Reviewer's report

Title: Multicenter phase II study of weekly docetaxel, cisplatin, and S-1 (TPS) induction chemotherapy in locally advanced squamous cell cancer of the head and neck

Version: 2 Date: 23 September 2012

Reviewer: Voichita Bar Ad

Reviewer's report:

Dear Sirs,

I read with great interest the review by Woo Kyuan Bae, “Multicenter phase II study of weekly docetaxel, cisplatin, and S-1 (TPS) induction chemotherapy in locally advanced squamous cell cancer of the head and neck”.

Please, find below my suggestions:

- Page 2, Abstract “Conclusions” paragraph. Please, reformulate the conclusions focusing on the response rate and toxicity. I suggest deleting the part “Although most patients had stage IV HNSCC”.

- Page 2, “Keywords” paragraph. I suggest reformulating the keywords, for example “Head and neck squamous cell carcinoma, induction chemotherapy, cisplatin-based regimen containing S-1 and weekly docetaxel”. I would suggest that the term “cisplatin-based induction chemotherapy regimen containing S-1 and weekly docetaxel” will also apply to the title.

- Page 3, paragraph 1. “Surgery coupled with radiotherapy and/or chemotherapy is considered the standard treatment for those patients...” It is unclear from the context for which group of patients is this approach considered the standard of care. Please, re-formulate the paragraph.

- Page 3, paragraph 3. It should be emphasized that in the context of increased loco-regional control, associated with CCRT for locoregionally HNSCC, an increased number of patients will experience systemic failure. Please, re-phrase and add the relevant references from the literature.

- Page 3, paragraph 3. Please, add the references to support your statement “Induction chemotherapy with cisplatin nd fluorouracil (PF) has failed to demonstrate any survival benefit”.

- Page 3, paragraph 3 It should be emphasized that the phase III studies discussed in this paragraph compared PF with TPF before RT or CCRT, meaning compared two different systemic induction chemotherapy regimen before RT or CCRT, and NOT induction chemotherapy before RT or CCRT versus CCRT upfront.

- Page 3, last paragraph and Page 4 first paragraph, I suggest changing the terms used. Instead of “TPF (three-weekly docetaxel regimen)” I suggest using the term “TPF regimen containing docetaxel delivered every three weeks”, in
order to avoid any confusion. And, instead of “weekly docetaxel” regimen I suggest using the term “TPF regimen containing weekly docetaxel”

- Page 4, paragraph 4. Please, explain the reason the oral cavity HNSCC cases were excluded from the trial.

- Page 6, paragraph 1. Please, give details about RT technique (3DCRT vs IMRT); the treatment-related toxicity may be influenced by the RT technique.

- Page 6, paragraph 2. Please, give more details about the time from the end of CCRT, when the PET/CT was performed. How was the PET/CT information used for additional treatment evaluation (eg. neck dissection).

- Page 8, paragraph 1. The RT interruption rate was high. Please, explain and compare your data with the previously published literature. The RT interruptions were shown to significantly impact the long term outcome. Please, discuss. Was PEG-tube used for these patients?

- Page 8, paragraph 2. You reported a case of asphyxia, as not related to the treatment. Which was the case of this patients’s death? Which was the primary tumor site in this case? Was a tracheostomy performed in this case or other cases? Was fatal aspiration pneumonia ruled out?

- Page 9, paragraph 1. I suggest that you used the term of locoregional recurrence only for the patients achieving a CR after the whole treatment package and having a period of disease free survival. For the patients who did not achieve a CR, most probably a persistent disease was present. Please, report separately these two categories of patients and give details about the local or regional or loco-regional persistent disease rate.

- Page 9, paragraph 4. The discussion should be focused on HNSCC not NSCLC; please, re-formulate the paragraph. Please, discuss the relevant literature with the use of S-1 and weekly docetaxel for HNSCC

- Page 11, paragraph 1. Please, give the references to support your statement “…we believe that HPV status may not affect the response”

- Page 11, paragraph 1. With a median follow up of 30.3 months, it is expected that also the late treatment related toxicities are reported (eg. PEG-tube dependence at 6-months, 1-year, and 2-years, etc)

- Please, revise the grammar for the entire manuscript.

Thank you,

Level of interest: An article of importance in its field

Quality of written English: Not suitable for publication unless extensively edited

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.