Reviewer’s report

Title: Phase II clinical trial of sorafenib plus interferon-alpha treatment for patients with metastatic renal cell carcinoma in Japan

Version: 2

Date: 14 March 2015

Reviewer: Sebastiano Buti

Reviewer’s report:

The work by Eto M et al. is well written, generally clear and of interest in the field of metastatic renal cell carcinoma treatment.

Minor Essential Revisions.

1. In the abstract, Results, lines 70-73: these sentences are not clear when read before the following full text of the manuscript.

2. Only IFN-alpha tolerant patients were enrolled in this trial: this could be a cause of bias. To comment in the discussion section.

3. Background page 6, lines 92-93: to add also the development of resistance as limitation of new agents

4. Page 8, lines 119-121: to better clarify why the authors specify the possible adjuvant IFN therapy...It is not a standard!! How many patients received this therapy?

5. Page 8, lines 123-124: to clarify what means “could tolerate IFN treatment”....grade 3 toxicity? At discretion of clinician?

6. Page 9, line 151: to specify that 12,4% of response rate was in patient after failed at least 1 prior cytokine containing therapy in the Akaza study.

7. Page 11, lines 167-168: high rates of adverse events and patient’s request as reasons for treatment discontinuation: this data should be discussed in the discussion section.

8. Page 12, toxicity: to add mood depression rate (patients treated with IFN!, it is a relevant toxicity to report).

9. Page 13, line 197: the response rate 26% is inferior (not compatible) compared to response rate of Bracarda study.


11. Page 14 line 226: yes but to specify that in the Bracarda study the complete responses were only in the arm with 9 MUI x 3 of IFN.
Major Compulsory Revisions

1. Page 12, lines 179-180: the OS was excellent but it may be strongly influenced by treatments administered after protocol drugs. To add in the discussion that also the post-treatment is a relevant potential factor that influenced the good OS.

2. Page 13, lines 200-202: To add in the discussion that also the distribution of prognostic factors could be a relevant potential factor that influenced the good OS. The patient distribution according to motzer score or Heng score should be added to the results section.

3. Page 15, line 250: a study comparing sorafenib alone versus a combination of sorafenib with an optimal dose of IFN-a would be not ethical because the standard globally accepted first line is sunitinib or pazopanib or bevacizumab + interferon, not sorafenib.

4. Page 16, line 259: the word “may” should be changed in “could” and to add “in the future” at the end of the sentence.

5. Table 1: to add prognostic score (MSKCC or Heng or both). To add subsequent treatments.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

No competing interests to declare.