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Effects of Demographics on the Antihypertensive Efficacy of Triple Therapy With Amlodipine, Valsartan, and Hydrochlorothiazide for Moderate to Severe Hypertension

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Abstract

Objective—To compare the antihypertensive efficacy and safety of once-daily triple therapy with amlodipine (Aml) 10 mg, valsartan (Val) 320 mg, and hydrochlorothiazide (HCTZ) 25 mg versus dual-therapy combinations of these components in patients with moderate to severe hypertension.

Research design—Subgroup analysis of a multinational, randomized, double-blind, parallel-group, active-controlled trial.

Methods—After antihypertensive washout and a placebo run-in of up to 4 weeks, 2271 patients were randomly allocated in a 1:1:1:1 ratio to receive Aml/Val/HCTZ triple therapy or dual therapy with Val/HCTZ, Aml/Val, or Aml/HCTZ for 8 weeks. Forced titration to the full dose was done over the first 2 weeks of treatment. Efficacy and safety parameters were determined by age group

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(<65 vs. ≥65 years), gender, race (White vs. Black), ethnicity (Hispanic/Latino vs. non-Hispanic/Latino), and body mass index (BMI, <30 vs. ≥30 kg/m²).

Main outcome measures—Change from baseline to endpoint in mean sitting systolic blood pressure (MSSBP) and mean sitting diastolic blood pressure (MSDBP); blood pressure (BP) control rate <140/90 mmHg.

Results—Triple therapy was numerically superior and, for the majority of comparisons, statistically superior to each dual therapy in reducing MSSBP and MSDBP and in improving BP control rates in all subgroups. Across subgroups, triple therapy reduced MSSBP by 5.7–10.7 mmHg more than Val/HCTZ, 3.4–8.3 mmHg more than Aml/Val, and 4.4–9.4 mmHg more than Aml/HCTZ. Triple therapy was well tolerated across all subgroups. Limitations of our analysis included the lack of stratification of patients by subgroup at randomization and the small sample size of some subgroups (eg, Blacks, elderly).

Conclusions—Triple therapy with Aml/Val/HCTZ is effective and well tolerated in patients with moderate to severe hypertension regardless of age, gender, race, ethnicity, or BMI.

Keywords

amlodipine; blood pressure; hydrochlorothiazide; hypertension; triple therapy; valsartan

INTRODUCTION

While the pathogenesis of hypertension is multifactorial, the prevalence and treatment response may vary across population subgroups. For example, hypertension affects approximately 30% of adults in the United States according to the National Health and Nutrition Examination Survey (NHANES), with prevalence rising to 66% in those aged 60 years or older^{1,2}. This is consistent with the prevalence in Europe, with rates exceeding 70% for those aged 65 to 74 years³. The age-adjusted prevalence of hypertension is higher in men than women, particularly in Europe, and in Blacks compared with Whites^{1–3}. However, in older age groups, hypertension is more common in women than men and occurs at particularly high rates in the Black population^{1,4}.

Demographic factors, including age, gender, race, ethnicity, and body mass index (BMI), may influence responses to antihypertensive agents⁵. For example, Blacks are more likely to have a low-renin, salt-sensitive profile compared with Whites, and as a result, some agents when administered as monotherapy (eg, angiotensin-converting enzyme [ACE] inhibitors, beta-blockers) have been shown to be less effective in lowering blood pressure (BP) in this population⁶. With respect to age, an increase in peripheral resistance leads to mostly diastolic hypertension in younger adults, but starting at around 60 years of age, reductions in arterial compliance, particularly in large vessels, lead to age-related increases in systolic blood pressure (SBP) and decreases in diastolic blood pressure (DBP)⁷. Many elderly patients have isolated systolic hypertension, which is more difficult to reduce to target BP levels⁸.

