

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 63631

Title: Disease Control and Failure Patterns of Unresectable Hepatocellular Carcinoma Following Transarterial Radioembolization with Yttrium-90 Microspheres and with/without Sorafenib

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03537016

Position: Peer Reviewer

Academic degree: PhD

Professional title: Consultant Physician-Scientist

Reviewer's Country/Territory: Spain

Author's Country/Territory: United States

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-03-22 10:20

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection

Re-review	[<input checked="" type="checkbox"/>] Yes [<input type="checkbox"/>] No
Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [<input type="checkbox"/>] Onymous Conflicts-of-Interest: [<input checked="" type="checkbox"/>] Yes [<input type="checkbox"/>] No

SPECIFIC COMMENTS TO AUTHORS

This is a study that continues the previous research carried out by the same expert group, already published. The main contribution of this work refers to the assessment of disease control and failure patterns in patients treated by radioembolization with and without sorafenib. The work is of great interest, since it provides recommendations on the therapy that patients should follow after this local treatment, according to their clinical characteristics. However, I consider it necessary to make certain clarifications and modifications in the manuscript. First of all, I consider that the number of patients in whom the post-treatment study was carried out exclusively within the first month after RE, should be clarified. As it is an excessively short time, it is not possible to detect any tumor response to treatment. Only in the event that during that time evident progression of the disease has been detected, the patient should be included in the analysis. Another main issue concerns the conclusion of the study. The authors state that "disease progression among TARE-sorafenib procedures was commonly extrahepatic". But this statement is misleading, because the most common location for this strategy was intrahepatic (38%), followed by intra + extrahepatic + extrahepatic only (32%). Therefore, the correct statement is that extrahepatic progression was more common in this strategy (32%) than in TARE alone (13%). This should also be corrected throughout the manuscript. Other recommendations refer to: 1. In order for the title to reflect the objective of the study, "with and without sorafenib" should be included after "Transarterial Radioembolization" 2. The abstract is excessively long (more than 500 words). 3. Based on Table 2, the following should be clarified: a. The limits of the LSF



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and absorbed doses by lung used by the center to consider the patient as a candidate for RE. The upper limit is 49 Gy, which seems excessive according to current guidelines. b. An interval between 99mTc-MAA and TARE of 125 days is striking. Do not the authors consider it necessary to re-evaluate the patient when more than 30 days have elapsed after the assessment with MAA? c. Likewise, it is striking that for different activity medians by groups, the absorbed dose medians remain the same between groups. d. When patients were treated with the whole liver approach, was it done in a single session or in two different sessions? 4. In the Discussion section, when the authors refer to the changes in the DCR between TARE alone and TARE-sorafenib, they refer to percentage points (arithmetic difference of two percentages): 6.3% and 12%, respectively. The decrease in DCR would actually be 7.3% (from 85.7 to 79.4%) and 21.43% (from 56 to 44%). As a final recommendation, I would encourage the authors to include the absorbed doses per tumor for a more accurate analysis of the factors that predict the response to treatment in both strategies. As the authors themselves state, there is increasing evidence (some of them presented in the last month for glass spheres) of the importance that dosimetry has in the outcome of patients with HCC treated by RE.