CROI Roundup: All the HIV News That's Fit to Print

A review of all of the big HIV science revelations coming out of the 2016 Conference on Retroviruses and Opportunistic Infections, including the PrEP failure case.

March 2, 2016 By Benjamin Ryan

Imagine 4,000 major stakeholders in the HIV movement gathered in a convention space for one purpose: to combat the epidemic. The sheer volume of attendance at the annual Conference on Retroviruses and Opportunistic Infections (CROI), held this year in Boston from February 22 to 25, is an awesome testament to how many brilliant and devoted scientists, nonprofit leaders, activists and, yes, even journalists, hailing from the four corners of the globe, have devoted their lives to the HIV cause.

This summary of major scientific presentations at CROI offers a glimpse into the future of the epidemic, which will likely include safer, easier-to-take treatments for the virus, expanded options for pre-exposure prophylaxis (PrEP), and, ultimately, success in getting more people on HIV treatment, thereby curbing the spread of the virus.

For more details about any of the studies, click the hyperlinks.

The first documented case of PrEP failure:

Since POZ broke the story on February 25, the general public has stirred itself into a clamor over the news of a Canadian man who contracted multi-drug resistant HIV while apparently adhering well to the daily Truvada (tenofovir/emtricitabine) as PrEP regimen.

A considerable portion of the online chatter over this case is divided into two camps: Those crowing "I told you so," using the news of PrEP's failure as supporting evidence for ongoing efforts to denigrate PrEP, discourage its use, and promote condom use instead; and those who have stressed that this case is rare. At times, members of the PrEP-promoting camp take pains to denigrate and discourage condom use. Lost in this polarized debate is the notion that there is often an overlap between PrEP and condom use.

The effectiveness of either HIV prevention method aside, a major question remaining is how evidence of PrEP's potential for failure, however slight the overall risk of such an outcome, may affect the anxieties of individuals who count on Truvada to keep them protected from HIV.

It is indeed rare to find strains of HIV that are so resistant to both drugs in Truvada that PrEP will not protect against such strains; far less than 1 percent of HIV strains likely fit this category. However, there is also evidence that resistance to the tenofovir component of Truvada is increasing.

More than 9,000 people participated in clinical trials of PrEP and an estimated 40,000 Americans are currently taking it. So the two years the Canadian man spent on PrEP is but a tiny fraction of the tens of thousands of years all HIV-negative individuals have cumulatively spent taking Truvada for prevention thus far. However, it's still possible that there have been other similar cases of PrEP failure. The Canadian man had a highly proactive physician, who was savvy enough to recognize the potential that he was seeing a PrEP failure case once the man tested positive for HIV, and who was hasty enough to conduct the tests necessarily to provide evidence that would support this suspicion before too much time had elapsed. Others taking Truvada for HIV prevention may also have failed on PrEP, but slipped under the radar because they lacked a physician with such a keen eye and scientific know-how.

Antiretrovirals of the future: PrEP 2.0 and long-acting HIV treatment:

The PrEP science presentations that apparently excited CROI attendees the most concerned two large trials examining the effectiveness of an antiretroviral-containing vaginal ring as PrEP among sub-Saharan African women. The ring was only partially effective in both trials, but worked much better in older women for reasons that are unclear. The ring reduced HIV risk by more than half among women older than 21 in one study.

While these results may seem modest, they were met with marked enthusiasm by the CROI attendees; both researcher presenters received fervent applause as well as standing ovations from some in the audience.

CROI saw several reports of other upcoming versions of PrEP, suggesting that Truvada may have company one day (although probably not until 2020—check out POZ's December 2015 feature on PrEP 2.0 development).

The antiretroviral (ARV) Selzentry (maraviroc) performed well in comparison to the components of Truvada in a Phase II safety and tolerability study. Researchers are in talks to start a large Phase III trial, one that won't wrap up for several more years.

In another Phase II study, transgender women and men who have sex with men (MSM) adhered well to a tenofovir-containing rectal PrEP gel.

Research into long-acting injectable ARVs, for use as PrEP as well as HIV treatment, is advancing. In a Phase IIa trial, researchers examined a long-acting injectable version of ViiV Healthcare's investigative antiretroviral cabotegravir as PrEP. Given every 12 weeks, the drug proved safe in most participants, although researchers concluded that future studies need to narrow the dosing frequency to every eight weeks. The goal is to bring this version of PrEP to market in 2020.

Meanwhile, a Phase IIb trial of injections of long-acting cabotegravir and Janssen's non-nucleoside reverse transcriptase inhibitor (NNRTI, or non-nuke) Edurant (rilpivirine), given every eight weeks as HIV treatment, proved safe and generally well tolerated and also suppressed the virus as well as a daily oral regimen in an ongoing trial. The combination will move into phase III trials later this year, with a goal for approval in 2019.

