Reviewer’s report

Title: Retrospective comparison between a regular and a split-dose protocol of 5-fluorouracil, cisplatin, and mitoxantrone for the treatment of far advanced hepatocellular carcinoma

Version: 2 Date: 28 September 2010

Reviewer: Franck Bonnetain

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Major Revisions

To my mind, this study is clearly underpowered to provide results with accuracy. Statistical analyses and report of them are not well describe

For example number of death or progression should done as well as post hoc power for statistical analyses of OS and TTP

Patients at risk for survival curves should be done

Strategy of multivariate Cox and logistic model is not described regarding number of variables that could be included in the final model: ratio 1 variable/event. Maybe too many variables were introduced in multivariate model to achieve a stable model

A propensity score, at least should be calculated using logistic regression in order to assess which variables were associated with split treatment and then used in multivariate cox model to take into account bias associated with treatment choice

Regarding TTP and OS definition, authors should précised if all deaths were used as event, censoring rules should be also done. Why they did not used PFS in order to increase statistical power with more events?

Discussion section should include more clearly limitation regarding number of patients and selection bias for treatment

While Okuda is provide please reports also BCLC and CLIP classification

Clearly state the exploratory purpose of the study

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.

Declaration of competing interests:

I declare that I have no competing interests'