Reviewer's report

Title: Multiple Gene Aberrations and Breast Cancer: Lessons from Super-Responders

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Reviewer: Eliane Tabea Taube

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The case report examines tissue by NGS from three patients with metastatic breast cancer who respond by partial- or complete remission when treated with Everolismus and Anastrozole. A number of mutations are detected, some of which influence the pik3ca/akt/mtor pathway. The authors conclude that this might explain the good response to the combining therapy of Everolismus and Anastrozole.

The article is categorized as "case report" and thus only these three patients are analyzed, naturally no statistical analysis or comparison with other patients is possible. And although this limits the conclusions drawn, it is an interesting concept to analyze the patients that respond well to therapy. Finding mutations that influence the Pik3ca/akt/mtor pathway could be anticipated in a group of patients responding well to a therapy with Everolismus. Interesting however is the fact that all three patients had multiple mutations. Of further interest is that only one showed directly mutated pik3ca, one PTEN loss, whereas one had mutations only indirectly influencing the pathway of pik3ca/akt/mtor. The author deduct that Everolismus might have a benefit even in that context.

Discretionary revisions: Especially in the third patient the conclusion drawn that Everolismus is efficient even in the absence of a direct mutation is one possible explanation. Nevertheless the authors might also state that the positive evolution of the patient could also be due to Anastrozole or due to an unknown mutation in the pik3ca pathway since the tissue tested was from the time of first diagnosis and in the meantime the tumor might have acquired additional mutations.

Level of interest: An article whose findings are important to those with closely related research interests

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.