Efficacy and safety of valsartan/amlodipine single-pill combination in patients with essential hypertension (PEAK LOW)

Hipertansif hastalarda valsartan/amlodipin tek tablet kombinasyonunun etkinlik ve güvenliliği (PEAK LOW)

Pınar Kızılırmak, M.D., PhD, İdilhan Ar, M.D., Barış İlerigelen, M.D.[#]

Novartis Pharmaceuticals, Istanbul

[#]Department of Cardiology, Istanbul University Cerrahpasa Faculty of Medicine, Istanbul

ABSTRACT

Objectives: This study evaluated the efficacy as well as the safety and tolerability profile of low-dose valsartan/amlodipine (Val/Amlo) single-pill combination (SPC) (160/5 mg) in patients with essential hypertension in Turkey.

Study design: Adult patients with essential hypertension [systolic blood pressure (SBP) >140 mmHg and/or diastolic blood pressure (DBP) >90 mmHg], who were on low dose Val/Amlo (160/5 mg) SPC before enrollment and gave informed consent, were accepted for this multi-centric observational study performed at 30 sites. The absolute changes in SBP and DBP from baseline were the primary efficacy outcomes. Safety assessments consisted of recording all adverse events.

Results: Of 381 patients enrolled, 327 completed the study; 39% were females. The mean age was 57.3±11.8 years. Median duration of hypertension was 38 months. Both SBP and DBP values showed reductions from 162.6±16.6 mmHg and 94.0±13.2 mmHg to 137.6±14.2 mmHg and 81.9±9.0 mmHg at 4th week and to 131.6±11.5 mmHg and 79.7±7.6 mmHg at 12th week, respectively. The control and response rates at the end of the study were 82.0% and 92.6%, respectively. Twelve patients (3.2%) experienced a total of 12 adverse events; there were no serious adverse events. The most common adverse event was edema (1.3%). Patient compliance was approximately 99%.

Conclusion: Low-dose (160/5 mg) Val/Amlo SPC is efficacous and has a good tolerability and safety profile for the management of essential hypertension in Turkey.

ÖZET

Amaç: Bu çalışmada, Türkiye'de esansiyel hipertansiyonlu hastalarda düşük doz valsartan/amlodipin (Val/Amlo) (160/5 mg) tek tablet kombinasyonunun (TTK) etkinliği, güvenliliği ve katlanabilirlik profili değerlendirildi.

Çalışma planı: Esansiyel hipertansiyonu (sistolik kan basıncı [SKB] >140 mmHg ve diyastolik kan basıncı [DKB] >90 mmHg) olan, düşük doz Val/Amlo (160/5 mg) TTK ile tedavi edilen ve bu çok merkezli, gözlemsel çalışmaya katılmayı kabul eden, erişkin hastalar çalışmaya alındı. Çalışma toplam 30 merkezde yürütüldü. Primer etkinlik sonucu, SKB ve DKB'nin bazale göre mutlak değişimi olarak belirlendi. Güvenlilik değerlendirmesi amacıyla tüm istenmeyen olaylar ve ciddi istenmeyen olaylar izlendi ve kaydedildi.

Bulgular: Çalışmayı, 381 hastanın 327'si tamamladı. Hastaların %39'u kadın olup ortalama yaş 57.3±11.8 idi. Ortanca hipertansiyon süresi 38 aydı. SKB değerinin 162.6±16.6 mmHg'dan dördüncü haftada 137.6±14.2 mmHg'ya ve 12'nci haftada 131.6±11.5 mmHg'ya düştüğü gösterildi. DKB değerinin de 94.0±13.2 mmHg'dan dördüncü haftada 81.9±9.0 mmHg ve 12'nci haftada 79.7±7.6 mmHg'ya düştüğü gözlendi. Çalışma sonunda kan basıncı kontrol oranı %82.0, yanıt oranı %92.6 idi. Hastaların 12'sinde (%3.2) toplam 12 istenmeyen olay görüldü. En sık görülen istenmeyen olay ödemdi (%1.3). Ciddi istenmeyen olay gözlenmedi. Hasta uyumu yaklaşık %99 idi.

Sonuç: Türkiye'de esansiyel hipertansiyonun tedavisinde düşük doz (160/5 mg) Val/Amlo TTK'nun etkili, iyi tahammül edilebilen ve güvenli bir tedavi olduğu gösterilmiştir.

