Author's response to reviews

Title: Prognostic role of CD133 expression in colorectal cancer: a meta-analysis

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Author's response to reviews: see over
Dear Dr Andreas Jung,

RE: Submission ID: 9158779678617237

We would like to thank BMC cancer for giving us the opportunity to revise our manuscript. We sincerely appreciate the reviewer’s comments and felt encouraged by their positive feedback. The concerns of the reviewers, editor, and all suggestions for improvement of the manuscript have been addressed. Below we provide a point-by-point response to the comments.

We are looking forward to hearing from you,

Sincerely,

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Editor's comment:

Q1: First of all your manuscript needs some spell checking and grammatical corrections which should be done best by a native speaker.

A1: According to your recommends, manuscript have edited by Edanz (www.edanzediting.com/bmc1) (See additional material). In the revised manuscript, some errors of basic grammatical spelling have already corrected. And manuscript is correctly formatted in accordance with journal style.

Q2: Second it is not clear how the selection of articles finally included in your work was made. You describe in Material and Methods that you used a logic search string. This results in about 220 hits. When using ¿CD133 AND (colon cancer OR colorectal Cancer) AND (overall survival OR OS) NOT review¿ only 67 articles show up. Comparably it would be great if you might specify your search string or explain in more depth how manuscripts were in- or excluded.

A2: We agree with your viewpoint. In the revised manuscript, we have used search string ¿CD133 AND (colon cancer or colorectal cancer) AND (overall survival or OS)¿. The results were 67 hits up to October 15, 2012. Additional 4 relevant articles were identified by manually cross-referencing. We also explain in more details the criteria for included and excluded. Updated individual patient data were collected, and included in meta-analyses (See materials and methods section).

Q3: Third it is not clear if your significance tests (p-values) were calculated one- or
two sided.

A3: Thanks. We have made it clear that “P values were two-sided, with significance at $P < 0.05$”.

Q4: Fourth when comparing things with each other it is important that the same parameters are used for the comparison. In your case there are many reasons why comparison might be difficult. Therefore it would be of a great help if you prepare a table where these parameters are given/ listed. These are at least: 1) TNM Grading/ UICC staging, 2) size of collection, 3) technique used, 4) antibody used, 5) score (cut off) used. As there are only 11 publications it should be not such a big effort.

A4: According to your instructions, we have corrected table 1 and enclosed: author, publication year, patient’s country, tumor stage, number of patients, research technique used, antibody used, cutoff value of CD133, and tumor site.

Q5: Fifth when stating that something was done “for the first time” (DISCUSSION) this is difficult to claim. Where do you know that up to now no one did such a meta-analysis and published it in her/ his native language in a journal which is not indexed in the PubMed. When you still would like to state that you did “for the first time” then you might wish to give the base for this statement, for example: PubMed search using the search string “

A5: Thanks to editor for the suggestion. We have replaced “for the first time” with
“To our knowledge, the present meta-analysis is the first English language study”.

Referee #1:

Major comments:

Q1: The manuscript must be rewritten in grammatical English with the help of a native English speaking-scientist or scientific English editing service.

A1: Thanks. The manuscript has been edited by Edanz (www.edanzediting.com/bmc1).

Q2: One of the biggest limitation of this study is, as noticed by the Authors, that studies using different methods (i.e., immunostaining and RT-PCR) to evaluate CD133 expression have been included in the analysis. This is an important bias and a great limitation especially because several studies have suggested a lack of correlation between CD133 mRNA and protein level. Thus, it is very important to verify how and whether results change by including in the analysis only the studies that use immunohistochemistry.

A2: We thank the reviewer for raising this issue. In the revised manuscript, CD133 expression was evaluated using immunostaining (Table 1), and relevant articles using RT-PCR were excluded. We also change search time from the original May 2012 to October 2012, and now 12 publications incuded. In addition, the explanatory variables did not significantly influence RR estimates for OS
Minor issues

Q3: Table 1: Horsta should be corrected in Horst. The indication Case/Control likely referring to Positive/Negative is not appropriate.

A3: Thanks. We have corrected this mistake in table 1, and dada analysis was described in statistical analysis section.