Sponsor

Novartis

Generic Drug Name

Valsartan/Hydrochlorothiazide

Therapeutic Area of Trial

Hypertension

Approved Indication

Each drug is approved, by itself, for the treatment of hypertension. Valsartan is also approved in combination with hydrochlorothiazide for the treatment of hypertension.

Study Number

CVAH631D2301

Title

A 6-week, multicenter, randomized, double-blind, parallel group study to evaluate the combination of valsartan/HCTZ (160/12.5 mg with forced titration to a maximum dose of 320/25 mg) compared to valsartan monotherapy (160 mg with forced titration to 320 mg) as initial therapy in patients with severe hypertension.

Phase of Development

Phase III

Study Start/End Dates

28 Nov 2005 to 05 Jul 2006

Study Design/Methodology

This was a 6-week multicenter, randomized, double-blind, parallel-group trial. Following a 3-28 day washout period, (Visit 1), patients were randomized (Visit 2) to receive valsartan (val)/ hydrochlorothiazide (HCTZ) 160/12.5 mg combination therapy or valsartan 160 mg monotherapy, once daily. After 2 weeks (Visit 4), combination therapy was force-titrated to a dose of 160/25

mg and monotherapy was force-titrated to a dose of 320 mg. On Day 28 (Visit 6), combination therapy was force-titrated to a maximum dose of 320/25 mg and monotherapy was maintained at a dose of 320 mg. Patients remained on these doses for the final 2 weeks of the trial.

Centres

93 centers in 8 countries: Belgium (2), Croatia (3), Guatemala (5), The Netherlands (9), Poland (2), Slovenia (1), Spain (5), United States (66)

Publication

Ongoing

Objectives

Primary objective(s)

To compare the blood pressure control rates between a once daily regimen of the combination therapy valsartan/hydrochlorothiazide (HCTZ) 160/12.5 mg (with forced titration to 160/25 mg after 2 weeks and 320/25 mg after 4 weeks) and the monotherapy of valsartan 160 mg (with forced titration to 320 mg after 2 weeks) as initial therapy in patients with severe hypertension.

Secondary objective(s)

- Percentage of patients achieving systolic and diastolic blood pressure control mean sitting systolic blood pressure (MSSBP)/ mean sitting diastolic blood pressure (MSDBP) < 140/90 mmHg) after 6 weeks of treatment
- Percentage of patients achieving MSDBP < 90 mmHg after 4 and 6 weeks of treatment
- Percentage of patients achieving MSSBP < 140 mmHg after 4 and 6 weeks of treatment
- Change from baseline in MSSBP and MSDBP after 4 and 6 weeks of the study
- Safety and tolerability of valsartan/HCTZ 160/12.5 mg as initial therapy in patients with severe hypertension

Test Product (s), Dose(s), and Mode(s) of Administration

- Valsartan tablets (160, 320 mg), valsartan/hydrochlorothiazide tablets (160/12.5, 160/25 and 320/25 mg), taken orally, once daily (o.d.)

Reference Product(s), Dose(s), and Mode(s) of Administration

Not applicable

Criteria for Evaluation

Primary variables

- Control rate of blood pressure at week 4 (Visit 6/Day 28), defined as MSSBP/MSDBP < 140/90 mmHg

Secondary variables

Secondary efficacy variables were:
• Percentage of patients achieving MSSBP/MSDBP < 140/90 mmHg after 6 weeks (Visit 8, Day 42) of treatment
• Percentage of patients achieving MSDBP <90mmHg after 4 and 6 weeks of treatment
• Percentage of patients achieving MSSBP <140 mmHg after 4 and 6 weeks of treatment
• Change from baseline (Visit 2/Day 1) in MSDBP and MSSBP at Week 4 and Week 6

Safety and tolerability

The assessment of safety was based mainly on the frequency of adverse events (AEs), serious adverse events (SAEs), vital signs, and the number of post-baseline laboratory values outside pre-determined ranges during the double-blind, randomized treatment phase.

