Reviewer's report

Title: TP53 mutations in ovarian carcinomas from sporadic cases and carriers of two distinct BRCA1 founder mutations; relation to age at diagnosis and survival

Version: 2 Date: 29 April 2005

Reviewer: Andrew Roddam

Reviewer's report:

General

This review deals solely with the statistical issues of the current manuscript.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Page 10 – how was the difference between mean age at diagnosis tested, details needed in the statistical analysis section. The test of difference in mean age between the familial cases should probably be non-parametric due to small sample size.
2. I am not always convinced of the necessity in this paper to test for differences between groups by means of a Cox PH model especially when some of the groups contain very few observations – surely some of the basic tests like between BRCA1 status, TP53 status, age at diagnosis (categorised into two groups) could be more efficiently tested by means of a log-rank test.
3. Figure 1 is not an appropriate representation of the data due to censoring. What is plotted on the y-axis is not always an exact survival time since some people will still be alive and will be living for at least as long as their survival time. The authors need to redraw this figure more in line with a classical survival analysis/Kaplan Meier type plot with separate lines for each of the subgroups they wish to show.
4. In the middle of page 10 it is stated that TP53 mutation reduced survival time but is really survival rates.
5. The results are not always very clearly presented since they are mainly in the text. I would recommend for some (not all) of them to be presented in a table in a similar way to Table 3 thus allowing a more direct visualisation of the results and hence reducing the amount of text needed for this section.
6. The discussion in the results section with respect to the interaction between TP53 and BRCA1 status should be followed with reference to Table 3 (currently at the end of the results section) since this is directly relevant to this.
7. I would recommend that the authors re-read parts of the discussion/summary section and ensure that their interpretations of the results are correct. Even though a subgroup estimate of familial versus sporadic cases in those >50 at diagnosis was significant the test of interaction was not and there is nothing more than a suggestion of a difference rather than as the authors suggest a clear trend. As the authors rightly note this study is very underpowered to detect differences in subgroups and they should also be mindful of the multiple numbers of tests in multiple subgroups and whether differences at the 0.05 level are conservative enough.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1. In the statistical analysis (and all references elsewhere in the paper) section the outcome from a Cox model is a hazard rate not a relative risk
2. The statistical significance level is normally set at 0.05, not <0.05.
3. At the bottom of page 9 on the manuscript there appears to be some text editing error over referencing to the IARC TP53 database which appears twice.

Discretionary Revisions (which the author can choose to ignore)

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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

**Quality of written English:** Acceptable

**Statistical review:** Yes

**Declaration of competing interests:**

I declare that I have no competing interests