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: 1 Date: 11 February 2005

Reviewer: richard buller

Reviewer's report:

- Major Compulsory Revisions
1) This study of the inter relationship of TP53 mutation in sporadic and hereditary BRCA1 related ovarian cancers presents several interesting observations. First, the hereditary ovarian cancers contain either of the two prevalent Norwegian founder mutations. With the conflicting literature on the impact of BRCA1 mutation status on ovarian cancer survival, publication of additional studies from different ethnic populations will allow investigators to determine whether the clear survival benefits seen in the Ashkenazi population likely is due to BRCA1 mutation, or may in fact be secondary to other commonly inherited genetic factors shared by the ethnic population under study. The authors should address this important issue in their discussion.

- Minor Essential Revisions

There are a couple of potential methodological problems which should also be discussed:
1) It is well known that DNA isolated from paraffin embedded tissue may give rise to artifactual sequence abnormalities. With perhaps 8 such events in the BRCA1 cancers, it is difficult to know the true relationship of the TP53 mutation to BRCA1 mutation status.
2) No reference is made to the % tumor within the samples studied. Either a laser capture technique, use of only high % tumor samples, or isolation of the abnormal band from the TTGE followed by reamplification and sequencing could get around this problem. I don’t think in this era that it is acceptable to equate the gel abnormality with a functional mutation; otherwise you might as well just use the gel results and skip the sequencing.

Table 3 is not labeled in a way that a reader could pick it up and understand what was reported. Furthermore, I don’t see any reference to Table 3 in the text of the manuscript.

Statistical review:
- Yes

When a negative study (BRCA1 mutation doesn’t impact survival) is reported, it is critical to understand the power of the study to detect a difference and then to report this statistical analysis.

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

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes
Declaration of competing interests:

I declare that I have no competing interests