

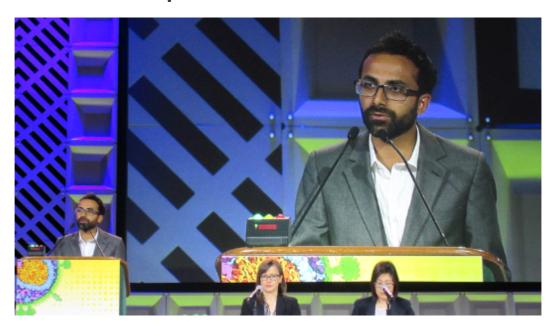
Wednesday 6 March 2019

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London patient in long-term HIV remission after stem cell transplant



Ravindra Gupta presenting at CROI 2019. Photo by Liz Highleyman.

A London man has had no remaining detectable HIV a year and a half after stopping HIV treatment, following a bone marrow stem cell transplant to treat lymphoma, according to a presentation at the Conference on Retroviruses and Opportunistic Infections (CROI 2019), taking place this week in Seattle.

His case has been likened to that of Timothy Ray Brown, the so-called 'Berlin patient', who was the first person to be cured of HIV. Brown had leukaemia and underwent stem cell transplants from a bone marrow donor who had double copies of a rare gene mutation known as CCR5-delta-32. The mutation results in missing CCR5 co-receptors on T-cells, the gateway most types

of HIV use to infect cells, creating a resistance to HIV. Brown underwent intensive conditioning chemotherapy and whole-body radiation therapy to kill off his cancerous immune cells, allowing the donor stem cells to rebuild a new HIV-resistant immune system. He stopped HIV treatment and has been free of HIV for 12 years.

Professor Ravindra Gupta of University College London presented the case of the so-called 'London patient', who remains anonymous. He underwent stem cell transplantation to treat Hodgkin lymphoma in May 2016. Like Brown, his donor had a double CCR5-delta-32 mutation. He underwent less aggressive conditioning chemotherapy and the transplant led to complete lymphoma remission.

The man stopped antiretroviral therapy 16 months after the transplant. His blood viral load remains undetectable 18 months later using a sensitive assay with a 1 copy/ml limit, no HIV DNA can be found in peripheral CD4 cells and tests showed no "reactivatable" virus in 24 million resting T-cells.

Gupta noted that the man's viral load could still rebound. He suggested that two or three years without detectable virus would be enough time to speak of a cure, saying he was "highly confident this will be achieved".

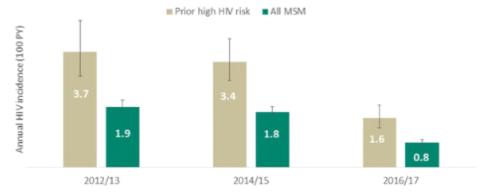
Although these cases hold interesting lessons for the HIV cure research field, experts caution that even if CCR5-delta-32 stem cell transplantation can lead to a functional cure of HIV, this high-risk procedure will not be an option for most people.

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55% drop in HIV incidence in gay men in England in just two years

Annual HIV incidence in MSM attending SHCs in England, 2012/13, 2014/15, 2016/17



Graph from Dana Ogaz's presentation at CROI 2019.

In just two years, the incidence of new HIV infections in men who have sex with men (MSM) attending English sexual health clinics fell by 55%, according to data presented at CROI 2019 by Dana Ogaz of Public Health England. The figures come from routinely collected data from gay, bisexual and other MSM who attend the same sexual health clinic twice or more in the same year.

Incidence was measured in 2012-2013, then in 2014-2015, and again in 2016-2017. In the first year, incidence was 1.9% (meaning that two in every 100 men acquired HIV during the year), remaining stable at 1.8% in the second time period. But just two years later, incidence was only 0.8%.

A similar pattern was seen in MSM who had both had an HIV-negative test and a bacterial sexually transmitted infection (STI) in the past year – a group at higher risk of HIV infection. Incidence fell from 3.7% to 3.4% and then to 1.6% (a 53% fall in the last two years).

The fall in HIV diagnoses coincides with a period when increasing numbers of men accessed pre-exposure prophylaxis (PrEP), while efforts to improve testing and prompt initiation of HIV treatment continued.

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Point-of-care viral load testing improves treatment outcomes and retention in care



Paul Drain presenting at CROI 2019. Photo by Liz Highleyman.

Results from the first randomised controlled trial to test the impact of rapid, point-of-care viral load testing were presented at CROI 2019.

Providing patients with same-day results of a point-of-care viral load test - rather than waiting

weeks for laboratory results – resulted in a 14% improvement in virological suppression and retention in care in a public clinic in South Africa.

Dr Paul Drain, presenting, said that delays in obtaining laboratory test results in resource-limited settings present challenges for monitoring HIV treatment. If viral load results are available while the patient is still in the clinic, any problems can be quickly identified and supportive interventions can be offered immediately.