Pharmacology

None

Other

None

Statistical Methods

The primary efficacy variable was analyzed using a logistic regression model with treatment regimen, region, and severity of systolic blood pressure at randomization as factors. Randomization was stratified for severity of baseline systolic blood pressure (BP). The test for the treatment comparison was made at a two-sided significance level of 0.05 in the intent-to-treat (ITT) population. Interaction terms (treatment-by-region and treatment-by-severity) were added to the primary model for supplementary analyses to assess the interactions. The null hypothesis was that there was no difference in the overall BP control rate between the two treatment regimens at Week 4. The number and percentage of patients achieving overall, systolic and diastolic BP control were summarized for all post-baseline visits and treatment regimens. Secondary efficacy variables for control rate were analyzed using a similar method to that used for the primary efficacy variable. For continuous secondary variables, appropriate summary statistics were summarized for all treatment regimens and visits. Changes from baseline were summarized and 95% confidence intervals for the difference between the two treatments reported.
Primary and secondary efficacy variables were also summarized by subgroup (age, race, sex and

baseline MSSBP) for the ITT population.

Study Population: Inclusion/Exclusion Criteria and Demographics

Inclusion criteria:

1 Male or female patients, 18 to 80 years of age (inclusive). Female patients must have been either post-menopausal for one year or surgically sterile, or using effective contraceptive methods such as barrier method with spermicide or an intra-uterine device. Hormonal contraceptive use was disallowed.
2. Diagnosis of severe hypertension (MSDBP ≥ 110 mmHg and < 120 mmHg) at Visit 2. Patients must also have had a MSSBP ≥ 140 mmHg and < 200 mmHg.
3. Written informed consent to participate in the study prior to any study procedures.
4. Ability to communicate and comply with all study requirements.

Exclusion criteria:

1. Inability to discontinue all prior antihypertensive medications and/or the inability to completely taper off of medications per the manufacturer's recommendations safely for a period of 3 to 28 days as required by the protocol.
2. Refractory hypertension. Defined as patients on two or more antihypertensives and their MSSBP ≥ 180 mmHg and/or MSDBP ≥ 110 mmHg at Visit 1.
3. Known moderate or malignant retinopathy. Defined as: moderate (retinal signs of hemorrhage, microaneurysm, cotton-wool spot, hard exudates, or a combination thereof) or malignant (signs of moderate retinopathy plus swelling of the optic disk).
4. History of hypertensive encephalopathy or cerebrovascular accident any time prior to Visit 1.
5. Transient ischemic attack, myocardial infarction, all types of revascularization procedures at any time prior to Visit 1.
6. Heart failure of any kind.
7. Second or third degree heart block with or without a pacemaker.
8. Angina pectoris of any type.
9. Concurrent potentially life threatening arrhythmia or symptomatic arrhythmia.
10. Clinically significant valvular heart disease.
11. Evidence of a secondary form of hypertension, including but not limited to any of the following: coarctation of the aorta, hyperaldosteronism, unilateral or bilateral renal artery stenosis, cushing disease, pheochromocytoma, polycystic kidney disease.
12. Diabetes with poor glucose control as defined by fasting glycosylated hemoglobin (HbA1c) > 7% at Visit 1.
13. Administration of any agent indicated for the treatment of hypertension after Visit 1, with the permitted exception of those anti-hypertensive medications requiring tapering down commencing at Visit 1.
14. Known or suspected contraindications, including a history of allergy to angiotensin receptor blockers or thiazide diuretics.
15. Any surgical or medical conditions which might significantly alter the absorption, distribution, metabolism, or excretion of any drug including but not limited to any of the following: history of major gastrointestinal tract surgery such as gastrectomy, gastroenterostomy, bowel resection, gastric bypass, gastric stapling, or gastric banding, currently active or active inflammatory bowel syndrome within 12 months prior to Visit 1, currently active gastritis, ulcers, or gastrointestinal/rectal bleeding, or urinary tract obstruction regarded as clinically meaningful by the investigator.
16. Any history of pancreatic injury, pancreatitis or evidence of impaired pancreatic func-

