Reviewer's report

Title: Randomized phase II study of pemetrexed/cisplatin with or without axitinib for non-squamous non-small-cell lung cancer

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Reviewer: Thierry Berghmans

Reviewer's report:

Belani et al are presenting a randomised phase II study assessing the effectiveness in adding axitinib to cisplatin-pemetrexed in non squamous NSCLC. The study cannot demonstrate an additional value of axitinib to conventional chemotherapy for PFS, its primary endpoint. This is in agreement with a recent meta-analysis on the role of oral antiangiogenic agents showing an increase in response rate without survival improvement by adding those agents to chemotherapy (Eur J Clin Pharmacol 2013; 69(2):151-9).

Major compulsory revisions

1. The authors are presenting data obtained at different time-point. If all patients completed follow-up on May 18, 2012 then it can be suggested that PFS and safety also can be obtained at this date. Further, if duration of response is available on December 21, 2011, I do not understand why the authors are presenting PFS data obtained 9 months before.

2. The primary endpoint is PFS. Can the authors precise if the follow-up post chemotherapy was similar in the three arms, also for the axitinib maintenance period?

3. In the statistical analysis, it is unclear why the authors are suggesting that “The emphasis of the final analysis was not on hypothesis testing”. I suggest suppressing this confusing sentence. The primary endpoint on which are based the statistical considerations is the subject of the final analysis and secondary objectives have only exploratory value. With the same idea, p values are not for reference only at least for the primary endpoint.

4. As the authors are presenting statistical comparisons for response rate and MDASI, they also have presenting p value for toxicity comparisons among the 3 arms.

5. Figure 1: which was the reason for study termination by the sponsor in 34 cases?

Minor essential revisions

1. The editorial independence from the sponsor has to be explicated.

2. References 4 and 5 are inappropriate when meta-analyses on antiangiogenic agents have been published (one for oral antiangiogenic agents and two for bevacizumab).
3. Can the authors specify if patients with recurrent NSCLC are eligible if not amenable to a curative treatment?

4. It is unclear if patients in the phase I lead-in are included in the analysis of the randomised phase II.

5. The dose adaptation plan must be available, at least in an appendix.

6. How many chemotherapy cycles were planned? 4 or 6?

7. Dates of first and last inclusion have to be provided.

8. More information on the dose intensity in each arms are needed

9. The authors are presenting the investigator-assessed data. Will it say that data were centrally revised? If yes, did it a significant discrepancy between investigator and central assessments?

10. As there is no statistical difference, we cannot conclude that the HR for PFS is favouring axitinib when comparing arms I and III (page 9).

11. Table 2: what means “indeterminate”

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests