Response to the National Institute for Health and Care Excellence's Appraisal Consultation Document on Erlotinib and Gefitinib (post chemotherapy) (rev TA162 and TA175) [ID620]

This response is submitted by Roy Castle Lung Cancer Foundation

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- We are very disappointed that the Appraisal Committee's preliminary decision is not to recommend Erlotinib for EGFR mutation negative patients (Paragraph 1.3), as a second line therapy. This will limit a therapy option which for some years has been standard clinical practice. This would adversely affect future treatment options for many patients affected by this devastating disease.

- We welcome the recommendations that Erlotinib and Gefitinib are available for use after chemotherapy, in EGFR mutation positive patients, in whom there was a delayed confirmation of EGFR mutation status. (Paragraphs 1.1 and 1.2). The number of patients impacted by these recommendations, however, is extremely small.

- We also welcome the recommendation that Erlotinib is available for use after chemotherapy, in EGFR mutation status unknown, as in Paragraph 1.4.

Our comments below are confined to those patients, in whom EGFR mutation status is negative (including those where it is unknown but assumed to be negative). The questions we are asked to comment on are as follows:

i) Has all of the relevant evidence been taken into account?

We do not have any additional evidence. However, we believe the Committee has failed to take sufficient account of the differences between Docetaxel (the only other anti-cancer drug therapy available in this indication) and Erlotinib, as described in section (ii) below. We also do not think that the Committee has addressed the implications of a false negative EGFR mutation test result.

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

Comments: No. There are two particular issues.

Comment 1 : We are deeply concerned that the Appraisal Committee has placed so much emphasis on the TAILOR study, in its assessment, deliberations and decision. Whilst we understand that this represents the only published direct comparison of Docetaxel and Erlotinib, we are very aware that this Italian Study does not reflect practice here in the UK. In the TAILOR Study, Docetaxel is given weekly, whereas in the UK it is administered three weekly. Also, on discussion with clinicians, we note the side effects of Docetaxel reported in this Study are considerably less than we see in practice here (in particular, the febrile neutropenia rate). We do not agree with the conclusions in paragraph 4.3.10 – we are aware that international consensus has concluded that the result of the TAILOR Study should not be used to make decisions about second line therapy in non small cell lung cancer. It is deeply worrying that should this Appraisal Committee decision be finalised, it will ensure a change to standard clinical practice for a significant number of patients, based on a study of questionable relevance to our UK practice,

Comment 2: We believe that the Committee has failed to recognise that Erlotinib is not simply an alternative chemotherapy to Docetaxel, but is a totally different type of therapy, with a very different side effect profile and administration route, making Erlotinib much more acceptable for patients.

- The side effects of Erlotinib are much less significant than Docetaxel – for which severe neutropenia can be life threatening.
- Many patients comment on the 'toxic' nature of Docetaxel – we have heard it referred to as "*doceterrible*" by patients.
- As an oral medication, Erlotinib does not involve repeated day case admissions for iv administration – offering a much greater prospect of treatment closer to home. We are ever mindful that, in the main, this group of patients has a short life expectancy. It is important to ensure that they are able to spend as much time as possible away from the hospital setting.

In this group of patients, at a second line treatment stage, there would be a number, who would reject Docetaxel as a treatment option, based on the side effect profile. Should Erlotinib be denied to this patient group, then no recommended anti-cancer therapy will be available.
Also, for those of borderline fitness for Docetaxel, at present, clinicians can offer oral Erlotinib as a more easily tolerated anti-cancer therapy to this patient group. Should this option be denied, then only the more toxic option will be available.

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

Comments: No, there are three issues.

Comment 1: The previous Technology Appraisal confined the use of Erlotinib in this indication, to patients who were suitable for Docetaxel therapy. As in (ii) above, this Appraisal Committee decision, if finalised, will remove the option of active second line anti-cancer therapy for these patients. As noted in (ii) above, we are deeply concerned that this decision is being made based on a single study of questionable relevance to UK clinical practice. We therefore do not conclude that assumptions and assessments made in coming to this provisional recommendation are sound.

Comment 2: We note that in EGFR negative patients, unfit for Docetaxel, where the comparator is 'best supportive care', both the manufacturer and the Assessment Group, had similar outcomes in their economic assessments – both at just over £50,000 per QALY gained. We note in 4.3.16 that, in this patient group, as in the original Technology Appraisal, it is concluded that Erlotinib is not deemed cost effective. We take this opportunity to remind the Appraisal Committee that, for this patient group, Erlotinib remains the only active anti-cancer therapy option and with this decision, access will continue to be denied.

Comment 3: Across the globe, Erlotinib has become a standard therapy option, in second line, for patients with non small cell lung cancer. Clearly, we do not wish to see the NHS in England deprive lung cancer patients of therapies routinely available elsewhere. Changing the current standard of care for English patients will not only have a negative impact on patients but, will limit English participation in clinical research in this patient group, amongst whom, there is much unmet need.

The patient's viewpoint:

Finally, as a lung cancer charity, we have contact with patients through our social media outlets and on line forums. The public announcement of this Appraisal Committee Document has provoked some of the most comments on any single topic, we have seen. Below are a few quotes:

- *"My mum has been taking Tarceva as a second line treatment since June and she is stable and enjoying life again..... . Apparently, you can, it seems put a price on life... . Mum nearly lost all her will to live. ... Tarceva is saving her life."*

- *"Seems ridiculous when generally, quality of life on Tarceva is good and work possible. While chemo is a killer and I was in hospital with an infection while I was on it and on the sick for four months. ...."*

- *"..... I have been on Tarceva since August 22 2013 and although I am not EGFR positive, it seems to be working, at least keeping it at bay. ....."*

- *"I cannot believe that a decision like this can be made. Yet, if you live in Scotland, it won't affect you. If this is carried out, it will seem like a death sentence when chemo isn't an option. ....."*

- *"..... I was diagnosed in July with Adenocarcinoma T4, EGFR negative. .... Tarceva was recommended after chemo which was not successful. I have been on Tarceva for just over 3 months. The scan a couple of weeks ago showed the tumours have started to shrink. Which was very positive news and I was told I would be on tablets as long as the treatment kept working. I am now very disappointed to read that it may be withdrawn..... . This looks to me like a backward step. ...."*

We welcome the ongoing nature of the appraisal process and hope that the Appraisal Committee will re-consider their decision at the earliest opportunity and also include, within its recommendations, that Erlotinib is also available within the NHS, in the second line setting, as a therapy option for EGFR mutation negative patients.

Jesme Fox
Medical Director
Roy Castle Lung Cancer Foundation
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