Author's response to reviews

Title: Is overexpression of HER-2 a predictor of prognosis in colorectal cancer?

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Author's response to reviews: see over
Editor
BMC-series journals

Re: MS: 6693711082186227. Is overexpression of HER-2 a predictor of outcome in colorectal cancer?

Dear Editor,

Thank you for reviewing my manuscript and considering it for publication in your journal. I have made the amendments to the manuscript to the best of my ability and herewith enclose a summary of these.

Reviewer 1 – A Rishi.

1. I have made the change to the last line of the background as recommended. It now reads ‘……….gene amplification and establish whether overexpression of HER-2 is a predictor of outcome.’

2. I have changed the first line of the materials & methods section on immunohistochemistry to read: ‘staining for Her-2/neu protein was performed on 5 μm (micro-meter) thick slides.’

3. I have modified the legend for figure 2 and incorporated arrows into the image to denote sites of gene amplification as recommended. It now reads: ‘Figure 2 Fluorescence in situ hybridisation of HER-2 gene amplification. Amplified HER-2/neu gene forms multiple scattered signals as illustrated with the white arrows.’

Reviewer 2 – I Zlobec

1. I have recalculated the interobserver of kappa coefficient and have included a Table 2 which demonstrates the components of the calculation. In fact the correct calculation was 0.907 (corrected to 0.91) rather than 0.97 as illustrated in my initial draft. I have amended this in the results section

2. I have changed the title as recommended.

3. This work was performed during the initial 6 months of 2006. The final scoring was completed at that time using the recommended scoring system as per the manufacturer. The pathologists involved on my request have attempted to review these slides but are not in a position to do so as they feel that the slides are no longer assessable at three months after initial staining. It is now almost 3 years. In a clinical scenario if asked to review Her-2 slides on a patient which was stained over three months prior they will not review it and will request a new stain. Furthermore they felt that the slides had not maintained sufficient staining quality to be called as they were three years ago using the recommended scoring system.
The recommendation of the reviewer is certainly a useful and interesting task. Previous papers in this field have adopted the standard scoring technique as recommended by the manufacturer identical to what I have used (References 12, 18, 20 & 24). In order to address this point adequately I would need to repeat the entire study. At present this is not a feasible option on a number of fronts. I have left that institution two and a half years ago and work over 200 miles from it in Dublin. Secondly, the equipment necessary was expensive and I would not be in position to acquire a second grant from Astrazeneca to fund this at present.

If possible I may examine this in the future. In order to do this:
What percentage of positive cells would the reviewer recommend as a cut-off for a positive or negative tumour?
Would one still use the 1+, 2+ and 3+ system?
I have not come across this system in the published literature.

Finally, I have included a line in the methods on ethics: ‘The study was approved by the institutions’ ethics committee.’ and I have also included a section on competing interests.

I hope you can look favourably upon these revisions despite my inability to address point 3 of reviewer 2 sufficiently.

Many thanks
Yours sincerely,

Mr Dara Kavanagh MCh MRCS