The following trials were presented at the 48th Scientific Sessions of the American College of Cardiology, March 7–10, 1999, in New Orleans, La.

Unstable Angina

The Trial: FRISC II

Presenters: Lars Wallentin and Bo Lagerqvist, Cardiovascular Centre, University Hospital, Uppsala, Sweden.

The study: A randomized, placebo-controlled trial of low-molecular-weight heparin (dalteparin) in conjunction with either early revascularization or conservative medical therapy in 2457 patients with unstable angina or non–Q-wave myocardial infarction (MI). On admission, all patients received dalteparin (120 IU/kg every 12 hours) for the acute treatment phase (5 to 7 days) and were randomized to receive either invasive (n = 1222; routine angiography and intervention, if indicated, within 2 to 7 days) or conservative (n = 1235; angiography and intervention only if driven by refractory clinical symptoms) treatment. After the acute treatment phase, patients were further randomized to treatment with dalteparin (5000 or 7500 IU BID) or placebo in a prolonged (90 day), double-blind treatment phase. The primary endpoint of the study was a clinical outcome of death or MI (defined both conservatively [2/3 of pain, ECG changes, and enzyme elevation] or using enzymatic markers); initial 3-month follow-up data were presented.

The results: A total of 98% (95% within 6 days) of the invasive treatment group underwent angiography, compared with 48% (14% within 6 days) of the conservative treatment group. Revascularization was performed in 78% of patients in the invasive treatment group (44% had percutaneous coronary intervention [PCI] and 34% had coronary artery bypass grafting [CABG]) and 38% of patients in the conservative treatment group (18% had PCI and 19% had CABG); abciximab was used in ≈10% of coronary interventions. The composite primary endpoint was significantly reduced in the invasive treatment group (8.6% versus 11.8% using a conservative definition of MI; 9.5% versus 12.0% using enzymatic markers). Despite slightly higher initial in-hospital mortality (1.2% versus 0.4%), by 3 months, mortality tended to be lower in the invasive treatment group (1.9% versus 3.0%). The clinical benefits of the invasive strategy were largely confined to male patients; endpoint events at 3 months (using enzymatic markers) were significantly reduced in men (9.1% versus 13.9%), whereas they tended to be slightly, but not significantly, higher in women (10.5% versus 8.2%). Invasive treatment significantly reduced mortality in men (1.5% versus 3.2%) but not women (2.9% versus 2.6%). The invasive treatment group had fewer symptoms of angina and fewer readmissions than the conservative treatment group. During the prolonged treatment phase in the noninvasively treated patients, composite endpoint events in the low-molecular-weight heparin group were significantly reduced at 45 days (3.7% versus 6.5% with placebo); however, continuing therapy to 3 months provided no additional benefit. At 3 months, the incremental benefit in the low-molecular-weight heparin group had eroded somewhat (6.7% versus 8.0%) and was not statistically significant.

Summary: In patients with unstable angina, an invasive strategy results in significantly better clinical outcomes than a conservative strategy. However, the survival benefits seem to be confined to men; an invasive strategy resulted in no mortality benefit in women. Invasive therapy was associated with fewer symptoms and fewer readmissions than conservative therapy. Three months of low-molecular-weight heparin therapy after hospitalization provided little or modest benefit. There did seem to be some incremental benefit with low-molecular-weight heparin in the first 4 to 6 weeks after admission; however, this benefit mainly occurred when combined with a noninvasive strategy; longer term therapy provided no advantage over placebo in the invasive strategy group.

The Trial: OPUS-TIMI 16

Presenter: Christopher Cannon, Brigham and Women’s Hospital, Boston, Mass.

