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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

The efficacy and safety of valsartan and combination of valsartan and hydrochlorothiazide in the treatment of patients with mild to moderate arterial hypertension — the VICTORY trial

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Abstract

Background and aim: The aim of the trial was to establish the efficacy and safety of Valsacor® (valsartan) and Valsacombi® (combination of valsartan and hydrochlorothiazide) in a wide variety of patient populations with mild to moderate arterial hypertension.

Methods: We performed an international, multicentre, open-label, prospective trial. After one week of washout in previously treated patients, the patients were treated for 16 weeks according to the protocol. Naïve patients entered the treatment period immediately. During the active treatment, four visits were planned for each patient to obtain the data for the primary and secondary efficacy endpoints analysis. The principal methods were blood pressure (BP) measurement, additionally in a subgroup of patients, assessment of erectile function. The initial dosage of valsartan 80 mg/day was titrated up to 320 mg/day to achieve the BP goal, with the addition of hydrochlorothiazide (HCTZ) in a fixed-dose combination (FDC), if needed.

Results: Mean ± standard deviation changes from baseline at week 16 were –26.6 ± 10.4 mm Hg (systolic BP) and –14.8 ± 7.6 mm Hg (diastolic BP). A total of 91% of the patients treated with either valsartan or valsartan FDC achieved the BP goal. Adverse reactions were experienced by 7.1% of the patients, with the most common being headache (1.9%), palpitation (1.6%), dizziness (1.6%), and fatigue (1.6%), during the whole trial.

Conclusions: The results of the VICTORY trial show that valsartan and valsartan FDC effectively reduce the BP in patients with mild to moderate arterial hypertension and have a good tolerability profile.

Key words: arterial hypertension, fixed-dose combination, valsartan

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INTRODUCTION

Arterial hypertension (AH) is one of the most important risk factors for cardiovascular morbidity and mortality. It is defined as blood pressure (BP) persistently at or above 140/90 mm Hg [1, 2]. Usually it is asymptomatic initially, but sustained hypertension over time is symptomatic due to target organ damage [3]. As of 2000, nearly one billion people, or approximately 26% of the adult population of the world, had hypertension. It was common in both developed (333 million) and undeveloped (639 million) countries [4]. In Europe hypertension

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occurs in about 30–45% of people as of 2013 [5]. However, rates vary markedly in different regions with rates as low as 3.4% (men) and 6.8% (women) in rural India and as high as 68.9% (men) and 72.5% (women) in Poland [6].

Dietary and lifestyle changes can improve BP control and decrease the risk of health complications, although treatment with medication is still often necessary in people for whom lifestyle changes are not enough or not effective [7].

Angiotensin receptor blockers (ARBs, e.g. valsartan) are among first-line medications for hypertension treatment. They can be used either alone or in combination with other antihypertensive agents (e.g. hydrochlorothiazide [HCTZ]).

The aim of the trial and primary endpoint was to evaluate the efficacy and safety of valsartan and fixed combination of valsartan and HCTZ in wide populations of adult patients with mild to moderate AH. The secondary endpoints were to compare primary endpoints between the monotherapy versus combination therapy and to evaluate adverse events (AE).

METHODS

Patients

Inclusion criteria for recruitment were patients of both genders, age 18 years or above, with mild to moderate essential hypertension (according to European Guidelines for the management of arterial hypertension 2013), with systolic blood pressure (SBP) of 140–179 mm Hg, and diastolic blood pressure (DBP) of 90–109 mm Hg. All patients gave written consent to participate in the trial. The main exclusion criteria were BP values 180/110 mm Hg or higher during washout period, secondary hypertension, malignant hypertension, treatment-resistant hypertension, hypovolemia due to salt-restricted diet, dialysis, diarrhoea or vomiting, haemodynamically significant aortic stenosis or bilateral stenosis of the renal artery or arterial stenosis of a solitary kidney, history of angioedema, hypertensive encephalopathy, angina pectoris or heart failure requiring treatment with a beta-blocker or a calcium antagonist or cardiovascular accident within former three months, acute liver disease or hepatic dysfunction and other acute diseases within the period of the past three months, renal failure (creatinine clearance < 60 mL/min) or clinically significant pathologic laboratory values of serum creatinine or potassium and diabetes mellitus treated with insulin, or uncontrolled diabetes mellitus with fasting blood glucose greater than 11 mmol/L.

Patients can withdraw from the trial after being included, if they want to discontinue the treatment and withdraw (patient's dropouts). The reasons for withdraw is either noncompliance (three or more missed consecutive doses, or 20% or more missed doses in a trial period [i.e. between visit 2 and 3]), do not appear at more than one visit, inefficient treatment in such a way that their health is endangered, serious or severe AE, treatment with a medicine that might influence the results of the trial, pregnancy during the trial, or some other reasons (e.g. after agreement with the monitor, the principal investigator, and the coordinator).

