IAS 2023 Highlights Advances in HIV Prevention, Treatment and Cure Research

Researchers preview studies on circumcision, PrEP for women, mpox, COVID-19 and HIV functional cure.

July 20, 2023 By International AIDS Society

IAS 2023, the 12th IAS Conference on HIV Science, will feature an array of studies that represent important advances in HIV prevention, treatment and cure research.

Highlights include results from the first randomized trial to show that voluntary medical male circumcision reduces HIV acquisition among men who have sex with men, a study showing that cisgender women in seven African countries prefer long-acting injectable to daily oral PrEP for HIV prevention, WHO analyses examining how mpox and COVID-19 have affected people living with HIV, and three studies that offer new insights in the quest for an HIV cure.

“This is an incredibly exciting time in HIV research, and the studies at IAS 2023 reflect that,” Sharon Lewin, IAS President, IAS 2023 International Chair and Director of the Peter Doherty Institute for Infection and Immunity at the University of Melbourne in Australia said. “The science presented at this conference will guide rollout of game-changing prevention tools like long-acting PrEP, shed light on how to reduce the impact of mpox and COVID-19 on people living with HIV, and identify new approaches to achieve an HIV Cure.”

Hosted by IAS – the International AIDS Society – IAS 2023 will take place in Brisbane, Australia, as well as virtually from 23 to 26 July. The conference will bring together thousands of scientists, policy makers and advocates to examine the latest advances in HIV research and forge a more equitable and innovative HIV response.

Today’s scientific highlights press conference featured seven studies that were selected from among hundreds of abstracts being presented at IAS 2023.

Voluntary medical male circumcision reduces HIV acquisition among men who have sex with men, first-ever randomized controlled trial finds

Voluntary medical male circumcision (VMMC) is “very likely” to prevent HIV acquisition among men who have sex with men who primarily engage in insertive anal sex, a study in China found.

According to presenter Huachun Zou of Fudan University, this is the world's first randomized controlled trial to assess the efficacy of VMMC among men who have sex with men.

About 15 years ago, three large randomized controlled trials in Africa found that VMMC reduces female-to-male transmission of HIV by 50% to 60%. Since then, VMMC has been scaled up in some countries with generalized HIV epidemics as a prevention option for heterosexual men, and modelling studies have estimated that VMMC has prevented hundreds of thousands of HIV acquisitions. Among men who have sex with men, however, there have only been observational studies of VMMC for HIV prevention, and these studies have had mixed results.

The Chinese study enrolled nearly 250 HIV-negative men who predominantly practiced insertive anal sex and were willing to undergo VMMC. (The study did not provide PrEP to participants; however, a small number of men reported taking PrEP during the study.) Over time, there were no HIV seroconversions in the intervention arm (immediate VMMC) and five in the control arm (delayed VMMC). The study team concluded that VMMC is "very likely to be efficacious" in preventing HIV acquisition in men who have sex with men, but notes that "large-scale trials with long-term follow-up may be necessary to further confirm this efficacy."

"These results provide further evidence that voluntary medical male circumcision is a viable HIV prevention option, including for men who have sex with men," Lewin said. "While this represents another HIV prevention option, we know that other tools, like PrEP, have very high efficacy, are far less invasive and must our highest priority."

Abstract and session: Voluntary medical male circumcision and incident HIV acquisition among men who have sex with men: a randomized controlled trial, Poster exhibition (1002, Track C)

Cisgender women in seven African countries prefer long-acting injectable to daily oral PrEP for HIV prevention

Nearly eight out of 10 cisgender women prefer long-acting injectable cabotegravir to daily oral PrEP for HIV prevention, a study conducted in seven African countries found.

The study was an open-label extension of HPTN 084, a landmark clinical trial which demonstrated that long-acting injectable cabotegravir is superior to daily oral PrEP for HIV prevention in individuals assigned female at birth. Based on those results, long-acting injectable PrEP is now poised to be rolled out in multiple African countries.

This follow-up study, presented by Sinead Delany-Moretlwe of the University of the Witwatersrand, took place in Botswana, Eswatini, Kenya, Malawi, South Africa, Uganda and Zimbabwe. It found that of nearly 2,500 participants, 78% chose long-acting PrEP while 22% chose daily oral PrEP.

A variety of factors influenced product choice, including personal preference regarding whether to get an injection every eight weeks or take a pill each day. Participants who chose long-acting PrEP were more likely to be sexually active but not live with a partner, to have experienced recent physical intimate partner violence and to have been paid for sex.

“These results suggest that long-acting PrEP could have a huge prevention impact in Africa, where uptake of daily oral PrEP has been disappointingly low,” Lewin said. “I hope these findings will accelerate momentum to make long-acting PrEP accessible to all those who need it.”

