While downtown Atlanta was a dreary disappointment, the 20th Conference on Retroviruses and Opportunistic Infections (CROI) held in Atlanta from March 3 to March 6, 2013 certainly was not. There was lots of important data on HIV “cure” research, antiretroviral therapy, emerging prevention strategies, co-morbidities, and HCV co-infection data presented at this year’s conference. I will be reporting on “cure” research, antiretroviral and prevention highlights.

HIV “cure” research was an important and highly publicized part of the 2013 meeting. The Mississippi Baby’s apparent HIV “cure” was the leading story at this year’s CROI. While this research is a top priority to activists working in the field, it is always prudent to keep “cure” research in a realistic perspective. It will be many years before a “cure” for HIV is a reality for all HIV infected people. Nevertheless, we are off to a great start.

The story of the “Mississippi baby” is very interesting. The baby was born prematurely to a mother who did not know she was HIV infected and who as a result did not use preventive antiretroviral (ARV) therapy. After confirmation that the baby was HIV infected, a potent ARV treatment combination was initiated. This combination consisted of 3 drugs, not the usual 2 drug preventative drug combination and was administered 31 hours after the baby’s birth. The baby’s caretaker stopped treatment at 18 months. Despite remaining off ARVs, no evidence of active HIV was found in the baby’s body by Hopkins’ researchers at months 24 and 26.

Questions remain about this important case. Was the baby “cured” because therapy was started early enough and/or because the 3 drug therapy used was strong enough to actually “cure” HIV? What actually happened to prevent the spread of HIV through the baby’s system with the top speed that usually propels HIV infection to all areas of the body?

The Visconti Cohort of French patients is another fascinating example of patients who may also be “functionally cured” of HIV which means their viral load is suppressed without ARV treatment much like the extremely small group known as “elite controllers”. “Elite controllers” are able to control their HIV without ever starting ARV therapy. There are 14 patients in the Visconti Cohort, 10 men and 4 women, who were treated...
with ARVs within 2 months of HIV infection. All patients remained on treatment for at least 1 year. The median time on treatment was 3 years and the maximum time was 8 years. All 14 patients have been off therapy between 4 and 18 months. So far, all patients have maintained viral suppression without ARVs and have extremely low HIV reservoirs, (dormant cellular reserves of HIV in the body). Even though these 14 patients lack the protective HLA B alleles (genetic makeup) of “elite controllers”, they were nevertheless able to control their HIV after early treatment with ARV therapy and are known as “post-controllers” who may be “functionally cured”. The Visconti Cohort will obviously need to be followed for a very long period of time to confirm that they have actually been “functionally cured”.

Data presented at CROI suggests that therapy administered immediately after HIV infection has the ability to prevent “seeding of reservoirs” in adults. Recent data has shown that after HIV enters the blood stream, it appears in the gut where it very quickly “seeds this important HIV reservoir”. Thereafter, HIV is very quickly disseminated throughout the body. Although we will need a lot more studies to explore whether a “functional cure” in both infants and adults is possible by administering immediate treatment of a sufficient duration treatment, this does seem to be promising. If this approach does prove to be successful, we will still have our work cut out for us. Realistically, the logistics of identifying people immediately after HIV infection is unfortunately a daunting prospect, especially in the US where our healthcare is less than optimal.

Because of the novel research of Hopkins Professor Bob Siliciano, we also know that there are active and dormant HIV cells in the body. The current thinking is that HIV will never be “cured” unless we can force these dormant cells out of HIV reservoirs and destroy them. Scientists are referring to this as the “kick and kill” approach. Researchers have been exploring a class of drugs known as HDAC inhibitors in hopes these drugs will be able to force HIV out of dormant cellular reservoirs in the body so that we can then obliterate HIV reservoirs, reducing the risk of the virus returning once standard HIV treatment is stopped.

Data at CROI, showed that multiple doses of the HDAC inhibitor vorinostat (SAHA) which is an approved treatment for a type of lymphoma, increased the expression of virus by these cells, but was not able to actually shrink the size of the reservoir. This data suggests that vorinostat alone is not likely to eliminate HIV reservoirs. Just like ARV therapy, we will probably need combination “cure” approaches, including drugs that are highly effective against both active HIV as well as dormant HIV cellular reservoirs. Combination approaches will be especially necessary for people who have been HIV infected for long periods of time and who have comprised immune systems. These patients will probably require a jump start with an immuno-modulator, possibly a therapeutic vaccine, so they will be able to successfully fight the HIV remaining in their systems. Unfortunately, this work will take years to complete, but we have started the long labor-intensive process.

Antiretroviral (ARV) therapy was also well covered at CROI this year. New data from ARV clinical trials, studying the safety and efficacy of four promising new ARVs were presented, including ViiV Healthcare’s new integrase inhibitor dolutegravir (DTG), Merck’s non-nucleoside reverse transcriptase inhibitor, (NNRTI), MK-1439, Gilead’s new nucleotide reverse transcriptase (NRTI) inhibitor tenofovir alafenamide, known as TAF, and Tobira’s CCR5 and CCR2 antagonist cenicriviroc.

