**Reviewer’s report**

**Title:** Tumour Shrinkage at 6 weeks Predicts Favorable Clinical Outcomes in a Phase III Study of Gemcitabine and Oxaliplatin with or without Erlotinib for Advanced Biliary Tract Cancer

**Version:** 1  
**Date:** 4 January 2015

**Reviewer:** Lars Henrik Jensen

**Reviewer’s report:**

Biliary tract cancer is a relatively rare cancer and especially larger trials in molecular markers and newer targeted agents are much needed. This article is based on a previously published randomised trial comparing combination chemotherapy alone or with erlotinib. In the manuscript, the authors explore a new endpoint, tumour shrinkage at 6 weeks, as a potential clinically meaningful marker in the systemic treatment of biliary tract cancer. KRAS mutation and the treatment with erlotinib are included as variables.

**Major Compulsory Revisions**

Only 103 out of 268 patients were included. There is a high risk of selection bias that cannot be corrected for.

The inclusion of KRAS as a marker in biliary tract cancer is not justified. It is neither an established prognostic factor nor a predictive factor for effect of erlotinib.

**Minor Essential Revisions**

In the introduction lines 74-78 the interpretation of the results from the randomised trial is overoptimistic and not according to good statistical practice.

Please check the definition of PFS in ‘Statistical analysis’. Was survival and not just progression included as an event?

Due to small numbers (only 8 KRAS mut), the speculative phrases in the abstract, discussion and conclusion about ETS as a marker for adding erlotinib in KRAS wt are not justified.

In conclusion, the manuscript is very interesting as a first report of early tumour shrinkage as a potential clinical marker in the systemic treatment of biliary tract cancer. Data derives from an investigator-driven, randomised trial, but too few patients are included. The manuscript is not yet ready for publication. It is suggested to include all possible patients with relevant scans. Erlotinib and KRAS may be included in a small paragraph in ‘Results’, but the main message should be focused on all patients irrespective of these variables.

**Level of interest:** An article of importance in its field
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests