Reviewer’s report

Title: Decentral gene expression analysis: analytical validation of the Endopredict genomic multianalyte breast cancer prognosis test

Version: 1 Date: 14 August 2012

Reviewer: Rolf Jaggi

Reviewer’s report:

The manuscript by Kronenwett et al. is a clearly written and well-structured manuscript on EndoPredict (EP), a gene expression test based on 8 test and 3 control/reference genes. EP is a score between 0 and 15, low scores (<5) correspond to relatively good and high score (≥5) to relatively poor prognosis in women with ER-positive, Her2-negative breast cancer. EP was previously developed from women receiving endocrine therapy alone (ABCSG-6 and ABCSG-8). This manuscript characterizes the parameters of real-time PCR (linearity of Cq, amplification efficiency and range of input RNA). The authors estimate several parameters of variation (variation of day, time, instrument, operator, reagent lot) on resulting score. The work documents that EP can reliably be measured in different laboratories and by different operators without major variation of Cq values and final scores. These are important criteria for commercialization of EP and testing in decentralized laboratories. The work does not describe any novel aspects on EndoPredict and its application area.

Major Compulsory Revisions
None

Minor Essential Revisions
The authors mention that the total variation of EP in different laboratories is in the range of 1%. It would be interesting if this number was compared to other diagnostic tests like antibody-based assays which are regularly used in pathologies.

Although instruments and reagents are standardized for EP, the results of this study very likely depend on the experience of each laboratory and the personnel performing the assay. For sure the Institute of Pathology in Berlin is more experienced with RNA work than many other pathology. Eventually, this aspect should be considered, especially for laboratories with less experienced operators.

Discretionary Revisions
page 14: please delete "can" (… which can must be performed in laboratories, …)

Level of interest: An article of limited interest
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