

Kidney Transplant Patients

Genotypes 1 and 4

Recommended regimens listed by evidence level and alphabetically for:

Treatment-Naive and -Experienced Kidney Transplant Patients With Genotype 1 or 4 Infection, With or Without Compensated Cirrhosis^a **i**

RECOMMENDED	DURATION	RATING i
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) ^b	12 weeks	I, A ^c IIa, C ^d
Daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg)	12 weeks	I, A

^a For [decompensated cirrhosis](#), please refer to the appropriate section.
^b This is a 3-tablet coformulation. Please refer to the prescribing information.
^c Evidence for patients without cirrhosis
^d Evidence for patients with compensated cirrhosis

Genotypes 2, 3, 5, and 6

Recommended and alternative regimens for:

Treatment-Naive and -Experienced Kidney Transplant Patients With Genotype 2, 3, 5, or 6 Infection, With or Without Compensated Cirrhosis^a **i**

RECOMMENDED	DURATION	RATING i
Daily fixed-dose combination of glecaprevir (300 mg)/pibrentasvir (120 mg) ^b	12 weeks	I, A ^c IIa, C ^d
ALTERNATIVE	DURATION	RATING i
Daily daclatasvir (60 mg) plus sofosbuvir (400 mg) plus low initial dose of ribavirin (600 mg; increase as tolerated)	12 weeks	II, A

^a For [decompensated cirrhosis](#), please refer to the appropriate section.
^b This is a 3-tablet coformulation. Please refer to the prescribing information.
^c Genotypes 2, 3, and 6
^d Genotype 5

DAA Therapy in Kidney Transplant Patients

A recent phase 2, open-label clinical trial evaluated the safety and efficacy of the daily fixed-dose combination of ledipasvir (90 mg)/sofosbuvir (400 mg) in 114 kidney transplant recipients who were more than 6 months post transplant ([Colombo, 2017](#)). Enrolled patients had genotype 1 (91%) or 4 infection; 69% were treatment naive, and 15% had compensated cirrhosis. Patients were randomized to 12 weeks or 24 weeks of ledipasvir/sofosbuvir. Median eGFR prior to treatment was 50 mL/min for patients in the 12-week study arm and 60 mL/min for those in the 24-week arm. Overall SVR12 was 100% (114/114). Adverse events were common (64%) and serious adverse events occurred in 13 patients (11%); only 1 participant discontinued treatment because of an adverse event ([Colombo, 2017](#)). Four patients with an eGFR >40 mL/min at baseline experienced a decrease to <30 mL/min during therapy. In 3 of these patients, eGFR increased to >30 mL/min at the last visit recorded; 1 patient who had interrupted study treatment had a final value of 14.4 mL/min. All but 1 of the 6 patients with compensated cirrhosis whose eGFR decreased to <40 mL/min continued study treatment without interruption; none permanently discontinued study treatment.

Several additional reports have described successful outcomes with combination direct-acting antiviral (DAA) therapy in kidney transplant recipients ([Sawinski, 2016](#)); ([Kamar, 2016](#)); ([Saxena, 2017](#)). Sawinski and colleagues treated 20 HCV-infected kidney transplant recipients (88% genotype 1; 50% with advanced fibrosis; 60% treatment-experienced with an interferon-based regimen) with sofosbuvir-based therapy. Various regimens were used, including simeprevir plus sofosbuvir (n=9); ledipasvir/sofosbuvir (n=7); sofosbuvir plus ribavirin (n=3); and daclatasvir plus sofosbuvir (n=1). SVR12 was 100% ([Sawinski, 2016](#)). Two patients required dose reductions due to anemia (associated with ribavirin use). However, no significant changes in serum creatinine or proteinuria, or graft rejection were seen before or after treatment. Forty-five percent of patients required dose reduction of immunosuppressive agents while on antiviral therapy ([Sawinski, 2016](#)).

Real-life data from the ongoing HCV-TARGET study have also demonstrated the efficacy of DAA therapy in patients with kidney transplant and in those with dual liver kidney transplant ([Saxena, 2017](#)). Various regimens were used, including sofosbuvir/ledipasvir ± ribavirin (85%); sofosbuvir plus daclatasvir ± ribavirin (9%); and ombitasvir/paritaprevir/ritonavir plus dasabuvir ± ribavirin (6%). The SVR12 rate was 94.6% in those with kidney transplant and 90.9% in dual liver kidney transplant recipients.

A pilot study conducted by Kamar and colleagues evaluated 25 kidney transplant recipients with chronic HCV infection who were treated with sofosbuvir-based regimens. The reported SVR12 was 100% ([Kamar, 2016](#)). Among the study participants, 76% were infected with genotype 1 and 44% had advanced fibrosis. All participants had an eGFR >30 mL/min. Treatment regimens included ledipasvir/sofosbuvir (n=9); daclatasvir plus sofosbuvir (n=4); sofosbuvir plus ribavirin (n=3); ledipasvir/sofosbuvir plus ribavirin (n=1); simeprevir and sofosbuvir plus ribavirin (n=1); simeprevir and sofosbuvir (n=6); and sofosbuvir plus peginterferon/ribavirin (n=1). Treatment was well tolerated without any discontinuations, dose reductions, graft rejections, or changes in serum creatinine levels. No drug interactions with calcineurin inhibitors were observed ([Kamar, 2016](#)).

Another small study that treated 3 genotype 4-infected kidney transplant patients with sofosbuvir (400 mg) plus ribavirin (1000 mg) for 24 weeks reported 100% SVR ([Hussein, 2016](#)). Anemia was reported in 2 patients related to concomitant ribavirin use. No other adverse events were reported.

The phase 3, open-label, single arm MAGELLAN-2 study evaluated a 12-week course of the pangenotypic regimen of glecaprevir/pibrentasvir in 100 liver (n=80) and kidney (n=20) transplant recipients. SVR 12 was achieved in 99% of patients ([Reau 2017](#)). The safety profile was excellent, and there was only 1 rejection episode in a liver transplant recipient. While this is an effective pangenotypic regimen as demonstrated in the nontransplant population, there were no genotype 5 transplant recipients in the study.

Drug interactions are an important consideration with antiviral therapy in renal transplant recipients. Please see [Unique Patient Populations: Patients Who Develop Recurrent HCV Infection Post Liver Transplantation](#) for a table of drug interactions with DAAs and calcineurin inhibitors.

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Related References

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Hussein NR, Sidiq Z, Saleem M. [Successful treatment of hepatitis c virus genotype 4 in renal transplant recipients with direct-acting antiviral agents](#). *Am J Transplant*. 2016th ed. 2016;.

Kamar N, Marion O, Rostaing L, Cointault O, Ribes D, Lavayssière L, et al.. [Efficacy and Safety of Sofosbuvir-Based Antiviral Therapy to Treat Hepatitis C Virus Infection After Kidney Transplantation](#). *American Journal of Transplantation: Official Journal of the American Society of Transplantation and the American Society of Transplant Surgeons*. 2016;16(5):1474 - 1479.

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Sawinski D, Kaur N, Ajeti A, et al. [Successful treatment of hepatitis C in renal transplant recipients with direct-acting antiviral agents](#). *Am J Transplant*. 2016;16(5):1588-1595.

Saxena V, Khungar V, Verna EC, Levitsky J, Brown RS, Hassan MA, et al. [Safety and Efficacy of Current DAA Regimens in Kidney and Liver Transplant Recipients with Hepatitis C: Results from the HCV-TARGET Study \[Epub ahead of print\]](#). *Hepatology (Baltimore, Md.)*. 2017;.