Transcript: New Hope for Treatment Experienced

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At the 15th Conference on Retroviruses and Opportunistic Infections (CROI) in Boston, David Evans talks with UCLA researcher, David Hardy, MD, about the latest data on antiretroviral options for people who are heavily treatment experienced and learns that the treatment landscape has changed radically. To see the video click here.

David Evans: Hi, this is David Evans for AIDSmeds.com. I'm reporting from the 2008 Conference on Retroviruses and Opportunistic Infections in Boston, Massachusetts. With us today is Dr. David Hardy, who is director of the division of infectious diseases at Cedars Sinai Medical Center, and an associate professor of medicine at the David Geffen School of Medicine at UCLA, in Los Angeles. We're going to talk a little bit about treatment for treatment-experienced people today. So with the recent back-to-back approvals of Selzenetry (maraviroc), Isentress (raltegravir), and Intelence (etravirine), it's been a pretty good year for people who are treatment experienced. How have these approvals changed what we can offer people who are heavily treatment experienced?

David Hardy, MD: David, I would say this has been a great year, a phenomenal year, particularly for persons who are treatment experienced with HIV infection—primarily because never in the history of HIV therapeutics have we had the approval of two brand new classes, and what may turn out to be a true next generation NNRTI (Non-nucleoside Reverse Transcriptase Inhibitor); a drug in an old class but working very differently. I think that the possibilities now are wonderful, incredible really, as to what persons who are HIV positive and have had a lot of experience can expect and should be able to achieve, in terms of new treatment regimens. This is a time when we're talking about a paradigm shift, doing away with some of the old medications we have relied upon heavily, that have been kind of tried and true from the past, but are probably no longer going to be, number one, very active, and often times have already caused some amount of adverse events and toxicities in people already. I look forward to these next few months when I can use these drugs together in new, exciting, and hopefully, beneficial ways. The good news is also that the studies so far that we've seen with Selzenetry or maraviroc, and also with raltegravir or Isentress, the integrase inhibitor, is that the side effect profiles have looked great. It's really difficult to find any additional side effects that using those medications add to a HAART regiment (Highly Active Antiretroviral Therapy). With the third drug, etravirine or Intelence, there is some rash associated with that, but it seems to be a very low incidence of rash, and one that has not been responsible for having to stop the medication but in a very small number of people. So not

only are the medications going to work better, because people have never taken drugs like them before—even if they have taken an NNRTI in the case of Intelence; it looks like that drug, for many people will add to a therapeutic regimen—but also, they seem to add very few side effects. So thus is really great news, and I think that people who are HIV positive and treatment experienced have a lot to look forward to in the future.

DE: At the conference this morning, there were some presentations and poster presentations on all three of the drugs, showing how effective they've been over forty-eight weeks. We knew how effective they could be over twenty-four weeks; is that efficacy holding up, and the lack of side effects?

DH: All four of those studies on the newly approved CCR5 antagonist (type of entry inhibitor) Selzentry, and also the new integrase inhibitor, Isentress, and also Intelence, are looking great. At forty-eight weeks we are seeing that in all of those studies on the new medications, the same level of efficacy, of effectiveness, is persisting, that none of these drugs, so far, look like a flash in the pan, they all continue to have good activity, and the patients who were responding well at six months are responding well at twelve months now. And the other good news is that so far there have been no additional side effects seen; so as patients continue to use these medications in clinical trials, the good news that we've been seeing at twenty-four weeks or six months is continuing to be seen six months later at about one year. So, continued great news.

DE: That's excellent. There's another new drug that's not yet approved called Vicriviroc, from Schering; it's an entry inhibitor, a CCR5 antagonist like maraviroc. They've reported forty-eight week data here as well; what does that look like?

