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LETTER TO THE EDITOR

Sorafenib for hepatocellular carcinoma according to Child-Pugh class of liver function

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Dear Sir,

We read with interest the article by Kim et al. [1], aimed at assessing sorafenib effectiveness and safety in patients with Child B cirrhosis. The work addresses the question whether the drug is advisable or not in this setting, a relevant concern in clinical practice [2], since a large number of patients eligible for sorafenib present with suboptimal liver function. The question is actually unanswered, because both the phase III registration SHARP trial and the Asia–Pacific trial were conducted mostly in patients with Child A cirrhosis [3, 4].

There is no doubt that, both in terms of survival and of disease control, sorafenib obtains the best results in Child A patients. For patients in Child C status, it has been clearly shown that the short life expectancy and the high risk of deterioration advise against the treatment [5]; for patients in Child B, the first retrospective analyses reported results that are worse than in Child A, but still acceptable in the absence of severe side effects. Overall, Child-Pugh score is a rough method for classifying patients with cirrhosis. Child B category includes an inhomogeneous group of patients and the idea is that, for instance, having a mild ascites is not as relevant as having increased bilirubin levels. In any case, there is a strong need to evaluate the safety of sorafenib in this subset of patients and to identify which are actually eligible for the treatment and which is the optimal dose. Data from the phase II trial, indeed, showed that pharmacokinetics and side effects were comparable between Child A and B, and no dose reduction was recommended. In contrast, a phase I trial, testing sorafenib in patients with solid tumors and impaired liver or renal function [6], concluded that the treatment should be started at lower dose in case of an increased bilirubin, to prevent dose-limiting toxicity. Also, the first trial on sorafenib in HCC, by Abou Alfa et al. [7], identified a difference in liver function worsening between Child A and Child B patients, the latter having more often bilirubin elevation, ascites, encephalopathy, and a shorter overall survival (41 weeks vs. 14 weeks). Some case series and retrospective studies have also been published, among which the one we are referring to, confirming a higher risk of liver impairment and a frequent need to reduce the dose in case of Child B, and this is also our own experience.

Additional studies are ongoing at the moment, and in Italy, a prospective trial in Child B patients started under the sponsorship of the National Agency for Medicines (AIFA). The results of all these studies are eagerly awaited to identify when and at which dose sorafenib is safe and, possibly, cost-effective, in Child B patients. In the mean time, the use of the drug is, in our mind, to be proscribed in Child C patients and prescribed in selected Child B patients (i.e. score 7), only when a hepatologist is directly involved in managing the patients.

Conflict of interest None.

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