Reviewer's report

Title: Combination chemotherapy of intermittent erlotinib with pemetrexed for pretreated patients with advanced non-small cell lung cancer: a phase I dose-finding study.

Version: 1 Date: 9 April 2012

Reviewer: dr atul sharma

Reviewer's report:

The study is well defined with satisfactory methods and data. However, the following points may be considered for correction-

a) Minor Essential Revisions:
   1. Abstract: background paragraph, 4th line; stylistic suggestion – may be changed to “We investigated the safety of erlotinib in combination with pemetrexed in pretreated NSCLC patients”.
   2. Methods: subtitle ‘Definition of DLT and MTD’ paragraph: 2nd last sentence seems incomplete - grammatical errors/ stylistic correction
   3. Results: patient characteristics paragraph, last sentence, spelling of “Patients” is wrongly printed
      2nd main subtitle, “Safety” is wrongly printed in the subtitle
      ‘Safety, DLT and RD’ subtitle paragraph, 2nd sentence seems incomplete

b) Discretionary Revisions:
   1. In results section, subtitle ‘patient characteristics’, the second line ‘The clinical data were collected up to May 2011 when the antitumor efficacy and the RD were fixed.’ seems incomplete and uninterpretable.
   2. In noting the antitumor efficacy, the time line for attainment of best response and the number of cycles needed before achievement of response (partial response / stable disease) or progressive disease has not been mentioned.
   3. Being a phase I study it looked into the safety and MTD of the regimen. Since there is a high rate of adverse events even though much of them being Gr1/2, a QOL questionnaire would have been more helpful in assessing the impact of AEs on the patient.
   4. Inclusion of pharmacokinetic analysis of the drugs in this phase I study could have permitted assessment of drug–drug interactions and other parameters for comparability.
   5. In the discussion part, the authors have put emphasis on the response rates and survival aspects of their own as well as the other studies and two thirds of
the discussion is devoted to this. This could be avoided as phase I studies cannot definitely comment on efficacy and survival benefits. More importance should be given to the toxicity and safety issues.

6. The authors have not clearly described the limitations of their work.

**Level of interest:** An article whose findings are important to those with closely related research interests

**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