Reviewer’s report

Title: Elevated preoperative peripheral blood monocyte count predicts poor prognosis for hepatocellular carcinoma after hepatic resection

Version: 1 Date: 7 May 2014

Reviewer: Michele Barone

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The authors explored the prognostic role of blood monocyte count for the prognosis of HCC patients after hepatic resection. A number of studies have been published in the last years on the prognostic impact of inflammatory markers in several field of oncology.

Major Revision

Although the topic is of interest, a lot of issues have been found that stand against the publication of the present paper on BMC cancer.

1) The current study is not the first paper exploring the impact of high monocyte levels on outcomes after resection in HCC patients (See Sasaki et al, Surgery 2006). Therefore, concerns raise about the novelty of the work.

2) It’s not clear what dependent parameter the authors used for ROC analysis. Disease-free survival rate at 1 year? 3 years? 5 years? Moreover, for prognostic purposes, the dependent variable should be overall survival (i.e. the primary endpoint in oncologic studies). Instead, in order to find a reliable cut-off point, authors stratified patients at high/low risk of recurrence. What does it mean recurrence? Disease-free survival? If so, a secondary endpoint has been erroneously taken into account.

3) The definition of OS that authors give in Materials and methods is wrong. OS is the time from treatment to death for any cause (not only HCC-related death). See Llovet et al, Design and endpoints of clinical trials in hepatocellular carcinoma., J Natl Cancer Inst. 2008, for the details.

4) ROC analysis is not the best way to find prognostic cut-off of a continuous parameter because OS and DFS are time-dependent variables. ROC can obviously be drawn but requires an artificial method (i.e. transforming OS or DFS in rates at predefined time periods). Such method could lead to biases because doesn’t encompass all study period but only a predefined limit (for example 1 or 3 years). Running log-rank test doesn’t present the aforementioned bias and should be performed in this setting. See Facciorusso et al. Serum Ferritin as a New Prognostic Factor in Hepatocellular Carcinoma Patients Treated with Radiofrequency Ablation. J Gastroenterol Hepatol. 2014 Apr 14. doi: 10.1111/jgh.12618, for the details.

5) All 351 patients underwent a biopsy before surgery? In Methods the authors state “351 newly diagnosed, histologically proven HCC”. This procedure stands against current guidelines (both American and European) that consider biopsy
only in case of discordance between CT and RMI. Please, better define the diagnostic algorithm followed in the study.

6) The study lacks a validation cohort, hence the results reported by the authors are weak and need further validation. Please develop this issue in Discussion.

Minor Revision

A careful language editing is needed. There are several typos and grammatical errors: for instance, page 11, raw 233 “the median monocyte count was two times higher Sasaki’s”. The word “than” should be added to this phrase.


**Level of interest:** An article of limited interest

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

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