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Inflammatory, Cardiac, and Lipid-Related Biomarkers in Relation to Residual MACE Risk in the REPRIEVE Trial

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Background

People living with HIV (PWH) have an increased risk for developing heart disease. Although REPRIEVE showed that pitavastatin (a cholesterol lowering medication) lowers this risk, our team wanted to better understand why some risk remains by studying certain markers in the blood (blood biomarkers).

Goals of the Study

We aimed to evaluate whether blood biomarkers related to inflammation, heart function, and cholesterol levels could help identify PWH who remain at higher risk for cardiovascular disease controlling for statin therapy. The blood biomarkers we assessed were inflammatory biomarkers such as high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), cardiac biomarkers such as high-sensitivity troponin (hs-TnT), N-terminal pro-B-type natriuretic peptide (NT-proBNP) and lipid biomarkers such as apolipoprotein B-100 (ApoB-100), oxidized low-density lipoprotein (oxLDL), and lipoprotein(a) (Lp(a)).

REPRIEVE enrolled PWH between ages 40-75 with low-to-moderate traditional heart disease risk, randomized these participants to a cholesterol-lowering medication called pitavastatin or to placebo (a pill that contains no medication). Participants were followed for heart disease events like a heart attack or stroke. Main findings from REPRIEVE were that statin therapy reduced heart disease events among people with HIV by 36%, prompting guideline changes recommending statin use in PWH.

➤ The participants:

- 7,005 REPRIEVE participants with blood biomarker data available at study entry (90% of total)
 - Median follow-up time: 5.6 years
 - On stable antiretroviral therapy with CD4 + T-cell count (CD4) >100 cells/mm³
 - Low-to-moderate traditional risk for CVD (CVD) by the Pooled Cohort Equations (PCE)

The Findings:

- Participants had elevated markers of inflammation (49% for hs-CRP, 33% for IL-6), and elevated markers for heart stress or injury (35% for hs-TnT, 33% NT-proBNP)
- Higher baseline levels of several biomarkers were associated with a greater chance of experiencing a major cardiovascular event during follow-up
- The strongest associations were seen with Interleukin (IL)-6 and high-sensitivity cardiac troponin T (hs-cTnT), which are markers of inflammation and heart muscle injury, respectively. Participants with the highest levels of these biomarkers had twice the risk of experiencing a cardiovascular event compared to those with lower levels
- The biomarkers associations remained even after accounting for traditional cardiovascular risk factors and statin treatment
- Combining several biomarkers improved the ability to identify participants at higher risk beyond traditional cardiovascular risk prediction alone

In Summary: These results suggest that biomarkers may help identify PWH at higher risk for future cardiovascular disease events and may guide future research into additional therapies to further reduce cardiovascular disease risk.

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