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Use of the Child-Pugh score in anticancer drug dosing decision making: proceed with caution

Authors' reply

Carlo Palmieri and Iain Macpherson expressed an important concern regarding the use of the Child-Pugh score for dose recommendations in cancer patients with hepatic impairment. We share this concern and agree that the Child-Pugh criteria were not developed nor validated to predict pharmacokinetic alterations, and are therefore far from ideal for making dose recommendations, particularly for cancer patients, in whom extrahepatic symptoms might lurk beneath elevated Child-Pugh scores.

However, the Child-Pugh score is currently the most widely supported grading system available and accepted by the US Food and Drug Administration and European Medicines Agency to study pharmacokinetics in hepatic impairment, although the importance of ensuring that changed Child-Pugh scores are attributable to hepatic impairment instead of other comorbidities is emphasised.[1,2] We concur that it is challenging to clarify the cause of liver function test abnormalities in patients with advanced metastatic cancer. Additionally, the thresholds used to define liver function abnormalities in clinical studies are not harmonised,[3] which perhaps calls for the use of a simpler classification system—such as the National Cancer Institute Organ Dysfunction Working Group criteria for hepatic dysfunction—which uses only bilirubin and aminotransferase levels.[4]

The aim of our Review[5] was to aid clinicians in selecting dose adjustments and to summarise the available literature. Decisions on dose adjustments have to be made with the evidence available, and since patients with chronic liver disease are often excluded from clinical trials, pharmacokinetic and pharmacodynamic knowledge in this group is very scarce. Knowledge in such patients can be limited to pharmacokinetic studies that use the Child-Pugh score. For anticancer drugs, this information can still be used to help guide dosing in patients with hepatic impairment.

In conclusion, we agree that information regarding dose adjustments for patients with abnormal organ function, including those based on Child-Pugh scoring, should be interpreted with caution. Identifying the underlying causes of test abnormalities, and taking each patient's individual condition into consideration, remain essential.

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1 US Food and Drug Administration. Guidance for industry. Pharmacokinetics in patients with impaired hepatic function: study design, data analysis, and impact on dosing and labeling. May, 2003. https://www.fda.gov/media/71311/download (accessed May 13, 2019).

2 European Medicines Agency. Guideline on the evalution of the pharmacokinetics of medicinal products in patients with impaired hepatic function. Feb 17, 2005. https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-evaluation-pharmacokinetics-medicinal-products-patients-impaired-hepatic-function_en.pdf (accessed May 13, 2019).

3 Wang E, Song F, Paulus JK, Hackenyos D, Mathew P. Qualitative and quantitative variations in liver function thresholds among clinical trials in cancer: a need for harmonization. *Cancer Chemother Pharmacol* 2019; published online April 22. DOI:10.1007/s00280-019-03821-6.

4 Mansfield AS, Rudek MA, Vulih D, Smith GL, Harris PJ, Ivy SP. The effect of hepatic impairment on outcomes in phase I clinical trials in cancer subjects. *Clin Cancer Res* 2016; **22:** 5472–79.

5 Krens SD, Lassche G, Jansman FGA, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; **20:** e200–07.