New data on ViiV’s once daily integrase inhibitor DTG was reported from the Phase III SAILING study of DTG naive, but otherwise ARV treatment-experienced patients were reported in a late-breaker session. In this study 750 people were randomized to receive either DTG or Merck’s twice daily raltegravir (RAL), also known as Isentress, combined with an optimized background regimen (OBR). Seventy-nine percent (79%) of patients in the DTG group had undetectable viral loads, compared with 70% in the RAL group. DTG is expected to be approved by the FDA this August. It is also important to note that unfortunately liver complications were more common among people co-infected with both hepatitis B and hepatitis C receiving DTG compared with those receiving RAL.

Merck’s new once daily NNRTI MK-1439 is active against NNRTI resistant mutations at least in test tubes. In a Phase I study presented at CROI involving 18 treatment-naïve people, seven days of either 25 mg or 200 mg
MK-1439 monotherapy reduced viral loads by 1.26 and 1.37 log copies respectively. No cases of rash or central nervous system side effects which are common among NNRTIs were seen in this small study. Much larger and longer studies will be needed to confirm these data. Another Phase I study involving HIV-negative individuals showed that MK-1439 can be taken either with or without food and also suggests that doses as low as 12mg may be effective.

Gilead’s TAF is a new experimental drug which is a low-dose prodrug (increased potency) of tenofovir (TDF), also known as Viread that is being studied as an alternative to TDF which carries the risk of serious kidney side effects as well as bone density loss. TDF is the active ingredient in Viread which is a component of the fixed dose, one pill once per day combinations Atripla, Complera and Stribild. Gilead believes that TAF will reduce the risk of kidney side effects and bone loss. A 24 week Phase II study of TAF showed that 90% of the HIV+ treatment naive patients using an experimental version of Stribild containing 25 mg of TAF achieved undetectable viral loads, compared with 88% of those using the approved version of Stribild which contains 300 mg of TDF. Kidney toxicity and bone loss represented by increases in creatinine levels and decreases in bone mineral density were noted in both groups, but the changes were less pronounced among those using Stribild containing TAF, likely due to the lower concentrations of TDF.

In a 24 week Phase 2 study of Tobira’s CCR5 and CCR2 antagonist cenicriviroc (CVC), rates of undetectable viral loads were similar among HIV treatment naive patients using either 100 mg or 200 mg of CVC plus TDF and Emtriva compared with those using Sustiva/TDF/Emtriva. Patients in the CVC group were more likely to be virologic non-responders, but those in the Sustiva group were more likely to discontinue treatment because of side effects. CVC’s ability to block the CCR2 receptor on CD4 cells resulted in a reduction in soluble CD14, a monocyte activation marker that has unfortunately been linked to all-cause mortality in people with HIV. We obviously need much more study of CVC especially its effect on soluble CD14.

The more data we have, the more we know that Pre-Exposure Prophylaxis (PrEP) works to prevent HIV transmission in up to 90% of patients IF they take their medication. But studies in Botswana evaluating daily Truvada (emtricitabine + tenofovir), in men who have sex with men and transsexual women, HIV discordant couples, and heterosexual men and women, showed overall PrEP efficacy rates of between 39% and 75%. FEM-PrEP, a study in high-risk women, failed to find any PrEP benefit. The results of the VOICE study presented at CROI which was conducted in 5,000 women at risk for HIV in South Africa, Uganda and Zimbabwe were also very discouraging. The women received daily oral tenofovir (TDF), also known as Viread which was stopped early for lack of efficacy, daily vaginal tenofovir microbicide gel which was also stopped early, daily oral Truvada, or either a gel or oral placebo. The VOICE results were similar to FEM-PrEP study results. HIV infection rates were similar in both the oral Truvada group and the oral placebo group. How did this happen? The answer is simple. Patients were not taking their drugs. Even though people reported that they were taking their assigned drugs, TDF was detectable in less than 30% of blood samples collected during quarterly follow-up visits. Unmarried women, those less than 28 years of age and those with a partner younger than 28 years of age were the least likely to take their assigned PrEP regimen. Importantly, researchers seem to be gaining a better understanding of the behavioral factors associated with poor adherence. We need to identify the reasons why people are not taking their medications so we can actually prevent HIV transmission. This is critical to the success of developing demonstration projects and roll-out programs that are being started in the real world.

As usual, CROI 2013 was a great success and a non-stop source of new HIV research information. Important data across the HIV spectrum was presented to researchers from across the globe. You can access full abstracts from the meeting at: www.retroconference.org/2013.

You may also want to surf our web site for links to more articles from HIV community writers from across the nation.