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ORIGINAL ARTICLE

# Antihypertensive efficacy and safety of olmesartan medoxomil compared with amlodipine for mild-to-moderate hypertension

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**The antihypertensive efficacy of the angiotensin II receptor blocker olmesartan medoxomil has been shown to compare favourably with that of other antihypertensive agents. This randomized, double-blind study compared the antihypertensive efficacy of the starting dose of olmesartan medoxomil with that of the calcium channel blocker amlodipine besylate (amlodipine) in subjects with mild-to-moderate hypertension. Following a 4-week, single-blind, placebo run-in period, 440 subjects aged ⩾18 years were randomized to the starting dose of olmesartan medoxomil (20 mg/day), amlodipine (5 mg/day), or placebo for 8 weeks. Subjects were evaluated by 24-h ambulatory blood pressure monitoring (ABPM) and by seated cuff blood pressure (BP) measurements at trough. The primary end point was the change from baseline in mean 24-h diastolic blood pressure (DBP) by ABPM at Week 8. Secondary end points included change from baseline in mean 24-h ambulatory systolic blood pressure (SBP) at 8 weeks, change from baseline in mean seated trough cuff DBP and SBP measurements, and response and control rates for DBP <90 and <85 mmHg. Control rates for SBP <140 and <130 mmHg were also calculated. Olmesartan medoxomil and amlodipine produced significantly greater reductions in ambulatory and seated DBP and SBP compared with placebo. Mean reductions in ambulatory and seated BP were similar between the two active agents; however, in the olmesartan medoxomil group, significantly more patients achieved the SBP goal of <130 mmHg and the DBP goal of <85 mmHg. Both drugs were well tolerated at the recommended starting dose. Although amlodipine was associated with a higher incidence of oedema, this did not reach statistical significance. Olmesartan medoxomil is an effective antihypertensive agent, with BP-lowering efficacy at the starting dose similar to that of amlodipine, and is associated with more patients achieving the rigorous BP goals of SBP <130 mmHg and DBP <85 mmHg.**
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**Keywords:** olmesartan medoxomil; amlodipine; angiotensin II receptor blocker

## Introduction

Angiotensin II receptor blockers (ARBs) comprise the most recently approved class of antihypertensive agents. Randomized, placebo-controlled trials have consistently shown that ARBs, as a class, are effective blood pressure (BP)-lowering agents that exhibit a tolerability profile similar to that of placebo.[1–3] Olmesartan medoxomil—a long-acting, once-daily ARB—was approved in 2002 for the treatment of hypertension. Efficacy data from placebo-controlled clinical trials suggest that the BP-lowering efficacy of olmesartan medoxomil monotherapy at starting (20 mg/day) and maximum (40 mg/day) doses should compare favourably with other antihypertensive agents, both within and across drug classes.[4] Olmesartan medoxomil has exhibited antihypertensive efficacy that compares favourably with that of atenolol, captopril, felodipine, and the ARBs losartan potassium (losartan), valsartan, and irbesartan in randomized, double-blind, head-to-head comparative trials.[5–7]

The present study was conducted to compare the efficacy and safety of the starting doses of olmesartan medoxomil and amlodipine besylate (amlodipine), currently the most widely prescribed antihypertensive agent, in patients with mild-to-moderate hyper-

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tension, as well as to compare the BP control rates achieved by olmesartan medoxomil and amlodipine. These data are useful in order to provide clinicians with information on alternative therapeutic regimens in the treatment of hypertension. This study employed ambulatory blood pressure monitoring (ABPM) and assessed the efficacy of olmesartan medoxomil and amlodipine in attaining rigorous BP goals, thus providing robust data with which to evaluate the comparative efficacy of these two agents.

## Methods

### Study population

A total of 440 male and female subjects were enrolled in the study. Subjects were aged $\geqslant 18$ years and had mild-to-moderate hypertension, defined as an average seated diastolic blood pressure (SeDBP) of 100–115 mmHg during Week 3 and Week 4 of the placebo run-in period (with a difference of $\leq 10$ mmHg between the two visit means), and a mean daytime diastolic blood pressure (DBP) that was 90–119 mmHg as measured via ABPM.

### Study design

This was a randomized, double-blind, placebo-controlled, parallel-group trial conducted at 43 study centres. Eligible subjects discontinued all antihypertensive agents and entered a 4-week, single-blind, placebo run-in period. Subjects who met the eligibility criteria were then randomized to an 8-week, double-blind treatment period. Subjects ($n = 440$) were assigned randomly in a 3 : 3 : 1 ratio to oral, once-daily treatment with the recommended starting dosages of olmesartan medoxomil 20 mg/day ($n = 188$), amlodipine 5 mg/day ($n = 186$), or placebo ($n = 66$).

Subjects were evaluated by 24-h ABPM at baseline and at the conclusion of the 8-week treatment period and by seated cuff BP measurements during the placebo run-in period and at Treatment Weeks 2, 4, and 8. Subjects were instructed to take their study medication at 08 : 00 h ($\pm$ 1.5 h), except on the day of a scheduled visit, when the medication was given after the BP was recorded (as close to 08 : 00 h as possible). At each study visit, subjects were evaluated for the occurrence of adverse events (AEs). Clinical AEs, including oedema, were either observed by the investigator or reported spontaneously by the patient.

### Efficacy variables

The primary end point was the change from baseline in mean 24-h DBP by ABPM at Week 8. Secondary end points included the change from baseline in mean 24-h ABPM systolic blood pressure (SBP) at Week 8 and the change in mean cuff SeDBP and cuff seated systolic blood pressure (SeSBP) at Week 8. Mean ambulatory daytime (08 : 00 to 19 : 59 h) and night time (20 : 00 to 07 : 59) BP measurements were also obtained. In addition, the responder and controlled DBP rate by 24-h ABPM and by cuff, the diastolic trough-to-peak ratio by 24-h ABPM, and the controlled SBP rate by 24-h ABPM and by cuff were calculated. All seated BP determinations were obtained by cuff at trough and were defined as the mean of three readings. The responder rate was defined as a DBP $< 90$ mmHg or a decrease in DBP $\geqslant 10$ mmHg from baseline. The controlled DBP rate was defined in two ways: DBP $< 90$ and $< 85$ mmHg. The controlled SBP rate was also defined in two ways: SBP $< 140$ and SBP $< 130$ mmHg. The lower DBP goal of $< 85$ mmHg was chosen to evaluate the potential efficacy of olmesartan medoxomil and amlodipine in achieving the more rigorous BP goal recommended for high-risk patients with diabetes or renal insufficiency.[8–10]

### Statistical analyses

Baseline characteristics were compared among the three treatment groups by using $\chi^2$ tests or Fisher's exact test for categorical variables and one-way analysis of variance for continuous variables. The sample size required to achieve a 5% significance level and 80% statistical power was determined to be 150, 150, and 50 for the two active treatment arms and the placebo arm, respectively. Based on a potential 15% dropout rate, the final sample size was 175, 175, and 60, respectively.

The null hypothesis tested was that the difference between the two active treatment groups was outside the equivalence limit of 3.5 mmHg for the primary efficacy variable, and it would be rejected (and equivalence inferred) if the entire 90% confidence interval (CI) fell within this equivalence limit. The treatment effects of olmesartan medoxomil 20 mg/day *vs* placebo and amlodipine 5 mg/day *vs* placebo were also tested. An analysis of covariance (ANCOVA), with baseline BP as covariate and treatment and centre as factors, was used for all BP reduction comparisons between treatment groups. For the comparison between olmesartan medoxomil and amlodipine, least-squared means derived from the ANCOVA model were used to calculate the 90% CI for the difference between the two treatment groups for each variable.

The primary efficacy analysis (24-h DBP by ABPM) and all secondary ABPM analyses were performed on the intention-to-treat (ITT) ABPM population, defined as subjects who received at least one dose of a randomized study drug and had at least one postbaseline BP measurement by ABPM. Secondary efficacy analyses of seated cuff BP evaluations were based on the ITT cuff population, defined as subjects who received at least one dose of a randomized study drug and had at least one

postbaseline seated cuff BP measurement. The safety evaluation included all patients who received at least one dose of study medication. Analysis of clinical AEs during the randomized, double-blind treatment period involved comparison of the incidence rates for all randomized patients treated with olmesartan medoxomil, amlodipine, or placebo from Day 1 through Week 8+1 day. The descriptive *P*-value was calculated using Fisher's exact test with treatment as a factor.

## Results

In all, 440 subjects were randomized into the three treatment groups. The ITT population for ABPM consisted of 397 subjects, and the ITT population for cuff BP measurements consisted of 438 subjects. There were no statistically significant differences between groups in terms of baseline demographic or clinical characteristics (Table 1). The mean age was 52 years, and approximately two-thirds of the subjects were male. Approximately 15% of the subjects were African American and 20% were Hispanic. The mean baseline 24-h ambulatory BP values for the olmesartan medoxomil, amlodipine, and placebo groups, respectively, were 153.9/95.5, 153.9/95.1, and 153.8/95.8 mmHg. The mean baseline seated cuff BP values were 154.9/104.0, 155.1/103.8, and 154.2/103.3 mmHg in the olmesartan medoxomil, amlodipine, and placebo groups, respectively.

Between Day 1 and Week 8 of the study, 14 patients (7.4%) in the olmesartan medoxomil group, seven patients (3.8%) in the amlodipine group, and 12 patients (18.2%) in the placebo group discontinued participation in the study. Patient request was the most common reason cited for discontinuation in the treatment groups, and accounted for eight discontinued patients in the olmesartan medoxomil group and three patients in the amlodipine group. Uncontrolled BP accounted for discontinuation of one patient in the olmesartan medoxomil group and four patients in the placebo group; and AEs accounted for discontinuation of one patient in the olmesartan medoxomil group, one patient in the amlodipine group, and two patients in the placebo group. Other reasons for discontinuation included loss to follow-up, noncompliance, and protocol violation.

**Table 1** Baseline characteristics for all randomized subjects

| | *Olmesartan medoxomil 20 mg/day* (n=*188*) | *Amlodipine 5 mg/day* (n=*186*) | *Placebo* (n=*66*) |
|---|---|---|---|
| Mean age (years) | 51.7 | 51.1 | 52.0 |
| Male sex (%) | 61.7 | 62.9 | 66.7 |
| *Race (%)* | | | |
| Caucasian | 63.8 | 61.8 | 57.6 |
| African American | 14.4 | 17.2 | 19.7 |
| Hispanic | 19.7 | 19.4 | 19.7 |
| Other | 2.1 | 1.6 | 3.0 |
| Mean hypertension history (years) | 9.5 | 8.9 | 12.3 |
| *Mean seated cuff BP (mmHg)* | | | |
| SBP | 154.9 | 155.1 | 154.2 |
| DBP | 104.0 | 103.8 | 103.3 |
| *Mean 24-h ABP (mmHg)* | | | |
| SBP | 153.9 | 153.9 | 153.8 |
| DBP | 95.5 | 95.1 | 95.8 |

BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; ABP, ambulatory blood pressure.

### Efficacy

The changes from baseline in mean 24-h ambulatory DBP (the primary end point) and SBP at Week 8 are displayed in Table 2 and Figure 1. Both olmesartan medoxomil and amlodipine, at the recommended starting dose, produced significantly greater reductions from baseline in mean 24-h ambulatory DBP compared with placebo (−7.7, −7.0, and −1.4 mmHg, respectively; $P<0.001$ for each active drug *vs* placebo), and in mean 24-h ambulatory SBP compared with placebo (−12.2, −12.3, and −2.3 mmHg, respectively; $P<0.001$ for each active drug *vs* placebo). The 90% CI for the difference between olmesartan medoxomil and amlodipine was within the equivalence limit of $\pm$ 3.5 mmHg for both mean 24-h ambulatory DBP and SBP, indicating equivalent BP reductions, as measured by ABPM.

