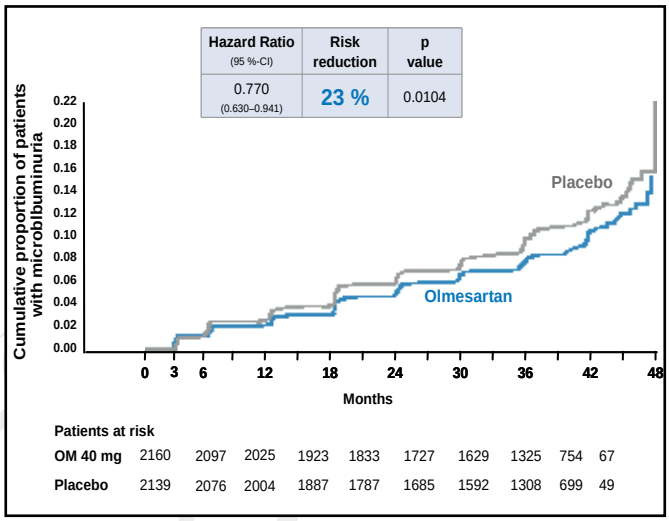
Patients in the olmesartan group were 23% less likely than those in the placebo group to develop microalbuminuria at 48 months (HR, 0.770; p=0.0104). The renoprotective benefit of olmesartan was independent of its effect on BP. MAU was less common in the olmesartan group after correcting for differences in diastolic BP (HR, 0.810; p=0.0398) and systolic BP (HR, 0.814; p=0.0451: Figure 1) between the ARB and placebo groups.

Figure 1. Time to First Occurrence of MAU.



According to a safety analysis, olmesartan showed no detrimental effects on renal outcomes at 48 months. The composite risk of CV morbidity and mortality was 4.3% in the olmesartan group and 4.2% in the placebo group (HR, 1.00; p=0.99). Fatal CV events were rare, but occurred more frequently in the olmesartan group (n=15) than in the placebo group (n=3; HR, 4.94; p=0.01). The risk of CV mortality with olmesartan relative to placebo was significantly increased only among patients with pre-existing CVD (p=0.02). CV deaths in the olmesartan group were also associated with hypotension, occurring more frequently in patients with the lowest systolic BP levels and in those who experienced the greatest reduction in systolic BP.

On June 11, 2010, the U.S. Food & Drug Association (FDA) announced that it is reviewing interim safety data from ROADMAP and the Olmesartan Reducing Incidence of End Stage Renal Disease in Diabetic Nephropathy Trial (ORIENT), which also showed excess CV mortality with olmesartan compared with placebo. According to Prof. Haller, an observational follow-up study of ROADMAP is underway to further understand the long-term benefits of preventing the onset of MAU in patients with type 2 diabetes.

Further Reading: FDA MedWatch. Benicar (olmesartan) Ongoing Safety Review. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm215249.htm.

Self-Management Better Than Usual Care in Reducing Blood Pressure Levels in Patients with Uncontrolled Hypertension

Self-management of hypertension with self-monitoring of blood pressure (BP) levels and self-titration of antihypertensive medications results in significantly lower systolic blood pressure (SBP) compared with usual care, according to findings from the Telemonitoring And Self-Management In The Control Of Hypertension (TASMINH2) trial.

Recent improvements in automated BP meters have lead to the widespread use of self-monitoring by patients with hypertension. However, the effectiveness of a self-management intervention that combines self-monitoring with self-titration of antihypertensive medication in the primary care setting is unknown. Richard J. McManus, University of Birmingham, Birmingham, UK, reported findings from the TASMINH2 trial (ISRCTN17585681), which was designed to evaluate the role of dual-intervention self-management in reducing BP levels in patients with poorly controlled hypertension.

The TASMINH2 trial included 480 patients with elevated BP levels (>140/90 mm Hg) who had previously been treated with up to 2 antihypertensive medications. Patients were randomly assigned to self-management (n=246) or usual care (n=234). Patients in the self-management group agreed to perform monthly self-monitoring of BP levels. Based on BP findings, patients in the self-management group also followed medication titration schedules that were individually tailored to each patient's guideline-recommended BP goals. The primary endpoint was SBP at 6 and 12 months.

Self-management was associated with greater reductions in mean SBP compared with usual care at 6 months (-12.9 mm Hg vs -9.2 mm Hg; p=0.013) and at 12 months (-17.6 mm Hg vs -12.2 mm Hg; p=0.0004). At 6 months, patients in the self-management and usual-care groups showed similar decreases in diastolic BP (DBP; -5.4 mm Hg vs -4.2 mm Hg; p=0.108). However, by 12 months, self-management showed a significant advantage in DBP reduction compared with usual care (-7.6 mm Hg vs -5.0 mm Hg; p=0.001).

Greater BP control within the self-management group may be due to increased use of antihypertensive medication. Overall, 212 patients (80%) in the self-management group adhered to the self-monitoring and self-management regimen for the full 12 months of the study. Of these, 148 patients (70%) made at least one change to their antihypertensive treatment regimen during the course of

the study. Indeed patients in the self-management group were significantly more likely than those in the usual care group to change medications during the study, with a mean of 0.46 more changes by month 12 (p=0.001). The most common agents added to the antihypertension treatment regimens were thiazide diuretics and calcium channel blockers.

