Sterol	Pbo (n=62)	EZE 10 mg (n=55)	Simva (n=232)	EZE 10 mg + Simva (n=229)

	% change	Ratio	% change	Ratio	% change	Ratio	% change	Ratio
Sitosterol	-0.5	-4.1	-46.5*	-37.8*	-3.3	21.4*	-52.1**	-25.1†
Campesterol	-2.0	-6.8	-50.5*	-78.6*	-1.6	39.8*	-60.7**	-68.3†
Lathosterol	4.7	2.7	35.5*	36.8*	-53.5*	-37.8	-47.6	-22.1†
Desmosterol	6.5	5.1	16.1	25.7*	48.0*	-22.8	-45.6	-11.1†

Simva: pool of all doses of Simva. Comparisons: EZE & Simva vs Pbo; EZE+Simva vs Simva

% change: Mean % change. Ratio: Mean change (10^2 mmol/mol)

*P<0.001 vs Pbo; †P<0.001 vs Simva (pooled)

Conclusion: The net effect of ezetimibe/simvastatin is to inhibit cholesterol synthesis and the absorption of phytosterols (in conjunction with cholesterol). Clinical relevance and implications with respect to atherosclerosis development and progression warrant further studies.

1008-184 The Effects of Pravastatin and Atorvastatin on Markers of Oxidant Stress In Vivo

Bonnie Ky, Megan L. Wolfe, Anne Burke, Philippe O. Szapary, Muredach P. Reilly, Jennifer B. Dykhouse, Leanne T. Bloedon, Garret A. FitzGerald, Daniel J. Rader, University of Pennsylvania School of Medicine, Philadelphia, PA

Treatment with inhibitors of 3-hydroxy-3methylglutaryl coenzyme reductase(statins) decreases low density lipoprotein (LDL) cholesterol, but their effects on oxidative stress are unclear.We performed a randomized, controlled clinical trial in which subjects received pravastatin 40, atorvastatin 10, atorvastatin 80 or placebo therapy with the goal of assessing the effects of statins on markers of oxidant stress. METHODS: 120 patients (68 males and 52 females) between the ages of 21-80 with an LDL cholesterol between 130-220 mg/dl without known atherosclerotic disease, diabetes mellitus, chronic renal insufficiency, or exposure to prior lipid lowering therapy were recruited. Patients were randomized to one of the four arms and treated for 16 weeks. At baseline and 16 weeks, plasma oxidized LDL was measured using a commercially available ELISA assay and urinary isoprostanes were determined using GC/MS. RESULTS: After 16 weeks, reductions in LDL cholesterol with statin therapy were as expected. With regards to changes in oxidized LDL, pravastatin 40mg led to an 18.8% reduction, atorvastatin 10mg led to a 28% reduction and atorvastatin 80mg led to a 32% reduction. In the placebo group, there was a nonsignificant change in oxidized LDL over 16 weeks (3.65 %). However, there were no significant changes in urinary isoprostane levels across all treatment arms. CONCLUSIONS: Pravastatin and atorvastatin led to statistically significant decreases in plasma oxidized LDL concomitant with changes in LDL cholesterol, but did not lead to reductions in urinary isoprostane excretion.

1008-185 Benefit of Statins in Secondary Prevention After Acute Myocardial Infarction: Evidence of a Class Effect

Zheng Zhou, Elham Rahme, Jack Tu, Karin Humphries, Mark Eisenberg, Michal Abrahamowicz, Peter Austin, Louise Pilote, Montreal General Hospital, Montreal, PQ, Canada, Institute for Clinical Evaluation Science, Toronto, ON, Canada

Background: Clinical trials have shown several statins to improve survival after acute myocardial infarction (AMI). However whether all statins have a similar effect in reducing recurrent AMI and death remains unclear. We conducted a population-based study to assess whether a class effect exists among statins for secondary prevention. **Methods**: A retrospective cohort study (1997~2002) was used to compare 5 statins based on the hospital discharge and prescription claims databases from 3 provinces of Canada (Quebec, Ontario and British Columbia). The cohort consisted of patients $\geq$ 65 years with a first-recorded AMI since 1997. The effect of statin use on outcome was evaluated using a Cox survival model adjusting for patient demographic and clinical characteristics as well as specialty of treating physician, hospital type and the year of AMI. Switching, stopping treatment and dosage change were also analysed. **Result:** A total of 18,637 statin users were studied with a median follow-up of 2.5 years [atorvastatin (n=6420), pravastatin (n=4480), simvastatin (n=5518), lovastatin (n=1736) and fluvastatin (n=483)]. Similar baseline characteristics and statin usage patterns were found across different statin groups and provinces. Compared to atorvastatin, the hazard ratios and 95% confidence intervals for recurrent MI or death whichever occurred first revealed an equivalent effect among statins: pravastatin 1.00 (0.90- 1.11), simvastatin 1.01 (0.91-1.12), lovastatin 1.09 (0.95-1.24) and fluvastatin 1.01(0.80-1.27). The conclusion remained unchanged when studying all-cause mortality alone while treating recurrent MI as a time dependent covariate. Censoring patients at switching or stopping treatment did not alter the results. **Conclusion:** Our results suggested that, despite the differences in their chemical structure and metabolic properties, a beneficial class effect can be assumed for statins in the secondary prevention post AMI.

1008-186 Encapsulation of Pravastatin Tablets Produces Greater Low-Density Lipoprotein Cholesterol Lowering in Patients With Human Immunodeficiency Virus Infection Dyslipidemia Taking Protease Inhibitors

Matthew K. Ito, Victoria E. Aldridge, Jennifer J. Howard, Eric K. Gupta, Scott T. Johns, Joseph K. Wong, University of the Pacific, Stockton, CA, VA San Diego Healthcare System, San Diego, CA

Background: Dyslipidemia is well recognized in patients with Human Immunodeficiency Virus (HIV) disease receiving antiretroviral therapy. Pravastatin is moderately effective at reducing LDL cholesterol and has documented efficacy in reducing cardiovascular events. Biotransformation of pravastatin occurs primarily by isomerization in the gut to a relatively inactive (1/40 the reductase inhibitory activity) metabolite (SQ31,906). We have shown that this biotransformation contributes to interindividual variability in the reduction in LDL cholesterol. It is suggested that encapsulating or enteric coating pravastatin may reduce this biotransformation and increase the efficacy of the drug.
Methods: We randomized 12 adult males with HIV to pravastatin 10 mg tablets either encapsulated (placed within gel capsule with lactose) or non-encapsulated for 4 weeks and were crossed-over following a 4 week washout.
Results: Lipid and pharmacokinetic parameters are shown in the table. Encapsulation of pravastatin produced greater reductions in total (22% vs 12%, p=0.012) and LDL (25 % vs 13%, p=0.021) cholesterol compared to non-encapsulation. The one hour post dose ratio of plasma pravastatin to SQ31,906 were higher (2.2 vs 1.1, p=0.061) following encapsulation compared to non-encapsulation. No differences in C-reactive protein (hs-CRP) were noted.
Conclusion: Encapsulation of pravastatin significantly improves its LDL-lowering efficacy by reducing biotransformation to SQ31,906.

	Encapsulated	Non-encapsulated	p-value
Total cholesterol (mean % change $\pm$ sd)	-22 $\pm$ 12	-12 $\pm$ 9	0.012
LDL cholesterol (mean % change $\pm$ sd)	-25 $\pm$ 9	-13 $\pm$ 16	0.021
HDL cholesterol (mean % change $\pm$ sd)	-1 $\pm$ 11	3 $\pm$ 13	0.23
triglycerides (mean % change $\pm$ sd)	-8 $\pm$ 36	-19 $\pm$ 25	0.21
hs-CRP (median % change)	-12	17	0.21
pravastatin/SQ31,906 (mean $\pm$ sd)	2.2 $\pm$ 2	1.2 $\pm$ 0.7	0.061

1008-187 Effect of Pravastatin on Endothelial Function in Human Immunodeficiency Virus-Infected Persons on Protease Inhibitor-Containing Antiretroviral Combination Therapy

David Hurlimann, Jr., Remy Chenevard, Frank Ruschitzka, Sr., Jorg Muntwyler, Sr., Thomas Luscher, Sr., Georg Noll, Sr., Markus Flepp, Jr., Bruno Ledergerber, Sr., Rainer Weber, Sr., University Hospital Zurich, Zurich, Switzerland

Background: Antiretroviral combination therapy has altered cardiovascular risks and manifestations in HIV-infected persons. Protease inhibitors in particular have been linked to dyslipidemia, glucose intolerance, an increase in cardiovascular events and endothelial dysfunction. Treatment of the pro-atherogenic lipid profile as well as improving endothelial function may be important for the long-term prognosis of these patients. The aim of this study was to evaluate the effects of pravastatin on endothelial function and plasma lipid profile.
Methods: 31 patients (mean age 45 ±9.3 years) with HIV-1 infection who were treated with stable proteinase inhibitor-containing antiretroviral combination therapy for at least 4 months were randomly assigned to receive pravastatin 40mg daily or matching placebo for 8 weeks in a double-blind cross-over fashion. Flow-mediated vasodilation (FMD) of the brachial artery was assessed by high-resolution ultrasound at baseline and after each treatment period, and plasma lipid levels were measured.
Results: Pravastatin significantly improved flow-mediated dilation compared to baseline after 8 weeks treatment (3.2±1.6% vs. 2.3±1.0%, p=0.003). Further, improvement in endothelial function was superior to placebo (3.2±1.6% vs. 2.5±1.2%, p=0.013). Total cholesterol was lowered from 6.6±1.1 to 5.6±1.1mmol/l (-14.8%) p<0.0001) and LDL from 3.7±0.9 to 3.1±0.9mmol/l (-16.3%) p=0.0003. Alterations in flow-mediated dilation were inversely correlated to changes in LDL cholesterol (r=0.36, p=0.014).
Conclusions: Our study demonstrates that pravastatin in HIV patients improves PI-containing HAART associated endothelial dysfunction. The observed effects on the vascular endothelium seem at least in part to be mediated by lowering LDL cholesterol. Thus, pravastatin might hold the potential to improve prognosis in HIV infected patients with protease inhibitor induced dyslipidemia.

1008-188 Trends in Use of Statins in Older Patients With Heart Failure

JoAnne M. Foody, Deron Galusha, Frederick A. Masoudi, Saif S. Rathore, Edward P. Havranek, Harlan M. Krumholz, Yale University School of Medicine, New Haven, CT

Background: Statin therapy improves outcomes in patients with ischemic cardiomyopathy and may improve cardiac function and functional class in patients with idiopathic dilated cardiomyopathy irrespective of serum cholesterol levels or atherosclerotic heart disease. Little is known regarding trends in the use of statins in a population-based sample of older patients with heart failure.
Methods and Results: In national cohorts of 39,477 and 39,405 older patients hospitalized between 1998-9 and 2000-1 respectively with heart failure, we assessed change in rates of use of statins at discharge in patients surviving to discharge without contraindications to statins. Overall, 11.9% and 21.8% of patients were discharged in 1998-9 and 2000-1, respectively. While patients with prior history of PTCA or CABG were more likely to receive these agents, as were those with elevated total cholesterol, women and the