Reviewer's report

Title: Inhibitory effect of ginsenoside Rg3 combined with gemcitabine on angiogenesis and growth of lung cancer in mice

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Reviewer: Charles Rosser

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The manuscript ‘Inhibitory effect of ginsenoside Rg3 combined with gemcitabine on angiogenesis and growth of lung cancer in mice’ by Liu and others is an interesting in vivo study illustrating combination therapy directed at cytotoxicity and angiogenesis may prove to be beneficial. This group possesses the most experience in the world on Rg3. Though the study is compelling there are several issues that must be addressed to strengthen the manuscript.

Below are some key points...

1) Title: No problems
2) Abstract: No problems
3) Introduction: Both Avastin and Macugen were approved the same year. Avastin was approved for the treatment of cancer whereas Macugen was associated with macular degeneration.
4) Last paragraph of introduction is worded oddly. Please consider revising to flow better and to get your point across better.
5) Materials and Methods: Was animal experiment approved by an animal care committee?
6) Can delete last sentence of first paragraph of Materials and Methods. It does not add anything.
7) What is the meaning of the following sentence from the Materials and Methods section…The tumor tissue from Lewis lung carcinoma mice were triturated and made into cell suspensions (dilution 1:5 with normal saline). Were these cells from xenograft tumors or were they grown in vitro?
8) A daily dose of 20 mg/kg of Rg3 was administered. Is this achievable in humans? How is it metabolized and excreted?
9) If I understand correctly, cells were injected and 7 days later treatment began for 18 days. This is a very short experiment. How big were the tumors when you began treatment? How big were they at the end of treatment?
10) Check manuscript for grammar and spelling.
11) ‘Quality of life’ was measured. A lot of what we know of quality of life in humans is subjective, thus impossible to assess in a mouse. For example, psychosis was measured. I think in animals this is near impossible to measure. Perhaps instead of saying quality of life can say you are measuring or assessing...
whether the animal is distress.

12) I have never heard of the inhibitive rate of tumor. Please provide a reference for the assay. Same for necrosis rate of tumor. Necrosis is important but must consider proliferative rate and apoptosis as well.

13) 7 MHz ultrasound was used to assay the tumors. This size probe is routinely used to image larger organs, i.e. prostate. Though the pictures included look impressive, would a higher MHz be more effective?

14) By scanning the field for CD31 hotspots, bias may be introduced.

15) Results: The Table is not helpful. Consider describing only in text and removing table.

16) To better illustrate survival, survival curves, Kaplan Meier curves should be utilized (Figure 1 A).

17) Again not sure what the inhibitive rate of tumor is showing. Please plot tumor growth curve over time for each group.

18) Considering doing apoptosis and Ki-67 or PCNA for IHC to better elucidate the mechanism behind Rg3. In my experience when high rates of necrosis are evident, there may be a higher incidence of toxicity, though none was reported here.

19) Discussion: Nicely stated discussion. Please incorporate some of the issues raised above. In addition, I am unsure of what a one-class new drug means in China? Has it been used in clinical trials? If so what has been the outcome?

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: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests