Reviewer's report

Title: Phase I study of intermittent and chronomodulated oral therapy with capecitabine in patients with advanced and/or metastatic cancer

Version: 1 Date: 13 December 2005

Reviewer: sridhar mani

Reviewer's report:

General.

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

1. What is the rationale for chronomodulating capecitabine. Please provide scientific data or a well established principle that demonstrates that dose intensity with capecitabine matters or it doesn't. Would saturation of enzymes in tumor be rate-limiting for more 5-FU to form as you escalate capecitabine. I am not clear of why dose intensify ??

2. Limit and shorten sections of the paper (e.g., patient selection etc.... are too long and may be referenced to other manuscripts and abbreviated).

3. There was no PK done which would have established whether concentrations were leveling off at a top dose or sub-MTD doses suggesting saturability of the system. This would have been especially worthwhile given the responses observed.

4. Comment on other strategies to make dosing more predictable like "flat dose" (mg) programs and how that may have improved chronomodulation or not.

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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. Correct minor spelling errors throughout manuscript..spellcheck and grammar check is important.

2. 

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Discretionary Revisions (which the author can choose to ignore)

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: Not suitable for publication unless extensively edited

Statistical review: No

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