Reviewer's report

Title: Association of Fascin-1 with Cancer-Specific Mortality, Disease-free Survival and Metastasis in Carcinomas: a Systematic Review and Meta-analysis

Version: 2 Date: 24 July 2012

Reviewer: Konstantinos Tsilidis

Reviewer's report:

This is a nice systematic review on the prognostic role of fascin-1 with cancer. I applaud the authors' idea to synthesize evidence from clinical IHC studies, and such evidence synthesis attempts should appear more frequently for basic and clinical science papers. However, I would like to see some more detail in certain areas of the manuscript, which are outlined below.

Major Compulsory Revisions

1) Some subgroup meta-analyses would be very helpful to explain some of your results for all cancers combined, even though I realize that you may end up with few studies in some of those subgroups. You stated in the Methods that you stratified the results according to the method of scoring fascin-1 staining, but I didn't see the analysis in the Results. In addition, could you also perform a sub-analysis by whether the results of the individual studies were adjusted or crude? To what extent do you believe that the prognostic role of fascin-1 is independent of stage and grade of cancer?

2) I am not quite sure why you haven't performed any formal assessment for publication bias. It seems that you have info on relative risk (95% CIs) and number of participants in each study. You could alternatively use the Harbord test if you have got information from a 2x2 table. I am afraid that this literature, as most basic/clinical science literature, will have lots of it.

3) Alternatively, you could also perform a formal test for excess significance bias for your all-cancer endpoint. This test examines whether there are too many reported statistically significant results in single studies based on what would be expected under different assumptions about the plausible effect size of each association. This test can supplement the tests for publications bias above, and may even be better, because the publication bias tests may not be very sensitive or specific for detecting such bias, especially when a limited number of studies is included in a meta-analysis. Check for more info at: Ioannidis JP, Trikalinos TA. An exploratory test for an excess of significant findings. Clin Trials. 2007;4(3):245-253.

4) It would be great if the authors could also provide some more details (and discussion about them) of the overall design and quality of the individual studies included in the meta-analysis. How were the subjects selected? Consecutive, random, other? Were the pathologists blinded to the outcome of the cancer
cases? Was the same pathologist used for all plates in a study? What were the characteristics of the study population: race/ethnicity, stage and grade of cancer at diagnosis, cancer treatment? This information could be added to Table 1. In complement to the above, the authors could elaborate a bit more on the issues of retrospective study design, selective reporting and heterogeneity that they mention in the Conclusions.

Minor Essential Revisions

1) The total number of participants and by case/control status (e.g., dead case vs. alive case) for all 25 included studies should be provided in the Abstract.

2) In several instances in the Methods, you stated that the authors of the original papers were contacted and asked for additional information. Could you be more explicit and state which authors provided what additional info? This could be part of the supplemental material if it is too long.

3) The wording in the Results when you are evaluating the heterogeneity of the literature is not consistent. In one instance, I-sqr is 55.3% and is deemed moderate heterogeneity, while when I-sqr is 45.3 it is strong evidence of heterogeneity.

4) In Figure 1, please list the number of exclusions next to the reason for exclusion.

5) In Figures 2-5, could you list the number of cases/controls instead of the total number of participants?

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