The changes from baseline in mean cuff SeDBP and SeSBP at Week 8, last observation carried forward (LOCF), are displayed in Table 3. Similar to the ABPM results, both active treatments produced significantly greater mean reductions in SeDBP than placebo (−10.8, −10.1, and −3.6 mmHg, for the olmesartan medoxomil, amlodipine, and placebo groups, respectively; $P<0.001$ for both active drugs *vs* placebo), and in SeSBP compared with placebo (−10.3, −10.3, and −0.8 mmHg, respectively; $P<0.001$ for each active drug *vs* placebo). The 90% CI for the difference between olmesartan medoxomil and amlodipine at Week 8 LOCF was again within the equivalence limit of $\pm$ 3.5 mmHg for both SeDBP and SeSBP.

Both olmesartan medoxomil and amlodipine were associated with significantly greater mean reductions in daytime and night time ambulatory BP than placebo, and the reductions achieved with the two active treatments were equivalent (Table 2). The placebo-adjusted diastolic trough-to-peak ratios by 24-h ABPM for olmesartan medoxomil and amlodipine were 0.7 and 0.8, respectively, suggesting that both active study drugs were effective when dosed once daily.

Olmesartan medoxomil demonstrated significantly higher ambulatory DBP response and control

**Table 2** Study results at Week 8 (ITT population): ambulatory blood pressure

| | *Olmesartan medoxomil* (n=*171*) | *Amlodipine* (n=*172*) | *Placebo* (n=*54*) | *90% CI, olmesartan medoxomil* vs *amlodipine* |
|---|---|---|---|---|
| *Mean change from baseline at Week 8 (mmHg)*[a] | | | | |
| 24-h DBP | −7.7[b] | −7.0[b] | −1.4 | −1.88, 0.47 |
| 24-h SBP | −12.2[b] | −12.3[b] | −2.3 | −1.96, 1.96 |
| Daytime SBP/DBP | −13.7/−8.5[b] | −13.2/−7.9[b] | −2.5/−1.6 | SBP: −2.69, 1.77<br>DBP: −1.97, 0.71 |
| Night time SBP/DBP | −10.6/−6.9[b] | −11.1/−6.1[b] | −2.0/−1.1 | SBP: −1.61, 2.56<br>DBP: −1.98, 0.56 |
| *Percentage at Week 8* | | | | |
| Responders[c,d] | 71.3[b] | 69.8[b] | 31.5 | |
| Controlled DBP to <90 mmHg[c,e] | 67.3[b] | 64.0[b] | 27.8 | |
| Controlled SBP to <140 mmHg[c,e] | 50.9[f] | 50.0[g] | 27.8 | |
| Controlled DBP to <85 mmHg[e,h] | 48.0[b] | 34.3[i] | 11.1 | |
| Controlled SBP to <130 mmHg[e,j] | 33.9[b] | 17.4[k] | 3.7 | |

ITT, intention to treat; CI, confidence interval; DBP, diastolic blood pressure; SBP, systolic blood pressure.
[a]Least-squared means.
[b]$P<0.001$ *vs* placebo.
[c]$P$=NS, olmesartan medoxomil *vs* amlodipine.
[d]Responders had a mean 24-h DBP <90 mmHg or a decrease in DBP ⩾10 mmHg from baseline value.
[e]Mean 24-h blood pressure.
[f]$P=0.004$ *vs* placebo.
[g]$P=0.005$ *vs* placebo.
[h]$P=0.01$, olmesartan medoxomil *vs* amlodipine.
[i]$P\leqslant 0.003$ *vs* placebo.
[j]$P<0.001$ olmesartan medoxomil *vs* amlodipine.
[k]$P=0.02$ *vs* placebo.

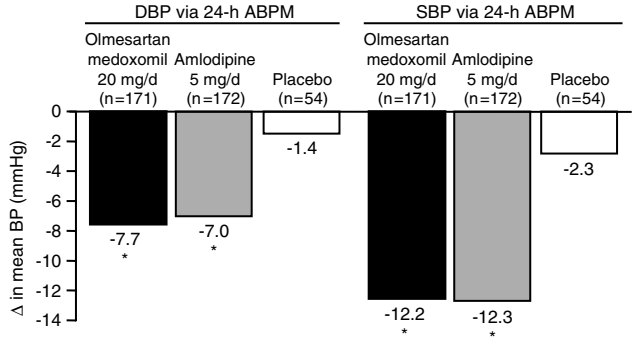


**Figure 1** Change from baseline in mean ambulatory DBP and mean ambulatory SBP at Week 8 with olmesartan medoxomil 20 mg/day, amlodipine 5 mg/day, and placebo. ABPM, ambulatory blood pressure monitoring. *$P<0.001$ *vs* placebo.

