

Clinical Coordinating Center
Massachusetts General Hospital
50 Staniford Street Suite 750
Boston, MA 02114

Data Coordinating Center
Massachusetts General Hospital
165 Cambridge Street Suite 400
Boston, MA 02114

Cardiovascular hazards of abacavir- versus tenofovir-containing antiretroviral therapies: Insights from an analysis of the REPRIEVE trial cohort

Emma Davies Smith, Carlos Malvestutto, Heather Ribaud, Markella Zanni, Steven Grinspoon and colleagues
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Background

Effective antiretroviral therapy is available for people living with HIV (PWH). However, large observational studies have reported that some therapies are linked with increased risk of heart disease events like heart attack and stroke. Despite belonging to the same class of antiretroviral therapy drugs known as nucleoside reverse transcriptase inhibitors (NRTIs), the drug named abacavir (ABC) has been associated with a 2-times increase in the risk of heart attack while the drug named tenofovir disoproxil fumarate (TDF) has not. Since these links were discovered, new NRTIs like the drug named tenofovir alafenamide (TAF) are now available, but their impact on heart disease risk is not well understood. Because people living with HIV already have twice the risk of heart disease events compared to the general population, it is important to understand how antiretroviral therapy further contributes to the risk of heart disease events.

The Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) enrolled PWH between ages 40-75 with low-to-moderate traditional heart disease risk, randomized these participants to a statin medication called pitavastatin or to placebo (a pill that contains no medication), and followed these participants for, on average, 5 years, to see if they developed heart disease events like a heart attack or stroke. Main findings from REPRIEVE were that [statin therapy reduced heart disease events among PWH by 36%](#), prompting guideline changes recommending statin use in PWH. REPRIEVE also collected high-quality data from all participants on their use of antiretroviral therapy before and during the study which can be used to investigate these risks.

Goal of the Study

The goal of this study was to use the antiretroviral therapy data collected from REPRIEVE participants to compare the risk of heart disease events between three commonly used NRTI drugs: abacavir (ABC), tenofovir disoproxil fumarate (TDF), and tenofovir alafenamide (TAF).

Methods

Unlike statin medication in the REPRIEVE trial, antiretroviral therapy was not randomized. This means that some participants may have chosen their antiretroviral therapy because they have other health conditions that restrict which drugs they can use. Some of these health conditions, like kidney disease, are also linked to higher heart disease risk. If some people living with HIV must take ABC because their kidneys cannot handle TDF, for example, it can make ABC look artificially riskier than TDF. This study tried to avoid unfair comparison by adjusting how much participants with certain risk factors count towards their drug's risk.

People living with HIV also commonly change their antiretroviral therapy for several reasons including concern for side effects, harmful interactions with other drugs, ease of administration, or preference. If someone changes from a higher-risk drug to a lower-risk drug during the study, it can make the higher-risk drug appear less risky. To avoid this, adjustments were made to capture differences between those that changed during the study and those that did not.

Findings

After accounting for participant characteristics like age, sex, and medical history that may contribute to heart failure risk and changes to antiretroviral therapy during the study, the risk of abacavir was found to be at least 1.4-times higher than the risk of both types of tenofovir when considering all heart disease events captured by REPRIEVE at the same time. There did not seem to be a difference in risk for the two types of tenofovir. However, TAF appeared higher risk than TDF for heart attack when

REPRIEVE Trial Website: reprivetrial.org

The findings shared in this summary are from the REPRIEVE population at a specific point in time. These findings are descriptive and not intended to change clinical care. If you have questions about what you've read, please talk to members of the REPRIEVE study team at your local site or a health care provider



MASSACHUSETTS
GENERAL HOSPITAL

Clinical Coordinating Center
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165 Cambridge Street Suite 400
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considered on its own, and TDF appeared higher risk than TAF for stroke. Most notably, the risk of heart attack when using abacavir was 3.5-times higher than TDF.

Summary

It is important to understand how antiretroviral therapy contributes to heart disease risk in people living with HIV so individual needs can be met and risks effectively managed. This study used data on antiretroviral therapy collected from all participants in the REPRIEVE trial to understand how the risks of commonly used drugs known as NRTIs differ. Findings demonstrate that abacavir meaningfully increases the risk of heart disease events when compared to different forms of tenofovir, and indicate it would be a good idea to avoid abacavir use to limit risk in people living with HIV.

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