TRIPLE-COMBINATION TREATMENT WITH OLMESARTAN MEDOXOMIL/AMLODIPINE/HYDROCHLOROTHIAZIDE IN HISPANIC/LATINO PATIENTS WITH HYPERTENSION: THE TRINITY STUDY

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Objective(s): Evaluate efficacy/safety of olmesartan medoxomil (OM)/amlodipine (AML)/hydrochlorothiazide (HCTZ) in Hispanic/Latino adults with hypertension.

Design: Randomized, double-blind, 12-week, parallel-group study followed by a 40-week open-label extension phase.

Setting: Clinical sites (317) in the United States and Puerto Rico.

Patients or Participants: Individuals ≥18 years of age with mean seated blood pressure (BP) ≥140/100 or ≥160/90 mm Hg divided into Hispanic/Latino (369) and non-Hispanic/Latino (2122) subgroups.

Interventions: Participants were randomized to OM 40/AML 10 mg, OM 40/HCTZ 25 mg, AML 10/HCTZ 25 mg, or OM 40/AML 10/HCTZ 25 mg during the double-blind phase. During the open-label extension, all participants received OM 40/AML 5/HCTZ 12.5 mg; participants not reaching BP goal within 2 weeks were randomly titrated to OM 40/AML 10/HCTZ 12.5 mg or OM 40/AML 5/HCTZ 25 mg, then to OM 40/AML 10/HCTZ 25 mg after another 2 weeks.

Main Outcome Measure: Change in mean seated diastolic BP (SeDBP) from baseline (double-blind phase).

Results: Triple-drug therapy vs the dual therapies resulted in greater mean reduction in SeBP (Hispanic/Latino: 35.0/20.9 mm Hg vs 27.8–30.9/15.3–17.7 mm Hg; non-Hispanic/Latino: 39.0/21.7 mm Hg vs 28.9–31.5/14.6–17.8 mm Hg) and enabled more participants to reach BP goal (Hispanic/Latino: 56.8% vs 40.6%–51.2%; non-Hispanic/Latino: 65.7% vs 33.8%–46.6%) irrespective of ethnicity. The efficacy of triple-drug therapy in achieving BP goal was sustained long-term (40-week open-label extension period) in Hispanic/Latino (63.3%) and non-Hispanic/Latino (64.2%) participants. Triple-drug therapy was well tolerated in Hispanic/Latino and non-Hispanic/Latino participants.

Conclusions: In this study, OM/AML/HCTZ was an effective treatment option in Hispanic/Latino patients with hypertension. (*Ethn Dis.* 2014;24[1]:41–47)

Key Words: Angiotensin Receptors, Calcium Channel Blockers, Hispanic Americans, Hypertension, Thiazide Diuretics

INTRODUCTION

Awareness, treatment, and control of hypertension differ across racial/ethnic groups with a resultant disparity in hypertension-associated morbidity and mortality.[1,2] The fastest growing ethnic group in the United States is Hispanic/Latino Americans.[3,4] Currently, 16% of the US population are of Hispanic or Latino origin and it is estimated that this will increase to 24% by 2050.[3,5] Although the proportion of patients with hypertension in this group is comparable to or less than that of White Americans, treatment and control rates are significantly lower.[1,6] Only 36.9% of Hispanic/Latino Americans with hypertension have their blood pressure (BP) controlled compared with 48.5% of White Americans.[6] This low control rate, most likely related to a combination of lifestyle, cultural, educational, and economic factors,[4,7] increases the risk of cardiovascular events, including death.[8] Data from the Centers for Disease Control and Prevention (1995–2002) indicate that Puerto Rican Americans had a consistently higher hypertension-related death rate than all other Hispanic subpopulations and non-Hispanic Whites.[9] Increasing BP control is crucial in order to reduce cardiovascular risk.

Current guidelines state that most patients with hypertension will require combination therapy to control their BP.[8,10] The proportion of antihypertensive medication use increased from 63.5% during 2001–2002 to 77.3% during 2009–2010 (P_{trend} <.01), accompanied by a large increase in the use of multiple antihypertensive agents (from 36.8% to 47.7%, P_{trend} <.01).[11]

The Triple Therapy with Olmesartan Medoxomil, Amlodipine, and Hydrochlorothiazide in Hypertensive Patients Study (TRINITY; ClinicalTrials.gov Identifier: NCT00649389) demonstrated that the triple-drug combination of olmesartan (OM) 40 mg, amlodipine (AML) 10 mg, and hydrochlorothiazide

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The objective of our prespecified TRINITY subgroup analysis was to evaluate the efficacy and safety of the 3 drugs (OM 40/AML 10/HCTZ 25 mg) in combination in Hispanic/Latino and non-Hispanic/Latino Americans compared with the corresponding-component dual combinations

(HCTZ) 25 mg reduced seated diastolic BP (SeDBP) and seated systolic BP (SeSBP) to a greater extent and enabled a larger proportion of participants to reach BP goal than any of the corresponding-component dual combinations.[12] The objective of our prespecified TRINITY subgroup analysis was to evaluate the efficacy and safety of the 3 drugs (OM 40/AML 10/HCTZ 25 mg) in combination in Hispanic/Latino and non-Hispanic/Latino Americans compared with the corresponding-component dual combinations after 12 weeks of treatment and to assess long-term efficacy and safety of varying doses of OM/AML/HCTZ using a sequential algorithm tailored to the individual needs of participants.

METHODS

Study Design and Participants

The study design and primary results of TRINITY have previously been reported for the total cohort.[12,13] TRINITY was a 12-week, randomized, double-blind, parallel-group study that tested whether the triple combination of OM 40/AML 10/HCTZ 25 mg has a clinically significant benefit compared with dual combinations of the individual components in participants with moderate to severe hypertension. Patients aged ≥18 years with mean seated BP (SeBP) ≥140/100 or ≥160/90 mm Hg (off antihypertensive medications) were enrolled at 317 clinical sites in the United States, including 4 sites in Puerto Rico (n=14 patients). Patients could identify themselves as Hispanics and no attempt by the sponsor was made to further subdivide this category. The protocol was approved by the applicable Institutional Review Boards and each individual gave written informed consent before participating in any study procedure.

Participants (stratified by age, race, and diabetes status) were randomized to a treatment sequence that led to their final treatment assignment (OM 40/AML 10 mg, OM 40/HCTZ 25 mg, AML 10/HCTZ 25 mg, or OM 40/AML 10/HCTZ 25 mg) by week 4 of the double-blind period, and this treatment was maintained throughout the double-blind period (week 12). At the conclusion of the double-blind period, participants were switched to open-label treatment with OM 40/AML 5/HCTZ 12.5 mg so that all participants would be on a common regimen with a new baseline BP. Participants not achieving BP goal (<140/90 mm Hg [<130/80 mm Hg in participants with diabetes, chronic kidney disease, or chronic cardiovascular disease]) after 2 weeks (week 14) were randomly titrated to either OM 40/AML 10/HCTZ 12.5 mg or OM 40/AML 5/HCTZ 25 mg and participants not achieving BP goal after another 2 weeks (week 16) were further titrated to OM 40/AML 10/HCTZ 25 mg. Participants who reached BP goal remained on the same treatment throughout the open-label treatment period. Participants who were previously at BP goal but subsequently lost achievement of BP goal after week 16 could have their antihypertensive therapy up-titrated. Participants could be back-titrated to a lower dose of triple-combination treatment if they experienced symptoms of hypotension or intolerance to study drug, but could not be back-titrated to dual-combination treatment. The open-label treatment period ended at week 52. Following week 52, participants were treated per investigator's discretion.

Study Measures

The primary efficacy analysis for the double-blind period included participants who received at least one dose of study medication, had a baseline assessment of SeDBP, and had at least one post-dose assessment of SeDBP. The main outcome was least-squares (LS) mean change from baseline in SeDBP in participants at week 12. Additional efficacy parameters included LS mean change in SeSBP, proportion of participants reaching BP goal, and mean change in SeBP in participants with severe hypertension at baseline (SeSBP ≥180 mm Hg or SeDBP ≥110 mm Hg) in Hispanic/Latino and non-Hispanic/Latino participants. The mean change in SeBP in participants with severe hypertension was a post hoc analysis.

Efficacy was assessed during the open-label extension period in participants who received at least one dose of open-label study medication and provided at least one post-dose assessment of BP. Efficacy parameters during this period included the mean change from baseline in SeBP and the proportion of participants reaching BP goal (<140/90 mm Hg [<130/80 mm Hg in participants with diabetes, chronic kidney disease, or chronic cardiovascular disease]) at week 52/early termination (ET). Safety was assessed using adverse events, vital signs, physical examinations, 12-lead electrocardiograms, and clinical laboratory tests during both treatment periods. Since the objective of our study was to evaluate the efficacy and safety of triple-drug therapy, the safety analysis for the double-blind period was restricted to participants who received at least one dose of study medication at

Table 1. Baseline demographic and clinical characteristics by subgroup and randomized treatment[a]

	Hispanic/Latino (*n*=369)				Non-Hispanic/Latino (*n*=2122)			
	OM 40/ AML 10 mg (*n*=90)	OM 40/ HCTZ 25 mg (*n*=85)	AML 10/ HCTZ 25 mg (*n*=98)	OM 40/ AML 10/ HCTZ 25 mg (*n*=96)	OM 40/ AML 10 mg (*n*=538)	OM 40/ HCTZ 25 mg (*n*=551)	AML 10/ HCTZ 25 mg (*n*=502)	OM 40/ AML 10/ HCTZ 25 mg (*n*=531)
Age, mean (SD), yrs	56.4 (9.6)	55.2 (10.4)	54.9 (10.8)	54.3 (11.4)	54.9 (11.1)	56.0 (10.8)	54.6 (10.8)	54.7 (11.2)
Male, *n* (%)	51 (56.7)	43 (50.6)	61 (62.2)	41 (42.7)	274 (50.9)	296 (53.7)	273 (54.4)	279 (52.5)
Race								
White, *n* (%)	83 (92.2)	70 (82.4)	86 (87.8)	80 (83.3)	349 (64.9)	351 (63.7)	309 (61.6)	335 (63.1)
Black, *n* (%)	7 (7.8)	11 (12.9)	7 (7.1)	9 (9.4)	174 (32.3)	189 (34.3)	185 (36.9)	175 (33.0)
Obesity								
Body mass index ≥30 kg/m^2, *n* (%)	44 (48.9)	35 (41.2)	49 (50.0)	42 (43.8)	353 (65.6)	348 (63.2)	321 (63.9)	333 (62.7)
Diabetes, *n* (%)	21 (23.3)	18 (21.2)	13 (13.3)	15 (15.6)	79 (14.7)	81 (14.7)	79 (15.7)	81 (15.3)
Chronic kidney disease, *n* (%)	1 (1.1)	2 (2.4)	3 (3.1)	2 (2.1)	28 (5.2)	23 (4.2)	26 (5.2)	18 (3.4)
Cardiovascular disease, *n* (%)	8 (8.9)	5 (5.9)	7 (7.1)	8 (8.3)	48 (8.9)	56 (10.2)	48 (9.6)	47 (8.9)
Hypertension duration, mean (SD), yrs	8.5 (9.6)	8.3 (8.9)	7.5 (7.0)	8.6 (8.1)	10.4 (9.9)	10.7 (9.9)	10.2 (9.3)	9.7 (9.8)
Baseline blood pressure, mean (SD), mm Hg	167.5/99.4 (11.6/6.4)	164.1/99.2 (14.0/6.6)	168.0/100.2 (15.0/7.4)	165.7/100.6 (12.8/7.1)	168.2/101.2 (13.8/8.0)	169.7/100.9 (15.0/8.4)	169.1/101.5 (14.4/7.6)	168.3/101.0 (13.5/7.5)
Severe hypertension, *n* (%)[b]	17 (18.9)	15 (17.6)	26 (26.5)	14 (14.6)	143 (26.6)	147 (26.7)	145 (28.9)	125 (23.5)

[a] The number of participants in the Hispanic/Latino subgroup (*n*=369) and non-Hispanic/Latino subgroup (*n*=2122) does not add up to the total number of participants in TRINITY (*n*=2492) since 1 participant did not have ethnicity data.

[b] Severe hypertension was defined as SeSBP ≥180 mm Hg or SeDBP ≥110 mm Hg at baseline.

AML, amlodipine; HCTZ, hydrochlorothiazide; OM, olmesartan; SD, standard deviation.

or beyond week 4 (the earliest time participants could receive triple-drug therapy). The analysis for the open-label period included all participants who entered the open-label period and received at least one dose of open-label study medication.

Statistical Analyses

During the double-blind period, reduction in SeBP was assessed using an analysis of covariance model with baseline SeBP as a covariate and fixed effects of final randomized treatment, subgroup, and final randomized treatment by subgroup interactions. Least squares mean difference and standard error (SE), derived from this model, were used to calculate the change from baseline in SeBP for each treatment, and the difference in this change for triple-drug vs each dual-drug treatment was analyzed using 2-sided *P*. Efficacy in reaching BP goal was assessed using summary statistics and analyzed using chi-square and Fisher's exact tests. A last observation carried forward approach was used to account for missing measurements during double-blind treatment. Summary statistics by dosing regimen were used to describe SeBP and the proportion of participants reaching BP goal at week 52/ET by Hispanic/Latino and non-Hispanic/Latino subgroup. This study was not designed or powered to compare the efficacy of the treatments between the subgroups.

RESULTS

Of the 2492 participants, 369 (14.8%) were Hispanic/Latino and, of these, 72 (19.5%) had severe hypertension, which approximated the 25% prevalence of severe hypertension in the total cohort. In general, demographic and clinical characteristics of Hispanic/Latino and non-Hispanic/Latino participants, except for race and prevalence of obesity, were comparable at baseline (Table 1).

All 4 treatments significantly reduced SeBP at week 12; however, triple-drug therapy compared with dual-drug therapies resulted in greater mean reductions in SeDBP and SeSBP in both Hispanic/Latino and non-Hispanic/Latino subgroups (Figure 1). As a result, a greater percentage of participants receiving triple-drug therapy compared with dual-drug therapies reached BP goal at week 12 in both Hispanic/Latino (56.8% vs 40.6%–51.2%; $P \leq .457$) and non-Hispanic/Latino (65.7% vs 33.8%–46.6%; $P < .0001$) subgroups. Similarly, triple-drug therapy compared with dual-drug therapies resulted in greater mean reductions in SeBP from baseline to week 12 in participants with severe hypertension in both subgroups (Hispanic/Latino: 45.1/23.7 mm Hg vs 34.6–38.6/17.7–20.0 mm Hg; non-Hispanic/Latino: 47.8/23.5 mm Hg vs 36.4–37.7/17.0–20.1 mm Hg).

Mean SeBP at the beginning of the double-blind period (randomized set) was 166.4/99.9 mm Hg in Hispanic/Latino and 168.8/101.1 mm Hg in non-Hispanic/Latino participants; mean SeBP at the beginning of the open-label period was 135.2/82.0 mm Hg in

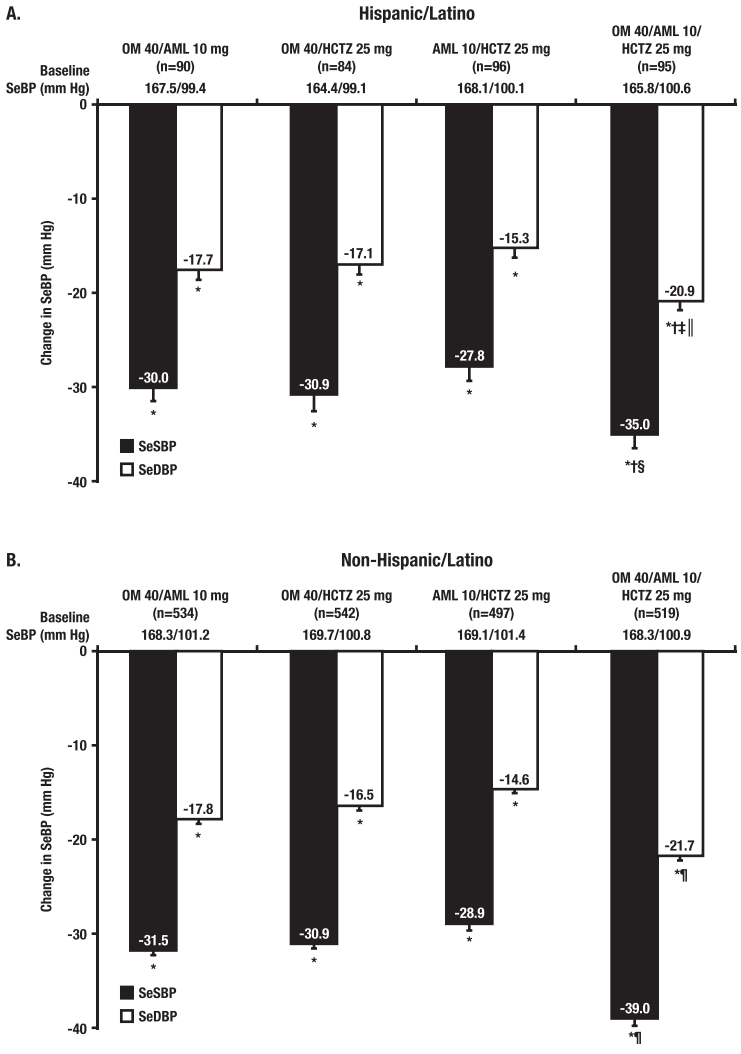

Fig 1. Least-squares mean reductions in seated BP at week 12 last observation carried forward. Error bars represent standard error. **P*<.0001 vs baseline; †*P*<.05 vs OM/AML; ‡*P*<.01 vs OM/HCTZ; §*P*<.005 vs AML/HCTZ; ‖*P*<.0001 vs AML/HCTZ; ¶*P*<.0001 vs each dual-drug treatment. AML, amlodipine; HCTZ, hydrochlorothiazide; OM, olmesartan; SeBP, seated blood pressure

Hispanic/Latino and 134.8/82.4 mm Hg in non-Hispanic/Latino participants. Mean SeBP at week 52 of the open-label period ranged from 127.3–137.3/77.3–82.8 mm Hg in Hispanic/Latino and from 124.5–136.7/77.8–82.5 mm Hg in non-Hispanic/Latino participants, depending upon dosing regimen. Overall, 63.3% (range: 45.9%–76.8%) of Hispanic/Latino and 64.2% (range: 44.3%–80.3%) of non-Hispanic/Latino participants, depending upon dosing regimen, were at BP goal at week 52.

No safety concerns that were not known to occur with the individual component therapies that made up the various combinations were identified during the double-blind treatment period for either the triple-combination or any of the component dual-combination therapies. The overall prevalence of treatment-emergent adverse events (TEAEs), drug-related TEAEs, serious adverse events, and discontinuations due to a drug-related TEAEs was 48.0%, 26.0%, 1.5%, and .3%, respectively, in Hispanic/Latino participants and 57.3%, 25.3%, 1.5%, and 1.6%, respectively, in non-Hispanic/Latino participants at week 12 (Table 2). Most TEAEs and drug-related TEAEs were considered mild or moderate in severity; the most common TEAEs in both subgroups were headache, dizziness, peripheral edema, and fatigue (Table 2). Participants receiving treatment with AML combination therapy experienced more peripheral edema than participants receiving combination therapy without AML (statistical analyses were not performed on safety data).

No important differences in extent of exposure to open-label study medication were noted in the 2 subgroups (median: 280 days in both subgroups). During the open-label period, the overall frequency of adverse events was lower in Hispanic/Latino (58.9%) compared with non-Hispanic/Latino (73.9%) participants; however, interpretation of this difference may not be meaningful given the large difference in the number of participants in the 2 subgroups. The most common adverse events during this period were urinary tract infection (8.1%), headache (8.1%), and dizziness (6.1%) in Hispanic/Latino participants and dizziness (8.0%), upper respiratory tract infection (6.5%), peripheral edema (6.2%), and nasopharyngitis (5.7%) in non-Hispanic/Latino participants.

DISCUSSION

The prevalence of Hispanic/Latino participants in TRINITY (14.8%) is similar to that in the US population (16%).[3] This prespecified subgroup analysis demonstrated the efficacy and safety of triple-drug therapy with OM/AML/HCTZ in this ethnic cohort. Triple-drug therapy resulted in greater mean reductions in SeBP and enabled a greater percentage of participants to reach BP goal (<140/90 mm Hg [<130/80 mm Hg in participants with diabetes, chronic kidney disease, or

Table 2. Study participants with TEAEs at week 12

	Hispanic/Latino (*n*=342)				Non-Hispanic/Latino (*n*=1959)			
	OM 40/ AML 10 mg (*n*=86)	OM 40/ HCTZ 25 mg (*n*=78)	AML 10/ HCTZ 25 mg (*n*=86)	OM 40/ AML 10/ HCTZ 25 mg (*n*=92)	OM 40/ AML 10 mg (*n*=510)	OM 40/ HCTZ 25 mg (*n*=501)	AML 10/ HCTZ 25 mg (*n*=466)	OM 40/ AML 10/ HCTZ 25 mg (*n*=482)
All TEAEs[a]	31 (36.0)	41 (52.6)	46 (53.5)	46 (50.0)	277 (54.3)	277 (55.3)	279 (59.9)	289 (60.0)
Drug-related[b]	19 (22.1)	21 (26.9)	27 (31.4)	22 (23.9)	119 (23.3)	100 (20.0)	137 (29.4)	140 (29.0)
Severe TEAEs								
All	2 (2.3)	1 (1.3)	1 (1.2)	4 (4.3)	22 (4.3)	16 (3.2)	17 (3.6)	20 (4.1)
Drug-related	2 (2.3)	1 (1.3)	0	1 (1.1)	7 (1.4)	3 (0.6)	2 (0.4)	6 (1.2)
Serious Adverse Events	1 (1.2)	1 (1.3)	1 (1.2)	2 (2.2)	8 (1.6)	6 (1.2)	8 (1.7)	8 (1.7)
Discontinuations								
TEAEs	0	0	3 (3.5)	2 (2.2)	6 (1.2)	12 (2.4)	8 (1.7)	21 (4.4)
Drug-related TEAEs	0	0	0	1 (1.1)	4 (0.8)	5 (1.0)	5 (1.1)	17 (3.5)
TEAEs (≥5% in any treatment group)								
Headache	9 (10.5)	11 (14.1)	5 (5.8)	11 (12.0)	33 (6.5)	27 (5.4)	28 (6.0)	26 (5.4)
Dizziness	2 (2.3)	9 (11.5)	2 (2.3)	5 (5.4)	27 (5.3)	49 (9.8)	15 (3.2)	52 (10.8)
Fatigue	1 (1.2)	7 (9.0)	8 (9.3)	1 (1.1)	33 (6.5)	24 (4.8)	28 (6.0)	23 (4.8)
Edema, peripheral	3 (3.5)	1 (1.3)	6 (7.0)	8 (8.7)	39 (7.6)	5 (1.0)	40 (8.6)	36 (7.5)
Hypokalemia	0	0	6 (7.0)	2 (2.2)	2 (.4)	3 (.6)	19 (4.1)	2 (.4)
Upper respiratory tract infection	2 (2.3)	5 (6.4)	2 (2.3)	2 (2.2)	24 (4.7)	13 (2.6)	12 (2.6)	14 (2.9)
Nasopharyngitis	0	4 (5.1)	3 (3.5)	2 (2.2)	11 (2.2)	16 (3.2)	13 (2.8)	18 (3.7)
Nausea	1 (1.2)	4 (5.1)	1 (1.2)	2 (2.2)	11 (2.2)	18 (3.6)	11 (2.4)	15 (3.1)

[a] TEAEs were adverse events that emerged during treatment (absent pre-treatment or worsened relative to pre-treatment). TEAEs are defined as having a start date on/after the first dose of double-blind study medication and up to the first dose of open-label study medication for participants continuing into the open-label period; or, for early terminated participants, up to and including 14 days after the last dose date of double-blind study medication. All TEAEs are counted under the treatment the participant received from week 4 to week 12.

[b] Drug-related was defined as definitely, probably, or possibly related to randomized study medication.

All data are *n* (%).

AML, amlodipine; HCTZ, hydrochlorothiazide; OM, olmesartan; TEAE, treatment-emergent adverse event.

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chronic cardiovascular disease]) compared with dual-drug therapy in both Hispanic/Latino and non-Hispanic/Latino participants during the double-blind phase of the study. Recently, the American Diabetes Association suggested that the SBP goal for many people with diabetes and hypertension should be <140 mm Hg, but that lower SBP targets (ie, <130 mm Hg) may be appropriate for certain individuals (ie, younger patients) if they can be achieved without undue treatment burden.[14] The magnitude of the BP-lowering effects of the various treatment regimens was similar in both subgroups. The BP reductions observed with OM/AML/HCTZ during the double-blind period were sustained throughout the open-label period, documenting the durable antihypertensive efficacy of this regimen. Triple-drug therapy was generally well tolerated in both subgroups, with low discontinuation rates due to drug-related TEAEs.

Effectively managing hypertension in Hispanic/Latino Americans is important in order to reduce the risk of cardiovascular events.[2] Compared with non-Hispanic Whites, Hispanic/Latino Americans have a higher prevalence of obesity, insulin resistance, diabetes, and metabolic syndrome.[4,15] In addition to increasing cardiovascular morbidity and mortality, these comorbidities complicate hypertension management[4] and may contribute to the lower BP control rates in Hispanic/Latino Americans compared with non-Hispanic Whites.[6,16]

Studies have shown that most Hispanic/Latino Americans with hypertension who are treated with angiotensin

receptor blockers as part of their therapeutic regimen can achieve BP goal.[17–19] In one study, AML/valsartan/HCTZ combination therapy was efficacious at lowering BP across racial/ethnic subgroups, with maximal efficacy obtained in patients receiving intensive (vs moderate) treatment.[18] In another study, switching to a combination of AML/OM with or without HCTZ significantly reduced BP and enhanced BP control (SeBP <140/90 mm Hg) in Hispanic and non-Hispanic patients with hypertension who were previously not controlled on monotherapy (prespecified subgroup analysis).[17] In the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT), Hispanic patients had equivalent or superior BP control compared with non-Hispanic patients when provided with equal access to medical care and no-cost medications (ie, common barriers to treatment were removed). In ALLHAT, the multivariate-adjusted odds of achieving BP control was 20% greater for Hispanic compared with non-Hispanic whites.[20]

There are many barriers to achieving BP control in Hispanic/Latino Americans, including acculturation, dietary patterns, communication issues, lack of awareness concerning hypertension, limited access to treatment, economic factors, clinical inertia, and nonadherence.[21–27] Data from the National Health and Nutrition Examination Survey (NHANES) demonstrated that lack of health insurance and/or a usual source of health care, both common in Hispanic/Latino Americans,[21,27] are associated with an approximately 1.6-fold increase in the probability that hypertension will not be treated.[6] These data also indicate that 24.8% (95% confidence interval [CI]: 17.2%–34.5%) of Hispanic Americans, other than Mexican Americans, with diagnosed hypertension are untreated.[6] Importantly, language has been identified as a major barrier to hypertension management in Hispanic/Latino Americans.[22,23,25]

Nonadherence to antihypertensive treatment is one of the most important barriers to hypertension management. In a retrospective evaluation, Hispanic Americans with hypertension were more likely to be nonadherent with their treatment regimen than White Americans (multivariate-adjusted odds ratio [OR]: 1.30; 95% CI: 1.28–1.32).[26] Because adherence is inversely related to the number of pills prescribed,[28] single-pill, combination antihypertensive therapy should increase adherence.[29,30] In separate meta-analyses, use of single-pill, fixed-dose combination therapy reduced the risk of noncompliance (risk ratio: .76; 95% CI: .71–.81) and improved adherence (OR: 1.29; 95% CI: 1.11–1.50) compared with individual drugs prescribed in combination.[29,30]

It is important to consider cardiovascular comorbidities common among Hispanic/Latino Americans when treating hypertension in this ethnic group and to implement therapies that effectively address both hypertension and comorbidities in order to reduce morbidity and mortality.[4] These therapies must be economically feasible for the patient and should include educational programs that help the patient modify unhealthy behaviors.[4] Pharmacotherapy may need to be more aggressive in order to improve BP control. Through simplification of the therapeutic regimen and increasing adherence, single-pill triple-drug combination therapy may prove beneficial in these individuals.

Limitations of this subgroup analysis of the TRINITY study include the absence of statistical analyses comparing the Hispanic/Latino and non-Hispanic/Latino subgroups because TRINITY did not stratify treatment by ethnicity and there were unequal numbers of participants in treatment subgroups. This study excluded individuals with symptomatic heart failure and other specific clinical/laboratory abnormalities; therefore, caution must be exercised regarding generalizability of these data to the overall population. In this study, Hispanic/Latino participants were included from clinical sites in the United States and Puerto Rico. There were fewer Black participants, obese participants, and participants with comorbid conditions, all of which usually result in more difficult control of high BP in the Hispanic/Latino subgroup.

In conclusion, this TRINITY subgroup analysis demonstrated the efficacy and safety of triple-drug combination therapy with OM 40/AML 10/HCTZ 25 mg in Hispanic/Latino participants with hypertension. Reduction in BP was similar in both Hispanic/Latino and non-Hispanic/Latino subgroups. This combination was generally well tolerated and may provide an effective treatment option for individuals in this ethnic group whose BP is not adequately controlled with the component dual-drug combinations. Additional studies are needed to evaluate the effects of other renin-angiotensin-aldosterone system inhibitors and other drug classes on BP lowering and cardiovascular disease outcomes in this population.

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