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Transmission of HCV NS5A Inhibitor–Resistant Variants Among HIV-Infected Men Who Have Sex With Men

To the Editor—the use of direct-acting antiviral agents (DAAs) targeting hepatitis C virus (HCV) nonstructural proteins (NS3 protease; NS5A and NS5B polymerase) has revolutionized the treatment of chronic HCV infections in patients with and without human immunodeficiency virus (HIV) infection. However, there is a growing number of cases of acute hepatitis C infections and reinfections among HIV-infected men who have sex with men (MSM) in Europe, and phylogenetic analysis has revealed an international network of HCV transmission among HIV-positive MSM [1].

We have studied 5 HIV-infected MSM suffering from acute HCV infections or reinfections in 2015. Two of them were anti-HCV negative in 2014, and became HCV infected at the end of 2015 with HCV genotype 1a. The other three patients were reinfected with HCV (genotype 1a) during the same period after successful treatment of their HCV genotype 4 infection. One was given pegylated interferon for an acute HCV infection in 2010. The other 2 were successfully treated with combinations of DAAs in 2015. Sequencing of the NS5A regions to assess the presence of DAA-resistant variants identified the M28V mutation conferring reduced susceptibility to the NS5A inhibitors daclatasvir and ombitavir [2]. Phylogenetic demonstrated that the viruses of all 5 patients belonged to the same cluster, and alignment of NS5A sequences indicated the presence of the M28V resistance mutation (Figure 1).

NS5A inhibitor-resistant viruses persist for years [3] and their presence at baseline may influence treatment outcome, especially in patients with genotype 1a, those with cirrhosis, and/or those who do not respond to interferon-based treatment [4]. While the new regimens are highly efficacious for treating HCV, these patients require optimal therapeutic schedules [5]. Because outbreaks of acute HCV infections have occurred among HIV-infected MSM in several European countries with high rates of HCV

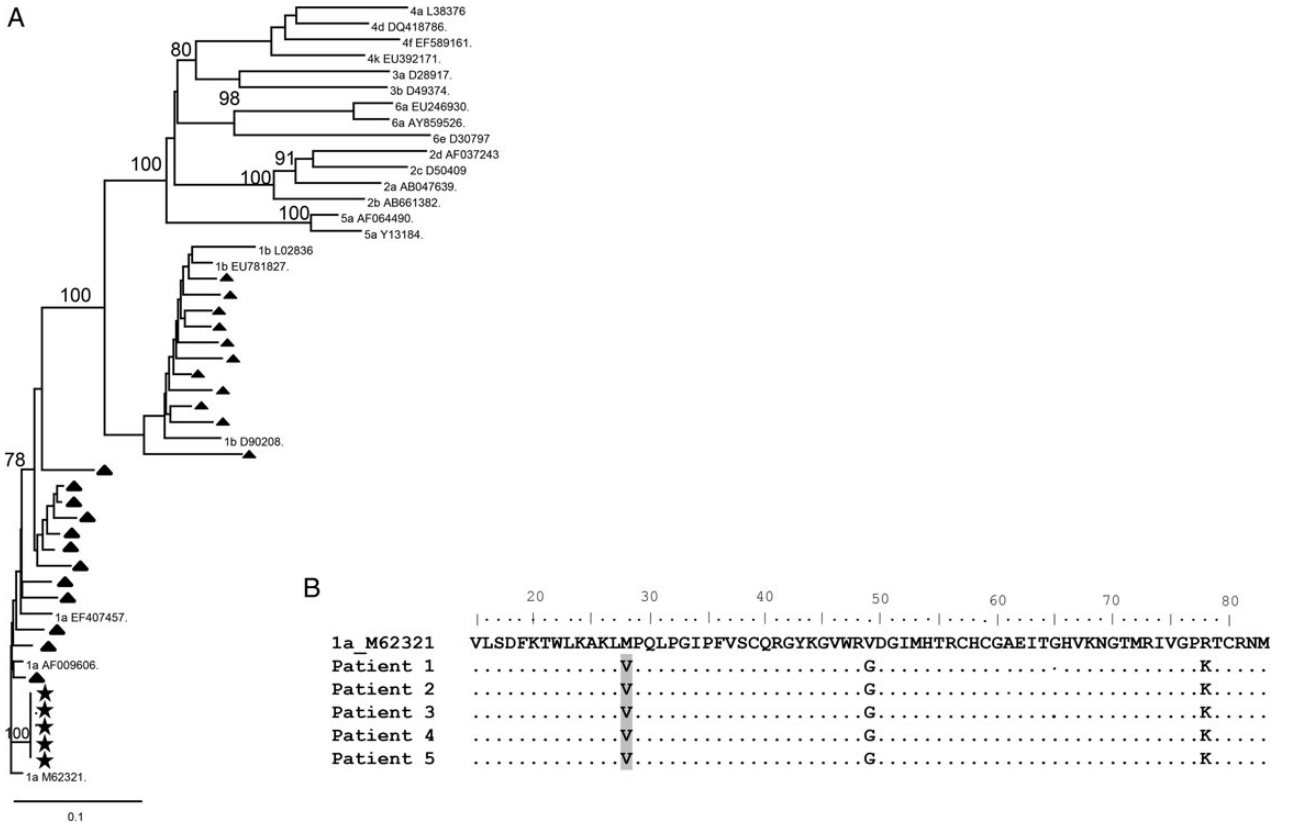

Figure 1. *A*, Phylogenetic analysis of the NS5B region of 5 human immunodeficiency virus (HIV)–infected men who have sex with men (MSM) with a hepatitis C virus (HCV) infection and reference strains identified with their GenBank accession number. Stars are the 5 sequences from HIV-infected MSM. Triangles indicate the sequences from patients in the same area. Numbers at the nodes indicate bootstrap values. *B*, Alignment of the NS5A sequence from HCV genotype 1a reference sequence (M62321) and the NS5A sequences of the 5 HIV-infected MSM with an HCV infection. The M28V resistance mutation is highlighted in grey.

reinfections, attention should focus on the transmission of DAA-resistant variants. Implementation of effective public health interventions is needed to limit onward transmission of HCV. Targeted prevention, such as raising awareness and routine testing, is needed to stop the further spread of HCV among HIV-infected MSM, and to prevent possible spillover to HIV-uninfected MSM.

Note

Potential conflicts of interest. All authors: No potential conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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