Reviewer's report

Title: A randomized multi-center phase II trial of the angiogenesis inhibitor Cilengitide (EMD 121974) and gemcitabine compared with gemcitabine alone in advanced unresectable pancreatic cancer [ISRCTN13413322]

Version: 1 Date: 2 April 2006

Reviewer: Henry Q Xiong

Reviewer's report:

General

Congratulations on the authors’ effort in conducting and reporting the trial. In this randomized phase II trial, gemcitabine in combination with cilengitide, an angiogenic inhibitor, was compared with gemcitabine in patients with advanced pancreatic cancer. The sample size was determined clinically and the results indicated that there were no clinically important differences regarding efficacy, safety between the two regimens.

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

1. The major concern is the statistical design. The author stated that the sample size of the trial was determined clinically and was not based on any consideration of statistical power. The author needs to explain why statistical design was not considered (in statistical analysis section or discussion section). Was the sample size (89 patients) predetermined? Were there any early stopping rules?
2. There was confusion in documenting and reporting safety. The author used NCI-CTC Version 2 for monitoring toxicities and reported toxicities based on AE and SAE, grades, and severity (mild, moderate, severe, and life-threatening). There was great redundancy as the author tried to report toxicity or safety based on these classifications. For example, life-threatening events could be either AE or SAE (Table 5). I’d recommend deleting Table 5 and . The readers are interested in toxicities and its grades. Serious adverse events usually include severe and life-threatening events or grade 3 and 4 events. I am not sure same definition applies here. If it doesn't, the author needs to change the title of Table 6b to: serious adverse and life-threatening events possibly related to study treatment.
3. There was discrepancy of toxic events reported between the text (safety) and the table 6a. For example, nausea was 64% vs 50% in the text (page 9, line 6 of second paragraph), but was 36% vs 38%.
4. The discussion on safety can be deleted or rewritten.

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

1. The author needs to be more specific in defining eligibility criteria. The criterion, a history of cerebrovascular accident or repeated transient ischemic attacks and cardiac or cardiovascular abnormality (page 4, patients), is not clear.
2. Why the author uses different starting date for calculation of overall survival (from the start of study drug administration to death) and PFS (the time between the date of randomization and the
date of disease progression)?
3. Define “condition reduced”(Table 6b) since it is not commonly reported as serious adverse event.

Discretionary Revisions (which the author can choose to ignore)

1. The authors may want to add "randomized phase II trial" as a key word.
2. Typo: Area under the curve (page 6, second to the last line).

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes

Declaration of competing interests:
I declare that I have no competing interests