NIAID Study Describes Successful Treatment of a Person with Multidrug-Resistant HIV

Experimental regimen included lenacapavir and the monoclonal antibody semzuvolimab.

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Although antiretroviral therapy (ART) is safe and highly effective at treating HIV, some HIV variants do not respond to most ART regimens. Those HIV variants are known as multidrug-resistant (MDR) HIV. People who acquire or develop MDR HIV have few treatment options and a greater likelihood of experiencing or dying from HIV-related complications.

A study from NIAID researchers published in Nature Medicine found that a novel treatment regimen including an investigational monoclonal antibody (mAb) called UB-421 (semzuvolimab), and the Food and Drug Administration (FDA)-approved antiretroviral drugs (ARVs) including lenacapavir, suppressed HIV in a person with MDR HIV. This finding could pave the way for further research and development on a novel treatment approach for people with MDR HIV.

MDR HIV can occur in people who have been prescribed an ART regimen that does not fully suppress HIV replication, had a lapse in treatment, or acquired MDR HIV directly. While MDR HIV is relatively uncommon in high-resource settings, it is an increasing threat to people with limited access to quality health care.

In the new study, the researchers aimed to identify a regimen that could be used to manage MDR HIV in people with limited treatment options. UB-421 was included in the regimen because prior studies have shown that it may be effective against drug-resistant HIV variants. The regimen also included lenacapavir, which is currently used for the treatment of MDR HIV, and the ARVs tenofovir and emtricitabine. Because drug-resistant HIV variants continue to emerge, the researchers are investigating new avenues of treatment for people with MDR HIV.

The study was led by Tae-Wook Chun, PhD, chief of the HIV Immunology Section in NIAID's Laboratory of Immunoregulation, and conducted at the Institute's HIV Outpatient Clinic.

The regimen was evaluated in a man with MDR HIV and Kaposi sarcoma (KS), a rare cancer that occurs in people with suppressed immune systems. The 58-year-old participant had taken several ART regimens over three decades living with HIV and developed resistance to all available

antiretroviral drugs. Analysis of virus from the participant indicated that it was also resistant to nearly all currently licensed and investigational mAbs except for UB-421.

During the 70-week treatment period, the participant received UB-421 and lenacapavir-based ART to suppress HIV replication, as well as the antibiotics trimethoprim/sulfamethoxazole and azithromycin, and chemotherapy and immunotherapy drugs for KS.

Within two weeks of beginning the regimen, the levels of HIV in the participant's blood rapidly decreased. HIV levels continued to decrease at a lower rate for the next 30 weeks. The researchers also found that the participant experienced an increase in the levels of immune cells called CD4+ T cells, indicating a recovery in the patient's immune system. UB-421 acts by attaching to the surface of the T cells at the CD4+ T-cell receptor, preventing HIV from binding and thus blocking a critical step in HIV infection. Examination of the participant's T cells found that UB-421 fully blocked the CD4 receptors during the majority of the treatment period. The regimen suppressed replication of MDR HIV in the patient, lowering the level of virus in the blood serum below the detection limit of 20 particles per milliliter after one year of treatment.

This study lays the groundwork for possible new treatments for people with MDR HIV for whom treatment options are limited. The authors note that UB-421 is a promising therapeutic alongside ART regimens for MDR HIV. These findings also support the evaluation of the study treatment regimen in a larger group of people.

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