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Novartis CTRD Results Template

Sponsor Novartis
Generic Drug Name Valsartan
Therapeutic Area of Trial Pediatric hypertension
Approved Indication Indicated for the treatment of hypertension.
Protocol Number CVAL489K1101
Title A multicenter, open-label, single-dose study to evaluate the pharmacokinetics of valsartan in Japanese pediatric patients 6 to 14 years of age
Phase of Development Phase I
Study Start/End Dates 11 Aug 2011 to 08 Oct 2011
Study Design/Methodology Multicenter, open-label, single dose study to evaluate the pharmacokinetics (PK) of valsartan in 6-14 year old Japanese pediatric patients with hypertension, chronic kidney disease (CKD), or nephrotic syndrome. Patients with body weight < 35 kg and ≥ 35 kg were treated with a single dose of 20 mg and 40 mg valsartan, respectively.
Centres 3 centers in 1 country: Japan (3)

Publication

None

Outcome measures

Primary outcome measures(s)

- Area under the plasma (or serum or blood) concentration-time curve (AUC) of valsartan in plasma: up to 24 hours post-dose
- Observed maximum plasma (or serum or blood) concentration following drug administration (Cmax) of valsartan in plasma: up to 24 hours post-dose
- Time to reach the maximum concentration after drug administration (Tmax) of valsartan in plasma: up to 24 hours post-dose
- Terminal elimination half-life (T1/2) of valsartan in plasma: up to 24 hours post-dose
- Apparent systemic (or total body) clearance from plasma (or serum or blood) following extravascular administration (CL/F) of valsartan in plasma: up to 24 hours post-dose

Secondary outcome measures(s)

- Electrocardiogram (ECG) evaluations: 24 hours post-dose
- Standard clinical laboratory evaluations: 24 hours post-dose
- Vital signs: 2, 4, and 24 hours post-dose
- Physical examination: 24 hours post-dose
- Number and severity of adverse events (AEs): Up to 24 hours post-dose

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

Valsartan 20 mg tablet and Valsartan 40 mg tablet were administered orally. Patients with body weight < 35 kg and ≥ 35 kg were treated with a single dose of 20 mg and 40 mg valsartan, respectively.

Statistical Methods

Descriptive statistics of PK parameters included mean, SD, and CV, min and max. When a geometric mean was presented it was stated as such. Since Tmax is generally evaluated by a nonparametric method, median values and ranges were given for this parameter. The relationship between PK parameters (AUC and Cmax) and weight adjusted dose (dose/weight) was explored.

Descriptive statistics were used to assess the safety and tolerability endpoints. Summary tables with the number, percentage, and severity of AEs were provided to assess safety and tolerability per treatment group. The number and percentage of subjects with AEs was tabulated by body system and preferred term with a breakdown by treatment group.

Study Population: Inclusion/Exclusion Criteria and Demographics

Key inclusion criteria

- Japanese pediatric patients with hypertension, chronic kidney disease, or nephrotic syndrome

Key exclusion criteria

- GFR < 30 mL/min/1.73 m2
- Inability to safely tolerate the temporary discontinuation of concomitant antihypertensive medications (expect amlodipine or atenolol) from 24 hours prior to study drug administration to study completion.
- Inability to safely tolerate the temporary discontinuation of any drug known or suspected to effect hepatic or renal clearance capacity from 24 hours prior to study drug administration to study completion (this includes drugs that are known to cause induction or inhibition of hepatic enzymes).
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Other protocol defined inclusion/exclusion criteria applied.

Participant Flow

	Valsartan 20 mg	Valsartan 40 mg	All subjects
	n (%)	n (%)	n (%)
Subjects			
Enrolled	6	6	12
Completed	6 (100%)	6 (100%)	12 (100%)

Baseline Characteristics

		Valsartan 20 mg	Valsartan 40 mg	All subjects
		N=6	N=6	N=12
Age (years)	Mean	8.5	11.5	10.0
	(SD)	(1.05)	(1.64)	(2.04)
	Range	7-10	9-14	7-14
Height (cm)	Mean	128.5	155.8	142.2
	(SD)	(5.47)	(8.45)	(15.80)
	Range	124-139	143-165	124-165
Weight (kg)	Mean	26.10	48.40	37.25
	(SD)	(4.872)	(8.398)	(13.359)
	Range	20.2-32.1	38.8-61.3	20.2-61.3
BMI (kg/m^2)	Mean	15.71	20.03	17.87
	(SD)	(2.110)	(3.710)	(3.654)
	Range	13.14-18.27	15.35-24.95	13.14-24.95
Gender – n (%)	Male	6 (100)	2 (33.3)	8 (66.7)
	Female	0 (0.0)	4 (66.7)	4 (33.3)
Race – n (%)	Asian	6 (100)	6 (100)	12 (100)
Ethnicity – n (%)	Japanese	6 (100)	6 (100)	12 (100)
Disease – n (%)	Chronic kidney disease (CKD)	3 (50.0)	3 (50.0)	6 (50.0)
	Nephrotic syndrome	1 (16.7)	0 (0.0)	1 (8.3)
	CKD + Hypertension	2 (33.3)	3 (50.0)	5 (41.7)

BMI = body mass index

Outcome measures

Primary Outcome Result(s)

Summary statistics of PK parameters per treatment group

	Valsartan 20 mg (Weight < 35 kg) N=6	Valsartan 40 mg (Weight >= 35 kg N=6	All treatments N=12
PK parameter	Mean ± SD (CV%)	Mean ± SD (CV%)	Mean ± SD (CV%)
Cmax (ng/mL)	2450 ± 856 (35.0)	2110 ± 837 (39.7)	
Cmax/dose (ng/mL/mg)	122 ± 42.8 (35.0)	52.7 ± 20.9 (39.7)	87.5 ± 48.5 (55.4)
Cmax-adjusted (ng*kg/mL/mg) #	3120 ± 1080 (34.6)	2460 ± 850 (34.5)	2790 ± 986 (35.4)
AUClast (hr*ng/mL)	12000 ± 3850 (32.1)	11300 ± 6130 (54.2)	
AUClast/dose (hr*ng/mL/mg)	600 ± 192 (32.1)	283 ± 153 (54.2)	441 ± 234 (53.1)
AUClast-adjusted (hr*ng*kg/mL/mg) #	15400 ± 5350 (34.7)	13200 ± 6900 (52.1)	14300 ± 5990 (41.9)
AUCinf (hr*ng/mL)	12300 ± 3930 (32.0)	11800 ± 6610 (56.0)	
AUCinf/dose (hr*ng/mL/mg)	615 ± 197 (32.0)	295 ± 165 (56.0)	455 ± 241 (52.9)
AUCinf-adjusted (hr*ng*kg/mL/mg) #	15800 ± 5620 (35.5)	13800 ± 7490 (54.2)	14800 ± 6400 (43.2)
T1/2(hr)	4.9 ± 0.763 (15.6)	5.2 ± 0.864 (16.6)	5.05 ± 0.792 (15.7)
CL/F (L/hr)	1.82 ± 0.72 (39.7)	4.44 ± 2.46 (55.5)	3.13 ± 2.2 (70.5)
CL/F/weight (L/hr/kg) [@]	0.071 ± 0.027 (37.7)	0.093 ± 0.047 (51.2)	0.082 ± 0.038 (47.1)
Tmax (hr) [$]	2.03 (1.92-2.08)	2.02 (1.93-2.1)	2.02 (1.92-2.1)

Adjusted = body-weight adjusted dose normalized = (PK result/dose) × weight (pre-dose)

@ Adjusted by body weight = PK parameter / weight at pre-dose

$ Median (range)

Secondary Outcome Result(s)

- **Electrocardiogram (ECG) evaluations: 24 hours post-dose**

Summary of ECG intervals: Valsartan 20 mg tablet

Treatment : Valsartan 20 mg tablet (Subjects with body weight of < 35 kg at predose)

