Clinical trial results:
A 6 week, randomized, multicenter, double-blind, double dummy study to evaluate the dose response of valsartan on blood pressure reduction in children 1-5 years old with hypertension, with or without chronic kidney disease, followed by a 20 week open-label titration phase

Summary

EudraCT number	2011-005991-40
Trial protocol	BE HU DE IT PL FR ES LT
Global end of trial date	24 January 2017

Results information

Result version number	v1 (current)
This version publication date	09 August 2017
First version publication date	09 August 2017

Trial information

Trial identification

Sponsor protocol code	CVAL489K2306

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01617681
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000005-PIP01-07
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	24 January 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate if a dose dependent reduction in mean systolic blood pressure (MSBP) exists when comparing two doses of valsartan solution (0.25 mg/kg/day and 4 mg/kg/day) over a 6 week period in children 1-5 years old with hypertension (MSBP ≥95th percentile for age, gender and height), 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	07 November 2012
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	Belgium: 7
Country: Number of subjects enrolled	Brazil: 36
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Guatemala: 20
Country: Number of subjects enrolled	Hungary: 10
Country: Number of subjects enrolled	Italy: 6
Country: Number of subjects enrolled	Lithuania: 6
Country: Number of subjects enrolled	Poland: 37
Worldwide total number of subjects	127
EEA total number of subjects	71

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	31
Children (2-11 years)	96
Adolescents (12-17 years)	0
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:

Overall, 156 patients were screened, of which 127 patients were enrolled in the double blind period 1 of the study. A total of 120 patients (94.5%) completed Period 1 and entered Open Label Period 2.

Parallel= Period 1 (Double Blind phase)
Single= Period 2 (Open Label phase)

Period 1

Period 1 title	Period 1 Double Blind
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Carer, Data analyst, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	CKD patients Valsartan 0.25 mg/kg

Arm description:

CKD patients: Valsartan oral solution 0.25mg/kg once daily + matching placebo of valsartan oral solution 4 mg/kg once daily for 6 weeks (period 1)

Arm type	Experimental
Investigational medicinal product name	Valsartan
Investigational medicinal product code	VAL489
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Valsartan 0.25 mg/kg/day oral solution for 6 weeks

Arm title	CKD patients Valsartan 4 mg/kg

Arm description:

CKD patients: Valsartan oral solution 4 mg/kg once daily + matching placebo of valsartan oral solution 0.25 mg/kg once daily for 6 weeks (period 1)

Arm type	Experimental
Investigational medicinal product name	Valsartan
Investigational medicinal product code	VAL489
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Valsartan 4 mg/kg/day oral solution for 6 weeks

Arm title	Non-CKD patients Valsartan 0.25 mg/kg

Arm description:

Non-CKD patients: Valsartan oral solution 0.25mg/kg once daily + matching placebo of valsartan oral solution 4 mg/kg once daily for 6 weeks (period 1)

Arm type	Experimental

Investigational medicinal product name	Valsartan
Investigational medicinal product code	VAL489
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Valsartan 0.25 mg/kg/day oral solution for 6 weeks

Arm title	Non-CKD patients Valsartan 4 mg/kg

Arm description:

Non-CKD patients: Valsartan oral solution 4 mg/kg once daily + matching placebo of valsartan oral solution 0.25 mg/kg once daily for 6 weeks (period 1)

Arm type	Experimental
Investigational medicinal product name	Valsartan
Investigational medicinal product code	VAL489
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Valsartan 4 mg/kg/day oral solution for 6 weeks

Number of subjects in period 1	CKD patients Valsartan 0.25 mg/kg	CKD patients Valsartan 4 mg/kg	Non-CKD patients Valsartan 0.25 mg/kg
Started	32	31	33
Full Analysis Set (FAS)	31	31	33
Completed	29	30	32
Not completed	3	1	1
Consent withdrawn by subject	1	1	1
Adverse event, non-fatal	2	-	-

Number of subjects in period 1	Non-CKD patients Valsartan 4 mg/kg
Started	31
Full Analysis Set (FAS)	31
Completed	29
Not completed	2
Consent withdrawn by subject	-
Adverse event, non-fatal	2

Period 2

Period 2 title	Period 2 Open Label
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Valsartan 1 mg/kg (Period 2)

Arm description:

Open-label (Period 2) valsartan will be optionally titrated from 1 mg/kg to 2 mg/kg. Valsartan will continue to be optionally up titrated in 1 mg/kg increments every 4 weeks until maximum dose of 4 mg/kg is achieved. Duration 20 weeks.

Arm type	Experimental
Investigational medicinal product name	Valsartan
Investigational medicinal product code	VAL489
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Valsartan 1 mg/kg/day oral solution for 20 weeks

Number of subjects in period 2	Valsartan 1 mg/kg (Period 2)
Started	120
Completed	114
Not completed	6
Consent withdrawn by subject	3
Adverse event, non-fatal	3

Baseline characteristics

Reporting groups	
Reporting group title	CKD patients Valsartan 0.25 mg/kg
Reporting group description:	
CKD patients: Valsartan oral solution 0.25mg/kg once daily + matching placebo of valsartan oral solution 4 mg/kg once daily for 6 weeks (period 1)	
Reporting group title	CKD patients Valsartan 4 mg/kg
Reporting group description:	
CKD patients: Valsartan oral solution 4 mg/kg once daily + matching placebo of valsartan oral solution 0.25 mg/kg once daily for 6 weeks (period 1)	
Reporting group title	Non-CKD patients Valsartan 0.25 mg/kg
Reporting group description:	
Non-CKD patients: Valsartan oral solution 0.25mg/kg once daily + matching placebo of valsartan oral solution 4 mg/kg once daily for 6 weeks (period 1)	
Reporting group title	Non-CKD patients Valsartan 4 mg/kg
Reporting group description:	
Non-CKD patients: Valsartan oral solution 4 mg/kg once daily + matching placebo of valsartan oral solution 0.25 mg/kg once daily for 6 weeks (period 1)	

Reporting group values	CKD patients Valsartan 0.25 mg/kg	CKD patients Valsartan 4 mg/kg	Non-CKD patients Valsartan 0.25 mg/kg
Number of subjects	32	31	33
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	10	12	5
Children (2-11 years)	22	19	28
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	2.99	2.72	3.7
standard deviation	± 1.47	± 1.33	± 1.51
Gender, Male/Female Units: Subjects			
Female	12	8	14
Male	20	23	19

Reporting group values	Non-CKD patients Valsartan 4 mg/kg	Total	
Number of subjects	31	127	
Age categorical Units: Subjects			
In utero	0	0	

Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	4	31	
Children (2-11 years)	27	96	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Age Continuous			
Units: years			
arithmetic mean	3.62		
standard deviation	± 1.36	-	
Gender, Male/Female			
Units: Subjects			
Female	13	47	
Male	18	80	

End points

End points reporting groups

Reporting group title	CKD patients Valsartan 0.25 mg/kg
Reporting group description:	
CKD patients: Valsartan oral solution 0.25mg/kg once daily + matching placebo of valsartan oral solution 4 mg/kg once daily for 6 weeks (period 1)	
Reporting group title	CKD patients Valsartan 4 mg/kg
Reporting group description:	
CKD patients: Valsartan oral solution 4 mg/kg once daily + matching placebo of valsartan oral solution 0.25 mg/kg once daily for 6 weeks (period 1)	
Reporting group title	Non-CKD patients Valsartan 0.25 mg/kg
Reporting group description:	
Non-CKD patients: Valsartan oral solution 0.25mg/kg once daily + matching placebo of valsartan oral solution 4 mg/kg once daily for 6 weeks (period 1)	
Reporting group title	Non-CKD patients Valsartan 4 mg/kg
Reporting group description:	
Non-CKD patients: Valsartan oral solution 4 mg/kg once daily + matching placebo of valsartan oral solution 0.25 mg/kg once daily for 6 weeks (period 1)	
Reporting group title	Valsartan 1 mg/kg (Period 2)
Reporting group description:	
Open-label (Period 2) valsartan will be optionally titrated from 1 mg/kg to 2 mg/kg. Valsartan will continue to be optionally up titrated in 1 mg/kg increments every 4 weeks until maximum dose of 4 mg/kg is achieved. Duration 20 weeks.	

