Comparison of *Olmesartan Medoxomil* Versus *Amlodipine Besylate* on Regression of Ventricular and Vascular Hypertrophy

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Reversal of left ventricular (LV) hypertrophy is an important goal of antihypertensive therapy. This phase 3b study compared the ability of the angiotensin receptor blocker olmesartan medoxomil with the calcium channel blocker amlodipine besylate to induce regression of LV hypertrophy and vascular hypertrophy after achieving blood pressure (BP) goal. After a washout phase, 102 patients with hypertension and LV hypertrophy were randomized to olmesartan medoxomil 20 mg/day, up titrated to 40 mg/day, or amlodipine 5 mg/day, up titrated to 10 mg/day, for up to 4 weeks until a BP goal of <140/90 mm Hg (<130/85 mm Hg for diabetes) was achieved (hydrochlorothiazide 25 mg/day and terazosin 1 to 5 mg/day 2 times/day could be added if needed). Upon achieving the BP goal or by week 8, and again at weeks 26 and 52, assessments of LV mass and compliance and arterial structure and function were performed by echocardiography, Doppler flow, and arterial ultrasonography, respectively. There was no statistically significant percent change in LV mass at 52 weeks in either treatment group (11.6% with olmesartan medoxomil vs 2.9% with amlodipine) and no statistically significant difference between treatment groups. There were no significant changes in LV compliance or carotid or femoral artery wall-to-lumen ratios in either treatment group at 52 weeks. In conclusion, there did not appear to be a clinically significant BP-independent effect with olmesartan medoxomil or amlodipine on LV mass decrease, diastolic function or vascular structure, and compliance in patients with hypertension and LV hypertrophy. Published by Elsevier Inc. (Am J Cardiol 2009; 104:359–365)

From currently available study results, renin–angiotensin system (RAS) blockers and calcium channel blockers (CCBs) have emerged as recommended first-line antihypertensive agents for patients with left ventricular (LV) hypertrophy.[1] However, there is still some uncertainty as how best to decrease LV hypertrophy in patients with hypertension.[2,3] Olmesartan medoxomil is a relatively long 1/2-life angiotensin receptor blocker (ARB) that exhibits insurmountable blockade of angiotensin II binding to the angiotensin type 1 receptor,[4] leading us to hypothesize that, by virtue of its inhibition of angiotensin II–mediated proliferative effects on the cardiovascular system, this agent would be an appropriate choice of treatment for patients with hypertension and LV hypertrophy. The aim of the present study was to evaluate the ability of olmesartan compared with the long-acting dihydropyridine CCB amlodipine besylate to induce regression of LV and vascular hypertrophy after controlling for blood pressure (BP) in a cohort of patients with hypertension and LV hypertrophy. These patients are at high risk for further progression of LV and vascular hypertrophy. This unique study design differed from that of several previous studies of RAS-inhibiting agents in that patients were treated to achieve specified BP targets before evaluating the treatment effects of olmesartan or amlodipine on LV hypertrophy.

Methods

This was a single-center, prospective, randomized, double-blind, parallel-group phase 3b study comparing the efficacy of olmesartan with amlodipine in reversing LV hypertrophy in patients with LV hypertrophy and primary hypertension after 52 weeks of double-blind therapy. Patients were titrated on their assigned medications using a predefined algorithm to achieve target BPs before evaluating the treatment effect on reversing LV hypertrophy.

This study was conducted in accordance with good clinical practice and the principles of the Declaration of Helsinki regarding the ethical conduct of clinical trials and approved by the institutional review board of the James J. Peters VA Medical Center (Bronx, New York). Written informed consent was obtained before any study procedures.

Patients included in the study were ≥18 years of age with a diagnosis of hypertension and LV hypertrophy and were required to have a mean systolic BP of 140 to 200 mm Hg and/or a mean diastolic BP of 90 to 120 mm Hg. Patients could not take antihypertensive drug therapy for 1 week to 3 weeks before these BP measurements. LV hypertrophy was diagnosed in patients who had any 1 of the following electrocardiographic characteristics: sum of S wave in lead V_1 and R wave in lead V_5 or V_6 >32 mm, R wave in lead

