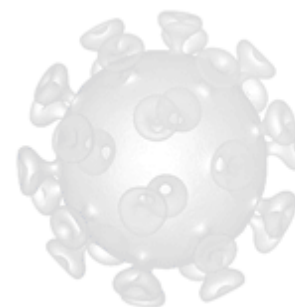


# CROI 2014

## 21st Conference on Retroviruses and Opportunistic Infections

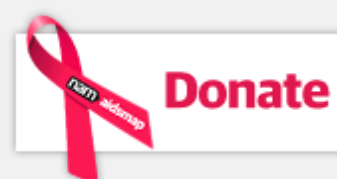
Boston, USA, 3-6 March 2014



### Friday 7 March

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## Gene therapy



Gary Blick presenting at CROI 2014. Photo by Liz Highleyman, [hivandhepatitis.com](http://hivandhepatitis.com).

Genetically modified CD4 cells lacking CCR5 co-receptors reach high levels in the body and are resistant to HIV, potentially enabling people to maintain a low viral load while off antiretroviral therapy (ART), according to the latest reports from studies evaluating zinc finger technology.

The technique uses a zinc finger nuclease to disrupt the gene in CD4 T-cells that controls expression of CCR5, the co-receptor that most strains of HIV use to enter cells.

Samples of CD4 T-cells are collected from HIV-positive participants, treated with the zinc finger protein in a laboratory and allowed to multiply. The modified cells, called SB-728-T, are then re-infused back into the same participant. The idea is that these modified cells – being protected against HIV entry – will persist while normal T-cells are killed off by the virus.

Researchers have previously reported that the procedure is safe and generally well tolerated.

The study presented at CROI evaluated the effect of pre-treatment with a chemotherapy drug, cyclophosphamide, prior to re-infusion of the modified cells.

The 12 participants in the study were all taking HIV treatment at the start of the study, had high CD4 counts and undetectable viral load.

They each received intravenous cyclophosphamide at doses of 200, 500 or 1000mg/m<sup>2</sup> given one to three days prior to a single infusion of modified cells. Six weeks later they started an HIV treatment interruption.

Cyclophosphamide was generally safe and well tolerated. Both total CD4 counts and numbers of modified cells increased depending on the dose given, with the largest gains seen in the

1000mg dose group. People receiving the highest dose of pre-treatment saw the greatest reductions in HIV viral load during the treatment interruption.

The researchers explained that the 1000mg dose appeared to approach the threshold for a functional cure.

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[Read the personal story of a participant in a previous trial of this technique](#)

## Self-testing for HIV



A community-based self-testing programme in Blantyre, Malawi achieved a 76% uptake of HIV testing, new research shows. Test results were highly accurate and more than 75% of patients reported being successfully linked to care.

Self-testing using the *OraQuick* oral fluid test is already available in the US and approval in Europe is expected in 2014. The test is also already in use in many middle- and low-income countries, but there is limited evidence on its large-scale use.

The research in Malawi involved 16 neighbourhoods with an adult population in excess of 16,000. In each neighbourhood, two households were trained to distribute the HIV self-test.

Younger people and single people had the highest use of the self-test.

Over 40% of men and women using the self-test had not had an HIV test before and three-quarters of those using the test had not had an HIV test in the previous year.

Nine per cent of people who used the test were prepared to reveal, in confidence, that they had tested HIV positive. Of these, 78% had accessed HIV care and 25% had started ART.

The accuracy of the tests was found to be high, and there was a high level of acceptability of self-testing.

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## Male life expectancy in South Africa



The life expectancy of HIV-positive men lags behind that of women due to lower uptake of HIV treatment, research conducted in rural South Africa shows.

Over half (57%) of deaths among men with HIV compared to 41% of deaths among women with HIV occurred before any kind of HIV care was sought.

The study was conducted in the Hlabisa district of northern Kwa-Zulu Natal. Since 2004, antiretroviral therapy (ART) has been rolled out in the district via nurse-led clinics. Seven per cent of all adults in Hlabisa are now receiving ART, achieving an improvement in life expectancy in the area of one additional year for each year that ART has been available. According to the researchers, this is among the fastest improvements in life expectancy in public health history.

In sub-Saharan Africa overall, women are more likely to benefit from ART roll-out than men. An important reason is that women present earlier for care than men.

