Lapatinib for the treatment of advanced and metastatic breast cancer:

a review of the response to the ACD provided by the manufacturer of Lapatinib

Addendum to report of 7 September 2008

Report by the NICE Decision Support Unit.

6 October 2008

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1 Cost-effectiveness of lapatinib under patient access programme (blended comparator approach)

In response to the Appraisal Consultation Document on lapatinib issued in July 2008, the manufacturer of lapatinib (GSK) submitted an analysis which compared lapatinib plus capecitabine to a 'blended' comparator of several treatment regimens. The blended comparator analysis assumes that capecitabine monotherapy, trastuzumab plus vinorelbine and trastuzumab plus capecitabine are all used routinely in the NHS and could be potentially and appropriately displaced by lapatinib. The data used to inform the proportionate use of each of the treatment regimens was based on data from the IMS oncology analyzer database.

An exploratory analysis was presented in the DSU report ('*Lapatinib for the treatment of advanced and metastatic breast cancer: a review of the response to the ACD provided by the manufacturer of Lapatinib'*, 7 September 2008), which varied the proportions in which each of the different treatment regimens are assumed to be used in the NHS. The cost-effectiveness results ranged from lapatinib costing an extra £60,730 per additional QALY gained compared to the combined comparator, to lapatinib costing an additional £89,545 per additional QALY gained (see Table 11 of DSU report).

The manufacturer of lapatinib also provided NICE with details of proposed 'patient access programme' whereby the costs of up to 12 weeks of lapatinib acquisition costs would be reimbursed by the manufacturer. Table B.1 below shows the results of an exploratory analysis, using the same methods and assumptions as described in section 3.2.3 of the main DSU report cost-effectiveness results, but also including the costs of lapatinib if provided under the proposed 'patient access programme'.

Table B.1: Mean incremental cost-effectiveness ratios (cost per QALY) for lapatinib plus capecitabine compared to alternative weighted comparators (lapatinib provided under terms of patient access programme)

	C-Only	V-only	T-only	T+V	T+C	ICER
GSK IMS data (GSK base case)	44%	0%	0%	27%	29%	£ 16,387
Alternative split of IMS data	40%	6%	3%	25%	26%	£ 19,108
GSK survey data	38%	13%	3%	16%	30%	£ 26,993
Roche data	88%	0%	0%	6%	6%	£ 63,034

Based on the IMS data used in the GSK basecase, the additional cost per QALY gained of lapatinib is below the reported NICE threshold range of £20,000 to £30,000 when compared to a combined comparator. Using the data from the market research survey supplied by GSK the additional cost per QALY of lapatinib is within the threshold range. However, based on the estimates of trastuzumab use supplied by the manufacturer of trastuzumab (Roche Pharmaceuticals), the incremental cost effectiveness ratio (ICER) is much higher than the reported threshold range considered by NICE.

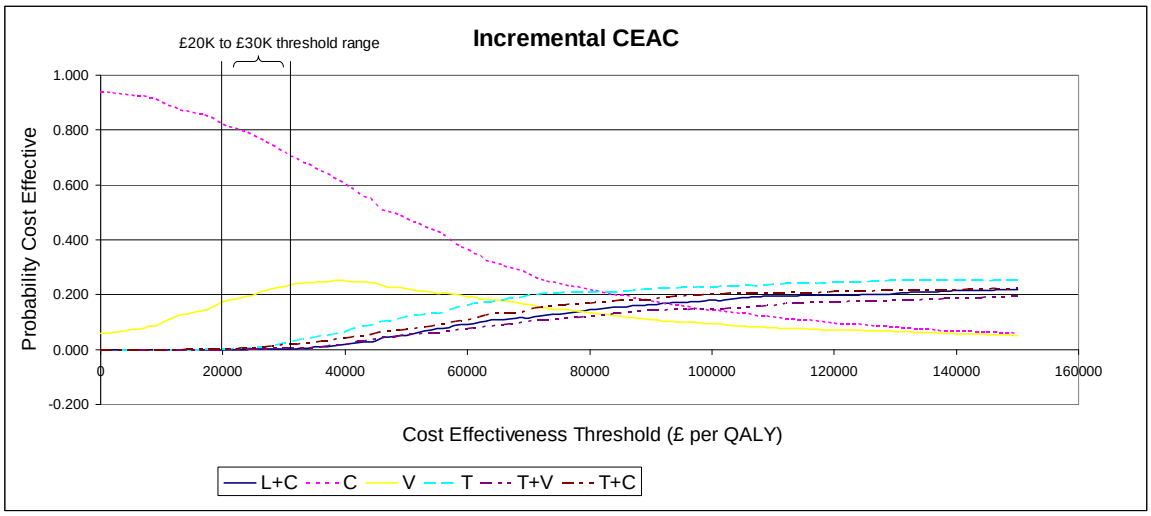
2 Simultaneous comparison of all treatment regimens

In the DSU report (7 September 2008) an incremental analysis was presented that compared all the treatment options in a single analysis. As stated in the DSU report, this approach assumes that it is appropriate to compare lapatinib to a combination of cost-effective and cost-ineffective technologies. The standard approach to considering multiple treatment strategies is to include them in a single incremental analysis as described in Section 3.2.2 of the DSU report. This approach enables the treatment of interest to be compared with the next best alternative, rather than the combined analysis which includes a combination of treatment strategies that may be considered inefficient as well as efficient.

To further illustrate that approach to analysis, cost-effectiveness acceptability curves are presented below. Cost-effectiveness Acceptability Curves (CEACs) allow a clear interpretation of the level of uncertainty in a model, and therefore the probability that a strategy is cost-effective at various thresholds of cost-effectiveness. Figure B.1 presents the cost-effectiveness acceptability curves for the GSK basecase analysis and corresponding to the data presented in Table 8 of the DSU report. Figure B.2 presents the cost-effectiveness acceptability curve for the GSK analysis including the proposed 'patient access programme' and corresponding to the data presented in Table 13 of the DSU report.

For accurate incremental PSA analysis, and the production of incremental CEACs, it is required that the model runs all comparators from the same set of parameter samples to clearly determine the most cost-effective for that sample, and then repeat this a large number of times. However in the case of this model, it was not possible to run PSA on the manufacturer's model simultaneously for all comparators. This means that there may be slight inaccuracies in the probabilities obtained, particularly where the differences in costs and QALYs between treatment options are small, however this is unlikely to affect the general results.

Figure B.1: Cost effectiveness acceptability curves (cost per QALY) for lapatinib plus capecitabine, capecitabine monotherapy, vinorelbine monotherapy and trastuzumab containing regimens



The figure above shows that up to a threshold of approximately £80,000 per additional QALY gained, capecitabine monotherapy is most likely to be the cost effective treatment strategy. Beyond this threshold value, there appears to be little difference in the probability of lapatinib plus capecitabine or any of the trastuzumab-containing regimes being the cost effective treatment option.

From the figure, trastuzumab monotherapy appears to be marginally more likely to be the cost effective treatment strategy for values of the threshold of approximately £80,000 or greater. This may appear to contradict the mean results which showed that lapatinib was on average more effective and more costly than trastuzumab monotherapy with an ICER of £24,227. This may in part be due to noise in the estimates arising from the sampling process which affects the results for this comparison. However, it is also due to the uncertainty around the estimates and the small differences in costs between the two treatment options. The mean cost difference between lapatinib plus capecitabine and trastuzumab monotherapy reported in the submission is £638 and the mean QALY gain is 0.026. Replicating the probabilistic sensitivity analysis for a larger number of iterations (n=5000) the difference between the two treatment strategies becomes even smaller (cost difference £231; QALY gain 0.018).

Figure B.2: Cost effectiveness acceptability curves (cost per QALY) for lapatinib plus capecitabine, capecitabine monotherapy, vinorelbine monotherapy and trastuzumab containing regimens (lapatinib provided under terms of patient access programme)

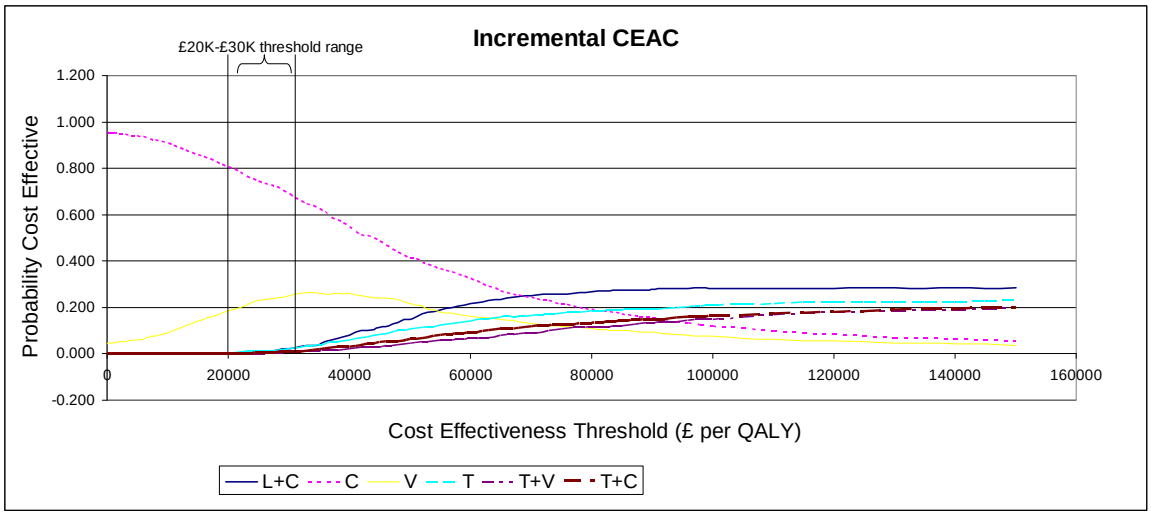


Figure B.2 shows the probability that each treatment is cost effective taking into account the proposed 'patient access programme' for lapatinib. The figure illustrates that up to a value of approximately £70,000 per additional QALY gained, capecitabine monotherapy is most likely to be the cost effective treatment option. If the threshold was higher than this, lapatinib plus capecitabine would be the most likely cost effective, although subject to considerable uncertainty.

Both sets of cost-effectiveness acceptability curves illustrate that capecitabine monotherapy is the most likely to be cost effective at the £20,000 to £30,000 threshold range usually considered by NICE.