tion/injury within 1 year of Visit 1.
17. Evidence of hepatic disease as determined by any one of the following: SGOT (AST) or SGPT (ALT) values > 2 x ULN at Visit 1, a history of hepatic encephalopathy, a history of esophageal varices, or a history of portocaval shunt.
18. Evidence of renal impairment as determined by any one of the following: serum creatinine > 1.5 mg/dL (men) and > 1.3 mg/dL (women), a history of dialysis, or a history of nephrotic syndrome.
19. History of clinically significant allergies including asthma, multiple drug allergies.
20. History of systemic lupus erythematosus.
21. History of gouty arthritis.
22. Serum sodium and/or serum potassium less than 132 mEq/L and 3.2 mEq/L, respectively at Visit 2.
23. Volume depletion.
24. Currently taking excluded concomitant medication(s).
25. Any chronic inflammatory condition needing chronic anti-inflammatory therapy.
26. History of malignancy including leukemia and lymphoma (but not basal skin cancer) within the past five years.
27. Pregnant or breast feeding women.
28. Any condition, not identified in the protocol, that in the opinion of the investigator or the Novartis monitor, placed the patient at higher risk from his/her participation in the study, or was likely to prevent the patient from complying with the requirements of the study or completing the trial period.
29. History of drug or alcohol abuse within the last 2 years.
30. History of non-compliance to medical regimens, or patients unwilling to comply with the study protocol.
31. Participation in any investigational drug trial within 30 days prior to Visit 1.
32. Unwillingness or inability to give informed consent.
33. Persons directly involved in the execution of this protocol.

Number of Subjects

	Valsartan/ HCTZ	Valsartan
Planned N	264	264
Randomised n	307	301
Intent-to-treat population (ITT) n (%)	303 (98.7%)	298 (99%)
Completed n (%)	262 (85.3%)	252 (83.7%)
Withdrawn n (%)	45 (14.7%)	49 (16.3%)
Withdrawn due to adverse events n (%)	7 (2.3%)	2 (0.7%)
Withdrawn due to lack of efficacy n (%)	8 (2.6%)	18 (6.0%)
Withdrawn for other reasons n (%)	30 (9.8%)	29 (9.6%)

Demographic and Background Characteristics

	Valsartan/ HCTZ	Valsartan
N (Randomized)	307	301

Females (%) : males (%)	123 (40.1) : 184 (59.9)	138 (45.8) : 163 (54.2)
Mean age, years (SD)	51.6 (10.5)	51.6 (11.2)
Mean weight, kg (SD)	90.74 (21.64)	90.23 (23.48)
Race White n (%) Black n (%) Asian n (%) Native American Pacific Islander Other n (%)	 191 (62.2) 77 (25.1) 10 (3.3) 17 (5.5) 2 (0.7) 10 (3.3)	 201 (66.8) 70 (23.3) 6 (2.0) 14 (4.7) 1 (0.3) 9 (3.0)
Characteristics relevant to study population Mean seated DBP mmHg (SD) Mean seated SBP mmHg (SD)	 112.19 (3.07) 168.68 (13.97)	 112.38 (2.87) 168.20 (13.65)

Primary Objective Result(s)

- **Overall blood pressure control (MSSBP/MSDBP < 140/90 mmHg) rates at Week 4 (LOCF) (ITT population)**

Control criterion		Valsartan/HCTZ † N = 303	Valsartan ‡ N = 298
MSSBP/MSDBP<140/90 mmHg	N	303	298
	Yes – n (%)	120 (39.6)	65 (21.8)
	No – n (%)	183 (60.4)	233 (78.2)
Comparison	Odds ratio estimate	2.50	
	95% CI (1)	1.72, 3.63	
	p-value (2)	< 0.0001*	

† These patients were treated with a once daily regimen of the combination therapy valsartan/HCTZ 160/12.5 mg (with forced titration to 160/25 mg after 14 days and 320/25 mg after 28 days) as initial therapy.
‡ These patients were treated with the monotherapy of valsartan 160 mg (with forced titration to 320 mg after 14 days, and sham titration to 320 mg after 28 days) as initial therapy.
(1) Wald confidence intervals.
(2) P-value was from a logistic model with treatment, region and severity of mean sitting systolic blood pressure at randomization as factors.
LOCF = last observation carried forward.
* Indicates statistical significance at 0.05 level.

Secondary Objective Result(s)

- **Overall blood pressure control (MSSBP/MSDBP < 140/90 mmHg) rates at Week 6 (LOCF) (ITT population)**

Control criterion		Valsartan/HCTZ † N = 303	Valsartan ‡ N = 298
MSSBP/MSDBP < 140/90 mmHg	N	303	298
	Yes – n (%)	146 (48.2)	81 (27.2)
	No – n (%)	157 (51.8)	217 (72.8)
Comparison	Odds ratio estimate	2.66	
	95% CI (1)	(1.86, 3.79)	
	p-value (2)	< 0.0001*	

† These patients were treated with a once daily regimen of the combination therapy valsartan/HCTZ 160/12.5 mg (with forced titration to 160/25 mg after 14 days and 320/25 mg after 28 days) as initial therapy.
‡ These patients were treated with the monotherapy of valsartan 160 mg (with forced titration to 320 mg after 14 days, and sham titration to 320 mg after 28 days) as initial therapy.
(1) Wald confidence intervals.
(2) P-value was from a logistic model with treatment, region and severity of mean sitting systolic blood pressure at randomization as factors.
LOCF = last observation carried forward.
* Indicates statistical significance at 0.05 level.

- **MSDBP (< 90 mmHg) and MSSBP (< 140 mmHg) control rates at Week 4 and Week 6 (ITT population)**

Study week Control criterion		Valsartan/HCTZ † N = 303	Valsartan ‡ N = 298
Week 4 (LOCF)			
MSDBP < 90 mmHg	N	303	298
	Yes - n (%)	154 (50.8)	87 (29.2)
	No - n (%)	149 (49.2)	211 (70.8)
Comparison	Odds ratio estimate	2.73	
	95% CI (1)	(1.92, 3.89)	
	p-value (2)	< 0.0001*	
MSSBP < 140 mmHg	N	303	298
	Yes - n (%)	167 (55.1)	96 (32.2)
	No - n (%)	136 (44.9)	202 (67.8)
Comparison	Odds ratio estimate	2.81	
	95% CI (1)	(1.99, 3.97)	
	p-value (2)	< 0.0001*	

Week 6 (LOCF)			
MSDBP < 90 mmHg	N	303	298
	Yes - n (%)	181 (59.7)	100 (33.6)
	No - n (%)	122 (40.3)	198 (66.4)
Comparison	Odds ratio estimate	3.12	
	95% CI (1)	(2.21, 4.40)	
	p-value (2)	< 0.0001*	
MSSBP < 140 mmHg	N	303	298
	Yes - n (%)	184 (60.7)	117 (39.3)
	No - n (%)	119 (39.3)	181 (60.7)
Comparison	Odds ratio estimate	2.63	
	95% CI (1)	(1.86, 3.72)	
	p-value (2)	< 0.0001*	

† These patients were treated with a once daily regimen of the combination therapy valsartan/HCTZ 160/12.5 mg (with forced titration to 160/25 mg after 14 days and 320/25 mg after 28 days) as initial therapy.
‡ These patients were treated with the monotherapy of valsartan 160 mg (with forced titration to 320 mg after 14 days, and sham titration to 320 mg after 28 days) as initial therapy.
(1) Wald confidence intervals.
(2) P-value was from a logistic model with treatment, region and severity of mean sitting systolic blood pressure at randomization as factors.
LOCF = last observation carried forward.
* Indicates statistical significance at 0.05 level.