Visit	Statistics	Heart rate (bpm)	PR interval (msec)	QRS duration (msec)	QT interval (msec)	QTcF $ interval (msec) #	QTcB * interval (msec) #
SCR	n	6	6	6	6	6	6
	mean	75.2	126.3	89.3	372.7	401.6	416.9
	SD	3.06	5.75	11.96	13.88	13.56	14.16
	minimum	72	120	70	348	375	389
	median	74.5	127.0	93.5	376.5	405.5	422.3
	maximum	81	135	102	388	412	426
EOS	n	6	6	6	6	6	6
	mean	76.5	129.7	87.8	375.2	403.6	419.0
	SD	13.49	11.96	8.95	43.19	27.52	21.46
	minimum	59	114	78	314	370	390
	median	74.0	127.0	89.0	387.5	411.7	419.7
	maximum	99	148	98	422	438	453

'$' QTcF: QT interval corrected fridericia = QT uncorrected /cube root of (60/heart rate).
'*' QTcB: QT interval corrected bazett = QT uncorrected /square root of (60/heart rate).
The repeated measurements are not taken into account for the calculation of the statistics.

SCR: Screening, EOS: End of study (24 hours post-dose)

Summary of ECG intervals: Valsartan 40 mg tablet

Treatment : Valsartan 40 mg tablet (Subjects with body weight of > =35 kg at predose)

Visit	Statistics	Heart rate (bpm)	PR interval (msec)	QRS duration (msec)	QT interval (msec)	QTcF $ interval (msec) #	QTcB * interval (msec) #
SCR	n	6	6	6	6	6	6
	mean	67.5	131.3	88.8	389.0	400.2	406.7
	SD	15.71	12.29	6.34	37.43	13.28	16.55
	minimum	51	120	78	348	390	380
	median	67.0	128.0	89.0	380.0	397.3	409.0
	maximum	90	154	96	450	426	426
EOS	n	6	6	6	6	6	6
	mean	68.3	125.2	89.3	394.0	411.0	419.8
	SD	4.68	14.78	6.02	15.34	8.31	6.85
	minimum	62	112	80	374	399	413
	median	70.0	121.0	90.0	393.0	414.4	419.5
	maximum	73	154	98	412	419	430

'$' QTcF: QT interval corrected fridericia = QT uncorrected /cube root of (60/heart rate).
'*' QTcB: QT interval corrected bazett = QT uncorrected /square root of (60/heart rate).
The repeated measurements are not taken into account for the calculation of the statistics.

SCR: Screening, EOS: End of study (24 hours post-dose)

- **Standard clinical laboratory evaluations: 24 hours post-dose**

Summary of biochemistry: Valsartan 20 mg tablet

Treatment : Valsartan 20 mg tablet (Subjects with body weight of < 35 kg at predose)

Visit	Statistics	SOD mEq/L	POT mEq/L	CHLOR mEq/L	CALC mg/dL	PHOS mg/dL	MAG mg/dL
SCR	n	6	6	6	6	6	6
	mean	139.3	4.43	105.8	9.87	4.25	2.00
	SD	1.97	0.441	3.06	0.554	0.207	0.200
	minimum	137	4.0	102	9.3	4.0	1.8
	median	139.0	4.35	105.5	9.80	4.25	2.00
	maximum	142	5.2	111	10.7	4.6	2.3
EOS	n	6	6	6	6	6	6
	mean	137.5	4.18	105.0	9.58	4.57	1.73
	SD	2.43	0.194	3.03	0.354	0.344	0.350
	minimum	133	4.0	100	9.0	4.2	1.1
	median	138.0	4.15	105.0	9.65	4.50	1.75
	maximum	140	4.5	109	9.9	5.0	2.1

Treatment : Valsartan 20 mg tablet (Subjects with body weight of < 35 kg at predose)

Visit	Statistics	CREA mg/dL	BUN mg/dL	UACID mg/dL	ALB g/dL	TPROT g/dL	GLUC mg/dL
SCR	n	6	6	6	6	6	6
	mean	0.630	18.03	5.17	4.260	6.880	98.5
	SD	0.2836	4.897	1.021	0.5339	0.6097	5.92
	minimum	0.35	13.7	3.8	3.79	6.36	93
	median	0.615	16.10	5.45	4.150	6.680	97.0
	maximum	1.14	24.3	6.4	5.20	8.00	107
EOS	n	6	6	6	6	6	6
	mean	0.652	18.85	5.12	4.015	6.568	109.5
	SD	0.3145	7.677	0.845	0.2163	0.1777	27.30
	minimum	0.36	13.3	3.9	3.81	6.30	84
	median	0.580	16.65	5.10	3.970	6.565	101.0
	maximum	1.21	33.6	6.2	4.40	6.80	143

Treatment : Valsartan 20 mg tablet (Subjects with body weight of < 35 kg at predose)

Visit	Statistics	TBIL mg/dL	SGOT U/L	SGPT U/L	GGT U/L	ALKPHS U/L
SCR	n	6	6	6	6	6
	mean	0.705	25.7	13.5	13.3	823.3
	SD	0.2501	4.76	2.35	2.58	112.64
	minimum	0.40	21	10	11	701
	median	0.800	24.5	13.5	12.5	812.0
	maximum	0.93	34	16	17	992
EOS	n	6	6	6	6	6
	mean	0.740	24.0	12.8	12.3	763.8
	SD	0.2683	2.53	2.71	1.86	108.32
	minimum	0.50	21	10	9	615
	median	0.700	24.5	12.0	12.5	737.5
	maximum	1.20	27	17	14	909

Treatment : Valsartan 20 mg tablet (Subjects with body weight of < 35 kg at predose)

Visit	Statistics	LDH U/L	ALPAMY U/L	CK U/L	TRIGLY mg/dL	TCHOL mg/dL
SCR	n	6	6	6	6	6
	mean	246.5	133.2	124.7	91.3	184.3
	SD	39.70	67.12	21.88	42.34	22.58
	minimum	199	69	105	53	154
	median	250.0	127.5	120.0	75.5	192.0
	maximum	299	233	164	163	207
EOS	n	6	6	6	6	6
	mean	203.3	103.8	112.5	85.2	182.3
	SD	25.76	44.53	19.23	32.08	22.77
	minimum	167	58	91	49	152
	median	205.5	96.0	109.5	84.5	185.5
	maximum	235	170	146	124	213

SCR: Screening, EOS: End of study (24 hours post-dose)

Summary of biochemistry: Valsartan 40 mg tablet

Treatment : Valsartan 40 mg tablet (Subjects with body weight of > =35 kg at predose)

Visit	Statistics	SOD mEq/L	POT mEq/L	CHLOR mEq/L	CALC mg/dL	PHOS mg/dL	MAG mg/dL
SCR	n	6	6	6	6	6	6
	mean	140.2	3.95	106.0	9.28	4.43	2.02
	SD	0.98	0.295	3.03	0.760	0.916	0.183
	minimum	139	3.5	101	8.1	3.0	1.7
	median	140.5	4.05	107.0	9.40	4.70	2.10
	maximum	141	4.3	109	10.3	5.5	2.2
EOS	n	6	6	6	6	6	6
	mean	139.5	3.92	105.7	9.42	4.45	2.05
	SD	0.84	0.376	1.97	0.852	0.647	0.315
	minimum	139	3.4	104	8.0	3.7	1.6
	median	139.0	4.05	105.0	9.65	4.50	2.20
	maximum	141	4.3	108	10.3	5.4	2.3

Treatment : Valsartan 40 mg tablet (Subjects with body weight of > =35 kg at predose)

Visit	Statistics	CREA mg/dL	BUN mg/dL	UACID mg/dL	ALB g/dL	TPROT g/dL	GLUC mg/dL
SCR	n	6	6	6	6	6	6
	mean	0.587	12.90	5.53	3.953	6.380	105.5
	SD	0.1713	3.516	1.703	0.8448	1.2001	15.00
	minimum	0.39	8.5	3.4	2.30	4.20	89
	median	0.555	13.65	5.15	4.135	6.610	105.5
	maximum	0.80	17.1	8.1	4.70	7.60	126
EOS	n	6	6	6	6	6	6
	mean	0.553	14.47	5.88	3.918	6.425	101.7
	SD	0.1901	4.276	2.056	0.8559	1.1651	5.99
	minimum	0.39	9.1	3.8	2.40	4.50	95
	median	0.460	15.55	5.40	4.105	6.825	101.5
	maximum	0.82	19.8	9.4	4.70	7.70	111

