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LETTER TO THE EDITORS

Sorafenib before liver transplantation for hepatocellular carcinoma: risk or give up

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Dear Sirs,

We read with interest the article by Truesdale *et al.* [1] regarding their experience in the use of sorafenib before liver transplantation (LT) in patients with hepatocellular carcinoma (HCC). The authors compare ten patients who were administered sorafenib during waiting time for LT with twenty-three patients to whom the drug was not given. No difference in terms of overall and HCC recurrence-free survival was seen between the two groups. Indeed a higher incidence of biliary complications (67% vs. 17%) and acute cellular rejections (67% vs. 22%) was observed in the first group. The authors assume that the higher amount of complications is secondary to the use of sorafenib because of its main effect in inhibiting the vascular endothelial growth factor (VEGFR), reducing the resistance to apoptosis of cholangiocytes and thus both hindering the integrity of biliary vascularization and altering the immune pathway leading to cellular rejection. However, some major issues arise reading this paper: the authors do not specify the inclusion criteria for the use of sorafenib, the extension of the tumour burden before LT, the number of locoregional treatments before the drug was given and in general the efficacy of down-sizing procedures in this group of patients.

An interesting matter of debate is the time to stop the administration of sorafenib. Infact the authors assert that the drug was stopped on the day of LT. In our experience [2], it seems not to be safe to continue with the administration of the drug until the day of LT: although there is no international agreement about this point [2–5], we usually interrupt the drug at least 3 weeks before a surgical procedure such as LT, because of the increased risk of bleeding of impaired wound healing and of liver dysfunction in the perioperative period in this setting of patients.

Another intriguing issue is that doubtlessly sorafenib cannot still be considered nowadays in the group of the standard down-staging procedures of HCC in terms of safety and cost–effectiveness, but it should be reserved to the patients with advanced HCC traditionally treated with locoregional therapies/hepatic resection in whom sorafenib plays as important role in bringing them within the accepted criteria for LT with HCC. So as to exploit as much as possible the potential of the drug, we believe that sorafenib should not be reserved to patients with advanced HCC to whom any other curative treatment is not possible, but it should be offered also to a different setting of patients such as young patients outside standard criteria to LT.

In the future, the challenge will be to break the *Damocles sword* of medical therapies for HCC, until now no effective therapy exists. The integration of sorafenib in the medical practice and its fully comprehension may permit the best management of these patients as possible.

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Conflicts of Interest

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