Reviewer’s report

Title: Bevacizumab plus irinotecan improves both response and survival in patients with recurrent malignant glioma: a survival gain analysis

Version: 1 Date: 13 February 2010

Reviewer: Antonis Valachis

Reviewer’s report:

This paper evaluates the role of bevacizumab plus irinotecan in recurrent malignant glioma by performing a survival gain meta-analysis of phase II studies. The authors have come up with the conclusion that the combination of those two regimens can improve the survival in patients with recurrent malignant glioma.

The question the authors are trying to answer is important but the data that are available in literature are from uncontrolled phase II studies. We cannot drive any implication for these uncontrolled data. In my opinion the data from this survival gain analysis are extremely weak, despite the statistical significance.

I would suggest the authors to change the form of the paper to a systematic review (with all the phase II studies) and to include the pooled analysis data as secondary outcomes, underscoring that we cannot use these data to give any firm conclusion. Randomized controlled trial is mandatory.

Specific comments

Major Compulsory Revisions:

1. The title of the article should be change. The data are too weak to support the title: “Bevacizumab plus irinotecan improves both response and survival in patients with recurrent malignant glioma: a survival gain analysis”.

2. Abstract. In the conclusion of the abstract, the authors stated that: "The combination of bevacizumab and irinotecan can improve outcome in patients with recurrent malignant glioma". The verb “can” is too “strong” for the available uncontrolled data and should be change.

3. Introduction section. In the last paragraph the authors stated: “Here we describe a second application of the same mathematical technology and its expansion to also analyze response to describe results from several phase II trials of bevacizumab and irinotecan for recurrent HGG”. This sentence should change so as to state more clear the aim of the study.

4. Table 1 and 2 are important for the systematic review and authors should include those in the manuscript and they should pay more attention to discuss those tables in Results section.

5. In Results section the authors describe the toxicity of the combination bevacizumab plus irinotecan but they do not include any numbers. A table with all the toxicities reported in phase II trials is necessary so as to justify the paragraphs in the Discussion section in which the authors adequately discuss
that the toxicities may be a drawback for this combination of drugs.

Discretionary Revisions:
1. In both table 1 and 2, the list of the phase II studies are not in a specific order. Authors can choose a specific order to present their tables: number of patients included (e.g. from the study with the highest to the study with the lowest number of patients included or vice versa) or alphabetical order etc.

Minor Essential Revisions:
1. Page 7. Results section. Overall survival of the database subsection. “…13.7 months (SD 11.1 months).” There is a need for a space between 11.1 and months.
3. Page 17. Figure Legends. Figure 3.
   After the “… irinotecan group (b)” comma should be replaced with full stop.
4. Page 17. Figure Legends. Figure 4.
   After the “… irinotecan group (b)” comma should be replaced with full stop.
5. Reference section. Please write the full citation of references 9 and 23.
6. Reference section. Please correct the citation of reference 25.

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.