Study design

The trial was designed as an international, multicentre, open-labelled, prospective, phase IV trial performed in 25 centres in five countries: Slovenia (seven clinical centres), Czech Republic (three clinical centres), Croatia (three clinical centres), Ukraine (three clinical centres), and Russian Federation (nine clinical centres).

The duration of the active treatment was 16 weeks.

The trial population was treatment-naïve or previously treated and uncontrolled patients with mild to moderate AH. The treatment consisted of administration of valsartan or fixed-dose combination (FDC) valsartan/HCTZ tablets in doses of up to 320 mg valsartan and up to 12.5 mg HCTZ for 16 weeks. The previously treated patients underwent one week of washout period before commencement of the treatment. Patients who were naïve at least one month before the study did not go through the washout period (Fig. 1).

The tested drugs were valsartan in the dosage of 80 mg, 160 mg, 320 mg and FDC valsartan/HCTZ in the dosage of 160/12.5 mg and 320/12.5 mg.

Patients took the medication once daily between 7 a.m. and 10 a.m. On the day of the control visit patients did not take the trial drugs before the BP measurement at the visit was performed. The treatment was initiated with one tablet of valsartan of 80 mg daily in all patients (naïve and previously treated patients). Only in Russia, previously treated patients at the first visit received valsartan in a dose of 160 mg (request from the Ethical Committee), which did not have any influence on study results. After four weeks of treatment, the dose was adjusted to one tablet of valsartan 160 mg (in Russia also to one tablet of valsartan 320 mg or FDC valsartan/HCTZ 160/12.5 mg) daily in patients whose BP was not lowered to 140/90 mm Hg or less. After consequent four weeks in insufficiently treated patients the dose was increased to valsartan 320 mg or FDC valsartan/HCTZ 160/12.5 mg (in Russia also to one tablet of FDC valsartan/HCTZ 320/12.5 mg). If target BP levels were not achieved after an additional four weeks, the dose was increased to FDC valsartan/HCTZ 320/12.5 mg (in Russia also to one tablet of FDC valsartan/HCTZ 320/25 mg).

The duration of the active treatment was 16 weeks. Previous therapy that could in any way affect the efficacy and safety endpoints was included in the exclusion criteria. During the 16 weeks of active treatment period any concomitant treatment that could itself affect the results was prohibited. This therapy included medicines with a hypotensive effect, medicines that may produce an increase in BP (oral corticosteroids, hormonal contraceptives, sympathomimetic), and potassium sparing diuretics or potassium salts and/or salt substitutes.

