Reviewer's report

Title: The pan-HDAC inhibitor panobinostat acts as a sensitizer for erlotinib activity in EGFR-mutated and -wildtype non-small cell lung cancer cells

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Reviewer: jhanellle gray

Reviewer's report:

This is a well-written manuscript where the authors set out to investigate the molecular mechanisms of the combination of the pan-HDACi panobinostat with erlotinib, we utilized three NSCLC cell lines with known different genotypes. There is Good molecular characterization of the cell lines. With companies looking for next steps with their compounds, this is very timely and scientifically important manuscript. Please see suggestions below.

1) Lines 90-96 appear to belong in the results section not the background section. If these are actually results from a prior trial then Please reference.

2) Line 110 should state no instead of not

3) The authors comment that their studies demonstrated some possible effects of combination treatment with panobinostat and erlotinib even in the EGFR WT population based upon cell line data. While the authors make note of the phase 1 clinical trial combining these compounds, it is important to note the pertinent conclusions from the trial as they interpret their results. This is particularly true for the conclusions: where they recommend an phase II trial evaluating the combination in lung adenoca patients. A notation of EGFR mutation positivity is an additional likely criterion that would key to eligibility is needed so as not to mislead the reader.

4) Further they make no notation of the predictability of the CHK1 data also noted in the already published clinical trial. While pre-clinical work can support translation of projects to the clinic, Pre-clinical work that is performed on a combination that has already undergone clinical testing (ref 13) should add to the mechanistic understanding of the agents and further the exploration of biomakers. The authors should revamp not only their conclusions but also the results as presented, which I am confident they can do, to demonstrate how their data is additive to what has already been published and to further interrogate CHK1 as they did for e-cadherin. Examining Next steps for this combination overall can be better delineated and would significantly add to the impact of the manuscript.

5) would also recommend outlining where these findings fit in the this era of the third-generation EGFR TKIs such as AZD9291 and CO-1686.

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 am first author on reference #13 but am not working with this combination currently.