The study recruited 390 people living with HIV, who joined the study six months after starting HIV treatment. In the intervention arm of the study, participants received point-of-care testing with the Xpert assay and same-day counselling, while those in the standard-of-care arm of the study had laboratory viral load testing.

The study's primary outcome looked at retention in care and viral load below 200 copies/ml 12 months after study entry. This was achieved by 89.7% of people in the intervention arm and 75.9% of people in the standard-of-care arm.

In the intervention arm, all six participants who had virological failure were switched to second-line therapy, a median of one day after the test was taken. In the standard-of-care arm, only four of nine participants with virological failure were switched, after a median of 76 days.

Patients reported that they liked getting real-time feedback on their adherence and having problems dealt with quickly.

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Women with HIV may have higher breast cancer mortality



Katrin Sadigh presenting at CROI 2019. Photo by Liz Highleyman.

A study from Botswana, presented at CROI 2019, found that HIV-positive women with breast

cancer appear to have decreased survival rates compared with HIV-negative women. Having HIV was associated with a nearly twofold reduction in survival.

While prior research in the US and Africa has found that women with HIV do not have higher breast cancer incidence, or likelihood of developing cancer, some studies with a small number of HIV-positive participants suggested that survival may be reduced.

This prospective analysis drew from the Thabatse Cancer Cohort, which enrolled nearly 4000 people with cancer at four major oncology centres in Botswana. Participants are evaluated at study entry and followed for five years. The breast cancer cohort included 510 women who sought cancer care between October 2010 and September 2018. Of these, 151 were HIV positive and 327 were HIV negative.

The women in the HIV-positive group were a few years younger than the HIV-negative group, on average, but the two groups were similar in terms of breast cancer stage and type. Types of cancer treatment also did not differ significantly by HIV status. The majority of the women living with HIV were taking HIV treatment and around 70% had a viral load below 1000 copies/ml.

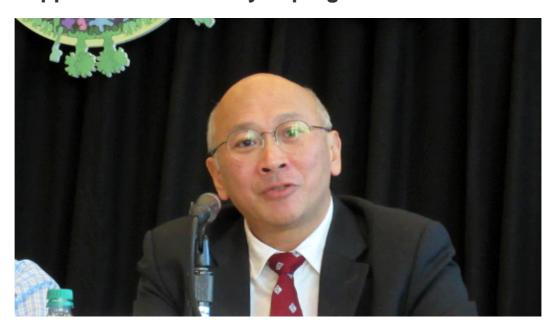
During the course of the study, 70 HIV-positive women (46%) and 101 HIV-negative women (31%) died. In a multivariate analysis controlling for other factors, HIV-positive women had an 82% reduction in survival compared with HIV-negative women.

Dr Katrin Sadigh, presenting, emphasised that survival was poor for both HIV-positive and HIV-negative women in this study, and better strategies are needed to speed up diagnosis and improve care.

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Integrase inhibitors give greater chance of viral suppression at delivery in pregnant women



Saye Khoo, presenting the results of the DOLPHIN-2 study to CROI 2019. Photo by Liz Highleyman.

Findings from two randomised studies presented at CROI 2019 show that starting integrase inhibitor-based treatment with either raltegravir (*Isentress*) or dolutegravir (*Tivicay*, also in *Triumeq*) reduces viral load more rapidly than efavirenz if started later in pregnancy.

Many women with HIV learn of their HIV status when they are tested during pregnancy, often after the first trimester. Reducing viral load rapidly during pregnancy is essential to achieve an undetectable viral load at the time of delivery. Undetectable viral load at delivery maximises the chance that HIV will not be transmitted from mother to baby.

The NICHD P1081 trial was carried out in South America, Africa, Thailand and the United States between 2013 and 2018. It randomised women who were starting antiretroviral therapy (ART) in later pregnancy (after week 20) to receive either raltegravir- or efavirenz-based ART.

In the analysis of over 300 women, the researchers found that significantly more women randomised to raltegravir had a viral load below 200 copies/ml at delivery (94% vs 84%) and this association was strongest in women who had started treatment after week 28 (93% vs 71%). The median time to viral suppression below 200 copies/ml was 8 days in women receiving raltegravir and 15 days in women receiving efavirenz. There was no difference in adverse outcomes for mother or infant between the two study arms.

A second study presented at CROI, DOLPHIN-2, randomised women starting ART from week 28 of pregnancy to receive either dolutegravir- or efavirenz-based ART. An analysis of 237 women found that women in the dolutegravir arm of the study were 66% more likely to have an undetectable viral load by the time of delivery. There was no difference between the two study arms in terms of adverse outcomes for mother or premature births. Three cases of HIV transmission occurred in this study, all in the dolutegravir arm. The researchers say it is likely that the transmissions occurred *in utero*, not at the time of delivery.

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