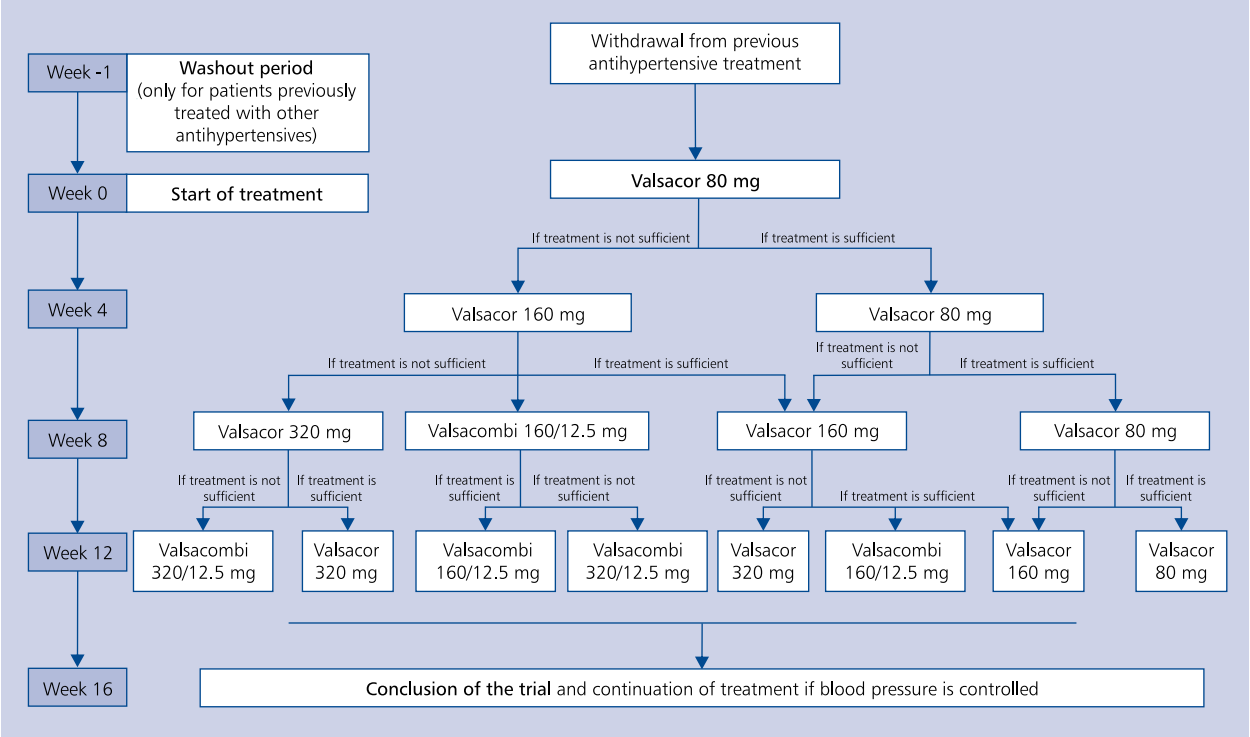

Figure 1. Study design

Assessments during the trial

Besides standard procedures to assess medical history, general physical examination, and vital signs assessment, special procedures were applied to assess baseline status of the disease and changes after the therapeutic intervention (Table 1).

Blood pressure measurement

Blood pressure was measured at every visit in the morning hours (7–10 a.m.) prior to administration of the morning dose of drug. In each patient, at all visits, BP was measured with the same device and by the same investigator or another member of the authorised medical staff.

Before BP measurement, a patient had at least 5 min of rest in a sitting position. Patients refrained from smoking or ingesting caffeine during the 30 min preceding the measurement.

During the measurement patients sat in a chair with their back supported and their arms bared and supported at heart level. Three measurements were performed in at least 2-min intervals and the obtained values were recorded with an accuracy of at least 2 mm Hg. The mean of the last two measurements was considered as the final BP value.

At the first visit BP was measured on both arms. At the following visits BP was only measured on the arm that showed higher BP value at the first visit measurement.

Target BP values were defined according to the 2013 ESH/ESC Guidelines for the management of AH [8].

Treatment compliance

The treatment compliance was monitored on visits 2, 3, 4, and 5. The following parameters were set: X — number of investigational medicinal product (IMP) units given to the patient at the previous visit (initial dose included); Y — number of prescribed doses since the last visit excluding the day of the current visit; and Z — number of unused IMP units checked at the current visit. Compliance (%) was given as a percentage, derived from the following formula:

$$\% = \frac{(X - Z)}{Y} \times 100$$

After the calculation was performed the compliance criterion was verified for further continuation of study participation. Patients who missed more than 20% of all doses were excluded from the trial.

Safety assessment

To assess the safety profile an interview and physical inspection were used.

The patients were asked about any signs or symptoms they experienced since the last visit, and a physical examination was carried out to identify any possible pathological signs of AEs. All captured AEs were stratified according to time of occurrence, frequency, relation with the IMP, severity, therapeutic measures, and outcome.

Table 1. Assessments during the trial

Parameter	At visit –1 (washout — only for previously treated patients)	At visit 1 (start of active treatment for all eligible patients)	At visit 2 (first control visit)	At visit 3 (second control visit)	At visit 4 (third control visit)	At visit 5 (last control visit: end of the trial)
Medical history		×				
Physical examination		×				
Systolic blood pressure	×	×	×	×	×	×
Diastolic blood pressure	×	×	×	×	×	×
Heart rate	×	×	×	×	×	×
Electrocardiogram		×				
Clinical chemistry (fasting glucose, potassium, creatinine)		×				×
Urine test (microalbuminuria)		×				×
Questionnaire on erectile function (men only)		×				×
Concomitant therapy		×	×	×	×	×
Compliance assessment			×	×	×	×
Monitoring adverse events			×	×	×	×

Statistical and analytical plans

Patients who prematurely discontinued the trial because of AE or because of an untoward effect on BP values that could be a threat to their health, or who discontinued the trial for other reasons, were not included in the per-protocol (PP) analysis, but were included in intention-to-treat (ITT) analysis. We did not include patients with violations of protocol in PP analysis (e.g. not increasing the dose despite not reaching the target BP).

The data was statistically processed: the largest and the smallest data, arithmetic mean of data with standard deviation of data, and standard error of mean and the value of t variable in t-test. The unpaired two-tailed Student's t-test and 95% confidence interval was used to compare values between the treatment groups. Differences were considered to be significant at $p < 0.05$.

RESULTS

Patients

Intention-to-treat analysis of primary and secondary endpoints includes 365 patients. PP analysis of primary and secondary endpoints included 230 patients. Four patients discontinued the treatment due to adverse reactions (AR) related to the treatment. At the end of the trial, 351 patients attended the last control visit. The study completion rate was 96% (351/365).

There were 365 patients (196 [54.0%] females and 169 [46.0%] males) enrolled in the trial. The mean age was 54.6 ± 12.0 years.

Based on body weight and body height parameters, body mass index (BMI) was calculated. The BMI stayed almost the same throughout the course of the trial with a mean value of 29.16 ± 4.4 on the first visit and 29.11 ± 4.4 on the final visit. The change of mean BMI from the first to the last visit was statistically insignificant.

