# Abacavir and Tenofovir Associated With Heart Troubles

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A new study of HIV-positive military veterans has found that abacavir (found in Ziagen, Epzicom and Trizivir) is associated with an increased risk of heart attacks, whereas tenofovir (found in Viread, Truvada and Atripla) may increase the risk of heart failure. The study, published online April 21 in the journal AIDS, may add a new layer of complexity to the already unclear process of selecting antiretrovirals (ARVs) that won't heighten the risk of cardiovascular disease (CVD).

There has been an ongoing debate over whether abacavir increases the risk of heart attacks. Back in 2008, researchers first presented data showing that people currently taking abacavir had about twice the risk for experiencing a heart attack as people not currently taking abacavir.

Subsequent studies echoed these results. Specifically, they showed poorer efficacy with abacavir in people starting ARV therapy with viral loads over 100,000 copies. As a result of these combined data, the committee tasked with developing HIV treatment guidelines for the U.S. Department of Health and Human Services (DHHS) downgraded abacavir from a "preferred" regimen to an "alternative" regimen.

Other more recent studies, including two large multi-study analyses—one by abacavir's maker, ViiV Healthcare, and the other by the U.S. Food and Drug Administration (FDA)—found no increased CVD risk among people living with HIV using abacavir. Needless to say, the conflicting results have left some confused about when to prescribe the drug, especially regarding people with underlying risks for CVD.

One explanation that's been given for the inconsistent study results is the possibility that people taking abacavir in the studies showing a heart attack risk just happened to have higher risks anyway. For example, it has been known that tenofovir can potentially exacerbate kidney problems—a major risk factor for CVD—as a result, health care providers may have put their at-risk patients onto a regimen containing abacavir instead of tenofovir to circumvent the problem. In other words, it may have been underlying kidney disease, not the abacavir, the contributed to the increased heart attack risk in the studies.

To get at this question, Andy Choi, MD, from the University of California in San Francisco, and his colleagues analyzed data from nearly 11,000 HIV-positive people receiving care in the Veterans Affairs (VA) health system.

As with most VA studies, the vast majority were men; in this case, the average age was 49. It was also a racially diverse group. Roughly 30 percent of the participants were taking a regimen containing abacavir, and 39 percent took tenofovir.

In addition to a straight comparison of tenofovir with abacavir, Choi and his colleagues considered the likelihood of VA health care providers preferentially selecting abacavir for their patients with kidney problems. Researchers established evidence of such practices very early: The percentage of those with chronic kidney disease on abacavir was nearly twice that of those taking tenofovir.

After accounting for this and other potential risk factors, such as diabetes, high blood pressure and coinfection with either hepatitis C virus (HCV) or hepatitis B virus (HBV), Choi's team still found that recent abacavir use increased the risk for a heart attack by 49 percent.

People taking tenofovir did not have an increased risk of heart attacks, but they did have a significant added risk for heart failure, whereby a person's heart is no longer able to adequately pump blood through the body. The risk of heart failure among tenofovir users was increased 82 percent. This added risk was somewhat larger in those with chronic kidney disease or other heart disease risk factors, such as diabetes and high blood pressure.

The authors note that their findings add more complexity to the evolving story about abacavir and present a potential new twist in the safety profile for tenofovir. However, given the design of the study and population included in the analysis, these results can't be applied to women, non-veterans or those without guaranteed health care. The authors also acknowledge that retrospective studies looking backward in time at a group of people—rather than blindly randomizing one group to one regimen and another group to a different regimen and then seeing what happens—may be more prone to false results.

They conclude, however, by stating:  "These findings suggest a need for raising the level of vigilance in the HIV community, continued ''comparative effectiveness' studies to characterize the cardiovascular risk of specific ART agents, and studies to identify mechanisms underlying these relationships."

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