Reviewer's report

Title: Celecoxib Concentration Predicts Decrease In Prostaglandin E2 Concentrations In Nipple Aspirate Fluid From High Risk Women

Version: 3 Date: 12 November 2007

Reviewer: Gillian Mitchell

Reviewer's report:

General
My previous comments have been addressed and I think that the current version of the manuscript is much improved.

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

I am still concerned about:

1. the observation that the NAF PGE2 levels increase in premenopausal women and clearly demonstrated in fig 1. If the underlying hypothesis is that NAF PGE2 levels somehow reflect the chemprotective effect of celecoxib on breast cancer, then this observation implies that the breast cancer risk could increase in premenopausal women using celecoxib. Simply concluding that no reduction in PGE2 levels in premenopausal women was observed in contrast to the reduction seen in postmenopausal women because postmenopausal women have higher serum levels of celecoxib post treatment is not a sufficient discussion of these observations.

2. the role of celecoxib as a chemopreventive agent.
   a. in premenopausal women as outlined above
   b. due to the cardiovascular risks. This study was started before these effects were appreciated and they probably mean that these NSAIDS are unlikely to be used as a chemopreventive agent for breast cancer, particularly as there are other proven alternatives (tamoxifen and raloxifene +/- aromatise inhibitors). A greater emphasis has to be given to this state of affairs, which means that even if the results presented in this study are in support of a breast cancer chemopreventive effect, it probably will not support further efforts being expended in developing this class of drugs as a chemopreventive option.

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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)

Background: Para 1 line 6, should read “Women with breast cancer with TUMOR PGE2 levels above etc”
Results: Subjects, para 1 line 10. “Side effects are discussed in detail IN THE TOXICITY SECTION IN THE METHODS SECTION.”

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, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare I have no competing interests