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7th July 2010

Dear Dr Longson

Re: Single technology appraisal (STA) Erlotinib monotherapy for the maintenance treatment of non-small cell lung cancer - Appraisal consultation document

I write on behalf of the NCRI/RCP/RCR/ACP/JCCO with relation to this ACD consultation. We are grateful for the opportunity to respond and would like to make the following comments. Our thanks go to our clinical expert nominee, Dr Clive Mulatero for coordinating the response.

Has all of the relevant evidence been taken into account?

It is noted, given the recent post-hoc sub-group analysis of the SATURN data, that the Committee decided to consider evidence only for those who had stable disease after first-line chemotherapy as outlined in section 3.1. While post-hoc analyses are generally to be regarded with caution, there is a reasonable case for allowing it in this appraisal rather than limiting the review to the intention to treat study population.

It is accepted by most oncologists that the use of pemetrexed as maintenance therapy will decline over time. This is because it has become established as standard first-line therapy in patients with non-squamous NSLCL, as outlined in Section 4.5.

Similarly, there is agreement that there is little use of docetaxel as maintenance therapy. We therefore agree that best supportive care (BSC) is an appropriate comparator for this appraisal, as outlined in Section 4.6.

The Appraisal Committee's opinion that there is a similar relative likelihood of benefit of maintenance erlotinib therapy in a UK population when compared to an Asian population matched for EGFR mutation status as outlined in Section 4.10, is also reasonable.

Overall, our experts believe that the ACD has taken account of all relevant evidence.

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

Despite there having been no patients treated on the SATURN trial following first-line pemetrexed and cisplatin chemotherapy as noted by the Committee in Section 4.10, there is no reason to believe that the potential clinical benefit in this group would be different to those treated with other doublet chemotherapy regimens.

The estimations of wastage made by the ERG as outlined in Section 3.14 seem high given that in standard clinical practice patients are generally provided only enough erlotinib tablets to take until the next response assessment is made.

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

We believe that the decision not to consider the application under the of 'end-of-life advice' rules is surprising and that this decision could be reconsidered by the Committee.

Both the manufacturer and the ERG agreed that the projected overall survival advantage would exceed 3 months, as stated in Section 4.21.

At present, the estimate of 3,000 patients eligible for maintenance erlotinib PA in the UK would represent less than 10 percent of those diagnosed with one of the most common malignancies. In addition, there appears little relevance to the comments on the use of erlotinib in its other licensed indications, other than the fact that the use of maintenance erlotinib would reduce the use of erlotinib as second line treatment for NSCLC.and has not been considered by NICE for use in pancreatic cancer. Similarly, the increase in use of first line gefitinib in EGFR mutation positive patients would reduce the pool of those considered eligible for maintenance erlotinib by over 1,000 PA.

Cost effectiveness models are, by their nature, subjective and assessment of their relative merits is beyond the expertise of our experts. However, given that a significant benefit in progression free survival and overall survival were achieved in the SATURN trial for the stable disease subgroup, were either 'end-of-life advice' rules to apply or the manufacturer able to provide erltonib at below a cost of £50,000 per QALY gained using a model that could be agreed by the Appraisal Committee then the draft guidance should be reviewed.

The draft recommendations were also circulated among our expert groups. In reply, the SOeN of the Royal College of Radiologists commented that they agreed with the Appraisal Committee's decision not to recommend maintenance erlotinib in NSCLC. They felt that in their opinion the majority of the benefit derived from patients actually receiving any second-line of therapy. They added that ensuring that as few as possible 'miss the boat' of receiving a second line of therapy by ensuring careful follow-up after first line therapy should be an ongoing focus of the oncology community.

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?

It is sensible that the Appraisal Committee have commented that there is no evidence to suggest that the UK population would be any less likely than an Asian population to respond to manitenance erlotinib. It should probably be spelled out in Seciton 4.10 that this would hold specifically if the groups were matched for EGFR mutation status.

There do not appear to be any other aspects of the recommendations that would lead to unlawful discrimination.

Yours sincerely

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