


# Critique on “Real-World Effectiveness of First-Line Lenvatinib Therapy in Advanced Hepatocellular Carcinoma: Current Insights” [Response to Letter]

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## Dear editor

We thank Goyal et al for their interest in our recent paper “Real-World Effectiveness of First-Line Lenvatinib Therapy in Advanced Hepatocellular Carcinoma: Current Insights” published in Pragmatic and Observational Research. We would like to share our thoughts about the concerns raised by these correspondents.

Since 2020, immune-checkpoint inhibitors (ICI) have been incorporated in first-line treatment for HCC, and atezolizumab/bevacizumab and durvalumab/tremelimumab are the preferred option in all recent guidelines including NCCN and ASCO. It is worth mentioning that our paper focused on scenarios in which immunotherapy is not a viable option given that tyrosine kinase inhibitors are not preferred first-line treatment in HCC anymore.

As to the concern regarding the toxicity related to lenvatinib, we agree that this can affect quality of life and should not be underestimated. The REFLECT trial showed non-inferior overall survival (13.6 vs 12.3 months, HR 0.92, 95% CI 0.79–1.06) as well as a statistically significant improvement compared with sorafenib for all secondary efficacy endpoints: progression-free survival (7.4 vs 3.7 months,  $p < 0.0001$ ) and response rate (24% vs 9%,  $p < 0.0001$ ). Although the toxicity profiles were similar, lenvatinib caused more G3 or higher hypertension (23% vs 14%), which is usually easier to manage compared to palmar-plantar erythrodysesthesia which occurred in grade 3 or higher in 3% and 11% of patients receiving lenvatinib and sorafenib, respectively. Also, a clinically meaningful delay in deterioration for multiple domains was observed with lenvatinib compared with sorafenib.<sup>1</sup>

Also, our paper focused on scenarios with contra-indication to ICI or in second-line treatment following immunotherapy. There are currently no guidelines available to assist with the decision-making process in these cases, and expert opinions are still necessary. We respectfully disagree that non-preplanned analysis or retrospective studies should determine whether to use lenvatinib or sorafenib, and, considering REFLECT data, lenvatinib is typically favored by the authors when available and in the absence of contraindications.

## Disclosure

Tiago Biachi de Castria receives honoraria from Bristol-Myers Squibb, Eli Lilly, Merck Sharp & Dohme Corp., Ipsen, Moderna, AstraZeneca, and A2Bio. Richard D Kim receives honoraria from AstraZeneca, Exelixis, Ipsen, Eisai, Roche, and Pfizer (consulting/advisory role); and Incyte and AstraZeneca (speaker's bureau). The authors report no other conflicts of interest in this communication.

## Reference

1. Kudo M, Finn RS, Qin S, et al. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised Phase 3 non-inferiority trial. *Lancet*. 2018;391(10126):1163–1173. doi:10.1016/S0140-6736(18)30207-1

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