HIGHLIGHTS FROM EASL 2014

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Fixed-Dose Sofosbuvir/Ledipasvir Potent in Treatment-Experienced Patients with Genotype 1 HCV Infection

Twelve-week sustained viral response (SVR) rates ranging from 94% to 99% have been reported in treatment-experienced patients infected with genotype 1 hepatitis C virus (HCV) infection following 12 to 24 weeks of therapy with sofosbuvir (Sovaldi, Gilead) and ledipasvir (fixed-dose combination) with or without ribavirin. The study population included patients with cirrhosis and those who failed previous therapy or relapsed. No significant differences were seen between study arms. The findings of this phase 3 study, termed ION-2, were reported by Nezam H. Afdhal, MD, chief of hepatology and director of the Liver Center at Beth Israel Deaconess Medical Center in Boston, Massachusetts, at the 49th annual meeting of the European Association for the Study of the Liver (EASL 2014), which took place April 9-13, 2014 in London, England (Abstract O109).

A total of 440 adult patients (mean age, 56 years) infected with genotype 1 HCV, including patients who had failed previous interferon-based therapy and patients with cirrhosis, were included in the study. Patients were divided into 2 groups that received 12 or 24 weeks of therapy, and these groups were, in turn, divided into groups of patients who received sofosbuvir plus ledipasvir or sofosbuvir plus ledipasvir plus ribavirin. Each group included a relatively equal proportion of patients who were cirrhotic, previous nonresponders to therapy, or had the *IL28B* CC genotype (Table 1).

The SVR12 was the least robust—but still strong—among those patients with cirrhosis who received 12 weeks of therapy (86% in patients receiving sofosbuvir plus ledipasvir and 82% in patients receiving triple therapy), although the SVR12 reached 100% in cirrhotic patients receiving 24 weeks of therapy regardless of whether the treatment regimen included ribavirin. Otherwise, SVR12 rates exceeding 90% were achieved regardless of type of previous treatment failure, sex, race, baseline body mass index, HCV genotype, *IL28B* genotype, baseline HCV RNA, cirrhosis status, or type of previous HCV therapy received.

Rapid, High Efficacy of Sofosbuvir/Ledipasvir Seen in Patients with HCV/HIV Coinfection

Interim results of ERADICATE, a nonrandomized phase 2 trial of 12 weeks' treatment with fixed-dose sofosbuvir plus ledipasvir, are suggesting that the combination may provide extremely high SVR rates in HCV treatment–naive patients with genotype 1 HCV/HIV coinfection. All patients responded to therapy by Week 4 and maintained response through Week 12 of active treatment. All patients who reached the 4-week follow-up had SVR (Table 2). SVR was sustained in all patients who were not taking antiretroviral (ARV) therapy who completed 12 weeks of follow-up. SVR12 rates for patients receiving ARV therapy are pending. The interim data were reported by Anu O. Osinusi, MD, MPH, assistant professor of medicine in the Division of Infectious Diseases at the University of Maryland, at EASL 2014 (Abstract 14). The study is expected to run to 48 weeks.

Table 1. Distribution of HCV Infection and Treatment Characteristics

	12 Weeks		24 Weeks	
	SFR/LDR (n=109)	SFR/LDR + RBV (n=111)	SFR/LDR (n=109)	SFR/LDR + RBV (n=111)
Mean HCV RNA, $\log_{10}$ IU/mL (range)	6.5 (5.0-7.5)	6.4 (4.6-7.3)	6.4 (4.7-7.4)	6.5 (3.1-7.4)
HCV RNA ≥ 800,000 IU/mL, %	95	88	85	87
Genotype 1a HCV, %	79	79	78	79
IL28B CC genotype, %	9	10	15	16
Previous nonresponder, %	45	41	45	46
Previous PI failure, %	61	58	46	46
Cirrhosis, %	20	20	20	20

HCV, hepatitis C virus; LDR, ledipasvir; PI, protease inhibitor; RBV, ribavirin; SFR, sofosbuvir.