Given the multiple factors involved in hypertension, it is not surprising that many patients require 3 or more antihypertensive agents to achieve their BP goals^{9,10}. However, limited

data are available on the efficacy of triple antihypertensive therapy in the different demographic subgroups. In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), the proportion of patients who achieved long-term BP control at 5 years who were taking at least 3 drugs included 31.5% of Black men and 27.2% of non-Black men, 27.2% of Black women and 24.5% of non-Black women, 27.5% of patients 55 to 69 years of age and 27.0% of patients ≥70 years of age, and 25.3% of patients with BMI <30 kg/m² and 30.0% with BMI ≥30 kg/m²¹⁰.

The results of the first large-scale (N=2271), randomized, double-blind trial designed to compare the efficacy and safety of once-daily triple therapy with amlodipine (Aml) 10 mg, valsartan (Val) 320 mg, and hydrochlorothiazide (HCTZ) 25 mg versus dual therapy with its components were previously reported¹¹. Triple therapy with Aml/Val/HCTZ was statistically superior in reducing mean sitting SBP (MSSBP) and DBP (MSDBP) compared with each of the dual therapies (Val/HCTZ, Aml/Val, and Aml/HCTZ). Moreover, triple therapy provided significantly higher systolic and diastolic control rates and significantly greater reductions in 24-hour ambulatory SBP and DBP than the dual therapies¹². Triple therapy was well tolerated with a safety profile consistent with its components. The objective of the present report differs from that of the primary publication¹¹ and others¹² in that it provides detailed results related to blood pressure reduction and tolerability of triple versus dual therapies in subgroups based on age, gender, race, ethnicity, and BMI from this large trial.

METHODS

Patients and Study Design

Patients aged 18 to 85 years were eligible if they had moderate to severe (grade 2 or 3¹³; stage 2⁵) hypertension (MSSBP ≥145 mmHg and MSDBP ≥100 mmHg). Patients who were receiving 4 or more antihypertensive agents at screening were excluded as were those taking 3 antihypertensive drugs with an MSSBP/MSDBP ≥140/90 mmHg or 2 antihypertensive drugs with an MSSBP/MSDBP ≥180/110 mmHg. Patients were also excluded if they had known hypersensitivity to any study medication; history of hypertensive encephalopathy, stroke, transient ischemic attack, myocardial infarction, or any revascularization procedure; angina pectoris; clinically significant heart block, arrhythmia, or valvular heart disease; type 1 diabetes or uncontrolled type 2 diabetes; significant pancreatic, hepatic, or renal disease; hyponatremia (serum sodium <132 mmol/L); hypokalemia (serum potassium <3.2 mmol/L); or required concomitant treatment with any medication known to significantly affect BP.

The design and patient eligibility criteria for this multinational, randomized, double-blind, parallel-group, active-controlled trial (NCT00327587) have been previously reported¹¹. Briefly, the study consisted of a 1-week washout period (for patients on antihypertensives requiring gradual withdrawal), a single-blind placebo run-in period of up to 4 weeks, and an 8-week double-blind treatment period. Patients meeting BP criteria during the run-in period (MSSBP 145 to <200 mmHg and MSDBP 100 to <120 mmHg) were randomly allocated in a 1:1:1:1 ratio using a validated interactive voice response system to triple therapy with Aml/Val/HCTZ 10/320/25 mg or dual therapy with Val/HCTZ 320/25 mg, Aml/Val 10/320 mg, or Aml/HCTZ 10/25 mg. Treatment was initiated with lower doses of study medications

and, over the first 2 weeks of the treatment period, the doses were escalated in 2 steps in the triple-therapy group and 1 step in the dual-therapy groups to reach the full dose. Patients took the full dose for the final 6 weeks of the treatment period. Treatment was administered once daily at approximately 8 AM, except on clinic visit days, when patients were instructed to delay treatment until later in the day after all assessments had been completed. Each treatment consisted of 2 tablets (valsartan 160 mg or placebo) and 2 capsules (amlodipine, HCTZ, or placebo) to maintain blinding; thus, each patient received 4 pills (2 tablets plus 2 capsules) daily. Investigators assessed compliance with therapy by tablet and capsule counts at scheduled visits and counseling was provided on an individual basis as required. This information was retained in investigators' records but was not analyzed formally.

Efficacy and Safety Assessments

Automated arterial BP measurements were made at screening and during each clinic visit using a validated BP monitor (Omron, Healthcare, Inc., IL, USA) and appropriate cuff size in accordance with published guidelines 14. Triplicate measurements were taken at 2-minute intervals after the patient had been sitting with both feet on the floor for 5 minutes. The MSSBP and MSDBP were calculated as the mean of the 3 BP determinations. The safety assessment included regular monitoring for all adverse events, which were defined as any undesirable sign, symptom, or medical condition occurring after initiation of study treatment.

Statistical Analysis

The primary efficacy variables (change from baseline to endpoint in MSSBP and MSDBP using a last-observation-carried-forward strategy), a key secondary efficacy variable (BP control rates <140/90 mmHg), and the key safety variable (frequency of adverse events) were summarized on an intent-to-treat basis for the following subgroups: age (<65 years and 65 years), gender (men and women), and race (White and Black). Subgroup analyses were not performed for Asian, Native American, Pacific Islander, or other races because they had insufficient numbers to allow a meaningful evaluation. In addition, a post hoc analysis was conducted to evaluate the effect of ethnicity and BMI (<30 kg/m² and ≥30 kg/m²) on the above variables. For ethnicity, Hispanics/Latinos were compared with non-Hispanics/Latinos (including Chinese, Indian subcontinent, Japanese, mixed ethnicity, or other).

In each subgroup, the changes from baseline to endpoint in MSSBP and MSDBP with triple therapy were compared with the corresponding changes with the dual therapies using a 2-way analysis of covariance (ANCOVA) model with treatment and region as factors and baseline MSSBP (or MSDBP) as a covariate. Four regions (East Coast US/Canada, West Coast US, European Union, and South America), defined from pooled centers before treatment unblinding, were used in the statistical analysis due to centers enrolling small numbers of patients. Comparisons of BP control rates for triple therapy versus dual therapies were made using a logistic regression model with treatment and region as factors. Adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA). The frequencies of adverse events with triple therapy and the dual therapies were compared using descriptive statistics.

RESULTS

Baseline Characteristics of Subgroups

The disposition of patients in this study was previously described¹¹. A total of 2271 patients were randomly allocated to the 4 treatment groups, which were well balanced with respect to demographic characteristics. Overall, 1255 (55.3%) patients were men, 317 (14.0%) were aged ≤ 65 years, 1627 (71.6%) were White, and 389 (17.1%) were Black. Approximately one fourth of the cohort was Hispanic/Latino and more than half of the cohort was obese (BMI ≥ 30 kg/m²). MSSBP/MSDBP at baseline for the entire cohort was 169.9/106.5 mmHg, and MSSBP/MSDBP was well matched across the 4 treatment arms within each subgroup classified by gender, age, race, ethnicity, or BMI (Table 1).

Change From Baseline in MSSBP and MSDBP

The reductions in MSSBP and MSDBP achieved with triple therapy were numerically superior and, for the majority of comparisons, statistically superior to each of the dual therapies regardless of age group, gender, race, ethnicity, or BMI (Figure 1). Triple therapy produced least-square mean reductions in MSSBP/MSDBP of 39.0/24.4 mmHg in patients aged ≤ 65 years and 43.9/26.4 mmHg in those aged > 65 years (Figure 1A). In the younger subgroup, between-treatment comparisons showed that the reductions in both MSSBP and MSDBP were significantly greater with triple therapy than with each of the 3 dual therapies (all $P < 0.0001$). In the smaller subgroup of older patients (14.0%), triple therapy produced significantly greater reductions in MSSBP and MSDBP than Val/HCTZ (both $P < 0.0001$) and Aml/HCTZ ($P = 0.0055$ and $P = 0.0233$, respectively), and showed a trend for reducing MSSBP and MSDBP by an additional 2 to 3 mmHg compared with Aml/Val ($P = 0.1589$ and $P = 0.0793$, respectively).

In terms of gender, triple therapy produced least-square mean reductions in MSSBP/MSDBP of 36.0/24.0 mmHg in men and 44.1/25.4 mmHg in women (Figure 1B), which were significantly greater than the corresponding BP reductions measured with each of the dual therapies (all $P < 0.0001$, except $P = 0.0005$ for comparison of triple therapy vs. Aml/Val on MSDBP reduction in women).

Triple therapy produced least-square mean reductions in MSSBP/MSDBP of 40.0/25.1 mmHg in Whites and 35.5/21.8 mmHg in Blacks (Figure 1C). Between-treatment comparisons showed that triple therapy was statistically superior in reducing MSSBP and MSDBP than each of the dual therapies in Whites (all $P < 0.0001$). In the smaller subgroup of Blacks (17.1%), triple therapy produced significantly greater reductions in MSSBP and MSDBP than Aml/Val ($P = 0.0004$ and $P = 0.0164$), and significantly greater reductions in MSSBP than Val/HCTZ ($P = 0.0079$) and Aml/HCTZ ($P = 0.0476$).

Triple therapy produced least-square mean reductions in MSSBP/MSDBP of 42.7/25.8 mmHg in Hispanics/Latinos and 40.6/25.1 mmHg in non-Hispanics/Latinos (Figure 1D). Between-treatment comparisons showed that triple therapy was statistically superior in reducing MSSBP and MSDBP than each of the dual therapies in both Hispanics/Latinos (all $P < 0.002$) and non-Hispanics/Latinos (all $P < 0.0001$).

Triple therapy produced least-square mean reductions in MSSBP/MSDBP of 41.6/26.0 mmHg in patients with BMI <30 kg/m² and 38.1/23.7 mmHg in those with BMI ≥30 kg/m² (Figure 1E). Between-treatment comparisons showed that triple therapy was statistically superior in reducing MSSBP and MSDBP than each of the dual therapies, regardless of BMI (all $P<0.0001$).

Across all subgroups, the full BP-lowering effects of triple therapy and the dual therapies were achieved after 2 weeks on the maximum dose (ie, end of Week 4). The greater BP reductions with triple therapy compared with the dual therapies were apparent by the end of Week 4 and were maintained through the end of the double-blind treatment period.

BP Control Rates

Triple therapy provided significantly higher BP control rates <140/90 mmHg compared with each of the dual therapies regardless of age group, gender, race, ethnicity, or BMI (Figure 2A–E). Triple therapy produced BP control in 70.3% of patients <65 years of age, 73.8% of those ≥65 years of age, 66.3% of men, 76.1% of women, 72.2% of Whites, 64.1% of Blacks, 75.3% of Hispanics/Latinos, 69.1% of non-Hispanics/Latinos, 75.9% of patients with BMI <30 kg/m², and 67.1% of those with BMI ≥30 kg/m². Between-treatment comparisons showed that triple therapy was statistically superior to each of the dual therapies in all subgroups (all $P<0.03$).

SBP control rates <140 mmHg in the ≥65 years of age subgroup were also determined given that isolated systolic hypertension is highly prevalent in elderly patients. Consistent with the overall BP control rates, triple therapy was statistically superior to each of the dual therapies in producing SBP control (all $P<0.005$).

Safety

Adverse events were reported in 1041 of the 2268 patients (46%) who received at least 1 dose of study drug. The overall incidence of adverse events was 45% with triple therapy, Val/HCTZ, and Aml/Val, and 48% with Aml/HCTZ, and was generally comparable among the 4 treatment groups within each subgroup (Figure 3). When compared between subgroups, the adverse event incidence was lower in elderly patients (age ≥65 years) than in younger patients (age <65 years), with the lowest rate seen in elderly patients who received triple therapy (Figure 3A). By gender, the adverse event incidence occurred at similar rates in men and women with triple therapy as well as with Val/HCTZ and Aml/HCTZ, whereas the adverse event rate with Aml/Val was nearly 10% higher in women than men (Figure 3B). By race, a higher incidence of adverse events was seen among Blacks compared with Whites in the groups receiving an HCTZ-containing dual therapy (Figure 3C). By ethnicity, adverse event rates were consistently lower among Hispanics/Latinos compared with non-Hispanics/Latinos (Figure 3D). Based on BMI, the adverse event incidence was generally similar in patients with BMI <30 kg/m² versus ≥30 kg/m² (Figure 3E).

