NIH launches study to test combination antibody treatment for HIV infection

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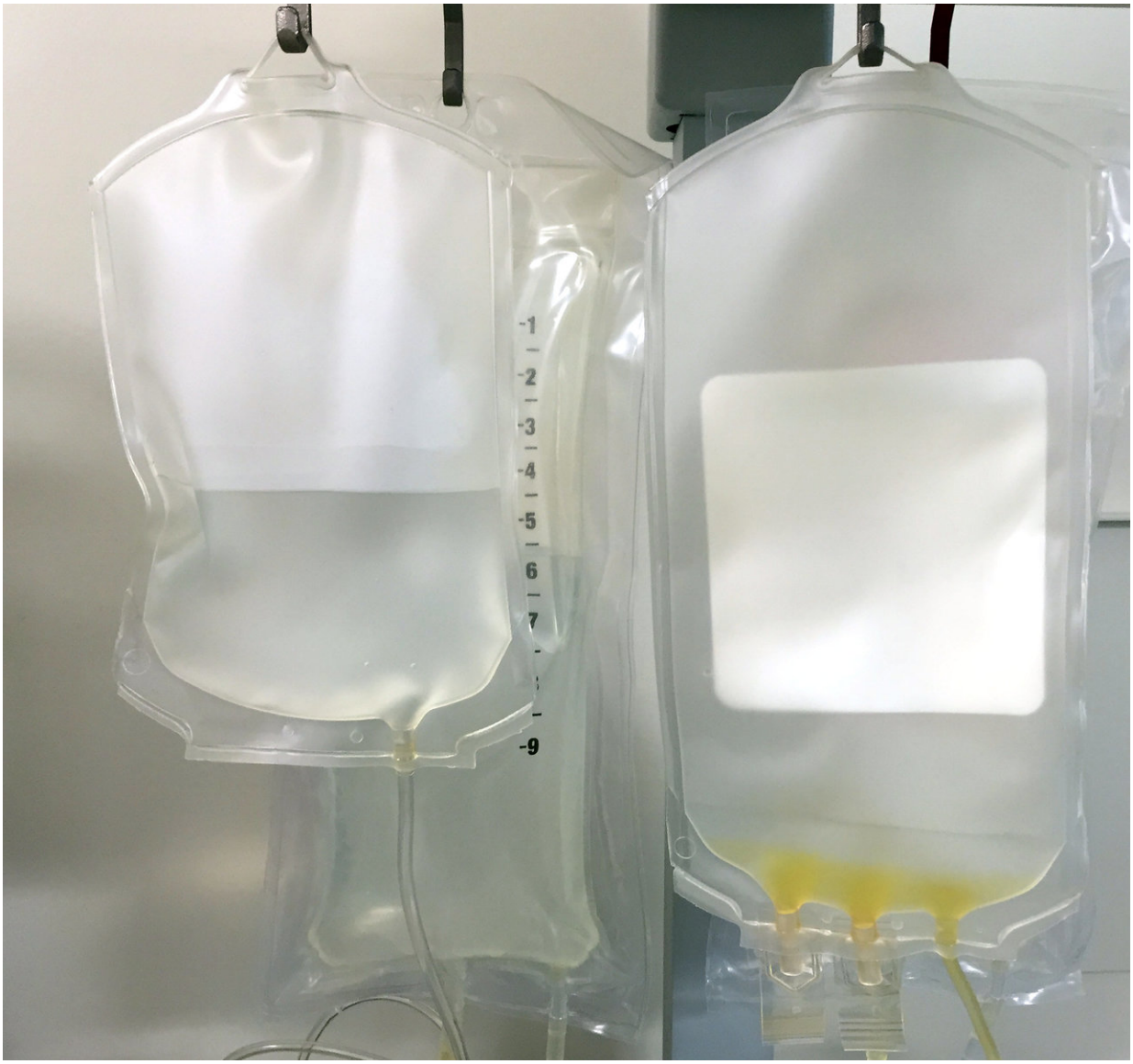

