Current and Soon-to-Be-Approved Regimens Offer High Cure Rates for HCV

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A choice of all-oral regimens to treat patients with hepatitis C virus (HCV) is available in the United States, and more are expected to be approved soon. Andrew J. Muir, MD, Duke University Department of Medicine, Durham, North Carolina, USA, reviewed the current regimens and trial data from those that are expected to be approved soon.

Key data on which to base treatment decisions include prior HCV treatment; if it included interferon and ribavirin, a protease inhibitor, or sofosbuvir; and whether these treatments failed. Fibrosis, if present, should be managed. Decompensated cirrhosis might indicate the need for a transplant evaluation.

US Food and Drug Administration-approved all-oral regimens for HCV include treatments for HCV genotypes 1, 2, and 3. There are no approved all-oral regimens for HCV genotypes 4, 5, or 6. For HCV genotype 1, the sustained virologic response (SVR) rates are >90%, which should be considered the benchmark for treatment. Treatment regimens for patients with genotype 1 are summarized in Table 1.

The TURQUOISE-II study [Poordad F et al. *N Engl J Med.* 2014] compared 12 vs 24 weeks of paritaprevir/ritonavir, dasabuvir, ombitasvir, and ribavirin in treatment-naïve and treatment-experienced patients (n=380) with genotype 1 HCV and compensated cirrhosis. The overall SVR was 92% at 12 weeks and 96% at 24 weeks; responses for genotype 1b were 99% and 100%, respectively, and for genotype 1a were 89% and 94%, respectively.

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American Association for the Study of Liver Diseases (AASLD)–Infectious Disease Society of America (IDSA) guidelines recommend sofosbuvir and ribavirin for treatment-naïve and peginterferon alpha/ribavirin-resistant, genotype 2 HCV.

Treatment of genotype 3 HCV remains challenging. AASLD–IDSA guidelines recommend sofosbuvir plus ribavirin for treatment-naïve and peginterferon alpha/ribavirin-resistant, genotype 3 HCV. However, in treatment-experienced patients, particularly those with cirrhosis, response rates are low [Zeuzem S et al. AASLD 2013. Abstract 1085]. The addition of ribavirin to sofosbuvir plus ledipasvir improves SVR rates in treatment-naïve (100%, n=26) and treatment-experienced (82%, n=50) patients with genotype 3 HCV, although the SVR rates are lower in patients with (73%, n=22) than without (89%, n=28) cirrhosis [ELECTRON2; Gane EJ et al. EASL. 2014. Abstract O6; Gane EJ et al. AASLD 2014. Abstract 79]. Response rates were 90% (n=101) vs 86% (n=51) for treatment-naïve versus treatment-experienced patients with genotype 3 HCV treated with daclatasvir plus sofosbuvir [ALLY 3; Nelson DR et al. AASLD 2014. Abstract LB-3].

For treatment-naïve and peginterferon alpha/ribavirin-nonresponsive, genotype 3 HCV, AASLD–IDSA guidelines recommend sofosbuvir and ribavirin for patients ineligible for interferon, adding peginterferon alpha for those eligible for interferon. A small study (n=25) suggests that the off-label combination of sofosbuvir plus ledipasvir is an option for genotype 6 HCV [ELECTRON2; Gane EJ, et al. AASLD. 2014. LB-11].

A key message for patients with HCV is that effective therapies are available, and more treatments, including ribavirin-free regimens, are expected to be approved soon.

Table 1. Treatment Regimens for HCV Genotype 1

Regimen	Weeks	Study	Sustained Virologic Response, n/N (%)
Treatment-Naïve, Noncirrhotic			
Sofosbuvir + ledipasvir (HCV RNA < 6 M IU/mL)	8	ION-3 [Kowdley KV et al. *N Engl J Med.* 2014]	119/123 (97%)
Sofosbuvir + ledipasvir (HCV RNA > 6 M IU/mL)	12	ION-3 [Kowdley KV et al. *N Engl J Med.* 2014]	206/216 (95%)
Simeprevir + sofosbuvir	12	COSMOS [Olysio Pkg Insert. 2014]	20/21 (95%)
Paritaprevir, dasabuvir, ombitasvir (genotype 1b)	12	PEARL III [Ferenci P. *N Engl J Med.* 2014]	207/209 (99.5%)
Paritaprevir, dasabuvir, ombitasvir (genotype 1a)	12	PEARL IV [Ferenci P. *N Engl J Med.* 2014]	97/100 (97%)
Sofosbuvir + daclatasvir	12	[Sulkowski M et al. *N Engl J Med.* 2014]	41/41 (100%)
Treatment-Naïve, Cirrhotic			
Sofosbuvir + ledipasvir	12	ION-1 [Afdhal N et al. *N Engl J Med.* 2014]	32/33 (97%)
Simeprevir + sofosbuvir	24	COSMOS [Olysio Pkg Insert. 2014]	10/10 (100%)
Paritaprevir, dasabuvir, ombitasvir, ribavirin	12 to 24	TURQUOISE II [Poordad F et al. *N Engl J Med.* 2014]	See text.
Treatment-Experienced, Noncirrhotic			
Sofosbuvir + ledipasvir	12	ION-1 [Afdhal N et al. *N Engl J Med.* 2014]	83/87 (95%)
Simeprevir + sofosbuvir	12	COSMOS [Olysio Pkg Insert. 2014]	20/21 (95%)
Paritaprevir, dasabuvir, ombitasvir, ribavirin	12	SAPPHIRE II [Zeuzem S. *N Engl J Med.* 2014]	286/297 (95%)
Treatment-Experienced, Cirrhotic			
Sofosbuvir + ledipasvir	24	ION-2 [Afdhal N et al. *N Engl J Med.* 2014]	22/22 (100%)
Simeprevir + sofosbuvir	24	COSMOS [Olysio Pkg Insert. 2014]	10/10 (100%)
Paritaprevir, dasabuvir, ombitasvir, ribavirin	12 to 24	TURQUOISE II [Poordad F et al. *N Engl J Med.* 2014]	See text.

HCV, hepatitis C virus; IU, international unit; M, million; mL, milliliter; SVR, sustained virologic response.