**Reviewer’s report**

**Title:** HPV positive, wild type TP53, and p16 overexpression correlate with the absence of residual tumors after chemoradiotherapy in anal squamous cell carcinoma.

**Version:** 0  **Date:** 04 Nov 2017

**Reviewer:** Veronika Vymetalkova

**Reviewer’s report:**

Soares et al. aimed to investigate the impact of HPV and HIV status, p16 expression level and TP53 mutations as predictors of the local response in Squamous Cell Carcinoma (SCC) of the anal canal.

Although it is engaged in interesting topic, it has several important discrepancies which should be addressed. Also, the novelty of the study is limited. All above do together interact in a way that makes publication less relevant. I clearly suggest major revision.

There are some typos and grammatical errors in the manuscript—therefore the final version would benefit from proofreading by native speaker or language editor.

**Introduction:**

The study lacks novelty, there are several other articles already published on all factors analyzed in this study. For this reason, the rationale for focusing on analyzed parameters should be more elaborated.

Second paragraph in introduction is not clear, please reformulate it.

When mention gene, use italics.

**Material methods:**

Why only 6 months follow up was analyzed, if patients have been recruited since 2003, it is beneficial if authors could analyze also overall and recurrence free interval. The majority of discussion is already based on prognostic factors of evaluated parameters.

Why exon 1 of TP53 gene was not analysed for mutations?

Page 7, row 24, the term "and" is redundant

**Results:**
Page 8, last three sentences in first paragraph in results section could be merged together

What about the concomitant analysis of all studied parameters? Are patients with any combination of parameters in higher risk for clinical response to chemoradiotherapy?

Table 2 is difficult to understand, please define it more in the result section. Especially, when mention the particular cases (cases 50,60, 19 and 10)

Discussion:

Discussion is very wordy and explaining the same results several times. This could be merged and thus shorten the text

The statement about the importance of HPV to study for their role in SCC of the anal cancer is not very clear in the connection with head and neck cancer as stated in discussion, please enlarge this more.

Authors state that homozygous DNA mutations can result from a loss of heterozygosity. The term homozygous refers to individuals that have identical alleles for a given trait. This part is not comprehensive. Please state clearly if it concerns allelic loss.

Page 13, last paragraph, authors mentioned three mechanisms of explanation for chromosome 17 and tP53 mutations, however above are mention only two.

Page 14, last paragraph is not clear at all, please reformulate it

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.
I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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