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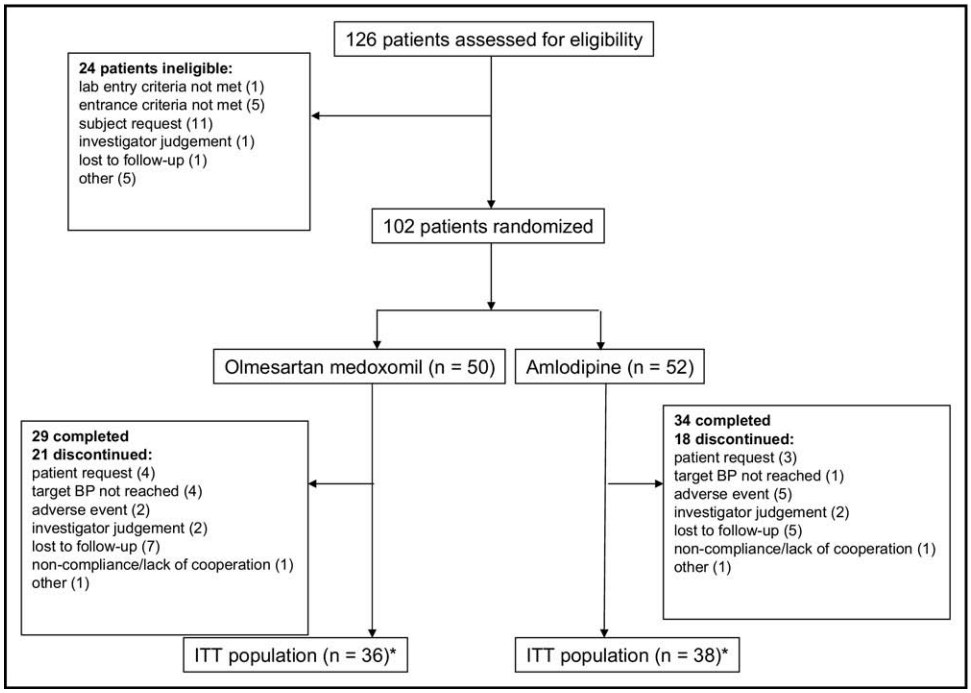

Figure 1. Patient disposition. *Intent-to-treat (ITT) population includes all randomized patients who received ≥1 dose of study drug and had baseline and postbaseline efficacy measurements.

V_5 or V_6 >27 mm, or R wave in lead aVL >11 mm. A history of severe hepatic or renal impairment was grounds for exclusion, as was a history of allergic response to any ARB, dihydropyridine, CCB, thiazide diuretic or α-adrenoceptor antagonist. Laboratory safety screening was required; patients were excluded if hemoglobin levels were <10 g/dl in men and <9 g/dl in women, white blood cell count was <2,000 /ml, neutrophil count was <1,500 /ml, platelet count was <100,000 /ml, creatinine level was >3.0 mg/dl, alanine aminotransferase/serum glutamic pyruvic transaminase level was >2.5 times the upper limit of normal, aspartate aminotransferase/serum glutamic oxaloacetic transaminase level was >2.5 times upper limit of normal, potassium level was <3.3 mg/dl, and any other laboratory abnormalities that could compromise patients' safety. Patients took no antihypertensive agents other than those specified by the protocol.

The study was divided into 3 phases: a 1- to 3-week washout/screening period during which all antihypertensive therapy was discontinued; a dose titration phase of ≤4 weeks; and a maintenance therapy period (end of dose titration to the end of 52 weeks of active therapy). Eligible patients were randomized 1:1 to olmesartan 20 mg/day or amlodipine 5 mg/day, with randomization stratified according to a diagnosis of diabetes mellitus. During the 4-week titration period, BP was checked at least every 2 weeks, with assigned medication titrated to reach a target BP <140/90 mm Hg (patients without diabetes) or <130/85 mm Hg (BP goal for patients with diabetes at the time the study was conducted). The titration sequence consisted of (1) doubling of initial doses to olmesartan 40 mg or amlodipine 10 mg; (2) addition of open-label hydrochlorothiazide 25 mg/day; (3) addition of open-label terazosin 1 mg 1 time/day; and (4) terazosin up titration to a maximum dose of 5 mg 2 times/day. At the end of titration, any patient with a diastolic BP ≥5 mm Hg above target or whose systolic BP remained above target were withdrawn. BP was measured at all study visits (scheduled during weeks 1 to 2, 2 to 4, 3 to 6, 4 to 8, and 8 to 14 and at weeks 26, 39, and 52). If target BP was not achieved at any visit, the regimen was adjusted according to the titration algorithm. The antihypertensive regimen was back-titrated for any patient who, in the investigator's opinion, had too low a BP. Compliance was determined by unused pill counts at each study visit.

The primary efficacy end point was percent change in LV mass from "on-treatment" baseline to the end of 52 weeks of active therapy. Percent change in LV mass after 26 weeks of treatment was a secondary study end point. Additional secondary end points obtained at 26 and 52 weeks were percent change in LV compliance and wall-to-lumen ratio and arterial compliance for common carotid and femoral arteries.

LV mass was obtained using standard 2-dimensional M-mode echocardiography, which was performed at the attainment of target BP during the titration phase or after 8 weeks of blinded therapy (whichever came first for the baseline measurement) and at 26 and 52 weeks. LV mass was corrected for height to generate the LV mass index. LV compliance was assessed using Doppler transmitral flow velocity curves to generate the E/A ratio and deceleration time. To measure arterial wall-to-lumen ratio and compliance, carotid and femoral ultrasonograms, using a 7.0- to 7.5-MHz probe ultrasound system, were obtained. Arterial compliance was defined as $(\Delta D/D)/\Delta P$, wherein ΔD is the change in arterial diameter during 1 cardiac cycle, D is the end-systolic diameter, and ΔP is the pulse pressure. Echocardiographic, Doppler flow, and ultrasonographic procedures were performed during the same study visits (on-

Table 1
Baseline demographic and clinical characteristics and cardiovascular history for all randomized patients (safety cohort)

Variable	Olmesartan (n = 50)	Amlodipine (n = 52)
Age (years)	63.7 ± 12.1	64.1 ± 11.3
Men	50 (100.0%)	51 (98.1%)
Ethnic origin		
Black	38 (76.0%)	35 (67.3%)
White	7 (14.0%)	4 (7.7%)
Hispanic	5 (10.0%)	10 (19.2%)
Other	0 (0.0%)	3 (5.8%)
Weight (lb)	200.3 ± 41.2	192.8 ± 37.4
Height (in)	68.8 ± 3.4	68.7 ± 2.8
BP (mm Hg)	163.2 ± 18.1/92.2 ± 12.1	164.9 ± 13.8/92.1 ± 13.6
Family history of hypertension	28 (56.0%)	28 (53.8%)
Diabetes mellitus	7 (14.0%)	10 (19.2%)
Angina pectoris	2 (4.0%)	3 (5.8%)
Myocardial infarction	3 (6.0%)	1 (1.9%)
Heart failure	0 (0.0%)	1 (1.9%)
Stroke	2 (4.0%)	4 (7.7%)
Transient ischemic attack	0 (0.0%)	1 (1.9%)
Peripheral vascular disease	3 (6.0%)	0 (0.0%)
Arrhythmia	4 (8.0%)	3 (5.8%)

Data are presented as mean ± SD or number of patients (percentage).

treatment baseline and weeks 26 and 52). Inflammatory markers of atherosclerosis (C-reactive protein and transforming growth factor-β) were also measured.

Adverse events, clinical laboratory values, and vital signs were monitored during the study. Physical examination, serum chemistry profiles, and complete blood counts were performed at screening and at 26 and 52 weeks (absolute neutrophil count was performed only at screening). Vital signs (BP and heart rate) were obtained at screening and each study visit. BP readings were reported to the nearest 2 mm Hg as the average of 2 readings taken after ≥5 minutes in the sitting position. As part of the safety assessment, a 12-lead electrocardiogram was obtained at screening and at weeks 26 and 52.

Analysis of efficacy was based on an intent-to-treat study population consisting of patients who received ≥1 dose of randomized study drug, had a baseline measurement, and ≥1 baseline efficacy measurement after baseline measurement. The safety population consisted of patients who received ≥1 randomized dose of study medication.

If normally distributed, analysis of the primary efficacy variable, percent change in LV mass, was to be based on analysis of covariance, with baseline LV mass as a covariate and treatment and diabetes strata as factors. If analysis of covariance assumptions were violated, analysis was to be based on analysis of variance, with treatment and diabetes strata as factors. Ninety-five percent confidence intervals were calculated for differences in treatment effects, but if the data were not normally distributed, nonparametric methods were used. One-sample t test or, as appropriate, nonparametric Wilcoxon signed-rank test was to be used to test whether the change from baseline to week 52 was statistically significant within each treatment group. Analyses of secondary end points were handled similarly to the primary efficacy variable.

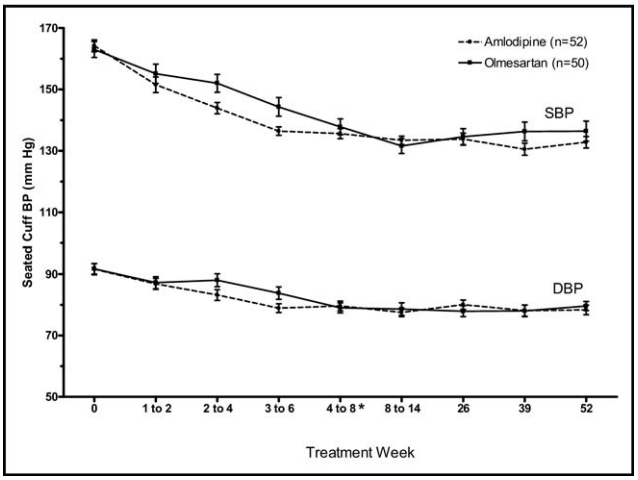

Figure 2. Timing of electrocardiography and echocardiography in relation to changes in systolic and diastolic BP (between-group differences not statistically significant). Electrocardiograms were obtained at weeks 0, 26, and 52. Echocardiograms were obtained at weeks 8, 26, and 52. *On-treatment echocardiographic baseline (week 8); expected deadline for target BP. DBP = diastolic BP; SBP = systolic BP.

Based on an estimation (from published studies) that, at week 52, treatment with olmesartan and amlodipine would be associated with LV mass decreases of approximately 15% and 10%, respectively, a sample of 84 patients (42 per treatment group) would provide 80% power at a 5% 2-sided significance level, assuming a common SD of 8%.

Results

As shown in Figure 1, 126 patients were screened for eligibility, 102 patients were randomized to treatment and received ≥1 dose of study medication (50 for olmesartan and 52 for amlodipine), and 39 patients did not complete the study. The efficacy dataset comprised 74 patients available for intent-to-treat analysis (36 for olmesartan and 38 for amlodipine). Of the intent-to-treat patient set, 72 patients (36 in each treatment group) had an echocardiogram at week 26 and 69 patients (32 for olmesartan and 37 for amlodipine) had an echocardiogram at week 52. As presented in Table 1, the randomized treatment groups were closely matched. Most patients in the 2 treatment groups were black (72% overall) and men (99% overall). There were 2 times as many Hispanic patients in the amlodipine group as in the olmesartan group. With regard to cardiovascular disease status, ≥92% of patients reported no history of cardiovascular disease diagnoses or episodes other than LV hypertrophy. During the 3 months before randomization, 88 patients (86.3%) received antihypertensive therapies, which included angiotensin-converting enzyme inhibitors, CCBs, β blockers, α blockers, loop or thiazide diuretics, or spironolactone. Many patients also received previous and ongoing therapy with lipid-lowering medications and/or aspi-

Table 2
Adjusted mean percent changes in left ventricular mass and compliance from baseline* at weeks 26 and 52 of treatment (efficacy cohort)

Variable	Olmesartan (n = 36)		Amlodipine (n = 38)		Between-Group Difference†	
	Percent Change‡	p Value§	Percent Change‡	p Value§	95% CI	p Value‖
Left ventricular mass						
52 weeks (primary end point)	11.6 ± 4.9	0.469	2.9 ± 4.3	0.832	−1.7 to 19.1	0.099
26 weeks	8.0 ± 5.2	0.221	6.0 ± 4.9	0.163	−9.3 to 13.3	0.727
Left ventricular compliance						
E-A ratio						
26 weeks	8.3 ± 5.7	0.650	13.7 ± 5.6	0.127	−18.0 to 7.3	0.399
52 weeks	9.4 ± 8.7	0.121	8.0 ± 7.8	0.123	−17.4 to 20.1	0.882
Deceleration time						
26 weeks	3.7 ± 4.4	0.277	2.3 ± 4.3	0.273	−8.3 to 11.0	0.784
52 weeks	−1.0 ± 4.9	0.578	4.9 ± 4.4	0.150	−16.3 to 4.4	0.257

* Baseline measurements were taken at attainment of target BP during the 4-week titration period or after a total 8 weeks of therapy (whichever came first).
† Mean olmesartan change minus mean amlodipine change.
‡ Data are adjusted means ± SE.
§ Calculated using 1-sample *t* test.
‖ Calculated using analysis of covariance with baseline LV mass, E/A ratio, or deceleration time as a covariate, and diabetes and treatment strata as factors.
CI = confidence interval.

rin. Patients were >90% compliant with olmesartan and amlodipine treatment regimens at each study visit. Compliancy ranged from 88.7% to 96.6% with terazosin and from 41% to 100% with hydrochlorothiazide.

Mean ± SD BPs at week 52 were 136.4 ± 18.21/79.6 ± 8.10 mm Hg in the olmesartan group and 132.8 ±11.32/78.3 ± 9.31 mm Hg in the amlodipine group. Changes in systolic BP are presented in Figure 2. Most patients (62 of 102) required additional open-label antihypertensive therapy to reach BP targets (68.0% in the olmesartan group and 53.8% in the amlodipine group).

Mean ± SD LV masses of 252.9 ± 73.06 g in the olmesartan group and 236.9 ± 59.94 g in the amlodipine group at on-treatment baseline were decreased to 248.2 ± 69.31 and 223.9 ± 53.18 g, respectively, after 52 weeks of therapy. Analysis of covariance analysis indicated that mean ± SD percent changes from baseline were 3.4 ± 25.82 in the olmesartan group and −0.9 ± 23.69 in the amlodipine group, which translated into adjusted treatment least squares mean changes of 11.6% in the olmesartan group and 2.9% in the amlodipine group (Table 2). Neither of these changes was significantly different from baseline, and the difference between the 2 treatment groups was not significant. At 26 weeks, adjusted percent changes in LV mass were 8.0% with olmesartan and 6.0% with amlodipine. As with the primary 52-week end point, changes occurring at the 26-week assessment were not significantly different from baseline or from each other.

Mean ± SD baseline LV mass indexes were 145.0 ± 39.70 g in the olmesartan group and 136.0 ± 34.50 g in the amlodipine group. At 52 weeks, mean ± SD LV mass indexes were 142.6 ± 38.02 and 128.9 ± 30.89 g in the olmesartan and amlodipine treatment groups, respectively.

With regard to LV compliance, mean ± SD E/A ratios at on-treatment baseline were 0.9 ± 0.34 in the olmesartan group and 0.8 ± 0.21 in the amlodipine group, and mean ± SD deceleration times were 205.9 ± 36.87 and 206.9 ± 38.31 ms, respectively. By week 52, mean ± SD E/A ratio was still 0.9 ± 0.34) in the olmesartan group and had increased to 0.9 ± 0.37 for patients treated with amlodipine, and mean ± SD deceleration values were 206.5 ± 32.87 and 218.9 ± 53.63 ms, respectively. Analysis of adjusted percent changes in E/A ratio and deceleration times from baseline to weeks 26 and 52 are presented in Table 2. Neither olmesartan nor amlodipine was associated with significant changes compared with on-treatment baseline, and there were no significant differences between the 2 groups with regard to percent change in E/A ratio or deceleration time.

Clinically significant changes from baseline, indicating regression of LV hypertrophy (decrease in voltage) in most cases, were noted on electrocardiogram for the 2 treatment groups (Figure 3).

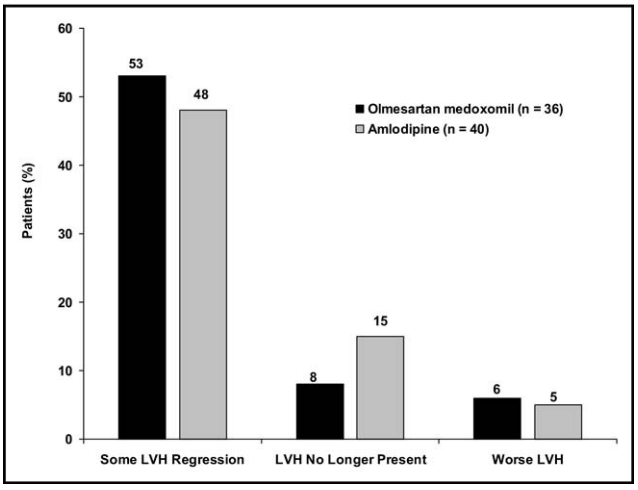

Figure 3. Proportions of patients with clinically significant changes in electrocardiographic voltage suggesting some LV hypertrophic regression, complete regression of LV hypertrophy (LVH; LV hypertrophy no longer present), or worse LV hypertrophy after 52 weeks of treatment with olmesartan medoxomil or amlodipine.

Table 3
Median percent change in carotid and femoral artery wall-to-lumen ratios and compliance from baseline* at weeks 26 and 52 of treatment

Variable	Olmesartan		Amlodipine		Between-Group Difference†
	Median Percent Change‡	p Value§	Median Percent Change‡	p Value§	p Value‖
Arterial wall-to-lumen ratio					
Carotid					
26 weeks	0.00% (30)	0.3252	−1.56% (31)	0.8935	0.5985
52 weeks	3.81% (29)	0.3788	5.48% (33)	0.1557	0.6315
Femoral					
26 weeks	11.29% (30)	0.0828	9.38% (31)	0.0256	0.9482
52 weeks	4.85% (28)	0.9470	−2.78% (33)	0.9235	0.9481
Arterial compliance					
Carotid					
26 weeks	−0.76% (30)	0.6964	10.81% (32)	0.0853	0.3139
52 weeks	13.97% (26)	0.1708	5.99% (31)	0.8334	0.4038
Femoral					
26 weeks	9.50% (31)	0.1892	4.29% (31)	0.4775	0.6728
52 weeks	10.51% (27)	0.0881	4.64% (33)	0.4144	0.6451

* Baseline measurements were taken at attainment of target blood pressure during the 4-week titration period or after a total 8 weeks of therapy (whichever came first).

† Mean olmesartan change minus mean amlodipine change.

‡ Patients having >200% increase or >200% decrease in arterial wall-to-lumen ratio or in arterial compliance at 26 or 52 weeks were considered to be outliers and were excluded from statistical analysis. Data are presented as percentage (number of patients).

§ Calculated using 1-sample *t* test.

‖ Calculated using analysis of covariance with baseline carotid or femoral wall-to-lumen ratio or compliance as a covariate, and diabetes and treatment strata as factors.

Table 4
Adverse events

Variable	Olmesartan (n = 50)	Amlodipine (n = 52)
≥1 adverse event	36 (72.0%)	38 (73.1%)
Possibly treatment related	7 (14.0%)	10 (19.2%)
Probably treatment related	1 (2.0%)	4 (7.7%)
Definitely treatment related	1 (2.0%)	0 (0.0%)
Events reported by ≥6% of patients		
Arthralgia	4 (8.0%)	4 (7.7%)
Back pain	3 (6.0%)	3 (5.8%)
Chest pain	5 (10.0%)	5 (9.6%)
Diarrhea	3 (6.0%)	3 (5.8%)
Dizziness	6 (12.0%)	5 (9.6%)
Fatigue	3 (6.0%)	3 (5.8%)
Headache	8 (16.0%)	3 (5.8%)
Impotence	3 (6.0%)	4 (7.7%)
Peripheral edema	0 (0.0%)	6 (11.5%)
Rhinitis	0 (0.0%)	4 (7.7%)
Upper respiratory tract infection	5 (10.0%)	3 (5.8%)

Analyses of percent changes in carotid and femoral arterial wall-to-lumen ratios and compliance are presented in Table 3. There were no statistically significant between-group differences in percent wall-to-lumen ratio changes at week 26 or 52, and, compared with on-treatment baseline there were no statistically significant within-group changes. There was a numerically greater percent increase in carotid and femoral compliance in the olmesartan group than in the amlodipine group (13.97% vs 5.99% and 10.51% vs 4.64%, respectively, at 52 weeks), although the difference was not statistically significant. Increases from on-treatment baseline to week 52 were not statistically significant for carotid or femoral artery compliance in the olmesartan or amlodipine treatment group.

Assessment of changes in markers of inflammation demonstrated that there were no significant changes in plasma levels of C-reactive protein and transforming growth factor-β.

Adverse events are listed in Table 4. The frequencies and patterns of reported adverse events were generally comparable between the 2 treatment groups. Most adverse events were of mild to moderate severity and were considered unrelated to the study drug. Serious adverse events were also considered unrelated or unlikely to be related to treatment. There were no deaths during the study or within 30 days of the last administration of study drug. Laboratory parameters remained relatively stable during the study.

