Reviewer's report

Title: MicroRNA-21 and the Clinical Outcomes of Various Carcinomas A Systematic Review and Meta-Analysis

Version: 3 Date: 26 August 2014

Reviewer: Marie Stampe Ostenfeld

Reviewer's report:

Wang WJ and co-workers bring an updated meta-analysis of the potential role of miR21 as a predictive marker for reduced overall survival among patients with different cancer diseases. The aim to address such potential is of high relevance to cancer research. The literature field often lacks combined analyses of several studies to reveal the potential utility of novel biomarkers in the clinic, and therefore the study is of interest.

The study is, however, insufficiently communicated due to inadequate English scientific language that sometimes makes it difficult for this reviewer to understand and evaluate methods and results described.

Specific points:

- The meta-analysis covers studies of different cancer types. It would be very informative to list the cancer types (either in table 1 or in the forest plot)

- Please discuss that the meta-analysis is conducted on the basis of different methods (mostly qPCR, but also microarray and ISH). Other types of studies (e.g. p53 mutation status) may have been conducted in a similar manner which could strengthen the choice of analysis. Is ISH a suitable quantification tool? In this reviewers opinion, it is very suitable for localization analysis but not for quantitative analysis. Studies based on ISH could therefore be excluded.

- The follow up time is quite short for some studies (Bovell 2013, Jamieson 2012, Capodanno 2013, Zhi 2010). The authors should consider using a cut-off of minimal accepted follow-up time (In fact many of these studies show reduced HR and the data would look better if these studies were censored out). The difference in follow-up time should be considered and/or discussed. E.g. a different used follow-up time can depend highly on the aggressiveness of tumor subtype.

- Graphical representation of meta-analysis (forest plot): 31 studies are listed. Where is e.g. Kjaer-Frifeldt 2012? The study mentions either 30 publications or 36 cases. How does the number of 31 studies arise here? And please insert a legend on the x-axis (Hazard ratio)

Language/writing comments (examples):

- Do not use Spaces in between parantheses (as in line 60)
The miR21 target is maspin (not spelled mapsin) (line 76)

"The existing prognostic and predictive factors are relatively crude" (line 85) is not scientifically sound writing

"...independent prognostic factor for poor survival of tumor" (abstract, line 50) is not scientifically sound writing

Authors should avoid using unscientific phrasing such as: “But this is only part of the story” (p. 10, line 285)

Do not use abbreviations such as "It didn’t". It should be spelled out: "It did not" (e.g. line 237, line 257, line 258)

Please rewrite to achieve a more concise, understandable, and to-the-point text.

Evaluation of the study requires review by a statistician as I do not have the expertise to evaluate this (choice of random-effect vs fixed effect model, heterogeneity analysis by I2 Eggers test, Beggs funnel plot testing, etc).

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

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

**Declaration of competing interests:**

I declare to have no competing interests.