

## CROI 2010: All that's new in HIV

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The Conference on Retroviruses and Opportunistic Infections (CROI) has just happened in San Francisco. This meeting is held annually and focuses on the very latest in basic science and [clinical](#) [1]Pertaining to or founded on observation and treatment of participants, as distinguished from theoretical or basic science. research. Jo Watson was there and gives us an overview.

As a meeting, CROI is very academic. Studies presented are not only critiqued but their findings discussed with regard to how they can best be applied clinically around the world. It is the conference that has the biggest impact on how international guidelines are determined.

One major session is about the drugs coming through the research and development pipeline. This session is always a good indicator of what we'll be seeing in the future.

After the excitement of recent years, where a striking and steady number of new drugs have been added to our arsenal, this year the theme could best be described as 'sobering'.

HIV research and development is now a mature field and the current number of novel agents in development is small. Compared to previous years, there is now just a trickle of new drugs coming through and some of these already have a questionable future.

Vicriviroc looks to be one of these. This new agent in the CCR5 inhibitor class showed very disappointing results in the latest [phase III](#) [2]A large clinical trial designed to establish whether a drug is effective and safe enough for widespread use. Phase III studies include expanded controlled and uncontrolled trials after preliminary evidence suggesting effectiveness of the drug has been obtained, and are intended to gather additional information to evaluate the overall benefit-risk relationship of the drug and provide an adequate basis for physician labeling. studies for treatment-experienced people. Put up against those on currently available [antiretrovirals](#) [3]A medication or other substance which is active against retroviruses such as HIV., investigators were not able to show any real benefit in using the drug.

These results raised a discussion about the future of study design. Is it enough now to just put new agents up against the best standard-of-care drugs? Beyond safety and [efficacy](#) [4](Of a drug or treatment). The maximum ability of a drug or treatment to produce a result regardless of dosage. A drug passes efficacy trials if it is effective at the dose tested and against the illness for which it is prescribed. In the standard procedure, Phase II clinical trials gauge efficacy, and Phase III trials confirm it., is it also the long-term durability and toxicity profiles that will have to be better understood?

The new generation of integrase inhibitors is moving along. But there was a lot of interest in how their [resistance](#) [5]

Resistance continues to be a critical issue in terms of the long-term challenges for people on therapy.

Another sobering theme at the conference was how limiting antiretroviral therapy is and what it means for long-term life expectancy and quality of life. The main challenges faced are drug resistance, the limitations to immune recovery and control, longterm toxicities (those known and those still emerging) and the impacts of HIV disease itself. These are themes we will be following-up in future stories in this magazine.

This year's meeting also saw major sessions devoted to the complications surrounding HIV and how we currently treat it. We were reminded of the complexities faced by clinicians and researchers when trying to analyse across many confounding scenarios. These sessions also underlined how important it is that HIV research continues with force and commitment, as so much is still debated and goes unanswered.

The START study hopes to answer one of these most fundamental questions: at what CD4 count is it best to initiate treatment? The results will deliver some vital clues as to how the disease progresses and how it is most effectively treated.

Throughout the CROI meeting, the importance of the START study was acknowledged, as was Australia's contribution to research generally.

I was reminded that when we contribute to HIV research in Australia we help shape the future for all populations living with HIV and contribute to a better quality of life for all positive people.

Recruitment of the START study is currently underway in Australia.

## **SOME HIGHLIGHTS**

### **TREATMENT AS PREVENTION**

Susan Buchbinder from the San Francisco Department of Public Health and University of California, focused on 'biomedical' rather than 'change of behaviour' prevention and surveyed some of the trials which were looking at such things as suppressing herpes simplex virus-2 (HSV2), vaccines and microbicides, all of which have had limited success in reducing new HIV infections.

She considered the role antiretroviral drugs play in preventing HIV infections, and highlighted trials using daily PrEP (pre-exposure prophylaxis) including a major study called iPrEx in which around 2,500 MSM have been [enrolled](#) [6]

The whole 'test-and-treat' discussion (in which an at-risk population is regularly tested and those found to be positive immediately start life-long antiretroviral treatment) was reviewed.

There is substantial biological plausibility for this but, of course, lots of social, behavioural and ethical questions, including whether it will lead to risk inhibition.

### **PURGING THE RESERVOIRS**

Scott Hammer from Columbia University Medical Centre in New York talked about purging the reservoirs where HIV infection is latent, with a view to eradicating HIV altogether. Currently, HIV which is able to replicate is 'archived' in reservoirs early in infection history and is 're-seeded' as HIV replication proceeds.

He described potential therapies to disrupt latent HIV infection, explaining that the immunology theoretically exists whereby HIV-infected cells from reservoirs are released into the circulating blood plasma where they can be blocked by the anti-HIV drugs present. The risk is that by activating these resting cells the pool of memory CD4 cells will be depleted and people will not be able to launch an immune response to common pathogens.

### **WHEN TO START AND WHAT TO USE**

Hammer also reviewed the evidence to date as to why we should start treatment earlier. He highlighted that our drug options are not only better and safer now but also that by taking them earlier we diminish our chances of developing resistance and the damage caused by uncontrolled HIV. This is still a debate that clinical studies such as START can help resolve. Hammer also discussed newer strategies to make treatment more effective.

These include treatment simplification (fewer drugs, fixed-combination drugs such as the 'Quad' pill, more convenient dosing) and drug intensification using, in particular, raltegravir, enfuvirtide (T-20) and maraviroc.

### **AGEING AND CO-MORBIDITIES**

Judith Currier from the University of California suggested that organ system diseases (particularly those associated with ageing) will increasingly become a major concern for people with HIV. These 'non-AIDS' events include cancers, cardiovascular disease, neurological deficits and kidney disease.

She provided some disturbing evidence that even people who successfully control their HIV have damage to their gut tissues which allow microbes to constantly transfer into their circulatory systems, leading to the production of toxic molecules which damage major organ systems.

Finally Currier suggested that some targets for preventing these bad health outcomes include effective, fully suppressive treatment, commenced earlier; treating co-infections; possible use of anti-inflammatory agents; and modifying known lifestyle factors: smoking alcohol, nutrition and recreational drug use.

**DISCLOSURE AND PREVENTION**

On the issue of HIV disclosure to partners, one paper noted that sero-status disclosure to partners is associated with less risky sexual behaviours, improved quality of life and better adherence to treatment and care.

The observation was also made in a study from Amsterdam that young gay seroconverters today are more likely to have contracted HIV from a steady partner than from a casual partner, compared with early in the AIDS epidemic and compared also with older gay seroconverters. This has obvious implications for HIV educators crafting campaigns aimed at younger gay men and those in serodiscordant relationships.

**For more detailed coverage from CROI including links to webcasts and abstracts, go to**

[www.aidsmap.com](http://www.aidsmap.com) [7]

**For podcasts of key presentations go to**

[www.retroconference.org](http://www.retroconference.org) [8]

- [Treating HIV](#)
- [basic science](#)
- [clinical research](#)
- [conference reports](#)
- [HIV treatments](#)
- [opportunistic infections](#)
- [The global HIV epidemic](#)

**Links:**

[1] <http://www.napwa.org.au/glossary/term/475>

[2] <http://www.napwa.org.au/glossary/term/92>

[3] <http://www.napwa.org.au/glossary/term/122>

[4] <http://www.napwa.org.au/glossary/term/486>

[5] <http://www.napwa.org.au/glossary/term/109>

[6] <http://www.napwa.org.au/glossary/term/489>

[7] <http://www.aidsmap.com>

[8] <http://www.retroconference.org>