Abstract #771

Long-term Changes in Bone Mineral Density and Insulin Resistance on Statins in HIV

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BACKGROUND

- Statins are associated with a beneficial effect on bone mineral density (BMD) and lean body mass, but increased diabetes risk, in HIV-uninfected cohorts.
- We previously demonstrated increased hip BMD and worsening in insulin resistance after 48 weeks of rosuvastatin in HIV-infected adults on antiretroviral therapy (ART).
- Here, we present the final 96 week results.

METHODS

- HIV-infected subjects on stable ART with a low-density lipoprotein (LDL) cholesterol level of ≤ 130 mg/dL and evidence of heightened immune activation (≥19% CD8+CD38+DR+ T-cells) *or* inflammation (hsCRP ≥2 mg/L)
- Subjects were randomized to rosuvastatin 10mg daily or placebo for 96 weeks
- Fasting specimens were obtained at weeks 0, 24, 48, and 96
- Insulin resistance was estimated by the homeostatic model assessment of insulin resistance (HOMA-IR)
- Bone and body composition were measure by dual-energy X-ray absorptiometry (DXA).

Statistical Approach

- This was a pre-specified secondary analysis
- Comparisons were made using t tests, paired t tests, Wilcoxon rank-sum tests, or signed-rank tests.
- Multivariable regression models were constructed to explore the effect of covariates on the association between statin and relative change in HOMA-IR.

RESULTS

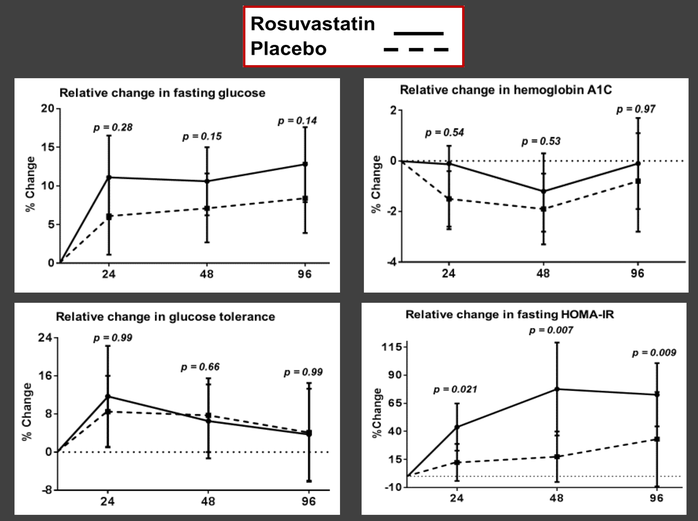
Table. Characteristics by randomized study arm

- *Characteristics were well-balanced between study arms*

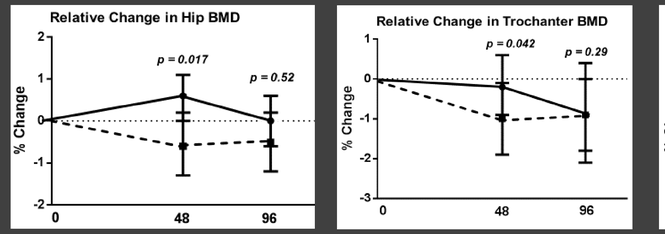
Characteristic	Statin (n=72)	Placebo (n=75)
Demographics		
Age (years)	45.6 (41.1-51.4)	46.9 (39.2-53.6)
Male	58 (81)	57 (76)
African American	51 (71)	52 (69)
Current smoker	43 (60)	54 (72)
HIV-related characteristics		
CD4+ count (cells/μL)	608 (440-848)	627 (398-853)
Nadir CD4+ count (cells/μL)	173 (84-312)	190 (89-281)
HIV-1 RNA <50 copies/mL	56 (78)	58 (77)
ART duration (mo)	63 (37-119)	71 (39-116)
Current protease inhibitor regimen	36 (50)	36 (48)
Hepatitis C	5 (7)	7 (9)
Clinical characteristics		
Body mass index (kg/m^2)	26.6 (23.4-30.0)	27.2 (23.5-30.5)
Fat mass (kg)	23.3 (14.3, 32.0)	22.4 (14.0, 32.2)
Lean body mass (kg)	56.3 (50.6, 61.9)	57.2 (48.9, 61.3)
Lumbar spine T-score < 1	19 (26)	13 (17)
Total hip T-score < 1	18 (25)	17 (22)
Fasting glucose (mg/dL)	84 (75, 95)	87 (79, 94)
Fasting insulin (μIU/mL)	8 (5, 15)	11 (6, 23)
Fasting HOMA-IR	1.7 (1.0, 3.1)	2.2 (1.3, 4.8)
LDL (mg/dL)	96 (76, 107)	97 (77, 121)

Values presented as median (25th, 75th percentile) or number (%).

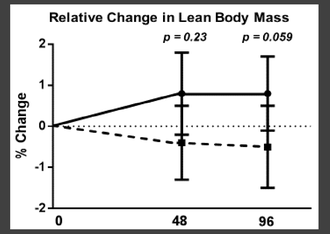
Relative change in markers of glucose tolerance & insulin resistance



Relative change in BMD at the hip, trochanter, or lumbar spine



Relative change in lean body mass



- <u>At study entry</u>: 18% in rosuvastatin and 15% in placebo arm had fasting glucose >100 mg/dL
- <u>By week 96</u>: 32% in rosuvastatin and 21% in placebo arm had glucose 101-125 (p=0.34); 2% in rosuvastatin and 3% in the placebo arm had fasting glucose ≥126 mg/dL
- There were no significant differences between groups in relative changes of trunk, limb, or total fat (p ≥ 0.19)
- In multivariable models, the difference in HOMA-IR with statin use did not change significantly when including week 96 change in BMI, lean body mass, trunk fat, or limb fat
- Despite the increase in lean body mass in the statin arm, self-reported physical activity was not significantly greater in the statin vs placebo arm (187 vs 248% relative increase; p=0.10).

SUMMARY/CONCLUSIONS

- Rosuvastatin led to significant increases in serum fasting insulin and HOMA-IR, robust indicators of worsening insulin resistance.
- Relative changes in glucose, glucose tolerance, and diabetes did not differ between study arms.
- The effect of statin therapy on insulin resistance was not explained by changes in BMI, fat distribution, or lean body mass.
- The week 48 improvement in BMD in the rosuvastatin arm did not persist at week 96 while gain in lean body mass did.
- Although statins clearly have a highly effective role in reducing death due to cardiovascular disease in certain populations, our findings suggest that statin therapy should be accompanied by a careful consideration of the risks and benefits, particularly in patients with lower cardiovascular disease risk.

ACKNOWLEDGEMENTS

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