



### PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastrointestinal Pharmacology and Therapeutics*

**Manuscript NO:** 97570

**Title:** Downstaging of Advanced Hepatocellular Carcinoma followed by Liver Transplantation using Immune Checkpoint Inhibitors - Where Do We Stand?

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05575380

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Italy

**Author's Country/Territory:** India

**Manuscript submission date:** 2024-06-02

**Reviewer chosen by:** Jia-Lin Zhang

**Reviewer accepted review:** 2024-08-07 14:24

**Reviewer performed review:** 2024-08-15 03:01

**Review time:** 7 Days and 12 Hours

<b>Scientific quality</b>	<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 Grade E: Do not publish
<b>Novelty of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
<b>Creativity or innovation of this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

Dear Editor, thank you so much for inviting me to revise this manuscript about cancer IO and HCC. Over the last two decades, the development of cancer immunotherapy has led to unprecedented clinical outcomes improvements in several tumor types. Immune checkpoint have represented and currently represent a fundamental research avenue in this setting, since agents targeting programmed cell death protein 1 (PD-1), programmed death-ligand 1 (PD-L1), cytotoxic T-lymphocyte antigen 4 (CTLA-4), lymphocyte-activation gene 3 (LAG-3), T-cell Immunoglobulin domain and Mucin domain 3 (TIM-3), and others, have reported practice-changing results in phase I to III clinical trials. In fact, the development of agents such as the PD-1 inhibitors pembrolizumab and nivolumab, the PD-L1 inhibitor atezolizumab, and the anti-CTLA-4 antibody ipilimumab, has revolutionized the clinical practice of hematological and solid tumors, such as malignant melanoma, lung cancer, and hepatocellular carcinoma. The manuscript is quite well written and organized. English could be improved. The introduction explains in a clear and coherent manner the background of this paper. We suggest the following modifications: • Introduction section: although the authors correctly included important



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papers in this setting, we believe the evolving systemic treatment scenario for HCC and predictors of response to ICIs should be further discussed and some recent papers added within the introduction ( PMID: 38791914 ), only for a matter of consistency. • Of note, the authors should expand some sections, including a more personal perspective to reflect on. For example, they could answer the following questions – in order to facilitate the understanding of this complex topic to readers: What are the knowledge gaps and how do researchers tackle them? How do you see this area unfolding in the next 5 years? We think it would be extremely interesting for the readers. We suggest a linguistic revision and the addition of some references for a matter of consistency. Moreover, the authors should better clarify some points.