At the beginning of the trial patients reported their smoking and alcohol consumption habits. 284 (78%) patients were not smoking at the beginning of the trial and 80 (22%) patients were smokers. Fifty (14%) of them were regular smokers, nine (2%) were occasional smokers, and 21 (6%) were ex-smokers. For one patient there was no data regarding smoking habit.

Two hundred and twenty three (61%) patients were not alcohol consumers, and 142 (39%) were alcohol consumers. Out of 142 alcohol consumers, 14 (4%) were regular consumers, 108 (30%) were occasional consumers, and 20 (5%) were other not specified consumers.

In Table 2 all medical history and concomitant diseases are presented. The most frequent concomitant disease was hyperlipidaemia.

In the last 12 months before the start of the trial, 244 (67%) patients were not treated for hypertension and 121 (33%) patients were already treated. Forty (11%) patients were treated with monotherapy and 81 (22%) with combina-

Table 2. Concomitant diseases

	N	Per cent (all patients)
Cardiovascular diseases:		
Chronic heart failure	27	7%
Myocardial infarction	6	2%
PTCA or CABG	2	1%
Peripheral artery disease	7	2%
Cerebrovascular disease	6	2%
Other	24	7%
Respiratory disease	9	2%
Gastrointestinal, hepatic disease	26	7%
Renal disease	26	7%
Metabolic syndrome	40	11%
Diabetes mellitus type II	35	10%
Hyperlipidaemia	131	36%
Neurogenic and locomotor illnesses	25	7%
Surgery	30	8%
Allergy	9	2%
Other	103	28%

CABG — coronary artery bypass grafting; PTCA — percutaneous transluminal coronary angioplasty

Table 3. The number and proportion of patients (previously treated for hypertension) according to therapeutic groups

Previous treatment of hypertension	N	Per cent (all patients)
ACEI (monotherapy and combinations)	73	20.0%
Calcium channel blockers	45	12.2%
ARBs (monotherapy and combinations)	42	11.5%
Diuretics	36	9.9%
Beta-blockers	30	8.2%
Alpha-blockers	6	1.6%
Antiadrenergics	5	1.4%

ACEI — angiotensin-converting enzyme inhibitors; ARB — angiotensin receptor blockers

Table 4. The number and proportion of patients with abnormal electrocardiogram examination

	N (119)	Per cent (all patients) (33%)
Left atrial hypertrophy	5	1%
Left ventricular hypertrophy	61	17%
Left ventricular load	2	1%
Other	51	14%

tion therapy. Previous antihypertensive treatment is presented according to the therapeutic groups (Table 3).

Before the start of the trial, patients carried out an electrocardiogram (ECG) examination. 245 (67%) patients had normal ECG, while 119 (33%) patients had abnormal ECG results. Abnormal results are shown in Table 4.

On the first and the last visit, patients carried out urine test to determine the presence of microalbuminuria. On the first visit, 33 (9.0%) patients out of 365 had positive test on microalbuminuria, while on the last visit, 28 patients out of 351 (8.0%) had a positive test. The proportion of patients testing positive on microalbuminuria declined during the course of the trial.

Efficacy

Antihypertensive efficacy of valsartan and FDC valsartan/HCTZ was evaluated by BP lowering effect and in achieving target BP control in patients with mild to moderate hypertension.

Blood pressure

The primary efficacy endpoint was to evaluate (according to the ITT analysis) the effect of valsartan and FDC valsartan/HCTZ on BP reduction and achievement of target BP. At each control visit the BP was measured, and according to the results the achievement of target BP was obtained.

During the trial, the mean values of SBP and DBP were steadily decreasing. The mean absolute decreases of SBP and DBP were 26.60 ± 10.41 mm Hg and 14.84 ± 7.57 mm Hg, respectively. On the other hand, the mean relative decreases of both SBP and DBP were 16.8 ± 6.1% and 15.2 ± 7.3%, respectively. The decrease of mean SBP and DBP between two consecutive visits was in every case statistically significant ($p < 0.0001$) (Fig. 2).

Achievement of target BP according to the 2013 ESH/ESC Guidelines for the management of AH was monitored on each control visit. On the last visit, 91% of patients who attended the last visit achieved target BP. The achievement of target BP was higher on each subsequent visit, which can be seen in Figure 3.

Overall, 230 patients were included into PP analysis of target BP control. Fifty of them were receiving combination therapy on at least one control visit, and 180 of them were receiving monotherapy throughout the whole trial. The combination therapy was initiated in patients who did not reach target BP on visit 3 and visit 4. Comparison of mean absolute and relative decrease of SBP and DBP from visit 3 to visit 5 between monotherapy and combination therapy was statistically significant ($p < 0.0001$). Patients treated with combination therapy were patients who did not achieve target BP on visit 3 and/or visit 4, meanwhile patients treated with monotherapy were patients mostly with controlled BP (with the exception of patients who start treatment with valsartan 320 mg on visit 3).

