Reviewer's report

Title: Comparative analysis of novel and conventional Hsp90 inhibitors on HIF activity and angiogenic potential in clear cell renal cell carcinoma: Implications for clinical evaluation

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Reviewer: Oliver Stoeltzing

Reviewer's report:

The study entitled „Comparative analysis of novel and conventional Hsp90 inhibitors on HIF activity and angiogenic potential in clear cell renal cell carcinoma: Implications for clinical evaluation“ by Bohonowych et al. investigates in vitro activity of various Hsp90 inhibiting compounds in renal cell carcinoma, with a particular focus on HIF-1/-2 since these transcription factors are key players in RCC. The study addresses an important point. HIF-1 targeting has gained great interest and early Hsp90 inhibitors actually have failed in clinical trials, although displaying promising anti-HIF-1 activity. Thus there is a great need for a) identifying novel and more potent inhibitors and b) finding molecular read outs to predict efficacy. This study is quite interesting since novel compounds are being compared head to head with a clear focus on the HIF-axis.

Although the manuscript is well written with a clear hypothesis and convincing data, some points should be addressed prior to publication.

minor essential revisions:

1.) Constitutive HIF-1 can obviously be reduced (Fig.) , however it would be valuable to see effects of inhibitors under hypoxic conditions as well (1%O2 or CoCL2)

2.) the authors should further clarify that an LBH589 mediated increase in HIF-2 does obviously not result in an increased HIF-2 activity, as determined by down-stream genes.

3.) the figures are quite colorful and authors should consider a more legible format

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