Reviewer's report

Title: Cyclo-oxygenase-2 (Cox-2) expression is associated with resistance to platinum but not platinum/paclitaxel containing chemotherapy in advanced ovarian cancer

Version: Date: 11 May 2006
Reviewer: Joanna Stewart

Reviewer's report:

General
The rationale for the study has been clearly presented and is easily understood by one knowing nothing about the particular field. The actual data collected would seem appropriate, however the terminology used to describe what was done is incorrect. The data is simple and presented in full. Some of the analysis is incorrect but this can be remedied (and in fact can been carried out from the data presented.) The paper is clearly written. The correct analysis would reveal that they have been unable, in this study, to conclusively demonstrate that there is a difference in the influence of COX-2 inhibitors on response depending on the treatment regime, although there is a possible indication that this could be so, indicating that a larger study needs to be carried out to confirm or refute this. This necessitates a modification to the title and discussion. However, given the presentation is altered, the basis of the paper is sound and should be reported.

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

Study description
1. The study is not a case control study. In a case control study the outcome is case or control - ie the response, not the treatment as described in the paper. It appears to have simply been a retrospective review of patients with ovarian cancer receiving chemotherapy.
2. There is mention of ‘matching’ but this is ignored in all analyses and does not appear to have happened at any rate - the sample sizes are quite different and the number of factors supposedly matched on would have rendered this impossible. It is not clear if there were other patients available for inclusion so some better description of patient selection needs to be made.

Analysis
1. While it is acceptable to list the characteristics of the subjects included in this study who received the 2 treatment regimes they should not be statistically tested for differences as the methods have indicated that in fact some attempt was made to ‘match’ on these characteristics. ie they were not a random sample of patients receiving these treatments and it is therefore not possible to test to see whether the populations of people who receive the 2 treatments differ on these characteristics, using these samples. If any of these factors are likely to influence response then they should be included in the analysis of response, irrespective of the comparability of there distribution in the 2 treatment groups.
2. The main thrust of the paper is to investigate whether the influence of COX-2 inhibitors on response differs according to treatment regime. This has not actually been statistically tested. You can not compare p values from 2 different tests and conclude the results are different because one is significant and one not. You can not conclude no effect because the p value was >.05 - simply that you could not demonstrate one with this sized sample.
   A logistic regression analysis needs to be run with response as the outcome and including treatment, COX-2 status and their interaction as explanatory variables (plus any other variable which could be expected in influence response). The interaction is the indicator of a difference in the effect of COX-2 in the different treatments. Using the raw data presented in the paper, without any other confounding variables included, the p value associated with this interaction appears to be 0.13. The conclusions of the paper need to reflect this - ie with this sized sample there is not enough evidence to conclude that COX-2 has a differential effect on response, depending on treatment. A larger study would be required to discover whether the trend seen in the observed data is real or a chance occurrence.

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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. The heading on table 2 appears to be wrong
2. The label on the Y axis of the survival curve appears to be wrong
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: No

Declaration of competing interests:
I declare that I have no competing interests