- **Mean change from baseline in MSDBP (mmHg) at Week 4 (LOCF) and Week 6 (LOCF) (ITT population)**

Study week	Treatment	N	Mean change from baseline (SD)	LSM change from baseline (SE)
Week 4 (LOCF)				
	Valsartan/HCTZ †	303	-22.67 (9.81)	-22.65 (0.62)
	Valsartan ‡	298	-17.53 (10.39)	-17.52 (0.63)
	Comparison	LSM difference in change from baseline (SE)	95% CI for LSM difference	p-value
	Valsartan/HCTZ † vs. Valsartan ‡	-5.13 (0.79)	(-6.68, -3.57)	< 0.0001*
Week 6 (LOCF)				
	Valsartan/HCTZ †	303	-24.38 (10.28)	-24.24 (0.66)
	Valsartan ‡	298	-17.93 (11.10)	-17.79 (0.67)
	Comparison	LSM difference in change from baseline (SE)	95% CI for LSM difference	p-value
	Valsartan/HCTZ † vs. Valsartan ‡	-6.45 (0.84)	(-8.10, -4.79)	< 0.0001*

† These patients were treated with a once daily regimen of the combination therapy valsartan/HCTZ 160/12.5 mg (with forced titration to 160/25 mg after 14 days and 320/25 mg after 28 days) as initial therapy.
‡ These patients were treated with the monotherapy of valsartan 160 mg (with forced titration to 320 mg after 14 days, and sham titration to 320 mg after 28 days) as initial therapy.
P-values were from an ANCOVA model containing severity of mean sitting systolic blood pressure, treatment and region as factors and baseline value as a covariate.
Baseline is the Week 0 (Visit 2/Day 1) value.
LOCF = last observation carried forward.
* Indicates statistical significance at 0.05 level.

- **Mean change from baseline in MSSBP (mmHg) at Week 4 (LOCF) and Week 6 (LOCF) (ITT population)**

Study week	Treatment	N	Mean change from baseline (SD)	LSM change from baseline (SE)
Week 4 (LOCF)				
	Valsartan/HCTZ †	303	-29.81 (16.59)	-30.75 (1.02)
	Valsartan ‡	298	-20.44 (16.39)	-21.73 (1.04)
	-Comparison	LSM difference in change from baseline (SE)	95% CI for LSM difference	p-value
	Valsartan/HCTZ † vs. Valsartan ‡	-9.02 (1.22)	(-11.41, -6.62)	< 0.0001*
Week 6 (LOCF)				
	Valsartan/HCTZ †	303	-32.06 (17.80)	-33.21 (1.09)
	Valsartan ‡	298	-22.34 (17.24)	-23.81 (1.11)
	-Comparison	LSM difference in change from baseline (SE)	95% CI for LSM difference	p-value
	Valsartan/HCTZ † vs. Valsartan ‡	-9.41 (1.30)	(-11.96, -6.85)	< 0.0001*

† These patients were treated with a once daily regimen of the combination therapy valsartan/HCTZ 160/12.5 mg (with forced titration to 160/25 mg after 14 days and 320/25 mg after 28 days) as initial therapy.
‡ These patients were treated with the monotherapy of valsartan 160 mg (with forced titration to 320 mg after 14 days, and sham titration to 320 mg after 28 days) as initial therapy.
P-values were from an ANCOVA model containing severity of mean sitting systolic blood pressure, treatment and region as factors and baseline value as a covariate.
Baseline is the Week 0 (Visit 2/Day 1) value.
LOCF = last observation carried forward.
* Indicates statistical significance at 0.05 level.

Safety Results

Adverse Events by System Organ Class (Safety population)

	Valsartan/HCTZ N (%)	Valsartan N (%)
Patients studied		
Safety population	307	300
Patients with drug-related AE	34 (11.1)	23 (7.7)
Drug-related AEs by preferred term		
Dizziness	9 (2.9)	5 (1.7)
Fatigue	4 (1.3)	5 (1.7)
Pollakiuria	4 (1.3)	3 (1.0)
Diarrhoea	2 (0.7)	1 (0.3)
Dyspepsia	2 (0.7	1 (0.3)
Headache	2 (0.7)	2 (0.7)
Hypokalemia	2 (0.7)	1 (0.3)
Nausea	2 (0.7)	1 (0.3)
Arthralgia	1 (0.3)	0 (0.0)
Blood uric acid increased	1 (0.3)	0 (0.0)
Decreased appetite	1 (0.3)	0 (0.0)
Erectile dysfunction	1 (0.3)	0 (0.0)
Hyperhidrosis	1 (0.3)	0 (0.0)
Hypoaesthesia	1 (0.3)	0 (0.0)
Hyponatremia	1 (0.3)	0 (0.0)
Hypotension	1 (0.3)	0 (0.0)
Insomnia	1 (0.3)	0 (0.0)
Micturition urgency	1 (0.3)	0 (0.0)
Myalgia	1 (0.3)	0 (0.0)
Oedema peripheral	1 (0.3)	0 (0.0)
Orthostatic hypotension	1 (0.3)	0 (0.0)
Palpitations	1 (0.3)	0 (0.0)
Peripheral coldness	1 (0.3)	0 (0.0)
Polyuria	1 (0.3)	0 (0.0)
Pruritus	1 (0.3)	0 (0.0)
Swelling face	1 (0.3)	0 (0.0)
Vision blurred	1 (0.3)	0 (0.0)
Visual disturbance	1 (0.3)	0 (0.0)
Abdominal discomfort	0 (0.0)	1 (0.3)
Abdominal pain upper	0 (0.0)	1 (0.3)
Agitation	0 (0.0)	1 (0.3)
Blood creatinine increased	0 (0.0)	1 (0.3)
Cough	0 (0.0)	1 (0.3)
Dry mouth	0 (0.0)	2 (0.7)
Dysgeusia	0 (0.0)	1 (0.3)
Flatulence	0 (0.0)	1 (0.3)
Frequent bowel movements	0 (0.0)	1 (0.3)
Nasal congestion	0 (0.0)	1 (0.3)
Night sweats	0 (0.0)	1 (0.3)
Pruritus generalized	0 (0.0)	1 (0.3)
Thirst	0 (0.0)	1 (0.3)

10 Most Frequently Reported AEs Overall by Preferred Term n (%) (safety population)

	Valsartan/HCTZ	Valsartan
Dizziness	17 (5.5)	6 (2.0)
Headache	17 (5.5)	16 (5.3)
Nasopharyngitis	8 (2.6)	13 (4.3)
Upper respiratory tract infection	8 (2.6)	3 (1.0)
Fatigue	7 (2.3)	6 (2.0)
Diarrhea	5 (1.6)	3 (1.0)
Nausea	4 (1.3)	4 (1.3)
Pollakiuria	4 (1.3)	4 (1.3)
Sinusitis	4 (1.3)	2 (0.7)
Constipation	3 (1.0)	3 (1.0)

Serious Adverse Events and Deaths (safety population)

	Valsartan/HCTZ	Valsartan
No. (%) of subjects studied	307	300
No. (%) of subjects with AE(s)	107 (34.9)	110 (36.7)
Number (%) of subjects with serious or other significant events		
Death	0 (0.0)	0 (0.0)
SAE(s)	1 (0.3)	0 (0.0)
Discontinued due to SAE(s)	1 (0.3)	0 (0.0)

One SAE in the Valsartan/HCTZ group: acute thrombosis of the right brachial vein

Other Relevant Findings

Number (%) of patients with hematology values exceeding prespecified percentage changes from baseline at endpoint (safety population)

Parameter		Valsartan/HCTZ† N = 307 n (%)	Valsartan‡ N = 300 n (%)	Total N = 607 n (%)
Hemoglobin		N' = 279	N' = 279	N' = 558
	>50% increase	0 (0.0)	0 (0.0)	0 (0.0)
	>20% decrease	1 (0.4)	1 (0.4)	2 (0.4)
Hematocrit		N' = 279	N' = 279	N' = 558
	>50% increase	0 (0.0)	0 (0.0)	0 (0.0)
	>20% decrease	2 (0.7)	0 (0.0)	2 (0.4)
RBC count		N' = 279	N' = 279	N' = 558
	>50% increase	0 (0.0)	0 (0.0)	0 (0.0)
	>20% decrease	2 (0.7)	0 (0.0)	2 (0.4)
WBC count		N' = 279	N' = 278	N' = 557
	>50% increase	11 (3.9)	11 (4.0)	22 (3.9)
	>50% decrease	1 (0.4)	0 (0.0)	1 (0.2)

Platelet count		N' = 279	N' = 279	N' = 558
	>75% increase	2 (0.7)	0 (0.0)	2 (0.4)
	>50% decrease	2 (0.7)	0 (0.0)	2 (0.4)

- **Number (%) of patients with biochemistry values exceeding prespecified percentage changes from baseline at endpoint (safety population)**

Parameter		Valsartan/HCTZ† N = 307 n (%)	Valsartan‡ N = 300 n (%)	Total N = 607 n (%)
Sodium		N' = 293	N' = 288	N' = 581
	> 5% decrease	4 (1.4)	1 (0.3)	5 (0.9)
Potassium		N' = 293	N' = 286	N' = 579
	> 20% increase	8 (2.7)	17 (5.9)	25 (4.3)
	> 20% decrease	10 (3.4)	6 (2.1)	16 (2.8)
Chloride		N' = 282	N' = 279	N' = 561
	> 10% increase	0 (0.0)	0 (0.0)	0 (0.0)
	> 10% decrease	2 (0.7)	1 (0.4)	3 (0.5)
Calcium		N' = 282	N' = 278	N' = 560
	> 10% increase	15 (5.3)	8 (2.9)	23 (4.1)
	> 10% decrease	4 (1.4)	6 (2.2)	10 (1.8)
Creatinine		N' = 293	N' = 288	N' = 581
	> 50% increase	6 (2.0)	5 (1.7)	11 (1.9)
BUN		N' = 293	N' = 288	N' = 581
	> 50% increase	62 (21.2)	23 (8.0)	85 (14.6)
Glucose		N' = 279	N' = 274	N' = 553
	> 50% increase	10 (3.6)	7 (2.6)	17 (3.1)
	> 50% decrease	0 (0.0)	1 (0.4)	1 (0.2)
SGOT (AST)		N' = 283	N' = 277	N' = 560
	> 150% increase	1 (0.4)	0 (0.0)	1 (0.2)
SGPT (ALT)		N' = 283	N' = 277	N' = 560
	> 150% increase	1 (0.4)	1 (0.4)	2 (0.4)
Alkaline phosphatase		N' = 283	N' = 279	N' = 562
	> 100% increase	0 (0.0)	0 (0.0)	0 (0.0)
Total bilirubin		N' = 283	N' = 277	N' = 560
	> 100% increase	5 (1.8)	7 (2.5)	12 (2.1)
Uric acid		N' = 283	N' = 279	N' = 562
	> 50% increase	13 (4.6)	4 (1.4)	17 (3.0)

† These patients were treated with a once daily regimen of the combination therapy valsartan/HCTZ 160/12.5 mg (with forced titration to 160/25 mg after 14 days and 320/25 mg after 28 days) as initial therapy.
‡ These patients were treated with the monotherapy of valsartan 160 mg (with forced titration to 320 mg after 14 days, and sham titration to 320 mg after 28 days) as initial therapy.
N'=number of patients with baseline and post-baseline values for the specific laboratory parameter.
n = number of patients with a specified laboratory parameter abnormality.
%=n/N'.

Date of Clinical Trial Report 09 November 2006
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Date of Latest Update 26 October 2007