Author's response to reviews

Title: A phase II trial of docetaxel and erlotinib as first-line therapy for elderly patients with androgen-independent prostate cancer

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Author's response to reviews: see over
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Dr. J. A. Le Good
Assistant Editor
BMC-series journals

RE: MS 5131998191350760

Dear Dr. Le Good,

Included in this transmission is a minor revision of the above referenced manuscript entitled “A phase II trial of docetaxel and erlotinib as first-line therapy for elderly patients with androgen-independent prostate cancer” submitted for publication in BMC Cancer.

I believe from our initial exchange of emails in March, that a trial registration number is not required for this report.

The comments of the reviewers are directly addressed in this revised manuscript as discussed below.

Dr. Laber’s review focused on the statistical methods and conclusion of our manuscript. We tend to agree with Dr. Laber that the small numbers included in this clinical trial limit definitive conclusions regarding the efficacy of this combination. Specific responses to his queries are below.

1. “It is not clear why the authors chose the current statistical methods…the single agent response rate have been well established between 25-50%”
2. “The conclusion seems misleading…this combination should not be studied any further since it has not <met> the minimum criteria of superiority of the single-agent docetaxel.”

As carefully described in the manuscript, the prospectively defined statistical design was directed at estimating the response rate to this combination. The statistical plan was not changed during the conduct of the trial and the trial was not stopped prematurely. We observed a response rate (95% confidence interval) of 23% (8-45%). Due to the wide confidence intervals in our data, we argue that it is misleading to conclude that this regimen is clearly worse (or better) to that of the single agent. We highlighted this point in the discussion and conclusion sections of the manuscript and argue that any conclusion for “single agent superiority” would need to be supported by an appropriately powered comparison trial.

As data for the docetaxel-erlotinib was not available in AIPC, we choose to include a statement regarding the power of the trial to exclude the null
hypothesis of a response rate of <5%. As we expected greater activity of docetaxel when used as a single agent, this reflects the ability of our study to reject antagonism when erlotinib is used with docetaxel. Subsequent data have shown a response rate of 45% in a general (not elderly) population of AIPC patients treated with single agent docetaxel. Our finding for the docetaxel-erlotinib combination and the focus on elderly patients remain both novel features of our report.

Dr. Rosenberg’s review included two requests for additional data.

1. “The authors do not mention any secondary hormonal manipulations…”
   In response to this requested we have included this data in Table 1 and a description in the text.

2. “Gleason scores should be reported…if available. “
   Unfortunately Gleason score information was not prospectively acquired from all patients at all sites. Therefore, we are not able to provide this data.

Dr. Berry recommended the manuscript be accepted without revision.

In summary, we summit this revised manuscript for publication.

Sincerely,

Mitchell Gross, M.D., Ph.D.