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Correspondence: Dr. Pınar Kızılırmak. Novartis İlaçları, Suryapı - Akel İş Merkezi, Rüzgarlıbahçe Mah. Şehit Sinan Eroğlu Cad. No 6, 34805 Kavacık, Beykoz, İstanbul, Turkey.
Tel: +90 216 - 681 20 00 e-mail: pinar.kizilirmak@novartis.com

Hypertension is the most prevalent modifiable risk factor for cardiovascular and cerebrovascular morbidity and mortality. An estimated 30% of the adult population in the United States has hypertension.[1] The importance of lowering blood pressure (BP) to reduce the risk of cardiovascular events has been demonstrated in numerous clinical trials. More drugs will likely be required for individuals with coronary artery disease, chronic kidney disease, or diabetes, for whom goals lower than 140/90 mmHg have been recommended.[2,3]

The American ALLHAT study (The Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial) demonstrated that 60% of patients who had achieved a good BP control of <140/90 mmHg had received two or more antihypertensive agents, and only 30% of the patients had achieved BP control with a single drug.[4] In a recent meta-analysis, it was demonstrated that patients treated with triple combinations had significantly lower BP level and higher BP control rate than those treated with a dual combination of the same molecules.[5]

Drug combinations recommended by the British Hypertension Society (BHS)[6] and the European Society of Hypertension (ESH)[7] include the combination of an angiotensin receptor blocker (ARB) and calcium channel blocker (CCB). Benefits of ARB/CCB combination therapy include additive BP-lowering effects and lower incidences of adverse events. The ARBs confer stroke protection, renal protection, and tolerability similar to placebo, without dose-related symptomatic and metabolic adverse events, while CCBs are beneficial in reducing stroke and treating angina and cardiac ischemia. The results of the recent clinical trials involving ARB/CCB combination therapy suggest that this therapeutic strategy offers potent lowering of BP, and in particular, marked reductions in systolic BP (SBP). Given the strong association between SBP and cardiovascular risk, the fixed-dose formulations of ARB/CCB combinations are useful in the management of hypertension and in the subsequent reduction in cardiovascular morbidity and mortality.

Blood pressure (BP) control rates were reported as 5.4% and 8% for all hypertensive patients and 21% and 24% for treated patients in the first half of 2010 in Turkey.[8,9] These figures have shown much improvement within a couple of years; BP control rates reported in more recent years increased to 28% and 29% for all hypertensive patients and 54% and 73% for treated patients.[10,11] The results of a subsequent incidence study in 2007 showed that the overall BP control rates for patients with hypertension rose to 14%, while in treated patients the control rates increased to 27%[12] Improvement in BP control is more easily maintained when patient compliance is high. Since most hypertensive patients need two or more agents to control BP, combining different antihypertensives in a single-pill combination (SPC) is recommended to increase compliance.[13]

Abbreviations:

ACEI	*Angiotensin converting enzyme inhibitor*
ARB	*Angiotensin receptor blocker*
BMI	*Body mass index*
BP	*Blood pressure*
CCB	*Calcium channel blocker*
DBP	*Diastolic BP*
ITT	*Intent-to-treat*
PP	*Per protocol*
SBP	*Systolic BP*
SD	*Standard deviation*
SPC	*Single-pill combination*
Val/Amlo	*Valsartan/amlodipine*

In a recent study of adult Turkish hypertensive patients, the treatment regimen with either 160/5 mg or 160/10 mg valsartan/amlodipine (Val/Amlo) SPC was evaluated in terms of efficacy, patient compliance and safety.[14] Thus, the present study was designed to evaluate the efficacy of low-dose Val/Amlo SPC (160/5 mg) in Turkish patients with essential hypertension. Data related to adverse events were also collected to evaluate the safety and tolerability profile of the therapy.

Therefore, the primary objective of this study was to evaluate the effects of low-dose Val/Amlo combination as antihypertensive therapy in patients with essential hypertension, and secondary objectives were to determine the BP control rate as well as the safety and tolerability of the regimen.

PATIENTS AND METHODS

Study design

This was a multi-centric non-interventional observational study. The patients were followed for 12 weeks, and evaluated at the baseline visit and again at the 4th week and 12th week. At the baseline visit (Day 0), the patients were evaluated considering vital signs, medical history, cardiovascular risk factors, antihypertensive therapy, physical examination, routine laboratory tests, and comorbidities. Current clinical status, antihypertensive treatment, comorbidities, and adverse events were evaluated, and efficacy parameters were measured at the 4th and 12th week visits. Compliance

to medications was also questioned by the investigators at the 4th and 12th week visits. Since the design was non-interventional, no drug accountability was accomplished.

The study protocol was approved by the local ethical committees. All patients provided written informed consent. The study was conducted according to the International Committee on Harmonisation Guidelines for Good Clinical Practice and in compliance with the ethical principles of the Declaration of Helsinki.

Study population

Patients using low-dose Val/Amlo SPC from study sites in Turkey were planned to be included in the study. Male or female patients aged ≥18 years with essential hypertension [SBP >140 mmHg and/or diastolic BP (DBP) >90 mmHg] were eligible for study participation. Patients who were prescribed to use low-dose Val/Amlo (160/5 mg) combination before enrollment and gave informed consent were accepted for the study. Since this was a "non-interventional observational" study, no measures to make or confirm the diagnosis of hypertension were planned or performed. The diagnosis made by the physician who treated the patient according to his/her routine practice was regarded as the only criterion for diagnosis. Exclusion criteria were pregnancy, breastfeeding or presence of serious diseases that might prevent the participation and continuation of the patient in the study. Patients with an allergy or sensitivity to any molecule of the Val/Amlo combination were also excluded.

Study drug

There were no investigational medications, but all patients were using low-dose Val/Amlo SPC. Thiazide diuretics and all other treatments or therapies unrelated to hypertension were allowed, while all other antihypertensive treatments were prohibited, since they could interfere with the safety and efficacy effects of the study drugs allowed. Since this was a "non-interventional observational" study, no intervention to alter any decision of the physician in patient management that would be a change to the routine daily practice was planned or performed. The physicians made their own decisions to increase or not increase the dosage and to add or not add another antihypertensive medication, etc. The patients whose Val/Amlo dosage was to be increased or who were to be given another antihypertensive medication (except thiazide diuretic) in addition to Val/Amlo within the study period were planned to be excluded from the analysis.

Efficacy parameters

The absolute changes in SBP and DBP measured in the office from baseline were the primary efficacy outcomes. Control rate was defined as SBP ≤140 mmHg and DBP ≤90 mmHg, and response rate was defined as decrease in DBP ≥10 mmHg or DBP <90 mmHg at the 12th week. The efficacy of the combination was evaluated using the change in average SBP and DBP values, control rate and response rate.

Safety parameters

Safety assessments consisted of monitoring and recording all adverse events (e.g., edema), serious adverse events (with their severity and relationship to the study drug) and pregnancies, the regular monitoring of hematology, blood chemistry and urine performed at the study center, and regular assessments of vital signs, physical condition and body weight.

Statistical analysis

The per protocol (PP) population included patients who fulfilled the protocol in terms of follow-up, whereas the intent-to-treat (ITT) population included those who attended to least one follow-up visit. Since ITT and PP analyses were quite similar, only ITT analysis results are presented.

Patient demographics and disease characteristics were analyzed using descriptive statistics. Continuous variables were summarized as mean (±standard deviation [SD]) or median (and interquartile range [IQR]). Categorical variables were evaluated using Friedman test. Binary comparisons, if needed, were performed using Wilcoxon tests and evaluated with Bonferroni correction. For the cases including three variables or more (e.g., comparisons between visits in terms of age, gender, body mass index [BMI], etc.) Kruskal–Wallis was used, and for comparisons between two independent variables, Mann-Whitney U test was used. For statistical significance, type-1 error level was accepted as 5%.

RESULTS

Patient demographics

In 30 sites nationwide, a total of 381 patients were enrolled, and 327 completed the study. The main reasons

for discontinuation were adverse events (n=3), protocol violation (n=16) and lost-to-follow-up (n=35). The ITT and safety population included 381 patients, and the PP population included 327 patients. As demonstrated in Table 1, 39% of the patients were females. The mean age was 57.3±11.8 years. The majority were <65 years of age. Approximately 45% of the patients had a BMI of ≥30 kg/m^2. Median duration of hypertension was 38 months. The mean±SD SBP and DBP values were 162.6±16.6 mmHg and 94.0±13.2 mmHg, respectively. The distribution of comorbidities was as follows: diabetes melitus (34.1%), coronary artery disease (14.3%), hyperlipidemia (27.9%), and asthma (3.2%).

Table 1. Demographic, clinical and laboratory characteristics of the study population (n=381)

	Summary statistics		
	n	%	Mean±SD Median (IQR)
Age (years)			57.3±11.6
Age ≥65	107	28.1	
Male	149	39.1	
Hypertension duration (month)			38 (78)
Already on treatment at baseline	35	9.2	
Systolic blood pressure (mmHg)			162.6±16.6
Diastolic blood pressure (mmHg)			94.0±13.2
Hypertension stage at baseline			
Normal	3	0.8	
Prehypertension	90	23.6	
Stage I	157	41.2	
Stage II	131	34.4	
Heart rate (beats/min)			79.7±11
Body mass index (kg/m^2)			30.7±6.0
Body mass index (≥30 kg/m^2)	170	44.6	
Cardiovascular disease	61	16.1	
Renal disease	8	2.1	
Dyslipidemia	106	27.9	
Tobacco use	64	16.8	
Alcohol use	13	3.4	
Fasting blood glucose (mg/dL)			121.7±51.8
HbA1c (%)			7.2±1.9
Cholesterol (mg/dL)			205.5±49.2
Triglyceride (mg/dL)			153 (110.1)
High density lipoprotein-cholesterol (mg/dL)			46.9±18.8
Low density lipoprotein-cholesterol (mg/dL)			125.8±37.0
Aspartate transaminase (U/L)			23.6±14.6
Alanine transaminase (U/L)			51.3±15.6
Urea (mg/dL)			26.3±13.9
Uric acid (mg/dL)			5.2±1.6
Creatinine (mg/dL)			1.0±0.3
Microalbuminuria (mg/dL)			6.7 (46.2)

Table 2. Blood pressure levels of the study population at baseline and follow-up visits (n=381)

	Baseline	4th week	12th week	p
Systolic blood pressure	162.6±16.6	137.6±14.2	131.6±11.5	<0.001
ΔSystolic blood pressure		25.2±17.8	31.3±18.3	
Diastolic blood pressure	94.0±13.2	81.9±9.0	79.7±7.6	<0.001
ΔDiastolic blood pressure		12.3±17.8	14.0±12.2	

Data are given as mean±SD. Δ: Absolute change compared to baseline value.

Half of the patients (n=190; 49.9%) had used an antihypertensive drug previously. The mean±SD number of antihypertensive drugs was 0.66±0.80. The most common antihypertensive drug used previously was amlodipine (11.9%), followed by ramipril (9.8%), Val/Amlo (8.5%), valsartan/hydrochlorothiazide (5.5%), perindopril (5.5%), metoprolol (4.7%), nifedipine (3.8%), nebivolol (3.0%), cilazapril (2.6%), losartan/hydrochlorothiazide (2.6%), and indapamide (1.7%).

During the 12-week study period, no change was made to the dose of Val/Amlo and no antihypertensive treatment, including thiazide diuretics, was added.

Evaluation of blood pressure

Since some patients had already been on Val/Amlo treatment for a period, 24.4% of the patients were at normal BP or prehypertension stage at baseline (Table 1). The SBP and DBP values showed reductions at follow-up visits compared to baseline. The changes in SBP and DBP values at follow-up visits in comparison to baseline and the changes between visits were statistically significant (by Wilcoxon test) (Table 2, Figure 1). Evaluation of the patients' control and response rates at the end of the study demonstrated a control rate of 82.0% and response rate of 92.6% (Table 3).

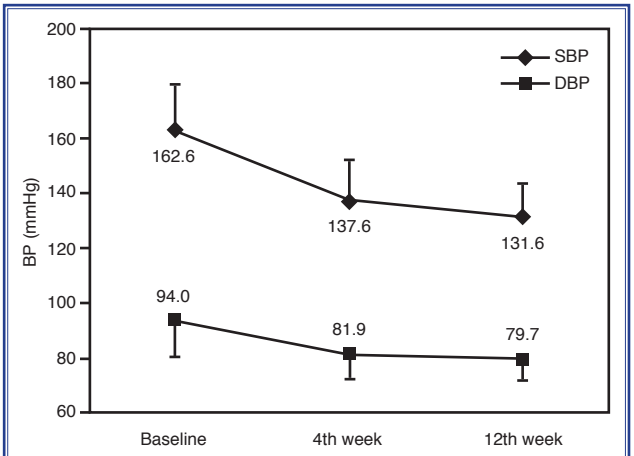

Figure 1. Blood pressure levels of the study population at baseline and follow-up visits. Error bars denote standard deviation. SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

