Dual Immunotherapy Delays—but Does Not Prevent—HIV Rebound

PD-1 immune checkpoint inhibitors are among the many approaches being studied in HIV cure research.

February 25, 2026 By Liz Highleyman

A pair of immune-modulating drugs, budigalimab and trosunilimab, appeared to slow viral rebound in about a quarter of people with HIV who stopped antiretroviral therapy, according to study results presented at the Conference on Retroviruses and Opportunistic Infections (CROI 2026) this week in Denver. Some participants eventually saw their viral load rise with further follow-up, however, and this combination will not move forward.

While antiretrovirals can keep HIV replication suppressed indefinitely, the virus inserts its genetic blueprints into the DNA of human cells, establishing a long-lasting reservoir that is unreachable by the drugs and usually invisible to the immune system, making a true cure nearly impossible. But researchers are exploring numerous approaches that may help keep the virus in remission after stopping treatment, known as a functional cure.

One approach is anti-PD-1 immune checkpoint inhibitors, monoclonal antibodies—such as Keytruda (pembrolizumab)—that block a receptor on T cells that regulates their activity. People with chronic HIV infection typically have high PD-1 expression and reduced T-cell responses. Widely used for cancer immunotherapy, checkpoint inhibitors can unleash T cells to attack tumors, and they could potentially also "reinvigorate" exhausted cytotoxic T cells to fight HIV and perhaps reactivate virus from the latent reservoir, Sharon Lewin, MD, of the University of Melbourne in Australia explained at her opening lecture on HIV cure science.

At the 2023 European AIDS Conference, researchers reported that the experimental PD-1 inhibitor budigalimab was associated with delayed HIV rebound or sustained low viral load in a majority of people who interrupted antiretroviral treatment in a small pilot study. The results were recently published in Nature Medicine.

At CROI, Dr Ana Gabriela Pires Dos Santos, MD, of AbbVie, presented findings from a Phase II randomized controlled clinical trial evaluating budigalimab plus trosunilimab (ABBV-382), a monoclonal antibody that binds to the alpha-4 beta-7 integrin receptor, which promotes viral replication and cell-to-cell spread.

This study enrolled 142 adults living with HIV at 80 sites in 12 countries in North and South America, Europe, Africa and Asia. Most (86%) were men, the mean age was approximately 47 years and they had been living with HIV for about 16 years, on average; 73% were white, 19% were Black 5% were Asian and a third had Latino ethnicity. At study entry, they were on antiretroviral treatment with an undetectable viral load for at least a year. The current mean CD4 T cell count exceeded 800, but more than half had previously had a level below 500.

The participants were randomly assigned to receive 10 milligrams budigalimab alone, 1,600 mg trosunilimab alone, 10 mg budigalimab plus either 800 mg or 1,600 mg trosunilimab, or a placebo. This budigalimab dose is about 25 times lower than the doses used in clinical trials for cancer.

At the start of the study, participants stopped their antiretrovirals in an analytical treatment interruption. Budigalimab was administered by IV infusion every two weeks through week 6 (four doses total), while trosunilimab or the placebo were given every four weeks through week 8 (three doses total).

The participants were closely monitored with weekly viral load tests during the analytical treatment interruption. The study protocol required that they restart antiretrovirals if they had two consecutive viral load measurements of 100,000 or greater, a confirmed viral load of 10,000 or higher for four weeks, a viral load of 1,000 or higher for six weeks, two consecutive CD4 counts below 350, severe retroviral rebound syndrome or became pregnant. They could also restart treatment by request at any time. Even a low-level persistent viral load can lead to health consequences, and 1,000 is around the level at which sexual transmission of HIV can occur.

The primary study outcome was the proportion of people who maintained a viral load below 1,000 at 24 weeks without restarting antiretrovirals. At that point, 24% of people in the budigalimab/low-dose trosunilimab group met the criteria, compared with 10% in the budigalimab/high-dose trosunilimab group, 10% in the budigalimab monotherapy group, 5% in the placebo group (similar to the rate typically seen during analytical treatment interruptions) and 0% in the trosunilimab monotherapy group. The difference between the budigalimab/low-dose trosunilimab and placebo groups was statistically significant. Using a viral load cut-off of 200, the corresponding proportions were 14%, 5%, 10%, 5% and 0%, respectively.

With further follow-up, however, viral control rates decreased in all the active treatment groups. Pires Dos Santos reported that at least two participants were no longer able to maintain control of HIV at 52 weeks. The median peak viral load and the time to viral rebound did not differ between the active treatment and placebo groups.

As a limitation, she noted that five people had detectable levels of antiretrovirals in their blood during the treatment interruption—including three who had used Cabenuva (injectable cabotegravir and rilpivirine) about a year prior—which could confound results.

Treatment with budigalimab, trosunilimab or both was generally safe, but side effects were common. Across all active treatment groups, 44% of participants experienced treatment-related

adverse events and 11% discontinued for this reason. Further, 20% had severe side effects (4% deemed treatment related), 7% experienced immune-related events (all in the arms containing budigalimab) and 12% had adverse effects associated with retroviral rebound syndrome.

Commenting after the presentation, Joseph Eron, MD, of the University of North Carolina at Chapel Hill, noted that PD-1 checkpoint inhibitors can cause immune-mediated adverse events even at very low doses. “I think this strategy is not a good one in terms of taking healthy volunteers [living with HIV] and giving them anti-PD-1 at any dose,” he said.

Based on these results, the researchers concluded, “Levels and durability of [antiretroviral]-free viral control are not sufficient to offer transformational benefits to people living with HIV and do not justify further development of budigalimab plus trosunilimab. These findings suggest that further studies of immune-mediated therapy with anti-PD1 agents may require approaches involving novel mechanisms.”

Click here for more news about HIV cure research.
Click here for more news from CROI 2026.
