Reviewer's report

Title: Intra-arterial carboplatin induction chemotherapy followed by surgery and/or radiotherapy for advanced head and neck cancer: single-center five-year results

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Reviewer: C. René Leemans

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General
This paper describes updated follow-up and adds six more patients to an initial report published in 2002 (European Archives of Oto-Rhino-Laryngology). It is a well written and well structured paper that deserves publication, but I have several points that need to be clarified and/or maybe discussed more thoroughly in the text.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
First of all this seems to be a phase I/II study, that was a dose finding study as well as a toxicity and feasibility study and also evaluated efficacy. The message of the manuscript is that similar response rates and survival data can be generated by this schedule using carboplatin, instead of the more widely used cisplatin, while having less toxicity. Secondly, intra-arterial administration was used under the premise that this would be more effective compared to intravenous usage. The protocol used neoadjuvant chemotherapy, which currently seems to be a little bit more en vogue in the context of being followed by concurrent chemo radiation (but not radiation therapy alone). Another finding of this study was that complete response to induction chemotherapy heralded a better outcome than lesser response rates. This feature however, remains a little elusive in the discussion and I am not quite sure whether the authors presently consider a partial response rate in their present protocol an indication for surgery, but I have the impression they do. This needs to be clarified in more detail.

As always with mono-institutional phase I/II studies results may be less favourable if performed in a multi-institutional setting, or compared in a randomised clinical trial. I find no mentioning of these items in the discussion but really think they deserve due attention to bring everything in proper perspective and I would certainly urge the authors to continue their work preferably in a phase III trial, that compares their present IA-schedule to an intravenous schedule using similar chemotherapy. The authors maybe aware that the initial data from the so called RADPLAT scheme when they were compared to intravenous usage of cisplatin proved to be equally effective as was reported by the group from the Netherlands Cancer Institute at the recent Head and Neck Conference in Chicago.

Some T1- of T2-patients were submitted to this protocol, because of poor general condition, or at the patients request. This needs further clarification as patients request is usually not an inclusion criteria for a protocol and furthermore being able to fulfil this protocol, I would think that the patients needed to have a certain general condition, at least in order to undergo major surgery in case of less than a partial response to be included in the first place.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
There are some minor essential revisions that I would like to suggest, such as the usage of the word organ preservation in the title and text since I believe this is the setting that the authors used their schedule, and this may be quite different from unresectable patients. In their background section the authors quote the paper by Pignon et al., and cite an absolute improvement of 8% in 5-years survival by using concurrent chemoradiation. Firs, I am not quite sure what this means in the setting that they were using chemotherapy since they used it in the neoadjuvant setting, which according to Pignon et al. has not proven to be of an advantage to the patients. Secondly, I wonder whether the toxic deaths are incorporated in the absolute gain percentage. Furthermore, the authors cite other workers that induction chemotherapy reduces micrometastases and downstages cancer in 90% of the cases. I find these remarks very optimistic and would like to suggest the authors to rephrase this a little bit since this is merely speculation and the downstaging effect, if it occurs at all, may not have clinical benefit.
What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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