Clinical trial results:
A Phase II, randomised, double blind, placebo controlled, seven way crossover study to assess the effect of single doses of RPL554 compared to salbutamol and placebo administered by nebuliser on lung function of patients with chronic asthma

Summary

EudraCT number	2014-005615-17
Trial protocol	GB SE
Global end of trial date	17 November 2015

Results information

Result version number	v1 (current)
This version publication date	25 October 2017
First version publication date	25 October 2017

Trial information

Trial identification

Sponsor protocol code	RPL554-008-2014

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02427165
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Verona Pharma plc
Sponsor organisation address	3 More London Riverside, London, United Kingdom, SE1 2RE
Public contact	Kenneth Newman, Verona Pharma plc, +44 203 283 4200, ken.newman@veronapharma.com
Scientific contact	Kenneth Newman, Verona Pharma plc, +44 203 283 4200, ken.newman@veronapharma.com

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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 November 2015
Global end of trial reached?	Yes
Global end of trial date	17 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the bronchodilator effect of single doses of RPL554 administered by nebuliser on peak and average* FEV1 over 12 hours compared with placebo and salbutamol.

*The average effect was calculated as the area under the curve divided by the length of the time interval of interest, and the peak effect as the minimum value for diastolic blood pressure or maximum value for other variables

Protection of trial subjects:

Standard procedures for emergency care were followed for any individual adverse events if clinically needed. Short acting bronchodilators could be used as rescue medication.

Background therapy:

Salbutamol was used as rescue medication

Evidence for comparator:

Two different single doses (2.5 mg and 7.5 mg) of nebulised salbutamol were included; 2.5 mg is the standard dose of salbutamol and was intended as a benchmark for bronchodilation, 7.5 mg is dose which may be used in acute asthma and was intended to show the maximum bronchodilation achievable using salbutamol

Actual start date of recruitment	13 May 2015
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	Sweden: 20
Country: Number of subjects enrolled	United Kingdom: 9
Worldwide total number of subjects	29
EEA total number of subjects	29

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	29
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was started on 13 May 2015 in the UK and 25 May 2015 in Sweden. Overall, 153 patients were screened for the study and 29 were treated . Patients received study treatment between 21 May 2015 and 15 November 2015. A total of 25 patients completed the study and four were withdrawn

Pre-assignment

Screening details:

153 patients were screened (128 in the UK and 25 in Sweden). The main reasons for screen failure were reversibility test criteria not met (50 patients), BMI out of range or vital signs out of range (13 patients each). Patients had to discontinue LABAs and LAMAs for 72 hours and SABAs and SAMAs for 8 hours before screening

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject, Carer, Assessor

Arms

Are arms mutually exclusive?	No
Arm title	0.4 mg RPL554

Arm description:

Single dose of 0.4 mg RPL554 administered using a nebuliser

Arm type	Experimental
Investigational medicinal product name	RPL554
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

Single dose of 0.4 mg RPL554 diluted to a 5 mL volume administered using a nebuliser.

Arm title	1.5 mg RPL554

Arm description:

Single dose of 1.5 mg RPL554 administered using a nebuliser

Arm type	Experimental
Investigational medicinal product name	RPL554
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

Single dose of 1.5 mg RPL554 diluted to a 5 mL volume administered using a nebuliser.

Arm title	6 mg RPL554

Arm description:

Single dose of 6 mg RPL554 administered using a nebuliser

Arm type	Experimental

Investigational medicinal product name	RPL554
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

Single dose of 6 mg RPL554 diluted to a 5 mL volume administered using a nebuliser.

Arm title	24 mg RPL554

Arm description:

Single dose of 24 mg RPL554 administered using a nebuliser

Arm type	Experimental
Investigational medicinal product name	RPL554
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

Single dose of 24 mg RPL554 diluted to a 5 mL volume administered using a nebuliser.

Arm title	Placebo

Arm description:

Single dose of placebo administered using a nebuliser

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser suspension
Routes of administration	Inhalation use

Dosage and administration details:

Single dose of placebo as a 5 mL volume administered using a nebuliser.

Arm title	2.5 mg salbutamol

Arm description:

Single dose of 2.5 mg salbutamol administered using a nebuliser

Arm type	Active comparator
Investigational medicinal product name	Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

Single dose of 2.5 mg salbutamol diluted to a 5 mL volume administered using a nebuliser.

