Author’s response to reviews

Title: Enhanced cytotoxic effect of radiation and temozolomide in malignant glioma cells: Targeting PI3K-AKT-mTOR signaling, HSP90 and Histone deacetylases

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Author’s response to reviews:

Dear Editor and Reviewers,

We are grateful to you for your helpful comments and for giving us the opportunity to respond. We have performed additional experiments, integrated the resultant data, and rewritten major sections to improve clarity. Please find attached a revised manuscript, which addresses the concerns raised and incorporates new figures. These revisions together should contribute to enhancing the appeal and relevance of our paper to the readership of “BMC Cancer”.

In the following paragraphs, we address specific points in detail:

Dr. Jann N Sarkaria

The authors have adequately addressed this reviewer’s concerns.

We really appreciate your thoughtful comments.

Dr. Chann Lagadec

As the dose used for the toxicity control, 2Gy while they are using 6Gy for all other experiments…

Although we repeated more than 5 times of clonogenic assays at the dose level of 6 Gy, we failed to get SF6 for the human astrocyte cells we used. Therefore, we removed SF2 data and description from supplementary Figure 1 and the results section (page 10).
The absence of standard deviation in Fig 4D and 5C and E.

We added standard deviation at Figure 4D, 5C and E.

Dr. Stefanie Galban

Before publication the authors need to address the PTEN status of these cell lines and discuss how that might affect treatment outcome. I failed to address this point in my previous review in more detail, but I feel that it is important to be added / addressed in the discussion of this study. To my knowledge are U251cells PTEN mutant whereas T98G cells are PTEN wt. Since PTEN status greatly affects PI3K/AKT/mTOR signaling, it is an interesting, yet not surprising finding that treatment outcome with agents impinging on this pathway varied between these cell lines.

We added the relevant description at the result (page 10) and discussion section (page15).

Dr. Peter Sminia

Is it correct that all those drugs stimulated cell migration and invasion?

Could you please show me the data?

We added the drug alone data without radiation at supplementary Figure S3.

We deeply appreciate all your helpful comments and excellent suggestions to improve our work.

Respectfully,

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