Reviewer’s report

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

Version: 2 Date: 06 Jan 2020

Reviewer: Reviewer 2

Reviewer's report:

PEER REVIEWER ASSESSMENTS:

OBJECTIVE - Full research articles: is there a clear objective that addresses a testable research question(s) (brief or other article types: is there a clear objective)?

No - there are minor issues

DESIGN - Is the current approach (including controls and analysis protocols) appropriate for the objective?

Yes - the approach is appropriate

EXECUTION - Are the experiments and analyses performed with technical rigor to allow confidence in the results?

Yes - experiments and analyses were performed appropriately

STATISTICS - Is the use of statistics in the manuscript appropriate?

Yes - appropriate statistical analyses have been used in the study

INTERPRETATION - Is the current interpretation/discussion of the results reasonable and not overstated?

Yes - the author's interpretation is reasonable

OVERALL MANUSCRIPT POTENTIAL - Is the current version of this work technically sound? If not, can revisions be made to make the work technically sound?

Probably - with minor revisions
PEER REVIEWER COMMENTS:

GENERAL COMMENTS:

This is a very interesting study that focuses on a scarcely studied problem. Overall is a well written study but it has some confusing sections.

REQUESTED REVISIONS:

There is a clear objective, but it would be better if it was more clearly stated.

Methods:

- Since the patients had not an echo at baseline and most of the valve abnormalities were mild, it is possible that some of them were present at baseline. Were there any murmurs at the first visit that could suggest the presence of valve disease before the start of the medication?

- In bromocriptine users, why was not examined the prevalence of significant valvular abnormalities by median cumulative dose

- The patient who had the echo done 12 months before the visit, the cumulative dose was considered at that time point?

- Why were the patients with mitral valve prolapse not excluded from the analysis?

- How and why was the dose of 115 mg of cabergoline chosen?

Results/abstract:

- According to the Table 1, there are 3 groups: cabergoline only users, bromocriptine only users and combined used. How is calculated the 4 groups in the abstract/results? "Median cabergoline use was 2.8 years in cabergoline only users and 3.2 years for those exposed to both cabergoline and bromocriptine; median 14 bromocriptine use was 5.5 years in bromocriptine only users and 1.1 years for those exposed to both cabergoline and bromocriptine". It is confusing.

- "Cabergoline only (37.1%, 3 P=0.02) and combined users (26.5%, P=0.26) were more likely to have ≥1 valve with grade 2+ regurgitation compared with bromocriptine only users (17.5%)". Combined users were not significantly more likely to have ≥1 valve with grade 2+ regurgitation. This should be corrected.

Discussion:

How do the authors explain the finding that lower cumulative cabergoline dose is no significantly associated with higher prevalence of valve dysfunction? How many patients were in each group?
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.

Yes

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 am able to assess the statistics

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

Acceptable

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