Dizziness, peripheral edema, and headache were the most frequently reported individual adverse events. The incidence of these individual adverse events was generally comparable among treatment groups within a given subgroup, and was also generally comparable

between subgroups within a given treatment group (Figure 3). However, several exceptions were noted. The incidence of dizziness with triple therapy and Val/HCTZ was higher than the incidence with the other dual therapies across each subgroup based on age, gender, race, and BMI. The incidence of peripheral edema with triple therapy was lower than the rates with Aml-containing dual therapies across the subgroups. The lowest rates of peripheral edema were seen with Val/HCTZ across all subgroups. Finally, the incidence of headache with triple therapy was lower in elderly compared with younger patients and was generally comparable across the other subgroups.

DISCUSSION

This subgroup analysis shows that regardless of age, gender, race, ethnicity, or BMI, Aml/Val/HCTZ triple therapy was more effective than dual therapy with any of the components in reducing MSSBP and MSDBP and in improving BP control rates in patients with moderate to severe hypertension. The results of this subgroup analysis are consistent with those previously reported for the overall population from the same study¹¹. Across the subgroups examined, triple therapy reduced MSSBP approximately 6 to 11 mmHg more than Val/HCTZ, 3 to 8 mmHg more than Aml/Val, and 4 to 9 mmHg more than Aml/HCTZ. The corresponding least-square mean differences in MSDBP favoring triple therapy over the 3 dual therapies ranged from approximately 3 to 6 mmHg, 2 to 4 mmHg, and 2 to 6 mmHg, respectively. These differences are clinically important given that SBP and DBP are directly and strongly related to cardiovascular morbidity and mortality in both epidemiologic and clinical studies. A reduction in DBP as small as 2 mmHg has been estimated to reduce the risk of coronary heart disease by 6% and stroke and transient ischemic attack by 15%¹⁵. While a 10-mmHg reduction in SBP has been associated with 40% lower risk of fatal stroke and 30% lower risk of death from ischemic heart disease (IHD) or other vascular causes in middle-aged individuals, even a decrease in SBP as small as 2 mmHg would be predicted to result in about a 10% lower mortality from stroke and a 7% lower mortality from IHD or other vascular causes throughout middle age¹⁶.

In a recent analysis of NHANES data divided into 3 timeframes (1988–1994, 1999–2004, and 2005–2008), older age, male gender, and Hispanic ethnicity were independently associated with uncontrolled BP in patients receiving 1 or 2 antihypertensive therapies in at least 2 NHANES timeframes. Patients with controlled BP were more likely to have been receiving diuretics and ACE inhibitors or angiotensin receptor blockers (ARBs). Obesity (BMI ≥ 30 kg/m²), older age, and Black race were independently associated with apparent treatment-resistant hypertension (ie, uncontrolled BP on 3 or more antihypertensive therapies) in 1 or more NHANES timeframes¹⁷.

Obesity increases BP through a variety of potential mechanisms, including increased activation of the sympathetic and renin-angiotensin-aldosterone systems, abnormal renal sodium handling, and endothelial dysfunction¹⁸. Black patients are known to have a reduced response to monotherapy with agents that suppress the renin-angiotensin-aldosterone system compared with Whites⁶. Lower BP control rates in the elderly may be attributed to a higher incidence of systolic hypertension compared with younger adults⁷ as well as the reluctance of some physicians to treat systolic hypertension compared with diastolic hypertension⁸. In

NHANES, therapeutic inertia was moderate or high in more than half of uncontrolled patients who had at least 2 visits annually¹⁷. The present analysis shows that triple therapy produced significantly higher BP control rates than the dual therapies across all subgroups by gender, age, race, ethnicity, and BMI.

Overall, triple therapy produced BP control <140/90 mmHg in 71% of the study cohort compared with 48% for Val/HCTZ, 54% for Aml/Val, and 45% for Aml/HCTZ (all $P<0.0001$)¹¹. A similar advantage with triple therapy over the dual therapies was generally seen across all subgroups. Triple therapy produced 30% to 43% higher BP control rates than Val/HCTZ, 18% to 36% higher rates than Aml/Val, and 24% to 44% higher rates than Aml/HCTZ across the multiple subgroups. The higher rates of BP control with triple therapy are consistent with previous studies showing that many patients, particularly those with more severe hypertension at baseline and those in difficult-to-treat subgroups, require 3 antihypertensive agents to achieve BP control^{9,10,19}.

In this study, patients in the triple-therapy group started treatment with low-dose Val/HCTZ 160/12.5 mg, and then had Aml 5 mg added in the second week followed by escalation to the full dose of each agent starting in the third week and continuing for the remainder of the double-blind treatment period. BP reductions were observed in all subgroups after just 1 week of treatment with lower-dose triple therapy (ie, Aml/Val/HCTZ 5/160/12.5 mg)¹¹. The maximum BP-lowering efficacy of triple therapy, as with each dual therapy, was observed after 2 weeks of treatment at the full dose across all subgroups and then was maintained until the end of the treatment period¹¹. Using this forced-titration approach, Aml/Val/HCTZ triple therapy was well tolerated across all subgroups. The overall incidence of adverse events with triple therapy was comparable to the rates seen with the dual therapies in each subgroup, which is consistent with the results seen in the overall population¹¹. In addition, the adverse event rates with triple therapy were generally comparable between subgroups based on gender, race, and BMI, and the rate tended to be somewhat lower in older than younger patients and in Hispanics/Latinos versus non-Hispanics/Latinos. Overall, the safety profile of triple therapy was consistent with the known pharmacological effects of an ARB, calcium channel blocker, and thiazide diuretic.

Current guidelines recommend a 2-drug combination—either as separate medications or in a single pill—as initial treatment for patients whose SBP is 20 mmHg above goal or whose DBP is 10 mmHg above goal⁵. Drug dosages should then be optimized or additional drugs added until the BP goal is achieved. The results of this subgroup analysis indicate that triple therapy with Val/Aml/HCTZ represents a viable option for patients whose BP remains uncontrolled with a 2-drug combination regardless of their age group, gender, race, ethnicity, or BMI. A 3-drug single-pill combination may offer improved control of hypertension compared with multiple separate medications by virtue of the potential for improved patient compliance²⁰. In this way, the 3-drug combination may allow physicians to better distinguish between truly resistant hypertension versus poorly controlled hypertension due to poor treatment adherence.

A limitation of the subgroup analyses reported herein is that patients were not stratified by subgroup at randomization and some of the subgroups (ie, Black and elderly patients)

contained a small number of patients. Also, to facilitate blinding, it was necessary to administer study medication as the free combinations of the 3 monotherapies. Thus, it was not possible to formally evaluate the compliance benefits of single-pill combination therapy in this study.

CONCLUSION

Triple therapy with Aml/Val/HCTZ is effective and well tolerated in patients with moderate to severe hypertension regardless of age, gender, race, ethnicity, or BMI.

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Figure 1.

Least-square mean change from baseline to endpoint in mean sitting systolic/diastolic blood pressure in the intent-to-treat population by age group (A), gender (B), race (C), ethnicity (D), and body mass index (BMI) (E). Aml, amlodipine; HCTZ, hydrochlorothiazide; Val, valsartan.

Figure 2.

Blood pressure control rates <140/90 mmHg in the intent-to-treat population by age group (A), gender (B), race (C), ethnicity (D), and body mass index (BMI) (E). Aml, amlodipine; HCTZ, hydrochlorothiazide; Val, valsartan.

