Reviewer’s report

**Title:** Transcriptional Changes Associated with Resistance to Inhibitors of Epidermal Growth Factor Receptor Revealed Using Metaanalysis

**Version:** 3  **Date:** 26 February 2015

**Reviewer:** Jae Cheol Lee

**Reviewer’s report:**

Discretionary Revisions;

Younis et al. conducted this meta-analysis to find changes of gene expression between EGFR inhibitor-sensitive and –resistant cells. They suggested that combined modulation of factors contributing to EGFR inhibitor-resistance would help to improve cancer treatment outcomes. This study is very interesting and well performed. However, the basic design of this study seems to be hard to be accepted.

EGFR mutation is an oncogenic driver of lung cancer and the definite predictive factor for EGFR-TKI, but not for EGFR blocking antibody. In the meantime, EGFR over-expression may be one of contributing factors for cancer development and progression, but it is not an oncogenic driver like EGFR mutation. Therefore, the meaning of EGFR-TKI in EGFR-mutant lung cancer is different from that of EGFR-TKI in EGFR over-expressed cancers including head & neck cancer and epidermoid carcinoma. It is also different from the meaning of EGFR blocking antibody both in EGFR-mutant lung cancer and EGFR over-expressed cancers. So, the rationale of putting these together into one analysis does seem a bit far fetched, considering the different context. It would be better to focus on the resistance to EGFR-TKI in lung cancer with EGFR mutation or the resistance to EGFR blocking antibody in head & neck cancer with EGFR over-expression.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests