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Glecaprevir/pibrentasvir + sofosbuvir for post-liver transplant recurrent hepatitis C virus treatment

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Abstract

Glecaprevir/pibrentasvir in combination with sofosbuvir may serve as a safe and effective option for treatment of recurrent hepatitis C virus post-liver transplant in those who previously failed direct-acting antivirals.

TO THE EDITOR

For direct-acting antiviral-experienced patients with recurrent hepatitis C virus (HCV), current national guidance recommends treatment with sofosbuvir/velpatasvir/voxilaprevir (SOF/VEL/VOX) or glecaprevir/pibrentasvir (GLE/PIB) and sofosbuvir (SOF) in combination with ribavirin (RBV) due to their established safety and efficacy profiles. However, for recurrent HCV treatment post-liver transplant, guidance recommends use of SOF/VEL/VOX +/- RBV for 12 wk. This recommendation is based on expert consensus from seven total cases, none of which included patients who failed SOF/VEL/VOX pre-transplant.[1-3] Current guidance does not provide any recommendation for the use of GLE/PIB with SOF +/- RBV post-liver transplant, and we are unaware of published studies describing its use in direct-acting antiviral-experienced patients with recurrent HCV post-liver transplant.

We report outcomes of recurrent HCV in two patients with a history of compensated cirrhosis and hepatocellular carcinoma treated with Y90 radioembolization who underwent 24 wk of GLE/PIB with SOF after orthotopic liver transplantation from HCV-negative donors. RBV was not started in either patient due to hemoglobin < 100 g/L at treatment initiation. At the time of transplant, Model for End-Stage Liver Disease – Sodium scores were 11 and 9 for patient 1 and 2, respectively. Neither patient was co-infected with HIV or hepatitis B virus. Patient 1, a 71-year-old man with genotype 3 HCV, failed two treatments pre-transplant: 1) 12 wk of SOF/VEL and 2) 12 wk of SOF/VEL/VOX after the patient developed hepatocellular carcinoma. Subsequent resistance testing found no mutations. Patient 2, a 67-year-old man with genotype 1 HCV, failed four regimens pre-transplant: 1) pegylated interferon + RBV + SOF, 2) 24 wk of ledipasvir/sofosbuvir, 3) 12 wk of GLE/PIB, 4) 12 wk of SOF/VEL/VOX and RBV. Treatment courses three and four occurred after the patient developed hepatocellular carcinoma. Subsequent resistance testing detected Q30R and Y93N mutations.

Prior to treatment initiation but post-transplantation, HCV RNA resulted as 337 and 667,114 IU/mL for patient 1 and 2, respectively. After 4 wk of treatment, HCV RNA levels were undetected and remained undetected throughout treatment. Both patients achieved sustained virologic response at 12 wk after treatment completion. Minor tacrolimus dose reductions were made in the immediate post-transplantation period, but neither patient achieved toxic levels. Neither patient experienced any treatment-related adverse events, transplant complications, acute cellular rejection, or antibody-mediated rejection during and through 12 wk post-treatment completion.

Drug-drug interactions between direct-acting antivirals and immunosuppressants must be carefully considered before use. A 1.5-fold increase in tacrolimus area under the curve can occur with GLE/PIB co-administration; therefore, therapeutic drug monitoring is imperative and tacrolimus dose reductions may be needed during

treatment. In those individuals taking cyclosporine, doses should be limited to <0.1 g/day because higher doses can increase glecaprevir exposure, which may lead to increased risk of adverse events. HCV in the post-transplant setting can cause rapid development of fibrosis and decompensation, leading to higher rates of rejection, graft failure, and mortality.[4] Direct-acting antivirals offer high cure rates, but in patients who fail to achieve sustained virologic response prior to liver transplant, national guidance offers limited recommendations for recurrent HCV treatment post-transplant. Use of GLE/PIB with SOF for 24 wk can offer an effective alternative to SOF/VEL/VOX +/- RBV in this small, yet complex cohort of patients, especially in those who failed SOF/VEL/VOX pre-transplant.

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PRIMARY SOURCES

1	Xiaoqing Liu, Zhiwei Chen, Qiao Tang, Peng Hu. "Phylogenetic signature and prevalence of natural resistance-associated substitutions for hepatitis C virus genotypes 3a and 3b in southwestern China", Journal of Virus Eradication, 2022 Crossref	13 words — 2%

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