Correspondence:
Steven K. Grinspoon, MD
sgrinspoon@mgh.harvard.edu

Relating Pitavastatin Effects on Inflammatory Biomarkers to Plaque Changes in REPRIEVE

773

Steven K. Grinspoon,[1] Michael T. Lu,[1] Sara McCallum,[1] Markella V. Zanni,[1] Borek Foldyna,[1] Kayla Paradis,[1] Carl J. Fichtenbaum,[2] Judith A. Aberg,[3] Gerald S. Bloomfield,[4] Carlos D. Malvestutto,[5] Judith S. Currier,[6] Thomas Mayrhofer,[1] Julia Karady,[1] Heather J. Ribaudo,[7] Pamela S. Douglas[4]

[1]Massachusetts General Hospital, Boston, MA, USA, [2]University of Cincinnati, Cincinnati, OH, USA, [3]Icahn School of Medicine at Mt Sinai, New York, NY, USA, [4]Duke University School of Medicine, Durham, NC, USA, [5]The Ohio State University, Columbus, OH, USA, [6]University of California Los Angeles, Los Angeles, CA, USA, [7]Harvard TH Chan School of Public Health, Boston, MA, USA

BACKGROUND

- The REPRIEVE trial demonstrated that pitavastatin reduced the risk of major adverse cardiovascular events (MACE) by 35% and LDL by 30% over median 5.1 years of follow up.
- The REPRIEVE mechanistic study further demonstrated that pitavastatin (vs placebo) was associated with a significant reduction in progression of noncalcified coronary plaque volume as well as reductions in oxLDL and Lp-PLA2.
- This analysis further interrogates these findings to examine whether pitavastatin effects on lipids and these inflammatory biomarkers relate to changes in plaque.

METHODS

- Coronary plaque volume was assessed at baseline and 24 months by CT angiography, using a threshold of <350 HU to define noncalcified plaque.
- Biomarker changes were analyzed on the log2 scale.
- Pearson correlation was used to assess associations between 24 month changes in LDL, biomarkers, and plaque.
- For this mechanistic assessment, analyses were restricted to participants who remained on randomized treatment for 24 months with biomarkers assessed.

Figure 1. Inclusion in Mechanistic Analysis

804 randomized
402 Pitavastatin; 402 Placebo

683 completed treatment
341 Pitavastatin; 342 Placebo

563 had complete data
281 Pitavastatin; 282 Placebo

Pitavastatin significantly reduced LDL and key biomarkers of lipid oxidation and arterial inflammation in people with HIV, but these changes were not associated with changes in noncalcified or total plaque volumes.

RESULTS

- The 563 participants included in the analysis were representative of the substudy population (mean age 51 years, sex 16% female, CVD risk median 4.5%) **(Table 1)**.
- No associations between changes in Lp-PLA2, oxLDL, hsCRP or LDL, and noncalcified plaque volume were apparent (|rho|<0.1) **(Figure 2)**.
- Similar results were seen in the the subset of the substudy population with plaque at baseline (not shown).
- Adjustment for changes in biomarkers did not impact the effect of pitavastatin to reduce noncalcified plaque volume **(Figure 3)**.
- Similar findings were seen for total plaque volumes (not shown).

Table 1. Participant demographics

Demographics	Total (N=563)
Age, mean	51 years
Female sex, N(%)	90 (16%)
Black race, N(%)	198 (35%)
CVD risk, median	4.5%
Plaque present	273 (48%)

Figure 2. Correlations between noncalcified plaque (NCP) volume, Lp-PLA2, oxLDL, hsCRP, and LDL among all participants

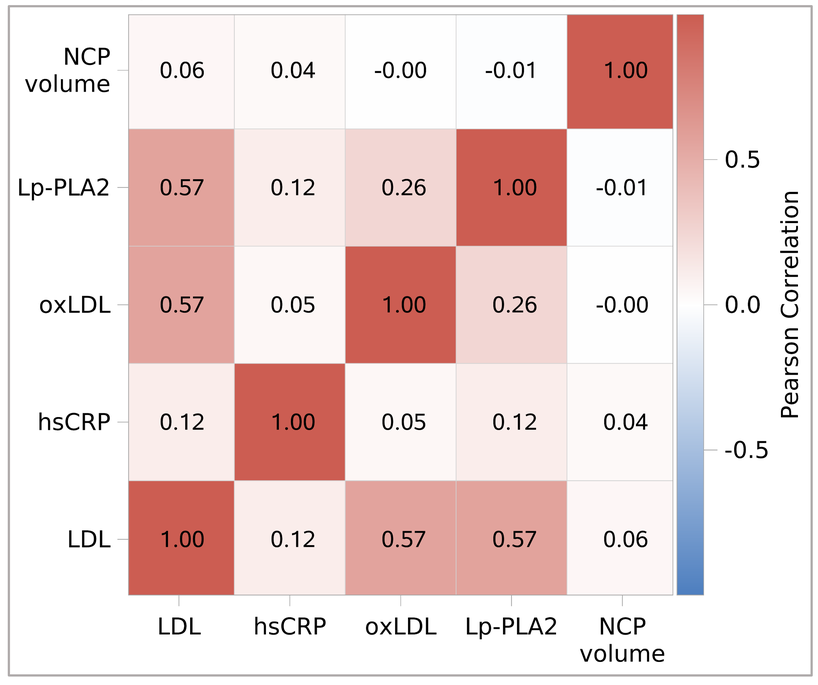
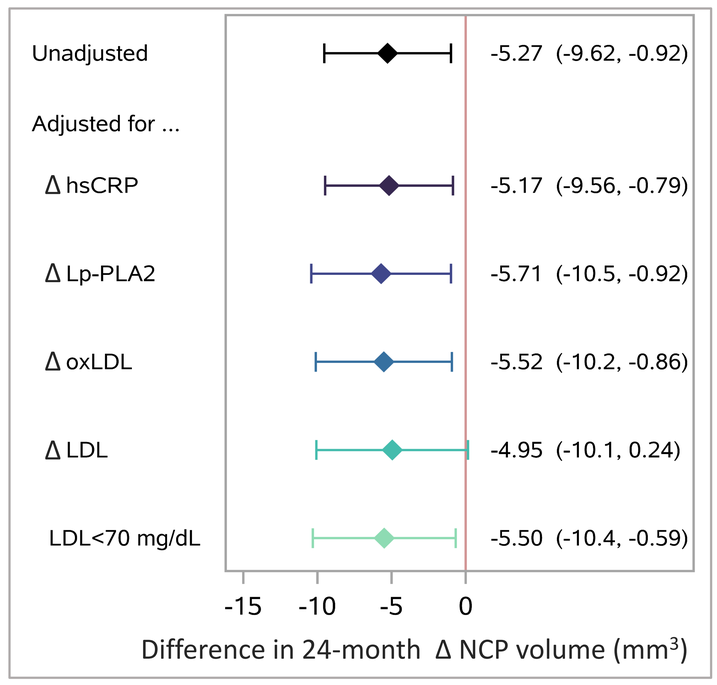


Figure 3. Pitavastatin effect on change in noncalcified plaque (NCP) volume. Estimates (95% CI) give the difference in change in NCP volume (pitavastatin – placebo) (mm^3) over 24 months without and with adjustment for changes in hsCRP, Lp-PLA2, oxLDL, and LDL.



CONCLUSIONS

- Pitavastatin significantly reduced LDL and key biomarkers of lipid oxidation and arterial inflammation in REPRIEVE, but these changes were not associated with changes in noncalcified or total plaque volumes.
- Further studies will assess effects of these pathways on MACE and also the effects of pitavastatin on other mechanistic pathways which might link statin effects to improvements in coronary artery disease indices and MACE in PWH.

Funding: REPRIEVE is supported through NIH grants U01HL123336, 1UG3HL164285, U01HL123339, and 1U24HL164284, the ACTG, Kowa Pharmaceuticals, Gilead Sciences, and ViiV Healthcare.