Reviewer's report

Title: Long term survival following the detection of circulating tumour cells in head and neck squamous cell carcinoma

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Reviewer: Daniel Zips

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Distant metastasis (DM) is an important issue in the treatment of head and neck cancer (HNC). Predictive assays to identify patients with a high risk of developing distant metastasis for therapeutic interventions are of great scientific and clinical interest. In the presented study a method to detect circulating tumour cells (CTC) in the peripheral blood was established for HNC. The preclinical experiments indicate that immunomagnetic enrichment and subsequent RT-PCR of four marker genes allows the detection of CTC with a sensitivity of about 5 CTC/ml. This method was then used in a group of 16 patients who underwent surgery for advanced HNC. No correlations of CTC with clinical or outcome parameters were found. The authors conclude that this method to detect CTC should be explored further.

Major compulsory revision/major limitation

The aim of the study is not well defined. Whereas in large parts of the methods and results section a series of logically structured pre-clinical experiments are described, the authors emphasize (title, abstract, conclusion) the clinical validation. However, the clinical results do not allow concluding on the predictive value of the described assay. This is because of the small sample size, large heterogeneity in clinical and treatment parameters and insufficient consideration of established predictors of DM. The latter would require a multivariate analysis to establish whether or not CTC independently predict for DM which appears not reasonable with the given sample size. Three patients developed local and distant failure. Distinction of primary and secondary DM is difficult or even impossible which adds further uncertainty to the presented data. The conclusion made by the authors that this method should be explored further is not adequately supported by the data. The assay showed an intermediate sensitivity and a very low specificity to predict for DM. In this group of patients the results don’t look very promising and it is difficult to understand why the assay should be further explored. It appears that the study is rather testing feasibility but not a hypothesis. If so, data should be presented and discussed accordingly.

Minor point:

The author’s statement that improved loco-regional control by optimized radiotherapy had not resulted in improved overall survival (page 3, first para) is not entirely correct (compare e.g. Bernier et al., N Engl J Med 2004;350:1945-52).
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

'I declare that I have no competing interests'