Reviewer’s report

Title: Impact of uPA/PAI-1 and disseminated cytokeratin-positive cells in breast cancer

Version: 0 Date: 12 Mar 2019

Reviewer: Serenella Eppenberger-Castori

Reviewer’s report:

uPA and PAI-1 are very well established biomarkers in breast cancer. The idea of this study to further investigate if the presence of these tumor aggressiveness markers correlates with disseminated disease in the bone marrow via detection of cytokeratin-positive cells (dCK+) is valid.

The reported associations of the uPA and PAI-1 expression levels with HR-, HER2- status, tumor grading and patients' overall survival are in accordance with data already published with larger collective, showing that this retrospective cohort as well as the detection of this protease and its inhibitor are representative.

The reported association between dCK+ cells with the occurrence of lymph node metastases (P < 0.005) is reported to be highly significant but dCK+ lack any prognostic impact as single marker. No association between dCK+ and PAI-1 is observed. The one with respect to uPA positivity is only marginally significantly: P = 0.028.

This is certainly due to the fact, as also discussed by the authors, that the number of cases in the subsets is very limited.

The p-values corresponding to the survival curves depicted in figures 2B and 3D refer to the overall difference between the curves and not between the triple plus and the two plus. Therefore, the authors should perform a statistical analysis comparing these two curves. Only if this would be significant the author could affirm the added synergistic values of dCK+.

Taking all together the message of this manuscript in the present form is underpowered and doesn't allow any clear conclusion.

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.

Yes
Are the conclusions drawn adequately supported by the data shown?
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No

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I am able to assess the statistics

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