Reviewer’s report

Title: A prospective study to investigate the role of serial serum mesothelin in monitoring mesothelioma.

Version: 0 Date: 06 Aug 2017

Reviewer: Giovanni Luca Ceresoli

Reviewer’s report:

The authors report the results of a small mono-institutional study of serum mesothelin (SM) as a marker of disease progression and prognostication during follow up of patients pretreated with chemotherapy or supportive care only for malignant pleural mesothelioma (MPM). The information provided is not new, even though it is focused on the follow-up period. SM is the most studied biomarker of prognostication or treatment response in MPM. Nearly 20 studies have been performed so far, as recently reviewed by the same group (Arnold et al., Br J Cancer 2017).

1. As stated by the authors themselves, heterogeneity regarding patient treatment is a major confounder in prognostic studies. In this study, 18/41 patients were not previously treated with chemotherapy, while 23 received first-line chemo with variable number of cycles of platinum/pemetrexed. However, they were grouped together in the analysis. The authors should discuss this limitation of the series. Furthermore, they should accurately report whether any patient received second-line treatment.

2. 13 patients only had non-epithelioid histology; therefore there are very limited data to state that SM should be tested also in non-epithelioid MPM. The authors should in this referee's opinion tone down their conclusion regarding this issue.

3. According to the authors, SM tracked the clinically reported CT results with greater accuracy than mRECIST CT reports. Moreover, half of follow-up CT in the reported series showed no measurable disease. This supported the use of clinically reported CT for the study analysis. However, this methodology is biased by a high inter- and intra-observer variability, and this represents a sort of "vicious circle". The referee opinion is that any comparison of a proposed biomarker should be with mRECIST, which is now standard in clinical practice and in the research setting.

4. Renal function was not routinely assessed during follow up; however, it is well known that renal function is inversely correlated with serum SM. The authors should acknowledge this bias in their discussion.

5. Reference section is inaccurate and must be checked carefully; for example, references 9-11 are wrong, because they are related to two first-line studies (Castagneto and Nowak) and to a study in which pemetrexed was not re-challenged, but used in patients who were pemetrexed-naive (Jassem).
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

Not relevant to this manuscript

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