Transcript: Coming Down the Pike: Expanding HIV Treatment Options

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Peter Staley asks Dr. Joe Eron about the latest data from the 47th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) on soon-to-be-approved Isentress and another integrase inhibitor called elvitegravir, and an entry inhibitor you might inject just once every other week. To see the video click here.

Peter Staley: Welcome, this is Peter Staley with AIDSmeds.com, reporting from ICAAC 2007 in Chicago. I'm here with Dr. Joe Eron, Professor of Medicine from the University of North Carolina at Chapel Hill. You remember Joe from our coverage in Sydney; he gave us a great overview of what was in the pipeline. Welcome, Joe.

Dr. Joe Eron: Great, thanks for inviting me.

PS: We're standing here in front of "PharmaFest," as I call it. At most of these conferences, all the pharma companies set up these huge booths, trying to sell their wares, basically, tell the doctors what's going on with these drugs, and all the HIV drugs are back there mixed in with some antimicrobials.

JE: Lots of antimicrobials here, lots.

PS: …Given the nature of this conference. This morning we had a great session and we're going to talk about that. First we're going to talk about some news on stuff that's in the pipeline, and then in a second videocast, you and I will discuss some news on drugs that are already in the market but might change how people use treatment.

JE: Absolutely. Sounds great.

PS: Let's start with the latest data on a drug that's just about to come out: Isentress, Merck's new integrase inhibitor. We heard some 48-wk data from a phase-2 trial that was a dose-ranging study. Did it add anything to what we know about Isentress?

JE: I don't think it added a whole lot, except that it added some durability information. It was kind of a complicated study, because there were 3 diff does and then at 24 weeks, patients changed to the current dose, which is 400 mg twice a day, and that presumably will be the approved dose, though we don't know for sure yet. But I think it gives us encouragement that the drug will be durable, that we will see prolonged activity in people who suppress below 50 copies.

PS: The drug was approved at 24-week data, but this is—

JE: Well, the drug was actually approved on 16-week data by the FDA, so this is three times as much information. Now a much a smaller group of people, so there's a little bit more variability, we see different numbers of the proportion suppressed below 50. I think the range was 46-64%, depending on the dose.

PS: On a highly treatment-experienced…

JE: Very treatment-experienced. So in this particular study, darunavir wasn't allowed, and tipranavir-ritonavir wasn't allowed, so the background therapy in this phase IIb study was actually quite a bit weaker than in the Benchmark study or the DUET studies that we talked about in Sydney.

PS: It's still showing to be a very powerful drug though, with pretty low toxicities.

JE: Right, I think that the tolerability appears very, very good. I think the one thing we're learning about integrase inhibitors in general is if you have virologic rebound, which, again, doesn't occur that commonly, you need that strong background therapy, but if you have rebound, you are going to see resistance, most likely.

PS: The resistance happens kind of like the non-nukes.

JE: Yeah, people try to make the comparison, like the non-nukes, like the PIs. Resistance occurs in the majority of patients that rebound, so that's similar to the non-nukes. On the other hand you tend to see multiple mutations, with a primary mutation and compensatory mutations, which is a little bit like the protease inhibitors. So I think we're gonna have to say, "it's like the integrase inhibitors."

PS: Staying on the same class, integrase inhibitors, we also heard about probably the next one that will come through the pipeline. Gilead has a drug, and they had follow-up data from again, a very highly treatment-experienced group, phase II dose-ranging study for elvitegravir. Um, "el-VIGH-tegravir…"

JE: Right, like "El*vi*ra, Mistress of the Dark" or whatever that is. El*vi*tegravir.

PS: Okay. Key differences between Isentress and elvitegravir?

JE: Okay, so one big difference is of course that the raltegravir, Isentress, is likely about to be approved. And elvitegravir is just starting their Phase III program. So that's a big difference. But in terms of clinical differences. One: the raltegravir is glucuronidated, so it's metabolized in a different way, so it's going to have different and probably fewer drug-drug interactions. On the other hand it has to be given BID, elvitegravir…

PS: Twice a day…

JE: Yes, twice a day, sorry. Elvitegravir is metabolized by P-450 which is the same enzyme that metabolizes protease inhibitors, so it's going to probably have more drug-drug interactions, but it is going to be combined with ritonavir, and it's going to be boosted, so it's going to be given once a day. So that's a substantial difference.

PS: Isentress you don't need Norvir and this one you're going to.

JE: That's exactly right. So this drug is being developed specifically with Norvir. So it's not being developed without Norvir.

PS: What about the comparative resistance profiles, are they going to be cross-resistant?

JE: That's a great question. I think Vicki Johnson, later in the session this morning went over some of the resistance to the integrase inhibitors and I think probably the safest thing to say is it looks like there's likely to be a substantial degree of cross-resistance. It may not be 100 percent, there may be patients who fail one of these, like raltegravir, and still might respond to elvitegravir. But I think for us as practicing clinicians, and for people with HIV, I wouldn't hold hope that we could obviously sequence these drugs. It looks like there's going to be a substantial amount of cross-resistance.

PS: We heard some very exciting news about a drug in very early development, but it's very different from every other drug people with HIV are used to. It's PRO 140, from Progenics, a small little company. They had follow-up data from…it's a CCR5-targeting drug, but it's different. It's a monoclonal antibody. Can you explain…at IAS they had stunning data, where they said you take an injection of this stuff, and the viral load goes down 90% and it stays down 90% for two to three weeks after one injection.

JE: So this is a CCR5 inhibitor, so it attacks the same step in the virus life-cycle as maraviroc, Selzentry, and vicriviroc. But it works in a different mechanism.

PS: And these are all entry inhibitors.

JE: These are entry inhibitors. And all three of these drugs bind to CCR5 but this PRO 140 actually binds in a different way, blocking the receptor in a different way, and because it's an antibody it has a big plus and a big minus. The big plus is it has a very long half-life so probably it's going to be dosed once a week, maybe even once every two weeks. So that's a big plus. The negative, of course, is that it can't be swallowed, so it's never going to be a pill. It's either going to be an IV injection, an IV infusion, or perhaps a subcutaneous injection.

PS: And they say the next trial they're going into they're going to use it sub Q…

JE: A subcutaneous infection, which…

PS: Which people can give themselves, hopefully.

JE: Sure. People should be able to give it to themselves. If it's one shot once a week or every other week, that's very different than currently with Fuzeon, where it's one shot twice a day. But we need to learn a lot more. How stable is it, are patients going to have to mix it themselves—all those sorts of things. But I think the promising data was just as you said. It wasn't a new study; it was the same study that was presented at Sydney. So it basically showed this prolonged activity with a single dose, and it showed that, maybe that even higher doses might even get a little more activity. So I think that's what the company is going to be shooting for.

PS: Well, it's one that we're definitely going to be following. Thanks for this overview of the experimentals. We're going to get right back to you on the currently approved drugs that have had some news out. We thank you for joining us, once again.

JE: Great, thank you very much. It’s my pleasure.