Table 2. Time to HCV RNA Less than the Lower Limit of Quantification

	ARV-Naive, % (n)	ARV-Treated, % (n)
Treatment Week 4	100 (n=13)	100 (n=37)
Treatment Week 12 (end of treatment)	100 (n=13)	100 (n=30)
SVR4	100 (n=12)	100 (n=22)
SVR12	100 (n=10)	pending

SVR4, sustained viral response at Week 4 posttreatment; SVR12, SVR at Week 12 posttreatment.

A total of 50 patients were enrolled in the study. Thirty-seven patients were on ARV therapy and 13 patients were not. The median baseline HCV RNA was 6.07-$\log_{10}$ IU/mL (range, 4.05-7.29) among patients not receiving ARV therapy and 5.97-$\log_{10}$ IU/mL among ARV-treated patients.

To date, the therapeutic regimen has been safe and well tolerated, with no deaths, grade 4 adverse events, discontinuations due to adverse events, or adverse impact on HIV infection.

3D–Magnetic Resonance Elastography Accurately Diagnoses NASH and Fibrosis

3D–magnetic resonance elastography (MRE) accurately diagnoses nonalcoholic steatohepatitis (NASH) and advanced fibrosis in patients with biopsy-proven nonalcoholic fatty liver disease (NAFLD), reported Rohit Loomba, MD, MHSc, associate professor of clinical medicine at the University of California at San Diego School of Medicine, at EASL 2014 (Abstract O80). Dr Loomba and his team sought to confirm whether 3D-MRE improved upon 2D-MRE in diagnosing NASH and fibrosis in persons with NAFLD.

During an 11-month enrollment, 80 consecutive patients with biopsy-proven NAFLD underwent a standard workup that included 3D-MRE. The diagnostic performance of 3D-MRE was assessed via an area-under-the-receiver-operating-characteristic (AUROC) analysis. The median time interval between biopsy and 3D-MRE was 1.3 months. Seventy of the 80 patients had NASH, and 33, 25, 10, 6, and 6 patients had stage 0, 1, 2, 3, and 4 fibrosis, respectively. 3D-MRE showed robust accuracy in identifying NASH, with an AUROC score of 0.852 (P=.0003), and in distinguishing advanced fibrosis from stage 0–2 fibrosis, with an AUROC score of 0.969 (P<.0001).

Livers of Moderate Drinkers Healthier than Livers of Teetotalers

Prevalence of hepatic steatosis is lower in persons who consume low or moderate amounts of alcohol than in persons who are abstinent, according to a study conducted by researchers from Johns Hopkins University in Baltimore, Maryland (Abstract O30). Mariana Lazo, MD, PhD, assistant professor of medicine at Johns Hopkins, reported the findings, derived from self-reports and ultrasound data of 12,454 adults, at EASL 2014. The adults were participants of the Third National Health and Nutrition Examination Survey, which was conducted between 1988 and 1994.

The study design was weighted to represent the US population and revealed that 45.5% of US citizens are nondrinkers. Fourteen percent of the US population consume 1 drink per day, 26% consume 2 to 3 drinks, and 15% consume 4 or more drinks. Persons consuming 1 drink per day were more likely to be physically fit, with less incidence of diabetes and hypertension, than nondrinkers or persons who consumed more than 1 drink per day, and this pattern was particularly noticeable in men. In fact, the adjusted prevalence of hepatic steatosis in nondrinking men and men who reported drinking 4 or more alcoholic beverages per day was about the same—about 26%, compared with about 19% in men who consume 1 alcoholic beverage per day. Prevalence of hepatic steatosis was lower in women than men across the board, although a slight increase in prevalence was also seen in nondrinking women compared with women who drank 1 to 3 drinks per day (about 18% vs 15% to 16%). The prevalence of hepatic steatosis in women who drank 4 or more drinks per day was about 24%.