Reviewer’s report

Title: A Phase II Study of LFP Therapy (5-FU (5-fluorourasil) continuous infusion (CVI) and Low-Dose Consecutive (Cisplatin) CDDP) in Advanced Biliary tract Carcinoma

Version: 4 Date: 15 November 2005

Reviewer: Nicolas Tsavaris

Reviewer’s report:

This is an extensive analysis of continuous infusion of 5FU + CDDP for advanced Billiary tract Carcinoma. In a group patients, of which 26% was previously treated by chemotherapy or radiotherapy, an interesting response rate of 42% was found. My main objection is that this study reports rather on the use of the pump than the basic points of such a study. These points would be:

1. Generally the Tables and Figures is of low quality with poor legends, without explanation of abbreviations, which makes it very difficult reading and understanding them.

2. Table 1 regarding the clinical characteristics of patients is inadequate; specifically there is no mention of disease extension (i.e. local or metastatic), of performance status and of the number of patients who had undergone surgery.

3. It is very difficult to evaluate the response rate in local disease pancreatic and billiary carcinomas. Authors used RECIST criteria, and they present overall response rate 42.9% which is very high for this type of cancer. This means that 18 patients which showed partial response had a more than 50% decrease in the sum of the products of the largest perpendicular diameters of the measurable lesions sustained for at least 1 month. This is not clear enough in the “material and methods” and the “results” sections.

4. The authors do not give any information about the 11 (26%) patients with previous therapy (radiotherapy/chemotherapy/ surgery).

5. PS is absent from Table 1, but it appears in Table 4.

6. In Table 3 there is no explanation for ascites and jaundice, were they the result of therapy (drug toxicity) or the outcome of the disease progression?

7. It is not clearly stated how was toxicity evaluated; was it expressed in respect with the administered courses of therapy or according to the number of patients?

8. The separation of patients in two groups ( >2 and <2A) is rather confusing. They refer to patients with only one course (<2) and 2 and more courses of therapy. From another point of view this means responders and no responders. The questions are firstly, when, how and by which criteria did the authors evaluated disease progression; and secondly why did they compare responders and no responders to chemotherapy, and included this element to survival and prognostic factors analysis?

9. The authors quote mild toxicity, mainly Grade 1 and 2. On the other hand, they used low doses of chemotherapy. It is well established in most types of
malignant tumors that by increasing the dose intensity of chemotherapy one might achieve better response rate. Why did the authors avoid to increase the doses of the administered drugs, although it was allowed at this phase of a study?

10. In Discussion I would expect a comment on the study by Kim et al. 2003, who had also used CDDP and Capecitabine, and reported RR 21.4% (half of the present study).

1. Is the question posed by the authors new and well defined?  
Yes
2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?  
Yes, but there are some methodological problems mentioned above.
3. Are the data sound and well controlled?  
It is a fair presentations of data, because authors have been oriented mainly to technical administration of drugs, with poor presentation of therapy’s results.
4. Does the manuscript adhere to the relevant standards for reporting and data deposition?  
Yes, but see above.
5. Are the discussion and conclusions well balanced and adequately supported by the data?  
Yes, but it needs to explain and support the findings of this effort, more.
6. Do the title and abstract accurately convey what has been found?  
Yes
7. Is the writing acceptable?  
Yes

- Major Compulsory Revisions  
Better quality of Tables and Figures, with brief legends, with explanation of abbreviations. More details of clinical characteristics, and evaluation of response. Think and decide about pretreated patients including in the study, also explain the relation of ascites and jaundice with disease or drug toxicity. More details about toxicity, and make clear its evaluation. Delete or re-write some confusing points such as the separation of patients in two groups ( >2 and <2 courses). Explain why they avoided to increase the doses of the administered drugs, or how they chose this doses. Discuss the response rate in correlation with other studies with platinum derives.

Level of interest  
- An article of importance in its field  
- An article whose findings are important to those with closely related research interests

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

Quality of written English: Needs some language corrections before being published

Statistical review: Yes

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