The study: A multicenter, randomized, placebo-controlled trial of orbofiban (an oral platelet glycoprotein [GP] IIb/IIIa antagonist) in patients with acute coronary syndromes. A total of 10 302 patients with unstable angina (rest pain within 72 hours, most with documented ECG and/or enzyme changes) were randomized to receive orbofiban 50 mg BID, orbofiban...
50 mg BID for 30 days and then 30 mg BID, or placebo. All patients received aspirin (150 to 162 mg/d). The primary endpoint was a composite of death, MI, recurrent ischemia leading to rehospitalization or urgent revascularization, or stroke. Analyses were performed at 30 days and through subsequent follow-up (mean, 7 months). Enrollment into the trial was halted early, before the target enrollment of 12,000 patients, because of excess 30-day mortality in one of the treatment groups.

The results: Preliminary results showed that the 30-day mortality rate was 1.4% in the placebo group, 2.3% in the orbofiban 50/30 group, and 1.6% in the orbofiban 50/50 group. Thirty-day composite primary endpoints were 10.7% in the placebo group, 9.7% in the orbofiban 50/30 group, and 9.3% in the orbofiban 50/50 group. Orbofiban was beneficial in reducing recurrent ischemic events leading to urgent revascularization (5.3% with placebo, 2.9% with orbofiban 50/30, and 3.3% with orbofiban 50/50). Follow-up composite event rates (Kaplan-Meier through 300 days) were 20.5%, 20.2%, and 19.5%, respectively; rates of death (3.2%, 4.7%, and 4.0%, respectively) and recurrent ischemia leading to revascularization (7.9%, 5.9%, and 5.8%, respectively) showed trends similar to those observed at 30 days. Severe or major bleeding was slightly, but significantly, increased with orbofiban: it was 1.9% (0.4% severe) with placebo, 3.3% (1.2% severe) with orbofiban 50/30, and 3.7% (0.7% severe) with orbofiban 50/50. Thrombocytopenia was rare, but slightly more frequent with orbofiban.

Summary: In patients with unstable angina or MI, the oral platelet IIb/IIIa antagonist orbofiban did not reduce clinical events at 10 months, and it may be associated with a small excess in early mortality. The reason for this excess mortality is not yet clear.

The Trial: FROST
Presenter: Robert Wilcox, University Hospital, Queen’s Medical Centre, Nottingham, UK.

The study: A randomized, placebo-controlled, dose-escalation trial of the oral GP IIb/IIIa antagonist lefradafiban in patients with acute coronary syndromes. A total of 531 patients who had chest pain within the past 24 hours and documented ECG changes (all treated with aspirin and heparin) were randomized to receive a placebo or 1 of 3 doses of lefradafiban (20, 30, or 45 mg TID). Treatment was continued for 1 month. The primary safety endpoint of the study was bleeding; the primary efficacy endpoint was the composite incidence of death, MI, or recurrent angina leading to revascularization.

The results: The high-dose lefradafiban group (45 mg TID) was stopped early because of excessively high bleeding rates (11% incidence of major bleeding compared with 1% in the placebo group, 3% in the 20 mg group, and 3% in the 30 mg group). Leukopenia (<4000 leukocytes/dL) and neutropenia (<1500 neutrophils/dL) were noted in 5.7% and 5.2% of lefradafiban-treated patients, respectively, compared with 3.1% and 1.5%, respectively, in the placebo group. This was an early-onset, rapid-recovery phenomenon, and it did not seem to be related to bone-marrow toxicity. The incidence of thrombocytopenia in lefradafiban-treated patients was 0.5%. There was a trend toward fewer recurrent ischemic events and fewer rehospitalizations in the higher dose (30 mg) lefradafiban group.

Summary: Lefradafiban produced a dose-dependent inhibition of platelet aggregation, but the 45 mg TID dose resulted in unacceptably high bleeding rates. Neutropenia (rapidly reversible, not related to marrow toxicity) was noted in 5.2% of patients; the incidence of thrombocytopenia was low. A trend toward fewer clinical events was noted, but given the observed safety profile, future trials are being carefully considered.

Heart Failure

The Trial: MERIT-HF
Presenter: Ake Hjalmarson, Goteborg University, Goteborg, Sweden.

The study: A randomized, placebo-controlled trial of metoprolol in patients with class II to IV congestive heart failure (CHF). A total of 3991 patients with CHF (65% ischemic, 35% nonischemic) were randomized to receive either metoprolol (starting dose, 12.5 to 25 mg; increased up to target of 200 mg; mean dose, 159 mg/d) or a placebo. The primary endpoint of the trial was total mortality. The trial was stopped prematurely because of excess benefit in metoprolol-treated patients.

The results: Annual mortality was 11% with placebo and 7.2% with metoprolol, a highly significant 34% relative decrease. This mortality benefit was evident in cardiovascular mortality (38% relative decrease), sudden death (41% relative decrease), and death due to progressive CHF (49% relative decrease). The mortality benefit was present across strata of left ventricular (LV) function and was significant in patients with both ischemic and nonischemic CHF.

Summary: Metoprolol therapy resulted in a significant mortality benefit in patients with CHF. The mortality benefit was consistent across clinical groups. β-Blocker therapy was well tolerated in this CHF population.

Na/H Exchange Inhibitors

The Trial: GUARDIAN
Presenter: Pierre Theroux, Montreal Heart Institute, Montreal, Canada.

The study: A randomized, placebo-controlled trial of cariporide (a Na/H exchange inhibitor) in patients at risk for MI or death. This class of compounds may provide protection to cardiac cells by reducing ischemia-associated damage and reducing reperfusion injury. The GUARDIAN study population included patients with unstable angina/non–Q-wave MI (n=5231), patients undergoing high risk percutaneous transluminal coronary angioplasty (PTCA; n=3441), and patients undergoing high-risk CABG (n=2918). Qualifying patients were randomized to 1 of 3 doses of cariporide (20, 80, or 120 mg IV TID) or placebo. Treatment was continued for 2 to 7 days in addition to standard medical therapy. The primary endpoint of the study was the composite incidence of death and MI (both Q-wave and non–Q-wave MI) 36 days after randomization.
The results: In the overall population, no significant differences existed in composite outcome events at 36 days between groups (13.4%, 13.5%, 14.1%, and 12.2% with placebo, 20 mg, 80 mg, and 120 mg of cariporide, respectively). Among the 3 subgroups of patients included in the study, a significant reduction of events occurred in patients undergoing surgical revascularization who were in the high-dose cariporide group (12.8% versus 16.7% with placebo). The high dose of cariporide also seemed to be effective in reducing the incidence of Q-wave MI (unstable angina, 1.5% versus 2.4% with placebo; PTCA, 0.8% versus 1.7% with placebo; CABG, 3.2% versus 4.9% with placebo; overall, 1.7% versus 2.8% with placebo). No increase in significant drug-related adverse events occurred with cariporide.

Summary: In the overall GUARDIAN study population, the Na/H exchange inhibitor cariporide did not significantly reduce composite adverse outcome events at 36 days. It did seem to be somewhat beneficial (in higher doses) in reducing the incidence of Q-wave MI, and it did seem to have some potential benefit (also in higher doses) in patients undergoing CABG.

Interventional Cardiology

The Trial: EXCITE


The study: A multicenter, randomized, placebo-controlled trial of the oral platelet GP IIb/IIIa antagonist xemilofiban in patients undergoing percutaneous coronary interventional procedures. A total of 7232 qualifying patients were randomized to receive 1 of 2 doses of xemilofiban (20 mg 30 to 90 minutes before the procedure and, subsequently, either 10 or 20 mg of xemilofiban TID) or placebo. Follow-up continued for at least 6 months. The primary endpoint of the study was the composite of death, MI, and urgent intervention. Stents were used in ~71% of patients; abciximab use was discouraged. Approximately 17% to 20% of patients were diabetic.

The results: At 30 days, no significant differences existed among the 3 groups in composite events (placebo, 8.1%; xemilofiban 10 mg, 8.1%; and xemilofiban 20 mg, 7.3%), although they tended to be somewhat less frequent in the higher dose xemilofiban group. A similar pattern was evident at 6 months (13.6%, 14.1%, and 12.6%, respectively). Disturbingly, mortality tended to be slightly higher in the lower dose xemilofiban group, both at 30 days (placebo, 0.4%; xemilofiban 10 mg, 0.9%; and xemilofiban 20 mg, 0.6%) and at 6 months (1.0%, 1.6%, and 1.1%, respectively). Interestingly, xemilofiban did seem to have a significant benefit in reducing clinical events in patients with diabetes.

Summary: In patients undergoing percutaneous coronary intervention, xemilofiban did not significantly reduce the composite incidence of death, MI, or urgent revascularization. There did seem to be some clinical benefit in patients with diabetes, but no other clinical group showed any demonstrable benefit. There was a disturbing trend toward increased mortality in the lower dose xemilofiban group.

The Trial: CLASSICS

Presenter: Michel Bertrand, Hospital Cardiologique de Lille, Lille, France.

The study: A multicenter, randomized, controlled trial of clopidogrel (a thienopyridine antiplatelet drug similar to ticlopidine) versus ticlopidine after coronary stenting. A total of 1020 patients undergoing coronary stent implantation at 48 European centers were randomized to post-stent antiplatelet therapy with aspirin (325 mg QD) plus ticlopidine (250 mg BID; n=340), aspirin plus clopidogrel (75 mg QD; n=335), or aspirin plus front-loaded clopidogrel (300 mg on day 1 followed by 75 mg QD; n=345). Therapy was initiated within 6 hours of a successful stent procedure and continued for 28 days afterward. The trial was primarily designed as a safety study; patients requiring the use of GP IIb/IIIa antagonists were excluded. The primary endpoint of the study was the composite of bleeding, neutropenia, thrombocytopenia, and early drug discontinuation for noncardiac adverse events. A secondary endpoint with clinical efficacy, assessed as the composite of cardiovascular death, MI, and target vessel revascularization, was determined at 30 days.

The results: Primary safety endpoint events were significantly reduced with clopidogrel; they occurred in 9.1% of the ticlopidine group, 6.3% of the 75 mg clopidogrel group, 2.9% of the 300/75 mg clopidogrel group, and 4.6% in the 2 clopidogrel groups combined. There were no instances of thrombocytopenia with clopidogrel. The major contribution to the primary endpoint came from a much higher percentage of early drug discontinuation (primarily due to allergic reactions, gastrointestinal disorders, and skin rash) with ticlopidine, specifically 8.2%, compared with 5.1% in the 75 mg clopidogrel group, 2.0% in the 300/75 mg clopidogrel group, and 3.5% in the 2 clopidogrel groups combined. The secondary endpoint of composite adverse cardiac events was not significantly different among the groups: 0.9% with ticlopidine, 1.5% in the 75 mg clopidogrel group, 1.2% in the 300/75 mg clopidogrel group, and 1.3% in the 2 clopidogrel groups combined.

Summary: In patients undergoing coronary stent implantation, post-procedure antiplatelet therapy with clopidogrel plus aspirin is much better tolerated than ticlopidine plus aspirin, with comparable clinical outcomes.

The Trial: PACIFIC

Presenter: Stephen Osterle, Massachusetts General Hospital, Boston, Mass.

The study: A multicenter, randomized trial comparing percutaneous transmyocardial laser revascularization (PMR) with medical therapy in patients who are not otherwise candidates for revascularization therapy. A total of 206 patients with class III/IV angina who were not candidates for PTCA or CABG were randomized to PMR (using the Cardiogenesis system) or continued medical therapy. The primary endpoints of the trial were angina score and exercise tolerance at 6-month follow-up.

The results: In the PMR group, significant symptomatic improvement occurred. Approximately 70% of the patients had class 0/1/II symptoms, and 46% of patients had a 2-class improvement in symptoms (compared with 6% of the medical
therapy group). The PMR group also had significantly better exercise tolerance. There were no deaths, MIs, or strokes during PMR, and only a 1% incidence of tamponade and a 1% incidence of heart block.

Summary: In patients with severe angina and no other revascularization options, PMR can be performed safely, and it seems to result in significant improvement in angina symptoms and exercise tolerance.

The Trial: ADMIRAL
Presenter: Gilles Montalescot, Pitie-Salpetriere Hospital, Paris, France.

The study: A randomized, placebo-controlled trial of adjunctive platelet GP IIb/IIIa antagonist therapy in patients treated with PTCA and primary stenting for acute MI. A total of 299 MI patients presenting within 12 hours of the onset of symptoms were randomized to receive abciximab (n = 149) or placebo (n = 150) before intervention. All patients were treated with aspirin, heparin, and ticlopidine. Patients with cardiogenic shock were excluded from the study. Stents were used in ≈85% of patients; ≈30% of patients received ≥2 stents. Study drug therapy was initiated before arrival in the catheterization laboratory in ≈25% of patients. The primary endpoint of the study was the 30-day composite incidence of death, MI, and ischemia-driven target vessel revascularization. Angiography was repeated 24 hours after the interventional procedure.

The results: Preliminary results showed that the 30-day primary composite clinical endpoint was significantly reduced in the abciximab group (10.7% versus 20% with placebo). Abciximab patients had a significantly higher incidence of TIMI (Thrombolysis in Myocardial Infarction) grade III flow before intervention (21% versus 10.3% with placebo); at the end of the interventional procedure, TIMI flow grades were 90% in both groups, but 24 hours after the procedure, abciximab-treated patients again had a significantly higher incidence of TIMI grade III flow (85.6% versus 78.4% with placebo) and higher ejection fractions (54.6% versus 51.4% with placebo). Major bleeding was slightly, but not significantly, higher in the abciximab group (4.0% versus 2.6% with placebo). Minor bleeding was more frequent with abciximab.

Summary: In patients undergoing primary angioplasty with stenting for acute MI, adjunctive abciximab results in better TIMI III flow, slightly better LV function at 24 hours, and better clinical outcomes at 30 days, with a slight excess of minor bleeding.

The Trial: VIVA
Presenter: Timothy Henry, Hennepin County Medical Center, Minneapolis, Minn.

The study: A randomized, placebo-controlled, clinical trial of vascular endothelial growth factor (VEGF), a natural angiogenic protein, in patients with viable, but underperfused myocardium (as documented by single photon emission computed tomography) who were not optimally eligible for PTCA or CABG. Qualifying patients were randomized to either low-dose VEGF (17 ng · kg⁻¹ · min⁻¹) intracoronary for 20 minutes and 3 subsequent 4-hour intravenous treatments on days 3, 6, and 9; n = 56), high dose VEGF (50 ng · kg⁻¹ · min⁻¹; n = 59), or placebo (n = 63). The primary endpoint of the study was exercise treadmill time at day 60.

The results: No significant differences existed in exercise treadmill times among the 3 groups at baseline or at 60-day follow-up. Similarly, no significant differences existed among groups in improvement in exercise time, angina class, improvement in angina class, or clinical events. VEGF infusions were well tolerated and not associated with adverse events.

Summary: In patients with viable, but underperfused myocardium who are not optimal candidates for revascularization, intracoronary and intravenous VEGF treatment did not result in a significant improvement in exercise time or angina class at day 60 compared with placebo. The fact that all 3 groups (including the placebo group) had significant improvement from baseline reinforces the importance of placebo-controlled trials in this area.

The Trial: OPUS
Presenter: Douglas Weaver, Henry Ford Heart and Vascular Institute, Detroit, Mich.

The study: A multicenter, randomized trial comparing routine stenting versus optimal angioplasty with stent deployment, if necessary, for inadequate results. A total of ≈500 patients with symptomatic angina (stable or unstable, excluding MIs within 24 hours) and single target vessels with a reference diameter ≥3 mm and lesions ≥20 mm in length were randomized to routine stenting or angioplasty with provisional stenting. Multivessel procedures were excluded. Aspirin and ticlopidine were administered for 4 weeks. Failure criteria in the provisional stent group included >20% residual stenosis (visual), >30% threatened closure (by quantitative coronary angiography), or a long or flow-limiting dissection. The primary endpoint of the study was the composite of death/MI and target-vessel revascularization over the 6 months after the procedure. Additional cost data and quality-of-life data were also collected.

The results: At 6 months, the routine stent group had significantly fewer primary outcome events (6.1% versus 14.9% in the angioplasty group; P < 0.003). The largest component contributing to this difference was target vessel revascularization (4.0% versus 10.7% with angioplasty); the rates of death (0.4% versus 1.2%), MI (1.7% versus 7.4%), and CABG (1.9% versus 3.9%) also tended to be lower in the stent group. Average in-hospital costs were higher in the stent group ($9200 versus $5400), but with the decrease in recurrent events, 6-month costs in the stent groups were actually slightly, but significantly, lower ($10 200 versus $10 400).

Summary: In isolated lesions ≤20 mm in target vessels ≥3 mm, primary stenting is superior to optimal angioplasty with provisional stenting; 6-month clinical outcomes (primary target vessel revascularization) were significantly better and 6-month costs were slightly, but significantly, lower.

Electrophysiology

The Trial: MUSTT
Presenter: Alfred Buxton, Temple University School of Medicine, Philadelphia, Pa.
The study: A multicenter, randomized, controlled trial evaluating the use of electrophysiological study–guided (EP-guided) therapy and the use of implantable cardioverter-defibrillators (ICDs) in high-risk patients with coronary artery disease, depressed LV function (ejection fraction ≤40%), and inducible sustained ventricular tachycardia. A total of 704 qualifying patients were randomized to EP-guided therapy or no antiarrhythmic therapy. If they received EP-guided therapy, initial therapy was with a randomly assigned Food and Drug Administration–approved agent; if initial therapy was unsuccessful, the patient could receive an ICD or the antiarrhythmic agent could be changed. Both groups received β-blockers and/or angiotensin-converting enzyme inhibitors as clinically indicated. The primary endpoint of the study was the incidence of arrhythmic death or cardiac arrest.

The results: A total of 46% of patients in the EP-guided therapy group underwent defibrillator placement after failing EP-guided drug testing. The mean duration of follow-up was 39 months. The incidence of arrhythmic death or cardiac arrest at 5 years was 32% in patients randomized to no antiarrhythmic therapy and 25% in the EP-guided therapy group. Primary endpoint events in the latter group who received EP-guided drug testing. The mean duration of follow-up was 39 months. The incidence of arrhythmic death or cardiac arrest at 5 years was 32% in patients randomized to no antiarrhythmic therapy and 25% in the EP-guided therapy group. Primary endpoint events in the latter group who received an ICD were reduced by >50% compared with patients in the EP-guided therapy group that did not receive an ICD. EP-guided pharmacological therapy alone did not seem to convey a survival benefit.

Summary: In high-risk patients with coronary artery disease, depressed LV function, and inducible sustained ventricular tachycardia, EP-guided therapy is useful in reducing the risk of arrhythmic death and cardiac arrest. This benefit seems to arise from the use of ICDs; EP-guided pharmacological therapy alone did not convey a survival benefit.

Acute Myocardial Infarction

The Trial: ASSENT II

Presenter: Frans Van de Werf, Gasthuisberg University Hospital, Leuven, Belgium.

The study: A multicenter, randomized, equivalence trial in patients treated with thrombolytic therapy for acute MI comparing standard front-loaded recombinant tissue-type plasminogen activator (rt-PA) with TNK t-PA, a modified form of t-PA with increased fibrin specificity, increased resistance to plasminogen activator inhibitor-I (PAI-1), and decreased plasma clearance (allowing single-bolus administration). The dose of TNK t-PA was weight-adjusted and between 30 to 50 mg. A total of 16 949 patients (3660 in the Angioplasty/CABG group and 56% in the aggressive medical/in-
Aortic balloon pumping therapy provide comparable 30-day outcomes with nonsignificant differences favoring early revascularization. Longer term outcomes in patients younger than 75 years may favor early revascularization. More complete and longer term follow-up data are awaited.

Preventive Cardiology

**The Trial: GISSI-Prevention**

**Presenter:** Franco Valagussa, Mario Negri Institute, Milan, Italy.

The study: A multicenter, randomized, placebo-controlled trial evaluating the efficacy of dietary supplementation with polyunsaturated fatty acid (n-3 PUFA) and/or vitamin E for secondary coronary prevention. In this study, 11,324 patients with a history of recent (within 3 months) MI were randomized to dietary supplementation with n-3 PUFA (1 g/day; n=2836), vitamin E (300 mg/day; n=2830), n-3 PUFA plus vitamin E (n=2830), or placebo (n=2828). The primary endpoint of the study was the composite incidence of total mortality, nonfatal MI, and nonfatal stroke at 3.5-year follow-up.

The results: Primary clinical endpoint events at 3.5 years were significantly reduced in patients receiving n-3 PUFA alone (12.2%) and n-3 PUFA plus vitamin E (12.3%) but not vitamin E alone (12.4%), compared with control patients (14.4%). Events increased when the 2 groups receiving n-3 PUFA were combined (12.4% versus 13.7% in the 2 groups that did not). Although a trend toward fewer events existed when the 2 groups of patients receiving vitamin E were combined (12.7% versus 13.4% in the 2 groups that did not), this did not achieve statistical significance. Total mortality was significantly reduced in the n-3 PUFA alone group (8.1%) and the n-3 PUFA plus vitamin E group (8.2%), but not the vitamin E alone group (8.8%), compared with the control group (10.1%). A large contributing factor seemed to be the incidence of sudden cardiac death, which was 1.9%, 2.5%, 2.3% and 3.5% in the respective groups.

Summary: In patients with a recent history of MI, dietary supplementation with n-3 PUFA (1 g/day) but not vitamin E (300 mg/d) seems to significantly reduce long-term cardiac events, total mortality, and sudden cardiovascular death. Combining the 2 therapies provided no incremental benefit over n-3 PUFA alone.

**The Trial: SCAT**

**Presenter:** Koon K. Teo, University of Alberta, Alberta, Edmonton, Canada.

The study: A multicenter, randomized, placebo-controlled trial of the angiotensin-converting enzyme inhibitor enalapril and the hepatic hydromethylglutaryl coenzyme A reductase inhibitor simvastatin in slowing the progression of and promoting the regression of atherosclerosis in normotensive coronary artery disease patients with normal lipid levels. A total of 460 patients were randomized, in a factorial design, to receive simvastatin only, enalapril only, simvastatin plus enalapril, or placebo. The primary endpoint of the study was lesion severity at follow-up angiography.

The results: Simvastatin therapy was associated with slightly, but significantly, less disease progression. Enalapril alone or adding enalapril to simvastatin had no such effect. The simvastatin group tended to have less need for subsequent revascularization; the enalapril group tended to have fewer composite adverse clinical events (death/MI/stroke).

Summary: Simvastatin reduces atherosclerotic progression slightly but significantly. Adding enalapril to simvastatin conveys no additional angiographic benefit, but enalapril therapy was associated with fewer composite adverse clinical events.

APPENDIX. Trial Name Acronyms

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<th>Trial Name Acronyms</th>
<th>Description</th>
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<td>Assessment of the safety and efficacy of a new thrombolytic agent II</td>
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<td>Simvastatin and enalapril coronary atherosclerosis trial</td>
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<td>SHOCK</td>
<td>Should we emergently revascularize occluded coronaries for cardiogenic shock?</td>
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<td>VIVA</td>
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Meeting Highlights: Highlights of the 48th Scientific Sessions of the American College of Cardiology
James J. Ferguson

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