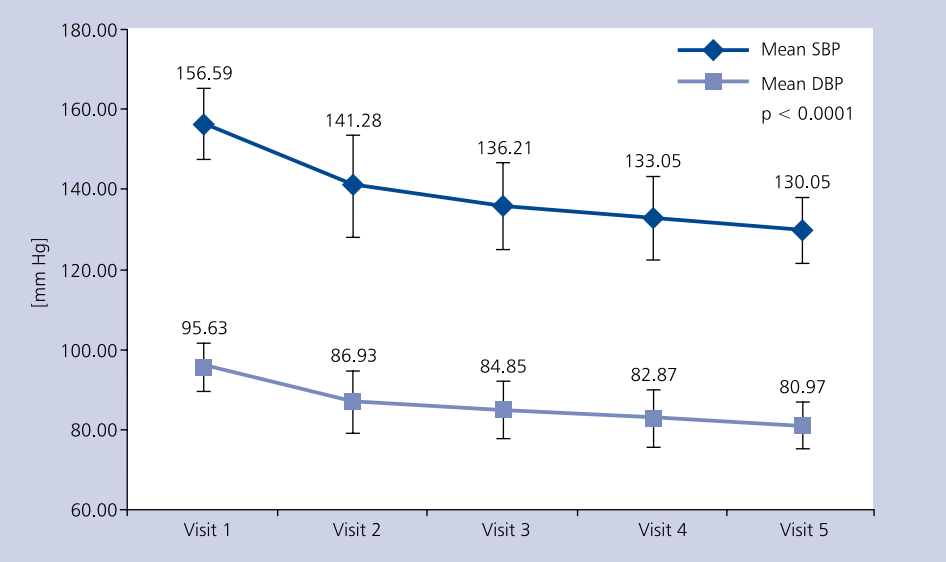

Figure 2. The mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) and standard deviation at each visit of the trial (all patients)

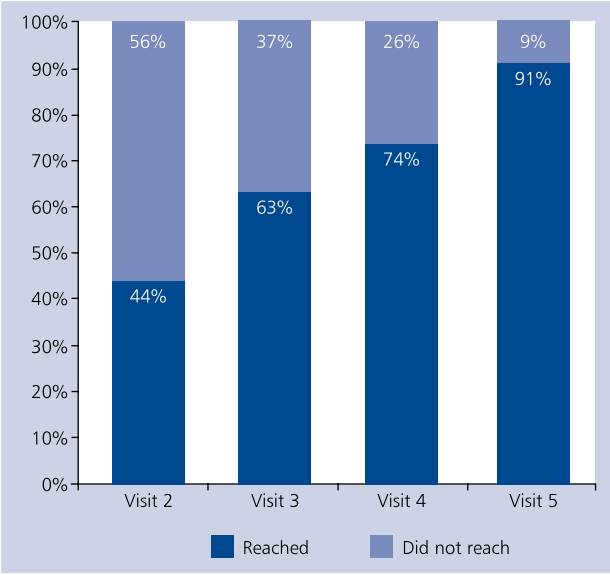

Figure 3. Achievement of target blood pressure during the trial

Besides that, mean SBP and DBP values between monotherapy and combination therapy were statistically significant ($p < 0.0001$, only on the last visit, the p for SBP was < 0.0005) on each visit of the trial (Fig. 4).

Comparison of target BP achievement shows that on the last visit 84% and 98% of patients in the combination and monotherapy groups achieved target BP, respectively. Combination therapy was introduced only in cases when monotherapy was insufficient for achievement of target BP.

Achievement of target BP according to the treatment group can be seen in the Tables 5 and 6.

Therapeutic effect

The therapeutic effect of the treatment was evaluated on the last visit of the trial:

- very good — if values of arterial BP are below 140/90 mm Hg at the end of the trial (< 140/85 mm Hg for high-risk and diabetic patients);
- good — if the SBP was reduced by at least 10 mm Hg, and the DBP by at least 5 mm Hg;
- satisfactory — if only the SBP was reduced by at least 10 mm Hg, or only the DBP by at least 5 mm Hg;
- unsatisfactory — if the SBP was reduced by less than 10 mm Hg, and the DBP by less than 5 mm Hg.

Very good therapeutic effect was achieved by 90.6% of patients who came on the last control visit. The remaining 9.4% were allocated between good, satisfactory, and unsatisfactory (Fig. 5).