Abstract and session: Initial PrEP product choice: results from the HPTN 084 open-label extension, HIV prevention: Novel approaches and promising findings (5998)

People living with HIV not more likely to be hospitalized with mpox unless immunosuppressed, finds WHO analysis

Among mpox cases globally in 2022, people living with HIV were not more likely to be hospitalized unless they were immunosuppressed, according to a study from the World Health Organization (WHO).

The multi-country outbreak of mpox – formerly known as monkeypox – emerged in May 2022, and countries have reported nearly 150 deaths to date. The vast majority of mpox cases have been among men who have sex with men, many of whom are living with HIV, and studies have shown that mpox can be much more severe in those who have a very low CD4 count (a key indicator of immune function).

The new analysis, presented by Ana Hoxha of WHO, describes clinical characteristics and outcomes of mpox cases among people living with HIV in 2022. It is based on more than 82,000 cases with detailed information in WHO’s mpox global surveillance system. Information on HIV status was available for 39% of reported cases; of these, 52% were people living with HIV. Among people living with HIV who had available information, 91% reported being men who have sex with men.

Based on the finding that uncontrolled HIV may lead to disproportionate mpox morbidity, the study team concluded that health systems must ensure that people living with HIV know their status, are linked to HIV care and treatment and achieve viral suppression. They also noted that for people with unknown HIV status, mpox testing can be an important opportunity for HIV testing, prevention and care.

Abstract and session: HIV among mpox cases: clinical characteristics and outcomes in the WHO global surveillance 2022, It’s all about the bugs: Other conditions in people with HIV (3953, Track B)

COVID-19 mortality risk declined only modestly among people living with HIV during Omicron

While COVID-19 mortality risk declined dramatically during the Omicron variant wave among HIV-negative people, it declined only modestly among people living with HIV – especially those with low CD4 counts, according to a late-breaking WHO analysis.

The study, presented by WHO’s Meg Doherty and Nathan Ford, is based on data from the WHO Global Clinical Platform comprising more than 821,000 people who were hospitalized with COVID across the pre-Delta, Delta and Omicron waves.

The study found that across all COVID waves, common factors associated with mortality for people living with HIV were having severe COVID and low CD4 counts. In addition, during the Delta and Omicron waves, COVID vaccination reduced the likelihood of death by 38% to 39% in people living with HIV.

According to the study team, the findings highlight the need to implement WHO recommendations for giving booster vaccine doses to all people living with HIV – even during the less severe and low-incidence Omicron wave.

“These findings underscore the need for equitable global access not only to COVID vaccines and boosters, but also antivirals,” Lewin said. “Today, global access to lifesaving antivirals for COVID-19 remains very limited.”

Abstract and session: High in-hospital mortality in SARS-CoV-2 infected patients living with HIV during pre-Delta, Delta and Omicron variant waves: finding from the WHO Global Clinical Platform for COVID-19, Track C late-breaker session (5988, Track C)

“Geneva Patient” in HIV remission 20 months after stem cell transplant from donor lacking CCR5-delta32 mutation

Asier Sáez-Cirión of Institut Pasteur and Alexandra Calmy from the Geneva University Hospitals presented the case of the “Geneva Patient,” a man who was diagnosed with HIV decades ago, but has been in HIV remission for 20 months without antiretrovirals following a stem cell transplant – and whose donor lacked the rare stem cell mutation that has been linked to all known HIV cure cases to date.

The Geneva Patient, whose name has not been disclosed, is a Caucasian male who was diagnosed with HIV in 1990. He initiated antiretrovirals shortly after diagnosis, and his HIV viral load was undetectable from 2005 onwards. In 2018, he received chemotherapy followed by a stem cell transplant to treat biphenotypic sarcoma. Later, in November 2021, he discontinued antiretroviral therapy. Now, 20 months later, his viral load remains undetectable even though he is not on antiretroviral treatment. However, the study team cannot exclude the possibility that the virus is still present in anatomical or cellular sanctuaries.

To date, five individuals have been considered “cured” of HIV; all received stem cell transplants from donors whose cells have a rare mutation that makes them resistant to HIV, known as the CCR5-delta32 mutation. But in this new case, the donor had normal or “wild type” stem cells – meaning they were susceptible to HIV.

Another pair of cases, known as the “Boston Patients,” were first discussed in detail a decade ago, at IAS 2013 in Malaysia. Both of those individuals also received transplants from donors whose stem cells were “wild type” and thus susceptible to HIV. Later, both interrupted antiretroviral treatment. In one of the individuals, HIV re-emerged four months after treatment interruption; in the other, it re-emerged after eight months. At 20 months, the Geneva Patient has already achieved much more durable HIV remission without treatment.

“This case is inspiring for people living with HIV and adds to a growing number of case reports of HIV cures. These cases are important to help understand the factors associated with the elimination of persistent HIV reservoirs,” Lewin said. “However, I remain cautious, given we learned previously from the two Boston patients that even a single virion can lead to HIV viral rebound. This person will need to be monitored closely in the coming months and years.”

Abstract and session: Absence of viral rebound for 18 months without antiretrovirals after allogeneic hematopoietic stem cell transplantation with wild-type CCR5 donor cells to treat a biphenotypic sarcoma, Track A late-breaker session (5819, Track A)

Among children born with HIV, boys may have a better chance of sustained remission due to innate immune sex differences

A study in South Africa identified five boys born with HIV who maintained undetectable viral load despite low adherence – or in some cases, non-adherence – to antiretroviral therapy, a discovery that ultimately led researchers to conclude that boys may have a better chance of sustained remission than girls due to innate immune sex differences.

Presented by Gabriela Cromhout of the University of KwaZulu-Natal, the study followed 281 mother-child pairs following in utero transmission of HIV. The main goal of the study was to determine whether children who are treated very early on can achieve post-treatment control of HIV without additional interventions, and if so, what mechanisms might contribute.

All children in the study received antiretroviral therapy at birth; 92% also received antiretrovirals prior to birth through their mothers. The study found that maintenance of viral control was highly dependent on adherence to antiretroviral therapy, irrespective of infant baseline plasma viral load. Over time, five males were identified who maintained viral control – ranging from 3+ to 19+ months – despite persistent non-adherence to antiretroviral therapy. This was not observed in any of the female children, even though the cohort was 60% female.

Higher rates of in utero transmission to female foetuses were associated with female susceptibility to type I interferon (IFN-I) resistant virus that tended to have low viral replication capacity. Viruses transmitted to male foetuses overall were typically IFN-I sensitive and of higher replicative capacity. However, those transmitted to males maintaining viral control despite persistent non-adherence to antiretroviral therapy had low replicative capacity.

The study team concluded that distinct immune interventions, taking into account early-life immune sex differences, are critical to optimize HIV cure potential in children.

Abstract and session: Sustained aviraemia in the absence of anti-retroviral therapy in male children following in utero vertical HIV transmission, Co-Chairs’ Choice session (5727, Track A)

Cancer drug shows promise in HIV cure study in humanized mice

A widely used cancer drug can be used to deplete HIV latently infected cells and delay viral rebound in humanized mice, according to a study from a team of researchers in Australia.

In the study, venetoclax – which is currently used to treat certain blood cancers – delayed viral rebound in a pre-clinical model of latent HIV infection and depleted HIV DNA ex vivo in CD4+ T-cells from people living with HIV who were on antiretroviral therapy.

Presented by Philip Arandjelovic of the Walter and Eliza Hall Institute of Medical Research in Melbourne, the study was a collaboration with the Doherty Institute, a joint venture of the University of Melbourne and Royal Melbourne Hospital, also based in Melbourne. The team assessed whether inhibiting host pro-survival proteins with venetoclax could preferentially prime latent cells to die and clear the viral reservoir.

In the CD4+ T cells treated ex vivo in a dose-dependent manner, intact DNA displayed a median-fold change of 0.58x with 100 nanomolars of venetoclax. The drug induced higher rates of death in naïve and central memory T-cells compared to other T-cell subsets, and cells with higher expression of transcripts of pro-apoptotic BH3-only proteins were overrepresented in the venetoclax-sensitive population.

In the humanized mouse model, researchers evaluated time to viral rebound following cessation of antiretroviral therapy.

When dosed on weekdays for six weeks, venetoclax significantly delayed viral rebound after cessation of antiretroviral therapy. When combined with the MCL1 inhibitor S63845 and dosed on weekdays for three weeks, the combination achieved a longer delay in viral rebound compared to either intervention alone; the median time to viral rebound was three weeks.

“These are very encouraging results,” Lewin, a member of the study team, said. “It’s exciting that venetoclax will soon be tested in a clinical trial in Australia and Denmark as a potential pathway to an HIV cure.”

Abstract and session: Venetoclax, alone and in combination with the BH3-mimetic S63845, depletes HIV-1 latently infected cells and delays rebound in humanized mice, Track A late-breaker session (5735, Track A)

Note: The summaries above are primarily based on submitted abstracts, but in some cases, study teams have provided updated or additional information. Final data presented at the conference may change.

This news release was published by the International AIDS Society on July 20, 2023 (Brisbane time).
