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## **HCV Viremic Donors With Hepatic Bridging Fibrosis: Are We Ready To Use Their Livers in The Era of Direct-Acting Antivirals?**

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*To the Editor:*

We read with interest the report from the American Society of Transplantation Consensus Conference on the use of hepatitis C (HCV) viremic donors in solid organ transplantation, which took place in Dallas in January 2017 (1).

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In the interferon-era, liver grafts from HCV-positive donors with no more than periportal fibrosis (F2 Ishak) did not show an outcome disadvantage compared with HCV-negative ones (2,3). In U.S., 16.9% of HCV-positive cirrhotics currently receive an organ from HCV-positive donors, 50% of whom are viremic and expected to transmit the infection (1). Considering the gap between organ demand and supply, the meeting participants felt that the availability of safe and effective direct-acting antivirals (DAAs) makes expansion of the criteria for transplanting HCV viremic organs into non-viremic recipients a possibility (1). However, no change was proposed to the current recommendations on accepting organs with higher fibrosis stages.

We recently reported the successful transplant of a liver with bridging fibrosis (F3 Ishak; Fig.1A,B) from a HCV-positive, genotype 3a, viremic (1,210,101 IU/mL) donor (46-year-old male) into a HCV-positive, genotype 1b, viremic (150,656 IU/mL) male recipient, nonresponder to peginterferon/ribavirin, MELD score 8, with multifocal hepatocellular carcinoma downstaged within Milan criteria (4). Cold ischemia time was 373 minutes, total warm ischemia time was 65 minutes and peak serum transaminases occurred on day zero after liver transplantation (LT) (AST 1,272 IU/L, ALT 824 IU/L). Post-LT course was complicated by pneumonia and he was discharged on day 26. The patient received sofosbuvir+daclatasvir+ribavirin for 24 weeks, starting immediately after LT and HCV viremia became undetectable from the 3<sup>rd</sup> week. At week 1, only the donor HCV genotype 3a was identified in the recipient. At week 12 after therapy, the patient reached a sustained virological response (SVR12); his liver stiffness (LS) evaluated by transient elastography, was

8.5 kilopascal (kPa), and liver biopsy showed a chronic hepatitis with persistent bridging fibrosis (Ishak grade 4/18, stage 3/6).

We have closely followed up this patient and here we report his outcome at week 48 after therapy (72 weeks from LT). Viremia is persistently negative (SVR48); LS has decreased to 6.0 kPa; liver biopsy shows fibrous expansion of some portal areas without septation (Ishak grade 1/18, stage 1/6; Fig.1C,D), in agreement with LS value; liver function tests are normal and Doppler-ultrasound shows normal liver echogenicity, regular biliary tree and blood perfusion with a spleen diameter reduced to 16 cm (from 20 cm at LT).

This report is a proof-of concept that treating HCV infection very early after LT with a pangenotypic DAA regimen, in carefully selected recipients, might allow not only to curb infection transmission into the recipient, but also to induce bridging fibrosis regression early after LT.

We submit that in the current DAA era, organs from HCV-viremic individuals represent an underutilized resource and prospective multicenter studies are urgently needed to evaluate not only transplantation of HCV viremic organs into non-viremic recipients, as discussed in Dallas, but also the criteria for acceptable graft fibrosis, provided that antiviral treatment is started very early post-LT.

## DISCLOSURE

The authors of this manuscript have conflicts of interest to disclose as described by the American Journal of Transplantation. SM is a Regional Advisory Board member for Gilead, FT is an Advisory Board member for Biotest, GMS is an Advisory Board member for AbbVie, Gilead and MSD and RR is an Advisory Board member for Biotest. The other authors have no conflicts of interest to disclose.

## FIGURE LEGEND

**Figure 1. HCV-positive donor liver and microscopic features of liver biopsy which was performed at retrieval (A, B) and at sustained virological response at week 48 after the end of therapy (C, D).**

(A) Portal tract inflammation with lymphocytic aggregate (arrowhead) and interface hepatitis (arrows); grading 4/18 according to Ishak score (hematoxylin-eosin staining, X100 magnification). (B) Portal fibrosis (arrowheads) with portal-portal bridging fibrosis (arrows; staging 3/6 according to Ishak score) and diffuse mild steatosis (Masson's trichrome staining, which was performed as an urgent procedure using rapid technique; X100 magnification). (C) Portal tract with mild lymphocytic inflammation (arrowhead); grading 1/18 according to Ishak score (hematoxylin-eosin staining, X100 magnification). (D) Central vein (arrow); fibrous expansion of portal area (arrowhead); staging 1/6 according to Ishak score (Sirius Red staining, X100 magnification).

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