rates (Table 2), as well as significantly higher cuff DBP response and control rates (Table 3), compared with placebo (Figures 2 and 3). Amlodipine also demonstrated significantly higher ambulatory DBP response and control rates and significantly higher cuff DBP response and control rates, compared with placebo, with the exception of the cuff control rate for DBP <85 mmHg, which did not reach statistical significance. More importantly, the percentage of subjects who achieved the more rigorous BP control rate for the ambulatory DBP goal of <85 mmHg with olmesartan medoxomil was significantly higher than that achieved with amlodipine (48 and 34%, respectively; $P=0.01$) (Figure 3). Olmesartan medoxomil and amlodipine also demonstrated similar ambulatory and cuff control rates for SBP <140 mmHg, and both were significantly greater than with placebo (Tables 2 and 3). As seen with DBP, for the more rigorous SBP goal of <130 mmHg, olmesartan medoxomil demonstrated a significantly higher control rate for both ambulatory ($P<0.001$) and cuff ($P<0.04$) measurements than amlodipine (Tables 2 and 3).

In order to better understand this difference in control rates, the ambulatory DBP responses to both active agents were further investigated (data not shown). More subjects in the amlodipine group than in the olmesartan medoxomil group had only modest reductions (⩽6 mmHg) in ambulatory DBP from baseline, and a similar percentage of subjects in both groups exhibited 7- to 12-mmHg reductions in ambulatory DBP. More subjects treated with olmesartan medoxomil than with amlodipine demonstrated 13- to 18-mmHg reductions in ambulatory DBP, and twice as many subjects treated with olmesartan medoxomil had very large reductions of 19 mmHg or more.

## Safety

The overall incidence of treatment-emergent clinical AEs was similar in the three treatment arms (35.1% in the olmesartan medoxomil group, 35.5% in the

**Table 3** Study results at Week 8 (ITT population): seated cuff blood pressure

| | *Olmesartan medoxomil* (n=*183*) | *Amlodipine* (n=*183*) | *Placebo* (n=*65*) | *90% CI, olmesartan medoxomil* vs *amlodipine* |
|---|---|---|---|---|
| *Mean change from baseline at Week 8 LOCF (mmHg)*[a] | | | | |
| SeDBP | −10.8[b] | −10.1[b] | −3.6 | −2.08, 0.68 |
| SeSBP | −10.3[b] | −10.3[b] | −0.8 | −2.23, 2.40 |
| *Percentage at Week 8* | (*n*=175) | (*n*=179) | (*n*=58) | |
| Responders[c,d] | 49.7[b] | 50.8[b] | 19.0 | |
| Controlled SeDBP <90 mmHg[c] | 36.0[e] | 35.2[e] | 13.8 | |
| Controlled SeSBP <140 mmHg[c] | 48.6[b] | 43.0[f] | 24.1 | |
| Controlled SeDBP <85 mmHg[c] | 20.0[g] | 13.4 | 6.9 | |
| Controlled SeSBP <130 mmHg[h] | 24.6[i] | 15.6 | 5.2 | |

ITT, intention to treat; CI, confidence interval; LOCF, last observation carried forward; SeDBP, seated cuff diastolic blood pressure; SeSBP, seated cuff systolic blood pressure.
[a]Least-squared means.
[b]$P \leqslant 0.001$ *vs* placebo.
[c]*P*=NS, olmesartan medoxomil *vs* amlodipine.
[d]Responders had an SeDBP <90 mmHg or a decrease in SeDBP ⩾10 mmHg from baseline value.
[e]$P < 0.003$ *vs* placebo.
[f]*P*=0.01 *vs* placebo
[g]*P*=0.03 *vs* placebo.
[h]*P*=0.04, olmesartan medoxomil *vs* amlodipine.
[i]*P*=0.004 *vs* placebo.

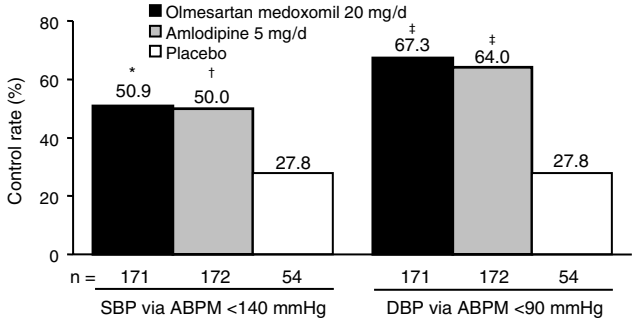


**Figure 2** Ambulatory SBP control rate of <140 mmHg and ambulatory DBP control rate of <90 mmHg at Week 8 for olmesartan medoxomil, amlodipine, and placebo. ABPM, ambulatory blood pressure monitoring. **P*=0.004 *vs* placebo; †*P*=0.005 *vs* placebo; ‡*P*<0.001 *vs* placebo.

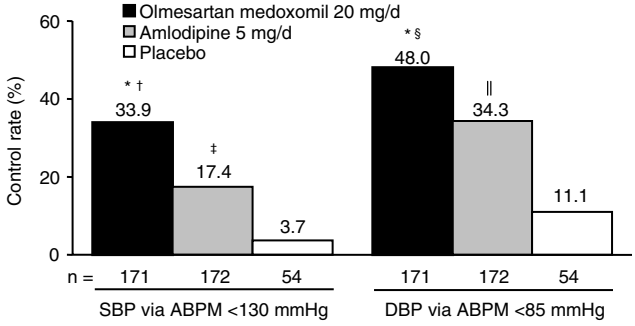


**Figure 3** Ambulatory SBP control rate of <130 mmHg and ambulatory DBP control rates of <85 mmHg at Week 8 for olmesartan medoxomil, amlodipine, and placebo. ABPM, ambulatory blood pressure monitoring. **P*<0.001 *vs* placebo; †*P*<0.001 *vs* amlodipine; ‡*P*=0.02 *vs* placebo; §*P*=0.01 *vs* amlodipine; ‖$P \leqslant 0.003$ *vs* placebo.

amlodipine group, and 25.8% in the placebo group); differences among the three groups were not statistically significant. Most AEs were judged by the investigators to be remotely or definitely not drug related, and were mild or moderate in severity. Headache, peripheral oedema, and upper respiratory tract infection were the most frequently reported treatment-emergent AEs.

Subjects who received amlodipine had a higher incidence of oedema (9.1%) than did those who received olmesartan medoxomil (4.3%) or placebo (4.5%), which is consistent with the AE profile of amlodipine.[11,12] Further, amlodipine resulted in a significantly higher incidence of nausea (2.7%) compared with olmesartan medoxomil (0%) and placebo (0%) ($P=0.039$). One subject in the olmesartan medoxomil group and one subject in the placebo group each experienced a serious AE, although both AEs were judged by the investigator to be only remotely or definitely not drug related. One subject in the olmesartan medoxomil group, one subject in the amlodipine group, and two subjects in the placebo group discontinued the study drug because of AEs.

The overall incidence of treatment-emergent laboratory AEs was 4.3% for olmesartan medoxomil, 9.1% for amlodipine, and 9.1% for placebo. These differences were not statistically significant. The most frequently reported treatment-emergent laboratory AEs were hyperglycaemia (0, 3, and 3% for olmesartan medoxomil, amlodipine, and placebo, respectively) and haematuria (1, 3, and 2%, respectively). All subjects with a laboratory AE of

hyperglycaemia had elevated fasting glucose levels at screening, baseline, or both.

