Reviewer's report

Title: Rosiglitazone synergizes anticancer activity of cisplatin and reduces its nephrotoxicity in 7, 12-dimethyl benz[a]anthracene (DMBA) induced breast cancer rats

Version: 1 Date: 11 November 2008

Reviewer: Marie H Hanigan

Reviewer's report:

Review of Tikoo et al

Cisplatin is not a first line therapy for breast cancer although it is first line for other types of tumors.

Major Compulsory Revisions

Did the rosiglitazone contain maleate? If so, how much maleate was administered?

In the methods the authors say that they divided the tumor bearing animals into groups on the basis of their tumor volume. This would introduce a major bias into the study. The DMBA treated rats should have been randomly distributed into the treatment groups. This bias calls all the data into question.

How many rats were in each group?

What is CMC? Why didn't the control groups also receive CMC?

The dose of cisplatin used (7.5 mg/kg) is an extremely high dose for a rat. Did any of the animals die following cisplatin treatment? BUN of 18 and creatinine of 5.5 would suggest a fatal dose of cisplatin. What day were those values measured? Were they the same time point for all groups?

In the methods the authors state that they measured visible tumors. This may have been the only method of monitoring the tumors post-cisplatin treatment but surface measurement of tumors is notorious for being inaccurate. All of the animals should have been sacrificed at the same time, the tumors excised and weighed.

Nine days is a very short time course for tumor regression (data presented in the tables). Nowhere in the methods does it state when the animals were sacrificed.

Fig 2 D was the rat treated with both rosiglitazone and cisplatin? The images in Fig 2 appear to be of distal tubules. The most prominent cisplatin toxicity is generally seen in the proximal tubules.

The histology of the kidney and mammary tumors - what day were the rats
sacrificed? Were they all sacrificed the same day? How many rats were sacrificed?

There are a series of papers on the effect of rosiglitazone protecting against cisplatin nephrotoxicity in mice. The authors cite one of these papers (ref 8) but do not indicate in their introduction that others have done these studies. The last paragraph of their introduction states that they hypothesize that rosiglitazone may protect against cisplatin nephrotoxicity. In fact they are repeating others work in a different species.

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

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.