The effect of treatment on the patient's quality of life

The effect of treatment on the patient's quality of life (QoL) was evaluated with the following statements/questions:

- the patient is feeling well [better than with previous antihypertensive(s)];
- the therapy did not aggravate the patient's overall feeling;
- adverse reactions are mild and not irritating to the patient;
- adverse reactions are irritating, but withdrawal of the drug was not necessary;

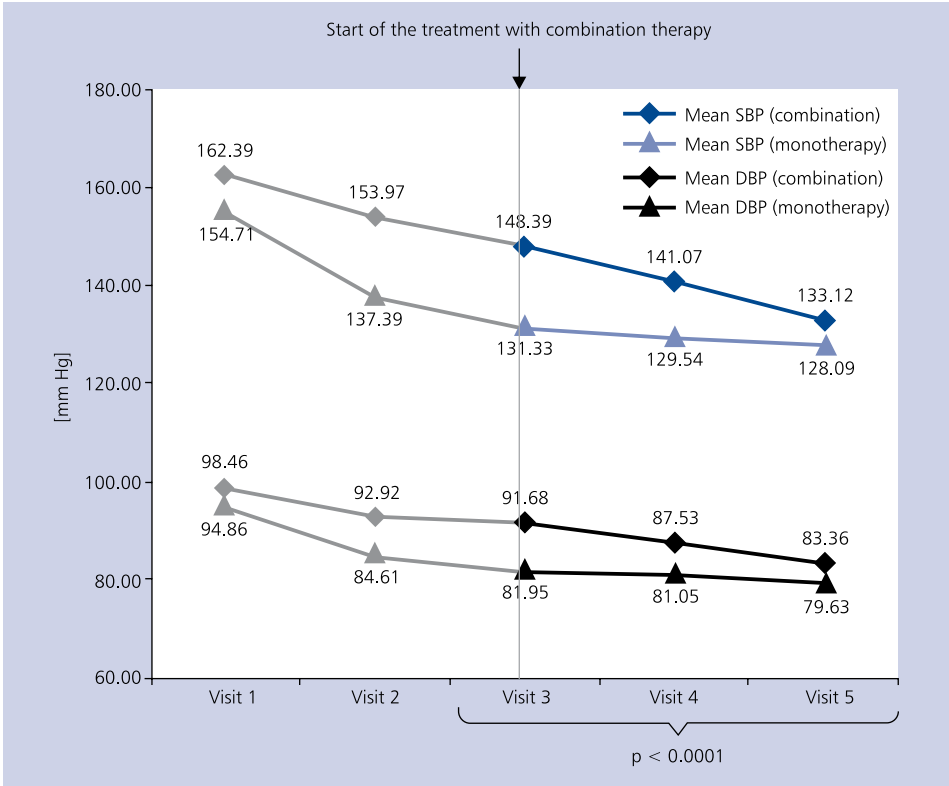

Figure 4. The mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) on each control visit for patients treated with monotherapy or combination therapy

Table 5. Achievement of target blood pressure at each control visit for patients treated with monotherapy

	Monotherapy				
	N	Reached		Did not reach	
		N	%	N	%
Visit 2	180	110	61%	70	39%
Visit 3	180	152	84%	28	16%
Visit 4	180	163	91%	17	9%
Visit 5	180	176	98%	4	2%

Table 6. Achievement of target blood pressure (BP) at each control visit for patients treated with combination therapy, who did not achieve target BP on monotherapy

	Combination therapy (for patients, who did not achieve target BP)				
	N	Reached		Did not reach	
		N	%	N	%
Visit 2	50	0	0%	50	100%
Visit 3*	50	5	10%	45	90%
Visit 4*	50	21	42%	29	58%
Visit 5*	50	42	84%	8	16%

*Combination treatment was firstly introduced on visit 3. On visit 3, 37 patients received combination therapy, and on visit 4, an additional 13 patients received combination treatment.

— the patient untimely discontinued the treatment due to severe AR.

At the end of the trial, 73.7% of patients who were questioned about the QoL answered that they feel well or better than with previous antihypertensive therapy. In most patients, the treatment improved patients QoL. In 22.3% of patients, the treatment did not aggravate the patients QoL. These results clearly show that patients treated with valsartan and FDC valsartan/HCTZ had improved QoL (Table 7).

Safety

Laboratory evaluation. We evaluated laboratory levels of glucose, potassium, and creatinine in plasma. There were no changes in levels of all three parameters comparing the initial visit and the end of the study (visit 5).

Adverse events. According to the safety analysis, patients tolerated valsartan and FDC valsartan/HCTZ very well;

