Many People From Africa Have Unusual Hepatitis C Genotypes

The presence of less studied HCV genotypes may compromise cure rates.

August 14, 2019 By Liz Highleyman

More than half of people from Africa may have less common—or in some cases, previously unrecognized—hepatitis C virus (HCV) genotypes, which could result in a lower likelihood of a cure, especially when using older direct-acting antiviral medications (DAAs), according to a recent study.

These findings indicate that expansion of hepatitis C treatment in Africa may require use of newer drugs that work against multiple HCV genotypes. Further, "the reality of global migration means that these data are also relevant for clinicians in high-income countries who should exercise caution in selecting regimens for African patients with unusual or un-subtypeable genotypes," the study authors concluded.

HCV genotypes 1a and 1b are the most common types in the United States and Europe, and consequently they have been the most widely studied in clinical trials of new therapies. The first DAAs used without interferon, including Sovaldi (sofosbuvir) and Harvoni (sofosbuvir/ledipasvir), work well against genotype 1. HCV genotypes 4, 5 and 6 are often treated with the same medications as genotype 1, though relatively few people with these less common types were included in trials. The newest DAA regimens, including Epclusa (sofosbuvir/velpatasvir) and Mavyret (glecaprevir/pibrentasvir), are pangenotypic, or active against all known types of HCV.

Kate Childs, of King's College Hospital Trust in London, and colleagues conducted a retrospective analysis of people with HCV who received care at King's College Institute of Liver Studies between 2010 and 2018. They identified 91 people who were born in 18 countries in Africa.

As reported in the Journal of Hepatology, just over half (52%) of the African patients had unusual HCV genotypes. While 22% had genotypes 1a or 1b, another 39% had other genotype 1 subtypes. Fifteen previously unknown genotype 1 subtypes were identified; three people had the same novel subtype, which was designated as subtype 1p.

Among the 22 people with unusual genotype 1 subtypes who received HCV genetic sequencing, 18 (82%) were found to have viral variants associated with resistance to NS5A inhibitors such as ledipasvir, pibrentasvir and velpatasvir. In contrast, in clinical trials of Harvoni, just 16% of participants had evidence of such resistance, according to the study authors.

In addition, 16% of patients had the known subtypes 4a and 4d, with another 13% having other, previously undesignated, genotype 4 subtypes. Only a small number of people had genotypes 2, 3, 5 or 6.

This genotype distribution differed from that of non-African patients treated at the clinic during the same period, among whom the most common HCV subtypes were 1a and 3a.

Overall, the treatment response rate was high, with 56 of the 63 treated African participants (89%) achieving sustained virological response (SVR), or continued undetectable HCV viral load after completing treatment, which is considered a cure. All 12 treated patients with HCV subtypes 1a or 1b were cured.

The SVR rate dropped to 75%, however, for those with unusual genotype 1 subtypes. All three people with subtype 1l and one of the two with subtype 1p experienced treatment failure. Of the seven people who were not cured, six were treated with Harvoni and one with Zepatier (grazoprevir/elbasvir).

All patients with unusual genotype 4 subtypes were cured. None had subtype 4a, which has been linked to poor response in other recent studies, according to the researchers.

“Population based studies to determine the frequency of unusual subtypes and the efficacy of DAA regimens against them, are urgently needed to formulate guidelines for treating HCV in Africa,” the study authors wrote. “The evidence indicates that the future desired expansion of HCV treatment in Africa may risk unacceptable rates of failure if first generation NS5A inhibitors are utilized without appropriate epidemiological and viral sequence data.”

Noting that Africa accounts for 15% of hepatitis C cases worldwide, they added, “Global equity of access to curative treatment is required to avoid jeopardizing the hepatitis C elimination agenda.”

Click here to read the study abstract.
