

REPRIEVE Study FAQs

The REPRIEVE (A5332) trial is the first-ever, large scale clinical trial to test a strategy to prevent heart disease among people with HIV. REPRIEVE showed that pitavastatin prevents heart disease in this population. REPRIEVE participants have contributed meaningfully to the attainment of new medical knowledge relevant to improving the health span of people with HIV.

FAQ About the Results of REPRIEVE

1. What were the main findings of the REPRIEVE trial?

- a. REPRIEVE results revealed that pitavastatin, a statin medication and the heart disease prevention strategy tested in the trial, reduced major heart disease events like heart attacks and strokes in people with HIV by 36% compared to placebo. Pitavastatin also reduced major heart disease events or death from any cause by 23% compared to placebo.

Pitavastatin was effective in both men and women, and the study participants experienced very few safety events.

The results of REPRIEVE are helping clinicians to better support the heart health needs of people with HIV, and there are many more questions that the REPRIEVE Team is working to answer in the future.

2. Why was pitavastatin used in REPRIEVE, and which statin medication is right for me?

- a. Revised treatment guidelines incorporating data from REPRIEVE that recommend statin therapy in this patient population were recently announced and are available [here](#). Pitavastatin was chosen for REPRIEVE because it has minimal interactions with antiretroviral therapy and has been shown to lower cholesterol and improve inflammation markers in people with HIV.

If pitavastatin is not available in your area, another statin medication that does not interact with your antiretroviral therapy may be a reasonable choice. Please discuss with your clinician about the choice that is right for you.

3. Should I start taking a statin, given the results of REPRIEVE?

- a. Revised treatment guidelines incorporating data from REPRIEVE that recommend statin therapy in this patient population were recently announced and are available [here](#). Before the results of REPRIEVE were known, the decision to take statin medications for people with HIV depended on cholesterol levels and other risk factors for heart and blood vessel (cardiovascular) disease.

REPRIEVE has shown that statins prevent heart disease in people with HIV in the absence of high cholesterol or other heart disease risk factors. However, you and your clinician should still consider all of your risk factors, like age, smoking history, and family history for heart attacks and strokes before starting a statin.

4. Pitavastatin is not available in my region or it is not covered by my health insurance. Will a different statin medication also protect me from heart disease?

- a. Revised treatment guidelines incorporating data from REPRIEVE that recommend statin therapy in this patient population were recently announced and are available [here](#). Pitavastatin was chosen for REPRIEVE because it has minimal interactions with antiretroviral therapy and has been shown to lower cholesterol and improve inflammation markers in people with HIV.

If pitavastatin is not available in your area or your health insurance does not cover it, another statin medication that does not interact with your ART regimen may be a reasonable choice. Please discuss with your clinician about the choice that is right for you.

5. Did REPRIEVE participants taking pitavastatin experience any muscle aches or pains?
 - a. A small proportion of REPRIEVE participants in REPRIEVE experienced general myalgias (muscle aches and pains), and muscle weakness, and this was slightly more common for participants taking pitavastatin vs. placebo (2.4% vs. 1.5%). But, these symptoms were mostly mild and only 1% of participants withdrew for muscle-related symptoms. These symptoms generally went away after the first year.
6. Did REPRIEVE participants taking pitavastatin develop diabetes?
 - a. The rates of diabetes were higher for participants taking pitavastatin group compared to participants taking placebo (6.0% vs. 4.7%). However, pitavastatin reduced the risk of heart disease even among people with diabetes. It is an important and personal choice to weigh your own risk of diabetes vs. heart disease like a heart attack or a stroke.
7. When will study participants find out if they were taking pitavastatin or placebo?
 - a. The study participants will be unblinded, meaning they will find out which medication they were taking, in mid-November 2023. A notification will be sent to the clinical research sites with this information, and the sites will then communicate this information with participants.
8. Should I wait to start a statin until I know which medication I was taking in the study, pitavastatin or placebo?
 - a. You can begin to discuss starting a statin with your clinician now and do not need to wait until you find out which medication (pitavastatin vs. placebo) you were randomized to in REPRIEVE. The decision to start a statin should be a shared decision between you and your clinician or healthcare provider.
9. Can someone living with HIV who already had a heart attack or a stroke in the past take a statin to reduce their chance of having another heart attack or stroke?
 - a. Yes, from many studies, we know that taking a statin may help prevent a second heart attack or stroke for people who already had a heart attack or stroke. It is important to discuss this with your healthcare provider your individual heart disease history and how best to protect your heart health.
10. Is there anything else I can do to protect myself from heart disease?
 - a. Don't forget that a healthy lifestyle is still key for preventing heart disease! Lifestyle changes are key for reducing your risk of heart disease, whether you take a statin or not. Data from REPRIEVE have shown that poor heart health is associated with more blockages in the heart arteries, and that heart healthy behaviors can be enhanced in people with HIV. To reduce your risk:

- Quit smoking and avoid secondhand smoke
- Eat a healthy diet rich in vegetables, fruits, fish, and whole grains and low in saturated fat, trans fat, refined carbohydrates and salt.
- Be physically active more often and sit less
- Maintain a healthy weight

FAQ About the REPRIEVE Trial:

1. What was the purpose of the REPRIEVE trial?
 - a. Previous studies have shown that people with HIV are at higher risk for heart disease than people without HIV. **The REPRIEVE trial tested a strategy to reduce the risk of heart disease—including heart attack and stroke—among people with HIV.** In people with HIV, cardiovascular disease risk is thought to be influenced by traditional risk factors—such as cigarette smoking, high blood pressure, diabetes, and high cholesterol—and also by factors unique to HIV, such as chronic inflammation.
2. What are we learning from your participation in REPRIEVE?
 - a. REPRIEVE found that pitavastatin, a statin medication and the heart disease prevention strategy tested in the trial, reduced major heart disease events like heart attacks and strokes in people with HIV by 36% compared to placebo. Pitavastatin also reduced major heart disease events or death from any cause by 23% compared to placebo. Pitavastatin was effective in both men and women, and the study participants experienced very few safety events. The results of REPRIEVE are helping clinicians to better support the heart health needs of people with HIV, and there are many more questions that the REPRIEVE Team is working answer in the future. A few of these questions are listed below:
 - Does pitavastatin help slow or prevent kidney disease in people with HIV?
 - How are people with HIV impacted by COVID-19?
 - What are the potential effects of a daily dose of pitavastatin and/or ART regimens on COVID-19?
 - Is COVID-19 a heart disease risk factor?
3. What are statins?
 - a. Statins are medications that lower cholesterol levels in the blood and have also been shown to have anti-inflammatory effects. Statins have already been shown to reduce heart disease in the general population among individuals at high risk for heart disease based on traditional risk factors. At the conclusion of REPRIEVE, we observed that statins reduce the risk of heart disease among people with HIV with low to moderate traditional risk scores.
4. How did this trial work?
 - a. Participants were randomized (like flipping a coin) to take either:
 - Pitavastatin calcium (Livalo) 4 mg, one pill daily
 - Placebo for pitavastatin calcium (Livalo), one pill daily
 Pitavastatin calcium (Livalo) is a statin that has been approved by the US Food and Drug Administration for the treatment of high cholesterol, even though not all participants in the trial had high levels of cholesterol, as per the trial design. Advice on healthy diet and

exercise was given to all participants in the trial. Pitavastatin calcium (Livalo) has been shown to be safe in individuals taking antiretroviral (ART) medications.

