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Clonal Hematopoiesis and Major Adverse Cardiac Events in People With HIV: Insights From the REPRIEVE Trial

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Background

People with HIV (PWH) have a higher risk of heart disease. The REPRIEVE study showed that the cholesterol-lowering drug pitavastatin helped lower the risk of major heart disease events (MACE), like heart attack or stroke, in PWH who were already on HIV treatment with low-to-moderate heart disease risk. Clonal hematopoiesis of indeterminate potential (CHIP), an emerging risk factor for cardiovascular disease in the general population, has been reported to be more prevalent in PWH.

Goals of the Study

The goal of the study was to investigate whether CHIP increases the risk of MACE among PWH, as well as whether HIV-associated factors like CD4+ levels were associated with greater CHIP prevalence among PWH.

REPRIEVE enrolled PWH between ages 40-75 with low-to-moderate traditional heart disease risk, randomized these participants to pitavastatin or to placebo (a pill that contains no medication). Participants were followed for, on average 5 years, for 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.

➤ The participants:

- 4490 REPRIEVE participants who had whole-exome and targeted CHIP sequencing analyzed
 - Low-to-moderate traditional heart disease risk, no known cardiovascular disease
 - Median age at enrollment: 50 years
 - 37% women and 84% men

The Findings:

- 837 (18.6%) had CHIP mutations, with 385 (8.6%) at variant allele fraction $\geq 2\%$ and 61 (1.4%) at variant allele fraction $\geq 10\%$
- No specific antiretroviral therapy regimens seem related to CHIP presence, but CD4+ nadir and CHIP variant allele fraction are associated, although the direction of causality needs further investigation.
- Large CHIP was associated with 3× risk of MACE, 5× risk of heart attack, and 15× risk of revascularization (a procedure to open blocked blood flow). These risks were not decreased by pitavastatin treatment, but need to be interpreted with caution, given the small number of events

In Summary: In PWH in the REPRIEVE trial who were low-to-moderate risk for cardiovascular disease, CHIP was not associated with increased risk of future MACE. However, a large CHIP was associated with increased risk of heart attack and revascularization.

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