Primary: Change from baseline in mean systolic blood pressure (MSBP) at Week 6 endpoint

End point title	Change from baseline in mean systolic blood pressure (MSBP) at Week 6 endpoint
End point description:	
Patient’s blood pressure will be measured in the same position at every visit Systolic and diastolic blood pressures will be measured three times at 2-3 minute intervals. The arithmetic mean of these three blood pressure measurements will be used as the mean office blood pressure (MSBP and MDBP) at Baseline and Week 6 endpoint in Period 1 Double Blind Phase	
End point type	Primary
End point timeframe:	
Baseline, week 6	

End point values	CKD patients Valsartan 0.25 mg/kg	CKD patients Valsartan 4 mg/kg	Non-CKD patients Valsartan 0.25 mg/kg	Non-CKD patients Valsartan 4 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	31	33	31
Units: mmHg				
least squares mean (standard error)	-1.2 (± 2.05)	-9.2 (± 2.05)	-6.9 (± 1.44)	-7.8 (± 1.48)

Statistical analyses

Statistical analysis title	Change from baseline in MSBP at Week 6
Comparison groups	CKD patients Valsartan 0.25 mg/kg v CKD patients Valsartan 4 mg/kg
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0096
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-7.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.86
upper limit	-2.01
Variability estimate	Standard error of the mean
Dispersion value	2.96

Statistical analysis title	Change from baseline in MSBP at Week 6
Comparison groups	Non-CKD patients Valsartan 0.25 mg/kg v Non-CKD patients Valsartan 4 mg/kg
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6531
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.07
upper limit	3.2
Variability estimate	Standard error of the mean
Dispersion value	2.07

Secondary: Change from baseline in mean diastolic blood pressure (MDBP) at Week 6

End point title	Change from baseline in mean diastolic blood pressure (MDBP) at Week 6

End point description:

Patient’s blood pressure will be measured in the same position at every visit Systolic and diastolic blood pressures will be measured three times at 2-3 minute intervals. The arithmetic mean of these three blood pressure measurements will be used as the mean office blood pressure (MSBP and MDBP) Baseline and Week 6 endpoint in Period 1 Double Blind Phase

End point type	Secondary

End point timeframe:
Baseline, Week 6

End point values	CKD patients Valsartan 0.25 mg/kg	CKD patients Valsartan 4 mg/kg	Non-CKD patients Valsartan 0.25 mg/kg	Non-CKD patients Valsartan 4 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	31	33	31
Units: mmHg				
least squares mean (standard error)	1.3 (± 1.79)	-6.5 (± 1.79)	-1.9 (± 1.26)	-7.2 (± 1.3)

Statistical analyses

Statistical analysis title	Change from baseline in MDBP at Week 6
Comparison groups	CKD patients Valsartan 0.25 mg/kg v CKD patients Valsartan 4 mg/kg
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-7.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.94
upper limit	-2.78
Variability estimate	Standard error of the mean
Dispersion value	2.54

Statistical analysis title	Change from baseline in MDBP at Week 6
Comparison groups	Non-CKD patients Valsartan 0.25 mg/kg v Non-CKD patients Valsartan 4 mg/kg
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0042
Method	ANCOVA
Parameter estimate	Mean difference (net)
Point estimate	-5.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.98
upper limit	-1.77
Variability estimate	Standard error of the mean
Dispersion value	1.8

Secondary: Patients achieving <90th percentile for age, gender and height at Week 6 endpoint in both MSBP and MDBP

End point title	Patients achieving <90th percentile for age, gender and height at Week 6 endpoint in both MSBP and MDBP

End point description:

Patient's blood pressure will be measured in the same position at every visit Systolic and diastolic blood pressures will be measured three times at 2-3 minute intervals. The arithmetic mean of these three blood pressure measurements will be used as the mean office blood pressure (MSBP and MDBP) Week 6

End point type	Secondary

End point timeframe:

Week 6

End point values	CKD patients Valsartan 0.25 mg/kg	CKD patients Valsartan 4 mg/kg	Non-CKD patients Valsartan 0.25 mg/kg	Non-CKD patients Valsartan 4 mg/kg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	31	31	33	31
Units: participants	6	9	7	8

Statistical analyses

Statistical analysis title	Achieving<90th% for age,gender&height in MSBP&MDBP
Comparison groups	CKD patients Valsartan 0.25 mg/kg v CKD patients Valsartan 4 mg/kg
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.411
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	5.8

Statistical analysis title	Achieving<90th% for age,gender&height in MSBP&MDBP
Comparison groups	Non-CKD patients Valsartan 0.25 mg/kg v Non-CKD patients Valsartan 4 mg/kg
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5443
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	4.79

Secondary: CKD patients achieving urine albumin creatinine ratio percentage reduction (UACR) >=25% at Week 6

End point title	CKD patients achieving urine albumin creatinine ratio percentage reduction (UACR) >=25% at Week 6[1]

End point description:

UACR response is defined as percentage change from baseline in UACR≤ 25%. UACR [mg/mmol] = urine albumin [mg/L] / urine creatinine [mmol/L] UACR was collected for CKD patients only. The UACR value at a given visit for a patient was to be derived by the median of the three lab values collected for that visit Week 6.