Gilead Sciences is set to receive word in April from the U.S. Food and Drug Administration (FDA) about its application for approval of a new version of Truvada that includes a safer version of the tenofovir component known as TAF. Research has shown that TAF is safer for the bones and kidneys.

Consequently, many people are wondering whether TAF-inclusive Truvada (which will receive a new name if approved) will ever be approved as PrEP. Researchers will have to conduct the series of clinical trials of the new tablet that are necessary for the FDA to green light it as PrEP, a process that would take many years. For now, research is only in the very early stages.

One study presented at BCROI found that TAF-inclusive Truvada protected monkeys from rectal exposures of the simian version of HIV, SHIV, and did so as well as standard Truvada had in a previous study. However, a small trial of TAF among HIV-negative women raised doubts about whether TAF-inclusive Truvada will lead to high enough drug levels in both vaginal and rectal tissues to protect against HIV as well as standard Truvada. (Researchers believe the findings in this study may apply to men where anal sex is concerned.)

Side effects: of PrEP, as well as of tenofovir among people with HIV:

Research presented at the conference showed that, among HIV-negative transgender women and MSM, the first 12 weeks of Truvada led to a modest initial drop in kidney function, one that stabilized thereafter. Previous research has shown that such a reduction in kidney function tends to reverse after an HIV-negative person goes off Truvada—which is always an option for anyone taking the drug as PrEP whose regular tests indicate worrisome results where the kidneys are concerned.

Another study found that, among young adult MSM and trans women on PrEP, the typically small drop in bone mineral density that tends to result from the tenofovir component in Truvada reversed after they stopped taking the drug.

Among HIV-positive people, the use of the traditional version of tenofovir, known as TDF, raises the risk of fractures, according to a large new study. This finding doesn't necessarily apply to HIV-negative people taking Truvada. HIV itself may contribute to the increased risk of fractures among positive people taking tenofovir. Also, in clinical trials of PrEP, tenofovir was not associated with the risk of broken bones. However, thus far there is no safety data available about the long-term use of Truvada—longer than about two years—among HIV-negative individuals.

The ability of PrEP, as well as HIV testing and treatment, to curb the epidemic:

The Centers for Disease Control and Prevention (CDC) estimated that expanding HIV treatment and testing, as well as PrEP, could slash the rate of new U.S. cases of the virus by 70 percent during the next five years. Some good news on this front is that, after years of gloom and doom where U.S. viral suppression rates are concerned, the CDC estimates that an increasing proportion of Americans living with HIV have an undetectable viral load, and therefore are very unlikely to transmit the virus to others.

The CDC contrasted these hopeful glimpses into the future with a dire prediction of the current risk of HIV among certain populations. The agency projected that half of all black MSM and one in four Latino MSM will contract HIV in their lifetimes if current trends continue.

Despite all of the talk in recent years about HIV treatment's power to reduce the spread of the virus, research shows that people taking antiretrovirals are greatly overestimating their own infectiousness.

A hopeful sign of Truvada's potential for success in helping to curb the HIV epidemic is a new study in which a targeted intervention was successful at getting black MSM interested in and adhering to PrEP. Previous research has raised questions about whether this population, which is disproportionately affected by HIV to a vast and troubling extent, will ultimately reap the benefits of PrEP.

Half-yearly STI screenings for those on PrEP isn't enough:

One final bit of PrEP news out of the conference came from research suggesting that the current CDC guidelines for sexually transmitted infection (STI) testing among those on PrEP are insufficient. Currently, the CDC recommends testing people on PrEP for STIs twice yearly or in the event of symptoms. CROI saw an emphatic call for changing these guidelines so that they recommend comprehensive STI tests at every one of the quarterly clinic visits required to maintain a PrEP prescription.

The benefits of HIV treatment, more work to do:

The average life expectancy of people treated for HIV has jumped 14 years during the combination ARV treatment era, but HIV-positive people still have a major gap in this department compared with their HIV-negative counterparts. This deficit narrows considerably if people have more than 500 CD4s, don't have hepatitis B or C viruses (HBV/HCV), don't abuse substances, and are non-smokers.

Meanwhile, treating HIV early, according to a substudy of the global START trial, reduces the risk of virus-related cancers, including cervical and anal cancers, cancers of the head and throat, Kaposi's sarcoma, and Hodgkin and non-Hodgkin lymphoma.

Finally, there is hopeful news that the World Health Organization's "90-90-90" call for high HIV diagnosis, treatment, and viral suppression rates was not just a pie-in-the-sky goal. WHO encourages nations to reach the following targets by 2020: diagnose 90 percent of their HIV

population, get 90 percent of that group on treatment, and get 90 percent of that group virally suppressed, for an overall viral suppression rate of 73 percent. Botswana's current figures are an impressive 83-87-96, vastly besting that infamous laggard, the United States.
