Clinical trial results:
A multicenter, open-label, 18 month study to evaluate the long-term safety and tolerability of valsartan in children 6 to 17 years of age with hypertension and with or without chronic kidney disease

Summary

EudraCT number	2009-017594-37
Trial protocol	DE FI PL
Global end of trial date	11 September 2015

Results information

Result version number	v1 (current)
This version publication date	14 July 2016
First version publication date	14 July 2016

Trial information

Trial identification

Sponsor protocol code	CVAL489K2305

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01365481
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 September 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the long-term safety and tolerability profile of valsartan and valsartan-based treatments in children with hypertension, with or without chronic kidney disease (CKD).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 August 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Colombia: 7
Country: Number of subjects enrolled	Finland: 2
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Guatemala: 27
Country: Number of subjects enrolled	Korea, Republic of: 7
Country: Number of subjects enrolled	Philippines: 34
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Romania: 16
Country: Number of subjects enrolled	Russian Federation: 23
Country: Number of subjects enrolled	Singapore: 7
Worldwide total number of subjects	150
EEA total number of subjects	45

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	45
Adolescents (12-17 years)	105
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A 1 arm study of valsartan but with 2 groups for analyses. These 2 groups were not randomized and considered to be 2 different populations since the patients in the valsartan+antihypertensive group had concomitant antihypertensive usage per individual patient's conditions at any time during treatment period.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	CKD Patients: valsartan + antihypertensive group

Arm description:

CKD Patients - Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35 kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg after Week 8 if the Mean Sitting Systolic Blood Pressure (MSSBP) and/or Mean Sitting Diastolic Blood Pressure (MSDBP) was higher than 95th percentile for age, gender and height under the maintenance valsartan dose then add amlodipine and/or Hydrochlorothiazide (HCTZ). The valsartan +antihypertensive group includes patients who received background antihypertensive medication or received antihypertensive medication including amlodipine or HCTZ during the study.

Arm type	Experimental
Investigational medicinal product name	valsartan
Investigational medicinal product code	val489
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

valsartan 80mg/160mg/320mg/day oral tablet for 78 weeks

Arm title	CKD Patients: valsartan alone

Arm description:

CKD Patients - Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35 kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg.

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Investigational medicinal product name	valsartan
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Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

valsartan 80mg/160mg/320mg/day oral tablet for 78 weeks

Arm title	Non-CKD Patients: valsartan + antihypertensive group

Arm description:

Non-CKD patients-Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35

kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg after Week 8 if the Mean Sitting Systolic Blood Pressure (MSSBP) and/or Mean Sitting Diastolic Blood Pressure (MSDBP) was higher than 95th percentile for age, gender and height under the maintenance valsartan dose then add amlodipine and/or Hydrochlorothiazide (HCTZ). The valsartan +antihypertensive group includes patients who received background antihypertensive medication or received antihypertensive medication including amlodipine or HCTZ during the study.

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Investigational medicinal product name	valsartan
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Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

valsartan 80mg/160mg/320mg/day oral tablet for 78 weeks

Number of subjects in period 1	CKD Patients: valsartan + antihypertensive group	CKD Patients: valsartan alone	Non-CKD Patients: valsartan + antihypertensive group
Started	23	52	18
Completed	16	37	14
Not completed	7	15	4
Abnormal laboratory value(s)	-	1	-
Consent withdrawn by subject	-	2	1
Adverse event, non-fatal	6	9	-
Protocol deviation	-	1	-
Unsatisfactory therapeutic effect	-	-	1
Administrative problems	-	1	-
Lost to follow-up	1	1	2

Number of subjects in period 1	Non-CKD Patients: valsartan alone
Started	57
Completed	50
Not completed	7
Abnormal laboratory value(s)	-

Consent withdrawn by subject	1
Adverse event, non-fatal	2
Protocol deviation	1
Unsatisfactory therapeutic effect	-
Administrative problems	-
Lost to follow-up	3

Baseline characteristics

Reporting groups	
Reporting group title	CKD Patients: valsartan + antihypertensive group
Reporting group description:	
CKD Patients - Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35 kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg after Week 8 if the Mean Sitting Systolic Blood Pressure (MSSBP) and/or Mean Sitting Diastolic Blood Pressure (MSDBP) was higher than 95th percentile for age, gender and height under the maintenance valsartan dose then add amlodipine and/or Hydrochlorothiazide (HCTZ). The valsartan +antihypertensive group includes patients who received background antihypertensive medication or received antihypertensive medication including amlodipine or HCTZ during the study.	
Reporting group title	CKD Patients: valsartan alone
Reporting group description:	
CKD Patients - Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35 kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg.	
Reporting group title	Non-CKD Patients: valsartan + antihypertensive group
Reporting group description:	
Non-CKD patients-Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35 kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg after Week 8 if the Mean Sitting Systolic Blood Pressure (MSSBP) and/or Mean Sitting Diastolic Blood Pressure (MSDBP) was higher than 95th percentile for age, gender and height under the maintenance valsartan dose then add amlodipine and/or Hydrochlorothiazide (HCTZ). The valsartan +antihypertensive group includes patients who received background antihypertensive medication or received antihypertensive medication including amlodipine or HCTZ during the study.	
Reporting group title	Non-CKD Patients: valsartan alone
Reporting group description:	
Non-CKD patients-Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35 kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg.	

Reporting group values	CKD Patients: valsartan + antihypertensive group	CKD Patients: valsartan alone	Non-CKD Patients: valsartan + antihypertensive group
Number of subjects	23	52	18
Age, Customized Units: participants			
6 – 11 years	10	22	3
12 – 17 years	13	30	15
Age Continuous Units: years			
arithmetic mean	12.9	12.3	13.79
standard deviation	± 3.35	± 3.2	± 2.64
Gender, Male/Female Units: participants			
Male	11	36	15
Female	12	16	3

Reporting group values	Non-CKD Patients: valsartan alone	Total	
Number of subjects	57	150	

Age, Customized Units: participants			
6 – 11 years	10	45	
12 – 17 years	47	105	
Age Continuous Units: years			
arithmetic mean	14.37		
standard deviation	± 2.83	-	
Gender, Male/Female Units: participants			
Male	37	99	
Female	20	51	

End points reporting groups

Reporting group title	CKD Patients: valsartan + antihypertensive group

Reporting group description:

CKD Patients - Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35 kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg after Week 8 if the Mean Sitting Systolic Blood Pressure (MSSBP) and/or Mean Sitting Diastolic Blood Pressure (MSDBP) was higher than 95th percentile for age, gender and height under the maintenance valsartan dose then add amlodipine and/or Hydrochlorothiazide (HCTZ). The valsartan +antihypertensive group includes patients who received background antihypertensive medication or received antihypertensive medication including amlodipine or HCTZ during the study.

Reporting group title	CKD Patients: valsartan alone

Reporting group description:

CKD Patients - Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35 kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg.

Reporting group title	Non-CKD Patients: valsartan + antihypertensive group

Reporting group description:

Non-CKD patients-Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35 kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg after Week 8 if the Mean Sitting Systolic Blood Pressure (MSSBP) and/or Mean Sitting Diastolic Blood Pressure (MSDBP) was higher than 95th percentile for age, gender and height under the maintenance valsartan dose then add amlodipine and/or Hydrochlorothiazide (HCTZ). The valsartan +antihypertensive group includes patients who received background antihypertensive medication or received antihypertensive medication including amlodipine or HCTZ during the study.

Reporting group title	Non-CKD Patients: valsartan alone

Reporting group description:

Non-CKD patients-Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35 kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg.

Subject analysis set title	valsartan + antihypertensive group
Subject analysis set type	Full analysis

Subject analysis set description:

Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35 kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg after Week 8 if the Mean Sitting Systolic Blood Pressure (MSSBP) and/or Mean Sitting Diastolic Blood Pressure (MSDBP) was higher than 95th percentile for age, gender and height under the maintenance valsartan dose then add amlodipine and/or Hydrochlorothiazide (HCTZ). The valsartan +antihypertensive group includes patients who received background antihypertensive medication or received antihypertensive medication including amlodipine or HCTZ during the study.

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during the study.

Subject analysis set title	valsartan alone
Subject analysis set type	Full analysis

Subject analysis set description:

Valsartan starting dose: ≥18 kg to <35 kg is 40 mg, ≥35 kg to <80 kg is 80 mg, ≥80 kg to ≤160 kg is 160 mg for 1 week then Valsartan maintenance dose: ≥18 kg to <35 kg is 80 mg, ≥35 kg to <80 kg is 160 mg, ≥80 kg to ≤160 kg is 320 mg.

Primary: Change from baseline in mean sitting systolic blood pressure (msSBP) at End Point (Week 78 or Last observation carried forward (LOCF)

End point title	Change from baseline in mean sitting systolic blood pressure (msSBP) at End Point (Week 78 or Last observation carried forward (LOCF)[1]

End point description:

Sitting blood pressure was measured using a calibrated standard sphygmomanometer after the participants remained in sitting position for 5 minutes at clinic during the visit. The repeat sitting measurements were made at 2 to 3 minute intervals and the mean of three sSBP measurements were used as the average sitting office blood pressure for that visit. No statistical analysis was planned for this primary outcome

End point type	Primary

End point timeframe:

Baseline, End Point (Week 78 or Last observation carried forward (LOCF)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary outcome.

End point values	valsartan + antihypertensive group	valsartan alone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	109		
Units: millimeter(s) of mercury (mmHg)				
arithmetic mean (standard deviation)	-13.3 (± 13.69)	-15.5 (± 13.35)		

Statistical analyses

No statistical analyses for this end point

Primary: Change from baseline in mean sitting diastolic blood pressure (MsDBP) at End Point (Week 78 or Last observation carried forward (LOCF)

End point title	Change from baseline in mean sitting diastolic blood pressure (MsDBP) at End Point (Week 78 or Last observation carried forward (LOCF)[2]

End point description:

Sitting blood pressure was measured using a calibrated standard sphygmomanometer after the participants remained in sitting position for 5 minutes at clinic during the visit. The repeat sitting measurements were made at 2 to 3 minute intervals and the mean of three sDBP measurements were used as the average sitting office blood pressure for that visit. No statistical analysis was planned for this primary outcome.

End point type	Primary

End point timeframe:

Baseline, End Point (Week 78 or Last observation carried forward (LOCF)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned for this primary outcome.

End point values	valsartan + antihypertensive group	valsartan alone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	109		
Units: millimeter(s) of mercury (mmHg)				
arithmetic mean (standard deviation)	-10.3 (± 11.94)	-10.8 (± 11.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with MSSBP, MSDBP and (MSSBP and MSDBP combined) < 95th percentile for gender, age, and height

End point title	Number of participants with MSSBP, MSDBP and (MSSBP and MSDBP combined) < 95th percentile for gender, age, and height

End point description:

Number of Participants with Mean sitting systolic (MSSBP) and mean sitting diastolic(MSDBP) blood pressure and both combined less than the 95th percentile for age, gender and height

End point type	Secondary

End point timeframe:

End Point (Week 78 or Last observation carried forward (LOCF)

End point values	valsartan + antihypertensive group	valsartan alone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	41	109		
Units: Number of Participants				
MSSBP (n=39, 105)	23	90		
MSDBP (n=28, 51)	20	47		
MSSBP and MSDBP combined (n=40, 105)	22	88		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Chronic Kidney Disease (CKD) patients who had >=50% reduction in urine albumin/creatinine ratio (UACR) from Baseline to end point

End point title	Percentage of Chronic Kidney Disease (CKD) patients who had >=50% reduction in urine albumin/creatinine ratio (UACR) from Baseline to end point

End point description:

Percentage of Patients with CKD who had Urine albumin creatinine reduction >/= 50% from baseline

End point type	Secondary

End point timeframe:

Baseline, End Point (Week 78 or Last observation carried forward (LOCF)

End point values	valsartan + antihypertensive group	valsartan alone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23	52		
Units: Percentage of patients				
number (not applicable)	50	41.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Chronic Kidney Disease (CKD) patients who had estimated Glomerular Filtration Rate (eGFR) decrease > 25 % from Baselinefrom Baseline to end point

End point title	Percentage of Chronic Kidney Disease (CKD) patients who had estimated Glomerular Filtration Rate (eGFR) decrease > 25 % from Baselinefrom Baseline to end point

End point description:

Percentage of Patients with CKD who had eGFR decrease > 25 % from Baseline

End point type	Secondary

End point timeframe:

Baseline, End Point (Week 78 or Last observation carried forward (LOCF)

End point values	valsartan + antihypertensive group	valsartan alone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	23	52		
Units: Percentage of patients				
number (not applicable)	30.4	27.5		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All adverse events reported in this record are from date of First Patient First Treatment until Last Patient Last Visit

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Valsartan + antihyp.
Reporting group description: Valsartan + antihyp.	
Reporting group title	Valsartan
Reporting group description: Valsartan	
Reporting group title	CKD: Valsartan + antihyp
Reporting group description: CKD: Valsartan + antihyp	
Reporting group title	CKD: Valsartan
Reporting group description: CKD: Valsartan	
Reporting group title	Non-CKD: Valsartan + antihyp
Reporting group description: Non-CKD: Valsartan + antihyp	
Reporting group title	Non-CKD:Valsartan
Reporting group description: Non-CKD:Valsartan	

Serious adverse events	Valsartan + antihyp.	Valsartan	CKD: Valsartan + antihyp
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 41 (19.51%)	7 / 109 (6.42%)	7 / 23 (30.43%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Hypertension			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 41 (0.00%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Somnolence			
subjects affected / exposed	0 / 41 (0.00%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Oesophageal polyp			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	0 / 41 (0.00%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Drug abuse			
subjects affected / exposed	0 / 41 (0.00%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IgA nephropathy			
subjects affected / exposed	0 / 41 (0.00%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus nephritis			
subjects affected / exposed	3 / 41 (7.32%)	1 / 109 (0.92%)	3 / 23 (13.04%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			
subjects affected / exposed	0 / 41 (0.00%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurogenic bladder			
subjects affected / exposed	0 / 41 (0.00%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Synovitis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 109 (0.92%)	1 / 23 (4.35%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 41 (0.00%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	CKD: Valsartan	Non-CKD: Valsartan + antihyp	Non-CKD:Valsartan
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 52 (7.69%)	1 / 18 (5.56%)	3 / 57 (5.26%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			

subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Somnolence			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Oesophageal polyp			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Drug abuse			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Chronic kidney disease			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IgA nephropathy			
subjects affected / exposed	1 / 52 (1.92%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus nephritis			
subjects affected / exposed	1 / 52 (1.92%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			
subjects affected / exposed	1 / 52 (1.92%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurogenic bladder			
subjects affected / exposed	1 / 52 (1.92%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Synovitis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 52 (1.92%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 52 (1.92%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	1 / 57 (1.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Valsartan + antihyp.	Valsartan	CKD: Valsartan + antihyp
Total subjects affected by non-serious adverse events			
subjects affected / exposed	34 / 41 (82.93%)	68 / 109 (62.39%)	18 / 23 (78.26%)
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Hypotension			
subjects affected / exposed	2 / 41 (4.88%)	2 / 109 (1.83%)	2 / 23 (8.70%)
occurrences (all)	4	2	4

Pallor			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	8 / 41 (19.51%)	17 / 109 (15.60%)	4 / 23 (17.39%)
occurrences (all)	17	46	11
Headache			
subjects affected / exposed	14 / 41 (34.15%)	23 / 109 (21.10%)	8 / 23 (34.78%)
occurrences (all)	27	70	21
Hypoaesthesia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 41 (4.88%)	1 / 109 (0.92%)	1 / 23 (4.35%)
occurrences (all)	2	2	1
Chest pain			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	12 / 41 (29.27%)	18 / 109 (16.51%)	8 / 23 (34.78%)
occurrences (all)	17	29	12
Eye disorders			
Myopia			
subjects affected / exposed	1 / 41 (2.44%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Retinal vascular disorder			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Vision blurred			

subjects affected / exposed	2 / 41 (4.88%)	0 / 109 (0.00%)	1 / 23 (4.35%)
occurrences (all)	2	0	1
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 41 (9.76%)	7 / 109 (6.42%)	2 / 23 (8.70%)
occurrences (all)	9	11	6
Abdominal pain upper			
subjects affected / exposed	2 / 41 (4.88%)	5 / 109 (4.59%)	2 / 23 (8.70%)
occurrences (all)	4	8	4
Constipation			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	2 / 41 (4.88%)	8 / 109 (7.34%)	1 / 23 (4.35%)
occurrences (all)	2	8	1
Nausea			
subjects affected / exposed	2 / 41 (4.88%)	3 / 109 (2.75%)	2 / 23 (8.70%)
occurrences (all)	2	3	2
Toothache			
subjects affected / exposed	3 / 41 (7.32%)	1 / 109 (0.92%)	2 / 23 (8.70%)
occurrences (all)	4	1	2
Vomiting			
subjects affected / exposed	5 / 41 (12.20%)	4 / 109 (3.67%)	4 / 23 (17.39%)
occurrences (all)	8	7	7
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	18 / 41 (43.90%)	18 / 109 (16.51%)	12 / 23 (52.17%)
occurrences (all)	35	52	23
Dyspnoea			
subjects affected / exposed	1 / 41 (2.44%)	2 / 109 (1.83%)	0 / 23 (0.00%)
occurrences (all)	1	2	0
Epistaxis			
subjects affected / exposed	2 / 41 (4.88%)	1 / 109 (0.92%)	1 / 23 (4.35%)
occurrences (all)	4	2	1
Nasal congestion			

subjects affected / exposed	3 / 41 (7.32%)	1 / 109 (0.92%)	1 / 23 (4.35%)
occurrences (all)	3	1	1
Oropharyngeal pain			
subjects affected / exposed	2 / 41 (4.88%)	2 / 109 (1.83%)	1 / 23 (4.35%)
occurrences (all)	3	4	1
Rhinitis allergic			
subjects affected / exposed	2 / 41 (4.88%)	0 / 109 (0.00%)	1 / 23 (4.35%)
occurrences (all)	2	0	1
Rhinorrhoea			
subjects affected / exposed	4 / 41 (9.76%)	3 / 109 (2.75%)	3 / 23 (13.04%)
occurrences (all)	4	3	3
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 41 (2.44%)	2 / 109 (1.83%)	0 / 23 (0.00%)
occurrences (all)	1	2	0
Papule			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 41 (0.00%)	3 / 109 (2.75%)	0 / 23 (0.00%)
occurrences (all)	0	5	0
Renal and urinary disorders			
Micturition urgency			
subjects affected / exposed	1 / 41 (2.44%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 41 (2.44%)	4 / 109 (3.67%)	1 / 23 (4.35%)
occurrences (all)	2	4	2
Neck pain			
subjects affected / exposed	2 / 41 (4.88%)	0 / 109 (0.00%)	0 / 23 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
subjects affected / exposed	3 / 41 (7.32%)	0 / 109 (0.00%)	2 / 23 (8.70%)
occurrences (all)	3	0	2
Infections and infestations			

Acarodermatitis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Enterobiasis			
subjects affected / exposed	1 / 41 (2.44%)	1 / 109 (0.92%)	0 / 23 (0.00%)
occurrences (all)	1	1	0
Influenza			
subjects affected / exposed	3 / 41 (7.32%)	1 / 109 (0.92%)	1 / 23 (4.35%)
occurrences (all)	4	1	2
Mycoplasma infection			
subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	11 / 41 (26.83%)	22 / 109 (20.18%)	7 / 23 (30.43%)
occurrences (all)	27	76	18
Pharyngitis			
subjects affected / exposed	2 / 41 (4.88%)	0 / 109 (0.00%)	2 / 23 (8.70%)
occurrences (all)	2	0	2
Respiratory tract infection			
subjects affected / exposed	2 / 41 (4.88%)	4 / 109 (3.67%)	1 / 23 (4.35%)
occurrences (all)	6	5	4
Rhinitis			
subjects affected / exposed	0 / 41 (0.00%)	3 / 109 (2.75%)	0 / 23 (0.00%)
occurrences (all)	0	3	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 41 (4.88%)	17 / 109 (15.60%)	1 / 23 (4.35%)
occurrences (all)	3	36	1
Urinary tract infection			
subjects affected / exposed	2 / 41 (4.88%)	3 / 109 (2.75%)	2 / 23 (8.70%)
occurrences (all)	2	3	2
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	1 / 41 (2.44%)	4 / 109 (3.67%)	1 / 23 (4.35%)
occurrences (all)	1	7	1
Hyperphosphataemia			

subjects affected / exposed	1 / 41 (2.44%)	0 / 109 (0.00%)	0 / 23 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	CKD: Valsartan	Non-CKD: Valsartan + antihyp	Non-CKD:Valsartan
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 52 (69.23%)	16 / 18 (88.89%)	32 / 57 (56.14%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Hypotension			
subjects affected / exposed	2 / 52 (3.85%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences (all)	2	0	0
Pallor			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 52 (11.54%)	4 / 18 (22.22%)	11 / 57 (19.30%)
occurrences (all)	12	6	34
Headache			
subjects affected / exposed	11 / 52 (21.15%)	6 / 18 (33.33%)	12 / 57 (21.05%)
occurrences (all)	19	6	51
Hypoaesthesia			
subjects affected / exposed	1 / 52 (1.92%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	1 / 57 (1.75%)
occurrences (all)	0	1	2
Chest pain			

subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	12 / 52 (23.08%)	4 / 18 (22.22%)	6 / 57 (10.53%)
occurrences (all)	19	5	10
Eye disorders			
Myopia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Retinal vascular disorder			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 52 (7.69%)	2 / 18 (11.11%)	3 / 57 (5.26%)
occurrences (all)	4	3	7
Abdominal pain upper			
subjects affected / exposed	2 / 52 (3.85%)	0 / 18 (0.00%)	3 / 57 (5.26%)
occurrences (all)	3	0	5
Constipation			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	5 / 52 (9.62%)	1 / 18 (5.56%)	3 / 57 (5.26%)
occurrences (all)	5	1	3
Nausea			
subjects affected / exposed	2 / 52 (3.85%)	0 / 18 (0.00%)	1 / 57 (1.75%)
occurrences (all)	2	0	1
Toothache			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	1 / 57 (1.75%)
occurrences (all)	0	2	1
Vomiting			

subjects affected / exposed	3 / 52 (5.77%)	1 / 18 (5.56%)	1 / 57 (1.75%)
occurrences (all)	6	1	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	12 / 52 (23.08%)	6 / 18 (33.33%)	6 / 57 (10.53%)
occurrences (all)	32	12	20
Dyspnoea			
subjects affected / exposed	2 / 52 (3.85%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	2	1	0
Epistaxis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	1 / 57 (1.75%)
occurrences (all)	0	3	2
Nasal congestion			
subjects affected / exposed	1 / 52 (1.92%)	2 / 18 (11.11%)	0 / 57 (0.00%)
occurrences (all)	1	2	0
Oropharyngeal pain			
subjects affected / exposed	1 / 52 (1.92%)	1 / 18 (5.56%)	1 / 57 (1.75%)
occurrences (all)	2	2	2
Rhinitis allergic			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	2 / 52 (3.85%)	1 / 18 (5.56%)	1 / 57 (1.75%)
occurrences (all)	2	1	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 52 (1.92%)	1 / 18 (5.56%)	1 / 57 (1.75%)
occurrences (all)	1	1	1
Papule			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	3 / 52 (5.77%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences (all)	5	0	0
Renal and urinary disorders			

