Reviewer's report

Title: Phase II Trial of Sequential Gefitinib After Response to Chemotherapy in Chinese Advanced Non-Small-Cell Lung

Version: Date: 25 September 2006

Reviewer: Martin Reck

Reviewer's report:

General
In this paper the role of a maintenance therapy with the EGFR TKI Gefitinib after front line chemotherapy is evaluated. This approach is of some interest facing the results of four randomised phase III trials which showed no benefit in adding an EGFR TKI to first line chemotherapy in general but which showed a trend towards improvement of efficacy in subgroups which received a maintenance therapy with an EGFR TKI after chemotherapy.
However the small sample size of this trial (33 patients in nearly 2 years) and the design of the study only can offer limited information about this topic which should be addressed in a randomised trial with a sufficient number of patients.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. In this study gefitinib was given after 2-3 cycles of chemotherapy which is no standard of care in chemotherapy of NSCLC with 4-6 cycles of chemotherapy. The reason for this decision and a possible explanation is not reported.
2. A broad range of Second-line, Third-line and Fourth-line patients were included in the study. Due to the differences in efficacy between the different settings no valid conclusion can be drawn by the results of this population.
3. Chemotherapy was not described. No information was given whether a combination chemotherapy was administered, whether a platinum based chemotherapy was used and whether a Cisplatinum or a Carboplatinum based chemotherapy was given. Furthermore no information about the used drug in second/third line therapy was given.
4. A Contradiction appeared between the patient’s characteristics and the description of Treatment assessment.
In the description of the patient’s population the criteria for inclusion was response to prior chemotherapy which was defined as Minor Response or Partial Response of the tumor.
Following the standardized guidelines (WHO and RECIST) for tumor assessment which were correctly described in the section of Treatment assessment no definition of Minor Response as a standardized tumor response can be found in both guidelines.
This contradiction should be clarified because it is impossible to use a response definition for characterizing a study population which is not mentioned in the standardized guidelines.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1. The manuscript and especially the discussion should be shortened.
2. The comparison of tumor response between adenocarcinoma and squamous carcinoma with the estimation of a statistical significance is overdone regarding the small sample size.
3. The report of the disease-related symptom improvement is very short without describing the symptoms which were improved and without explaining the method how the symptom improvement rate was assessed.

Discretionary Revisions (which the author can choose to ignore)
1. The conclusion which was drawn in the discussion that gefitinib after 2-3 cycles of chemotherapy offered a better toxicity profile than chemotherapy for 6 cycles should be evaluated in a randomised trial but it can not be concluded from the results of this trial.
2. The advice to offer Gefitinib only to patients who responded to previous chemotherapy is questionable and this advice is neither validated by data of the clinical trials with the EGFR TKI nor by the results of this trial.
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests.