Reviewer's report

**Title:** TIMP-1 and VEGF-165 serum concentration during first-line therapy of ovarian cancer patients

**Version:** 1  **Date:** 9 December 2009

**Reviewer:** Lindy Durrant

**Reviewer's report:**

When assessing the work, please consider the following points:

1. Is the question posed by the authors well defined? yes
2. Are the methods appropriate and well described? yes
3. Are the data sound? statistics need revising
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? yes
5. Are the discussion and conclusions well balanced and adequately supported by the data? no
6. Are limitations of the work clearly stated? no
7. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? yes
8. Do the title and abstract accurately convey what has been found? yes
9. Is the writing acceptable? yes

Reviewer's report

The authors look at the concentration of TIMP-1 and VEGF-165 serum concentrations during first line therapy of ovarian cancer patients. They conclude that high levels of CA-125, TIMP-1 and VEGF-165 after chemotherapy were associated with reduced overall survival. In addition elevated CA-125 and VEGF-165 post chemotherapy predicted poor progression free survival.

My main criticism of the study is that serum markers must be used to assess individual patient’s response to therapy and therefore all statistics should have been done for paired samples and assessed by a non parametric ranking test. The results should also be presented as linked data for each patient so it is possible to assess how many patients showed an increase in TIMP-1 and VEGF-165 serum concentrations post surgery and a decrease post chemotherapy.

Major Compulsory Revisions
It is unclear if TIMP-1 and VEGF-165 serum concentrations reflect tumour burden or biologic responses. Post surgery the increase in TIMP-1 and VEGF-165 serum concentrations could be due to the biology of wound repair. However, it is less clear whether there is a significant drop in TIMP-1 and VEGF-165 serum concentrations during chemotherapy when compared to before surgery or just a return to normal levels following wound repair. This needs clarifying. Normal levels of TIMP-1 and VEGF-165 serum concentrations need to be presented for an appropriate group of aged matched controls as it is difficult to evaluate if there is any elevation in cancer patients.

Similarly CA-125 is a good predictor of response to chemotherapy in 80% of patients the role of new serum markers is therefore in the 20% of patients where CA-125 is not indicative of response. The authors should show in this group of patients whether TIMP-1 and VEGF-165 serum concentrations where useful in predicting responses.

Table 3 is unintelligible. It is unclear why TIMP-1 and VEGF-165 serum concentrations where correlated with age? There are multiple comparisons leading to a type 1 statistical error. P values need to be adjusted for multiple comparisons. PFS and OS should be presented as Kaplan Meir plots. How do the authors explain that TIMP-1 after CTX was highly significant with overall survival but not progression free survival?

Minor Essential Revisions

Tumour types should be added to Table 1 as ovarian cancer has now been shown to be a diverse group of cancer with very different molecular profiles and biological outcome.