Reviewer's report

**Title:** Trop-2 Protein Overexpression is an Independent Prognostic Marker in Endometrioid Endometrial Carcinoma

**Version:** 3  **Date:** 24 July 2012

**Reviewer:** Emanuela Guerra

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In this paper Bignotti et al consider Trop-2 expression as measured by IHC in endometrial endometrioid cancer, using a subset of a group of cases already presented in a previously published paper (Bignotti et al, 2011). Here they correlate Trop-2 expression with a number of clinical parameters for these cases and found that high Trop-2 expression is significantly associated with tumor grade and cervical involvement. They also show that Trop-2 is an independent prognostic indicator for disease-free survival in endometrial endometrioid cancer.

The findings coming from this further analysis are per se interesting, although in my opinion the paper as it is relies too much on results already presented and discussed elsewhere (see below).

**Major Compulsory Revisions**

1. To avoid selection bias, it is important to describe the inclusion criteria according to which the patients were enrolled in the study. The authors should be more specific on this issue. Was this a series of sequential cases?

2. Information on the treatment of these patients was recorded, yet it does not appear in the manuscript. Treatment should be described and association (or lack of association) with outcome and Trop-2 expression should be investigated.

3. How were the limits used for the IHC evaluations chosen? Did the authors choose them on the basis of their previous work in epithelial ovarian cancers? Even if taken from a previous study, the basis for these should be justified here. How do they compare with the cut-off values used by other groups showing a negative prognostic value for Trop-2 (ie Fong et al 2008)?

4. The authors’ statement in the first paragraph of the results of “In all samples, Trop-2 immunoreactivity was localized exclusively to the membrane of neoplastic epithelium, with no positivity in adjacent stromal cells” as a result in this study has no data to support this in this manuscript. Although they refer back to their previous paper (Bignotti et al., 2011), such statements should be accompanied by the relevant data for the reader to form their own judgement. Indeed, the same phrase (word for word) is in their previous paper (Bignotti et al., 2011) to which they refer, and hence this result is not new, but just a repetition from their previous paper.

Also a significant correlation with higher tumor grade is shown (grade 1 vs grade
2 and 3 together). Again, this appears not to be absolutely novel since the authors have previously shown stronger Trop-2 staining in grade 3 vs grade 1 tumors (Bignotti et al., 2011).

(5) I am not an expert on Kaplan-Meier analysis. I therefore suggest the opinion of a statistician.

Minor Essential Revisions

(1) Reference 24 is not quoted correctly (Int J Cancer instead of Int J Gynecol Cancer); please check the full reference list carefully.

(2) The authors have not included any reference to three recent papers relevant to the Trop-2 literature. One demonstrates a direct link between Trop-2 upregulation and stimulation of cancer growth and appears relevant to the details in the second paragraph of the Introduction (Trerotola et al., Oncogene 2012, PMID: 22349828). The two others appear relevant for the Discussion, one relating directly to the pathways through which Trop-2 mediates tumor growth (Guerra et al., Oncogene 2012, PMID:22562244), the other to a different role for Trop-2 in cancer growth in lung adenocarcinoma, through modulation of IGF-1R signalling (Lin et al., Embo Mol Med 2012, PMID: 22419550).

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interest