Reviewer’s report

Title: Neoadjuvant Irinotecan (CPT-11), 5-Fluorouracil (5-FU) and Leucovorin (LV) for Colorectal Liver Metastases: A Means of Selecting Candidates for Resection

Version: 1 Date: 30 September 2008

Reviewer: Carmelo CP Pozzo

Reviewer's report:

This paper reports an interesting phase 2 experience on the use of neoadjuvant irinotecan-based chemotherapy for the treatment of resectable colorectal cancer liver metastases (CLM). There are few experiences of a perioperative treatment of CLM and the only phase 3 study published so far used a perioperative oxaliplatin-based and not irinotecan-based chemotherapy regimen. I have some doubts on the statistical design of the study, on the choice of a typical phase 3 objective, such as DFS, as primary endpoint, and as well on the historical control indicated in the text. Nevertheless, DFS, resection rate, and response rate are consistent with those reported by others. The authors reported also an unusual high rate of thromboembolic events and they state that these could be related to the central venous catheter (CVC) and the perioperative approach. With regards to the use of an infusional 5-FU combination, i.e. FOLFIRI or FOLFOX, several phase 2 and phase 3 studies, including also patients who underwent liver surgery, have been published so far and the CVC did not seem to increase significantly the number of TE, neither when Bevacizumab has been added to the conventional chemotherapy regimen. The authors should better outline the characteristics of patients who developed a TE, the time of onset, the type of CVC used and as well the protocol of medical management of the CVC etc etc. The discussion should be shorten and the conclusion should be more cautious. No matter if the statistical design is appropriate, it should be emphasized that decreasing the number of patients accrued to roughly half of the foreseen enrollment number, due to unusual adverse events or other reasons, also the results could be jeopardized.

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

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I received in the past five years payments from Pfizer as conference speaker and as consultant in advisory boards, with regards to the use of irinotecan in
colorectal cancer, with a total amount less than 10,000 US dollars.