Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/heart-matters/a-discussion-on-statins-to-lower-cvd-risk-for-hiv-patients/15746/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

A Discussion on Statins to Lower CVD Risk for HIV Patients

Dr. Cheeley:
You're listening to *Heart Matters* on ReachMD. I'm Dr. Mary Katherine Cheeley, and joining me today to discuss the key findings from the REPRIEVE study, which looked at the risk of heart disease in patients with HIV, is returning guest Dr. Steven Grinspoon. He is a Professor of Medicine at Harvard Medical School in Boston.

Dr. Grinspoon, it's lovely to see you again.

Dr. Grinspoon:
Hey, thanks for inviting me back. I really appreciate it.

Dr. Cheeley:
I am so excited for this discussion today, so let's jump right in. Tell me about the REPRIEVE study. What were the outcomes we were looking for? What question were we hoping to answer?

Dr. Grinspoon:
Right. So as we mentioned last time, the risk of cardiovascular disease is upward of two-fold increase among people living with HIV, and we think that's in part due to traditional risk factors, but also in part due to nontraditional risk factors, such as inflammation, residual immune activation, the body's effort to fight the virus, if you will, and going on antiretroviral therapy, which is so important, doesn't knock that down entirely, so we're left with a population that is relatively young, who has increased cardiovascular disease without an increased, necessarily, predicted cardiovascular risk using traditional risk scores. And we were thinking what strategy might be appropriate to prevent heart disease in that group, and we settled on a statin because it has both effects to lower LDL and traditional risk, but also effects to reduce inflammation and residual immune activation. And then we said, "Which statin would be safe?" Pitavastatin is a statin that is known not to interact with antiretroviral therapy. There are other ones as well, but that one is not metabolized by the SIP system.

So we endeavored to prevent heart disease in a global study across 12 countries, 7,769 participants who were followed on average five years, and the study was stopped early by the DSM-V in very late March for efficacy and without any safety signal beyond anticipated. And basically, the results showed that MACE, Major Adverse Cardiovascular Events, which includes heart attacks, strokes, cardiovascular death, revascularization, those were prevented by 35 percent in the pitavastatin group versus placebo. And a second key endpoint was MACE or all-cause death. That one was reduced by 21 percent in the pitavastatin versus placebo.

Dr. Cheeley:
Yeah, so tell me a little bit more about the patient population. I want to make sure that we think about the right group of folks. Was there anything special about these groups? Did they have comorbidities? Did they have anything? Or was it just if you're living with HIV, let's put you on a statin.

Dr. Grinspoon:
So the inclusion criteria were 40 to 75. The reason we picked 40 as the lower end is because the ACC pooled cohort equation doesn't go down below 40, and there's probably really relatively lower risk in that group, so 40 to 75 with a low-to-moderate risk. Those with a higher predicted risk, like above 20 percent, we told them they should be on a clinical statin, and it wasn't equipoise, but for the lower-to-moderate, the average is 4.5 percent. And they had to have a CD4 more than 100, but they had to be on ART, so this is an ART-treated group seemingly well with a modest ASCVD risk. The baseline LDL was only 108, which is not particularly high. Their CD4 count was healthy, and 31 percent were women.

And only 35 percent were white, so it was really diverse across multiple countries, Sub-Saharan Africa. So I think the population represents the global population that's relevant for primary care prevention. And in that group, we showed that it works. The number needed to treat was 106, about a hundred, which compares well to aspirin in 300s, the antihypertensives in the 200s. It is true that the event rate went up as your baseline ASCVD risk went up, within the low-to-moderate range, there were more events, for example, in the placebo group if you had a baseline risk of 10 to 15, and zero to two, so that means that as the number needed to treat went down, the higher your baseline risk. So those data are published in the paper, and I think clinicians can make an individual decision about this, but we think that this is practice-changing in that for that group, even relatively young with a modest ASCVD risk or low-ish LDL, you will save lives and prevent MACE by starting a statin therapy.

Dr. Cheeley:
I think it's really interesting, and I don't want it to be lost in our discussion that this is a relatively healthy population. In our last discussion we talked about HIV being a risk equivalent. It's great that we add a statin, and we can reduce MACE, but it further proves that even like you're saying with low risk, moderate—okay, we know statins help—but low-risk living with HIV is a risk enhancer or a risk equivalent probably even at this point. I think this is—I agree with you, practice changing. We now can do even better for folks living with HIV to reduce their comorbidities or critical outcomes that they could have that are not associated with what is considered to be one of their bigger disease states, meaning HIV.

