

Four Weeks May Be Too Short for Treatment of Recent Hepatitis C

Cutting the duration of Mavyret treatment also cut the likelihood of a cure.

March 6, 2023 By [Liz Highleyman](#)

A shorter four-week course of Mavyret (glecaprevir/pibrentasvir) for people with recent [hepatitis C virus \(HCV\)](#) infection led to a lower cure rate than treatment for six weeks or longer, according to study results presented at the [30th Conference on Retroviruses and Opportunistic Infections](#).

Direct-acting antiviral (DAA) treatment for hepatitis C is highly effective. More than 90% of people with chronic HCV infection can be cured with an eight-week course of [Mavyret](#) or a 12-week course of [Epclusa](#) (sofosbuvir/velpatasvir). But acute or recent HCV infection is generally easier to treat, so researchers have explored shorter courses of DAA therapy.

A [previous small study](#) by Marianne Martinello, MD, of the University of New South Wales, and colleagues showed that six weeks of Mavyret cured almost all patients who acquired HCV within the past year. So the researchers set out to determine whether treatment could be shortened even further.

The open-label [TARGET3D](#) pilot study included 23 participants with recent hepatitis C infection or reinfection. (Martinello noted that the study closed early due to COVID-19 with fewer than the planned number of participants.)

Recent primary infection was defined as a first positive HCV antibody or HCV RNA test within six months before enrollment and either HCV antibody seroconversion within the past 18 months or symptoms of acute hepatitis or elevated liver enzymes within the past 12 months. Recent reinfection was defined as a new positive HCV RNA test within six months before enrollment along with evidence of prior spontaneous HCV clearance or successful treatment.

Most participants were men who have sex with men, a group at risk for sexually transmitted HCV. The median age was 46 years. More than half (57%) had a history of ever injecting drugs, but 61% said they had not done so within the past six months. About two thirds had a recent primary infection, while a third had a recent reinfection. The estimated median duration of infection was 17 weeks. Most had HCV genotype 1 (78%), but five people had genotypes 2, 3 or 4. A majority (70%) were also living with HIV.

All participants were treated with Mavyret once daily for four weeks, and everyone completed treatment. The main study endpoint was sustained virological response, or continued undetectable HCV RNA at 12 weeks posttreatment (SVR12), which is considered a cure.

At the end of treatment, 20 participants (87%) had achieved viral suppression. But at 12 weeks posttreatment, just 18 (78%) overall and 82% of those who completed follow-up achieved a sustained response. This was substantially lower than the 90% overall and 96% per-protocol cure rates seen in the previous study of Mavyret treatment for six weeks.

There were four cases of virological failure, all of which were confirmed by genetic sequencing to be relapses rather than reinfections. Two of the four had a sustained response at four weeks after treatment but later relapsed. Everyone who relapsed had a high HCV viral load above 6.5 log, or about 3,000,000 copies. One of the four reported less than optimal treatment adherence. Three of the relapsers were treated again with a 12-week course of Epclusa or [Zepatier](#) (grazoprevir/elbasvir); two were cured and one was lost to follow-up.

“Glecaprevir/pibrentasvir for four weeks was safe and well tolerated among people with acute and recent HCV infection, but efficacy was lower than seen with longer treatment duration ($\geq$ six weeks),” the researchers concluded.

Studies are ongoing to look for biomarkers that can predict who can be cured with shorter treatment, Martinello noted.

Experts previously often recommend waiting six months after HCV infection to see whether the immune system would natural clear the virus, which happens in around a third of people (though less so among those with HIV coinfection). But treating hepatitis C as soon as possible breaks chains of transmission. What’s more, new DAA drugs are safe and well tolerated, so there is little downside besides cost.

“Treatment of recent HCV infection is needed for elimination,” Martinello said. “We need to ensure that all people with hepatitis C are considered for treatment regardless of the duration of infection.”

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