Most common adverse events								
Dizziness	7.8%	7.2%	2.0%	3.8%	7.3%	5.3%	3.9%	4.8%
Peripheral edema	4.6%	1.0%	8.4%	8.4%	3.7%	0%	9.2%	12.0%
Headache	4.8%	4.6%	5.1%	7.1%	1.2%	10.5%	3.9%	6.0%

Figure 3.

Incidence of any adverse event in patients who received at least 1 dose of study drug by age group (A), gender (B), race (C), ethnicity (D), and body mass index (BMI) (E). The data below each histogram shows the incidence of the 3 most common adverse events: dizziness, peripheral edema, and headache. Aml, amlodipine; HCTZ, hydrochlorothiazide; Val, valsartan.

Table 1
Demographic and Mean Baseline Sitting Blood Pressure by Treatment and Subgroup

Characteristic	Aml/V al/HCTZ (n=583)	Val/HCTZ (n=559)	Aml/V al (n=568)	Aml/HCTZ (n=561)	Total (N=2271)
Men, n (%)	316 (54.2)	303 (54.2)	319 (56.2)	317 (56.5)	1255 (55.3)
MSSBP/MSDBP	167.3/106.6	168.7/106.3	168.7/106.9	169.5/107.1	168.6/106.7
Women, n (%)	267 (45.8)	256 (45.8)	249 (43.8)	244 (43.5)	1016 (44.7)
MSSBP/MSDBP	172.4/106.2	170.4/106.0	170.8/106.1	172.4/107.0	171.5/106.3
Age <65 y, n (%)	501 (85.9)	483 (86.4)	492 (86.6)	478 (85.2)	1954 (86.0)
MSSBP/MSDBP	168.6/106.5	168.2/106.4	168.3/106.9	169.4/107.3	168.6/106.8
Age 65 y, n (%)	82 (14.1)	76 (13.6)	76 (13.4)	83 (14.8)	317 (14.0)
MSSBP/MSDBP	176.1/105.6	177.6/104.5	178.0/104.6	178.7/105.4	177.6/105.1
White, n (%)	420 (72.0)	412 (73.7)	403 (71.0)	392 (69.9)	1627 (71.6)
MSSBP/MSDBP	169.9/106.4	169.2/105.9	170.3/106.3	170.6/106.7	170.0/106.3
Black, n (%)	98 (16.8)	93 (16.6)	91 (16.0)	107 (19.1)	389 (17.1)
MSSBP/MSDBP	166.6/106.2	169.2/106.8	166.2/107.0	170.1/108.4	168.1/107.1
Hispanic/Latino, n (%)	152 (26.1)	141 (25.2)	148 (26.1)	147 (26.2)	588 (25.9)
MSSBP/MSDBP	171.7/107.2	170.6/106.3	171.9/107.1	172.9/107.3	171.8/107.0
Non-Hispanic/Latino, n (%)	431 (73.9)	418 (74.8)	420 (73.9)	414 (73.8)	1683 (74.1)
MSSBP/MSDBP	168.9/106.1	169.1/106.1	168.8/106.4	170.0/107.0	169.2/106.4
BMI <30 kg/m ² , n (%)	251 (43.1)	230 (41.1)	249 (43.8)	257 (45.8)	987 (43.5)
MSSBP/MSDBP	169.5/106.3	170.8/106.1	170.2/105.9	171.2/106.9	170.4/106.3
BMI 30 kg/m ² , n (%)	330 (56.6)	324 (58.0)	316 (55.6)	300 (53.5)	1270 (55.9)
MSSBP/MSDBP	169.8/106.5	168.8/106.2	169.2/107.0	170.4/107.2	169.5/106.7

Aml, amlodipine; BMI, body mass index; HCTZ, hydrochlorothiazide; MSDBP, mean sitting diastolic blood pressure; MSSBP = mean sitting systolic blood pressure; SD, standard deviation; Val, valsartan.