Bags of fluid for intravenous (IV) infusions. Credit: NIAID

A clinical trial testing infusions of combination antibodies in people living with HIV has begun at the National Institutes of Health. The early-phase clinical trial will evaluate whether periodic infusions of two highly potent, HIV-specific, broadly neutralizing antibodies (bNAbs)—3BNC117 and 10-1074—are safe in people living with HIV. The study also will gather preliminary data on how effectively the bNAb infusions, delivered together every two to four weeks, suppress HIV following discontinuation of antiretroviral therapy (ART).

"Antiretroviral therapy suppresses HIV to very low levels, normalizes life expectancy, and prevents sexual transmission of the virus. However, these benefits are lost if an individual stops taking the medications as prescribed," said Anthony S. Fauci, M.D., director of the National Institute of Allergy and Infectious Diseases (NIAID), part of NIH. "If proven safe and effective, periodic infusions of potent, broadly neutralizing HIV antibodies may be a potential alternative to daily antiretroviral therapy."

The new Phase 1 trial is being led by Michael C. Sneller, M.D., and Tae-Wook Chun, Ph.D. Dr. Sneller is a medical officer in the NIAID Laboratory of Immunoregulation (LIR), and Dr. Chun is chief of LIR's HIV Immunovirology Unit.

In 2016, Drs. Sneller and Chun and their collaborators found that the anti-HIV bNAb VRC01 could be safely delivered to people living with HIV, though it had only a modest effect on controlling HIV in the absence of ART. They found that the effect was modest because the virus quickly mutated in some individuals such that the antibody could no longer neutralize HIV. The two bNAbs used in the current study bind to distinct regions on an HIV surface protein, preventing the virus from entering and infecting cells. These regions are conserved, meaning they

remain the same across most HIV strains. Targeting two conserved regions on the virus may reduce the risk of resistance.

"When we first began developing antiretroviral medications more than two decades ago, we found that HIV mutated to escape the effect of any single drug acting alone," said Dr. Sneller. "However, we had remarkable success treating people with combinations of drugs, which targeted different parts of the HIV replication cycle," he added. "Our group hypothesized that a combination approach to infusions of broadly neutralizing antibodies might also help avoid the development of resistance that has been observed following treatment with individual bNAbs."

The 3BNC117 and 10-1074 bNAbs were developed by Michel Nussenzweig, M.D., Ph.D., and colleagues at Rockefeller University, New York City, with support from NIH and the Bill & Melinda Gates Foundation. The bNAbs have shown promise in nonhuman primates infected with the simian form of HIV.

The NIH study will enroll two groups of volunteers: 30 people who began ART during early HIV infection and who are still taking ART, and about 15 individuals whose HIV infections seem to be advancing at an abnormally slow rate even though they have never taken ART. Among the first group, volunteers will stop taking ART a few days after being assigned at random to receive either infusions of the combination antibodies or a saline placebo. This group will receive a total of eight infusions of the combination antibodies or placebo over 24 weeks. Participants will be closely monitored and will be restarted on ART if HIV levels in their blood rise above 1,000 copies per milliliter, if there is a significant decline in levels of their protective immune cells called CD4+ T cells, or if they develop any HIV-related symptoms. All volunteers in the second group, known as "slow progressors," will receive the combination antibody infusions on the same schedule but will remain

without ART throughout the study unless they experience a significant decline in CD4+ T cells, sustained increase in HIV levels in their blood, or an opportunistic infection. Researchers will monitor both groups closely for any side effects or other adverse events. Results are expected in 2021.

Drs. Nussenzweig and Marina Caskey, M.D., at Rockefeller University are conducting a related and ongoing NIAID-supported trial evaluating the safety of infusions of the same two bNAbs in people living with long-term HIV infection. Their study will enroll approximately 40 individuals, and results are expected in 2022.

Provided by NIH/National Institute of Allergy and Infectious Diseases