Reviewer’s report

Title: Ten-years breast cancer overall survival as an indicator of brca mutation in a caucasian population with high probability to be hereditary

Version: 1 Date: 19 July 2009

Reviewer: paul van diest

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This paper aimed to examine whether breast cancers (BCs) occurring in patients at high risk on the basis of the family history are associated with better outcome than patients with intermediate/slightly increased risk or without family history, and if the prolonged survival could be considered a good indicator for gene mutation. The following comments can be made.

Major comments

1. Before this study was conceived, there was no convincing evidence that BRCA carriers with breast cancer do better. Then, how can an aim be to examine “...if the prolonged survival could be considered a good indicator for gene mutation”?

2. The authors conclude that 10 years overall survival is an indicator for BRCA mutation in breast cancers. This is in practice however of no value. When one is faced with a patient (or even a family), no follow up data are usually available (let alone long term survival) so survival of breast cancers in a family will play no role in deciding on mutation testing. Further, there are many, many confounders here. Nobody would be surprised to see a patient with a ER+/PR+/HER2- grade 1 tubular carcinoma of 1 cm in size survive for over 10 years, while these will almost never occur in BRCA carriers. Although there may be trends in large groups, this is quite useless for an individual patient or a family.

3. In view of 2, the title can better be adopted (e.g. “FAVORABLE TEN-YEARS BREAST CANCER OVERALL SURVIVAL IN A CAUCASIAN POPULATION WITH HIGH PROBABILITY TO BE HEREDITARY”) as well as the aim.

4. A severe limitation of the study is that BRCA1 and BRCA2 mutations are consequently lumped. It is not even mentioned how many are BRCA1 and BRCA2. It is to be expected that BRCA1 and BRCA2 would differ in behavior, so this needs to be analyzed separately.

5. A severe limitation is that no formal matching for survival confounders such as age, type, grade, size and lymph node status has been performed. Stratifying for these in multivariate analysis may not suffice.

Minor comments

6. The sentence “One hundred-fifteen BRCA carriers were identified. Patients belonging to H risk category had a better OS than IS and sporadic groups (85%
vs.74% vs.73%, p<0.0001) such as BRCA carriers respect to BRCA negative and sporadic BC (82% vs.77% vs.73%, p<0.0001), despite no differences in DFS were seen. " very difficult to understand. Please rephrase.

7. The purpose to examine “whether BRCA carriers have a worse DFS despite to the better OS, demonstrating that chemotherapy might provide more benefit in this patients’ population” is questionable. DFS goes hand in hand with OS in breast cancer, just with a delay. Since we are talking ADJUVANT chemotherapy here, it is not to be expected that in case of relapse BRCA carriers would have prolonged survival after that when mutated. Maybe, maybe this could be hypothesized for BRCA mutation carriers receiving anthracycline chemo AFTER relapse.

8. How were ER/PR assessed?

9. Which chemotherapy was applied?

10. The English needs brushing up.

11. Would be interesting to plot in the BRCA+ group chemo vs no chemo.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests