# Transcript: Refining HIV Treatment for New Med Takers

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At the 2008 Conference on Retroviruses and Opportunistic Infections in Boston, David Evans talks with Los Angeles HIV specialist, David Hardy, MD, about research to refine and enhance treatment for people taking HIV medications for the first time. To see the video click here.

David Evans: Hi, this is David Evans from AIDSmeds.com. I'm here at the 2008 Conferences on Retroviruses and Opportunistic Infections. I'm here with 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. Dr. Hardy spoke with us a little bit about treatment-experienced patients, and now we're going to talk a little bit about people who have never been on therapy before. Those are the patients that a lot of scientists call treatment naive. We now have really potent and relatively safe combinations, and I'm wondering, is the bar now set really high for companies that are trying to get their drugs approved for people who are treatment naïve?

David Hardy, MD: The answer to that, simply, I think is yes. There have been some very good studies done with very effective--and getting simpler and simpler--regimens all the time. Probably the best example of that is the medication Atripla, which is a one pill, once a day medication that has a HAART (highly active antiretroviral therapy) regimen, three drugs, all in one pill. Which is probably the easiest, at least daily regimen, that we could ever get to. But the one thing that is very curious about all of this, David, is that many of the studies that we've been seeing for the past couple of years now, and even at this conference, is that the ceiling, the top, of where the proportion or percentage of patients who become undetectable at a year, which is the major cut off point we look at for the effectiveness of a drug, the major test of the effectiveness, still seems to be around eighty percent. That we seem to get it to be around eighty percent, maybe a little over that, eighty-five, but we never seem to get higher than that. And I think certainly one hundred percent is going to be a tough goal; eighty-percent has been something that's been very well established, and certainly good in many ways. But the question I have in my mind is, what's going on with that other fifteen or twenty percent? Certainly, a large part of it is side effects; why people do not become undetectable—well, for a variety of reasons—but probably one of the main reasons is because they can't tolerate the medication. Whether it be because of the gastrointestinal side effects of certain protease inhibitors, often times when they're boosted with Norvir (ritonavir), and they're just very sensitive to that medication even in low doses; whether it's

the central nervous system side effects—the dreams, the insomnia, the grogginess from a Sustiva (efavirenz) regimen, like Atripla (tenofovir, etricitabine and efavirenz), may be the other side of the coin. I think those are still areas for improvement, that we can certainly push that bar up a little higher. But you know it's going to take something pretty powerful to do it.

DE: Well in terms of, if not getting over the bar, at least meeting the bar, there were data presented on—it was actually the first head-to-head data in treatment naives, people who were on a [Norvir] boosted Reyataz (atazanavir) regimen compared to Kaletra (ritonavir plus lopinavir), and I'm wondering if you can tell me about that trial.

DH: Sure. This trial, call the CASTLE study, was large, international; it contained almost nine-hundred patients, so it was very well what we call powered, meaning that we can really believe the results of it, because certainly enough people were in the test, the study, to give us some good information; it's reliable. It basically showed something that really needed to be showed, in terms of what we look upon this drug of Reyataz boosted, in the fact that compared to Kaletra, given twice a day, Reyataz, given once a day with also Truvada (tenofovir plus emtricitabine) in both of the treatment arms, performed identically well. Identically well in terms of suppressing the virus. And that came as a surprise to many of us, because our previous impression was that Kaletra was the gold standard, the most potent drug, and that Reyataz was a little weaker in a sense. But in fact this study, the CASTLE study, that was not true at all. And really showed that boosted Reyataz is a very good option as a once a day medication with half the amount of Norvir too. The other good news I think in that is that even in patients with very high virus, and patients how had low T-cells, that in the case of high virus, the two medications, Reyataz or Kaletra, were exactly the same. And, interestingly, in the case of the patients with low T cell, the Reyataz boosted was better. Which came as a real surprise, because that was one area where Kaletra seemed to always be much, much better. The good news on the other side is that even though the proportion of patients having side effects like diarrhea were small the in the study, they were still greater with patients who took Kaletra than those who took Reyataz. Of course, patients who took Reyataz had a little higher incidence of yellow eyes, yellow skin, what we call jaundice, but not enough that it caused most patients to stop the medication. And then finally, I think the best medication news was a confirmation of something we had also suspected, and that is the effect that Kaletra is known to have, in terms of raising the patient's cholesterol, raising the patient's triglycerides, the kind of fatty substance measured in the blood, was much less with the Reyataz. So it's a really nice confirmation, something that many patients have been experiencing for several years really does ring true. I think that that concern, that patients who have high virus, high amount of virus in the blood, or low T-cells have to take Kaletra really is no longer true.

DE: That's great. So CASTLE compared Reyataz to Kaletra taken twice a day, and Abbott actually presented data here of Kaletra taken once a day versus twice a day. And I'm wondering how that data came out.

DH: That was another important study here as well. It was a study done as a follow up to a previous ACTG study. And in the ACTG study, it was found that the once a day Kaletra did not perform as well as the twice a day Kaletra; it had more side effects, because a larger dose of medication is taken at one time, and therefore there was the concern that once a day Kaletra really isn't not something that one could really offer, that the drug really needed to be taken twice

a day, as most of the studies done with it have shown it's best activity. This study that was done by the Abbott company in fact showed no difference, interestingly, over a year, of patients who received the Kaletra tablets either once a day, or the Kaletra tablets twice a day—both with Truvada as the backbone of both regimens.  And I think it was a little bit of a surprise in some ways, because all previous Kaletra once a day studies had actually shown more diarrhea and a drop off in effect, because patients were stopping their medication because of the diarrhea. This study did not show that for the first time. Although it did show about a fifteen, sixteen percentage of patients that did have moderate to severe diarrhea in both arms of the study, but not one worse than the other. So this was some new data that I think will make some individuals who would really like to use Kaletra to think about, perhaps, either starting it or perhaps switching it to once a day. And just seeing if it works for them.

DE: Looking a little further out to drugs that are not currently approved, are there any new drugs or any new ways to use drugs that we're starting to consider more seriously?

DH: I think in the area of treatment in naive patients, we have, as you already mentioned, set a pretty high bar for new medications. I look forward to, in this coming year, the results of a treatment naive study with raltegravir, Issentris, a drug, the integrase inhibitor that's already approved for patients who have resistant virus, treatment experienced patients. An ongoing study with this drug compared to efavirenz (Sustiva) regimens, with nucleosides, is ongoing. A short-term phase two type study showed initially very good results, and bottom line, equal efficacy as with Sustiva, but less side effects. So the phase III larger number patient studies will hopefully either confirm or refute that. As more people get involved in that kind of trial. So using an integrase inhibitor as a first medication may be a reality, you know, where that medication is going to work best and where we may want to choose to use it first is not clearly worked out yet. Certainly at the treatment naive end of the spectrum, for the person that's just starting medication, there are lots of options, all of which seem to be very good. But the biggest problem right now is side effects. And if the integrase inhibitor could really show equal effectiveness but smaller side effects, maybe we could push that number of people who become untouchable above eighty percent.  Because they wouldn't stop the medication because of side effects. Who knows.

DE: That's great. We'll look forward to that data. Again, thank you so much for speaking to us, and have a great conference.

DH: Thanks very much, David.

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