Reviewer's report

Title: A word of caution: Do not wake sleeping dogs. Micrometastases of melanoma suddenly grew after progesterone treatment.

Version: 2 Date: 22 January 2013

Reviewer: Kevin Kim

Reviewer's report:

Re: the manuscript, “A WORD OF CAUTION: DO NOT WAKE SLEEPING DOGS. MICROMETASTASES OF MELANOMA SUDDENLY GREW AFTER PROGESTERONE TREATMENT”

This manuscript is a case report of a patient whose disease progressed rapidly soon after the initiation of progesterone treatment for ovarian dysfunction. The authors speculated and hypothesized that progesterone treatment was the cause of the rapid disease progression through the negative effect on the immune system. They provided the literatures of both preclinical and clinical observations to base their hypothesis.

I believe that this case is interesting and worth publication. However, I have a number of major issues.

1. Please consider deleting the first paragraph of the Background section as this doesn’t seem to be essential to be included. Also, the second and the third paragraphs of Background may be a better fit for Conclusion/Discussion section. Please consider moving these 2 paragraphs to the discussion section where the authors mentioned the preclinical and clinical findings of progesterone in the immune system. Discussion section.

2. In Case Presentation, Please mention whether the liver was evaluated with the ultrasound at the time of the serum LDH of 369 U/L and a normal CXR between November and December 2011. It will be important to clarify that the liver was clear at the time of the initiation of progesterone.

3. In Case Presentation, in which month the new liver mets were seen for the first time on an ultrasound? The authors stated “three months later”, but was it 3 months after the initiation of the progesterone treatment or 3 months after the completion of the 3 cycle of the progesterone treatment?

4. In the Conclusion/Discussion, the authors stated “After a one month Pg treatment for her ovary cysts a rapid disease progression ensued”. From the Case presentation, it appears that the disease progression occurred within 3 months, so it may not be accurate to state “after one month”.

5. There are many grammatical errors. The manuscript should be revised with a help of a scientific editor.
There are a number of minor issues which may be easily addressed.

1. In the abstract, I am not sure what “(001-CSS)” means. If not essential info, please delete.
2. In the abstract and the body of the manuscript, “Breslow index” and “Clark’s stage” should be replaced with “Breslow thickness” and “Clark’s level”, respectively.
3. In the abstract, “CSF470” may be replaced with “melanoma cell lysate vaccine” because it will be easier for the readers to understand. It is appropriate that CSF470 was explained in the text body.
4. In Case Presentation, I would suggest that which sentinel lymph node basin was examined. Was it bilateral axillary node or left or right axillary nodes?
5. In Case Presentation, please describe how frequent the patient received a cycle of 4 daily injections of CSF470 vaccine. Was it repeated every 4 weeks? Or 3 months?
6. In Case Presentation, after the first description of the serum LDH level, please include the normal range in the parenthesis, so that it will be easier for the readers.
7. In Case Presentation, please describe the specific grade 2 toxicity at the injection site. Pain? Rash? Erythema? Edema?
8. In Case Presentation, Please describe the duration of the cycle of progesterone. Every 4 weeks? Every 2 weeks?

This manuscript is not publishable as is and needs major revision before it can be reconsidered for publication. I will be happy to rereview the manuscript after it is revised.

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

**Quality of written English**: Not suitable for publication unless extensively edited

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

**Declaration of competing interests**: None. No competing interests exist for me.