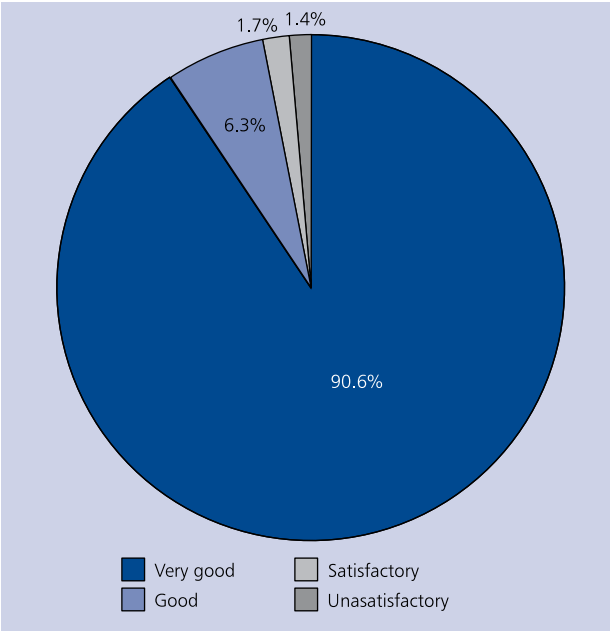

Figure 5. Therapeutic effect of the treatment

321 (87.9%) patients did not experience AEs. Investigators assessed that 26 (7.1%) patients experienced a total of 44 ARs that were related to valsartan and FDC valsartan/HCTZ treatment, in the investigators' opinion. ARs were assessed in 4.4% of patients during the first period and only nine (2.5%) patients maintained the ARs during the second period. During the third and fourth periods, six (1.6%) and five (1.4%) patients experienced ARs.

Eighteen (4.9%) patients experienced AEs that were not related to valsartan and FDC valsartan/HCTZ treatment. If a patient experienced both AEs not related to the study medicine as well as an AR, he or she was counted as a patient with AR. Among the ARs that patients experienced during the trial, none was severe (Table 8).

The most common ARs were headache (seven patients, 1.9%), palpitations (six patients, 1.6%), dizziness (six patients, 1.6%), fatigue (six patients, 1.6%), and diarrhoea (two patients, 0.5%).

None of the patients experienced severe ARs (for three patients we do not have data of severity). Other ARs were moderate or mild. Most frequently patients experienced mild ARs (20 patients, 5.5%). The majority of ARs occurred during the first period of the active treatment.

Four (1.1%) patients discontinued the active treatment during the study (three in the first period and one in the second period). Other patients who also experienced ARs did not take any other measures and continued with the active treatment.

DISCUSSION

Valsartan was first approved in 1996 for the treatment of AH in adults. In more than 10 years since its approval for hypertension, a wealth of experience with valsartan has been gained through an extensive clinical research programme. Valsartan has been included in more than 60 studies involving over 100,000 patients. Based on the results of these studies, valsartan also gained approval for two additional indications: heart failure and post-myocardial infarction. More than 50,000 patients have been included in valsartan cardiovascular morbidity and mortality studies. Some of them also proved that valsartan improves sexual function in hypertensive men. Besides that, valsartan was also proven in different types of patients including elderly, obese, and patients with diabetes mellitus, etc. [9].

Table 7. Effect of treatment on the patients' quality of life

	N (365)	Per cent (all patients) (100%)	Per cent (evaluated patients) (100%)
The patient is feeling well	261	71.5%	73.7%
Patient's overall feeling not aggravated	79	21.6%	22.3%
Mild adverse reactions	8	2.2%	2.3%
Irritating adverse reactions	5	1.4%	1.4%
Discontinuation due to severe adverse reactions	1	0.3%	0.3%
No data	11	3%	

Table 8. Patients with and without adverse events (AE) (n = 365; 100%)

	First period		Second period		Third period		Fourth period		All periods	
	N	%	N	%	N	%	N	%	N	%
Patients with AE:	21	5.8%	14	3.8%	16	4.4%	10	2.7%	44	12.1%
— Patients with adverse reactions	16	4.4%	9	2.5%	6	1.6%	5	1.4%	26	7.1%
— Patients with AE not related to the study medicine	5	1.4%	5	1.4%	10	2.7%	5	1.4%	18	4.9%
Patients without AE	344	94.2%	351	96.2%	349	95.6%	355	97.3%	321	87.9%

In the international, multicentre, open labelled, prospective phase IV trial the efficacy and safety of valsartan or its combination with HCTZ in patients with mild to moderate AH was studied. In the VICTORY trial, 365 patients from five countries were included. Prior to the start of the active treatment, previously treated patients had to undergo a one-week wash-out period. Patients who satisfied all inclusion criteria were included into the trial. All patients started the active treatment with valsartan in a dose of 80 mg (except in Russia, where previously treated patients started the treatment with valsartan in a dose of 160 mg), which was titrated on each control visit according to the dosing scheme and achievement of target BP.

The results of the VICTORY trial clearly suggest that valsartan and FDC valsartan/HCTZ effectively reduce SBP and DBP. Mean absolute decrease of SBP and DBP in all patients at the end of the trial, compared to the start values, were 26.60 ± 10.41 mm Hg and 14.84 ± 7.57 mm Hg, respectively, which was statistically significant ($p < 0.0001$). At the end of the trial, 90.6% of patients achieved target SBP and DBP levels. Seen from a population point of view, where we have many uncontrolled patients, these are high numbers that are rarely observed in real-life trials, with direct clinical implications.

A comparison of BP decrease between monotherapy and combination therapy from visit 3 to visit 5 was statistically significant ($p < 0.0001$), bearing in mind that combination therapy was initiated in patients who did not reach target BP on visit 3 and visit 4. This proves that the usage of FDC, which further decreases BP in patients with greater difficulty in controlling BP, is highly recommended when target BP is not achieved.

Of note, the treatment with valsartan and valsartan/HCTZ improved the QoL in 73% of investigated patients. With the aging of the population and increased number of comorbidities of these patients, we should not only aim for BP control, but we should also take into consideration the patient's feeling about their disease and how they live with it.

As a class, ARBs are noted for their improved tolerability profile and improved adherence relative to angiotensin-converting enzyme inhibitors. The AE profile of ARBs is similar to that observed with placebo; common AEs are usually transient and mild in severity and include dizziness, headache, nasopharyngitis, and malaise/fatigue [10]. The tolerability profile of valsartan is independent of dose and duration of treatment, and is consistent regardless of age, sex, and ethnic group at dosages up to 320 mg/day; headache and possibly dizziness appear to be dose related at very high doses [11]. In placebo-controlled clinical trials, the discontinuation rate due to AEs was low (2.3%), primarily for headache and dizziness. In trials of patients with HF, the tolerability profile of valsartan is as expected pharmacologically and based on the overall health status of the patients. Dizziness was the primary AE, reported by 17% of valsartan and 9% of placebo recipients. Rates of discontinuation due to AEs were similar for valsartan and placebo recipients.

Treatment with valsartan and FDC valsartan/HCTZ was well tolerated; 87.9% of patients did not experience any AEs throughout the trial. Investigators assessed that 7.1% of patients experienced ARs that were related to study medicines. On the other hand, 4.9% of patients experienced AEs that were not related to treatment. The majority of patients experienced mild ARs. The most common ARs were headache (1.9%), palpitations (1.6%), dizziness (1.6%), fatigue (1.6%), and diarrhoea (0.5%). Four (1.1%) patients discontinued the treatment due to ARs related to valsartan and FDC valsartan/HCTZ treatment.

CONCLUSIONS

The results of the present VICTORY trial show that valsartan and valsartan/HCTZ effectively reduce BP in patients with mild to moderate AH and provide a good tolerability profile because almost 93% of patients did not experience ARs during the whole trial.

Conflict of interest: *This study was sponsored by KRKA, Słovenia.*

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Skuteczność i bezpieczeństwo walsartanu oraz połączenia walsartanu z hydrochlorotiazydem w leczeniu pacjentów z nadciśnieniem tętniczym łagodnego do umiarkowanego stopnia — badanie VICTORY

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Streszczenie

Wstęp i cel: Celem badania była ocena skuteczności i bezpieczeństwa leków Valsacor® (walsartanu) i Valsacombi® (połączenie walsartanu i hydrochlorotiazydu) w dużej grupie pacjentów z nadciśnieniem tętniczym łagodnego do umiarkowanego stopnia.

Metody: Przeprowadzono międzynarodowe, wieloośrodkowe, otwarte, prospektywne badanie. Po okresie eliminacji leku z organizmu wynoszącym 1 tydzień u pacjentów wcześniej leczonych, chorzy byli poddani terapii przez 16 tygodni zgodnie z harmonogramem. U osób dotąd nieleczonych natychmiast włączano leczenie. U każdego pacjenta w okresie aktywnej terapii zaplanowano przeprowadzenie 4 wizyt, w celu uzyskania danych do analizy skuteczności pierwotnych i wtórnych punktów końcowych. Do głównych metod należały pomiar ciśnienia tętniczego (BP) i, dodatkowo w podgrupie pacjentów, ocena zaburzeń erekcji. W celu uzyskania docelowej wartości BP początkową dawkę walsartanu 80 mg/dobę zwiększano do 320 mg/dobę i w razie konieczności dodawano hydrochlorotiazyd (HCTZ) w ramach leku złożonego o ustalonej dawce (FDC).

Wyniki: Średnie ± odchylenie standardowe zmian w stosunku do wartości wyjściowej po 16 tygodniach wynosiły: –26,6 ± 10,4 mm Hg (skurczowe BP) i –14,8 ± 7,6 mm Hg (rozkurczowe BP). U 91% pacjentów leczonych za pomocą walsartanu lub walsartanu FDC uzyskano docelowe wartości BP. U 7,1% chorych wystąpiły reakcje niepożądane. Do najczęściej występujących reakcji obserwowanych w trakcie całego badania należały: ból głowy (1,9%), kołatanie serca (1,6%), zawroty głowy (1,6%) i zmęczenie (1,6%).

Wnioski: Wyniki badania VICTORY wskazują, że walsartan i walsartan FDC skutecznie obniżają BP u pacjentów z nadciśnieniem tętniczym łagodnego do umiarkowanego stopnia i są dobrze tolerowane przez chorych.

Słowa kluczowe: nadciśnienie tętnicze, połączenie o ustalonej dawce, walsartan

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