Reviewer's report

Title: Phase II Study of the Combination Carboplatin plus Celecoxib in Heavily Pre-treated Recurrent Ovarian Cancer Patients

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Reviewer: Stephen Ackland

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This paper describes a straight phase II study in 45 pts with ovarian cancer and prior Pt therapy. The treatment was carboplatin and celecoxib, with a 29% objective clinical response rate, a 40% biochemical response rate (>50% fall in CA125), a PFS of 5 months median and an overall survival of median 13 months. Toxicity was acceptable, similar to carboplatin alone, with no obvious toxicity interaction of the 2 agents. The study has been well conducted and analysed, but I find a number of minor issues.

Major Compulsory Revisions:

1. Selection of patients and the term platinum-resistant: these patients were required to have had primary treatment with a platinum, at least one prior line of treatment for recurrence, and >6mo since last platinum regimen. The definition of platinum resistance according to Ref 5 is <PR, or PD within 6 mo of platinum. Platinum refractory disease is progression while on platinum. For patients with an interval of >6mo since platinum, the probability of responding to a platinum re-treatment is about 20%, as the authors state. The patients in this study should be considered platinum-sensitive, since the interval from last platinum was median 22 mo. Therefore a response rate of 29% is not surprising. In “results” it is mentioned that 29% of patients had primary resistance, which is not consistent with the above accepted definitions and incorrect. Secondary platinum-resistance is not defined, and I think all patients should be considered platinum-sensitive. The first paragraph under results and the second paragraph under discussion therefore need revision.

2. Carboplatin schedule: most clinicians would have used carboplatin AUC5 every 3 weeks. The use of a 4-weekly schedule in this trial might have compromised the primary outcome variable. The relative lack of toxicity suggests that a larger AUC or a 3-weekly cycle would have been feasible. Why was a 4-weekly schedule used?

3. The rationale for measuring only 2 of a vast number of angiogenic compounds is not strong.

4. Was PD assessed only clinically and radiologically? Or were patients considered PD if CA125 was rising?

4. The future: the authors might like to speculate in “discussion” about where this line of research is leading. Is a phase III trial proposed?
Minor/discretionary comments:

1. Can it be stated that there is no known PK interaction between carboplatin and celecoxib? (I don’t think there are any interactions) Otherwise it is possible that any difference in effect of the combination may be based on PK.

2. Patients already taking an NSAID were not excluded. How did the authors manage to confirm that the patient population was “clean” in this regard?

3. Details about the serum separator tube should be included (page 8).

4. The study took 4 years to accrue 45 patients. However, I don’t think the field has advanced much in that time, except that there are a lot more “targeted new agents” to study in clinical trials. So it still has relevance.

5. It might be worthwhile detailing some of the post-study treatment that was used, since the median survival after PD was 8 months.

6. PGE-M needs to be defined.

7. Categories of platinum sensitivity (table 1) need to be defined. See comment above.

8. Figure 1 should either have ticks indicated censored patients on the curve, or number at risk below the x-axis. I note that follow-up is 3-46 months.

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 that I have no competing interests'