Reviewer’s report

Title: Boronic Prodrug of 4-Hydroxytamoxifen is More Efficacious than Tamoxifen with Enhanced Bioavailability Independent of CYP2D6 Status

Version: 2
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Reviewer: Anna Herman-Antosiewicz

Reviewer’s report:

This is a well written paper showing very interesting results on pharmacokinetics and bioavailability in mice of boronic prodrug developed to deliver active form of tamoxifen, 4-OH-tamoxifen. Presented results show its superiority over 4-OH tamoxifen and tamoxifen, as it reveals better bioavailability, even in low concentrations provides much higher plasma concentration of active tamoxifen metabolites, and their higher accumulation in tumor tissues.

Specific comments for the major compulsory revision:

1. Authors should show or at least mention the possible side effects of the tested pro-drug (overall body weight, effect on uterus, etc) in comparison to drugs already in use.
2. Authors should reevaluate t1/2 values, as these presented in Table 1 do not match with Fig. 3D (especially 4-OHT and ZB497). Besides, data presented in Fig.3 seems to refer to just one experimental animal (no SD provided); Y axis for tamoxifen (Fig.3D) is incorrect. The clearance time for the new drug should be commented in relation to tamoxifen or 4-OH tam.

Specific comments for minor essential revisions

1. Figure legends should be written in more detail,
2. Last sentence of Introduction: should be “with” instead of “of”

Specific comments for discretionary revisions

1. Fig.2- It would be helpful to present the amounts of respective metabolites (which is mentioned in the main text) in the figure

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

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

Declaration of competing interests:
I declare that I have no competing interests