Author's response to reviews

Title: Randomized controlled trial to evaluate the effects of ethyl-2-cyanoacrylate on pain intensity and quality of life in head and neck cancer patients suffering from cetuximab-induced rhagades during radioimmunotherapy: The SUPPORT Trial

Authors:

Karin Potthoff (karin.potthoff@med.uni-heidelberg.de)
Gregor Habl (gregor.habl@med.uni-heidelberg.de)
Thomas Bruckner (bruckner@imbi.uni-heidelberg.de)
Christian Suppan (christian.suppan@nct-heidelberg.de)
Jessica Hassel (jessica.hassel@med.uni-heidelberg.de)
Dirk Jaeger (dirk.jaeger@nct-heidelberg.de)
Martin Indorf (martin.indorf@iomedico.com)
Juergen Debus (juergen.debus@med.uni-heidelberg.de)

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Author's response to reviews: see over
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Martin Indorf (martin.indorf@iomedico.com)
Juergen Debus (juergen.debus@med.uni-heidelberg.de)

Version: 3 Date: 26 February 2014

Author’s response to reviews: see over
Thank you for consideration of our manuscript for publication in your journal.

We have reviewed the above manuscript according to your reviewer’s comments.

**Reviewer # 1 (Prof. Mario E Lacouture)**

1. I commend authors for this interesting study and await the results. However, this is a synopsis of the protocol and the results are not presented. this would be more suitable as a letter to editor in a supportive care journal, if the intentios is to enroll patients and give visibility to the study.
   - The manuscript should be considered for publication in the section “study protocol”. The article type is “study protocol”.

2. Also, consider include colorectal cancer patients, since these rhagades occur after 2-3 months of therapy
   - Colorectal patients are excluded first due to the homogeneity of the study population, second due to the reliability and validity of the data including the primary and secondary endpoints, and third due to the fact that the trial is led by radiooncologists that do not primarily care for colorectal patients.

3. Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal.
   - The article type is “study protocol”.

4. Quality of written English: Not suitable for publication unless extensively edited.
   - Done. The manuscript has been extensively edited.

5. Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Done. A statistical review was made by our co-author Thomas Bruckner, a well-experienced statistician. There were no changes made to the manuscript besides the addition of a detailed description of the randomization procedure as warranted by reviewer #2.

Reviewer #2 (Dr. Dr. Diana Steinmann)

Minor Essential Revisions:
The study protocol is well described and the study group considers a very important theme. I have some minor essential revisions only.

1. Some replications should be avoided: The "Treatment schedule" replies the "Primary and Secondary objectives". All sentences between "The therapeutic response... and...each institution" could be deleted. The second part of the sentence with explanation of cross-over possibility is a replication too and should be deleted. The first part of the next sentence: "Since the primary endpoint..." is a replication, too.

   • Done. Changes made as indicated by the reviewer.

2. The paragraph "Trial duration, Schedule and Follow-up" can be shortened and integrated into the "Treatment schedule".

   • Done. Changes made as indicated by the reviewer.

3. The "Assessment of Efficacy Parameters" can be deleted. All aspects are written in "Primary and Secondary objectives".

   • Done. Changes made as indicated by the reviewer.

4. "Analysis Populations" is an 1:1 replication of the first two sentences in "Statistical methods". The last sentence of "Analysis population" could be integrated into "Statistical methods".

   • Done. Changes made as indicated by the reviewer.

5. The "Discussion" replies most aspects of "Introduction". It should be shortened or revised.

   • Done. "Discussion" was shortened and revised as indicated by the reviewer.

6. I also missed but some aspects in consideration of CONSORT guidelines: Who enrolled participants, and who assigned participants to their groups? Please describe the randomization procedure in detail. Possibility of patients to drop out every time if they want and stopping rules, i.e. at toxic events were not described.

   • Done. The enrollment of participants, the assignment of participants to the groups and the randomization procedure in detail have been added as indicated by the reviewer. Furthermore, the possibility of patients to drop out any time if they want and stopping rules were added.
Reviewer # 3 (Prof. Stefano Maria SM Magrini)

Minor essential revisions:

1. Minor essential revisions: Figure 1 and 2 are included twice.
   - Done.

Reviewer # 4 (Prof. Siegfried Segaert)

Reviewer's report:
EGFR inhibitors are responsible for numerous side effects on the skin including fissures that can be painful and invalidating; Evidence on optimal treatment of fissures is lacking. This manuscript reports on the setup of a randomized clinical trial for the treatment of cetuximab-induced fissures comparing ethyl-2-cyanoacrylate with standard care. I have no comments on the article that can be published.

Level of interest: An article whose findings are important to those with closely related research interests.

Quality of written English: Acceptable.

Statistical review: No, the manuscript does not need to be seen by a statistician.

Editorial Requests:
1.) Acknowledgements Section
Please acknowledge anyone who contributed towards the article by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data, or who was involved in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria for authorship. Please also include the source(s) of funding for each author, and for the manuscript preparation. Authors must describe the role of the funding body, if any, in design, in the collection, analysis, and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication. Please also acknowledge anyone who contributed materials essential for the study. If a language editor has made significant revision of the manuscript, we recommend that you acknowledge the editor by name, where possible.

The role of a scientific (medical) writer must be included in the acknowledgements section, including their source(s) of funding. We suggest wording such as 'We thank Jane Doe who provided medical writing services on behalf of XYZ Pharmaceuticals Ltd.'

Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements section.

- Done.

2.) Please remove Ethics Statement from additional file and include it to the methods Section.

- Done. It already was included to the “Ethics, Informed Consent and Legal Aspects” section. The number of the positive vote was added. (The additional file was required from BMC in October 2012.)

3.) Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals). It is important that your files are correctly formatted.

- Done.

Best regards,

Karin Potthoff