Discussion

Using amlodipine as a comparator, this study sought to establish whether olmesartan was able to induce regression of LV hypertrophy after target BP was achieved. In contrast to many previous studies that investigated the effects of RAS inhibition on LV hypertrophy, patients involved in the present study were treated to achieve specified BP targets before assessing the effects of treatment on LV hypertrophy (e.g., baseline echocardiography was performed only after attainment of protocol-defined BP targets). This study design allowed for the simultaneous measurement of LV dimensions and diastolic function. Because the E/A ratio as a criterion for the assessment of diastolic dysfunction is load dependent, it was felt that the BP should be stabilized at normal levels before baseline echocardiographic and Doppler assessments were made. This study design might also allow the identification of any antihypertrophic effects that were additional to those attributable to decrease of BP

alone. However, despite the existing evidence that RAS inhibitors and CCBs can decrease LV hypertrophy,[1] a statistically significant regression of LV hypertrophy was not observed in either treatment group, and there was no significant difference between treatment groups based on echocardiographically determined LV mass measurements obtained after BP goals were attained. These results suggest that the beneficial effects of ARBs and CCBs on decreasing LV hypertrophy could be largely pressor dependent.

In the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) study, the ARB losartan was more effective than the β blocker atenolol in decreasing echocardiographically determined LV mass and electrocardiographic measurements of LV hypertrophy, despite similar decreases in BP.[5,6] In the present study, it is likely that the failure to achieve a significant improvement from baseline in LV mass with olmesartan or amlodipine was a consequence of the study design, which specified that baseline and subsequent echocardiographic assessments be conducted only after patients had achieved most, if not all, of the decreases in BP associated with antihypertensive treatment. The 2 agents were effective in decreasing BP as monotherapies, although slightly $>1/2$ of the patients required additional open-label therapy to reach predefined BP targets. Decreases in mean BP were achieved within 8 weeks of initiation of treatment with olmesartan or amlodipine, with no significant incremental decreases from 8 to 52 weeks. LV hypertrophic regression has been reported to occur within 8 to 12 weeks of treatment initiation with RAS-inhibiting agents.[7–9] In the LIFE study, baseline electrocardiography and echocardiography were performed before randomization of patients to losartan or atenolol.

LV mass by Framingham criteria[10] was within the upper limit of normal for patients in this study when determined by echocardiography performed 4 to 8 weeks after initiation of therapy with olmesartan or amlodipine, thus allowing little room for subsequent detection of further decreases in LV mass. To some extent, the relatively low mean LV mass may have reflected the large proportion of patients receiving antihypertensive agents before enrollment. Although it was not the case using relatively sensitive echocardiographic techniques, large proportions of patients in the olmesartan and amlodipine treatment groups were observed to have improvements in LV hypertrophy as assessed by electrocardiogram. It seems probable that this finding reflects the fact that, in contrast to baseline echocardiography, which was performed after 4 to 8 weeks of randomized treatment, baseline electrocardiogram was obtained during the washout/screening period, thus lending credence to the hypothesis that changes in LV mass would have been detected if baseline echocardiographic assessment had also been performed during the washout period and before randomization.

Another potential issue that may have affected the outcome of the study was the racial composition of the patient population. To minimize observer bias and ensure that treatment groups were consistently and accurately compared, this study was conducted at a single site. However, this site was an urban Veterans Affairs hospital, and the patients recruited for the study were mainly elderly African-American men. Hypertension in black patients is more frequently of the low-renin, salt-sensitive phenotype[11] and it has been suggested that RAS blockade may be a less effective antihypertensive treatment strategy in black than in nonblack patients.[12] Similarly, black patients may be more resistant to decrease of target-organ damage induced by angiotensin II type 1 receptor blockade. Indeed, a subanalysis of the LIFE study results indicates that occurrence of a favorable cardiovascular outcome because of RAS inhibition may be less likely in black than in nonblack patients with LV hypertrophy.[12] The large proportion of black patients in this study population may have contributed to the lack of LV hypertrophic regression as measured by echocardiography.

The finding that there were no clinically significant changes from baseline to week 52 in mean levels of the inflammatory markers assessed in this study (C-reactive protein and transforming growth factor-β) for either treatment group was perhaps unsurprising. Considering the high use rates of concurrent medications (including lipid-lowering agents, aspirin, and anti-inflammatory agents), it might be expected that these agents would have had an anti-inflammatory effect, thus decreasing the levels of such markers before the active treatment period of the study had been initiated.

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