Treatment : Valsartan 40 mg tablet (Subjects with body weight of > =35 kg at predose)

Visit	Statistics	TBIL mg/dL	SGOT U/L	SGPT U/L	GGT U/L	ALKPHS U/L
SCR	n	6	6	6	6	6
	mean	0.535	18.8	13.8	12.8	775.2
	SD	0.2230	3.31	2.93	3.37	459.49
	minimum	0.31	13	9	10	221
	median	0.450	19.5	14.5	11.5	864.5
	maximum	0.90	22	17	18	1350
EOS	n	6	6	6	6	6
	mean	0.680	17.5	14.5	14.0	747.7
	SD	0.2683	5.09	6.28	4.24	460.15
	minimum	0.38	12	8	9	189
	median	0.600	16.5	13.0	14.0	807.5
	maximum	1.10	25	25	19	1309

Treatment : Valsartan 40 mg tablet (Subjects with body weight of > =35 kg at predose)

Visit	Statistics	LDH U/L	ALPAMY U/L	CK U/L	TRIGLY mg/dL	TCHOL mg/dL
SCR	n	6	6	6	6	6
	mean	185.0	92.3	91.2	176.7	192.5
	SD	44.97	55.35	60.87	93.35	62.32
	minimum	135	57	21	105	128
	median	179.5	66.5	84.5	148.5	184.5
	maximum	264	198	173	357	295
EOS	n	6	6	6	6	6
	mean	178.3	87.0	67.8	201.0	196.0
	SD	47.47	55.35	42.81	158.02	62.08
	minimum	133	50	21	82	137
	median	164.0	61.5	63.0	147.5	179.0
	maximum	257	196	129	516	308

SCR: Screening, EOS: End of study (24 hours post-dose)

Summary of hematology: Valsartan 20 mg tablet

Treatment : Valsartan 20 mg tablet (Subjects with body weight of < 35 kg at predose)

Visit	Statistics	HGB g/dL	HCT %	RBC 10E10/L	WBC 10E6/L	DPLCNT 10E10/L
SCR	n	6	6	6	6	6
	mean	13.38	38.02	489.0	6618.3	28.63
	SD	1.403	3.245	57.61	960.86	6.422
	minimum	11.1	32.5	393	5170	18.9
	median	13.40	38.20	496.0	6505.0	28.75
	maximum	15.5	42.5	558	7810	38.2
EOS	n	6	6	6	6	6
	mean	13.07	37.53	476.0	5965.0	27.58
	SD	0.937	2.594	59.50	1225.57	7.639
	minimum	11.9	34.3	410	4750	17.9
	median	13.20	37.00	462.0	5755.0	26.80
	maximum	14.0	41.4	567	7880	40.0

Treatment : Valsartan 20 mg tablet (Subjects with body weight of < 35 kg at predose)

Visit	Statistics	NEU %	EOS %	LYM %	BAS %	MON %
SCR	n	6	6	6	6	6
	mean	56.17	4.80	33.57	0.45	4.62
	SD	7.684	5.886	2.324	0.315	0.574
	minimum	40.8	0.8	30.6	0.0	3.8
	median	58.40	2.55	33.30	0.45	4.65
	maximum	61.9	16.5	37.3	0.9	5.4
EOS	n	6	6	6	6	6
	mean	52.82	5.27	36.57	0.57	4.57
	SD	9.380	5.860	6.081	0.350	0.698
	minimum	37.2	0.8	25.8	0.1	3.6
	median	53.50	3.75	39.15	0.50	4.40
	maximum	64.9	16.9	41.7	1.1	5.6

SCR: Screening, EOS: End of study (24 hours post-dose)

Summary of hematology: Valsartan 40 mg tablet

Treatment : Valsartan 40 mg tablet (Subjects with body weight of > =35 kg at predose)

Visit	Statistics	HGB g/dL	HCT %	RBC 10E10/L	WBC 10E6/L	DPLCNT 10E10/L
SCR	n	6	6	6	6	6
	mean	12.67	36.97	433.0	8758.3	28.03
	SD	0.909	2.275	46.01	2963.84	4.105
	minimum	11.9	35.1	394	6450	23.1
	median	12.35	35.85	418.5	7355.0	27.75
	maximum	14.2	40.5	517	13430	33.9
EOS	n	6	6	6	6	6
	mean	13.12	38.50	448.5	10585.0	30.42
	SD	0.868	2.333	44.85	6505.26	5.669
	minimum	11.8	34.3	398	4970	25.9
	median	13.05	38.65	436.5	8280.0	27.80
	maximum	14.4	41.1	530	22020	39.2

Treatment : Valsartan 40 mg tablet (Subjects with body weight of > =35 kg at predose)

Visit	Statistics	NEU %	EOS %	LYM %	BAS %	MON %
SCR	n	6	6	6	6	6
	mean	54.30	3.75	35.50	0.45	5.75
	SD	9.001	3.110	8.529	0.197	1.450
	minimum	40.1	0.5	22.1	0.2	4.1
	median	54.30	3.25	35.95	0.40	5.70
	maximum	68.5	7.9	47.9	0.8	7.6
EOS	n	6	6	6	6	6
	mean	60.77	3.30	29.25	0.32	6.03
	SD	5.090	3.270	4.662	0.172	1.772
	minimum	53.6	0.0	23.0	0.0	4.0
	median	60.90	2.60	30.05	0.35	6.15
	maximum	67.0	8.3	35.8	0.5	8.0

SCR: Screening, EOS: End of study (24 hours post-dose)

Summary of urinalysis: Valsartan 20 mg tablet

Treatment : Valsartan 20 mg tablet (Subjects with body weight of < 35 kg at predose)

Visit	Statistics	UPH	USPGR
SCR	n	6	6
	mean	6.17	1.0168
	SD	0.258	0.00813
	minimum	6.0	1.009
	median	6.00	1.0145
	maximum	6.5	1.030
EOS	n	6	6
	mean	6.17	1.0220
	SD	0.516	0.00756
	minimum	5.5	1.008
	median	6.00	1.0245
	maximum	7.0	1.030

Treatment : Valsartan 20 mg tablet (Subjects with body weight of < 35 kg at predose)

Visit	Category	UGLUCST N=6 n(%)	UPROTST N=6 n(%)	UBILST N=6 n(%)	UKETST N=6 n(%)	ULEUKST N=6 n(%)	UBLOST N=6 n(%)
SCR	NEGATIVE	6(100)	3(50.0)	5(83.3)	6(100)	6(100)	3(50.0)
	TRACE	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
	1+	0(0.0)	1(16.7)	1(16.7)	0(0.0)	0(0.0)	1(16.7)
	2+	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
	3+	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	2(33.3)
	4+	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
EOS	NEGATIVE	6(100)	3(50.0)	6(100)	6(100)	6(100)	3(50.0)
	TRACE	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
	1+	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	1(16.7)
	2+	0(0.0)	3(50.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
	3+	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	2(33.3)
	4+	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

SCR: Screening, EOS: End of study (24 hours post-dose)

Summary of urinalysis: Valsartan 40 mg tablet

Treatment : Valsartan 40 mg tablet (Subjects with body weight of > =35 kg at predose)

Visit	Statistics	UPH	USPGR
SCR	n	6	6
	mean	6.92	1.0120
	SD	0.736	0.00341
	minimum	6.0	1.008
	median	6.75	1.0110
	maximum	8.0	1.017
EOS	n	6	6
	mean	5.83	1.0218
	SD	0.683	0.00794
	minimum	5.0	1.010
	median	5.75	1.0235
	maximum	7.0	1.030

Treatment : Valsartan 40 mg tablet (Subjects with body weight of > =35 kg at predose)

Visit	Category	UGLUCST N=6 n(%)	UPROTST N=6 n(%)	UBILST N=6 n(%)	UKETST N=6 n(%)	ULEUKST N=6 n(%)	UBLOST N=6 n(%)
SCR	NEGATIVE	5(83.3)	0(0.0)	6(100)	6(100)	5(83.3)	1(16.7)
	TRACE	0(0.0)	1(16.7)	0(0.0)	0(0.0)	1(16.7)	1(16.7)
	1+	1(16.7)	2(33.3)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
	2+	0(0.0)	3(50.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
	3+	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	4(66.7)
	4+	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
EOS	NEGATIVE	6(100)	0(0.0)	6(100)	6(100)	5(83.3)	1(16.7)
	TRACE	0(0.0)	1(16.7)	0(0.0)	0(0.0)	1(16.7)	0(0.0)
	1+	0(0.0)	3(50.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
	2+	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	2(33.3)
	3+	0(0.0)	1(16.7)	0(0.0)	0(0.0)	0(0.0)	3(50.0)
	4+	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

SCR: Screening, EOS: End of study (24 hours post-dose)

- Vital signs: 2, 4, and 24 hours post-dose

Summary of vital signs: Valsartan 20 mg tablet

Treatment : Valsartan 20 mg tablet (Subjects with body weight of < 35 kg at predose)

Visit	Hours post dose	Statistics	Weight (kg)	Body tempera ture (oC)	Sitting Blood pressure syst. (mmHg)	Sitting Blood pressure dias. (mmHg)	Sitting Pulse rate (bpm)
SCR		n	6	6	6	6	6
		mean	26.10	36.47	106.8	64.7	81.0
		SD	4.872	0.413	6.88	7.17	11.03
		minimum	20.2	35.9	100	53	61
		median	26.45	36.55	105.0	67.5	85.5
		maximum	32.1	37.0	118	72	90
DAY1	0.00	n	6	6	6	6	6
		mean	26.02	36.82	106.3	69.0	81.7
		SD	4.662	0.454	8.36	12.23	12.47
		minimum	20.2	36.4	97	57	65
		median	26.40	36.65	106.0	64.5	81.0
		maximum	31.3	37.6	120	88	100
	2.00	n	0	0	6	6	6
		mean			106.0	63.3	82.0
		SD			8.25	11.00	13.01
		minimum			97	44	65
		median			105.5	68.0	85.5
		maximum			119	74	96

Treatment : Valsartan 20 mg tablet (Subjects with body weight of < 35 kg at predose)

Visit	Hours post dose	Statistics	Weight (kg)	Body tempera ture (oC)	Sitting -Blood pressure- syst. (mmHg)	Sitting -Blood pressure- dias. (mmHg)	Pulse rate (bpm)
DAY1	4.00	n	0	0	6	6	6
		mean			102.0	61.7	84.0
		SD			9.78	8.14	10.53
		minimum			85	51	74
		median			106.0	65.0	81.5
		maximum			110	69	100
EOS		n	6	6	6	6	6
		mean	26.08	36.57	102.8	61.8	85.7
		SD	4.562	0.333	10.34	14.18	12.50
		minimum	20.4	35.9	92	50	70
		median	26.80	36.70	99.5	57.0	83.5
		maximum	31.5	36.8	116	82	103

The repeated measurements are not taken into account for the calculation of the statistics.

SCR: Screening, EOS: End of study (24 hours post-dose)

Summary of vital signs: Valsartan 40 mg tablet

Treatment : Valsartan 40 mg tablet (Subjects with body weight of > =35 kg at predose)

Visit	Hours post dose	Statistics	Weight (kg)	Body tempera ture (oC)	Sitting -Blood pressure- syst. (mmHg)	Sitting -Blood pressure- dias. (mmHg)	Pulse rate (bpm)
SCR		n	6	6	6	6	6
		mean	48.40	36.60	120.5	70.0	75.5
		SD	8.398	0.358	7.99	11.56	15.98
		minimum	38.8	36.1	113	56	61
		median	45.70	36.55	119.0	71.0	68.5
		maximum	61.3	37.2	135	84	98
DAY1	0.00	n	6	6	6	6	6
		mean	47.87	36.37	109.7	63.5	72.0
		SD	8.510	0.314	8.45	11.33	15.86
		minimum	38.9	36.0	102	46	48
		median	44.65	36.45	108.5	65.0	74.0
		maximum	61.1	36.8	123	79	88
	2.00	n	0	0	6	6	6
		mean			109.7	66.8	77.0
		SD			10.48	9.97	15.74
		minimum			91	52	55
		median			114.0	68.0	80.0
		maximum			118	81	95

Treatment : Valsartan 40 mg tablet (Subjects with body weight of > =35 kg at predose)

Visit	Hours post dose	Statistics	Weight (kg)	Body tempera ture (oC)	Sitting -Blood pressure- syst. (mmHg)	dias. (mmHg)	Pulse rate (bpm)
DAY1	4.00	n	0	0	6	6	6
		mean			105.3	53.7	75.0
		SD			9.50	7.03	10.60
		minimum			90	43	61
		median			105.5	54.0	75.5
		maximum			118	62	90
EOS		n	6	6	6	6	6
		mean	47.95	36.57	109.8	64.8	84.5
		SD	8.166	0.163	7.65	4.17	6.22
		minimum	39.7	36.4	97	59	77
		median	44.95	36.55	110.0	64.0	86.5
		maximum	60.8	36.8	118	71	92

The repeated measurements are not taken into account for the calculation of the statistics.

SCR: Screening, EOS: End of study (24 hours post-dose)

- Physical examination: 24 hours post-dose

Significant findings made after the drug administration which meet the definition of an AE were to be recorded as AEs. There were no such results.

Safety Results

- Number and severity of adverse events: Up to 24 hours post-dose

Adverse Events by System Organ Class

System organ class Preferred term	Valsartan 20 mg N=6 nE/nS (%)	Valsartan 40 mg N=6 nE/nS (%)	All subjects N=12 nE/nS (%)
Any body system	0/0 (0.0)	5/3 (50.0)	5/3 (25.0)
Blood and lymphatic system disorders	0/0 (0.0)	1/1 (16.7)	1/1 (8.3)
Leukocytosis	0/0 (0.0)	1/1 (16.7)	1/1 (8.3)
General disorders and administration site conditions	0/0 (0.0)	1/1 (16.7)	1/1 (8.3)
Feeling abnormal	0/0 (0.0)	1/1 (16.7)	1/1 (8.3)
Investigations	0/0 (0.0)	1/1 (16.7)	1/1 (8.3)
Blood pressure diastolic decreased	0/0 (0.0)	1/1 (16.7)	1/1 (8.3)
Vascular disorders	0/0 (0.0)	2/1 (16.7)	2/1 (8.3)
Hypotension	0/0 (0.0)	2/1 (16.7)	2/1 (8.3)

N = number of subjects studied, nE = number of AEs in the category
nS = number of subjects with at least one AE in the category, % = 100 × (nS/N)

Severity of all AEs by preferred term

Preferred term	Severity	Valsartan 20 mg N=6 nE/nS (%)	Valsartan 40 mg N=6 nE/nS (%)	All subjects N=12 nE/nS (%)
Any body system		0/0 (0.0)	5/3 (50.0)	5/3 (25.0)
Leukocytosis	Mild	0/0 (0.0)	1/1 (16.7)	1/1 (8.3)
Feeling abnormal	Mild	0/0 (0.0)	1/1 (16.7)	1/1 (8.3)
Blood pressure diastolic decreased	Mild	0/0 (0.0)	1/1 (16.7)	1/1 (8.3)
Hypotension	Mild	0/0 (0.0)	2/1 (16.7)	2/1 (8.3)

N = number of subjects studied, nE = number of AEs in the category

nS = number of subjects with at least one AE in the category, % = 100 × (nS/N)

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

Serious Adverse Events and Deaths

	Valsartan 20 mg	Valsartan 40 mg	All subjects
	N=6	**N=6**	**N=12**
	nE/nS (%)	nE/nS (%)	nE/nS (%)
Serious Adverse Events (SAEs)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)
Deaths	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)

N = number of subjects studied, nE = number of AEs in the category
nS = number of subjects with at least one AE in the category, % = 100 × (nS/N)

Other Relevant Findings

None

Date of Clinical Trial Report

20 Mar 2012

Date Inclusion on Novartis Clinical Trial Results Database

20 AUG 2012

Date of Latest Update