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ORIGINAL ARTICLE

Real-life effectiveness and safety of fixed amlodipine/irbesartan in hypertension management in Latin America: the PARCERIA study

Eficacia y seguridad en la vida real de amlodipino/irbesartán en combinación fija en el tratamiento de la hipertensión en América Latina: estudio PARCERIA

Álvaro J. Ruiz[1], Diego Funes[2], Claudio Higa[3], Marco Ramos[4], Omar Alonzo[5], and Leonardo Cobos[6]*

[1]Department of Clinical Epidemiology and Biostatistic, School of Medicine, Pontificia Universidad Javeriana, Bogotá, Colombia; [2]Sanofi Medical Affairs South Cone, Argentina; [3]Cardiology Service, Hospital Alemán, Buenos Aires, Argentina; [4]Department of Cardiology, Hospital San José Satélite, Naucalpan de Juárez, Estado de México, México; [5]Department of Non-invasive Cardiac Imaging, Centro Cardiovascular Avanzado, Guatemala, Guatemala; [6]Department of Cardiology, Hospital El Pino, Santiago, Chile

Abstract

Introduction: *Latin American population-based studies have shown suboptimal blood pressure control rates. Fixed-dose anti-hypertensive combinations are associated with improved convenience, adherence and effectiveness compared with monotherapy.* **Objective:** *to assess the real-life effectiveness and safety of a fixed amlodipine/irbesartan combination in long-term management of hypertension in Argentina, Chile, Colombia, Guatemala, and Mexico.* **Materials and method:** *this was a 48-week, prospective, observational, single-cohort study, which included adults with uncontrolled hypertension treated with a fixed-dose amlodipine/irbesartan combination per the treating physician's judgment, were followed in routine care. Target blood pressure was < 140/90 mmHg (< 130/80 mmHg for patients with diabetes or renal disease).* **Results:** *509 patients (57.6% females) were included. The mean (SD) age and 10-year Framingham risk score were 60.6 (12.5) years and 9.9 (8.78), respectively. Over 48 weeks, 97.4% of patients took ≥ 80% of prescribed doses. Statistically significant and clinically important blood pressure improvements (- 25.7/-13.5 mmHg; p < 0.001) were observed. Control was achieved by 62.7% of patients. Treatment compliance was one of the significant (p < 0.05) predictors of target blood pressure achievement. Eighty-seven (17.1%) patients experienced 117 treatment-emergent adverse events, including 7 serious events by 5 (1.0%) patients. Adverse events were generally mild (75.2%) and judged not to be treatment-related (76.1%). The most common adverse events were peripheral edema (3.9% of patients) and dizziness (1.0%). Based on Kaplan-Meier estimates, the mean (SE) time to adverse event-related discontinuation was 32.85 (0.08) weeks.* **Conclusion:** *Treatment with the fixed-dose combination of irbesartan/amlodipine demonstrated clinical effectiveness, with a significant improvement in blood pressure values and a higher rate of achieving the treatment goal in those who adhered to the regimen. The treatment was well-tolerated, with a low percentage of treatment-related adverse events, and few severe events. The fixed-dose combination is an important tool in the management of arterial hypertension.*

Keywords: *Hypertension. Amlodipine/irbesartan. Effectiveness. Safety. Latin America.*

***Correspondence:**
Álvaro J. Ruiz
E-mail: aruiz@javeriana.edu.co

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Resumen

Introducción: *los estudios basados en la población latinoamericana han demostrado tasas de control de la presión arterial subóptimas. La combinación de medicamentos antihipertensivos en dosis fijas se asocia con mayor comodidad, adherencia y efectividad en comparación con la monoterapia.* **Objetivo:** *evaluar la efectividad y seguridad en la vida real de la combinación fija de amlodipino/irbesartán en el tratamiento a largo plazo de la hipertensión en Argentina, Chile, Colombia, Guatemala y México.* **Materiales y método:** *estudio prospectivo, observacional, de cohorte única de 48 semanas, en el que incluyeron adultos con hipertensión no controlada, tratados con una combinación fija de amlodipino/irbesartán según criterio médico y fueron seguidos en la consulta ambulatoria habitual. La presión arterial objetivo fue < 140/90 mmHg (< 130/80 mmHg para pacientes con diabetes o enfermedad renal).* **Resultados:** *se incluyeron 509 pacientes (57.6% mujeres). La edad media (DE) y la puntuación de riesgo de Framingham a 10 años fueron 60.6 (12.5) años y 9.9 (8.78), respectivamente. Durante 48 semanas de seguimiento, 97.4% de los pacientes tomaron ≥ 80% de las dosis prescritas. Se observó mejoría en la presión arterial estadísticamente significativa y clínicamente importante (-25.7/-13.5 mmHg; p < 0.001). Se logró control en 62.7% de los pacientes. El cumplimiento del tratamiento fue uno de los predictores significativos (p < 0.05) de la presión arterial objetivo. Ochenta y siete (17.1%) pacientes experimentaron 117 eventos adversos emergentes del tratamiento, incluidos 7 eventos graves en 5 (1.0%) pacientes. Los eventos adversos fueron generalmente leves (75.2%) y se consideró que no estaban relacionados con el tratamiento (76.1%). Los acontecimientos adversos más frecuentes fueron edema periférico (3.9% de los pacientes) y mareos (1.0%). Según las estimaciones de Kaplan-Meier, el tiempo medio (SE) hasta la interrupción del tratamiento por acontecimientos adversos fue de 32.85 (0.08) semanas.* **Conclusiones:** *El tratamiento con irbesartán/amlodipino en combinación de dosis fijas mostró efectividad clínica, con mejoría significativa de las cifras de presión, y mayor llegada a la meta en quienes cumplieron con el tratamiento. El tratamiento fue bien tolerado, con un bajo porcentaje de eventos adversos relacionados con el tratamiento, y pocos eventos graves. La combinación en dosis fija es una importante herramienta en el tratamiento de la hipertensión arterial.*

Palabras clave: *Hipertensión. Amlodipino/irbesartán. Efectividad. Seguridad. Latinoamérica.*

Introduction

Hypertension is the leading cause of premature death and cardiovascular disease worldwide[1]. In 2010, a collaborative report by the World Bank and the World Health Organization showed that hypertension was the main single risk factor for the global burden of disease[2]. In 2000, a pooled analysis of available national and regional data estimated the worldwide prevalence of hypertension at 972 million individuals, the majority of whom (67.5%) resided in developing countries[3]. In Latin America, up to 40% of the adult population is affected by hypertension[4].

Randomized clinical trials have demonstrated that hypertension can be controlled and cardiovascular risk markedly reduced by changes in modifiable risk factors and the use of antihypertensive therapy[5]. In hypertensive patients, the primary goal of treatment is to achieve maximum blood pressure (BP) reduction while maintaining a good quality of life. However, despite improvements in the development of hypertension medications, including angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers and thiazide-type diuretics[6] that are efficient in reducing BP in clinical trials, the real-life effectiveness of marketed treatments is suboptimal. BP control rates remain low at 21% among hypertensive patients[7], which is far below the Panamerican Health Organization (PAHO) target of 35% established for 2019[8]. Complicated treatment regimens and algorithms, inadequate patient follow-up, and poor adherence to therapy represent barriers to effective treatment delivery[9,10].

Due to the multifactorial cause of hypertension[11] and based on meta-analyses and review studies[12-15], several BP management guidelines acknowledge the necessity of combination therapy for the majority of patients[16-18]. Fixed-dose combinations of anti-hypertensives are regarded as a suitable alternative for hypertension management since they have been associated with patient convenience, improved adherence and compliance with treatment, as well as higher effectiveness in achieving BP control compared with separate agents and monotherapy[19-21].

Fixed-dose amlodipine/irbesartan, a combination of an angiotensin II receptor blocker with a calcium channel blocker, has been approved for the treatment of hypertension as a first-line or subsequent regimen. Irbesartan is an orally active angiotensin II type 1 receptor antagonist whose pharmacological profile differs significantly from those of many other compounds of the same class. In particular, according to its pharmacokinetic and pharmacodynamics profile, irbesartan has a high bioavailability,

a long duration of action, and a small potential for pharmacological interactions due to the nature of the enzymatic pathway involved in its metabolic process[22]. Amlodipine, on the other hand, is a calcium channel blocker with comparable effectiveness to that of irbesartan in reducing BP when considered as monotherapy[23].

Even though combination therapy with antihypertensive agents having complementary mechanisms of action is reportedly more effective than monotherapy with the individual components, the efficacy observed in controlled clinical trials does not translate to real-life effectiveness in routine clinical care. This is mainly because regional variations in the patient profiles, cultural influences, access to care, as well as variations in physician decision-making and practice patterns are rarely considered in controlled clinical trials. The design and performance of studies that take into consideration regional needs and treatment gaps are therefore required for the adequate assessment of approved treatments.

The aim of this study was to assess the real-life effectiveness and safety of a fixed amlodipine/irbesartan combination in the long-term management of hypertension in Latin America, as well as to describe patient compliance and to identify determinants of response to treatment.

Materials and method

This was a 48-week, prospective, observational, single-cohort study conducted in Argentina, Chile, Colombia, Guatemala, and Mexico. Adults with uncontrolled hypertension treated with a fixed-dose combination of amlodipine/irbesartan as per the judgement of the treating physician were followed as per routine care (see complete admission criteria in supplementary data 1). Although there was no fixed study visit schedule imposed, the investigators were asked to collect data for study endpoint assessments after 4, 8, 24 and 48 weeks of treatment with a fixed-dose combination of amlodipine/irbesartan, provided this was in line with their clinical practice. During the study, office BP was to be measured at each visit. The patient was to remain in the sitting position for at least 5 minutes before any office BP readings were recorded. Two BP measurements with a 5-minute interval were to be obtained and the average of the two measurements was to be reported. These measurements were to be taken as part of routine clinical care, using the same standardized equipment throughout the study. Uncontrolled hypertension was defined as grade II hypertension (systolic blood pressure [SBP] ≥ 160 mmHg and/or diastolic blood pressure [DBP] ≥ 100 mmHg), or grade I hypertension (SBP 140-159 mmHg and/or DBP 90-99 mmHg) and two or more cardiovascular risk factors (tobacco use, obesity, physical inactivity, dyslipidemia, diabetes mellitus, microalbuminuria or estimated glomerular filtration rate < 60 ml/min, age [older than 55 for men, 65 for women], and a family history of premature cardiovascular disease [men under age 55 or women under age 65]). Patients were responsible for acquiring the study treatment. This study was approved by all required regulatory agencies and Independent Ethics Committees and was conducted in accordance with local regulations.

The primary effectiveness outcome was the absolute change in SBP and DBP from baseline to 48 weeks of treatment. Secondary effectiveness outcomes were: the proportion of patients achieving target BP defined as SBP/DBP < 140/90 mmHg for patients with no target organ damage and no associated clinical conditions, and SBP/DBP < 130/80 mmHg for patients with diabetes or renal disease; the patient-reported treatment adherence as assessed by the ratio of treatment doses taken in relation to prescribed doses and treatment compliance, with patients with an adherence rate ≥ 80% considered compliant. The safety outcomes were the incidence of treatment-emergent adverse events (TEAEs) and the proportion of patients who discontinued due to TEAEs occurrence during the 48-week study period.

Effectiveness analyses were conducted on patients who had a baseline assessment, had taken at least one dose of study medication and had a minimum of one post-baseline assessment, while the safety analyses were conducted on patients who were administered any amount of the study drug. All treated patients had a post-baseline assessment, therefore the two populations overlapped.

Changes in SBP and DBP from baseline to 48 weeks were assessed with a two-sided one sample t-test with the null hypotheses of –5.0 mmHg and –3.0 mmHg, respectively. In addition, repeated measure analysis using general linear models was used to assess the change of SBP and DBP over time. Target BP achievement was descriptively assessed using an intent-to-treat approach where the denominator was the number of patients included in the analysis population regardless of data availability and the 99% confidence interval (CI) around the point estimate was calculated based on the normal approximation method.

Descriptive statistics were used to assess the patient-reported adherence and compliance with treatment at each visit and during the overall follow-up period.

A logistic regression model was built to identify determinants of response to treatment with fixed-dose

combination amlodipine/irbesartan, where the dependent variable was the target BP achievement at 48 weeks (yes vs. no) and pre-selected potential determinants were the overall cumulative compliance with treatment (≥ 80% vs. < 80%), the baseline dose of the fixed-dose combination of amlodipine/irbesartan (150/10 mg, 150/5 mg and 300/10 mg vs. 300/5 mg) and the country of residence (Argentina, Chile, Guatemala and Mexico vs. Colombia). Potential confounders, including country of residence, sex, age, and cardiovascular risk factors (body mass index [BMI], waist circumference, tobacco and alcohol consumption, diet, stress exposure, physical activity, family history of premature cardiovascular disease, co-morbid conditions [dyslipidemia, diabetes mellitus, microalbuminuria], Framingham score, fasting triglyceride levels, total cholesterol, high-density lipoprotein [HDL] and low-density lipoprotein [LDL] cholesterol) were assessed for statistical significance with Fisher's exact/Chi-square test for categorical variables and the t-test for continuous variables. Only statistically important ($p < 0.15$ when comparing patients who did and did not achieve BP at 48 weeks) and clinically important (a more than two-fold difference between patients who did and did not achieve the target BP at 48 weeks) confounders were considered in the multivariate logistic regression model.

All adverse events (AE) were coded according to the Medical Dictionary for Regulatory Activities (MedDRA) terminology. The proportion of patients who experienced an AE during the treatment period was summarized by body system and preferred term. Descriptive statistics were used to assess the proportion of patients who discontinued due to an AE, while Kaplan-Meier survival analysis was used to determine the time to discontinuation due to an AE occurrence.

All statistical analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC).

Results

Figure 1 summarizes the patient disposition in the study. Five hundred forty-four (n = 544) patients were screened, of which 528 were enrolled in the study and 509 met the analysis population definition. Among the latter, 447 (87.8%) patients completed the 48-week follow-up period and 62 patients (12.2%) were discontinued prematurely due to losses to follow-up (n = 29; 5.7%), protocol deviations (n = 5; 1.0%), administrative problems (n = 5; 1.0%), adverse events (n = 4; 0.8%), withdrawal of consent (n = 3; 0.6%), death (n = 2; 0.4%), lack of effectiveness (n = 1; 0.2%) and other reasons (n = 13; 2.6%).

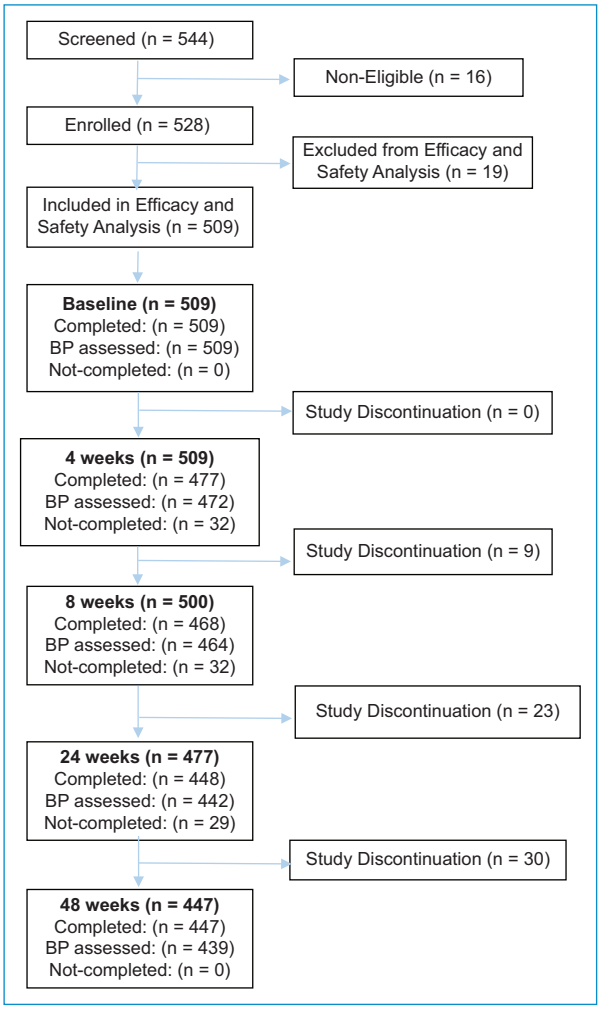


Figure 1. Patient disposition.

The baseline patient characteristics and cardiovascular risk factors are presented in table 1. The mean (SD) age was 60.6 (12.5) years, and 57.6% (n = 293) of patients were female. Patients were mainly from Colombia (n = 175; 34.4%), Argentina (n = 105; 20.6%) and Mexico (n = 101; 19.8%), while 85 (16.7%) were from Guatemala and 43 (8.4%) from Chile.

The mean (SD) 10-year Framingham risk score was 9.9 (8.78). Physical inactivity was reported by 76.8% (n = 391) of patients, 43.2% (n = 220) had comorbid dyslipidemia, 24.8% (n = 126) had ever smoked (5.9% current), and 19.3% (n = 98) were alcohol consumers.

At baseline, the mean (SD) SBP/DBP was 159.6 (14.61)/92.1 (93.0) mmHg. The results of a repeated measure analysis assessing the change in BP over time from baseline through follow-up are presented in figure 2. Statistically significant and clinically important

Table 1. Baseline characteristics and cardiovascular risk factors

Parameter	Analysis population (n = 509)
Age, years, mean (SD)	60.6 (12.5)
Sex, n (%) Male Female	 216 (42.4%) 293 (57.6%)
Country of residence, n (%) Argentina Chile Colombia Guatemala Mexico	 105 (20.6%) 43 (8.4%) 175 (34.4%) 85 (16.7%) 101 (19.8%)
Use of tobacco, n (%) Smoked in last 3 months Ex-smoker Never smoked	 30 (5.9%) 96 (18.9%) 383 (75.2%)
Alcohol user, n (%)	98 (19.3%)
BMI, kg/m^2, mean (SD)	29.0 (5.01)
Waist circumference, cm, mean (SD)	97.7 (12.83)
Use of salt at meals, n (%)	256 (50.3%)
Physical inactivity (less than 150 minutes of exercise per week), n (%)	391 (76.8%)
Daily hassles, n (%) Never Occasionally Frequently	 78 (15.3%) 275 (54.0%) 156 (30.6%)
Respond to stress with anger, n (%) Never Occasionally Frequently	 150 (29.5%) 289 (56.8%) 70 (13.8%)
Feeling tense or anxious, n (%) Never Occasionally Frequently	 89 (17.5%) 294 (57.8%) 126 (24.8%)
Family history of premature cardiovascular disease, n (%)	67 (13.2%)
Dyslipidemia, n (%)	220 (43.2%)
Total cholesterol level, mg/dl, mean (SD)	204.6 (53.34)
HDL level, mg/dl, mean (SD)	46.8 (15.83)
LDL level, mg/dl, mean (SD)	118.6 (41.17)
Triglyceride level, mg/dl, mean (SD)	172.1 (90.29)
Microalbuminuria, n (%)	21 (4.1%)
Diabetes mellitus, n (%)	69 (13.6%)
Framingham 10-year score, mean (SD)	9.9 (8.78)

improvements in BP were observed as early as four weeks into treatment (ΔSBP [99% CI]: –21.7 [–19.9, –23.4] mmHg; ΔDBP [99% CI]: –11.2 [–10.3, –12.2] mmHg) which were further enhanced over 48 weeks (ΔSBP [99% CI]: –26.2 [–24.3, –28.1] mmHg; ΔDBP [99% CI]: –13.7 [–12.6, –14.9] mmHg). In terms of BP control, target BP was achieved by 62.7% of patients (99% CI: 57.5%, 68.6%) at their last available visit after the baseline (Fig. 3). More specifically, the proportion of patients who achieved target BP increased from 45.6% (99% CI: 43.2%, 55.1%) at 4 weeks to 58.0% (99% CI: 61.4%, 73.0%) at 48 weeks.

Adherence to treatment remained high during the study, with mean (SD) rates at 4 and 48 weeks of 97.8 (9.4) and 98.5 (8.39), respectively, and cumulative adherence during the total follow-up period of 97.7 (8.29). Overall, 97.4% of patients reported taking ≥ 80% of prescribed doses and were therefore considered compliant with fixed-dose combination amlodipine/irbesartan treatment.

On multivariable analysis, country of residence (p = 0.001), treatment compliance (p = 0.035), and absence of diabetes (p < 0.001) were found to be significant predictors of target BP achievement (Table 2). More specifically, patients compliant with treatment were ≅ 7 times more likely to achieve BP control than non-compliant patients (OR = 6.86; 95% CI: 1.15, 41.09) while patients with comorbid diabetes were less likely to achieve it (OR = 0.26; 95% CI: 0.14, 0.48).

