Reviewer's report

Title: High OX40 expression in recurrent ovarian carcinoma is indicative for response to repeated chemotherapy

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Reviewer: Rupert Langer

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Droeser et al. present an interesting study about the potential role of OX40 for chemoresistance in ovarian cancer

- The usage of the term «biopsy» may be misleading. I understood that surgical debulking was performed in all patients. Was the tissue taken from these surgical procedures or as a separate diagnostic biopsy

- How many cores were analyzed per tumor? Was there any considerable heterogeneity? As ovarian cancers may reach a considerable tumor mass, this issue should be taken into account (e.g. separate analysis of tumors)

- The quality of the TMA cores presented in figure 1 is very poor with large artifacts. This could negatively bias the results especially when counting single cells. How did the authors deal with this issue?

- It is confusing to read the cut offs (IHC section) before the description of the statistics.

- Apart from the approach using a cut-off for survival (overall or recurrence free survival? Please be more specific; moreover, this defines a good and a bad group, that of course would be expected to correlate with chemosensitivity), was there a significant difference using the raw values (medians/means) in the two groups (sensitive / resistant). Was there an increase or decrease of OX40 positive tumor and inflammatory cells in the respective groups?

- Describe tumoral positivity for OX40. I assume it is nuclear and cytoplasmic? Shouldn't it be membranous? Can the authors provide a rationale for this? One would expect OX40 positivity predominantly on T cells. Moreover, a higher magnification for tumor cell positivity and the exact location of OX40 on inflammatory cells would be helpful.
- The authors describe OX40 positivity in inflammatory cells excluding vessels. What about other stromal components, such as fibroblasts? Were macrophages included?
- Was there a correlation between tumoral and inflammatory cell OX40 positivity? What, if you combine both scores? Were double negative cases different from double positive?
- The results part is hard to read. I suspect that there are some mistakes, such as OX40 tumor cells are presented in the OX40 immune cells section. Please improve readability and structure.
- The authors mention MPO data, but I cannot see any results
- Did the authors try to combine their IL17 data with OX40?
- Bösmüller et al (2011) describe the potential predictive value of the density of tumor infiltrating lymphocytes. It would enhance the value of the paper, to test for this (CD3 / CD8) and to add it to OX40 and / or calculate against OX40.
- Which controls were used for immunohistochemistry?

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

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