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Daclatasvir plus sofosbuvir regimen sheds promising light on future hepatitis C virus genotype 3 therapies

Nelson DR, Cooper JN, Lalezari JP, et al. All-oral 12-week treatment with daclatasvir plus sofosbuvir in patients with hepatitis C virus genotype 3 infection: ALLY-3 phase III study. Hepatology 2015; 61: 1127-35.

The development of new direct-acting oral antiviral agents (DAAs) against the Hepatitis C virus (HCV) has garnered the attention of physicians because of its efficacy in delivering higher cure rates of HCV patients (1). DAAs have a high potency in curing HCV patients and fewer side-effects than all previous HCV treatment options. Furthermore, the therapy is considerably simpler than all interferon-based therapies, particularly for the treatment of HCV genotype 1 infection. Patients affected with genotype 3, which is common throughout the world, have been a soft spot of DAAs as a difficult-to-treat HCV population with suboptimal response rates (2). HCV genotype 3 is associated with a higher risk of progression to cirrhosis and hepatocellular carcinoma than other HCV genotypes (2).

Nelson et al. (3) conducted an open-label, two-cohort phase 3 study that included 152 HCV patients [n=101 (66%) treatment naive, n=51 (34%) treatment experienced]. They evaluated the 12-week regimen of daclatasvir [pangenotypic nonstructural protein (NS) 5A inhibitor] 60 mg plus sofosbuvir (pangenotypic NS5B inhibitor) 400 mg once daily for 12 weeks in patients infected with HCV genotype 3. Study participants had the following characteristics: whites, 90%; males, 59%; median age, 55 years; HCV- Ribonucleic acid (RNA)>800,000 IU/mL, 71%; and non-CC interleukin (IL) 28B genotype, 61%. Sustained virological response (SVR) 12 rates were higher in patients without cirrhosis (96%; 105/109) than in those with cirrhosis (63%; 20/32). SVR12 rates in treatment-naive and treatment-experienced patients were 90% (91/101) and 86% (44/51), respectively. Five of the seven patients who had previously failed the treatment with a sofosbuvir-containing regimen and two who had previously failed treatment with an alisporivir-containing regimen achieved SVR12. Baseline characteristics of gender, age, HCV-RNA levels, and interleukin-28B genotype did not have any influence on SVR12. During the treatment, there was only one serious adverse effect reported which was an event of gastrointestinal hemorrhage; however, it was not considered to be related to study medications. The most common adverse effects (in >10% of patients) were headache, fatigue, and nausea (3).

The initial DAAs were approved in 2011, and more oral medications are expected to be approved in the near future. Nelson et al. (3) report that daclatasvir plus sofosbuvir is currently at the forefront of HCV genotype 3 treatment. The same study also noted a lower SVR on cirrhotic patients' success and recommended that HCV genotype 3 infection and cirrhosis may benefit from a longer therapy of 24 weeks (3). In another cohort study on daclatasvir and sofosbuvir, the European compassionate use program presented the SVR rates at 12 and 24 weeks in HCV genotype 3 cirrhotic patients' treatment as 76% and 88%, respectively (4).

Finally, the United States Food and Drug Administration approved the use of daclatasvir plus sofosbuvir for antiviral therapy of HCV genotype 3 infection in July 2015. Daclatasvir plus sofosbuvir over 12 weeks is now our preferred regimen for HCV genotype 3-infected patients without cirrhosis. Daclatasvir plus sofosbuvir plus weight-based ribavirin regimen for 24 weeks is our preferred regimen for HCV genotype 3-infected patients with cirrhosis. However, over time it is imperative to stay up-to-date on these novel practices to maintain treatment efficacy that is specifically tailored toward HCV genotype 3 infections.

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