Reviewer's report

Title: Connexin 26 and 46 expression refines intermediate prognostic subgroups of residual tumor classifications in neoadjuvant treated breast cancers

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Reviewer: Marwan El-Sabban

Reviewer's report:

In the absence of markers that reliably predict the efficacy of primary neo-adjuvent systemic therapy in breast cancer, this study attempts to provide additional information (breast-specific connexin expression) to enhance the prediction and refine classification of prognostic subgroups, post therapy. The prognostic and predictive role of connexins in relation to neo-adjuvant chemotherapy is novel. The authors use immunofluorescence microscopy to detect the expression of four connexins (Cx26, Cx32, Cx43 and Cx46) in addition to Ki67 in 96 cases in tissue micro arrays. The manuscript is well written with adequate references (albeit incomplete) and well-discussed findings. Their data support the prognostic value of connexin detection in neo-adjuvant treated breast cancer. Using different classification and statistical analysis they found that reduced Cx26 expression post-chemotherapy and moderate to high Cx46 expression both pre- and post chemotherapy exhibited significantly improved survival rates especially in the intermediate subgroups of currently used classification systems. They have used sections from FFPE blocks, retrieved antigens and employed indirect immuno-histochemical analysis to the sections. Although the data collected appear convincing, it is important to set very specific and uniform criteria for positivity for laboratories to follow, if this evaluation to be followed by others. Detection and evaluation of connexin expression did not discriminate and included both cytoplasmic and membranous positivity in the analysis. This may confound interpretations since the authors made correlation with proliferation and cell cycle. The cellular distribution of connexins will be affected by the cell cycle. It would have been interesting to clearly demonstrate Ki76 staining with connexin expression in all conditions.

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 interests