Addendum

LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP (LRiG)

Afatinib for treating epidermal growth factor receptor mutation positive locally advanced or metastatic non-small cell lung cancer

This report was commissioned by the NIHR HTA Programme as project number 12/59/01

Revised 7th March 2014

DOES CONTAIN IN CONFIDENCE DATA

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1 INTRODUCTION

This document provides the results of an updated and more accurate estimation of the costs of treating patients with afatinib, erlotinib and gefitinib on the assumption of equivalent efficacy, as an illustrative cost-minimization exercise. It replaces the analysis previously presented as section 5.3.2 of the ERG report.

In addition further details are provided relating to the simple assessment of cost-effectiveness of afatinib vs pemetrexed/cisplatin shown in Appendix 10.4 of the ERG report.

2 COMPARABILITY OF EFFECT AND COST

If it is concluded that the three EGFR-TKI products are of equal effectiveness, the assessment of cost effectiveness reduces to a simple exercise of cost-minimisation, based primarily on the acquisition and administration cost of each drug.

Afatinib, erlotinib and gefitinib are all available as tablets and PAS prices are available for all three products. The PAS for afatinib and erlotinib both comprise [redacted]. The current list price for afatinib is £2023.28 (for 28 days' supply)[102] and that for erlotinib is £1631.53[98] (for 30 days' supply), i.e. daily costs of £72.26 and £54.38 respectively. If the relevant PAS discounts are applied to these prices the daily costs of treatment with afatinib and erlotinib become [redacted]respectively. The PAS for gefitinib is more complex, with a fixed cost of £12,200 being applied only to patients who continue on therapy beyond two months (i.e.on receipt of the third monthly pack).

The assumption of equal effectiveness may be interpreted in two ways:

- Assuming that patients experience the same OS hazard profile as experienced in the LUX-Lung 3 trial, but experience individual PFS hazard profiles drawn from the key clinical trial for each treatment (i.e. IPASS for gefitinib, EURTAC for erlotinib and LUX-Lung 3 for afatinib

- Assuming that patients experience both the same OS and PFS hazard profiles as experienced in the LUX-Lung 3 trial, irrespective of treatment

In each case, treatment is estimated for the duration of PFS until all patients have suffered disease progression or death without progression, using projective models developed by the ERG in this appraisal and in the previous STAs for gefitinib and erlotinib. Data for this

analysis from the afatinib trial is drawn from the non-Asian subgroup which is most relevant to the current appraisal. It should be noted that the estimated costs using these data are conservative compared with both the Asian subgroup and the overall trial population. Table 1 shows the results obtained by both methods and include only the acquisition costs of each treatment and any costs associated with the administration of the relevant PAS.

Table 1 Estimated treatment cost per patient assuming equal effectiveness

Treatment	Equal OS / separate PFS	Equal OS & PFS
Gefitinib	[redacted]	[redacted]
Erlotinib	[redacted]	[redacted]
Afatinib	[redacted]	[redacted]

The derivation of these estimates is detailed below:

Afatinib cost per patient

The estimated cost per patient of treatment with afatinib is calculated as the cost of the total number of packs issued in ten years, based on the estimated number of patient still alive and progression-free at the start of each 28 day period. This number was then multiplied by the PAS discounted cost per pack of afatinib. Progression-free survival was estimated using the ERG's 2-phase parametric model fitted to the LUX-Lung 3 non-Asian subgroup PFS data for those patients randomized to receive afatinib, as shown in Figures 3 & 4 of the ERG report.

Estimated cost of afatinib treatment = 16.50051 * [redacted] = [redacted] **per patient**.

Erlotinib cost per patient

To estimate the cost per patient of treatment with erlotinib, assuming that erlotinib provides **equal efficacy** to afatinib, it is only necessary to substitute the PAS discounted cost of erlotinib in the above calculation as follows:

Estimated cost of erlotinib treatment = 16.50051 * [redacted] = [redacted] **per patient**

To estimate the cost per patient of treatment with erlotinib, assuming that **erlotinib efficacy corresponds to that shown in the EURTAC trial**[1], the PFS Kaplan-Meier results from EURTAC were employed up to 390 days, and then an exponential projection was used to project PFS to 10 years. The exponential formula at time, t (expressed in months from baseline) is

$$\text{Estimated PFS} = \exp(-0.079842 * t / 30.4375 + 0.040353)$$

The estimated cost per patient of treatment with erlotinib is calculated as the cost of the total number of packs issued in ten years, based on the estimated number of patient still alive and progression-free at the start of each 30 day period. This number is then multiplied by the PAS discounted cost per pack of erlotinib.

Estimated cost of erlotinib treatment = 14.1773 * [redacted] = [redacted] **per patient**

Gefitinib cost per patient

To estimate the cost per patient of treatment with gefitinib, assuming that gefitinib provides **equal efficacy** to afatinib, it is necessary to estimate the proportion of afatinib in the LUX-Lung 3 trial who remained alive and progression-free at 60 days. This number is them multiplied by the fixed cost per patient (£12,200) and an administration cost is added for each subsequent pack issued.

Estimated cost of gefitinib treatment = 0.877317 * £12,200 + £523.62 = **£12,069 per patient**

To estimate the cost per patient of treatment with gefitinib, assuming that **gefitinib efficacy corresponds to that shown in the IPASS trial**, the PFS Kaplan-Meier results from IPASS[2] are used to estimate the proportion of patients who remained alive and progression-free at 60 days. This number is them multiplied by the fixed cost per patient (£12,000) and an administration cost is added for each subsequent pack issued.

Estimated cost of gefitinib treatment = 0.946341 * £12,200 + £340.95 = **£11,886 per patient**

3 SUMMARY OF COST TREATMENT COMPARISON

Regardless of the assumed interpretation of ‘equal effectiveness’ it is clear that the cost of treatment is [redacted]. The ranking by treatment cost [redacted] depending on the assumption made.

4 DATA SOURCES FOR APPENDIX 10.4

The simple assessment of cost-effectiveness of afatinib vs pemetrexed/cisplatin shown in Appendix 10.4 of the ERG report involves use of several sources of data drawn from the ERG report and the manufacturer’s model:

Overall survival (OS) is estimated using 2-phase projective trends (Figure 1 & 2 of the ERG report), and Progression-free survival (PFS) using 2-phase projective trends (Figure 3 & 4 of the ERG report) over a 10 year period. Post-progression survival (PPS) is estimated as the difference between OS and PFS.

Health state costs are taken from the manufacturer's model (monthly cost of care in the PFS and PPS states for afatinib patients). Adverse event unit costs are also taken from the manufacturer's model, and applied to the frequency of events reported in the LUX Lung 3 trial. Health state utility values relating to PFS and PD during first-line treatment are used in this assessment, derived from the manufacturer's model.

It must be emphasised that this exercise is only intended to offer a broad indication of the relative position of pemetrexed/cisplatin as an additional comparator to afatinib. The results shown in Tables 66 and 67 of the ERG report would need to be confirmed using a full and comprehensive decision model.

5 REFERENCES

1. Roche Products Ltd. Updated Analysis of ML20650 (EURTAC) (data cut 26 January 2011) Figure 1
2. Mok TS, Wu Y-L, Thongprasert S, et al. Gefitinib or Carboplatin-Paclitaxel in Pulmonary Adenocarcinoma. NEJM 2009; 361(10):947-957