Reviewer’s report

Title: Survival endpoints in colorectal cancer. The effect of second primary other cancer on disease free survival.

Version: 1 Date: 31 May 2011

Reviewer: Simone Mathoulin-Pelissier

Reviewer’s report:

1. Is the question posed by the authors well defined?
Partly

1.1 Context and definitions of survival endpoints are described; however, an explanation for focussing on second primary other cancer is missing. Moreover the sentence “to understand the effect…” is very short to be understood the meaning of “the effect”. Finally, in the result section, we discovered additional results: multivariate analyses, other endpoints (all according to the paper of Punt).

1.2 The question of survival endpoints is important in cancer trials and this study is an observational study: I think that these particular settings (endpoint and survival definition in observational studies) should be developed

Major Compulsory Revisions

1.3 Many sentences in introduction section were unclear; please give more explanations
“meta-analyses are not reliable”: with individual data?
“Selection of survival endpoints depends on the study question and the information available”

Minor

2. Are the methods appropriate and well described?
Partly

2.1 The methods section should describe where/how the data were abstracted.
We have no information about the whole-population sample related to the data source of “these population based study” (cf. abstract): cancer register or only XX hospitals or both and we cannot understand the role of “Clinical database for colorectal cancer”. More details about data information collected (and presented in the results and table 3) and the modality to evaluate quality of data (particularly on survival endpoints) are necessary.

Major Compulsory Revisions

2.2. The “statistical method” section defined the events and censure according to Punt paper; we have one table (table 1, table 1 is also present in introduction section) and the text. The text is not in accordance with the table (for instance:
DFS without distant metastasis? does the term “recurrence” means? (locoregional and distant); it necessary to explain it and the different terms using on the table and in the text are confusing. Moreover, censure mentioned in the text is different according to some items (no censure for DFS but for other survival endpoints?)

Minor

2.3 We discover a Cox model without explanation related to an objective in this study.

Minor

2.4 On page 7 last paragraph: the first sentence should moved in the method section (with and without second primary other cancers)

Minor

3. Are the data sound?

3.1 The lack of information on population representativeness, data abstraction methods, and record completeness is a weakness.

Major Compulsory Revisions

3.2 Moreover we have results without any explanation in the methods section (multivariate analysis for instance)

Minor

3.3 On page 6, the authors state that they “compare the survival curves of different endpoints”: Why? How? Please explain in method section.

I have the same concern about the analysis by stages: Why? How?

Finally, could you explain why you used all survival endpoints (and survival curves) in these figures related to you main objective?

Major Compulsory Revisions

3.4 In the first paragraph of the discussion section, the authors state that the effect of inclusion (or not) of second primary other cancers have an effect on multivariate analyses (“significant changes in the HR for emergency operation”) without any explanation to understand these result.

Minor

We have no elements for the study limits in the discussion section.

Major Compulsory Revisions

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?

These items are not mentioned in the manuscript.

The discussion section, as it currently stands, gives the reader no sense that this research contributes to the literature about what has already been done. There is
a need to better clarifying the author’s contribution with this study
Minor

6. Are limitations of the work clearly stated?
The authors don't describe any limitations as such
Major Compulsory Revisions

7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
The authors could track the literature about “observational studies and endpoints definition” and “about prognostic factors for CRC with curative intention” (particularly to more understand their results with DFS endpoint)
Discretionary

8. Do the title and abstract accurately convey what has been found?
No.
The abstract results should better describe the population and mains results
The title and the abstract conclusion do not reflect fully the purpose and results of this paper
Minor

9. Is the writing acceptable?
There could be more lively writing of the discussion, which is rather opaque at present.
Discretionary

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

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

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

'I declare that I have no competing interests'