Reviewer’s report

Title: Heterogeneous components of lung adenocarcinomas confer distinct EGFR mutation and PD-L1 expression

Version: 1 Date: 27 Aug 2019

Reviewer: Craig Stiles

Reviewer's report:

page 1 line 12 - after the "2.8" i think the word "years" is missing

page 7 line 20 - I disagree with your assertion regarding the meta analysis that "only 3 studies examined cabergoline exposure &gt;12 months". Reading back through the papers involved in this work - just looking at the first 5 cited in the data tables (Bogazzi, Boguszewski, colao, cordoba soriano and elenkova), ALL had a mean/median exposure &gt; 12 months

page 7 line 22 - the clinically significant 'moderate or worse' analysis from the meta analysis was heavily skewed by one particular paper (Colao) - the findings of which were not replicated in their subsequent work

page 11 line 9 - did you consider excluding the people who had used appetite suppressants in the past? It looks like no-one used dex/fen drugs in your analysis - but a few took an appetite suppressant and couldn't remember what they'd taken, just wondered if this would change your findings at all? a very minor point.

page 12 line 14-17 - a slightly counter-intuitive finding, the significance for valvulopathy being more common in the cabergoline exposed group is lost when the cumulative dose of cabergoline is &gt;115 (i.e. higher) but is present when it is lower. No explanation is offered for why this is.

page 14 line 11 - I understand that you are reporting your findings - however, it seems odd that if cabergoline is causing a rapid progression from (presumably) normal valves to mildly regurgitant years (over 2-3 years) that we aren't seeing a lot more people with moderate-severe valvulopathy as cabergoline therapy frequently continues for longer periods than 2-3 years and one might expect the valve to continue to deteriorate. Have you an explanation for why this might be?

In general, I still have a small problem with the categorisation of valve problems as being described as '2+'. You have only one moderately (grade 3) regurgitant valve (and therefore 1 incidence of clinically significant valvulopathy) in the whole study.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Unable to assess

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.
I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal