Reviewer's report

Title: A randomized, phase 2 study comparing pemetrexed plus best supportive care versus best supportive care as maintenance therapy after first-line treatment with pemetrexed and cisplatin for advanced, non-squamous, non-small cell lung cancer

Version: 1 Date: 26 April 2012

Reviewer: Bryan Schneider

Reviewer's report:

Abstract
1) The median PFS and OS numbers should be stated in the abstract and not use vague terms like “similar”.

Background
1) Would benefit from careful editing with particular focus on English usage and grammar. For example the first sentence ….typically a relatively brief… should be reworded.

2) Second paragraph, most practicing oncologists would know pemetrexed is not platinum.

3) Would expand briefly on why vitamin supplementation is given (to reduce cytopenias)

4) Second paragraph “…..despite more patients receiving additional systemic anticancer therapy……” should be removed as this is misleading and clearly reflects bias of the authors. If you consider the maintenance drug to be active 2nd line therapy, then 100% of the study arm received 2nd line therapy whereas only 67% of the control arm received 2nd line therapy. Furthermore, 51% of the study arm received 3rd line therapy with no data on the number of patients in the control arm that received 3rd line therapy (presumably less though).

Methods
1) Would specify the 6th edition of the TNM staging system was used.

2) Under study treatment, first paragraph, the sentence “Randomized patients who discontinued study treatment without progression…” is unclear. Patients were observed until disease progression?

Results
1) Under patient disposition: “inadequate response” does this mean they progressed during the therapy?

2) Last sentence of the paragraph “Fully completed the study” needs clarification. What defined completion of the study? Disease progression?
3) Progression-free and overall survival: These data need to be presented in a clearer fashion that a practicing oncologist will understand. The median PFS for both arms should be presented in this section. The interpretation of the hazard ratio could then be reviewed in the discussion section if the authors want to explain why the HR is potentially meaningful despite no improvement in the median PFS.

Safety
1) Would avoid vague descriptors like “relatively low”.
2) Death from AE not related to study drug should be presented in the text. What were the specific AEs?

Discussion
1) PARAMOUNT has been published in full manuscript form. Would update the reference. Lancet Oncol 2012;13:247-55
2) Would expand on the clinical relevance of the trial results.
3) The authors note more men and stage IV patients in the maintenance arm as potential reasons for the modest results. However there were only 2 more stage IV patients and 3 more men compared to the control arm. Is this enough to dilute a survival benefit?
4) A large portion of the patients were never-smokers in both arms (about 40%). This population typically has a good prognosis and could have also diluted a small but meaningful benefit with the maintenance pemetrexed. They typically do better with most therapy compared to the current/former smokers.

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