(10/20), EZ/S 40 mg (10/40), and EZ/S 80 mg (10/80) through Periods 1-4; and (3) EZ/S 20 mg titrated to EZ/S 40 mg (for Periods 2 and 3), then EZ/S 80 mg for Period 4. Primary endpoint was % change from baseline in LDL-C after the initial 6-week period. Secondary endpoints included % change from baseline in LDL-C to ends of Periods 2, 3, and 4; and HDL-C to ends of Periods 1, 2, 3, and 4. Safety measurements were clinical and laboratory adverse events including ALT or AST _3x upper limit of normal (ULN), CK _10x ULN.

Results: Baseline LDL-C and HDL-C levels were comparable between treatment groups. At the end of Period 1, mean LDL-C reduction and mean HDL-C increase were significantly (p_0.01) greater for the EZ/S 10 mg and EZ/S 20 mg groups compared with the A10 mg group (see Table). At the end of Period 4, comparing maximum doses, EZ/S 80 mg was superior to A80 mg in LDL-C reduction (–59.4 vs –52.5) and HDL-C increase (12.3 vs 6.5).

Table. Summary of Endpoints

				LS-Mean Percent Change from Baseline in:	
Period	Group	Treatment	n available for analysis†	LDL-C	HDL-C
1	1	Atorvastatin 10 mg	250	—37.2	5.1
	2	Ezetimibe/Simvastatin 10 mg	252	—46.1‡	8.0‡
	3	Ezetimibe/Simvastatin 20 mg	253	—50.3‡	9.5‡
2	1	Atorvastatin 20 mg	235	—44.3	6.9
	2	Ezetimibe/Simvastatin 20 mg	239	—50.2‡	9.0
	3	Ezetimibe/Simvastatin 40 mg	243	—54.3‡	12.4‡
3	1	Atorvastatin 40 mg	228	—49.1	7.8
	2&3*	Ezetimibe/Simvastatin 40 mg	466	—55.6‡	11.4‡
4	1	Atorvastatin 80 mg	223	—52.5	6.5
	2&3*	Ezetimibe/Simvastatin 80 mg	441	—59.4‡	12.3‡

LS means and p-values are from analysis of variance model with terms for treatment and baseline LDL-C strata. †Baseline values for LDL-C (mg/dL) were: (Group 1, 180.6; Group 2, 180.0; Group 3, 179.2), for HDL-C: (Group 1, 46.9; Group 2, 46.6; Group 3, 46.8). ‡p_0.01 for difference with Atorvastatin in the specified period.
*Treatment Groups 2 and 3 combined in Periods 3 and 4.

Conclusion: Greater LDL-C reduction and HDL-C increase can be attained by treating with EZ/S compared with atorvastatin. Treatments with EZ/S and A were well-tolerated.

1084-178 **Trends in Use of Statins in Older Patients With Acute Myocardial Infarction**

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

Background: Treatment with HMG CoA Reductase Inhibitors (statins) decreases cardiovascular events and mortality in patients with coronary artery disease (CAD). Little is known regarding trends in the use of statins in a population-based sample of older patients surviving acute myocardial infarction (AMI).
Methods and Results: In two national cohorts of 31,399 and 31,759 older patients hospitalized between 1998-9 and 2000-1 with confirmed AMI, we identified patients who survived to discharge. We assessed change in rates of use of statins at discharge in 'ideal candidates' without contraindications to statins. Overall, 27.5% and 46.2% of patients were discharged in 1998-9 and 2000-1, respectively. Of those patients with an LDL-c greater than the guideline-based threshold of 130 mg/dL, 55% received lipid-lowering therapy in 1998-9 compared to 71% in 2000-1. In general, women and the elderly were consistently less likely to receive statins on discharge.
Conclusions: In a national sample of older AMI survivors, significant increases in discharge prescription of statins occurred irrespective of patient age, sex, race and LDL cholesterol. Despite these increases, a significant proportion of older patients do not receive guideline-based lipid management.