Table 3. The control and response rates in the study population (n=323 evaluated)

	n	%
Control rate	265	82.0
Response rate	299	92.6

Table 4 and Figure 2 demonstrate the changes in the SBP and DBP levels of female and male patients during the course of the study. For both genders, BP decreased during the follow-up. Gender difference reached a statistically significant level for SBP. As given in Table 4, both SBP and DBP values showed significant reductions during the course of the study for all BMI subgroups. Although BMI subgroups did not differ in terms of baseline SBP and DBP levels, there were significant differences between BMI subgroups in terms of SBP values at both the 4th week and 12th week visits, with SBP being lowest in the BMI 25-30 kg/m^2 subgroup. SBP and DBP values of patients in the different age groups also reduced at the follow-up visits. However, age groups did not differ in terms of BP values during the course of the study. Further analysis comparing the patients who were previously untreated and those already on treatment before enrollment showed that, mean SBP and DBP levels had declined to similar levels at the 4th week, although mean SBP and DBP levels were significantly higher in previously untreated patients (Table 4).

Twenty-two percent of the patients at the 4th week and 7.7% of the patients at the 12th week had under-

gone changes in antihypertensive therapy. These were as follows: 93.7% dose increment, 2.5% drug cessation and 3.8% dose increment+addition of new drug. These rates were 26.9%, 3.9% and 3.9% at the 12th week, respectively. A new drug was added in 61.5% of the patients at the 12th week.

Table 4. Blood pressure values of the study population at baseline and study visits in terms of gender, age, treatment status, and body mass index (n=381)

	Baseline (Mean±SD)	4th week (Mean±SD)	12th week (Mean±SD)	p
Systolic blood pressure (mmHg)				
Gender				
Female	163.7±16.9	138.7±14.7	132.8±11.7	**<0.001**
Male	160.9±15.9	135.8±13.2	129.7±10.9	**<0.001**
p	0.058	0.051	0.029	
Age (years)				
<65	162.3±16.5	137.4±14.7	131.7±11.7	**<0.001**
≥65	163.4±16.9	138.0±12.9	131.5±10.8	**<0.001**
p	0.445	0.172	0.24	
Previously untreated				
Yes	164.5±14.5	137.5±13.6	131.7±11.5	**<0.001**
No	146.5±21.3	136.0±11.6	130.6±11.6	**<0.001**
p	**<0.001**	0.526	0.699	
Body mass index (kg/m^2)				
<25	162.0±14.0	140.0±10.4	133.1±11.1	**<0.001**
25-30	160.7±15.2	133.4±13.2	129.3±10.9	**<0.001**
≥30	164.5±18.3	140.9±15.0	133.4±11.7	**<0.001**
p	0.161	**<0.001**	**0.007**	
Diastolic blood pressure (mmHg)				
Gender				
Female	94.7±14.0	82.0±9.3	79.5±7.9	**<0.001**
Male	93.0±11.9	81.8±8.5	79.9±7.2	**<0.001**
p	0.576	0.714	0.220	
Age (years)				
<65	94.7±13.8	81.8±9.0	79.6±7.8	**<0.001**
≥65	92.3±11.7	82.2±9.1	79.8±7.2	**<0.001**
p	0.795	0.644	0.085	
Previously untreated				
Yes	94.1±11.6	82.0±9.0	80.0±7.6	**<0.001**
No	89.9±12.7	80.8±6.4	77.6±7.6	**<0.001**
p	**0.010**	0.618	0.047	
Body mass index (kg/m^2)				
<25	90.8±10.8	82.2±8.3	80.2±7.5	**<0.001**
25-30	93.2±11.6	80.4±8.5	78.7±7.1	**<0.001**
≥30	95.8±15.1	83.3±9.5	80.5±8.1	**<0.001**
p	0.129	0.047	0.399	

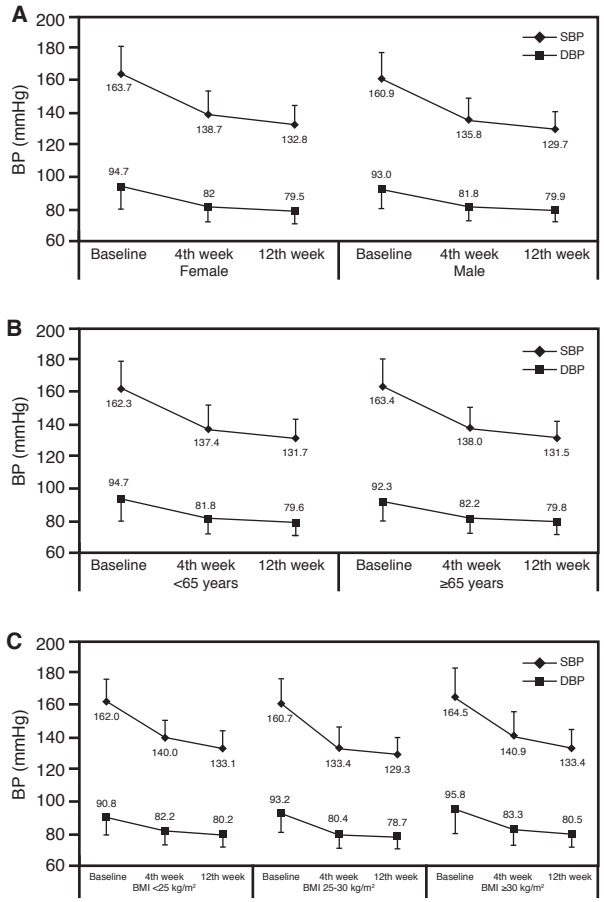

Figure 2. (A-C) Blood pressure values of the study population at baseline and study visits in terms of gender, age and body mass index. Error bars denote standard deviation. BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

Adverse events

Twelve patients (3.2%) experienced a total of 12 adverse events; there were no serious adverse events. The most common adverse event was edema (1.3%). Others included pruritis, hypotension, erectile dysfunction, dizziness, rashes, flushing, and coagulation. Table 5 summarizes the distribution of adverse events. 58.3% of the adverse events were mild. No action was taken for six adverse events (50%), and approximately three-quarters of the adverse events (83.3%) were considered related to the treatment.

Patient compliance

The compliance to medication as assessed by the study physician was 99.3±3.8% at the 4th week and 99.0±6.8% at the 12th week.

DISCUSSION

This 12-week, non-invasive, multi-center, observational study assessed the efficacy and safety profiles of low-dose combination treatment with valsartan and amlodipine in patients with hypertension. The data demonstrated the low-dose ARB/CCB SPC as efficient, tolerable and safe for the management of essential hypertension.

It is now well recognized that most patients require combination therapy, initiated as first line or early, to achieve guideline BP targets.[15] However, there is an inverse relationship between regimen complexity and patient adherence.[16,17] Treatment regimens that involve multiple medications are consistently associated with reduced compliance and adherence.[18] The use of fixed-dose combinations represents an alternative approach to multiple-drug therapy.[19,20] A number of fixed-dose combination therapies that are in clinical use include angiotensin converting enzyme inhibitor (ACEI)/CCB,[21,22] ACEI/diuretic[23,24] and ARB/diuretic.[25-27] A new strategy added to currently available treatment options is a fixed-dose combination of an ARB with a CCB.

In a study by Fogari et al.,[28] combination therapy with losartan/amlodipine (100/5 mg) or Val/Amlo (160/5 mg) provided an antihypertensive effect that was better than that attained with amlodipine monotherapy. This finding was consistent with the data of previous studies showing that addition of losartan or valsartan enhanced the efficacy of amlodipine.[29-32] A recent study of adult Turkish hypertensive patients under treatment with either 160/5 mg or 160/10 mg

Table 5. Adverse events in the study population (n=381)

	Frequency	
	n	%
Edema	5	1.3
Pruritis	2	0.5
Hypotension	1	0.3
Erectile dysfunction	1	0.3
Vertigo	1	0.3
Flushing	1	0.3
Coagulation	1	0.3

Val/Amlo SPC at baseline evaluated the efficacy, patient compliance and safety profile of the regimen and demonstrated a reduction in baseline BP of 165/98 mmHg to 131/81 mmHg 178 days after baseline.[14] The overall control rate was calculated as 97%.

