Reviewer's report

Title: PIK3R1 underexpression is an independent prognostic marker in breast cancer

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Reviewer: Katarina Ejeskär

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General
In this paper the authors have studied mutational status and expression levels of genes in the PI3K-pathway, with emphasis on PIK3CA and PIK3R1 in 458 well defined breast tumor samples. They can confirm the common mutations of PIK3CA, AKT1 and PIK3R1 from previous studies, and conclude that underexpression of PIK3R1 is common in metastatic tumors, contrary to PIK3CA-mutation that is a good prognostic marker. The finding is interesting; the sample size is good, methods used are good, and the English is acceptable:

- Minor Essential Revisions

- In Abstract, Results and Discussion: PIK3R1 and AKT1-mutations were more common in non-PIK3CA-mutated cases, however mutually exclusive is an incorrect term, since it did occur in PIK3CA-mutated cases, even if it was rare. Change in the text were this term was used.

- In Methods: Explanation is needed for the choice of the exons chosen to sequence, why not all exones were examined.

- In Results: PIK3R1-mutation: AAG-AAA gives no amino acid change for sure, in the text it says probably.

- In Table 2, 3 and 4: It is not clear to what differences the p-value is indicating significance, change to make it clear.

- Table 3 and 4 would benefit to be fused into one single table, for less repetition of data.

- Additional file 1: Figure 1: Important figure! It would be better as an original figure in the paper.

- Discretionary Revisions

- In Introduction: Information is missing regarding other isoforms of catalytic subunit p110, p110beta and p110delta, that also could influence the PI3K activity.

- In Methods: 170 patients developed metastases. Write in numbers.

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
'I declare that I have no competing interests'