Cancer Immunotherapy Is Safe and Effective for People With HIV

HIV-positive people who use checkpoint inhibitors have side effects, response rates and survival comparable to those of HIV-negative people.

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People living with HIV can safely use immune checkpoint inhibitors to treat advanced cancer, and the treatment is as effective as it is for HIV-negative people, according to a study published in the Journal of Clinical Oncology. HIV-positive people can also benefit from CAR-T therapy and stem cell transplants, which have led to a handful of HIV cures.

“This study should give some level of confidence to clinicians who are treating patients living with HIV and cancer,” lead study author Abdul Rafeh Naqash, MD, of the University of Oklahoma’s Stephenson Cancer Center, said in a press release. “It provides a level of assurance that immune checkpoint inhibitors are broadly safe for people with HIV and have the potential to effectively treat several types of solid tumor cancers.”

As people with HIV live longer thanks to effective antiretroviral treatment, non-AIDS cancers have become a leading cause of morbidity and mortality. Studies have shown that HIV-positive people are at increased risk for certain cancers compared with the general population, even if their HIV is well controlled.

The oncology field is undergoing a paradigm shift from traditional chemotherapy that indiscriminately kills fast-growing cells to targeted therapies and immune-based therapies that help the immune system fight cancer. But people living with HIV were excluded from the clinical trials that led to approval of these new treatments, leaving clinicians uncertain about their safety and effectiveness for this population.

Checkpoint Inhibitors

Immune checkpoint inhibitors, the most widely used type of cancer immunotherapy, interfere with receptors that regulate immune activity. Some cancers can hijack the PD-1 receptor on T cells to turn off immune responses. Drugs that block the interaction between PD-1 and PD-L1, its binding partner on cancer cells, release the brakes and restore T-cell activity. Keytruda (pembrolizumab), Opdivo (nivolumab) and Libtayo (cemiplimab) are PD-1 inhibitors, while Bavencio (avelumab),

Imfinzi (durvalumab) and Tecentriq (atezolizumab) block PD-L1. Yervoy (ipilimumab) blocks CTLA-4, which suppresses T-cell multiplication.

Naqash, Talal El Zarif, MD, of Dana-Farber Cancer Institute and colleagues with the Cancer Therapy using Checkpoint inhibitors in People With HIV-International (CATCH-IT) consortium looked at overall response rates (tumor shrinkage) and safety outcomes among HIV-positive people who received PD-1 or PD-L1 checkpoint inhibitors to treat various advanced or metastatic cancers. The researchers also compared progression-free survival (time until cancer worsens) and overall survival in matched groups of HIV-positive and HIV-negative patients with non-small-cell lung cancer (NSCLC). Study results were previously presented in part at last year's American Society of Clinical Oncology and Society for Immunotherapy of Cancer annual meetings.

The main analysis included 390 people with HIV who were treated at more than 30 academic medical centers in North America, Europe and Australia between January 2015 and October 2021. Most (85%) were men, the median age was 58 years, just over half were white, about a third were Black and 14% were Latino. They were on antiretroviral therapy (usually an integrase inhibitor regimen), 94% had an HIV viral load below 400 and 70% had a CD4 T-cell count of at least 200.

The participants had more than 10 types of solid tumors or blood cancers, the most common being NSCLC (29%), liver cancer (11%), head and neck cancer (10%), anal cancer (7%), melanoma (7%), small-cell lung cancer (6%) and Kaposi sarcoma (5%). A majority (70%) received PD-1 or PD-L1 inhibitors alone, while the rest combined them with chemotherapy (17%), targeted therapy (6%) or Yervoy.

The researchers found that overall response rates were 69% for non-melanoma skin cancer, 67% for Hodgkin lymphoma, 60% for Kaposi sarcoma, 47% for melanoma, 31% for NSCLC, 29% for non-Hodgkin lymphoma, 19% for small-cell lung cancer, 16% for liver cancer, 16% for anal cancer and 11% for head and neck cancer. These rates are comparable to those seen in studies of HIV-negative people.

One concern with checkpoint inhibitors is that in addition to restoring immune responses against cancer, they can also unleash the immune system more broadly, leading to inflammation of organs throughout the body. In this study, 20% of HIV-positive patients experienced immune-related adverse events of any grade, including 7.7% with severe events.