Rates of Statin Use in Older AMI Survivors

	1998-9 N =14,808 %	2000-1 N =14,606 %
Overall Use	27.5	46.2
Age >/= 75 years *	21.6	40.1
LDL <100 mg/dL	28.8	47.4
LDL 100-129 mg/dL	34.7	56.2
LDL >/=130 mg/dL	55.0	71.3
* in ideal patients with LDL-c ³ 130 mg/dL		

1084-179 **Ezetimibe/SimvastatinTherapy Is More Effective Than Simvastatin Alone at Reducing Remnant-Like Particle Cholesterol**

Harold E. Bays, Leiv Ose, Neil Fraser, Katherine L. Quinto, Robert Reyes, Aditi Sapre, Diane Tribble, Stephen R. Donahue, Louisville Metabolic and Atherosclerosis Research Center, Louisville, KY, Merck Research Laboratories, Rahway, NJ

Background: Levels of remnant lipoproteins are independent predictors of future coronary events in patients with coronary artery disease. We evaluated the effects of ezetimibe/simvastatin (EZE/SIM) combination therapy versus SIM alone on remnant-like particle cholesterol (RLP-C) in hypercholesterolemic patients.
Methods: After a 6- to 8-wk washout and a 4-wk diet/placebo run-in, 1528 patients with LDL-C 145 - 250 mg/dL and triglycerides ≤350 mg/dL, were randomized to one of the following daily treatments for 12 wks: EZE/SIM tablet (10/10, 10/20, 10/40, or 10/80 mg/mg); SIM alone (10, 20, 40, or 80 mg); EZE 10 mg; or placebo. The primary endpoint was % change from baseline in LDL-C for pooled EZE/SIM vs pooled SIM alone. RLP-C levels were measured using an immune separation assay.
Results: EZE/SIM produced significantly greater reductions in RLP-C than did SIM alone (table). For each SIM dose comparison, RLP-C was reduced more by the EZE/SIM combination (range: -31.8% to -47.4%) than by the corresponding dose of SIM alone (range: -22.5% to -37.5%; p<0.001 for all comparisons). The effects of EZE/SIM on RLP-C were consistent with the effects on LDL-C (-53.1% vs -39.0%; p<0.001); apolipoprotein B (-42.4% vs -31.6%; p<0.001); non-HDL-C (-48.7% vs -35.9%; p<0.001); and triglyceride (-24.3% vs -20.8%; p<0.001).
Conclusion: EZE/SIM in a single tablet (10/10 to 10/80 mg/mg) is more effective than the corresponding dose of SIM alone in reducing plasma levels of potentially atherogenic remnant lipoproteins.

Effect of Treatment on RLP-C

	Pbo (N=141)	EZE 10 mg (N=144)	Pooled SIM (N=597)	Pooled EZE/SIM (N=570)
Baseline RLP-C (mg/dL)	13.3	14.0	14.0	14.0
% Change from baseline	5.4	-15.6^	-29.31^	-40.6*^

*p<0.001 versus Pooled SIM; ^p<0.001 versus Pbo
RLP-C: remnant-like particle cholesterol; Pbo: placebo; EZE: ezetimibe; SIM: simvastatin

POSTER SESSION

1085

Hypertension Treatment Effects

Monday, March 08, 2004, Noon-2:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 1:00 p.m.-2:00 p.m.

1085-165 **Aliskiren, a Novel, Orally Effective Nonpeptide Renin Inhibitor, Lowers Blood Pressure After Once-Daily Dosing in Marmosets, Rats and Humans**

Jeanette M. Wood, Randy L. Webb, Frederic Cumin, Christian R. Schnell, Martin P. Bedigian, Novartis Institute for Biomedical Research, Basel, Switzerland, Novartis, East Hanover, NJ

Background: Renin inhibitors (RIs) provide an attractive new therapeutic approach to the treatment of hypertension, as they block the first and rate-limiting step of the renin-angiotensin system (RAS). The present study investigates the in vivo effects of aliskiren, the first of a new class of non-peptide RIs.
Methods: Aliskiren was administered orally to normotensive, sodium-depleted marmosets and to hypertensive (mean systolic BP ≥ 140 mmHg) human patients, and subcutaneously to spontaneous hypertensive rats (SHR). In animal studies, changes in mean arterial pressure (MAP; mean±s.e.mean) and heart rate were measured continuously by telemetry; 24 h ambulatory BP measurement was used in humans. Plasma renin activity was measured by antibody trapping assay.