Researchers wanted to establish a better understanding of disparities between men and women in outcomes before and after ART roll-out in Hlabisa. They therefore examined data for 52,964 women (3729 HIV-related deaths) and 45,688 men (3500 HIV-related deaths).

Between 2004 and 2011, the life expectancy of women increased by 13 years and that of men by 9 years. In 2011, men were 25% more likely to die of an HIV-related illness than women.

Even after taking into account use of ART during pregnancy, the investigators found that women were over twice as likely to be taking HIV treatment than men.

Between 2007 and 2011, 70% of HIV-related deaths in men involved men who had not sought HIV care. Overall, 40% of women died without accessing care, the proportion falling gradually.

The researchers couldn't explain the disparities. But they suggested efforts should be made to design male-friendly clinics and acknowledged that local attitudes towards masculinity may mean men don't access care. Health promotion initiatives need to address this issue, in order to ensure that men do not miss out on the benefits of antiretroviral treatment.

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## HIV treatment – raltegravir



A study has shown the integrase inhibitor raltegravir (*Isentress*) to be superior, in terms of the overall likelihood of treatment failure, when compared to the two ritonavir-boosted protease inhibitors atazanavir (*Reyataz*) and darunavir (*Prezista*).

In the study, 1809 people living with HIV, who had not taken HIV treatment before, were randomised into three groups and received either: raltegravir; atazanavir boosted with ritonavir; or darunavir boosted with ritonavir, and their progress was monitored for 96 weeks. All three drugs were taken alongside tenofovir and FTC (co-formulated in *Truvada*).

At 96 weeks, viral load was below 50 copies/ml in 88% of participants who had started treatment with atazanavir, 94% who had started with raltegravir and 89% for those who had started with darunavir.

Therefore, virological failure was not very different for the three drugs. However, more people stopped taking the other two drugs, mainly due to gastrointestinal symptoms (both related to atazanavir and darunavir) and to jaundice related to atazanavir.

These findings are likely to be taken into account the next time treatment guidelines are revised.

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## The HIV epidemic and intergenerational sex



Billboard, detail from slides by Guy Harling presented at CROI 2014.

**Having a sexual relationship with an older man is not putting young women at increased risk of HIV, new research conducted in rural South Africa concludes.**

The findings confound a theory, suggested by previous studies of HIV prevalence – that younger women in sub-Saharan Africa are put at high risk of acquiring HIV as a results of relationships with older men.

The latest research is the first study to follow women over a long period, looking at HIV incidence and age of sexual partners.

Over 2400 HIV-negative women, aged between 15 and 49, were recruited to the study and tested annually for HIV between 2005 and 2012.

Women in the 15 to 29 age group had sexual partners who were on average five years older than they were. But HIV incidence among these women did not differ according to the age of their partners.

For women aged 30 to 49, having an older partner actually reduced the risk of acquiring HIV. Women with a partner who was between five and ten years older were 37% less likely to acquire HIV compared to women who had partners of a similar age to themselves, while women with a partner who was ten or more years older had their risk of acquiring HIV reduced by 52%.

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# Disappointment in search for an HIV cure



Timothy Henrich presenting at CROI 2014. Photo by Liz Highleyman, [hivandhepatitis.com](http://hivandhepatitis.com).

HIV has re-emerged in two men in Boston who had stopped taking HIV treatment after receiving bone marrow stem cell transplants for cancer treatment.

The cases show that it will be difficult to achieve a 'functional cure' for HIV if even a tiny amount of the virus remains in the body.

Both men, sometimes referred to as the 'Boston patients' were previously controlling HIV without medication, after undergoing a bone marrow transplant. [The cases were reported at last year's International AIDS Society Conference.](#)

But the virus has re-emerged in both men – twelve weeks after [interrupting treatment](#) in one and after eight months in the other.

Once HIV was detected, it replicated rapidly, with [viral load](#) reaching millions of copies/ml in both individuals. They also experienced symptoms usually seen in people when they first acquire HIV.

Both men restarted ART. However, one had developed a new NNRTI resistance mutation and needed to change therapy. Treatment achieved full viral suppression, their symptoms disappeared and [CD4 counts](#) increased.

Long-lived reservoirs of virus appear to be the cause of the rebound. Genetic analysis showed the virus to be very similar, suggesting that the survival of just a few infected cells may be enough for a complete rebound once ART is stopped.

Although disappointing, these cases provide important information about the persistence of HIV which will be useful in the search for a functional cure.

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