Transcript: Are We Starting Treatment Early Enough?

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In this videocast from the International AIDS Society Conference in Sydney, Peter Staley interviews Dr. Fred Gordin from George Washington University, who explains why many experts think we might be waiting too long to put patients on HIV treatment. Dr. Gordin is also leading the effort to launch a large clinical trial called START, which hopes to determine if starting treatment at higher CD4 counts will save more lives. To see the video click here.

Peter Staley: Good evening from Sydney. This is Peter Staley with AIDSmeds.com and I'm here with Dr. Fred Gordin who is Chief of Infectious Diseases at George Washington University?

Dr. Fred Gordin: The VA Medical Center and George Washington University. Correct.

And you just gave a very interesting talk this evening titled "Is An Early Treatment Study Important Now?" I was actually the founder of TAG, the Treatment Action Group, back in 1992 and our organization pushed very hard early on for a trial to answer this question of "Should we be starting treatment earlier?" It's been a raging debate at almost all of these international AIDS conferences since the early '90s or mid '90s and the pendulum keeps swinging back and forth. Summarize what you spoke about tonight.

Well, I think the pendulum is a good analogy. Clearly in the early days of HIV/AIDS in the late '80s and early '90s before we had effective therapy, the emphasis really was, appropriately, on people with advanced infection who were dying from major infections, malignancies, and really both clinicians, patients, and researchers focused in that area. After the access to better drugs with first the protease inhibitors and then other agents people started to ask, "When should we use these drugs? Should we wait until people are very sick—one hundred, two hundred CD4 cells? Should we intervene at three or four hundred or really even at the time of infection?" So I agree that question's been unanswered and it's trying to be a balance between the benefits of the drug. And there's almost no other infectious disease where we have a drug or a therapy that works and we don't use it. But the drugs have toxicities with them, as obviously you and all of your listeners and readers know very well, and so how do you balance treating the virus with the problems of adherence, drug toxicity, not even just cost, but really the ability of people as individuals and society to take care of a large group of people on medicines that may not benefit from them.

The real story we're hearing more and more about though are these non-AIDS defining morbidities… that people with HIV are dying of kidney-, liver-disease, cancer, heart disease—not the traditional AIDS-defining illnesses—and they're doing so at higher rates if they're off treatment.

Exactly. So AIDS of course is not a single illness. HIV is a virus, but AIDS, for definition reasons, was invented as a catch all of very serious illnesses. And so in the early days, again, that made sense. It was an indicator of severe disease from HIV. But what we've learned from numerous cohort or studies or groups of people as well as some controlled trials is that people at higher CD4s, 350 through, say, 600 or 700, when you match them against non-HIV infected people or you look at people on therapy versus off therapy, HIV-infected people off therapy have higher rates of cancer, higher death from cancer, more liver disease, including severe, what's called, serosis, renal disease that can be major resulting in dialysis, as well as cardiac events and, overall, more death. I don't want to scare people. The absolute numbers are relatively low but they're higher than they should be, and so the question again is "Are they related to HIV?" I think the clear answer is yes and there's very little debate about that. But what's not clear again is should we be treating and what would the benefit of treatment in terms of reducing these events versus all the problems that go along with treatment. That's really the question right now.

Aren't we still dealing, though, with a theoretical speculation about why HIV is causing these traditional non-AIDS related diseases, specifically cancer, and what it is about immune stimulation that might be doing that?

Very good question and the answer's really not in. I've been at two different workshops that NIH sponsored in the past four weeks on this. There's no answer, I just want to start with that. So whether the virus is interfering, which we know it does, with the immune system, whether it's interfering with other, what are called, inflammatory markers, these are things that basically show inflammation in the body in a way that allows cancer cells, if you will, to thrive, I'll use that word, it's not very scientific, without other parts of the immune system being able to recognize this is a cancer cell, a malignant cell, and kill it early on. Whether inflammation in the coronary vessels result in more heart disease, more heart attacks—these are theories that a lot of blood that's been saved from studies that have gone on—SMART, which was a very large trial of 5000 people and other studies—is now being evaluated in the laboratory to try to understand kind of the answer to your question. So "we don't know" is the real answer.

So now people are finally talking about launching a trial. They've given it a great name. It's called START, but what's the status on it? Are they still arguing about it?

So it's called START, Strategic Timing of Antiretroviral Therapy. It would be targeted at people with high CD4 cells of over 500 half of whom would start immediately and half would wait until they reached 350.

CD4 cells?

CD4 cells, 350. Correct. NIH has stated that they're interested in the study. It's going through the

final approvals and sign-offs so that all studies that the NIH sponsors, while the outside investigators create the study, inside NIH they want to make sure that it's good science, and that's appropriate. So it's going through those stages now. Dr. Fauci, when asked this evening by one of the TAG members, Mark Harrington, "would he fund the study?" said "yes," they plan on funding the study. So I'd say it's in negotiations in terms of the final design, the final amount of funding but we hope to actually be enrolling patients by hopefully October/November.

It was a pretty dramatic moment when Mark mentioned that he had been in Fauci's office in 1997, asking him to do the same trial and Fauci said, "Sure I want to do it." But it never happened and he said it never got to his desk, basically.

Basically he said that, but in some ways I think it probably would have come up with a different answer back then. The drugs we have now are clearly more affective, easier to take and less toxic. So back then if people with very high CD4s had started on therapy, many of them would have stopped therapy fairly early and I don't think that would be the situation today. So for whatever reason it didn't happen then, it was probably was good that it didn't.

One last question. There was a lot of discussion also about the possible public health benefits of starting a larger group of people earlier on treatment in the sense that we would actually reduce HIV transmission.

Yeah, that was quite exciting work from Julio Montaner in British Columbia. His group is apparently modeling what would the benefit be, and I think most people agree there would be a lot of benefit without question, but that we shouldn't treat people who don't benefit themselves. There's good data that people who are on antiretroviral therapy with low viral loads are less able to transmit the virus, so looking at a population, the more people on therapy, the less transmission there'd be. It's still not 100% safe, people need to use appropriate precautions, but it would still be a positive gain if one could show that the individual benefits as well as society.

Well thank you very much and thank you for your stimulating talk tonight on this endless pendulum of when to start treatment.

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