www.medscape.com

Darunavir Linked to Heightened Heart Disease Risk

Heather Boerner | February 17, 2017

SEATTLE — People living with HIV who have been on a ritonavir-boosted darunavir protease inhibitor regimen for more than 5 years might be at increased risk for heart attack, stroke, invasive heart surgery, or sudden cardiac death, new research suggests.

The analysis from the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study shows that ritonavir-boosted darunavir is associated with a 59% increase in risk, but researchers found no such association for ritonavir-boosted atazanavir. They did not have enough data to include cobicistat.

"I can't say to a patient that if you stay on this drug, you will develop a myocardial infarction. I can only say that it increases your risk this much," said investigator Lene Ryom, MD, PhD, from the Centre for Health and Infectious Disease Research at the University of Copenhagen.

The study findings were presented here at the Conference on Retroviruses and Opportunistic Infections 2017.

Results from D:A:D have shown that the antiretrovirals abacavir and didanosine are associated with an increased risk for heart attack, and that tenofovir is associated with serious liver and kidney disease, as previously reported by *Medscape Medical News*.

In their study, Dr Ryom and her colleagues followed all 49,709 D:A:D participants to determine how many had a heart attack, stroke, major heart surgery, or died of cardiac arrest since 2009, and identified 1157 participants.

On univariate analysis — adjusted to control for other potential causes of cardiovascular disease, such as baseline diabetes, body mass index, dyslipidemia, and CD4 count — the risk for heart disease was 59% higher for every 5 years on the ritonavir-boosted darunavir regimen. For patients on a regimen of ritonavir-boosted atazanavir, the increase in risk was negligible.

Even after adjustment for smoking status, liver function, variation in CD4 counts, BMI, kidney function, and dyslipidemia, ritonavir-boosted darunavir was independently associated with a 53% increase in the risk for heart disease.

"The increase in risk was gradual but statistically significant," Dr Ryom reported. "The strength of this association is similar to that seen with first-generation protease inhibitors, so it's not minor."

Scientific Skepticism and Practice Change

The results might lead to some practice changes. "As a practicing physician, the findings are very significant in terms of the way we will be thinking about drug choice when selecting patients' regimens," one member of the audience told the panel after the presentation.

But, as with any new data, the results also raised concerns from the crowd about study methods and about the reliability of observational data.

The drugs we use are actually quite a small component of overall risk.

"Safety is our highest priority," Janssen said in a statement sent to *Medscape Medical News*, "and with an extensive clinical trial program and more than 10 years' clinical experience on the market, our surveillance program has not suggested an association between darunavir and cardiovascular events."

Results from the D:A:D study on abacavir led to years of replication studies and debate before physicians and researchers finally accepted the D:A:D findings, said Peter Hunt, MD, from the University of California, San Francisco School of Medicine.

He said he expects the same thing to happen now.

"It's an early observation, so there's no proof that darunavir is increasing the risk for cardiovascular disease," Dr Hunt told *Medscape Medical News*. "But there is an early signal that clinicians will now start to think about when they select regimens."

In the meantime, he said, he plans to focus on the things that we already know cause heart disease in people with HIV, such as smoking, cholesterol, and blood pressure.

"The drugs we use are actually quite a small component of overall risk," he pointed out.

Still, Dr Ryom said that when she returns to her patients in Copenhagen, she will start to consider individual risks and discuss these findings with patients.

Can you afford for the individual patient to take any additional risk?

"When a drug-safety issue is raised with a rigorously defined end point, I think you need to consider it, especially in patients who are at high risk already," she said.

"Can you afford for the individual patient to take any additional risk? Or should you try to find something more neutral in terms of CVD risk factors? It's something you should discuss with the patient themselves," she said.

Dr Hunt reports receiving funding from Gilead Sciences, ViiV, and Merck. Dr Ryom has disclosed no relevant financial relationships.

Conference on Retroviruses and Opportunistic Infections (CROI) 2017: Abstract OA 128LB. Presented February 16, 2017.

Send comments and news tips to news@medscape.net.

Cite this article: Darunavir Linked to Heightened Heart Disease Risk. *Medscape*. Feb 17, 2017.