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Sofosbuvir, Simeprevir, and Ribavirin for the Treatment of Hepatitis C Virus Recurrence in Human Immunodeficiency Virus/Hepatitis C Virus–Coinfected Liver Transplant Recipients

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TO THE EDITORS:

For human immunodeficiency virus (HIV) patients coinfecting with hepatitis C virus (HCV), poor graft survival after liver transplantation (LT) has prompted concerns about their suitability for LT.¹ The availability of oral direct-acting antiviral drugs for HCV offers new opportunities for managing HCV disease in LT recipients with HCV and HIV and potentially improving long-term survival,² as shown by the 2 patients reported here.

CASE 1

A 48-year-old HIV-infected transplant recipient with chronic HCV genotype 1a [interleukin-28B CT (rs12979860)] was found to have recurrent HCV disease with stage 3 fibrosis (Metavir) on her 1-year protocol biopsy. The immunosuppressive regimen was cyclosporine, mycophenolate mofetil (MMF), and corticosteroids. Her antiretroviral therapy (ART) was abacavir/lamivudine and efavirenz. She underwent antiviral treatment with peginterferon and ribavirin (PR) without a virological response. When protease inhibitors became available 2.5 years after LT, she was retreated with PR and boceprevir. To minimize drug-drug interactions, ART was changed to emtricitabine/tenofovir and raltegravir. She had a significant decline in her HCV viral load but developed virological breakthrough. Shortly thereafter, she developed decompensated cirrhosis with ascites and encephalopathy.

Four years after LT, the patient began treatment with sofosbuvir at 400 mg/day and ribavirin at 200 mg/day via an IRB-approved compassionate access program. Immunosuppression was MMF monotherapy; cyclosporine had been stopped previously for renal dysfunction. With treatment, HCV RNA became undetectable in week 8 of treatment (Table 1). The ribavirin dosage ranged from 200 mg every other day to 600 mg/day; this depended on anemia and depressive symptoms. Erythropoietin was needed. She completed 24 weeks of treatment, and with concerns about relapse due to her stage of disease and prior treatment history, treatment was administered for another 12 weeks with sofosbuvir, simeprevir at 150

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mg/day, and ribavirin. The therapy was well tolerated, with anemia, mild depressive symptoms, and mild hyperbilirubinemia the only noteworthy side effects. A sustained virological response at week 12 post-treatment (SVR-12) was achieved. Importantly, with treatment, her Child-Pugh score decreased from 10 to 5 with a resolution of her ascites and encephalopathy, and her Model for End-Stage Liver Disease score improved from 10 to 9.

CASE 2

A 55-year-old male with an HIV infection and chronic HCV genotype 1a infection (interleukin-28B CT) developed severe cholestasis and recurrent HCV 5 months after LT. His immunosuppressive regimen was cyclosporine, MMF, and corticosteroids. ART included atazanavir, lamivudine, and tenofovir. He was treated with PR with biochemical improvement but without a virological response. Two years later, he was retreated with daily consensus interferon and ribavirin, but again, there was no virological response. Over the next 4 years, his HCV disease progressed to cirrhosis complicated by ascites and nonbleeding varices.

Seven years after LT, he began treatment with sofosbuvir at 400 mg/day and ribavirin at 200 mg/day via an IRB-approved compassionate access program. His immunosuppression was cyclosporine and corticosteroids. No changes to his ART or immunosuppressant therapy were made. The HCV viral load became undetectable by week 4 of treatment. Ascites was resolved after the first month of treatment. He completed 24 weeks of therapy and then had an additional 12 weeks of sofosbuvir, simeprevir at 150 mg/day, and ribavirin. The maximum dose of ribavirin during treatment was 800 mg/day, but the doses had to be decreased to 200 mg/day, and finally ribavirin was stopped at week 32 because of gastrointestinal side effects. Before the start of simeprevir, his ART regimen was changed to rilpivirine, lamivudine, and tenofovir as a result of drug-drug interactions between atazanavir and simeprevir. No adjustment in the cyclosporine dose was required during the treatment, and SVR-12 was achieved. His Child-Pugh score improved from 11 at baseline to 5 at SVR-12, and his Model for End-Stage Liver Disease score decreased from 18 to 13.

These encouraging case reports highlight the use of new oral antiviral agents in HCV/HIV-coinfected patients in the setting of LT and provide hope for the future management of coinfecting transplant candidates and recipients.

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TABLE 1

Laboratory and Virological Course of Therapy

Test	Sofosbuvir + Ribavirin				Sofosbuvir + Simeprevir + Ribavirin			Off Treatment Week 48 SVR-12
	Baseline	Week 4	Week 8	Week 24	Week 28	Week 36		
Case 1								
HCV RNA (IU/mL)	1,120,000	<25	Undetectable	Undetectable	Undetectable	Undetectable	Undetectable	Undetectable
HIV RNA (copies/mL)	<40	<40	<40	<40	<40	<40	<40	<40
CD4 count (cells/μL)	161	Not determined	90	123	Not determined	84	127	127
Alanine aminotransferase (IU/L)	137	35	37	77	43	72	133	133
Bilirubin (mg/dL)	1.1	0.9	0.4	1.0	1.7	1.1	0.7	0.7
Creatinine (mg/dL)	1.5	1.3	1.0	1.0	1.1	1.1	1.3	1.3
International normalized ratio	1.0	1.0	1.0	1.0	1.0	1.0	1.1	1.1
Albumin (mg/dL)	2.3	2.3	2.6	3.3	3.3	3.3	3.6	3.6
Child-Pugh score	C-10	C-9	B-7	A-6	A-6	A-5	A-5	A-5
Case 2								
HCV RNA (IU/mL)	312,340	Undetectable	Undetectable	Undetectable	Undetectable	Undetectable	Undetectable	Undetectable
HIV RNA (copies/mL)	<40	<40	<40	<40	<40	Detected	<40	<40
CD4 count (cells/μL)	204	Not determined	Not determined	253	Not determined	279	278	278
Alanine aminotransferase (IU/L)	62	42	39	37	32	39	35	35
Bilirubin (mg/dL)	2.7	2.0	2.1	1.8*	1.6	1.4	1.0	1.0
Creatinine (mg/dL)	1.2	1.2	1.2	1.2	1.2	1.1	1.5	1.5
International normalized ratio	1.7	1.5	1.4	1.3	1.3	1.2	1.4	1.4
Albumin (mg/dL)	2.4	2.6	3.0	3.0	2.8	3.5	3.6	3.6
Child-Pugh score	C-11	C-8	B-7	A-7	A-6	A-6	A-5	A-5

NOTE: HIV lower limit of quantification (LLOQ) <40 copies/mL; HCV LLOQ <12 IU/mL.

* Simeprevir was initiated with bilirubin level of 1.8 mg/dL, without any related side effects.