Reviewer’s report

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

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Reviewer: Galatea Kallergi

Reviewer’s report:

The manuscript entitled "Impact of uPA/PAI-1 and disseminated cytokeratin-positive cells in breast cancer" is interesting. The authors tried to find combination of biomarkers that could be prognostic factors for breast cancer patients, however there are some questions that need to be addressed.

Why the authors have used an antibody targeting only cytokeratin 18 to detect DTCs while most of the studies for Circulating Tumor Cells and Disseminated Tumor Cells are using either CK19 or pan Cytokeratins antibodies. It is possible that they have lost some positive cases.

The authors have shown that the presence of DTCs concomitantly with uPA and PAI-1 is associated with poor prognosis. It will be interesting to examine the potential co-expression of these molecules in patients' DTCs. They could probably do this indicatively in some cases. This fact could explain why the triple positivity is a poor prognostic factor.

It is strange that DTCs are not prognostic in any group of patients in this study, since many other studies in the past have shown that DTCs could be a poor prognostic factor. Have the authors checked OS or PFS with Cox Regression regarding DTCs numbers in all different groups?

How the authors explain the fact that although the DTCs are not important for survival in this study the triple positivity is an independent prognostic factor.

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?  
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 recommend additional statistical review

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