Reviewer's report

Title: Potent inhibition of rhabdoid tumor cells by combination of flavopiridol and 4OH-Tamoxifen

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Reviewer: Judith Karp

Reviewer's report:

The authors present provocative data regarding the synergistic interaction between the cdk inhibitor flavopiridol and 4-OH-tamoxifen. However, the presentation leaves it unclear as to which effects of flavopiridol relative to p53 activity and G2 arrest result in net cytotoxicity. Moreover, the possibility that flavopiridol exerts 2 distinct p53-dependent activities (one via upregulation --> G2 arrest and the other paradoxically via downregulation --> abrogation of G2 arrest) deserves careful and explicit discussion. A case in point is the final paragraph of the Introduction, which needs to clearly separate the disparate relationships between flavopiridol and p53.

The authors should discuss their p53-related findings in the context of Ambrosini’s work (Cancer Res 2008;68:2312-2320), which demonstrates that flavopiridol can synergize with a G1-arresting agent (namely SN-38) by suppressing Rad51 in a p53-dependent fashion. This is pertinent to the flavopiridol + 4-OH-tam combination, given that the latter causes G1 arrest.

The p53-independent activities need to be discussed in great depth, as well. In this regard, the authors should discuss some of the other mechanisms by which flavopiridol is likely to induce apoptosis, in particular via down-regulation of MCL-1 (Gojo et al, Clin Cancer Res 2002;8:3527-3538) and attendant early mitochondrial damage (Hussain et al, Blood 2008;111:3190-3199).

Level of interest: An article of importance 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.