Reviewer’s report

Title: Is Symptom Reduction by Angiogenesis Inhibitors in GBM Patients Without a Price?

Version: 1 Date: 15 December 2008

Reviewer: Andrew D. Norden

Reviewer’s report:

General Comments:
This debate concerns an important, unresolved issue in contemporary neuro-oncology: whether anti-angiogenic therapy achieves true anti-tumor efficacy. This is a topic that should be of general interest to the oncology community because anti-angiogenic therapies are now being evaluated in nearly every known tumor type.

Major Compulsory Revisions:
1. Further editing for grammar and style is necessary to increase the clarity of the argument.
2. In referring to the results of phase II trials on page 4 (line 9), the authors should cite the Cloughesey data (reference 19). Overall survival of 8-9 months was reported in Cloughesey's study, and this should be discussed and compared to historical data.
3. The Macdonald criteria, which are used widely as the authors note on page 6 (line 5), should be defined and explained in further detail. Further discussion of alternatives to Macdonald criteria is needed.
4. On page 6 (line 12), the authors comment on the shift to an invasive tumor phenotype; citations 25 and 26 do not sufficiently support this claim in glioma.
5. The section entitled Vascularisation and vessel normalization (page 7) is insufficiently detailed to be convincing.
6. Is there other literature that could be discussed in the section on Blood Brain Barrier and chemotherapy (page 9)? This brief section is not persuasive, as it cites a single study as evidence that anti-angiogenic therapy may reduce chemotherapy penetration. The authors' argument may be correct, but a fair amount of published literature supports the counter-argument, that anti-angiogenic therapy promotes chemotherapy penetration.
7. Other literature that supports the vascular co-option hypothesis should be reviewed and discussed; see Lamszus et al. Acta Neurochir Suppl 2003;88:169-77.

Minor Essential Revisions:
1. Bevacizumab is FDA-approved for lung and breast cancers, in addition to colorectal cancer as noted by the authors.
2. On page 5 (lines 3-4), the authors note that anti-angiogenic drugs reduce the need for corticosteroids. This has been reported in a number of recent studies that should be cited here.

3. In Figure 1, ADC sequences are included. The potential significance of ADC must be discussed. Additionally, the size of the contrast-enhancing lesion in (c) appears to be larger (as opposed to smaller than baseline).

4. The implication in Figure 2 is that bevacizumab treatment has increased invasion and co-option. Perhaps a non-bevacizumab treated sample could be provided as a comparison.

Discretionary Revisions: none

**Level of interest:** An article of outstanding merit and interest in its field

**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:**

I declare that I have no competing interests.