

HIGHLIGHTS FROM CROI 2014*

The 21st Annual Conference on Retroviruses and Opportunistic Infection (CROI) was held in Boston, Massachusetts on March 3-6, 2014. CROI is often held in Boston at the Haynes Convention Center, just blocks from the site of the Boston Marathon bombings. It was wonderful to see high functioning Boston still doing just that and its citizens as hearty as ever, continuing to be "Boston Strong".

As always, CROI was packed full of the latest cutting edge information on HIV research, care and prevention. This article will provide the highlights of antiretroviral (ARV) therapy at CROI 21. The focus at CROI 21 was on new drugs and novel strategies. The bar is set very high in the ARV arena. We already have lots of relatively safe and highly effective ARVs on the market. The goal here is to develop safer ARVs that are just as effective and that are also easily administered with a small number of pills that can be taken once daily. Highlights of ARV studies that attempt to prove safety, efficacy and ease of and simplicity of administration in people who have never taken ARVs, known as ARV naïve, and also in treatment-experienced patients are presented below.

Studies in ARV Naïve patients

Viread with twice daily Isentress which is an integrase inhibitor with a good side effect profile was equally as effective as Viread, plus either Reyataz combined with Norvir or Prezista with Norvir which are both protease inhibitor boosted regimens. Viread plus Isentress was as effective as Viread and Prezista plus Norvir with less cardiovascular (CVD) side effects, like elevated cholesterol and triglycerides. Patients with CVD issues may wish to discuss switching to Viread plus Isentress with their providers.

Twice daily Isentress with once daily Prezista plus Norvir was just as effective as Truvada combined with Prezista plus Norvir. Truvada use presents the possibility of kidney side effects. Of note, there was a trend toward failure in the Isentress containing regimen in patients with viral loads above 100,000 and significant evidence of failure in this arm in patients with CD4s less than 200. If you have a low viral load and high CD4s, kidney issues, but no CVD issues, Isentress and Prezista plus Norvir may be the ticket for you.

Ziagen and Epivir, both NRTIs, plus Tivicay, the latest and arguable the most effective integrase inhibitor was superior to Truvada plus Sustiva which has known central nervous system (CNS) side effects. The superiority of the Tivicay containing regimen is driven by its superior tolerability profile to that of Sustiva. Tivicay continues to have the most favorable resistance profile of all the integrase inhibitors.

MK 1439 Phase 2b study results were also presented. MK1439, now known as doravirine is an NNRTI like Sustiva. At 24 weeks, doravirine showed promising efficacy and safety results. Doravirine may replace Sustiva as the preferred first line NNRTI if its efficacy remains as good as Sustiva and its tolerability profile remains superior to Sustiva in upcoming Phase 3 studies.

The community is very excited about new long acting drugs which will not require daily dosing and will be administered by monthly intramuscular (IM) injections. The LATTE study enrolled patients on oral Ziagen and Epivir plus different doses of the long-acting drug, GSK 1265744, known as 744. The goal of this study was to switch patients who became virally suppressed on this regimen to a maintenance regimen of 744 plus Edurant which has also been made into a long-acting formulation. This would enable people to switch to a monthly maintenance IM injection after they have become undetectable

and have taken the oral drugs long enough to ensure that they will be able to tolerate long-term use of the long-acting formulations.

Over 90% of those undetectable patients that switched to 744 plus Endurant maintained viral suppression after 24 weeks of maintenance therapy with good tolerability to the long-acting regimen. If these excellent results are maintained, we will have an entirely new exciting HIV treatment paradigm available to patients.

Studies in Treatment-Experienced Patients

Patients with undetectable viral loads were switched from NNRTI and boosted PI regimens to the Gilead fixed dose combination of more than one drug in one pill, now known as Stribild which contains four drugs, one of which is Gilead's integrase inhibitor, Vitekta. The reason to switch to Stribild is dosing simplification. The hope was also for a booster drug with a better side effect profile than Norvir. Tybost is another one of the four drugs within Stribild and is Gilead's version of Norvir, the long used ARV boosting drug. The hope was that Tybost would have less side-effects than Norvir.

The efficacy of Stribild was as good as the PI and NNRTI regimens. There was a significant, but very small decrease in cholesterol and a significant decline in triglycerides, diarrhea and bloating in the Stribild group. Unfortunately, Tybost use is related to increased creatinine levels, a kidney related side effect which may prove to be a double whammy as other component parts of Stribild, namely Truvada is also known to cause kidney side effects.

Patients on Stribild also experienced less neuropsychiatric side effects. Most of the patients in the non-Stribild arm of the study were on Sustiva, which is well-known for such side effects. Stribild may be easier to take, but this alone does not prove it is a better just because it is simple to take. Better ARV adherence has yet to be proved convincingly. Stribild may be easier take, if you can afford it. In spite of pleas from the activist community, including the Fair Pricing Coalition of which I am a member, Gilead priced Stribild at over \$28,000 per year annually which is thousands of dollars more expensive than ARVs that are just as effective, but that require more pills to be taken daily.

Exciting new data on a new drug from a new class known as BMS-626529 which is an attachment inhibitor was also presented at CROI. 529 has been shown to have activity against many strains of HIV. Patients were enrolled in a study in which they received Viread plus Isentress with different doses of 529 versus Viread plus Isentress and Reyataz plus Norvir. Of the near 200 patients enrolled in the 529 containing arm, approximately 70% achieved viral suppression with very favorable side effect profiles. This is very exciting news for the heavily treatment-experienced patients who have burned through other HIV ARVs and who need new treatments the most. BMS is to be commended for developing a new drug class for heavily treatment-experienced patients as this is a smaller and thus less lucrative patient population than ARV naïve patients.

As usual, the CROI presentations did not disappoint. The new strategies described are very exciting for so many patients with varying side effects and different degrees of treatment experience as well as adherence issues. Clearly, we continue to make great progress in the fight against HIV/AIDS.

*This article has been updated since March of 2013 to include the latest brand names of all drugs discussed.