For those of you just joining us, you're listening to *Heart Matters* on ReachMD. I'm Dr. Mary Katherine Cheeley, and I'm speaking with Dr. Steven Grinspoon about the REPRIEVE study.

All right, let's jump right back in. Let's look at the outcomes and the findings that you had. You mentioned side effect profile before. Did you find any additional safety signals, anything that made us think a little bit more about adding statins to patients living with HIV?

Dr. Grinspoon:
So we did find two things. We did find it increased risk of diabetes. The diabetes prevalence for new diabetes was 5.3 percent in the pitavastatin group, but four percent in the placebo group, so the difference was about one percent, and if you looked at it as a risk rate in both the placebo and the pitavastatin, the confidence intervals crossed what the CDC expects for people in that age range. So yes, there is a small prevalence of increased diabetes. It's not unlike other statin studies. And interestingly, in the relatively small group of people with diabetes who got MACE, it was half as much in the pitavastatin group than in the placebo group.

So we interpret this as a class effect and something people should know about. We're going to do more studies about who is at risk specifically for diabetes. There were more muscle aches and pains, but only two percent versus one percent, and very, very few were significant enough to withdraw from the study, and very, very few were serious, grade three or four, so the vast majority were mild-to-moderate. And there was a very large almost equivalent prevalence in the placebo group, which really tells you that a lot of the statin stuff is not specific. And you have to do an RCT to understand the real relative differences. As you know, this is known in statin studies. There have been studies to show that if you stop it and start it again, sometimes it's not there.

You can try a different statin. Our results were specific to pitavastatin because that's what we used, but our general feeling is that if that's not available, there are other statins, pharmacologically, which don't interact with ART—for example, pravastatin particularly—and then also, atorva and rosuva have some minor considerations with protease inhibitors but can generally be used, so there are a bunch of statins that could be used in areas where this is not available.

Dr. Cheeley:
Yeah. Like you mentioned, both of those are expected. We have seen this with other statins, so this REPRIEVE study finding it again shows us, okay, it really truly is a class thing. Statin intolerance is one of the things that I hang my hat on. I think that there's so much more work that needs to be done in that space, but it, to me, further proves the point that we have to be able to get someone on something they can tolerate because we've proved—you guys have proved in this study—it works when you take it, and so, if we can find something to lower atherogenic lipoproteins, then we're going to reduce events in these patients.

Any other key findings that you guys found?

Dr. Grinspoon:
Some interesting things. When we looked within MACE, it was a pretty consistent effect across strokes, heart attacks, so it was a very kind of equivalent effect of the different types of MACE. We found that there were equal numbers of strokes and MIs, so strokes were a big component of our MACE. It brings up that that should be studied further.

Another really interesting aspect is that a reduction in MACE was about twice what you'd predict for the change in LDL alone. So there are nomograms from the CTC collaborative, which show for X change in LDL there should be Y reduction in MACE, and we reduced LDL 30 percent, about 30 milligrams per decilitre, pretty standard. If you plot that along the nomogram, you'd expect a 17 percent

reduction in MACE, and we got a 35 percent.

Dr. Cheeley:
As we close, what future is there for patients living with HIV and statins?

Dr. Grinspoon:
Well, I think this is probably going to be a lifelong treatment, and we know that people can take statins lifelong because we've had 30 years of statins and people taking them. I think there's going to be a whole movement now for people to take their ART and a statin probably, and that's a combination that's well-tolerated, and probably, going to do a lot of good for people. I think other strategies will now need to be tested versus statin. I think bempedoic acid, which you need if you're statin-intolerant—well, there wasn't a lot of statin intolerance—and the MACE reduction rates in bempedoic acid are not as high as in statins. Other fancier anti-inflammatory, canakinumab, etc., would need to be tested against statins, and they have some risk for infection.

So I think statins makes sense, and for individual people, there may be different choices and options and discussion, but I think our findings will hold for the vast majority of people.

Dr. Cheeley:
These are exciting, exciting times in the world of cardiovascular risk reduction as we look at these subpopulations of people that haven't had answers before, so thank you so much for doing the study, for doing the hard work. It truly has moved cardiovascular risk reduction in HIV care forward. I am so grateful.

Thank you to my guest, Dr. Steven Grinspoon, for joining me again today to talk about this awesome topic. It has been a lovely discussion.

Dr. Grinspoon:
Thank you so much. I really enjoyed it.

Dr. Cheeley:
For ReachMD, I'm Dr. Mary Katherine Cheeley. To access this and other episodes in our series, visit ReachMD.com/HeartMatters where you can Be Part of the Knowledge. Thanks for listening.