Reviewer's report

Title: Metformin enhances tamoxifen-mediated tumor growth inhibition in ER-positive breast carcinoma

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Reviewer: Keivan Majidzadeh-A

Reviewer's report:

Tamoxifen (TAM) is one of the most important medicines in adjuvant therapy of Breast Cancer (BC). So finding new medicines for increasing its effects can be helpful. In this study the authors, based on previous studies, have used appropriate methods to consider the synergistic effects of Metformin (MET), a diabetes 2 therapeutic medicine, on TAM in proliferation and apoptosis of BC cell lines. They have generated sound in vitro and in vivo data to support their primary well defined hypothesis.

Major Compulsory revisions:

1. Results: Paragraph 1: The authors have mentioned that inhibitory effects of each TAM or MET were dose dependent, BUT did not mention the exact concentration of each TAM or MET in which the fall of cell survival has happened. They may refer this to the Figure 1, BUT the exact point is not clear in Figure 1 too. Based on the graph 1-A and 1-E it seems that at falling point of cell survival, there is no significant difference between TAM concentration in single and combination therapy. Also it would be better to show the result of combination and single therapy in the same form of graph.

2. Figure 2-C: It seems that DNA replication inhibitory effects of MET is significantly greater than TAM in ZR-75-1 cell line, and such a result is somehow strange. How do the authors convince this result?

3. Results: In vivo study: How did the authors select the day 39 for sacrificing the animals?

4. Discussion: Last Paragraph: The discussion about TAM resistance is beyond the scope of this paper because the result of this manuscript cannot be applied to TAM resistance and the mechanisms underlying resistance may be totally different from synergistic effects. So this part should be omitted or rephrased.

Minor essential Revisions:

In results part of the paper Figure 3 is not referred.

Figure labels and legends have some dictation errors.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being
published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests