**Reviewer’s report**

**Title:** Association between levels of tumor-infiltrating lymphocytes in different subtypes of primary breast tumors and prognostic outcomes: A meta-analysis

**Version:** 1  **Date:** 29 Feb 2020

**Reviewer:** Roberto Salgado

**Reviewer's report:**

The authors have replied well to the suggestions raised at the first review.

A few minor comments to improve the paper:

1. The first paragraph of the Discussion is incorrectly worded, but I know what the authors mean. I would rephrase its as follows "The prognostic and predictive importance of TILs in ER+ disease is still controversial. To investigate this issue, we evaluate all available evidence regarding ER positive and ER-negative breast tumors from a pool of clinical studies and demonstrate that each 10% increment of TILs in breast tumors improves OS in HER2-amplified and TN molecular subtypes but not in the luminal phenotype.", so basically removing line 222, 223, 224 and part of 225.
2. Lines 237, 238. I would rephrase the last sentence as follows "Prospective de-escalation clinical trials in HER2+ and TNBC are needed to identify the appropriate TIL-levels to safely de-escalate therapy in those patients that have an excellent outcome". Those trials are already in development, so the authors can hint to this development.
3. Lines 246, 247. I would rephrase this sentence as follows: "The prognostic outcome of TIL-levels in luminal disease remains an important area of investigation."
4. I would suggest adding the following in the discussion: "One of the reasons why TIL-counts are not associated with survival benefit in luminal disease is that the range of TILs is not very high, with most cases having less than 10% stromal TILs, so most series don't have a significant number of patients with luminal disease with very high TILs. In luminal disease, combined features of immunity and tumor cell characteristics, like for example tumor cell proliferation or histological grade, may be probably the best approach, while in TNBC and HER2+ disease immunity is probably sufficient to predict outcome, with cancer cell characteristics being less important in these subtypes."
5. Lines 250, 251: the authors should state the authors and abstract, not the Conferences.
6. I would remove the paragraph line 264 till 277 as this is highly speculative.
7. Line 279: I would propose to more neutral. Using the wording "Admittedly" is not good. I would propose the following "The limitations of this study are as follows:...."

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**Are the methods appropriate and well described?**

If not, please specify what is required in your comments to the authors.
Yes

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