Reviewer's report

Title: Circulating tumor cells and survival of patients with gastric cancer: a meta-analysis

Version: 2
Date: 13 June 2014
Reviewer: Zhen-Ning Wang

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Major Compulsory Revisions

The authors applied a meta-analysis of 26 studies containing 1950 patients. The authors said that this study is the first meta-analysis. E.g. Background, fourth paragraph “we performed the first meta-analysis on the topic”, but to my best knowledge, a meta-analysis of the Clinicopathological and prognostic value of CTCs in gastric cancer has been published (PubMed: 24901848; 24803400).

Comments

1. There were no excluded criteria on the redundant studies based on same patients’ population. The studies by Arigami32, Arigami 36, Arigami42, and Uenosono 48 (as well as studies by Wu25 and study by Uen26) were conducted by same institution and may be based on same patients, thus same patients are evaluated several times and the pooled results are doubtful and may be incorrect. Moreover, Statistical Approaches, third paragraph “For studies with multiple arms (i.e., resectable and unresectable groups) or multiple markers (i.e., cytokeratin 18 and 19), each of the subgroups was considered an independent data set”, it contributed double/treble patients evaluation.

2. Statistical Approaches, third paragraph “we used data from pre-therapy samples in prior to intra/post-therapy samples because those data were usually dependent”, in my opinion, clinical study and relevant meta-analysis (PubMed: 11176124, 20100481, and 22799295) indicated that the post-therapy sampling time might reflect the most relevant CTC status. And the authors also mentioned similar situation in Discussion and they are inconsistent. E.g. Discussion, fifth paragraph “Baseline detection had risks of failing to provide information about the actual burden of CTCs after therapies thus might be unable to accurately predict survival of patients post treatments.” and Subgroup Analyses and Meta-Regression, first paragraph “the prognostic role of CTCs for RFS was not observed in...” authors should clarify the difference on CTCs positivity level in pre-therapy and post-therapy and underlying reasons and mechanisms.

3. Statistical Approaches, fourth paragraph “We did not assess the quality of included studies, because widely accepted standard was not available for prognostic studies [19]”, the reference 19 is a meta-analysis, thus whether the citation is correct.

4. The subgroup analysis on detection methods was only based on cytological and molecular methods. For providing useful information to clinicians and
investigators, the authors should also conducted subgroup analysis by PCR, ICC, CellSearch, and HTCMA.

5. MicroRNA act as a novel marker for detection of CTCs, authors should brief clarity the sensitivity and specificity.

6. If the number of studies was available, the authors should conduct in-depth subgroup analyses considering the methods and sampling time simultaneously.

Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

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