DH: That drug looks like it's going to be very interesting as well. The one thing that, in my opinion, looks good about it, is that it so far is being dosed on a once a day basis. Which may be an improvement over the twice a day CCR5 antagonist, the twice a day integrase inhibitor, and the twice a day Intelence. In order to do that though, that drug needs to be boosted with a low dose of Norvir (ritonavir), so that comes with some cost in itself. However, it's assumed that many people who are going to be given a medication like a CCR5 antagonist, like a Vicriviroc, are probably going to be on a boosted inhibitor anyway. So what would be happening there is you kind of get two birds with one stone. The Norvir, the ritonavir would be used to boost not only the protease inhibitor but also the Vicriviroc. Today we saw forty-eight week data—which is nice long-term data—but in a small number of patients, only about a 115-120 patients were being studied here. New doses were being studied than in a previous trial done by the ACTG called 5211. Similar results, actually a little bit better results were being seen, in terms of number of patients with good repression of viral load. Side effect profile looks great so far. From what we could tell, from the study today, only one patient out of the treatment group developed lymphoma—out of about 60, I think, who were treated there. And so far, it's looking promising. This drug still has to catch up, in my opinion, to the other three drugs we just talked about: maraviroc, Selzentry Isentress, the integrase inhibitor, and etravirine, or Intelence. Because it has to be studied in a larger number of people--it's been studied in two relatively small trials so far, each about a hundred and twenty patients. And so far, so good. But we certainly need more experience and longer-term information with it as well.

DE: What are the main issues that you're dealing with now in your patients who are heavily

treatment experienced? Is there any data from this conference that's going to help you address some of those issues?

DH: I think the biggest issue I deal with in many of my treatment experienced patients is…probably the most common across the board is treatment fatigue; taking medications for a long period of time without good results. I think that's one thing that's been disheartening for many people, that the ability to get their viral load undetectable seems to be very tough, very much of a challenge. I think that issue can be certainly addressed by the fact that these new drugs can be used in persons who have taken all the protease inhibitors, or at least almost all the protease inhibitors, the previous NNRTIs like viramune and Sustiva, and many of the nucleosides—and expect to get a good result. These new drugs, really, I think, can challenge that treatment fatigue, that disappointment, that disillusionment, because of the fact that we're using brand new drugs that people should not have resistance to. The other part, also, I think is side effects. I have patients who have suffered many side effects over the years: peripheral neuropathy, gastrointestinal—diarrhea—side effects, problems like that. And they're just tired of having side effects. And again, there I think the good news is that the new medications that we just mentioned seem to have limited side effects and add very little to a regimen. So I think that it's great news on both counts there. The last thing I deal with is tough resistance problems. I often deal with patients that, when we get their genotypes, phenotypes (types of drug resistance tests), and we count up to six to eight mutations in nucleosides, two or three with the non-nucleosides, as many as ten to twelve in the protease inhibitor. Those genotype, phenotype tests look very frightening. Because it doesn't really show many, if any options at all, maybe one, one and half drugs. What we basically did was create a patchwork quilt of partially active medications, but no purely active medications; it was a real guessing game as to whether the regimens you put together were ever going to work. I think that kind of situation is also going to start fading away, and that with these new medications, we can put together… offer patients new medications that they've never taken before, and for that reason, expect that they will have full activity against their viruses. And we know they're combinable, at least the way that drugs don't interact, or that if they do, we know how to dose the medications. And for that reason, we can really take care of that high resistance of virus in patients, and offer an effective, fairly easy to take (as far as pill count and number of times per day), and also tolerable. So I think it's going to be sort of a whole different story. The term "salvage" will hopefully start to fall away. Because that's always been a term I've felt was never that descriptive of people; it's descriptive of their virus and the fact that physicians get frustrated with trying to find something for it, so they label the patient that way. And that's really not a fair way to go. I mean, the main reasons that people have resistance to HIV medication is often not through a fault of their own; they took their medications as told, as prescribed, and the virus still got resistant. It never was suppressed. So my feeling is that we can really work together honestly and hopefully now to achieve undetectable virus in many, many patients.

DE: Great. That's a very hopeful note to end on. And so really, thank you for taking the time to speak to us today and I hope you have a great conference.

DH: Thank you very much, David.