Executive Summary: The Mechanistic Substudy of REPRIEVE (A5333s)

Title	Effects of Pitavastatin on Coronary Artery Disease and Inflammatory Biomarkers: Mechanistic Substudy of REPRIEVE (A5333s)
Indication	Assess the effects of statins on critical plaque and inflammatory characteristics to understand mechanism of action in HIV
Location	Selected sites of the REPRIEVE (A5332) study
Brief Rationale	The Mechanistic Substudy of REPRIEVE (A5333s) will determine, among HIV-infected persons, potential statin effects to halt progression of non-calcified atherosclerotic plaque and to stabilize morphologic features of plaque vulnerability as assessed on coronary computed tomography angiography (CCTA). Moreover, the study will identify biological factors mediating these changes – be it lipid parameters, such as LDL cholesterol, or markers of inflammation and immune activation
Study Design and Duration	Randomized, placebo-controlled multicenter substudy oREPRIEVE (A5332) in 800 subjects, with individual subjects participating in the substudy for 2 years.
Treatment	Pitavastatin 4 mg PO daily or matching placebo
Primary Objective	To determine the effects of pitavastatin on the morphology and composition of non-calcified coronary atherosclerotic plaque (NCP) on CCTA, including the progression of plaque volume and whether these effects are modulated by markers of inflammation and immune activation.
Secondary Objectives	1. The effects of pitavastatin on the progression of high risk plaque features including low attenuation plaque and positive remodeling on CCTA. 2. The effects of pitavastatin on detailed markers of immune activation, immune activation, inflammation, coagulation and traditional CVD risk indices including detailed parameters of glucose homeostasis (insulin, glucose and related indices of insulin resistance such as HOMA-IR, HgbA1c). 3. The relative contributions of baseline and pitavastatin induced changes in HIV specific immune activation and traditional risk factors, including LDL, on the presence and progression of coronary plaque and high risk morphological features in HIV.
Primary Endpoint	Change in noncalcified plaque volume on CCTA at enrollment and 2 years.
Secondary Endpoints -	High risk plaque features on CCTA Detailed immune phenotyping measures and inflammatory and coagulation indices as well as detailed measures of glucose homeostasis