American College of Cardiology 58th Annual Scientific Session in Orlando, FL.

The primary objective of TIPS was to determine whether the Polycap™ is equivalent to its individual components in reducing blood pressure (BP) and heart rate (HR), modifying lipids, and suppressing urine thromboxane B2 and whether it has a similar adverse event profile. The secondary objective of TIPS was to determine whether the Polycap™ is superior in reducing BP compared with its components.

The study population comprised 2053 subjects aged 45 to 80 years (mean age 54 years; 44% women) without cardiovascular disease but with at least 1 risk factor. One-third (33.9%) of the subjects had diabetes, mean baseline BP was 134/85 mm Hg, and mean cholesterol was 180 mg/dl (HDL 44 mg/dL and LDL 117 mg/dL).

Subjects were randomly assigned to receive either the Polycap™ (n=412) or 1 of 8 other formulations (n≈200 each) for 12 weeks. The 8 other formulations, which used the same doses of agents as Polycap™, were: aspirin alone, thiazide alone, thiazide + either ramipril or atenolol or both, thiazide + ramipril + atenolol + aspirin, ramipril + atenenol, and simvastatin alone.

In the Polycap group, BP reductions (7.4 mm Hg systolic and 5.6 mm Hg diastolic) were comparable with those that were seen in the group that received 3 BP medications (6.9 mm Hg systolic and 5.0 mm Hg diastolic). Aspirin did not interfere with the BP-lowering effects of the Polycap™.

LDL reductions in the group that was randomized to Polycap™ (0.70 mmol/L [23.3%]), however, were significantly lower than those that were seen in the group that received simvastatin alone (0.83 mmol/L [27.7%]; p<0.04), leading the investigators to speculate that the 40 mg dose should be tried instead of the 20 mg dose of simvastatin in order to enhance the benefits. Reductions in LDL for both groups of individuals who received the polycap, however, were significantly (p<0.0001) better than for subjects who did not receive simvastatin.

The reductions in HR with Polycap™ (7.0 beats/min) and other arms using atenolol (7.0 beats/min) were similar, and both were significantly greater than those in subjects who did not receive atenolol (p<0.001). The reduction in thromboxane B2 that was seen with Polycap™ (-322.3) was similar to that seen with aspirin alone (-388.0) or the combination of thiazide, atenolol, and ramipril + aspirin (-389.3; all p<0.001 vs baseline).

Polycap™ was well tolerated, and there was no evidence of increasing rates of adverse effects or discontinuation of study drugs with increasing numbers of active components in the pill.

Based on the results of this study, the investigators estimate that in individuals who are at average risk of cardiovascular disease, the use of Polycap™ could potentially result in a 62% reduction in the relative risk for coronary heart disease and a 48% reduction in the relative risk for stroke. However, they emphasized the need for large, prospective randomized trials to evaluate this hypothesis.

The study was sponsored by Cadila Pharmaceuticals, India, which played no role in data collection, analysis, or interpretation.

Results of the TIPS study were simultaneously published in *The Lancet* (Online Publication, 30 March 2009).

No Benefit from Omega-3 Supplements in Addition to Optimal Medical Therapy

Results from the OMEGA (NCT00251134) trial, presented by Jochen Senges, MD, Heart Center Ludwigshafen, University of Heidelberg, Germany, show that dietary supplementation with omega-3 fatty acids offers no additional benefits when added to optimal medical therapy (OMT) in patients who have suffered a heart attack.

The OMEGA trial primarily evaluated the effect of 1g daily of highly purified omega-3 acid ethylesters for 1 year in addition to OMT on the rate of sudden cardiac death (SCD) in patients with recent acute myocardial infarction (AMI). Secondary endpoints were total mortality, arrhythmic events, and the rates of reinfarction, stroke, and revascularization.

The study involved 3851 subjects with AMI (74.4% males; mean age 64 years), 59% of whom were diagnosed with ST elevated myocardial infarction (STEMI). Approximately 24% of the subjects had an ejection fraction <45%; 66% had hypertension, 50% had hypercholesterolemia, and 27% had diabetes. Coronary angiography was performed in 94% of patients, 78% of subjects underwent percutaneous coronary intervention, and 8% received fibrinolytic therapy.

Three to 14 days after AMI, patients were randomly assigned to 1 year of treatment with highly purified omega-3 fatty acids along with OMT (n=1937) or placebo (1 g olive oil; n=1909) and OMT. At the time of discharge from the hospital, 95% of patients were prescribed

aspirin, 88% clopidogrel, 94% beta-blockers, 94% statins, and 83% ACE inhibitors.

After approximately 1 year of follow-up, there was no significant difference on the primary study endpoint of SCD or on any of the secondary endpoints between patients who were assigned to guidelines-based OMT alone or OMT plus omega-3 fatty acids (Table 1). At follow-up, triglyceride levels were very similar between groups (121 vs 127 mg/dL). No additional benefit for omega-3 supplementation in addition to OMT was evident across the prespecified subgroups that were analyzed.

Table 1. Effect of Omega 3 on Primary and Secondary Study Endpoints.

	Total	Omega-3 n=1919	Placebo n=1885	p value
Primary Study Endpoint				
SCD	1.5%	1.5%	1.5%	0.84
Secondary Study Endpoints				
Total mortality	4.2%	4.6%	3.7%	0.18
Arrhythmic events	0.9%	1.1%	0.7%	0.22
Reinfarction	4.3%	4.5%	4.1%	0.63
Stroke	1.1%	1.4%	0.7%	0.07
Revascularization	28.4%	27.7%	29.1%	0.36
MACCE*	9.6%	10.4%	8.8%	0.10

*MACCE = total death, repeat MI, stroke.

The findings from OMEGA contradict those of previous studies, which suggested that supplementation with omega-3 fatty acids improves long-term survival. "In our study, there was a very low rate of cardiac events after acute myocardial infarction," Dr. Senges said. "It would be incorrect to say that omega-3 fatty acids are not effective, but we could not find any additional benefits after optimizing medical therapy" after 12 months of therapy. The lower-than-anticipated event rate, resulting in a realized power of ~50%, and the absence of longer-term follow-up are important limitations of this study.

Early Routine Eptifibatide Use is Not Superior to Delayed Provisional Use in NSTE ACS

The early routine administration of eptifibatide is not superior to delayed provisional eptifibatide use among invasively managed patients with high-risk non-ST-segment elevation acute coronary syndrome (NSTE ACS), according to findings from the Early Glycoprotein IIb/IIIa Inhibition in Non-ST-Segment Elevation Acute Coronary Syndromes (EARLY-ACS; NCT00089895) study. Moreover, compared with delayed use, early eptifibatide use increases bleeding and transfusion rates.

L. Kristin Newby, MD, MHS, Duke University Medical Center, Durham, NC, and Robert P. Giugliano, MD, SM, Brigham and Women's Hospital, Boston, MA, reported findings from the EARLY-ACS trial, which was designed to compare a strategy of eptifibatide that was initiated shortly after presentation with a strategy of delayed provisional use of the glycoprotein IIb/IIIa inhibitor just prior to percutaneous coronary intervention (PCI).

The EARLY-ACS trial included 9492 patients with 2 or more high-risk criteria, including an age of 60 years or older, elevated troponin or creatine kinase MB, and ischemic changes on electrocardiography. Within 12 hours of presentation, patients were randomly assigned to treatment with a strategy of early, routine eptifibatide administration shortly after presentation (n=4722) or a strategy of delayed, provisional eptifibatide use at the treating physician's discretion after coronary angiography and prior to PCI (n=4684). The primary endpoint was a composite of death, myocardial infarction (MI), recurrent ischemia that required urgent revascularization, and thrombotic bailout within 96 hours of treatment.

The primary endpoint occurred in 9.3% of patients in the early eptifibatide group and 10.0% of those in the delayed eptifibatide group (OR, 0.92; 95% CI, 0.80 to 1.06; p=0.23). There was a nonsignificant trend toward a reduction in the risk of death or MI at 30 days with early versus delayed eptifibatide treatment (11.2% vs 12.3%; OR, 0.89; 95% CI, 0.79 to 1.01; p=0.08), but there was no difference between these groups in the 30-day mortality rate (2.8% vs 2.6%; p=0.46).

The early eptifibatide strategy increased bleeding risk through 120 hours, as measured by Thrombolysis in Myocardial Infarction (TIMI) and Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries (GUSTO) criteria. Compared with those in the delayed eptifibatide group, patients in the early eptifibatide group had a higher rate of TIMI major hemorrhage (1.8% vs 2.6%; p=0.02), TIMI major or minor bleeding (3.4% vs 5.8%; p<0.001), GUSTO moderate or severe bleeding (5.1% vs 7.6%; p<0.001), and red blood cell transfusion (6.7% vs 8.6%; p=0.001). However, there were no significant differences in the risks of