Reviewer's report

Title: Poor prognosis of single hormone receptor-positive breast cancer: No difference with triple negative breast cancer

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Reviewer: Ewa Mrozek

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The authors examined a large and well characterized series of 6,980 cases of primary invasive ductal carcinoma with ample clinicopathologic data including immunophenotyping on a wide range of proteins of known relevance in breast cancer, as well as data on endocrine therapy, chemotherapy and radiation therapy. The patients were stratified according to the estrogen receptor (ER) and progesterone receptor (PR) expression. The aim of the study was to assess and compare clinicopathologic features of the single hormone receptor (HR) positive breast cancers to double-positive and double –negative tumors. In addition the authors evaluated prognostic difference between the single HR positive breast tumors and the double-positive and double –negative tumors. The median follow up on this study was only 45 months, which can limit the value of this analysis.

The manuscript is quite well written. The aims of the study are well defined and developed. The methods paragraph describes methodology in details. The results paragraph is well presented; it provides clinicopathologic characteristics of the single HR positive breast cancer and compares them to the double –positive/-negative tumors. Analysis of outcome of single HR positive breast cancer was compared to the outcome of the double –positive/-negative tumors. This study has confirmed poor survival of patients with ER negative, PR positive tumors. The novelty of this analysis is to assess the outcome of the single HR positive breast cancer in subgroup of patients with and without HER2 overexpression. Interestingly, the authors found that single HR positivity is a significant prognostic factor in tumors without HER2 overexpression, but not in tumors with HER2 overexpression. They suggested that HER2 expression might be more significant prognostic factor than PR loss, especially while those patients are treated with trastuzumab. However, the 790 patients who received trastuzumab therapy had similar OS as did 586 patients who did not receive trastuzumab. They should clarify this discrepancy. The discussion paragraph is well organized and informative. Overall my recommendation is to accept the manuscript with minor revisions.

Below are the minor revisions that should be corrected in the manuscript:

Page 2, line 6. “HR-” should be replaced with “HR negative”

Page 2, lines 13-15. Please clarify the statement about survival. The multivariate analysis showed that ER+PR- tumors in patients without HER2 overexpression were associated with the lower not increased survival compared with ER+PR+ tumors. The same statement is for ER-PR+ tumors, they had lower not increased
survival compared with ER+PR+ tumors.

Page 2, line 24: “but” should be replaced with “and”

Page 6, line 8: add “frequently” between “more” and “in”. (tumors were found more frequently in postmenopausal) Page 6, line 9: eliminate “in”. (than other subtypes) Page 7, lines 1-3: correct this statement It should be: “More patients with ER+PR- (73.7%) and ER-PR+ (89.7%) tumors received chemotherapy than the patients with ER+PR+ tumors (68.7%), the group with ER-PR- tumors was treated with chemotherapy most frequently (91.9%, Table1). “ Page 8, line 6: add “found in” between “those” and “previous studies”

Page 8, line 11: add “to have” between “shown” and “worse”

Page 8, lines 12-13: provide information what is the connection between endocrine resistance and HER2 overexpression that is discussed in the next sentence.

Page 9, lines 3-7: it is unclear what authors are discussing here. It needs some clarification.

Page 10, line 5: add “treatment with” between “to” and “tamoxifen”

Page 11, line 2-3. The statement about single HR positivity being a surrogate marker for increased activity of growth factor receptor tyrosine kinase is out of context. It was never discussed in the discussion. Please revise.

Table 3. Multivariate analysis of disease-free survival (DFS) and overall survival (OS) in 4,549 women with HER2-positive breast cancer is not part of this manuscript. According to the authors only 1,376 patients had HER2 overexpressing tumors. Please remove or correct the table.

Similarly, the Table 4. Multivariate analysis of disease-free survival (DFS) and overall survival (OS) in 1,121 women with HER2-negative breast cancer, does not correlate with the manuscript. According to the authors 5,433 patients had HER2 negative disease. Please remove or correct the table.