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

life-threatening bleeding (GUSTO severe bleeding 0.8% vs 0.9%; p=0.97), peri-CABG bleeding, thrombocytopenia, or stroke between the early-routine and delayed-provision eptifibatide groups.

These findings do not support the routine use of early eptifibatide in patients with high-risk NSTE ACS that is managed with an invasive strategy. However, if subgroups of patients with high likelihood of benefit and low bleeding risk could be identified, it might be reasonable to consider early eptifibatide use in selected high-risk NSTE ACS patients who intend to undergo angiography, Dr. Giugliano said.

EARLY ACS joins an array of other trials—including PURSUIT, PRISM, PARAGON A, PARAGON B, ACUITY, and ACUITY Timing—that have examined the utility and timing of small molecule glycoprotein IIb/IIIa inhibition in NSTE ACS. Together, these trials suggest a role for glycoprotein IIb/IIIa inhibition in the management of selected high-risk patients. Future analyses may identify which subgroups of patients are most likely to benefit.

Findings from the EARLY-ACS trial were simultaneously published online in the *New England Journal of Medicine.*

Genetic Variants Associated with Early Onset Myocardial Infarction also Associated with Need for Future Revascularization

A genetic variant that is associated with early-onset myocardial infarction (MI) is also associated with the progression of coronary atherosclerosis and the need for revascularization years after an MI, according to study results that were presented by Diego Ardissino, MD, University of Parma, Parma, Italy.

Previous studies showed that genetic variants on chromosome 9 (9p21.3) are associated with ischemic heart disease [Samani N et al. *N Engl J Med* 2007; McPherson R et al. *Science* 2007], but it was not known if these genetic variants affected prognosis after MI.

The Italian Genetic Study in Early-Onset Myocardial Infarction was a nonrandomized, prospective, observational study that was conducted at more than 100 Italian coronary care centers to assess whether the 9p21.3 single nucleotide polymorphism rs1333040 would influence the occurrence of new cardiovascular events and the progression of coronary atherosclerosis after early-onset MI. Early-onset MI (defined as occurring at age 45 years or younger) was selected for the study, said Dr. Ardissino, because "the influence of genetic factors is greater when the acute coronary event occurs at an early age."

The study had 2 arms–a cross-sectional arm that included 2000 subjects with early-onset MI and 2000 healthy controls who were matched for age, sex, and geography, and a longitudinal arm, in which subjects (n=492) who had received primary percutaneous coronary intervention (PCI) were excluded. Dr. Ardissino reported on the longitudinal arm of the study, in which the subjects (n=1508) were followed for up to 20 years.

Subjects (mean age at first MI 41 years; >85% men) were tested for 5 allelic variants in the 9p21.3 region. Each subject was classified as being homozygous for the risk allele, heterozygous for the risk allele, or "wild-type" (reflective of the general population). Results showed that all 5 allelic variants were associated with early-onset MI. The marker that had the strongest association (rs1333040) was chosen for statistical analysis (heterozygous OR, 1.43; 95% CI, 1.22 to 1.67; homozygous OR, 2.04; 95% CI, 2.49 to 2.79; $p=1e^{-54}$). The clinical endpoint of the study was a composite of cardiovascular death, recurrence of MI, and need for coronary artery revascularization. The angiographic endpoint was progression of coronary atherosclerosis, as evaluated by the Duke Coronary Artery Disease Index.

Significant (p=0.01) differences in the time to the primary clinical endpoint were found between both the homozygous and heterozygous groups versus the wild-type group. Results diverged, however, when the components of the primary endpoint were analyzed separately, wherein a significant (p=0.00015) effect was shown on time to coronary artery revascularization (RR vs wild-type for heterozygous 1.38; 95% CI, 1.17 to 1.63 and for homozygous 1.90; 95% CI, 1.36 to 2.65) but not on time to cardiovascular death or MI recurrence. Angiographically, rs1333040 showed a significant (p=0.002) influence on progression of coronary atherosclerosis. The median change in the Duke Coronary Artery Disease Index was 19.

The investigators concluded that in patients with early-onset MI, the 9p21.3 single nucleotide polymorphism rs1333040 affects the progression of coronary atherosclerosis and the probability of undergoing coronary artery revascularization during long-term follow-up. Testing for genetic variants may influence treatment.