In the matched NSCLC groups, which included 61 HIV-positive and 110 HIV-negative people, the two-year progression-free survival rates were 17.8% for people with HIV and 18.4% for HIV-negative people, while the corresponding overall survival rates were 42.3% and 41.5%, respectively. The overall response rate was a bit lower in the HIV-positive group (28% versus 36%), but the difference was not statistically significant. Immune-related adverse events occurred with similar frequency (20% versus 22%), as did severe events (12% versus 9%).

The study was large enough to look at outcomes among people with more advanced immune suppression. Those with a CD4 count below 200 had comparable overall survival and a slightly lower adverse event rate, perhaps because those with a weaker immune system were less likely to

experience side effects due to an overactive immune response. The researchers concluded that arbitrary CD4 cutoffs for the use of checkpoint inhibitors are not warranted.

No significant changes in CD4 counts or HIV viral load were observed during treatment. The six people who had active opportunistic infections when they started checkpoint inhibitors did not experience worsening disease.

Checkpoint inhibitors are also being studied as a potential HIV cure strategy. PD-1 suppresses CD8 killer T cells that target HIV as well as cancer, and PD-1 is heavily expressed on exhausted T cells that have lost their ability to function. Some studies suggest that blocking the interaction between PD-1 and PD-L1 can restore HIV-specific CD8 cell activity, leading to a reduction in viral load. PD-1 is heavily expressed on CD4 helper T cells that harbor hidden HIV and may play a role in maintaining viral latency. However, the current study was unable to assess the impact of checkpoint inhibitors on the viral reservoir.

The results confirm those of a systematic review and two small prospective studies that found checkpoint inhibitors are safe for HIV-positive people, with response rates in line with those seen in HIV-negative people.

Taken together, these studies show that there is no reason to exclude people with well-controlled HIV from clinical trials of new cancer therapies. In recent years, the National Cancer Institute, the Food and Drug Administration and patient advocates have worked to expand eligibility criteria to enable more cancer patients with coexisting conditions, including HIV, to enroll in trials.

“In general, people with HIV should receive the same standard, full-dose cancer therapy used in the general population unless there are data for specific cancer regimens in people with HIV,” Kathryn Lurain, MD, MPH, of the National Institutes of Health, wrote in an accompanying commentary. “Learning from the experience in [PD-1 and PD-L1] agents, future cancer clinical trials should include and seek to actively enroll people with HIV, so that they have equal and timely access to emerging cancer therapies.”

CAR-T Therapy and Stem Cell Transplants

Chimeric antigen T-cell therapy, better known as CAR-T, is another type of immunotherapy that is increasingly used to treat advanced cancers (especially blood cancers), but has been largely inaccessible to people living with HIV. CAR-T uses gene therapy to modify T cells to help them attack cancer cells. A sample of T cells is collected from a patient, altered in a laboratory to recognize their cancer and infused back into the body.

While CAR-T therapy is a more arduous treatment than checkpoint inhibitors, requiring conditioning chemotherapy to kill off a patient’s existing immune cells to make room for the modified ones, it is feasible for people with HIV. One recent small study found that CAR-T therapy demonstrated acceptable safety and effectiveness for HIV-positive people with non-Hodgkin lymphoma, with outcomes comparable to those observed for HIV-negative patients.

Like checkpoint inhibitors, CAR-T is also being studied in HIV cure research. T cells can be engineered to help them recognize HIV, make them resistant to HIV infection by deleting a receptor the virus uses to enter cells or both.

Stem cell transplantation is an intensive and risky procedure, but it can lead to long-term remission in some patients with advanced blood cancers. In rare cases, it can also lead to a cure for HIV.

A small number of people with life-threatening leukemia or lymphoma remain free of HIV after receiving stem cells from donors with a rare mutation (CCR5-delta32) that blocks the virus from entering cells. The first, Timothy Ray Brown (the Berlin Patient), was HIV-free for 13 years at the time of his death due to a recurrence of leukemia in 2020. Marc Franke (the Düsseldorf Patient), the fifth person to come out as cured, shows no signs of HIV more than four years after stopping antiretroviral treatment.

Stem cell transplantation is too dangerous—not to mention too labor-intensive and expensive—for otherwise healthy people with HIV who are doing well on antiretroviral therapy, but lessons learned from these cases offer clues in the search for a more widely accessible functional cure for HIV.

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