Micturition urgency			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 52 (5.77%)	0 / 18 (0.00%)	1 / 57 (1.75%)
occurrences (all)	3	0	1
Neck pain			
subjects affected / exposed	0 / 52 (0.00%)	2 / 18 (11.11%)	0 / 57 (0.00%)
occurrences (all)	0	2	0
Pain in extremity			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Acarodermatitis			
subjects affected / exposed	1 / 52 (1.92%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	1	1	0
Enterobiasis			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	1 / 57 (1.75%)
occurrences (all)	0	1	1
Influenza			
subjects affected / exposed	0 / 52 (0.00%)	2 / 18 (11.11%)	1 / 57 (1.75%)
occurrences (all)	0	2	1
Mycoplasma infection			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	14 / 52 (26.92%)	4 / 18 (22.22%)	8 / 57 (14.04%)
occurrences (all)	46	9	30
Pharyngitis			
subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	4 / 57 (7.02%)
occurrences (all)	0	2	5
Rhinitis			

subjects affected / exposed	0 / 52 (0.00%)	0 / 18 (0.00%)	3 / 57 (5.26%)
occurrences (all)	0	0	3
Upper respiratory tract infection			
subjects affected / exposed	12 / 52 (23.08%)	1 / 18 (5.56%)	5 / 57 (8.77%)
occurrences (all)	28	2	8
Urinary tract infection			
subjects affected / exposed	2 / 52 (3.85%)	0 / 18 (0.00%)	1 / 57 (1.75%)
occurrences (all)	2	0	1
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	4 / 52 (7.69%)	0 / 18 (0.00%)	0 / 57 (0.00%)
occurrences (all)	7	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 52 (0.00%)	1 / 18 (5.56%)	0 / 57 (0.00%)
occurrences (all)	0	1	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 November 2011	Amendment 1: Estimated GFR <30 mL/min/1.73m2 was added as a reason for study discontinuation;complied with the current valsartan core data sheet, which does not recommend valsartan to be used in severely renal impaired pediatric patients (i.e. GFR <30 mL/min/1.73m2).Hemoglobin <8 g/dL was added as additional exclusion criteria.Text regarding immunosuppressive and steroid therapy was added to the prohibited treatment list to provide guidance to the study investigators. A statement regarding immunosuppressive therapy was also removed from the exclusion criteria.Bicarbonate (total CO2) was added as an additional lab parameter. At least 40% of patients enrolled were to have CKD.Revisions to visit and dosing times were added, in order to allow for morning or afternoon study visits. This added additional flexibility to the timing of study
14 May 2014	Amendment 2: Enrollment was complete with 150 patients. Enrolled patients meeting the revised CKD definition that included Stage 1 CKD (eGFR ≥ 90mL/min/1.73m2)were classified as such. This revised definition of CKD is consistent with the CKD definition from the National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (KDOQI).This revision removed the requirement that CKD patients need an eGFR < 90 mL/min/1.73m2 for ≥ 3 months to be considered CKD patients. There was no impact on study procedures or patient safety. This protocol amendment allowed:Non-CKD patients to be potentially re-classified following adjudication as having Stage 1 CKD, should they meet Stage 1 CKD criteria.Non-CKD patients who were misclassified by the investigator as having CKD using the original protocol definition were to be potentially classified as Stage 1 CKD following adjudication.Patients continued following the same study assessments they had been following since initial treatment assignment. For example, patients who had morning urine collections done for UACR continued to have urine collections for UACR. Patients who never had morning collections for UACR were not required to begin morning UACR collections because a baseline sample had not been collected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported