Author's response to reviews

**Title:** IMRT and carbon ion boost for malignant salivary gland tumors: interim analysis of the COSMIC trial

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**Version:** 2 **Date:** 9 March 2012

**Author's response to reviews:** see over
To whom it may concern

09th March 2012

Dear editors,

We would also like to take the opportunity to thank the reviewers for their friendly and constructive comments. We have tried to incorporate their advice in our revision of the text and hope this has helped to improve the manuscript. Please find our point-by-point-reply attached.

Thank you for reviewing this manuscript for publication.

Yours sincerely,

Alexandra Jensen, MD MSc (on behalf of the authors)
Reviewer's report

Title: IMRT and carbon ion boost for malignant salivary gland tumors: interim analysis of the COSMIC trial

Version: 1 Date: 23 January 2012

Reviewer: Ralf Schneider

Reviewer's report:
This is the first analysis of the prospective phase II trial COSMIC. A carbon ion boost followed by IMRT was performed in a patient cohort with malignant salivary gland tumors. Primary endpoint of this trial is mucositis grade III. Secondary endpoints are local control, progression-free survival and toxicity.
The authors included 29 patients into the analysis. 16 patients underwent radiation therapy after R2-resection and 13 patients after R1-resection. The sentences and the text body are well constructed. The figures and tables give a good overview and are an appropriate addition to the manuscript.
Thank you!

Minor essential revisions (spelling):
Target volumes / dose prescription and constraints
…dose to any point within the spinal cord should not exceed 5045 Gy…
Treatment planning and radiotherapy
…magnetically deflected so as to scan each of these iso-energetic…
Daily images guidance consists of orthogonal……
Agreed and corrected

Patients with salivary gland tumors are difficult to treat. High biologic effective doses to extensive volumes frequently involving base of skull are recommended to control efficiently the tumor. High grade acute toxicities are expected in these patients. Nevertheless the presented interim analysis is promising because of moderate acute toxicities especially when taking into account the significant higher RBEs of carbon ions.

Minor essential revisions:
Data with regards to secondary endpoints of this trial are very preliminary after such a short follow-up time. This should be stated in the conclusions in a more clear way.
Agreed and clarified

According to the COSMIC protocol < 5% of CTV 1 or CTV 2 should receive < 90%.
Was it feasible to observe these parameters for the treatment plans of the 29 patients? The authors should present the results.
Agreed and commented

I recommend the article for publishing after minor essential revisions, even though median follow-up time was only 3 months for this relatively small cohort and a longer follow-up period with a higher number of patients will be needed.
Reviewer's report

**Title:** IMRT and carbon ion boost for malignant salivary gland tumors: interim analysis of the COSMIC trial

**Version:** 1 **Date:** 6 March 2012

**Reviewer:** Robert Semrau

**Reviewer's report:**

The manuscript reports first toxicity and efficacy results of combined IMRT and carbon ion boost for inoperable or incomplete or marginally resected adenoid cystic carcinomas and other malignant salivary gland tumors. The question of the trial is important and follows the aim to set up clinical trials of carbon ion radiotherapy to collect clinical data for cancer types that will potentially benefit from heavy ion therapy.

Thank you!

The methods are mostly well described, patient selection is clearly shown. Toxicity results are thoroughly reported. However, frequency of toxicity analysis during treatment is not described and needs to be added. **Agreed and included**

Minor changes in English writing should be considered

- Page 7: ":" should not exceed 5045" – please clarify. **We are sorry, this is a typing error which has escaped our attention.**

- Discussion: “particle therapy has changed patients outlook in this rare condition”: patient’s prognosis seems more appropriate
- The term “complete resection” in the manuscript is misleading when also used for R1-resected patients. Please clarify.
- Page 15: “profit from combined treatment”, benefit seems more appropriate  **Agreed and corrected**

The work is suitable for publication

**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