Original Research | 24 November 2015

Four-Week Direct-Acting Antiviral Regimens in Noncirrhotic Patients With Hepatitis C Virus Genotype 1 Infection: An Open-Label, Nonrandomized Trial

ONLINE FIRST

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[+] Article, Author, and Disclosure Information

Ann Intern Med. Published online 24 November 2015 doi:10.7326/M15-0642

Background: Treatment of chronic hepatitis C virus (HCV) infection with direct-acting antivirals (DAAs) for 6 weeks achieves sustained virologic response (SVR) rates of 95% in some patients. If effective, shorter therapeutic courses could improve adherence and treatment costs.

Objective: To determine factors predictive of SVR to 4 weeks of DAA treatment in patients with stage F0 to F2 liver fibrosis.

Design: Open-label, nonrandomized, phase 2a trial. (Clinical Trials.gov: NCT01805882)

Setting: Single-center.

Patients: 50 treatment-naive and predominantly African American patients with HCV genotype 1 infection and early-stage liver fibrosis were sequentially enrolled into 2 treatment groups.

Intervention: 25 participants received a 3-drug regimen consisting of ledipasvir and sofosbuvir plus GS-9451 for 4 weeks, and 25 received a 4-drug regimen consisting of ledipasvir, sofosbuvir, GS-9451, and GS-9669 for 4 weeks.

Measurements: The primary efficacy end point was SVR12 (HCV RNA level below the lower limit of quantification at posttreatment week 12).

Results: Forty percent (10 of 25) (95% CI, 21% to 61%) of patients in the 3-drug group and 20% (5 of 25) (CI, 7% to 41%) of those in the 4-drug group achieved SVR12. Exploratory analysis suggested that lower baseline HCV viral load, younger age, and HCV genotype 1b were associated with SVR12. Ten patients had baseline HCV variants conferring greater than 20-fold resistance in vitro to at least 1 study DAA; all had viral relapse. Forty-eight percent (12 of 25) of patients receiving the 3-drug regimen and 72% (18 of 25) of those receiving the 4-drug regimen had adverse events, most of which were mild. One participant was lost to follow-up.

Limitation: Nonrandomized study design and small sample of patients with early-stage fibrosis.

Conclusion: Combination DAA therapy with 3 or 4 drugs for 4 weeks was well-tolerated but resulted in

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Primary Funding Source: National Institute of Allergy and Infectious Diseases, National Cancer Institute, and Clinical Center Intramural Program; supported in part by a cooperative research and development agreement between the National Institutes of Health and Gilead Sciences.

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Print ISSN: 0003-4819 | Online ISSN: 1539-3704