Self-management was well tolerated. Patients had similar rates of side effects in both treatment arms with the exception of leg swelling, which occurred more frequently in the self-management group than in the usual care group (32% vs 22%; p=0.022).

Findings from TASMINH2 demonstrate the effectiveness of the self-monitoring of BP levels and the self-titration of BP medication in patients with uncontrolled hypertension. Self-management represents an important new intervention in the management of hypertension in primary care, Prof. McManus concluded.

The Potential Blood Pressure Lowering Benefit of Azilsartan Medoxomil

In a recent study comparing azilsartan medoxomil (AZL-M) with olmesartan medoxomil (OLM-M) and placebo, AZL-M therapy was found to be safe and effective in patients with primary hypertension. Angiotensin receptor blockers (ARB) such as OLM-M are thought to be better tolerated than other classes of antihypertensives. However, many patients continue to experience inadequate blood pressure (BP) control despite medical therapy. Therefore, more therapeutic options are being investigated in the hopes of providing more reliable BP control. OLM-M was chosen as a comparative ARB due to its similarity to AZL-M with regards to its mechanism of action.

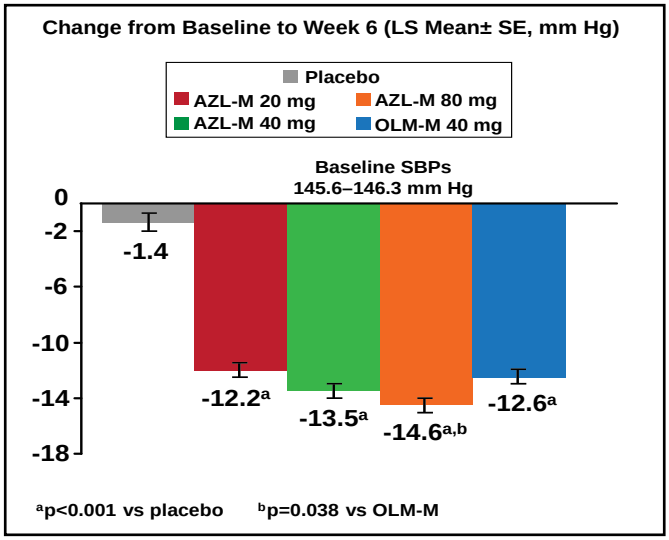
George L. Bakris, MD, University of Chicago Medical Center, Chicago, Illinois, USA, presented findings from this phase III, multicenter, parallel-group, double-blind, randomized placebo-and active-controlled trial (NCT00696241). The purpose of this study was to compare the BP lowering effects of AZL-M with OLM-M and placebo over a period of 6 weeks in patients with primary hypertension.

A total of 1275 patients were randomized to receive AZL-M 20 mg daily (n=283), AZL-M 40 mg daily (n=283), AZL-M 80 mg daily (n=285), OLM-M 40 mg daily (n=282) or placebo (n=142) and BP was evaluated using ambulatory BP monitoring (ABPM) and clinic BP measurement. Patients with trough sitting clinic diastolic BP >114 mm Hg, history of a major cardiovascular event, secondary hypertension, hyperkalemia, renal artery stenosis, or Type 1/poorly controlled diabetes were excluded from participation in the study. The groups were well-matched at baseline with regards to demographics and BP readings.

The primary endpoint was change in 24-hour mean systolic BP (SBP) from baseline to Week 6, as determined by ABPM. The secondary efficacy endpoints included change from baseline to Week 6 in trough sitting clinic SBP, 24-hour mean sitting diastolic BP (DBP) according to ABPM, and other ABPM parameters, such as mean trough BP at 22 to 24 hours post-dosing. Secondary safety endpoints included adverse events and laboratory data.

Treatment with all doses of AZL-M resulted in significantly lower 24-hour mean SBP compared with placebo at Week 6 (p<0.001 for all doses). This was also the case with 24-hour mean DBP in AZL-M patients versus placebo (0<0.001 for all doses). Patients taking AZL-M 80 mg had significantly reduced 24-hour mean SBP compared with OLM-M 40 mg (p=0.038; Figure 1). The AZL-M 80 mg group also demonstrated significant improvement in trough sitting clinic SBP and DBP at Week 6 compared with OLM-M 40 mg (p=0.043 and p=0.044, respectively).

Figure 1. 24-Hour Mean SBP by ABPM.



Serious adverse events occurred in 2.1% of patients in the placebo group, 2.8% in the AZL-M 20 mg group, 0.4% in the AZL-M 80 mg group, and 0.7% in the OLM-M group. No serious adverse events were reported in the AZL-M 40 mg group. A total of 30 patients discontinued treatment due to adverse events (6 in placebo, 11 in AZL-M 20 mg, 3 in AZL-M 40 mg, 6 in AZL-M 80 mg, and 4 in OLM-M 40 mg group). One death did occur in the AZL-M 20 mg group. Overall, the safety profiles of all AZL-M doses were similar to that of OLM-M and placebo.

These findings demonstrate that AZL-M is safe and effective for the treatment of primary hypertension. It is important to note that AZL-M is not currently licensed for the treatment hypertension. However, these results are quite promising and warrant further investigation.