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.

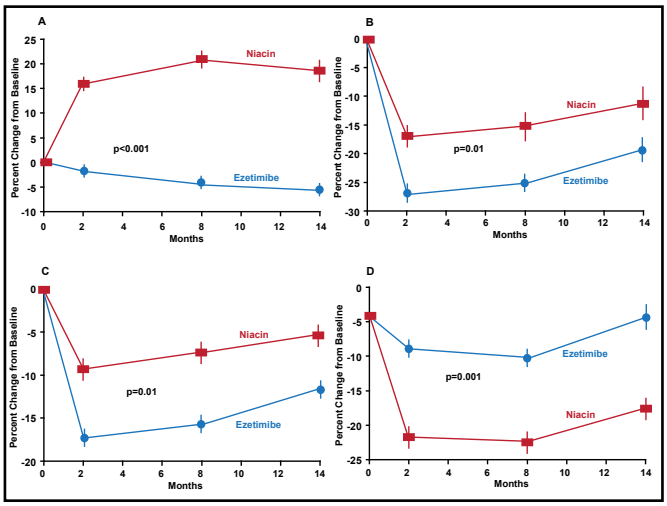
Statin plus Extended Release Niacin is More Effective Than Statin plus Ezetimibe in Reducing CIMT

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

with possible adverse clinical consequences was neither robust nor well supported by external data. Several large ongoing randomized double-blinded clinical trials are evaluating the clinical benefit and safety of niacin and ezetimibe (although none of these trials is comparing the two directly). Such large-scale trials will serve as the foundation for shaping future guidelines and clinical practice with niacin and with ezetimibe.

Additional reading:

- Taylor AJ et al. Extended-Release Niacin or Ezetimibe and Carotid Intima-Media Thickness. *N Engl J Med*. Published online 16 November 2009.
- Kastelein JJP & Bots ML. Statin Therapy with Ezetimibe or Niacin in High-Risk Patients. *N Engl J Med*. Published online 16 November 2009.

Collaborative Care Improves HRQoL, Physical Functioning, and Mood Symptoms in Patients with Post-CABG Depression

Results from the Bypassing the Blues trial (NCT00091962) indicate that depression screening shortly after coronary artery bypass graft (CABG) surgery, telephone follow-up using evidence-based depression treatment protocols, and patient education that is supervised by primary care physicians (ie, collaborative care) can improve health-related quality of life (HRQoL), physical functioning, and mood symptoms and thereby speed patient recovery following CABG surgery.

Post-CABG depression is common (20% to 25% incidence) and has been associated with delayed recovery, increased hospital readmissions, cardiovascular events, and death. The Bypassing the Blues trial was designed to test the effectiveness of a telephone-delivered collaborative care strategy for treating post-CABG depression versus doctors' usual care. Post-CABG patients who expressed mood symptoms that were indicative of depression (Patient Health Questionnaire [PHQ-2] positive screen) preceding discharge, followed by a PHQ-9 score ≥10 at 2 weeks posthospitalization, were randomly assigned to an 8-month course of collaborative care (n=150) or their physicians' "usual care" (n=152). Results were also compared with a group of 151 randomly sampled nondepressed post-CABG patients (PHQ-2 negative and PHQ-9 <5).

The intervention consisted of telephone contact at regular intervals, during which the nurses provided basic psycho education, assessed treatment preferences (eg, self-management workbook, antidepressant pharmacotherapy, referral to a mental health specialist), monitored treatment response, and suggested changes to patients and their primary care physicans (PCP) following a discussion with a study psychiatrist and PCP. The study investigators did not prescribe or dispense any antidepressant medications, and patients who were interested in pharmacotherapy were required to obtain this treatment from their PCP and at cost. No pharmaceutical or industry support was involved in this trial.

The primary outcome measure was mental HRQoL, as measured by the Short Form-36 Mental Component Summary (SF-36 MCS) at 8 months. Secondary outcome measures included assessment of mood symptoms (Hamilton Rating Scale for Depression [HRS-D]), physical HRQoL (SF-36 PCS), and functional status (Duke Activity Status Index [DASI]); and rehospitalization rate.

The 302 depressed subjects were well matched by baseline randomization status; however, depressed subjects were slightly younger than those in the nondepressed comparison group (mean age 64 vs 66 years; p=0.03). Approximately 25% of depressed patients were already using an antidepressant medication at baseline.

Depressed subjects who were randomized to collaborative care experienced a significant improvement in HRQoL compared with subjects in the usual care group beginning at 2 month follow-up that was equivalent to a small to moderate effect size (ES) of 0.30 (95% CI, 0.17 to 0.52; p=0.01) and a number needed to treat (NNT) of 4.9 (3.2 to 10.4; p<0.001) to achieve a 50% or greater decline from baseline HRS-D score. The improvement in mood symptoms appeared to be more prominent in men (ES, 0.53; 95% CI, 0.23 to 0.84; p<0.001). Patients who received collaborative care also had improved scores on the HRS-D for mood symptoms (ES, 0.30; 95% CI, 0.08 to 0.53; p=0.009), the SF-36 PCS (ES, 0.26; 95% CI, 0.03 to 0.48; p=0.03) for physical status, and DASI (ES, 0.32; 95% CI, 0.09 to 0.54; p=0.006) for physical functioning. The mean HRQoL and physical functioning of patients who received intervention did not reach those of the nondepressed comparison group for any of the measures.

Overall, while there was no difference in the incidence of rehospitalization between study arms by randomization status, there was a trend toward fewer rehospitalizations for cardiovascular causes among depressed men who were randomized to their intervention (13%) versus men who were randomized to usual care (25%; p=0.07). However, the study was underpowered to detect a difference in cardiovascular events of mortality (1% overall mortality by 8-month follow-up). Cost data are not yet available.