Reviewer’s report

Title: Phase I trial of bortezomib in combination with celecoxib in patients with advanced solid tumors

Version: 1 Date: 9 August 2007

Reviewer: Robert E Brown

Reviewer’s report:

General

I have reviewed the manuscript by Hayslip and co-workers entitled, "Phase I trial of bortezomib in combination with celecoxib in patients with advanced solid tumors". I offer the following impressions and comment:

1. The work combining bortezomib with celecoxib appears to be new and original, given the fact that no other articles of a similar nature were identified in a computer-assisted literature search of the National Library of Medicine’s MEDLINE database.

2. The work is clearly defined and the methods appear appropriate and well described in sufficient detail to permit others to replicate the study.

3. The data appear sound and well controlled.

4. The title and abstract appear to accurately convey what has been found.

5. The manuscript is well written.

Additionally, this reviewer respectfully requests that the authors respond to the following queries and suggestions and consider incorporating the discussion into their manuscript:

1. Why did they choose the selective COX-2 inhibitor, celecoxib instead of the nonselective COX inhibitor, indomethacin which also has antitumoral activity (see Takada, et al. Oncogene. 2004;23:9247-9258)--especially, in light of the cardiovascular risk associated with a selective COX-2 inhibitor?

2. Because other COX-2 inhibitors, such as rofecoxib, have been combined with single agent chemotherapy (e.g., trofosfamide) in a metronomic fashion (which may be targeting the NF-kappaB pathway, at least in part [see Reichle, et al. Cancer 2004;101:2247-2256; Reichle, et al. Br. J. Haematol. 2005;128:730-732 and Brown, RE. Br. J. Haematol. 2005;130:147-148]), do the authors forsee a similar application for combinatorial therapy employing bortezomib, celecoxib and a cytotoxic agent?

3. The authors appear to focus upon and emphasize COX-2 inhibition as the main target and action of celecoxib in the rationale for their initiative. For the sake of completeness, they should incorporate other observations that provide for an antitumoral effect of celecoxib independent of cyclooxygenase (see Kim, et al. J.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after discretionary revisions

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.