



# Ramucirumab and other new systemic therapies for hepatocellular carcinoma: still uncovered the problem of Child-Pugh B patients

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I read with great interest the Editorial Commentary by Longo *et al.* analyzing the role of ramucirumab as a systemic treatment of hepatocellular carcinoma (HCC) (1).

In addition to mentioning the clinical studies with ramucirumab, the authors rightly point out the relevant data regarding the evidence of efficacy of ramucirumab in HCC patients with a baseline alpha-fetoprotein (AFP) concentration of 400 ng/mL or higher, which demonstrated for the first time a prognostic marker that is able to effectively identify patients who may benefit from this therapy (2).

As appropriately mentioned by the Authors, in recent years, several systemic agents have demonstrated efficacy in randomized clinical trials for HCC, such as lenvatinib and the atezolizumab-bevacizumab combination in the first-line setting as well as regorafenib and cabozantinib in the second-line setting (3,4).

However, we would like to point out that despite the evidence of efficacy of several systemic therapies, to date there are still subgroups of HCC patients who cannot benefit from these therapies because they were not included in clinical trials.

In particular, this limitation concerns the numerous patients with advanced HCC who have Child-Pugh B liver function, who are regularly excluded from clinical trials.

To date, the only systemic therapy that has demonstrated evidence of efficacy and safety in HCC patients with Child-Pugh B liver function, particularly in those who have experienced sorafenib failure, is metronomic capecitabine (5-7).

Apart from this therapy, for HCC patients with Child-Pugh B liver function there are only data on the use of sorafenib, as reported by various clinical practice studies (8). The other aspect that in my opinion deserves to be emphasized concerns the possible prognostic significance of events as surrogate markers of therapeutic efficacy. Unlike sorafenib therapy for which a prognostic significance of adverse events has been reported, no other systemic therapy has ever been reported to have a prognostic significance of adverse events that could guide the maintenance and tailoring of systemic therapy (9,10).

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