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.