Reviewer's report

Title: Chemotherapy Followed by Surgery versus Surgery Alone in Patients with Oesophageal Squamous Cell Carcinoma: Long-term Results of a Randomized Controlled Trial

Version: 1 Date: 21 October 2010

Reviewer: Pierre G Thirion

Reviewer's report:

A. General Comments

1. Is the question posed by the authors well defined? Yes
2. Are the methods appropriate and well described? Yes, evidence level 1
3. Are the data sound? Yes
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, with modifications (see below)
6. Are limitations of the work clearly stated? Yes, with modifications (see below)
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes, with modifications (see below)
8. Do the title and abstract accurately convey what has been found? Yes
9. Is the writing acceptable? Yes

B. Specific comments and suggested modifications

1- Title: Discretionary Revision: I would suggest adding the term “resectable” (oesophageal) should be added, to better define the patients group

2- Abstract: Minor Essential Revision: In the material and method paragraph it should be clear that the primary end-point was OS, and the secondary end-points were DFS, pattern of failure and toxicity. The polymorphism study is an unplanned subgroup analysis

Minor Essential Revision: In the results paragraph, the pattern of failure results should be mentioned (as the end-point is mention in material and methods).
Minor Essential Revision: In the results paragraph, as the polymorphism profile is significant in multivariate analysis, the mention of the results of univariate analysis is not relevant. It should be clear that the polymorphism analysis was only conducted on the chemotherapy patients.

Minor Essential Revision: In the conclusion paragraph, given that the polymorphism analysis is an unplanned subgroup analysis, the conclusion should be more careful, e.g. Polymorphism profile could be associated with better clinical outcome..

3- Main text:

3-1 Introduction:

Discretionary Revision: Authors should give a comprehensive list of the potential rational of pre-operative chemotherapy: tumour shrinkage, increase R0 resection,

Major Compulsory Revision: Authors should provide evidences supporting the rational and reliability of polymorphism study on post-chemotherapy pathology

3-2 Results

Minor Essential Revision: Clarify the resectability criteria

Major Compulsory Revision: In the statistical method paragraph: the authors need to explain why with a sample size of 160, more than 160 patients were included

Discretionary Revision: The landmark method is used because of the difference in overall treatment duration

Minor Essential Revision: Table 1: age description should use median, min and max (not mean)

Major Compulsory Revision: Table 1: No comment in the text on the fact that 1 patient had a cervical tumour location (= not eligible)

Minor Essential Revision: pCR rate is 7% (in chemo group) and not 3%

Minor Essential Revision: Clarification is needed regarding postoperative morbidity figures. As I understand the table the number of patients experiencing at least one post-operative morbidity event is the same in the 2 groups, but lung toxicity was a more frequent event with preoperative chemotherapy. If so it should be clear if the number or percents mentioned are patients or events

Minor Essential Revision: Resection status. Is there a difference in R2 resection rate?

3-3 Discussion
The authors clearly identify the limitation of the study

Minor Essential Revision:: The authors should compare their results with other major preoperative chemotherapy trials (EO2 and Kelsen), both on the similarity and difference. Several aspects should be looked at:

1- Compliance (low in chemo arm) and toxicity
2- Postoperative morbidity and mortality
3- The clinical and pathological response rate
4- OS and DFS benefit
5- Pattern of relapse

Discretionary Revision: The authors should make better use of the data on the pattern of relapse in R0 resection patients. The latter results of the present study is one of its strength, and is hypothesis generating to explain the effect of preoperative chemotherapy (no effect on metastatic disease) and is in keeping with the UK experience

Major Compulsory Revision: the comments on chemo-radiation should be removed as they are not in keeping with the subject of the study and not supported by the present results

Level of interest: An article of outstanding merit and interest in its field

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'