End point type	Secondary

End point timeframe:

Week 6 weeks

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint only looked at CKD patients

End point values	CKD patients Valsartan 0.25 mg/kg	CKD patients Valsartan 4 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	27		
Units: participants	12	9		

Statistical analyses

Statistical analysis title	CKD patients achieving UACR >=25% at Week 6
Comparison groups	CKD patients Valsartan 0.25 mg/kg v CKD patients Valsartan 4 mg/kg

Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.2624
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	0.517
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.16
upper limit	1.64

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	17.0

Reporting groups

Reporting group title	Valsartan 0.25 mg/kg
Reporting group description:	
Valsartan 0.25 mg/kg	
Reporting group title	All open label Patients
Reporting group description:	
All open label Patients	
Reporting group title	Valsartan 4.0 mg/kg
Reporting group description:	
Valsartan 4.0 mg/kg	

Serious adverse events	Valsartan 0.25 mg/kg	All open label Patients	Valsartan 4.0 mg/kg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 64 (3.13%)	6 / 120 (5.00%)	2 / 62 (3.23%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Toxicity to various agents			
subjects affected / exposed	0 / 64 (0.00%)	1 / 120 (0.83%)	0 / 62 (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
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	0 / 64 (0.00%)	1 / 120 (0.83%)	0 / 62 (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
Gastrointestinal disorders			
Gastritis			

subjects affected / exposed	0 / 64 (0.00%)	0 / 120 (0.00%)	1 / 62 (1.61%)
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			
Aggression			
subjects affected / exposed	1 / 64 (1.56%)	0 / 120 (0.00%)	0 / 62 (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
Renal and urinary disorders			
Nephrotic syndrome			
subjects affected / exposed	0 / 64 (0.00%)	1 / 120 (0.83%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 64 (1.56%)	0 / 120 (0.00%)	1 / 62 (1.61%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 64 (0.00%)	2 / 120 (1.67%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastoiditis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 120 (0.83%)	0 / 62 (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
Pharyngitis			
subjects affected / exposed	0 / 64 (0.00%)	1 / 120 (0.83%)	0 / 62 (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

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

Non-serious adverse events	Valsartan 0.25 mg/kg	All open label Patients	Valsartan 4.0 mg/kg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 64 (29.69%)	62 / 120 (51.67%)	13 / 62 (20.97%)
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 64 (3.13%)	20 / 120 (16.67%)	3 / 62 (4.84%)
occurrences (all)	3	27	5
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 64 (6.25%)	10 / 120 (8.33%)	2 / 62 (3.23%)
occurrences (all)	4	13	2
Vomiting			
subjects affected / exposed	3 / 64 (4.69%)	9 / 120 (7.50%)	1 / 62 (1.61%)
occurrences (all)	3	9	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 64 (7.81%)	11 / 120 (9.17%)	1 / 62 (1.61%)
occurrences (all)	5	13	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 64 (4.69%)	7 / 120 (5.83%)	0 / 62 (0.00%)
occurrences (all)	3	9	0
Ear infection			
subjects affected / exposed	0 / 64 (0.00%)	7 / 120 (5.83%)	0 / 62 (0.00%)
occurrences (all)	0	8	0
Nasopharyngitis			
subjects affected / exposed	3 / 64 (4.69%)	9 / 120 (7.50%)	2 / 62 (3.23%)
occurrences (all)	5	11	2
Respiratory tract infection			
subjects affected / exposed	4 / 64 (6.25%)	6 / 120 (5.00%)	3 / 62 (4.84%)
occurrences (all)	6	10	3
Tonsillitis			
subjects affected / exposed	0 / 64 (0.00%)	8 / 120 (6.67%)	2 / 62 (3.23%)
occurrences (all)	0	8	2
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	1 / 64 (1.56%) 1	10 / 120 (8.33%) 12	0 / 62 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported