Reviewer's report

Title: Clinical implications of thymidylate synthetase, dihydropyrimidine dehydrogenase and orotate phosphoribosyl transferase activity levels in colorectal carcinoma following radical resection and administration of adjuvant 5-FU chemotherapy

Version: 6 Date: 18 December 2007

Reviewer: Carlo Barone

Reviewer's report:

Major Compulsory Revisions
The authors have addressed the minor essential revisions, but they did not realize the sense of the major criticisms. Furthermore, also in the revised parts of the manuscript there are other new mistakes, that are listed afterwards (see "Minor Essential Revisions")

First of all, the lack of significant difference in DFS between Dukes B and Dukes C stage is very unusual. It may be explained by the very low number of patients in each group, but this bias might affect also the statistically significant data, that would be purely random and due to the low number of patients.

Secondly, the discussion is still too long and rather chaotic; many arguments are generic, superfluous and unrelated to the study results. In particular, the discussion concerning DPD (page 13 lines 7 to 24) is clearly redundant and it might be shortened to a single sentence. In the next lines the meaning of "predictive" and "prognostic" remains confused as in order to support the authors' theory. Furthermore, in the paper of Kato et al no enzyme activity has been evaluated, therefore the results cannot be explained in relation to TS and/or OPRT. On the other hand, it is unclear how the enzyme activities might influence the study of Kato et al differently from that of Edler et al. The argumentation seems devoid of scientific evidence, so the paragraph should be removed.

Minor Essential Revision
- Page 2 line 11: The chemotherapy did not consist of 5-FU but of an oral fluoropyrimidine
- Page 3 line 27 "... changes 5FU to 5-FUMP ..." (not to UMP)
- Page 4 line 2: Which enzymes? OPRT and DPD?
- Page 4 lines 6 and 10: 5FU: see above
- Page 5 line 21: "...activity levels of ...
- Page 5 lines 24-28: The statements are repetitive
- Page 6 line 9: 37 what? 37Â°C?
- Page 6 line 20: "... measured ..." (not "measure")
- Page 6 line 24: Verify the centrifugation speed
- Page 8 lines 3-7: The sentences are confused and contain reiterations
- Page 8 line 22: Wrong phrase: the verb is missing
- Page 9 line 1: "Results ...". The term does not seem appropriate. Please, rewrite the sentence
- Page 11 lines 4-5: Lower OPRT expression in N+ than in N- patients in this small-sized study does not allow to state that the OPRT level predicts the node involvement
- Page 12 lines 10-12: The sentence is not related to the previous consideration and should be deleted
- Page 12 line 24: " ... activity ..." The word is wrong

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

Level of interest: An article of limited interest

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.