Reply:

We agree with Martin et al. that, as yet, late recurrence of hepatitis C virus (HCV) following treatment has not been studied in this highly exposed group of patients. To clarify the point made in our study,[1] the majority of cases labeled as HCV reinfection within the 24-week window posttreatment are likely to represent viral rebound rather than reinfection, even in the presence of a switch in genotype or subtype. In the absence of detailed sequencing data, it indeed seems likely that patients with recurrent HCV infection have a high rate of reinfection,[2] although there is a need to carry out an appropriately designed study to confirm this, as some studies in other highly exposed cohorts have shown that relapse is associated with recrudescence of similar strains, others have lacked analysis of paired samples, and none have employed a next-generation sequencing approach.[3,4] In the meantime, the proposed adjustment to the reinfection rate following removal of the 7% of patients who relapsed within the 24-week posttreatment would seem entirely appropriate.[5,6] We also agree that retreatment is indicated in patients with recurrent HCV infection. The role of the emergence of resistant variants will be of particular interest as direct-acting antivirals (DAAs) are rolled out, in particular when interferon-free regimens are used, as interferon resistance is likely to be heavily influenced by the host response and is unlikely to occur solely due to mutations within the viral genome.

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Waiting Time and Transplantation for Hepatocellular Cancer: A Balance Between *Tempus Fugit* and *Carpe Diem*

To the Editor:

We read with great interest the article by Halazun et al.,[1] in which United Network for Organ Sharing (UNOS) data regarding transplanted patients with hepatocellular cancer (HCC) coming from long waiting times regions (LWTR, n = 2,562) were combined and compared to data from short waiting times regions (SWTR, n = 3,604). Despite a higher incidence of death on the waiting list was observed in LWTR (8.4% versus 1.6%, $P < 0.0001$), both intent-to-treat and posttransplant survivals were better in this group. LWTR patients received more locoregional therapies (LRTs) and more Milan criteria-out tumors were transplanted. Being listed/transplanted in an SWTR was an independent predictor of poor patient survival on multivariate analysis ($P < 0.0001$, hazard ratio [HR] = 1.545). Another recent study from the United States similarly compared 3,278 versus 1,724 HCC patients waiting $\leq$ or $>$120 days. One-year posttransplant recurrence was significantly lower among patients waiting $>$120 days (2.2% versus 3.9%, $P = 0.002$).[2] Despite that these results can apparently appear as anticonceptual from an oncological point of view—the more a patient waits for cancer treatment, the higher his/her survival—data from these large multicenter experiences are in line with previous experience, in which "fast-track" transplantation, mainly in the scenario of living donation, is connected with worse results.[3] The most commonly adopted approach presently used for selecting patients is the "ablate-and-wait" strategy, in which a patient is treated with LRT and then waits for transplant: if HCC remains stable or positively responds to LRT (low biological aggressiveness), the patient is transplanted; otherwise, if HCC proceeds the patient is dropped from the waiting list (high biological aggressiveness). This paradoxical statement derives from the absence of worldwide acceptable biological markers able to preoperatively select high-risk patients for posttransplant recurrence.[4] Selection factors other than tumor size and number are strongly needed to further optimize the selection of HCC patients.

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