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Hepatitis C cured in co-infected HIV patients

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A multicenter team of researchers report that in a phase III clinical trial, a combination drug therapy cures chronic hepatitis C in the majority of patients co-infected with both HIV and hepatitis C.

"In many settings, hepatitis C is now a leading cause of death among HIV co-infected patients," says Mark Sulkowski, M.D., medical director of the Johns Hopkins Infectious Disease Center for Viral Hepatitis and professor of medicine at the Johns Hopkins University School of Medicine. Approximately one-third of HIV patients in the United States have hepatitis C, with an estimated 7 million co-infected patients worldwide.

Because of poor tolerability to the previous standard of treatments for hepatitis C, including injections of interferon-alpha and medications that can have interactions with anti-retroviral medications used to treat HIV, this population of co-infection patients has been considered difficult to treat. Data from this phase III clinical trial were incorporated into the FDA's approval of the new drug, sofosbuvir, last December, so treatment with this all-oral regimen—sofosbuvir and ribavirin—is considered on-label.

The trial, paid for by the developers of sofosbuvir, Gilead Sciences, is published in the July 23 issue of *The Journal of the American Medical Association*.

Researchers and doctors enrolled study participants from the United States and Puerto Rico through 34 academic, private practice and

community health centers. In total, doctors administered sofosbuvir and ribavirin to a total of 223 HIV-1 patients chronically co-infected with hepatitis C (genotypes 1, 2 or 3) either for 12 weeks (for treatment-naive patients with genotype 2 or 3) or for 24 weeks (for treatment-naive patents with genotype 1 or treatment-experienced patents with genotype 2 or 3). Twelve weeks after treatment ended, researchers tested patients again for hepatitis C infection to determine if treatment was effective.

For treatment-naive patients, 76 percent with genotype 1, 88 percent with genotype 2 and 67 percent with genotype 3 were cured. "We've always termed this to be 'sustained virologic response,'" says Sulkowski, "but we now know that means hepatitis C has been cured." Treatment-experienced patients had even better cure rates: 92 percent for patients with genotype 2 and 94 percent for patients with genotype 3. Seven patients discontinued treatment because of adverse events, but there were no observed adverse effects on HIV or its treatment.

"The likelihood that a patient with chronic, long-standing hepatitis C infection would have spontaneous cure is near zero," says Sulkowski, "so if these patients had not been treated, none would have been cured." Because of this, typically the control group of patients in a clinical trial undergoes the standard-of-care treatment, which for hepatitis C is weekly Interferon injections and twice-daily ribavirin orally. However, neither the investigators nor the potential clinical trial participants were willing to accept a therapy that for HIV co-infected patients had both low efficacy and poor tolerability.

In addition, says Sulkowski, "Doctors and patients alike recognize the idea that it would be difficult, if not impossible, to randomize clinical trial participants to an injectable treatment (interferon) that's linked to many side effects versus an oral treatment (sofosbuvir plus ribavirin)." For these reasons, the clinical trial, named PHOTON-1, was open-label, nonrandomized and uncontrolled. "The PHOTON-1 study represents the

first clinical trial to demonstrate that we can cure hepatitis C in patients with HIV co-infection without the use of interferon," says Sulkowski. "As such, it represents a transformative step in our approach to this therapeutic area."

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