Reviewer’s report

Title: Systemic chemotherapy with doxorubicin, cisplatin and capecitabine for metastatic hepatocellular carcinoma

Version: 1 Date: 3 November 2005

Reviewer: Tony Mok

Reviewer’s report:

General
This is a phase II study on a triplet chemotherapy of doxorubicin, cisplatin and capecitabine on 29 patients with metastatic HCC. Authors reported tumor response rate of 24%, PFS of 3.7 months and overall survival of 7.7 months. They reported very favorable toxicity profile that included grade 3-4 neutropenia rate of only 14%. However, they concluded that this combination is unlikely to play an important role in treatment of HCC.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. I find the manuscript to be confusing. In the background, authors proposed the replacement of 5-FU by capecitabine in the three-drug combination because of its lower myelosuppression. They achieved response rate of 24% and low toxicity profile, which was supposed to be the objective of this phase II study. But at the end, they concluded the triplet combination to be unworthy. Authors must clarify their objectives and conclusion.

2. Please explain why enroll only patients with metastatic disease. For assessment of tumor response, did the authors include the primary HCC? Majority of patients had metastatic abdominal lymph node. What was the size criteria for the lymph node.

3. I found the grade 3-4 neutropenia rate of 14% hard to believe. According to the paper by Yeo et al (ref 25), which is one of the largest randomized study on cytotoxic therapy for HCC, the grade 3-4 neutropenia rate of single agent doxorubicin 60mg was 68%. Most of other publications on single agent doxorubicin also reported higher neutropenia rate.

4. Inclusion criteria allows patients with Child A or B cirrhosis but all 29 enrolled patients were Child A. Did the investigators enroll consecutive patients?

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. Page 8 paragraph 1: Which version of Common Toxicity Criteria was used?
2. Page 11 paragraph 2: What is the incidence of hand-foot syndrome?
3. Page 15, paragraph 2: The discussion on the use of targeted therapy in HCC is shallow and irrelevant to this phase II study on triplet cytotoxic chemotherapy.
4. Ref 25 is now published in full paper at JNCI.

Discretionary Revisions (which the author can choose to ignore)
1. Author should include data from other studies of capecitabine in HCC.
**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:** Needs some language corrections before being published

**Statistical review:** No

**Declaration of competing interests:**

I declare that I have no competing interests