Letter to the Editor

The CRAFITY score can identify patients with hepatocellular carcinoma showing poor response to treatment with atezolizumab and bevacizumab

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With great interest we have read the comment of Dr. Khakoo on the recently published CRAFITY score for the prediction of response to anti-programmed death (ligand) 1 [PD-(L)1]-based immunotherapy in patients with unresectable hepatocellular carcinoma (HCC) (1). In his comment, The “CRAFITY” score, as the authors named it, is based on alpha fetoprotein (AFP ≥100 ng/mL) and C-reactive protein (CRP ≥1 mg/dL), and it stratifies patients by likelihood of increased survival and treatment response to subsequent immunotherapy containing systemic treatment (CRAFITY-low, 0 points; CRAFITY-intermediate, 1 point; and CRAFITY-high, 2 points) (2). The CRAFITY score is easy to adopt to clinical practice as the included parameters are available for most patients and measuring them is low cost.

Dr. Khakoo highlighted the potential importance of the CRAFITY score, but also the lack of validation of this score for patients receiving treatment with the current standard of care, the combination treatment with PD-L1 blocker atezolizumab and the vascular endothelial growth factor (VEGF) blocker bevacizumab (atezo/bev). Indeed, the combination treatment with atezo/bev was approved in 2020 by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for systemic treatment-naive patients with unresectable or metastatic HCC based on significantly prolonged overall survival (OS) and progression-free survival (PFS) compared to sorafenib (3,4). Since then, atezo/bev has become the recommended first line systemic treatment for HCC in Europe (5). Prediction of response to this treatment is not established. Although some patients within the patient populations in which the CRAFITY score has been developed and validated include patients treated with atezo/bev (n=25; 25%), their number is limited. To date, there are few real-life cohorts available for such analyses to date owing to the short duration of the approval. However, anticipating an increasing use of this regimen, the performance of the CRAFITY score in this population is of special interest. We have evaluated the performance of the CRAFITY score in a real-world population of HCC patients treated with atezo/bev as a first line systemic treatment.

Of the 45 patients in our analysis [44 Caucasians, 40 males, mean age 68±11 (range, 57–77) years], 40 had liver cirrhosis due to alcohol or fatty liver disease. Patients had intermediate or advanced stage HCC corresponding to Barcelona clinic liver cancer stages B (n=4) or C (n=41). Within the mean observation period of 7.5±5.5 (1.3–21.1) months, 26 patients (58%) showed radiologic disease control (mRECIST

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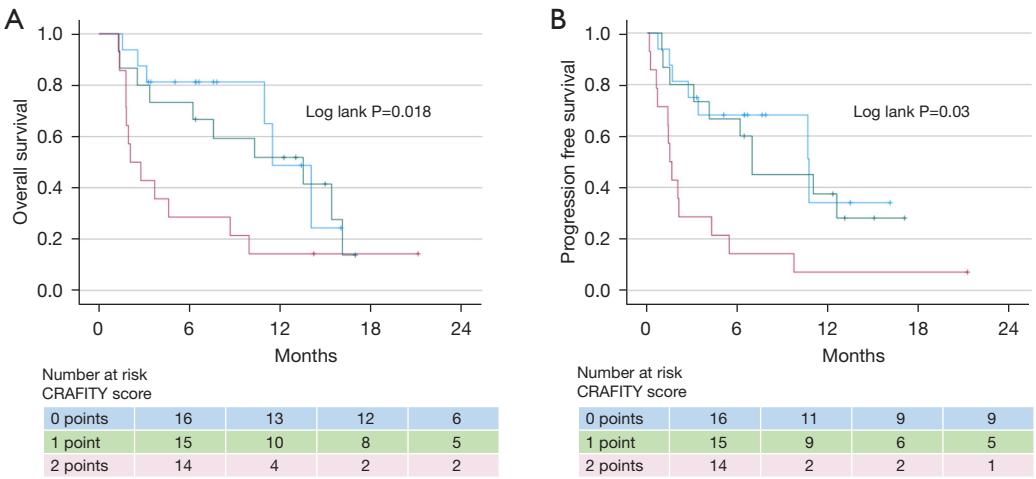

Figure 1 Survival of patients with HCC during first line treatment with atezolizumab and bevacizumab according to the CRAFITY score. Kaplan-Maier analyses showing overall survival (A) and progression free survival (B) by CRAFITY score results. HCC, hepatocellular carcinoma.

criteria), including 15 (33%) with stable disease, 9 (20%) with partial response and 2 (5%) with complete response, whereas 19 (42%) showed progressive disease. Mean OS and mean PFS after initiation of atezo/bev were 10±1.2 [range, 1.3–16.1, 95% confidence interval (CI): 7.6–12.2] and 8.5±1.2 (0.1–12.5, 95% CI: 6.1–11.0) months, respectively. Mean OS was found to be similar among CRAFITY-low [11.4±1.3 (1.5–14.0 months), 95% CI: 8.8–14] or CRAFITY-intermediate patients [10.4±1.6 (1.3–16.1 months), 95% CI: 7.4–13.4; P=n.s.], but significantly shorter in CRAFITY-high patients [6±1.8 (1.3–9.9 months), 95% CI: 2.5–9.5; P=0.018] (*Figure 1A*). Similarly, mean PFS was found to be similar among CRAFITY-low [9.7±1.6 (0.7–10.6 months), 95% CI: 6.5–14] or CRAFITY- intermediate patients [8.9±1.6 (0.9–12.5 months), 95% CI: 5.8–12; P=n.s.], but significantly shorter in CRAFITY-high patients [3.7±1.5 (0.1–9.7) months, 95% CI: 0.87–6.54; P=0.03] (*Figure 1B*).

In our patient population treated with atezo/bev, we can confirm the ability of the CRAFITY score to identify patients with poor treatment benefit. Our cohort was retrospective with limited sample size, however, our findings are similar to those of two cohorts of Chinese HCC patients, one treated with the tyrosine kinase inhibitor lenvatinib as monotherapy and the other cohort treated with the combination of lenvatinib plus immunotherapy that were recently published in response to the original publication (6). The accuracy of our observation needs confirmation, as does the question of whether different treatment regimens (e.g., including VEGF inhibitors) require adjusted use of the CRAFITY score. In conclusion, we feel that the CRAFITY score may provide an important impetus for the personalization of systemic HCC treatment and a helpful tool to increase tumour response and patient survival, however, it needs to be separately validated for different treatment regimens.

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Footnote

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Intercept, Ipsen, Janssen, MSD/Merck, Novartis, Roche, Sequana Medical, and Shionogi; reported honoraria from Abbvie, Alexion, Bayer, Gilead, Eisai, Intercept, Ipsen, Janssen, MedUpdate GmbH, MSD/Merck, Novartis, and Sequana Medica; reported support for attending meetings and/or travel from Gilead, Abbvie, Intercept, and Janssen. DS reported honoraria from Astellas, BTG, and Novartis; reported support for attending meetings and/or travel from Gilead, Abbvie, Intercept, Janssen, and Johnson & Johnson and DS was on the Data Safety Monitoring Board or Advisory Board of BTG, SIRTEX, and Olympus. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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