Reviewer's report

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

Version: 3 Date: 13 December 2012

Reviewer: Andy Reynolds

Reviewer's report:

Major Compulsory Revisions

I am happy with the revisions, but I suggest these further changes:

In response my point 1, the authors need to cite this paper when talking about induction of other growth factors by sunitinib treatment:

Multiple circulating proangiogenic factors induced by sunitinib malate are tumor-independent and correlate with antitumor efficacy, 2007. PNAS vol. 104 no. 43, 17069–17074

Also, suitable references for the evasive response to sunitinib in PNET and GBM should be cited (e.g. Casanovas 2005, Paez-Ribes 2009).

In response to my point 2, I am pleased to see the authors now include a statement on limitations. I agree with this new text. However, they raise the issue of the conditioning effect reported with sunitinib:

“It has been reported that prior administration of doses of 120mg/kg induce a "conditioning effect" which promote the formation of metastases by circulating tumor cells [46, 47]. While lower doses have not been shown to have a conditioning effect for the 4T-1 murine mammary carcinoma cell line, variability in response amongst cell lines is observed [47].”

Whilst these are important data to cite, the way this info is presented could be more helpful. Instead:

(1) Authors should make the point that although pre-treatment of mice with 120 mg/kg/day sunitinib promotes metastasis (ref 46), pre-treatment of mice in their study with the 40 mg/kg/day dose did not lead to enhanced metastasis.

(2) They then need to state that this observation is in keeping with other data (ref 47) which support the concept that lower doses of sunitinib do not promote metastasis.

(3) In addition to ref 47, this paper should also be cited:

(4) “4T1” is the correct way to write the name of these cells.

(5) The comment about "variability in response amongst cell lines is observed" is not relevant here and can be removed.

(6) The above information about conditioning effect is not a limitation of the study, it is an important observation. Therefore, this text should be moved to a different part of the discussion.

· Minor Essential Revisions

None

· Discretionary Revisions

None

Level of interest: An article of importance in its field

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