Reviewer's report

Title: Preclinical evaluation of Sunitinib as a single agent in the prophylactic setting in a mouse model of bone metastases.

Version: 1 Date: 28 August 2012

Reviewer: Andy Reynolds

Reviewer's report:

The authors have used a metastatic breast cancer cell line in a mouse model to examine the efficacy of sunitinib in preventing bone metastases. A clear rationale for the work is provided, since sunitinib appears to have effects on bone remodeling. The question itself is therefore of interest although, disappointingly, the results of this small study are largely negative. The study itself appears to be well conducted.

The manuscript would be improved by addressing the following points:

Major compulsory revisions:

1) It is unclear to the reviewer why there should be no effect of sutent on the the size of osteolytic lesions as measured by plain radiograph, but a significant effect of sutent on tumour size as measured by fluorescence. One assumes these two parameters should be correlated. The reason for this anomaly should be explained.

2) The limitations of the study should be made clear. A single cell line was employed. Sunitinib was commenced 2 days prior to injection and it is unclear whether a longer period may have had any influence. A more interesting question may have been to examine the effect of sutent in conjunction with another agent.

Minor essential revisions:

3) The authors should acknowledge the fact that sutent appears to have no useful activity in metastatic breast cancer, as recent data shows (Barrios CH et al., 2010; Bergh J et al, 2012), even though their results suggest an anti-tumour effect in the bones of mice.

4) The reference suggesting sunitinib is not associated with significant toxicity and is well tolerated is misleading. This is a very limited example, and the clinical reality with this drug is that many patients experience significant toxicity of CTC grade 3 or 4 requiring dose reduction or cessation. The authors should instead draw attention to the development of second generation TKIs such as pazopanib or tivozanib that have similar activity but appear to be much better tolerated.

5) Ref 10 has now been published in the NEJM (Coleman et al., 2011) and should be replaced.
6) It should be made clear that MDA-MB231 is a metastatic breast cancer cell line.

7) Point 2.2: The word ‘injected’ is misleading for vehicle mice and should be replaced.

Discretionary Revisions:

8) The term TRAP+/bone surface/mm² is unclear. It would be clearer expressed as TRAP+/mm² of bone surface.

9) Again, the term MVD/mm² is redundant and mm² can be removed.

**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.