Reviewer's report

Title: Anti-invasive and antiangiogenic effects of MMI-166 on glioma cells

Version: 1 Date: 26 March 2010

Reviewer: Ian Lorimer

Reviewer's report:

Major Compulsory Revisions:

1. As this is a preclinical evaluation of the potential of MMI-166 to treat glioblastoma, data on invasion, angiogenesis and proliferation/cytotoxicity for all three cell lines (U87MG, T98G and ONS12) should be shown.

2. For the VWF staining (Figure 6), there needs to be quantification from multiple sections to ensure that the differences in VWF staining are real and not a sampling artifact.

3. The structure of MMI-166 should probably be shown (I am not sure of the journal policy on this).

4. The authors should include a discussion of the limitations of the U87MG model, with particular reference to invasion.

5. There should be an explanation or discussion as to why an inhibitor down-regulates the total protein levels of the MMPs, rather than simply inhibiting their activity.

6. There should be an explanation/discussion as to why, in Figure 4, angiogenesis is further affected at 100uM drug, even though Figure 2 indicates that MMP inhibition is complete at 10 uM.

7. There should be some discussion of what stage this drug is at in clinical development. The drug has been around for ten years and has been assessed preclinically in multiple other cancer types - is there some obstacle to further development?

Minor Essential Revisions:

1. Details of the ONS12 cell line should be included (patient tumour classification, tumorigenicity in nude mice if known, available data on markers or genetic aberrations).

2. There should be a reference for the culture insert method used to evaluate angiogenesis.

3. It should be clarified that MTT assays assesses changes cell numbers: this can be due to changes in proliferation or cytotoxicity or both (not simply
cytotoxicity).

4. In Figure 2, there is no explanation for what the different lanes show. Similarly in Figure 3A and 4A, there is no explanation as to what the different panels show in the Figure legend.

5. In Figure 5, the data should be shown as a bar graph.

6. In Figure 1b, GAPGH should be GAPDH.

7. On p.20, it was unclear what was meant in the last sentence (“coeval” is not a word).

8. There are minor problems with English grammar in the text – perhaps the journal can help with this.

Discretionary Revisions:

1. The paper would be greatly strengthened if a second glioblastoma model was used that is more representative of the human disease.

**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