Reviewer's report

**Title:** Pre-radiotherapy plasma carotenoids and markers of oxidative stress are associated with survival in head and neck squamous cell carcinoma patients: a prospective study

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**Reviewer:** Hans Christiansen

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In the manuscript „Pre-radiotherapy plasma carotenoids and markers of oxidative stress are associated with survival in head and neck squamous cell carcinoma patients: a prospective study”, Amrit Kaur Sakhi et al. show that biomarkers of antioxidants and oxidative stress are unfavourable in HNSCC patients compared to healthy controls. The results are interesting and worthy of consideration. However, some points have to be addressed as follows:

1. In the “Methods”-section, the authors state that post-operative radiation doses ranged from 50 to 70 Gy. The patients treated with radiotherapy alone received 70 Gy except one that received 60 Gy in a hyperfractionated regimen. First, it would be interesting to know more details about the radiotherapy treatment (Fractionation? Radiation technique? How many patients received what total dose?). Second, what was the reason for 70 Gy in the adjuvant situation? Third, was chemotherapy given concomitantly (If yes: How many patients? Which chemotherapy regimens were used? Had the application of chemotherapy an influence on the data presented? If no: Why did the patients did not receive concomitant chemotherapy?)?

2. Moreover, it is stated in the “Methods”-section that 100 control individuals were selected from a separate study. First, why did the authors chose 100 controls compared to 78 patients in the study (Why did they not chose another 78 controls or recruited until they also had 100 patients in the study?)? Second, is it possible to know something more about the control individuals (What kind of study did they participate in? Did they have any relevant co-morbidities? Can the study by Anette Karlsen be cited (in the manuscript given as “personal communication”)?

3. In the “Results”-section, it is said that total tocopherols were also close significantly lower in patients as compared to healthy controls (first paragraph). A statistical analysis is either significant (p<0.05) or not – so what does “close significantly” mean. The authors are asked to change the sentence accordingly (for example: Total tocopherols showed a trend…).

4. Finally, all results are given for all patients together. In some paragraphs, it is stated that in multivariate analyses adjusting for treatment the results remained significantly – do the authors mean that there was no difference between the patients treated in the adjuvant situation and the patients treated by primary
radiotherapy in curative intent? The authors are asked to state more clearly whether there was a difference between these two groups concerning the study results or not. At least the clinical outcome (survival data) should be mentioned separately for these two groups as data potentially considerably differ. Furthermore, loco-regional control is also an important factor in HNSCC and should additionally be given. Probably, an additional table showing overall survival, loco-regional control, and progression-free survival for all patients, patients treated in the adjuvant setting, and patients treated with primary radiotherapy would be helpful to give an overview to the reader.

**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:**

I declare that I have no competing interests.