5. How many people participated in the REPRIEVE trial?
 - a. REPRIEVE enrolled over 7500 people with HIV into the trial from around the world.
6. How long did it take to finish the REPRIEVE trial?
 - a. Participants had visits approximately every 4 months during the trial. The median length of trial participation for individual participants was about 5 years.
7. Where was the REPRIEVE trial conducted?
 - a. The REPRIEVE trial was conducted at research sites in United States, Canada, Thailand, South Africa, Brazil, Peru, Haiti, Zimbabwe, Botswana, Uganda, and India. Over 100 research sites enrolled participants into REPRIEVE. A map is posted providing links to participating sites, as well as contact information for the site.
8. Are there any substudies or ancillary studies that are a part of the REPRIEVE trial?
 - a. There are 6 substudies and ancillary studies that are part of the REPRIEVE trial, including 2 additional study objectives included in REPRIEVE, they are:
 - The REPRIEVE Mechanistic Substudy (ACTG A5333s)
 - [Pitavastatin to REduce Physical Function Impairment and FRailty in HIV \(PREPARE\) \(ACTG #A5361s\)](#)
 - Sex-Specific Mechanisms of Cardiovascular Disease Risk and Risk Reduction
 - Evaluate the Effect of Pitavastatin on Kidney Function in Persons with HIV
 - Clonal Hematopoiesis of Indeterminate Potential (CHIP) and Incident Cardiovascular Outcomes
 - Mechanisms of Cardiac Dysfunction in HIV and the Effect of Statins: A Cardiac MRI Study

The **Mechanistic Substudy of REPRIEVE (ACTG A5333s)** is trying to understand ways in which statin therapy may achieve a reduction in cardiovascular disease. Some possible ways include:

- i. lowering cholesterol levels
- ii. lowering the degree of inflammation
- iii. stabilizing fatty plaques in the blood vessels surrounding the heart, preventing these plaques from rupturing.

805 participants enrolled in the REPRIEVE substudy and the last visit was completed summer of 2020. Substudy participants had some additional tests and monitoring, including CT scan of the heart's blood vessels.

[Pitavastatin to REduce Physical Function Impairment and FRailty in HIV \(PREPARE\) \(ACTG #A5361s\)](#)

PREPARE is an observational study of muscle strength and function among people with HIV who are receiving pitavastatin or placebo as part of the REPRIEVE study (A5332) and are also enrolled in the Mechanistic substudy (A5333s). 600 REPRIEVE participants are also participating in the PREPARE substudy.

Sex-Specific Mechanisms of Cardiovascular Disease Risk and Risk Reduction

This project is exploring among participants in REPRIEVE, sex-differences in immune activation in relation to heart disease events and statin-related heart disease

prevention. The project is also assessing how menopause influences heart disease risk and risk reduction specifically among women with HIV.

Evaluation of the Effects of Pitavastatin on Kidney Function in HIV-infected Persons

To evaluate the effects of pitavastatin on clinical and subclinical kidney function and to investigate the relationship between chronic kidney disease and cardiovascular disease.

Clonal Hematopoiesis of Indeterminate Potential and Incident Cardiovascular Outcomes

The objective is to estimate the prevalence of & characterize risk factors for CHIP in people with HIV, associate CHIP with incident clinical outcomes in people with HIV and discover mechanistic relationships of CHIP with HIV-associated outcomes.

Mechanisms of Cardiac Dysfunction in HIV and the Effect of Statins: A Cardiac MRI Study

This is a study assessing mechanisms of cardiac dysfunction among individuals with HIV on antiretroviral therapy and the effects of pitavastatin on myocardial fibrosis, myocardial steatosis, and cardiac function. Approximately 120 REPRIEVE participants also participated in this study and underwent additional testing including cardiac MRI.

9. Who funds the REPRIEVE trial?
 - a. REPRIEVE is funded by the National Heart Lung and Blood Institute (NHLBI) at the National Institutes of Health (NIH), with significant support and collaboration from the National Institute of Allergy and Infectious Diseases (NIAID) through its Division of AIDS (DAIDS). In addition, Kowa Pharmaceuticals America, Inc. is donating pitavastatin and providing support for the study. Gilead Sciences, Inc. and ViiV Healthcare are also providing support. The REPRIEVE trial is a collaboration of government agencies, academic centers, research institutes and industry support working in partnership to determine if pitavastatin can reduce the risk of cardiovascular disease in people with HIV.
10. How did COVID-19 impact people with HIV in the REPRIEVE trial?
 - a. The REPRIEVE team is evaluating whether participants randomized to statin (vs. placebo) experienced protection from developing COVID-19 or serious COVID-19. REPRIEVE trial leadership received a grant from the NIH National Heart Lung and Blood Institute to carry out this investigation.