this basis, as in the GSK and Roche economic evaluations, the estimated incremental cost effectiveness ratios (ICERs) for the two are of a similar magnitude (NICE 2010). However the Assessment Group applied different modelling techniques and assumptions to assess the long-term benefit of lapatinib plus letrozole relative to those used for trastuzumab plus anastrozole. This difference in approach was based on the tail end of the progression free survival curves when the number of patients remaining in the clinical trials was small and the data highly uncertain. This approach in the Assessment Group's models resulted in considerably higher ICER estimates for lapatinib plus letrozole compared to trastuzumab plus anastrozole. Since the ICER range

quoted in the summary table of the ACD is based on the manufacturers' base case estimates (lower end of the range) and the Assessment Group base case estimates (upper end of the ICER range) the ICER range for lapatinib plus an aromatase inhibitor is wider and goes higher than that given for the trastuzumab intervention. This may ultimately affect the perception of the relative clinical and cost-effectiveness of the lapatinib and trastuzumab interventions.

Section 4.3.10 of the ACD states:
"The Committee considered that the Assessment Group's estimates were likely to be an overestimate of the most plausible ICER for lapatinib on the basis of previous discussions in which the Committee had agreed that the progression-free survival had been underestimated (section 4.3.8) by the Assessment Group. The Committee discussed the manufacturer's estimate of the ICER. On the basis of previous discussions regarding post-progression survival (section 4.3.9) the Committee concluded that the most plausible ICER would be higher than £74,000 per QALY gained."

Given the comments above regarding the Assessment Group's estimates we suggest that it would be more appropriate in the 'key conclusions' section of the document (page 36) to state the Appraisal Committee's conclusion regarding the ICER for lapatinib rather than the range covered by the Manufacturer and Assessment Group estimates.

2.2. Factual inaccuracies

a) Section 4.3.4 page 25

"The Committee noted that, in TAnDEM, 9 patients had not progressed after 16 months, although in EGF30008 the number was also small (18 patients) and this added to the uncertainty in the estimation of meal survival"

'meal' should be replaced with 'mean'.

b) 'Summary of Appraisal Committee's key conclusions', 'Uncertainties around and plausibility of assumptions and inputs in the economic model', page 38.

"The Committee heard from clinical specialists that there is no reason why treatment with lapatinib prior to progression should result in either a shorter or longer duration of post-progression survival."

This statement also applies to trastuzumab refer to section 4.3.13 of the ACD.

The suggested revision is as follows:

The Committee heard from clinical specialists that there is no reason why treatment with lapatinib or trastuzumab prior to progression should result in either a shorter or longer duration of post-progression survival.

3. Are the provisional recommendations sound and a suitable basis for guidance to the NHS?

As stated above GSK remains concerned about the modelling approach employed by the Assessment group in this MTA and the impact that this may have on the perceived relative cost-effectiveness of the interventions under consideration. However we recognize that addressing this issue is unlikely to affect the provisional recommendation since the ICER estimates are not within the range normally considered cost-effective by NICE.

4. Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of gender, race, disability, age, sexual orientation, religion or belief?

GlaxoSmithKline does not believe that there are any aspects of the recommendation that need particular consideration to ensure that NICE avoid unlawful discrimination.

5. Are there any equality-related issues that need special consideration and are not covered in the appraisal consultation document?

GlaxoSmithKline does not believe that there are equality related issues needing special consideration which have not already been highlighted in our submission.

References

NICE 2010, Breast Cancer (Advanced) - Lapatinib and trastuzumab (1st line): Assessment report for consultation.

http://guidance.nice.org.uk/TA/Wave0/167/AssessmentReport/pdf/English (Accessed 2nd March 2012)

NICE 2011a, Breast cancer (metastatic hormone-receptor) - lapatinib and trastuzumab (with aromatase inhibitor): consultee and commentator comments on the assessment report - GlaxoSmithKlinehttp://www.nice.org.uk/guidance/index.jsp?action=download&o=52162 (Accessed 5th March 2012)

NICE 2011b, Breast cancer (metastatic hormone-receptor) - lapatinib and trastuzumab (with aromatase inhibitor): GlaxoSmithKline comments on the ACD

http://guidance.nice.org.uk/TA/Wave0/167/FAD/CCComment/GlaxoSmithKline/GSKCommentsACD/pdf/English (Accessed 5th March 2012)

NICE 2012, Breast cancer (metastatic hormone-receptor) - lapatinib and trastuzumab (with aromatase inhibitor): appraisal consultation 2.

http://guidance.nice.org.uk/TA/Wave0/167/ACD2 (Accessed 2nd March 2012)