

# Therapy Respond Well to AbbVie Hepatitis C Treatment

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Nearly all genotype 1 hepatitis C patients with a history of injection drug use who were on stable opiate substitution therapy with methadone or buprenorphine were cured using AbbVie's Viekira Pak regimen plus ribavirin for 12 weeks, according to a Phase 2 study described in the *August 2015 Journal of Hepatology*. No interactions were seen between opiate substitution therapy and the hepatitis C drugs.

Hepatitis C virus (HCV) is efficiently spread through shared needles or other injection equipment, and a large proportion of people who inject drugs have HCV infection. People with a history of injection drug use often were not treated with interferon-based therapy in the past due to its long course of treatment, difficult side effects, and suboptimal efficacy. But new direct-acting antiviral agents in interferon-free regimens offer short treatment duration, good tolerability, and high cure rates.

Jay Lalezari from Quest Clinical Research in San Francisco and colleagues evaluated the efficacy, safety, and pharmacokinetics of a 12-week all-oral treatment regimen for chronic hepatitis C patients on opioid substitution therapy.

AbbVie's "3D" regimen consists of the HCV protease inhibitor paritaprevir with a ritonavir booster plus the NS5A inhibitor ombitasvir in a once-daily coformulation, taken with the NS5B polymerase inhibitor dasabuvir twice-daily. In the U.S. the full regimen is sold together under the brand name Viekira Pak, while in Europe the coformulation (Viekirax) and dasabuvir (Exviera) are sold separately.

This Phase 2 multicenter study included 38 participants with chronic HCV genotype 1 infection who were on stable opioid substitution therapy for at least 6 months using either methadone (n=19) or buprenorphine with or without naloxone (n=19).

Two-thirds of participants were men, 95% were white, and the mean age was 48 years. More than 80% had harder-to-treat HCV subtype 1a. Most (95%) were starting hepatitis C treatment for the first time but a few had previously tried pegylated interferon plus ribavirin. About 20% had moderate or advanced liver fibrosis (stage F2-F3), but none had cirrhosis. People with HIV or hepatitis B coinfection were excluded.

All participants in this open-label, single-arm study were treated with the paritaprevir/ritonavir/ombitasvir plus dasabuvir combination along with 1000-1200 mg/day weight-based ribavirin for 12 weeks. The primary efficacy endpoint was sustained virological response, or continued undetectable HCV RNA at 12 weeks post-treatment (SVR12).

## Results

- 37 out of 38 participants (97%) achieved SVR12 and still had undetectable HCV viral load at 24 weeks post-treatment (SVR24).
- None of the patients experienced viral breakthrough while on treatment or post-treatment relapse.
- The 1 patient without SVR12 discontinued treatment prematurely due to serious adverse events.
- The 3D regimen was generally safe and well-tolerated.
- Most people experienced at least 1 adverse event, but these were usually mild to moderate.
- 2 patients (5%) experienced serious adverse events considered unrelated to the study drugs (stroke, sarcoma, and leukemia), and 1 discontinued treatment early for this reason.

- The most frequent side effects were nausea, fatigue, and headache.
- 8 patients developed anemia (hemoglobin <10 g/dL), a known side effect of ribavirin; 6 of these reduced their ribavirin dosage and all went on to achieve SVR.
- Pharmacokinetic analysis indicated no clinically meaningful interactions between the hepatitis C drugs and opiate substitution therapy.
- Neither methadone nor buprenorphine significantly affected paritaprevir, ritonavir, ombitasvir, or dasabuvir concentrations.
- No dose adjustments of methadone or buprenorphine were needed.

"The interferon-free regimen of ombitasvir/paritaprevir/ritonavir and dasabuvir + ribavirin for 12 weeks was well tolerated and achieved sustained virologic response in 97.4% of patients on opioid substitution therapy in this study," the researchers concluded. "This all-oral regimen may provide an effective alternative to interferon-based therapies for HCV-infected patients with a history of injection drug use."

"Improved treatment uptake and completion rates could significantly decrease the burden of liver disease in this underserved patient population, since sustained virologic response is associated with a lower risk of HCV-related clinical outcomes," the study authors wrote. "Mathematical models suggest that increased uptake of treatment among this patient population could substantially reduce HCV infection incidence, and prevalence, leading to tangible benefits for overall public health."

"Opioid substitution therapy clinics may be an ideal setting to implement all-oral, interferon-free therapies for patients with HCV genotype 1 infection," they continued. "These therapies have the potential to substantially limit disease progression and reduce transmission among patients with a history of injection drug use...Given the burden of disease and pending availability of better tolerated and more efficacious regimens, greater efforts should be undertaken to screen, evaluate, and treat HCV-infected patients with a history of drug use."

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### Reference

J Lalezari, JG Sullivan, P Varunok, et al. Ombitasvir/paritaprevir/r and dasabuvir plus ribavirin in HCV genotype 1-infected patients on methadone or buprenorphine. *Journal of Hepatology* 63(2):364-369. August 2015.