# ANSWERING REVIEWERS

April 20th, 2016

Dear Editor,

Please find enclosed the edited manuscript in word format (file name: 24641-Review.doc).

**Title:** Transarterial radioembolization vs chemoembolization for hepatocarcinoma patients: A systematic review and meta-analysis

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**Name of Journal:** *World Journal of Hepatology*

**ESPS Manuscript NO:** 24641

The manuscript has been improved according to the suggestions of reviewers:

**Reviewer 1:**
A good attempt to shed light onto which modality could possibly be preferred. However based upon a lack of properly conducted randomized prospective trials, this question currently cannot be answered adequately. Discussion response rates probably does not make sense, I should delete this paragraph, whereas it is unfortunate that no relevant information re toxicity or QoL could be retrieved from the retrospective datasets

**RE:** We agree with the reviewer on the lack of properly conducted RCTs in this field. In particular we consider a serious limitation the lack of stratified outcomes data according to baseline tumoral and clinical features. In the discussion we state: "*Unfortunately, subgroup analysis performed on the basis of baseline tumor stage or other clinical prognostic factors…… was not feasible due to the low number of available studies and the absence of outcomes stratification in most of them.*" and among the limitations to our study "*This, in addition to the aforementioned lack of data stratification and subgroup analysis, calls for a carefully interpretation of our findings.*"
On the other hand, we consider response rate an important outcome, although not the primary endpoint of our analysis, as tumor response is usually assessed in most studies conducted in the field of locoregional treatments for HCC patients. In fact, 8 out of 10 included studies reported this outcome. Therefore, we are willing to confirm our discussion on response rates as we think it completes our paper, although we acknowledge heterogeneity found with regard to tumor response as a limitation to this analysis.

**Reviewer 2:**
This meta-analysis aimed to compare the efficacy and safety of Y-90 transarterial radioembolization (Y90RE) and transarterial chemoembolization (TACE) in hepatocellular carcinoma (HCC). The analysis was well performed. Comments: 1. A table summarizing the clinical characteristics of the 10 studies included would be useful. 2. Is it possible to identify what type of patients would benefit more from Y90RE or TACE?

**RE:** We really thank reviewer 2 for his/her kind comments on our paper. We included in our manuscript a table summarizing main characteristics of the 10 studies (table 1). This table reports, among methodological and general characteristics of all the included studies, main clinical and tumoral features (in particular BCLC stage and Child-Pugh score). As commented above, unfortunately we were not able to stratify our summary estimates according to baseline patient characteristics. In fact, only 3 out of the 10 included studies, namely the papers by

Salem, Carr, and Moreno-Luna, reported this stratification. Honestly, only 3 studies are too fews to perform a separate subgroup analysis. Furthermore, criteria applied for stratification were rather different among the aforementioned 3 studies (for instance Carr differentiated between tumors < 5 cm and > 5 cm, while Salem and Moreno-Luna followed BCLC staging system). As reported above in response to Reviewer 1, we properly acknowledged this aspect as a limitation to our study in the Discussion.

**Reviewer 3:**
Facciorusso and colleagues compared the efficacy and safety of Y90RE and TACE in HCC patients. Comments: 1. The quality of figures are poor. Figures 2,4,5 and 6 are actually tables not figures. 2. The review needs more details about the effect of Y90RE and TACE on different classes of HCC patients.

**RE:** We admit that quality of figure 1 was suboptimal and in this new version of the paper we improved this aspect. Figures 2,4,5, and 6 are forest plots, which are universally considered as figures, not table (all the meta-analyses available in the literature consider forest-plot as figures). As above reported in response to reviewers 1 and 2, we were not able to perform this sub-analysis due to the lack of stratified data in the included studies. We properly acknowledged this aspect as a limitation to our study in the Discussion.

Thank you again for considering our manuscript for publication in the *World Journal of Hepatology*.

Sincerely yours,
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