Regimens for Cirrhotic Patients

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KEYWORDS

• Direct-acting antivirals • Hepatitis C • Cirrhosis • Sofosbuvir • Ledipasvir • Paritaprevir • Ombitasvir • Simeprevir

KEY POINTS

- It is now expected that patients with compensated cirrhosis will achieve sustained virologic response (SVR) rates similar to those who do not have cirrhosis.
- The most significant population requiring new therapies is the genotype 3 treatment-experienced cirrhotic patients, in whom the optimal therapy remains unclear.
- Once SVR is achieved, patients should continue to be monitored for complications, including varices, decompensation, and hepatocellular carcinoma.

Hepatitis C is a blood-borne virus that is found worldwide. Although precise epidemiologic data are not available it is estimated that there are 150 million persons globally who have chronic hepatitis C infection and 350,000 to 500,000 people die each year from hepatitis C–related liver diseases.[1] In the United States, the prevalence is 1.8% and recent estimates suggest that as many as 5 million individuals may be infected with chronic hepatitis C.[2] By the year 2020, it is estimated that there may be 1 million individuals with hepatitis C who have progressed to cirrhosis.[3] Hepatitis C infection progressing to cirrhosis is the most common cause of hepatocellular carcinoma in United States and the most common indication for orthotopic liver transplant worldwide. A recent estimate has suggested that effective therapy for hepatitis C could potentially substantially reduce the transplant requirement for those with chronic hepatitis C.[4]

In the evaluation of chronic hepatitis C, it is essential to assess for the presence or absence of cirrhosis. Historically, this has been achieved with liver biopsy, which is considered the goal standard. Recently, elastography has been approved in the United States, which allows a noninvasive measure of cirrhosis (for hepatitis C >12.5 kPa).[5] Moreover, serum markers of fibrosis are also available. In addition, imaging may also be used to show cirrhosis and, with a nodular liver, cirrhotic

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morphology and portal hypertension, all pointing to a diagnosis of cirrhosis. Once cirrhosis is diagnosed, these patients should be screened regularly for hepatocellular carcinoma with ultrasonography every 6 months.[6] Endoscopy should also be performed to assess for the absence or presence of varices.[7] The recent American Association for the Study of Liver Diseases (AASLD)/Infectious Diseases Society of America (IDSA) guideline (http://www.hcvguidelines.org/) confirms the importance of assessing for cirrhosis.

The treatment of chronic hepatitis C infection has undergone a revolution in the past 2 years. In December 2013, the first oral regimen, sofosbuvir and ribavirin, was approved without interferon for genotypes 2 and 3 based on 3 registration studies.[8–10] Moreover, the combination of 2 medicines, sofosbuvir and simeprevir, which were approved separately for the treatment of hepatitis C genotype 1 in 2013, could be combined with or without ribavirin for a genotype 1 all-oral regimen to be given with high sustained response rates.[11] Historically, lower sustained response rates have been observed in cirrhotic patients who received peginterferon with or without direct-acting antiviral agents (DAAs).[12–14] As treatment have evolved to all-oral regimens, many of the previous predictors of poor treatment response, such as race, viral level, and IL28B genotype, that predicted poor response to peginterferon and ribavirin no longer predict poor response to all-oral therapies with direct-acting antiviral agents for hepatitis C. However, even in this current era, patients with cirrhosis and advanced liver disease remain a population that may require additional strategies to achieve sustained virologic response (SVR) compared with those without cirrhosis. This requirement is particularly important because sustained response in this population has significant clinical impact with the potential to help fibrosis progression, reduce the risk of decompensation and liver cancer, and possibly prevent progression of chronic liver disease to a point at which orthotopic liver transplant must be considered.[15] However, in patients with Child A cirrhosis, the population that is discussed here, no dose adjustments are required for any of the DAA classes or ribavirin. Therapy in patients with Child B/C cirrhosis is discussed elsewhere in this issue.

TREATMENT OPTIONS: GENOTYPE 1

The treatment options for patients with hepatitis C differ by genotype. Historically, genotype 1 has been most the difficult genotype to treat. There are currently 3 approved treatment options for genotype 1 and all 3 treatment options may be used in patients with hepatitis C with cirrhosis in the United States. The treatment options for treatment-naive patients with cirrhosis are listed in **Table 1** and include sofosbuvir and ledipasvir for 12 weeks, sofosbuvir plus simeprevir for 24 weeks, and paritaprevir plus ombitasvir plus dasabuvir with ribavirin for 12 to 24 weeks depending on genotype 1 subtype (1a or 1b). The data for these recommendations come from landmark

Table 1
Genotype 1 regimens for patients with compensated cirrhosis

Treatment Naive	1a/1b	Duration (wk)	SVR (n/N)
Sofosbuvir + ledipasvir	1a/1b	12	94% (32 of 34)
Paritaprevir/r + ombitasvir + dasabuvir + RBV	1a	24	93% (52 of 56)
Paritaprevir/r + ombitasvir + dasabuvir + RBV	1b	12	100% (22 of 22)
Sofosbuvir + simeprevir ± RBV	1a/1b	24	100% (3 of 3) + RBV 100% (5 of 5) no RBV

Abbreviation: RBV, ribavirin.