Reviewer’s report

Title: High expression of Wee1 is associated with malignancy in vulvar squamous cell carcinoma patients

Version: 1 Date: 5 April 2013

Reviewer: Nathalie Scholler

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In the manuscript entitled “High expression of Wee1 is associated with malignancy in vulvar squamous cell carcinoma patients, Magnussen and colleagues studied the expression of Wee1, a central regulator of the G2/M DNA-damage checkpoint, that has been previously described as a prognostic biomarker and a potential target for therapies in other cancers. To do so, they analyzed the expression of Wee1 in a panel of 297 vulvar tumors versus 10 benign controls by immunohistochemistry, and they inhibited Wee1 expression in two vulvar cancer cell lines by siRNA. Wee1 kinase expression was found increased in vulvar squamous cell carcinomas, and Wee1 high expression was associated with markers of malignancy. But the association between Wee1 and different cell cycle regulatory proteins depended on cellular localization. In addition, while the biomarker for DNA double-strand breaks #H2AX was increased after Wee1 siRNA silencing, no significant reduction of viability were observed in two silenced vulvar cancer cell lines, and no significant association was found between disease-specific survival and Wee1 expression. The authors conclude that Wee1 may be involved in the progression of vulvar carcinomas, but that Wee1 silencing cannot arrest cell cycle or increase apoptosis thus limiting its use as mono-treatment for patients with vulvar carcinoma. These results are in accordance with previously published works in human glioblastomas and osteosarcomas, but not with some reports in breast cancer, melanoma, and non-small-cell lung cancer.

This manuscript is well written and clearly documents the expression of Wee1 kinase in vulvar carcinoma. Because of the existence of divergent reports on the expression and role Wee1 in different cancer forms, this work is important and should be published, even if the results do not support a therapeutic use of Wee1 silencing.

One Minor Essential Revision is recommended: the age of the control patients should be given, as Wee1 expression in vulvar cancer is correlated with age. Does Wee1 expression in control patients also correlated with age?

Level of interest: An article of importance in its field

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.