## Discussion

The emphasis in current BP management remains the achievement of appropriate BP goals established by expert panels.[8] Despite these established goals, only about one-quarter of patients with hypertension are controlled to JNC VI-recommended BP levels. Among the major reasons for these poor BP control rates, which are multifactorial, are poor patient compliance with BP medication regimens, due in part to AEs, and lack of aggressive treatment by practicing physicians.[13]

Many drug-related AEs are dose dependent—that is, they are far more prevalent at higher doses of the medication. Unfortunately, higher doses of antihypertensive medications are often required to achieve BP control. For example, in clinical studies of amlodipine,[14] the target BP was achieved in 56 and 73% of patients who received amlodipine 5 and 10 mg/day, respectively, but the increase in goal achievement rate was associated with a higher incidence of AEs. In the present study, amlodipine was chosen as the comparator for the newest ARB, olmesartan medoxomil, because despite the BP-lowering efficacy achieved with this calcium channel blocker (CCB), amlodipine is associated with a high rate of peripheral oedema, especially pedal oedema, at doses exceeding the recommended starting dose.[11,12,14] This particular dose-dependent AE is reported by many patients as being very unpleasant, and may lead to poor patient compliance and discontinuation of treatment.

In contrast, ARBs have demonstrated efficacy similar to that of other classes of antihypertensive agents, with placebo-like tolerability and no increase in the incidence of AEs reported at their maximum doses.[3] In large clinical trials involving ARBs,[15–18] the drug discontinuation rate was significantly lower among subjects treated with an ARB than among subjects treated with other classes of agents, including beta blockers and angiotensin-converting enzyme (ACE) inhibitors. Furthermore, in a study assessing the compliance rate for various classes of antihypertensive medications,[19] ARBs were associated with fewer patient discontinuations and longer patient persistence with therapy compared with other antihypertensive drug classes, including ACE inhibitors.

The ARB olmesartan medoxomil was approved in 2002 for the management of hypertension, and its efficacy has compared favourably with that of other ARBs, as well as that of beta blockers, ACE inhibitors, and the CCB felodipine, in head-to-head trials.[5] The present study sought to assess the antihypertensive efficacy and goal BP attainment rate with the recommended starting dose of olmesartan medoxomil, compared with that of the most widely prescribed antihypertensive agent, amlodipine. Although other ARBs have been compared with amlodipine in clinical trials,[20–23] the studies focused primarily on the absolute reduction in BP between the two agents and not on their ability to achieve a specific BP goal. Further, our study utilized ABPM and assessed the efficacy of these agents in attaining the rigorous control rates of SBP $<130$ mmHg and DBP $<85$ mmHg, thus providing robust data with which to evaluate the comparative efficacy of olmesartan medoxomil and amlodipine.

In this study, although olmesartan medoxomil and amlodipine demonstrated similar reductions, on average, in ambulatory and seated cuff BP measurements, the small differences observed in favour of olmesartan medoxomil translated into a significantly greater percentage of subjects who achieved SBP and DBP control rates of $<130$ and $<85$ mmHg, respectively, as assessed by ABPM. The fact that the distribution of ambulatory BP response appeared different with these two agents may help explain the significant difference obtained for this controlled BP rate. Thus, small changes in mean BP may lead to clinically observable results—in this case, an increased number of patients achieving BP goals. This is particularly important in light of evidence that lower BP goals have been shown to provide greater cardiovascular and renal benefits in numerous clinical trials in patients with diabetes and renal disease.[24–26]

In addition to demonstrating the superior rate of BP goal achievement with olmesartan medoxomil, this study demonstrated that numerically fewer reported oedema-related AEs were associated with olmesartan medoxomil compared with amlodipine when both drugs are administered at the recommended starting doses. It has been well established that many patients require dose titration in order to reach an appropriate BP target. Based on clinical evidence, increasing the dose of amlodipine would be expected to result in an increase in the incidence of AEs, particularly pedal oedema, whereas increasing the dose of olmesartan medoxomil would not be expected to have any negative impact on safety or tolerability.[3,4,11,12,14]

Appropriate and aggressive BP management today requires a simple, once-daily, well-tolerated antihypertensive regimen that can effectively lower BP to widely recommended treatment goals. The newest ARB, olmesartan medoxomil, has demonstrated antihypertensive efficacy similar to that of amlodipine, with significantly better DBP and SBP goal attainment rates, while being shown to be safe and well tolerated.

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## Appendix

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