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## on Drugs and Therapeutics

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### IN BRIEF

#### New Indications for *Harvoni*

*Harvoni*, a once-daily fixed-dose combination of the direct-acting antiviral agents ledipasvir and sofosbuvir approved by the FDA in 2014 for treatment of hepatitis C virus (HCV) genotype 1 infection,<sup>1</sup> has now been approved for use in patients infected with HCV genotype 4, 5, or 6, and in patients co-infected with HCV and HIV-1. A 12-week course of treatment with *Harvoni* plus ribavirin has also been approved as an alternative to 24 weeks of *Harvoni* alone for treatment-experienced, cirrhotic patients with HCV genotype 1 infection.

**HCV genotypes 4, 5, and 6** are responsible for <2% of HCV cases in the US and Canada. They are more prevalent in the Middle East, North Africa, and Central sub-Saharan Africa (genotype 4), Southern sub-Saharan Africa (genotype 5), and Southeast Asia (genotype 6).<sup>2</sup>

In two open-label trials (both summarized in the package insert), 44 patients infected with HCV genotype 4, 41 patients with genotype 5, and 25 patients with genotype 6 received 12 weeks of treatment with ledipasvir/sofosbuvir.<sup>3</sup> The rates of sustained virologic response 12 weeks after stopping treatment (SVR12) were 93%, 93%, and 96% in patients infected with HCV genotypes 4, 5, and 6, respectively.

In a single-arm trial (ION-4), 335 patients **co-infected with HIV-1 and HCV genotype 1** (98%) or 4 (2%) received 12 weeks of treatment with ledipasvir/sofosbuvir. An SVR12 was achieved in 322 patients (96%), including 94% of 67 cirrhotic patients and 97% of 185 treatment-experienced patients.<sup>4</sup>

In a randomized, double-blind trial (SIRIUS), 154 **treatment-experienced patients with HCV genotype 1 infection and cirrhosis** who had not responded to peg-interferon plus ribavirin with and without a protease inhibitor received either ledipasvir/sofosbuvir plus ribavirin 1000-1200 mg daily for 12 weeks or ledipasvir/sofosbuvir without ribavirin for 24 weeks. An SVR12 was achieved in 74 of 77 patients (96%) in the 12-week arm and in 75 of 77 patients (97%) in the 24-week arm.<sup>5</sup>

1. A combination of ledipasvir and sofosbuvir (*Harvoni*) for hepatitis C. *Med Lett Drugs Ther* 2014; 56:111.
2. JP Messina et al. Global distribution and prevalence of hepatitis C virus genotypes. *Hepatology* 2015; 61:77.
3. EJ Gane et al. Efficacy of ledipasvir and sofosbuvir, with or without ribavirin, for 12 weeks in patients with HCV genotype 3 or 6 infection. *Gastroenterology* 2015; 149:1454.
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5. M Bourlière et al. Ledipasvir-sofosbuvir with or without ribavirin to treat patients with HCV genotype 1 infection and cirrhosis non-responsive to previous protease-inhibitor therapy: a randomised, double-blind, phase 2 trial (SIRIUS). *Lancet Infect Dis* 2015; 15:397.

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