Table 3 shows an overview of the study safety analysis. There were 117 TEAEs experienced by 87 (17.1%) patients, including 7 serious TEAEs experienced by 5 (1.0%) patients. TEAEs were generally mild (75.2% of TEAEs) and judged not to be related to fixed-dose amlodipine/irbesartan combination (76.1% of TEAEs). Most of the TEAEs ended in patient recovery (77.8% of TEAEs) without any action taken (38.5% of TEAEs) or with the addition of a new concomitant medication (41.0% of TEAEs). The most frequently reported TEAEs (≥ 1% of patients) were peripheral edema (3.9%) and dizziness (1.0%) (Table 4). There were 6 (1.2%) patients who discontinued due to an AE. Of these, two died during the study, more specifically due to cardiac tamponade and myocardial infarction, neither of which was judged to be related to amlodipine/irbesartan, and the remaining four patients experienced peripheral edema. Based on the Kaplan-Meier analysis, the mean (SE) time to discontinuation due to an AE was 32.9 (0.1) weeks.

Discussion

In this real-life assessment of a fixed-dose combination of amlodipine/irbesartan in the management of uncontrolled hypertension in Latin America, statistically

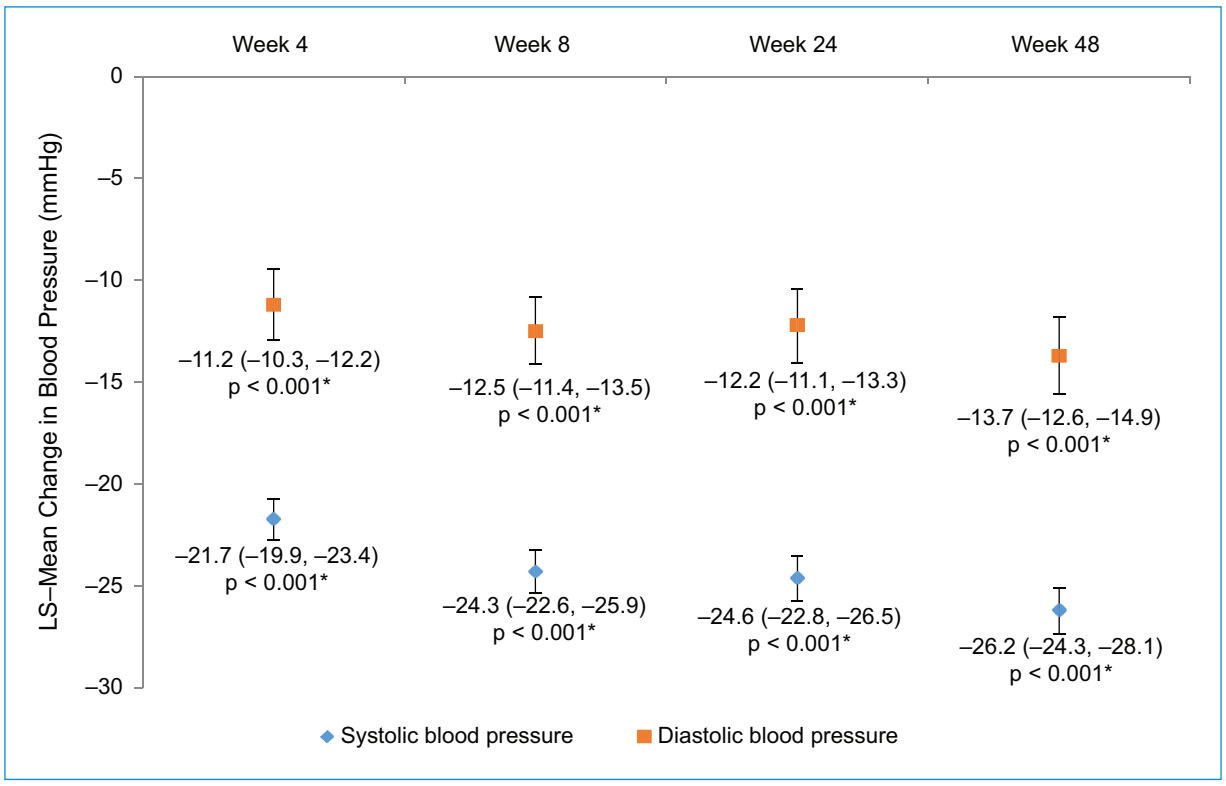


Figure 2. Repeated measure analysis for blood pressure change over time from the baseline. Error bars represent the 95% CI of the mean change in blood pressure.
*Compared to baseline values based on repeated measure analysis.

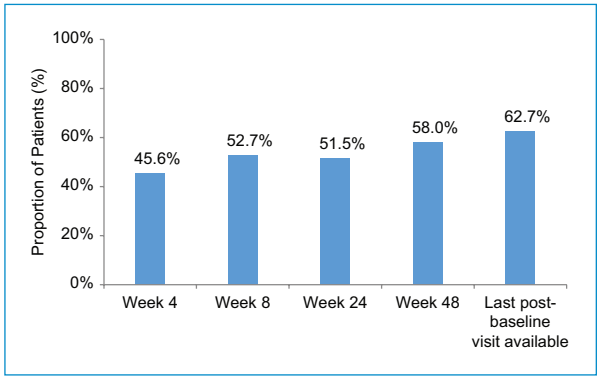


Figure 3. Blood pressure control rates over time. Target blood pressure control was defined as SBP/DBP < 140/90 mmHg for patients with no target organ damage and no associated clinical conditions; and SBP/DBP < 130/80 mmHg for patients with diabetes or renal disease. Percentages based on the total number of patients in the analysis population (n = 509).

significant and clinically important improvements in both SBP (–25.7 mmHg; p < 0.001) and DBP (–13.5 mmHg; p < 0.001) were observed over 48 weeks. The present findings are superior to those observed in two Phase III randomized clinical trials, I-ADD and I-COMBINE, which included patients inadequately controlled with amlodipine or irbesartan monotherapy. In the I-ADD and I-COMBINE studies, after 5 and 10 weeks of fixed-dose combination therapy, the mean (SD) SBP/DBP significantly decreased by –10.8 (1.0) / –3.8 (0.6) (p < 0.001) and –17.9 (1.2) / –7.7 (0.7) mmHg (p < 0.001), respectively.[24,25] Furthermore, the proportion of patients who achieved BP control over the treatment period was 62.7% (99% CI: 57.5%, 68.6%), which is close to the PAHO target of 70% established for treated patients for 2019[8]. The results observed in the current study are consistent with the results of the PARTNER study that demonstrated high therapeutic effectiveness of a fixed-dose combination of amlodipine/irbesartan combination for the management of hypertension.[26]

Over 48 weeks, 97.4% of patients reported taking ≥ 80% of prescribed doses and were therefore considered compliant with treatment. The high compliance with treatment reported in our observational study is consistent with previous studies showing that fixed-dose combinations of antihypertensives are associated with

Table 2. Multivariate logistic regression assessing predictors of target blood pressure achievement

Covariate	Odds ratio†	95% CI	p-value
Number of drinks per day*	0.909	0.749, 1.103	0.332
Country‡			**0.011**
Argentina vs. Colombia	1.567	0.518, 4.747	
Chile vs. Colombia	1.286	0.469, 3.528	
Guatemala vs. Colombia	0.227	0.090, 0.574	
Mexico vs. Colombia	0.920	0.434, 1.948	
Baseline dose (mg)‡			0.230
150/10 vs. 300/5	3.817	0.343, 42.537	
150/5 vs. 300/5	1.925	0.994, 3.727	
300/10 vs. 300/5	1.855	0.555, 6.198	
Cumulative compliance (≥ 80% vs. < 80%)‡§	6.862	1.146, 41.090	**0.035**
Regular use of salt at meals (yes vs. no)*	1.356	0.761, 2.417	0.301
Presence of diabetes mellitus (yes vs. no)*	0.257	0.138, 0.476	**< 0.001**
BMI (kg/m^2)*	0.959	0.888, 1.037	0.295
Triglyceride test (mg/dl)*	1.001	0.998, 1.005	0.524
Waist circumference (cm)*	1.000	0.968, 1.032	0.977

*Statistically important ($p < 0.15$) or clinically important (more than two-fold difference) variables identified in univariate analysis.
†Mutually adjusted.
‡Pre-selected covariates.
§Defined as the ratio of cumulative doses taken vs. prescribed using available data.
Statistical significance denoted by bold p-values.

Table 3. Overview of treatment-emergent adverse events

TEAE	Safety population (n = 509)		
	n of events	n of patients*	% of patients
Total			
TEAE	117	87	17.1
Serious TEAE	7	5	1.0
Severity			
Mild	88	69	13.6
Moderate	24	19	3.7
Severe	5	4	0.8
Relationship to amlodipine/irbesartan			
Not suspected	89	74	14.5
Suspected	28	23	4.5

*A patient may have reported more than one TEAE. TEAE: treatment emergent adverse events

Table 4. Most frequent (≥ 1% of patients) treatment-emergent adverse events by preferred term

PT of TEAE	Safety population (n = 509)		
	n of events	n of patients*	% of patients
Peripheral edema	22	20	3.9
Dizziness	5	5	1.0

*Two patients reported more than one TEAE. TEAE: treatment emergent adverse events; PT: preferred term.

improved adherence to and compliance with treatment and may explain the improved outcomes observed in our study compared to those of controlled clinical trials and PAHO[19-21,24,25].

Country of residence was identified as an independent predictor of BP control, which may be explained by differences in local patient management or by health care access[27]. Alternatively, although difficult to confirm, patient compliance may differ between countries despite what the patients may have reported. Increased treatment compliance and the absence of diabetes mellitus were also identified as significant determinants of target BP achievement, in line with the results of previous studies[28-30]. These findings highlight the need for additional initiatives for improving BP control, in addition to the use of fixed-dose combination treatments[15], such as patient programs to improve stress management and salt intake[31-36].

With respect to safety, treatment was generally well tolerated, as only a minority of patients experienced a TEAE. The most common TEAE was peripheral edema

(3.9% of patients) and the safety profile was in agreement with the product monographs[37,38].

The results should be interpreted in light of the study limitations. Although observational studies allow the assessment real-life effectiveness, this study design is prone to prescription bias. Furthermore, the assessment of treatment compliance may have been biased, as this was based on self-reported patient information. A strength of this study is the generalizability of the findings, since patients from various Latin American countries were included. Moreover, due to the observational nature of the study, the results are representative of the real-life long-term management of hypertension.

Conclusions

The findings of this study advocate the use of combination blood pressure-lowering therapy among patients with uncontrolled hypertension in Latin America. Improved effectiveness is expected, namely due to the high adherence associated with fixed-dose combination therapy. In addition, a favorable safety profile supports the administration of the fixed-dose combination amlodipine/irbesartan regimen. Future studies assessing fixed-dose combination amlodipine/irbesartan therapy may be performed in additional countries to further examine differences between countries regarding hypertensive patient profile as well as the effectiveness and safety of fixed-dose combination amlodipine/irbesartan.

In conclusion, the results of the current study support the real-life effectiveness of fixed-dose combination amlodipine/irbesartan in the long-term management of patients with hypertension. BP control rates close to the PAHO target were observed despite significant regional variability. Compliance with treatment was further shown to be independently associated with target BP achievement.

Novelty and significance

What is new?

– Among Latin American patients with uncontrolled hypertension, 62.7% achieve blood pressure control after 48 weeks of fixed-dose combination amlodipine/irbesartan treatment.
– Country of residence, treatment compliance, and diabetes presence are significant predictors of target blood pressure achievement.

What is relevant?

– Over 48 weeks of fixed-dose combination amlodipine/irbesartan therapy, 97.4% of patients were compliant with treatment.
– Fixed-dose combination therapy and a favorable safety profile are associated with high treatment effectiveness in hypertension management.

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Conflicts of interest

Dr. Álvaro J Ruiz is a speaker for Amgen, Abbott, Pfizer, Sanofi, Valentech, and Lafrancol, and receives financial support for research projects from Sanofi, Amgen, Abbott, Colciencias, and Pontificia Universidad Javeriana. Dr. Marco Antonio Ramos Corrales is a speaker for Sanofi and Siegfried Ingelheim. Dr. Omar Alonzo serves as a speaker for Bayer and Sanofi. Diego Funes was a Sanofi Argentina employee when the study was conducted. Thais Cocarelli declares that he was a Consultoria Estatistica employee providing services for Sanofi Brasil when the study was conducted.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective observational study.

Use of artificial intelligence for generating text. The authors declare that they have not used any type of

generative artificial intelligence for the writing of this manuscript, nor for the creation of images, graphics, tables, or their corresponding captions.

Supplementary data

Supplementary data are available at DOI: 10.24875/RCCAR.23000001. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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