Reviewer's report

**Title:** Customized Chemotherapy Based on EGFR Mutation Status for Elderly Patients with Advanced Non-Small-Cell Lung Cancer: a phase II trial

**Version:** 1  **Date:** 18 January 2012

**Reviewer:** Adolfo Favaretto

**Reviewer's report:**

Major Compulsory Revisions

This is a phase II study, so unable to answer the question of the better treatment in elderly patients. The patients were allocated to the different treatment based on the presence of mutation in EGFR exons.

The datum of a better disease control with TKI rather than chemotherapy in EGFR positive patients is well known, as well as the better prognosis; elderly patients are not different in this. Moreover TKIs are better tolerated than chemotherapy. So it is nothing new that TKIs are the winners in the competition with chemotherapy as the best treatment in elderly patients with EGFR positive NSCLC.

Minor Essential Revisions

Patient population is not so large for a study in NSCLC.

Moreover the choice of response rate as primary objective of the study about "comparison" of TKI and chemotherapy does not seem the best: TKIs are able to modify the PFS or OS despite minor results in response rate.

Some interest can derive from toxicity analysis and deserves to be better discussed:

- Gefitinib overall optimal tolerance in Elderly patients, and in particular the lack of ILD toxicity (that in the past caused concern, especially in Asian people).

- Conversely, the high rate of drug discontinuation for AEs, attributed to a supposed “Age-related decreases in organ function “ seems unlikely in a population with such restricted entry criteria (see: no prior chemotherapy; ECOG PS 0-1; adequate bone marrow, renal, and hepatic function; and a life expectancy of at least 3 months. Exclusion criteria included symptomatic brain metastasis, any evidence of interstitial lung disease on chest CT examination, other co-existing malignancies or malignancies diagnosed within the last 5 years other than carcinoma in situ, history of congestive heart failure, unstable angina pectoris or recent history (within 6 months) of acute myocardial infarction, uncontrolled cardiac arrhythmia, severe psychiatric illness, or concurrent disease or condition that would have made the patient inappropriate for study participation).

Discretionary Revisions
In the “background”:
- why the Authors define EGFR as a “presumptive” target of gefitinib?
- the statement “Responsiveness to gefitinib is a characteristic of distinct subgroups of patients” is not correct: responses are not restricted to women, non-smokers, adenocarcinoma, Asians.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**
'I declare that I have no competing interests'