Safety results were similar to the overall trial. There was no significant difference in the risk of PLATO major, TIMI major, or fatal bleeding between treatment groups. Episodes of dyspnea were more common with ticagrelor (13.8%) compared with clopidogrel (7.8%). The difference was statistically significant (p<0.0001) and led to significantly (p=0.002) more ticagrelor patients who discontinued treatment.

Ticagrelor differs from thienopyridines, such as clopidogrel, in a number of important ways. It is *not* a prodrug and thus does not require hepatic activation—instead, it directly inhibits the adenosine diphosphate (ADP) receptor P2Y12 (purinoceptors), which is involved in platelet activation. Ticagrelor has a rapid onset of action and can completely inhibit the sustained aggregation response to ADP; yet, it is reversible, wherein functional recovery of circulating platelets occurs within 48 hours of treatment cessation. Because patients with STEMI who undergo primary PCI require urgent and effective blockade of the P2Y12 platelet receptor and are at a greater risk of side effects from inconsistent platelet inhibition, the pharmacokinetic profile of ticagrelor is well suited for treating such patients.

One drawback, mentioned by the discussant of this trial, Lisa K. Jennings, PhD, University of Tennessee Health Science Center, Memphis, TN, was the need for twice-daily dosing due to ticagrelor's reversible binding properties and 12-hour half-life. This might cause problems for patients who are not fully compliant. In balance, however, the significant reduction in all-cause mortality and in clinically important cardiac events, without increased bleeding, makes this new agent a promising new addition to oral antiplatelet therapy for patients with STEMI who are undergoing PCI.

Primary PCI at Hospitals without On-Site Cardiac Surgery Increases Risk of Repeat Vascularization

According to a new analysis of data from the Massachusetts Data Analysis Center (MASS-DAC) registry, patients who are undergoing primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) face similar risks of death and MI but higher rates of repeat revascularization when treated at hospitals without on-site cardiac surgery (non-SOS) capabilities compared with hospitals with cardiac surgery capabilities (SOS).

If it can be performed quickly (within 90 minutes of initial medical contact), primary PCI is the preferred method of reperfusion in patients with STEMI, according to current American Heart Association/American College of Cardiology guidelines. However, most patients with STEMI present to hospitals without SOS, where primary PCI is generally discouraged (eg, in Massachusetts). With limited access to immediate PCI, many patients with STEMI either are treated with fibrinolytic therapy or face potential delays in treatment in transfer to PCI centers.

Allowing primary PCI in hospitals without SOS could greatly expand access to timely PCI for STEMI patients. In 1997, the Massachusetts Department of Health initiated a pilot program for primary PCI at non-SOS hospitals. Ather Anis, MD, Boston University Medical Center, Boston, MA, presented findings from the MASS-DAC analysis, comparing outcomes of primary PCI in hospitals depending on the availability of SOS.

Of a total of 6139 patients in the MASS-DAC registry with STEMI who underwent PCI between 2005 and 2007, there were 3018 patients with complete data who were not transferred and were treated at centers with (n=2041) and without (n=977) cardiac surgery capabilities. Demographic, clinical, and angiographic variables were included in multivariate analyses, with propensity score-matching to minimize confounding. The primary outcomes were 30-day and 1-year all-cause mortality, MI, repeat revascularization, and target vessel revascularization.

Patients who were treated at non-SOS hospitals were more frequently white, covered by HMO insurance, and had multivessel disease. All-cause mortality was similar in centers with and without cardiac surgery capabilities at 30 days (4.5% vs 5.7%; p=0.22) and at 1 year (9.4% vs 8.6%; p=0.51). Although there was a trend toward increased risk of MI at 30 days at non-SOS hospitals (4.35% vs 2.82%; p=0.05), the risk of MI was similar at 1 year (6.7% vs 5.1%; p=0.11).

Target vessel revascularization rates were also similar at 30 days (6.3% vs 5.0%; p=0.21) and at 1 year (10.9% vs 9.7%; p=0.39). However, repeat revascularization rates were significantly higher in non-SOS centers through 30 days (14.9% vs 7.6%; p<0.0001) and 1 year (21.0% vs 14.7%; p<0.0001).

This observational analysis suggests that primary PCI may be safely performed in patients who present with STEMI to non-SOS hospitals, with no differences observed in 30-day or 1-year mortality. Dr. Anis noted, however, that "STEMI patients undergoing primary PCI at hospitals without on-site cardiac surgery had a slightly higher incidence of

recurrence [MI] at 30 days for reasons that are unclear and will require further study." Further analyses that account for differences in the timing of procedures and selection of patients who underwent PCI and other differences in patients between hospital types are pending.

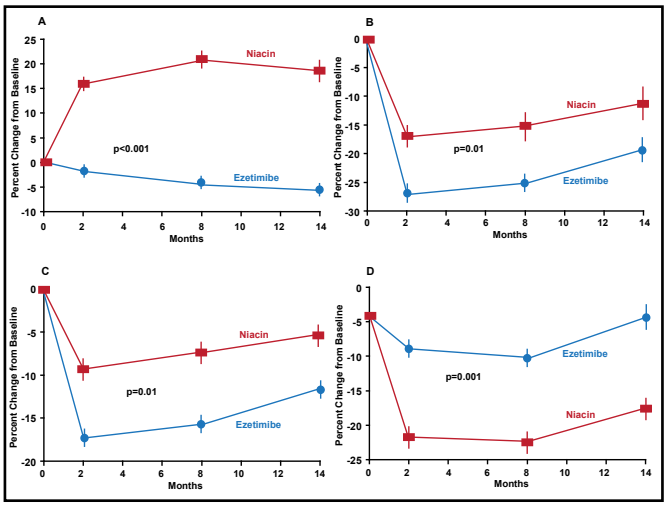
Statin plus Extended Release Niacin is More Effective Than Statin plus Ezetimibe in Reducing CIMT

Results from the Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol 6-HDL and LDL Treatment Strategies (ARBITER-6 HALTS; NCT00397657) trial, presented by Allen J. Taylor, MD, Walter Reed Army Medical Center, Washington, DC, showed that combination therapy that uses a statin plus niacin is more effective than the combination of a statin plus ezetimibe in reducing carotid intima-media thickness (CMIT).

The ARBITER-6 HALTS trial enrolled a total of 363 subjects (mean age 65 years; 80% men) with coronary heart disease (CHD) or a CHD risk equivalent who were receiving long-term (6±5 years) statin therapy (95% simvastatin or atorvastatin; mean dosage 42±25 mg/day) and who had an LDL-C level <100 mg/dL (mean 82.1±23.1 mg/dL) and an HDL-C level <50 mg/dL (<55 mg/dL for women). Subjects were randomly assigned in a double-blind fashion to receive open-label extended release (ER) niacin (target dosage 2000 mg/day) or ezetimibe (10 mg/day) along with their usual statin. The primary study endpoint was the between-group difference in the change from baseline in mean CMIT after 14 months. Secondary endpoints included change in lipid values, a composite of major adverse cardiovascular events (MACE; ie, myocardial infarction, myocardial revascularization, hospital admission for an acute coronary syndrome, and death from CHD), adverse event (AE)-associated discontinuations, and health-related quality of life (HRQoL).

The study was stopped prematurely, based on the consistency of findings in CMIT at 8 and 14 months; results of a sensitivity analysis, and a post hoc analysis that suggested potentially paradoxical effects of ezetimibe, after 208 patients (111 ezetimibe; 97 niacin) had completed the trial. When compared with baseline, the addition of niacin to statin therapy resulted in a significant regression of both mean and maximal CMIT at 8 and 14 months; the corresponding changes in CMIT with ezetimibe compared with baseline were not significant on either measure at either timepoint. At 14 months, the between-group comparisons were significant for both measures: -0.0142 mm±0.0041 reduction in mean CMIT for the niacin combination versus -0.0007 mm±0.0035 with ezetimibe (p=0.01) and -0.0181 mm±0.0050 versus -0.0009 mm±0.0039, ezetimibe and niacin combinations, respectively (p=0.006). Mean HDL-C levels in the niacin group increased by 7.5±9.2 mg/dL, while those in the ezetimibe group decreased by 2.8±5.7 mg/dL (p<0.001). Mean LDL-C levels decreased by 17.6±20.1 mg/dL in the ezetimibe group and by 10.0±24.5 mg/dL (p=0.01) in the niacin combination group. There was a significant reduction in triglyceride levels in both groups (Figure 1).

Figure 1. Mean Percent Changes in Cholesterol and Triglyceride Levels.



The incidence of MACE was significantly (p=0.04) higher in the ezetimibe group (5%; 9/165) compared with the niacin group (1%; 2/160). AE-related withdrawals were similar in the two groups. Adherence was significantly (p<0.001) higher in the ezetimibe group (95±8%) compared with the niacin group (88±15%). Cutaneous flushing was reported in 36% of patients in the niacin group. The final dosage of ER niacin was 2000 mg/day in 75%, 1500 mg/day in 3%, 1000 mg/day in 12%, and 500 mg/day in 10% of patients. HRQoL outcomes were similar in both groups.

A number of limitations of this study must be considered. ARBITER-6 HALTS was a small open-label trial that used a controversial surrogate endpoint, and thus these data can not be used to evaluate clinical benefit adequately. The study was prematurely terminated (which may have exaggerated the observed benefits), and the post hoc analysis that suggested a paradoxical effect with ezetimibe