A number of large, well-validated studies have shown that SBP is a better predictor of cardiovascular risk than DBP in most of the subjects allocated to chronic antihypertensive therapy in clinical practice. A meta-analysis of data from 61 prospective observational studies involving almost 1 million individuals with no vascular disease at baseline calculated the effect of a 20 mmHg difference in SBP on the risk of stroke and ischemic heart disease.[33] The authors demonstrated that a SBP value that was lower by 20 mmHg was associated with significantly lower risk of death from stroke (hazard rates, 0.36-0.67) and ischemic heart disease (0.49-0.67).[33] In a randomized, double-blind, placebo-controlled study involving 1940 patients with a mean baseline BP of 164/102 mmHg, olmesartan medoxomil (40 mg/day) and amlodipine besylate (10 mg/day) combination was associated with mean SBP reductions of 30.1 mgHg after eight weeks of treatment.[34] In a registration study using Val/Amlo (160/10 mg) combination therapy, the mean SBP reduction observed after eight weeks of treatment was 27.8 mmHg.[35]

In the present study, SBP values of the study population showed marked reductions during the 4th week and 12th week follow-up visits. Although the mean DBP values at the 4th week visit did not change significantly at the 12th week visit, the mean SBP values observed at the 4th week showed further decreases at the 12th week. These data are consistent with the findings of other recent clinical trials that showed lowering of BP, in particular, substantial decreases in SBP, with ARB/CCB combination therapy.[36] Thus, combination treatments with ARB/CCB offer convenient and potent BP reduction, including a powerful reduction in SBP.

An important factor in the long-term efficacy of antihypertensive therapy is the tolerability. Regimens involving multiple medications tend to be associated with low compliance.[15,17] On the other hand, combination regimens provide advantages in enhancing tolerability, in that ARBs prevent some of the adverse events related to CCBs, such as edema and headache.[35,37] As reported by Fogari et al.,[37] losartan/amlodipine (100/5 mg) and Val/Amlo (160/5 mg) combinations were well tolerated, with incidence rates of adverse events lower than the rate observed with amlodipine monotherapy. A double-blind, paralel group study by Poldermans et al.[36] evaluated the overall safety profile and efficacy of Val/Amlo combination therapy, and demonstrated that in a total of 63 patients, the regimen was well tolerated, with adverse events in 40.6% of the patients. The most common adverse events reported were headache (10.9%) and peripheral edema (7.8%). In the same study, the response rate (proportion of patients with mean sitting DBP <90 mmHg or a >10 mmHg reduction from baseline) at the end of the study was 100% and overall BP control of <140/90 mmHg was 67.2%. In our study, a total of 12 adverse events (58% mild) were experienced by the study population and approximately 50% of them required no action. The most common adverse event observed was edema (1.3%). Another important finding of the study was that fixed-dose ARB/CCB combination resulted in a very high patient compliance (99% at the follow-up visits). Evaluation of the patients' control and response rates at the end of the study demonstrated a control rate (SBP≤140 mmHg and DBP≤90 mmHg) of 82% and response rate (DBP<90 mmHg or a ≥10 mmHg reduction from baseline at the 12th week visit) of 93%. In the study conducted in Turkey, the most commonly reported adverse events were edema (10.8%), headache (0.4%), dizziness (0.3%), and pain (0.3%).[14] The severity of edema was mostly reported as mild (74.1%) and moderate (22.9%), and only 3.1% of edema occurrences were reported to be severe. The study reported no adverse event with the use of Val/Amlo.

In conclusion, the results of the study presented here demonstrated that monotherapy with Val/Amlo combination offered adequate BP control and was tolerated well, with a very low incidence of adverse events. Low-dose Val/Amlo SPC therapy is efficacous and has a good tolerability and safety profile for the management of essential hypertension in Turkey.

Limitations

Since this study was a "non-interventional observational" study, no measures to make or confirm the diagnosis of hypertension were planned or performed. The diagnosis made by the physician who treated the patient according to his/her routine practice was regarded as the only criterion of diagnosis. Furthermore,

no intervention that could minimize bias, like use of a control group or washout period, which would be a change to the routine daily practice, was planned or performed. We consider these limitations to be strengths of the study, since this design facilitated the collection of real-life data, not biased by the "overly standardized" management of patients in randomized clinical trials.

List of the participating physicians

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