Reviewer's report

Title: Cost analysis of erlotinib versus chemotherapy for first-line treatment of non small cell lung cancer (NSCLC) in fit elderly patients participating in a prospective phase 2 study (GFPC 0504)

Version: 1 Date: 6 May 2012

Reviewer: Chun-Ru Chien

Reviewer's report:

General comments:
1. Is the question posed by the authors well defined? Yes
2. Are the methods appropriate and well described? Yes
3. Are the data sound? Almost sound, also see below comment 2 & 5
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? Yes
5. Are the discussion and conclusions well balanced and adequately supported by the data? Yes, but it seems there is less discussion regarding implication of the study finding. Also see comment 6 below.
6. Are limitations of the work clearly stated? Yes
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes
8. Do the title and abstract accurately convey what has been found? Possibly does, please see comments 6 below
9. Is the writing acceptable? Yes

Specific comments:
1. Section “Introduction”, 1st paragraph: “The US National Institutes of Health estimated that $89 billion was spent on cancer care in the United States in 2007, and that the total economic burden reached $219.2 billion when indirect costs associated with lost productivity and death were taken into account. [Ref[”. It would be better to add the reference. (Discretionary Revisions)

2. Section “Patients and methods” subsection “cost”: The authors wrote: “Costs incurred after the second disease progression period were derived from a representative French nationwide sample of 428 patients, using chart review to assess the mean direct monthly cost of the first 18 months of NSCLC patient management (14).” The wording looks a little confusing for the reviewer: >> is cost during the first 18 months representative for cost after 2nd progression? But when the reviewer looked at their Ref 16, the reviewer wondered if the authors used the 5764 USD in table 2 of Ref 16 (3 months average cost without active treatment for distant NSCLC)? Assuming the reference year in Ref 16 was 2004, then the per month cost of palliative care might be (5764/3)\text{*power}
(1.035,7)=2444, which might be close to 2324, the number used in the current manuscript. The above was just the reviewer’s guess. It would be better for the authors to revise the wording to make it less confusing. (Minor Essential Revisions)

3. Section “Patients and methods” subsection “assessing uncertainty”: what is TTP2? The reviewer assumed that was “time to 2nd progression”? (Minor Essential Revisions)

4. Table 3: The reviewer assumed the authors were reporting per patient mean cost here. The reviewer felt it might be better to make it clear such as “Table 3. per patient mean costs in Arm A (erlotinib followed by docetaxel and gemcitabine (DG) and Arm B (DG followed by erlotinib)” (Discretionary Revisions). By the way, the cost of EPO in arm B was typo error? (Minor Essential Revisions)

5. Table 4: The reviewer felt it might be better to use “Table 4: one-way Sensitivity analysis. Arm A: erlotinib followed by docetaxel and gemcitabine (DG); Arm B: DG followed by erlotinib” (Discretionary Revisions). By the way, it would be better to add sensitivity by using lower utility value of patients treated by DG because the utility cited (0.653) was the optimal utility (without side effect) (Table 3 of the Ref 16) (Minor Essential Revisions)

6. Additional comments on implication: to the reviewer’s understanding, “Economic evaluation is almost always structured to compare one intervention with a competing alternative or alternatives. In most cases, the “standard of care” is chosen as the comparator for new interventions;” (CA Cancer J Clin 2008;58: 231–244). The two study arms in this study were erlotinib followed by DG vs. DG followed by erlotinib. From the point of view of implication, the reviewer wondered which was the standard of care and which was the alternative. The reviewer agreed with the authors that the optimal treatment for elderly NSCLC patients might be debated, but the reviewer wondered if DG was the first choice. In the NCCN guideline, “Single agent therapy or platinum based combinations are a reasonable alternatives in PS 2 patients of the elderly” (2011v3, slide NSCL-F 1-3). On the contrary, 1st line erlotinib might the considered as the standard of care, but only limited to EGFR mutant patients (NCCN 2011v3, slide NSCL-F 1-3). It would be great for the authors to perform a subgroup analysis limiting to only EGFR mutant patient (either by real genetic tests or just clinically orientated like the strategy used in the IPASS study (N Engl J Med 2009;361: 947-57)). If the results still showed high incremental cost-effectiveness ratio of DG followed by erlotinib vs erlotinib followed by DG, then we can concluded that when compared to the current standard of care (Erlotinib) for these either clinically or genetically selected EGFR mutant patients, 1st line DG was not cost-effective. Before the subgroup analyses results available, the reviewer felt the title of the current manuscript might be better as “Cost analysis of erlotinib versus chemotherapy for first-line treatment of non small cell lung cancer (NSCLC) in fit but genetically unselected elderly patients participating in a prospective phase 2 study (GFPC 0504)” (Discretionary Revisions)

**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