Reviewer’s report

Title: Prognostic Value of alpha-Fetoprotein and Des-gamma-Carboxy Prothrombin Responses in Patients with Hepatocellular Carcinoma treated with Transarterial Chemoembolization

Version: 5 Date: 31 August 2012

Reviewer: Hidenori Toyoda

Reviewer’s report:

The revised version of the article by Lee et al. was reviewed.

I have still several concerns on this article that should be clarified.

1. With regard to the response by the authors to my comment #1 for original version, they explained that the study population in their study is different from patients included in the previous study by Kang et al. (Eur J Gastroenterol Hepatol 2012; 24: 849-856) from the same institution. However, this previous study included 350 patients with pretreatment elevation of both AFP and DCP who underwent TACE, termed as “palliative therapy”, between 2003 and 2007 (please see Table 1 of this article). The study period of the present study is between 2003 and 2005. How is the difference between these patient population? If the study patients between these two groups are different as the authors mentioned, how did they divided these patients (i.e., patients with pretreatment elevation of AFP and DCP who underwent TACE) into two groups, one of the previous study and the other for the present study? This reviewer still cannot trust the response. Please explain this point. I believe that it can be O.K. if study patients of the two studies overlap, because the focuses of the two studies are clearly different (prognostic value of baseline AFP and DCP in the previous study vs. the value of responses of AFP and DCP by TACE in the present study). I recommend that the authors rather emphasize this difference.

2. With regard to the response to my comment #2 for original version, the authors described that they did univariate and multivariate analyses for PFS and OS including antiviral therapies (nucleoside analogue intake or interferon) and viral factors (HBeAg atatus and HBV DNA levels) as factors. They described that these factors did not show independent association with PFS and OS. However, they showed no data on these re-analyses in the revised version. In revised Table 3, only the size and the number of tumors were added as factors. Therefore, it would be questionable whether they really re-analyzed including viral factors. Please re-make Table 3 including factors of antiviral therapy and viral status for univariable and multivariate analyses for both PFS and OS.

3. With regard to the response to my comment #3 for original version, they stand their selection of patients (select only patients with both elevated pretreatment AFP and DCP). Nonetheless, it will make a strong selection bias and will importantly decline the value of the study, because the results can be true only
on the very limited population of patients with HCC that does not represent the entire patients with HCC. Especially because the authors concluded that baseline DCP elevation is the factor that affects OS, this conclusion should be based on all HCC patients treated by TACE including those without DCP elevation. (One cannot conclude that base line DCP elevation is a predictive factor for OS when they only analyzed patients with elevated baseline DCP.) At least, they should included all HCC patients treated by TACE when evaluating baseline elevation of AFP and DCP.

4. With regard to the response to my minor comment #1 for original version, the authors described that AFP usually return to normal range within 25-35 days after tumor removal. Please provide the literature for this.

5. Page 5, lines 3-4 of the revised version, conclusion of the abstract: This sentence should be corrected. This sentence can lead misunderstanding that the findings can be applicable for all HCC patients receiving TACE. This study can lead the conclusion that AFP response and higher baseline DCP level are significant predictors of OS in treatment-naïve patients with HCC receiving TACE, only when “patients showed pretreatment elevation of both AFP and DCP”, i.e., very limited subpopulation of HCC patients receiving TACE.

6. Page 9, lines 11-12 of the revised version: “at the time of best radiologic response” How did the authors determine the “best radiologic response”?

7. Page 12, lines 3-6 of the revised version: Here, they should described all factors included univariate analysis and the condition for that the factors are included to further multivariate analysis (usually p<0.05 by univariate analysis).

8. Page 21, line 8 of the revised version: “old age and poor general condition as cachexia” Please provide their criteria to avoid surgical resection.

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

**Quality of written English:** Acceptable

**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.