

Cancer drug leads to 'drastic decrease' in HIV infection in lung cancer patient

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Doctors in France have found the first evidence that a cancer drug may be able to eradicate HIV-infected cells in humans.

In a letter published in the leading [cancer](#) journal *Annals of Oncology* today, researchers led by Professor Jean-Philippe Spano, head of the medical oncology department at Pitie-Salpetriere Hospital AP-HP in Paris, France, report that while treating an HIV-infected lung cancer patient with the cancer drug nivolumab, they observed a "drastic and persistent decrease" in the reservoirs of [cells](#) in the body where the human immunodeficiency virus (HIV) is able to hide away from attack by anti-retroviral therapy.

These reservoirs of HIV-infected cells are found in the immune system in organs such as the brain, bone marrow and genital tract. They lie dormant and cannot be eliminated by anti-retroviral therapy, nor by the weakened immune system, so that if treatment is stopped at any time, the virus starts to replicate and infect more cells again, while the immune system cannot suppress this rebound of HIV infection. If scientists could find a way of clearing away the reservoirs of HIV-infected cells, then it might enable them to eradicate the virus completely, making it possible to cure HIV [patients](#).

HIV primarily infects CD4 T cells, which are a type of white blood cell that plays an important role in regulating the immune response. When under attack from HIV they not only become infected but also exhausted, meaning they are less able to fight the infection.

Professor Spano explained: "Dormant CD4 T cells infected with HIV are not actively producing HIV: they are latently infected. Latent HIV reservoirs are established during the earliest stage of HIV infection and throughout the course of the disease. When a latently infected cell is reactivated, the cell begins to produce HIV again. However, this re-activation is blocked in most latently-infected cells by cellular molecules called immune check-points. One of these check-points is programmed death-1 (PD-1), which also blocks the functions of CD4 T cells in fighting the virus.

"Increasingly, researchers have been looking into the use of certain drugs that appear to re-activate the latent HIV-infected cells. This could have the effect of making them visible to the immune system, which could then attack them. Drugs that inhibit immune check-points such as PD-1 are well known in the cancer field as being very efficient at restoring [immune defences](#) by removing the brake, enabling the immune cells to spring into action to reject the cancer cells. It was thought, but until now not demonstrated, that inhibitors of immune check-points could, in a similar way, wake up dormant HIV-infected cells and also the immune defences against the virus."

Nivolumab is PD-1 inhibitor, which is used to treat several cancers in their advanced stages, including melanoma, non-small cell lung cancer and kidney cancer. The researchers used it to treat an HIV-infected patient with non-small cell lung cancer after he relapsed following surgery and chemotherapy for his tumour. So far, the 51-year-old man has received 31 injections of nivolumab every 14 days since December 2016. He was diagnosed as HIV-positive in 1995 and the cancer was diagnosed in May 2015.

When the researchers first gave nivolumab to the patient, HIV was undetectable in blood samples. It then increased progressively up to day 45 before decreasing again. At the same time T cell activity increased,

with a marked increase in the activity of another T cell, CD8, from day 30 to 120. By day 120 the reservoirs of HIV-infected cells "showed a drastic and persistent decrease", report the researchers in their letter to *Annals of Oncology*.

Professor Spano said: "In this patient we observed, as expected, both a re-activation of HIV and an increase in CD8 T cell responses against HIV, which resulted in the drastic decrease in the HIV reservoir, thus leading to a sustained reduction of the HIV reservoirs.

"This is the first demonstration of this mechanism working in humans. It could have implications for HIV patients, both with and without cancer, as it can work on HIV reservoirs and tumour cells independently. The absence of side effects in this patient is also good news, and suggests this could be an optimum treatment for HIV-infected patients with cancer."

However, the researchers are also cautious about their results. Professor Spano continued: "Firstly, this is the first case of such a drastic decrease of the HIV reservoir, and we must remain careful, especially because this is only one case; we have published details of another case where there was no decrease of the HIV reservoir.

"Secondly, we have to evaluate - in clinical trials and in a group of 50 French patients we are treating currently - the potential toxicities of these drugs in HIV infected people. And finally, we have to identify markers that can predict HIV response to the anti-PD-1 therapy so that treatment can be personalised, especially as we observed one responder and one non-responder."

Editor-in-chief of *Annals of Oncology*, Fabrice André, Professor in the Department of Medical Oncology, Institut Gustave Roussy, Villejuif, France, commented: "Although this is a single case study, it is an exciting result. Anti-HIV drugs usually stop virus replication but don't

cure the patients who still have reservoirs of the virus. This study generates the hypothesis that drugs that make the virus disappear could, perhaps, cure patients."

The patient will be treated with more nivolumab later this month and his cancer will also be assessed then. "For the moment, he is doing quite well and doesn't show any signs of disease, even though the cancer is progressing slowly, which suggests it is not optimally controlled," said Professor Spano.

More information: "Drastic decrease of the HIV reservoir in a patient treated with nivolumab for lung cancer", Letter to the editor from Amélie Guihot et al. *Annals of Oncology* (2017). [DOI: 10.1093/annonc/mdx696](https://doi.org/10.1093/annonc/mdx696)

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