Reviewer’s report

Title: The frequency of BRCA1 mutation in breast cancer patients from Ukraine

Version: 2 Date: 17 June 2015

Reviewer: Rob B van der Luijt

Reviewer’s report:

General comment on the manuscript:

In the manuscript submitted by Gorodetska et al, the results of a study on the frequency of the BRCA1 founder mutation 5382insC (i.e. mutation nomenclature according to HGVS guidelines: c.5266dupC) in breast cancer patients from Ukraine are presented. This BRCA1 sequence change is a well-known founder mutation that most likely arose from a single ancestor about 1800 years ago in Northern Europe and since then has spread to several populations, including the Ukrainian. The authors used a mutation-specific assay to determine the frequency of this particular mutation in a series of 193 breast cancer patients from Ukraine. Although their report does not provide new insights into the characteristics and demographics of this mutation, the paper could still be interesting to the BRCA-genes associated breast cancer community. It re-emphasizes the important role of this mutation in the etiology of breast cancer in this particular population, where (if I understand correctly) genetic testing has not yet reached the mainstream in breast cancer diagnosis and management. However, before the paper is suitable for publication, several major and minor issues have to be addressed, as can be found below.

Major Compulsory Revisions:

(1) although the founder mutation discussed in the paper is well-known under its legacy or traditional name 5382insC, the authors should also describe the mutation according to the most recent HGVS guidelines for mutation nomenclature. A way to achieve this is, to describe this mutation at least once as c.5266dupC while referring also to the traditional name 5382insC.

(2) the title should be more specific. Suggestion: The frequency of the BRCA1 founder mutation c.5266dupC (5382insC) in breast cancer patients from Ukraine.

(3) the authors state that the patients were 'haphazardly selected'. It may be better to state that the patients were unselected cases of breast cancer (if indeed the case).

(4) The reference by Chan et al (1999) is numbered as [19] in the body of the text. However, in the references list it is numbered as [20].

(5) The authors conclude that the frequency of the BRCA1 mutation 5382insC is similar in patients with and without a family history (FH) of breast cancer.
However, they detected the mutation in 5 / 90 patients with a FH of (breast) cancer and in 1 / 45 patients without a FH of breast cancer.
- why do the authors reach their conclusion ?
- what about the remaining 3 mutation carriers (total is 9, of which 5 have positive FH and 1 has negative FH).
- 193 patients were tested for the BRCA1 mutation: how many had a positive or a negative FH of breast cancer ? This is only reported for (90 + 45 =) 135 patients.

(6) However plausible, the statistical significance of the difference in ages of onset between mutation-positive and mutation-negative patients may have to be stated.

Minor Essential Revisions:

(1) The name of the mutation is inconsistent throughout the manuscript: 5382insC as well as the incorrect 5328insC occur at several places.

(2) BRCA1 mutation 'bearers' could be replaced by mutation 'carriers'

(3) The article should state that BRCA1 (and BRCA2) mutations are not only associated with an increased risk of breast cancer, but also of ovarian cancer.

(4) The authors could include a statement that identification of the BRCA1 mutation may lead to appropriate management not only in symptomatic patients, but also allows presymptomatic (or predictive) testing in at-risk family member of patients, contributing to early detection and prevention of breast cancer.

Discretionary Revisions:

(1) As this journal primarily deals with genetics, there is no strict need to explain the meaning of DNA in the List of abbreviations.

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

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

**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.