**Author’s response to reviews**

**Title:** Infliximab therapy together with tyrosine kinase inhibition targets leukemic stem cells in chronic myeloid leukemia

**Authors:**
Oliver Herrmann (oherrmann@ukaachen.de)
Maja Kuepper (mkuepper@ukaachen.de)
Marlena Bütow (mbuetow@ukaachen.de)
Ivan Costa (ivan.costa@rwth-aachen.de)
Iris Appelmann (iappelmann@ukaachen.de)
Fabian Beier (fbeier@ukaachen.de)
Tom Luedde (tluedde@ukaachen.de)
Till Braunschweig (tbraunschweig@ukaachen.de)
Steffen Koschmieder (skoschmieder@ukaachen.de)
Tim Brümmendorf (tbruemmendorf@ukaachen.de)
Mirle Schemionek (mschemionek@ukaachen.de)

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**Author’s response to reviews:**

Dear Members of the editorial board,

Thank you for your response and the decision to potentially accept our manuscript for publication in BMC Cancer. We have implemented all remaining points that were addressed by the editorial board and reviewers. All text changes in the revised manuscript are included in this rebuttal letter. As requested, we have now uploaded our manuscript as a final, clean version.

Thank you and best regards,

Mirle Schemionek on behalf of all coauthors.
Editor Comments:

1 - If human cell lines are used, authors are strongly encouraged to include the following information in their manuscript:

- The source of the cell line, including when and from where it was obtained
- Whether the cell line has recently been authenticated and by what method
- Whether the cell line has recently been tested for mycoplasma contamination

Further information is available from the International Cell Line Authentication Committee (ICLAC). We recommend that authors check the NCBI database for misidentification and contamination of human cell lines. Please include the sources of all cell lines and their catalogue numbers.

We have now added the information to the Methods section as follows:

“32Dcl3 (here after named as 32D) and BA/F3 cells (ACC-411, ACC-300, DSMZ, 2018-01) were cultured as described previously [25, 26]. TF-1 cells (ACC-334, DSMZ, 2018-01) were cultured using RPMI 1640/10%FCS/GM-CSF (5ng/ml). All cell lines were routinely tested for mycoplasma using PCR. Authentication of cell lines was performed using qRT-PCR for murine or human housekeeping gene as well as cell surface expression of characteristic receptor expression pattern (CD34, CD11b, Gr-1) using FACS analysis.”

2 - Please confirm whether any of the cell lines required ethics approval for their use and include a statement in the Ethics approval and consent to participate section in the Declarations.

We have added the following text to the Declarations section:

“Ethics committee approval was not required for the cell lines applied in this study.”

3 - Please describe in the Methods the manner by which animals were sacrificed.

We have now added the following text to the Methods section:

“Mice were sacrificed by cervical dislocation in isoflurane anesthesia.”

4 - In the Funding section of the Declarations please indicate the role of the funding body in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript. If no specific funding was received for this study, please clearly indicate this in the Funding section.
We have added the following text to the Declarations section:

“The funding bodies were not involved in either the design of the study, nor in writing the manuscript, or the collection, analysis, or in interpretation of data.”

5 - At this stage, please upload your proofread manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethrough or text in different colours. All relevant tables and figures should also be clean versions. Figures (and additional files) should remain uploaded as separate files. Should you wish to respond to these revision requests, please include the information in the designated input box only.

We have now uploaded a clean version of the manuscript.

Reviewer reports:

Hsin-An Hou (Reviewer 1): The authors respond to my queries. I have no more comments.

Thank you

Eishi Ashihara (Reviewer 2): Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Please overwrite this text when adding your comments to the authors.

Paolo Gallipoli (Reviewer 4): The authors have addressed all of my comments. However with regards to my comment 2 about the TNF-alpha rescue experiment in IFX treated primary murine cells, I do believe that would be an important experiment to clarify the effects and possible mechanism of action of IFX in this setting. I do appreciate the issue regarding regulatory approval and the time delay associated with it. While I think the paper could be accepted in the absence of these experiments, I would personally grant the authors more time to do them. If however the Editor feels strongly about it and does not want to wait the time required, I would suggest the paper is approved without these experiments but with careful discussion about the limitations of current experiments in allowing to draw conclusion on the mechanisms of action of IFX. Ideally one sentence explaining this clearly should be added to the discussion.

We have now added the following text to the Discussion section of the manuscript:

„However, at this stage it cannot be excluded that IFX-induced effects, independent of TNFα, could contribute to the response of CML cells observed in this study”