Reviewer's report

**Title:** Differential efficacy of cisplatin plus pemetrexed between L858R and Del-19 in advanced EGFR-mutant non-squamous non-small cell lung cancer

**Version:** 0  **Date:** 06 Mar 2017

**Reviewer:** Anthony Faber

**Reviewer's report:**

The study by Yoshioka and colleagues is an analyses of two large trials reporting differential activity of cis/prem in L858R EGFR mutant lung cancers compared to Del 19. The analyses raises an interesting and clinically relevant point, especially as treatment plans become more nuanced, for instance, catered to specific activating mutations in an oncogene. I do have a critique for the discussion which should be considered.

**Major point:**

It is interesting that ORR was not different between L858R and exon 19 deletion, while PFS was. Along these lines, the authors discuss the possibility of different responses to PEM based on mutation rate. For me, particularly in light of the ORR non-difference, there is at least two explanations as plausible as the one the authors discuss, for the difference in PFS b/w the mutants:

1) is the biology of the two EGFR mutant proteins are different causing quicker regrowth sometime after the initial cycles of induction therapy.

2) because of the different potencies of the mutants reported (as the authors discuss), other events necessary for cancer formation, like EGFR amplification or other RTK co-amplification, is causing differences in regrowth sometime after the initial cycles of induction therapy. This becomes even more relevant (i.e. ErBB family receptor amplification), when Afatinib enters the picture (as an inhibitor of both EGFR and HER2). These points should at least in part be raised in the discussion.

**Minor points:**

On page 7, line 7, it is unclear what is the PFS for gem for L858R and what is It for exon 19 deletion.
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?
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