Author's response to reviews

Title: Cost-effectiveness analysis of pemetrexed versus docetaxel in the second-line treatment of non-small cell lung cancer in Spain: results for the non-squamous histology population

Authors:

Yumi Asukai (yasukai@uk.imshealth.com)
Amparo Valladares (valladares_maría_amaro@lilly.com)
Carlos Camps (camps_car@gva.es)
Eifiona Wood (ewood@uk.imshealth.com)
Kaisa Taipale (taipale_kaisa@lilly.com)
Jorge Arellano (arellano_jorge@lilly.com)
Alejo Cassinello (cassinello_alejo@lilly.com)
José Antonio Sacristán (sacristan_jose@lilly.com)
Tatiana Dilla (dilla_tatiana@lilly.com)

Version: 2 Date: 18 November 2009

Author's response to reviews: see over
Dear Ms Norton

I write on behalf of our research team to present our revised manuscript in response to peer review comments. We have responded to each of the comments raised by the two peer reviewers in a point-by-point fashion below.

Reviewer 1: From 12 August 2009
- Comparison to erlotinib was not possible due to lack of data available for erlotinib within the non-squamous sub-population. This point is made on page 25 of the revised manuscript.

Reviewer 2: From 13 October 2009 (in the order in which they appear on the reviewer’s report)
- Text has been added in the Model Inputs: Efficacy section to acknowledge that it is post-hoc, and that other trials since have reinforced the treatment-by-histology effect.
- Text has been added on page 22 to explain the cost of treatment for neutropenia.
- Text has been added on page 27 to list the effect of third-line therapy as a limitation of the study.
- Text has been added on page 12 to clarify that hospitalisation costs have been included.
- Text has been added to page 22, 2nd paragraph to explain the 50% reduction in BSC during active therapy.
- Text has been added to page 26, 2nd paragraph (page 25, 2nd paragraph in original manuscript)
- Text has been deleted from the Introduction (3rd paragraph of Introduction in original manuscript)
- The last paragraph of the Introduction has been revised to acknowledge that it is the health care system’s decision makers who would be influenced by economic evaluations; but at the same time we point out that the clinical evidence around different sub-groups that make a product in that indication more cost-effective may also play a role in the clinician’s awareness of the best-suited treatment choice.
- Text added first paragraph, page 7 to clarify that progressing during chemotherapy is possible in the model.
- EMEA defined on page 8, SmPC was already defined on page 5.
- Reference added for survival functions on page 9.
- A sensitivity analysis has been added assuming a proportion of patients are treated at home. The proportion of patients treated at home is based on a reference giving the place of death, and assumptions have been made around the resource use incurred by such patients who receive terminal care at home. The resulting impact on the ICER was an approximately €3,000 increase, still below the €30,000 threshold.
- VAT has been defined on page 11.
- These reports are not published, and therefore should not be included in the reference list according to BMC author guidelines.
- The word anaemia (page 12) is already spelled correctly according to UK Spelling, which the manuscript uses throughout.
- The grade 3/4 fatigue utility was only applicable to a standalone BSC arm (placebo) which was not used in this analysis. Text concerning this has therefore been removed entirely.
- The word tumour (page 12) is already spelled correctly according to UK Spelling, which the manuscript uses throughout.
The Sacristan reference which uses LYG is widely used in Spain as the threshold reference for both QALYs and LYG; however, another reference has been added which discusses QALYs more specifically, and text has been amended.

Text has been added on pages 22-23 to explain why the BSC costs on higher on average for pemetrexed.

Text from the Discussion (paragraph 4 in original manuscript) has been deleted.

Page 23 paragraph 1 and page 24 paragraph 2 wording has been changed.

Page 25, paragraph 2 (paragraph 1 in original): reference has been added for the mentioned cost-utility analysis.

Page 26, last paragraph (page 25, paragraph 3 in original) has been updated to reflect what impact the inclusion of societal perspective may have on the results.

Text from Table 3 has been removed.

In addition, the manuscript has undergone review for copyediting and the discretionary revisions have been taken into account at this time. This review was conducted with an eye towards punctuation, syntax and grammar.

We hereby submit a revised manuscript and one updated figure to reflect the additional new sensitivity analysis (Figure 3).

Thank you for taking the time to consider our submission and we look forward to receiving your reply.

Yours Sincerely,

Yumi Asukai

On behalf of:

M. Amparo Valladares
Carlos Camps
Eifiona Wood
Kaisa Taipale
Jorge Arellano
Alejo Cassinello
José Antonio Sacristán
Tatiana Dilla