Arm title	7.5 mg salbutamol

Arm description:

Single dose of 7.5 mg salbutamol administered using a nebuliser

Arm type	Active comparator
Investigational medicinal product name	Salbutamol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nebuliser solution
Routes of administration	Inhalation use

Dosage and administration details:

Single dose of 7.5 mg RPL554 administered as a 5 mL volume using a nebuliser.

Number of subjects in period 1	0.4 mg RPL554	1.5 mg RPL554	6 mg RPL554
Started	26	27	26
Completed	26	27	26
Not completed	0	0	0
Physician decision	-	-	-
Pre-dose FEV1 not comparable with baseline	-	-	-

Number of subjects in period 1	24 mg RPL554	Placebo	2.5 mg salbutamol
Started	27	26	28
Completed	27	26	26
Not completed	0	0	2
Physician decision	-	-	-
Pre-dose FEV1 not comparable with baseline	-	-	2

Number of subjects in period 1	7.5 mg salbutamol
Started	28
Completed	26
Not completed	2
Physician decision	1
Pre-dose FEV1 not comparable with baseline	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	29	29	
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)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	29	29	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	37.6		
full range (min-max)	21 to 62	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	26	26	

End points

End points reporting groups	
Reporting group title	0.4 mg RPL554
Reporting group description: Single dose of 0.4 mg RPL554 administered using a nebuliser	
Reporting group title	1.5 mg RPL554
Reporting group description: Single dose of 1.5 mg RPL554 administered using a nebuliser	
Reporting group title	6 mg RPL554
Reporting group description: Single dose of 6 mg RPL554 administered using a nebuliser	
Reporting group title	24 mg RPL554
Reporting group description: Single dose of 24 mg RPL554 administered using a nebuliser	
Reporting group title	Placebo
Reporting group description: Single dose of placebo administered using a nebuliser	
Reporting group title	2.5 mg salbutamol
Reporting group description: Single dose of 2.5 mg salbutamol administered using a nebuliser	
Reporting group title	7.5 mg salbutamol
Reporting group description: Single dose of 7.5 mg salbutamol administered using a nebuliser	

Primary: Peak FEV1	
End point title	Peak FEV1
End point description:	
End point type	Primary
End point timeframe: pre-dose (-30 and -15 minutes), 10, 20, 30, 60, 90 minutes and 2, 4, 6, 8 and 12 hours post-dose	

End point values	0.4 mg RPL554	1.5 mg RPL554	6 mg RPL554	24 mg RPL554
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	27	26	27
Units: Litres				
arithmetic mean (full range (min-max))	3.432 (1.86 to 4.57)	3.547 (1.93 to 4.93)	3.554 (2.03 to 4.89)	3.749 (2.02 to 5.59)

End point values	Placebo	2.5 mg salbutamol	7.5 mg salbutamol	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	28	28	
Units: Litres				
arithmetic mean (full range (min-max))	3.164 (1.77 to 4.29)	3.738 (2.05 to 5.26)	3.748 (2.08 to 5.3)	

Statistical analyses

Statistical analysis title	Peak FEV1 0.4 mg RPL554 versus placebo
Comparison groups	0.4 mg RPL554 v Placebo
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Ratio
Confidence interval	
level	95 %
sides	2-sided
lower limit	106.01
upper limit	111.13

Statistical analysis title	Peak FEV1 1.5 mg RPL554 versus placebo
Comparison groups	Placebo v 1.5 mg RPL554
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Ratio
Point estimate	110.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	107.76
upper limit	112.97

Statistical analysis title	Peak FEV1 6 mg RPL554 versus placebo
Comparison groups	Placebo v 6 mg RPL554

Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Ratio
Point estimate	111.47
Confidence interval	
level	95 %
sides	2-sided
lower limit	108.87
upper limit	114.13

Statistical analysis title	Peak FEV1 24 mg RPL554 versus placebo
Comparison groups	Placebo v 24 mg RPL554
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Ratio
Point estimate	115.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	112.42
upper limit	117.86

Statistical analysis title	Peak FEV1 2.5 mg salbutamol versus placebo
Comparison groups	Placebo v 2.5 mg salbutamol
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Ratio
Point estimate	115.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	113.16
upper limit	118.59

Statistical analysis title	Peak FEV1 7.5 mg salbutamol versus placebo

Comparison groups	Placebo v 7.5 mg salbutamol
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	LS Means Ratio
Point estimate	117.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	114.9
upper limit	120.36

Statistical analysis title	Peak FEV1 24 mg RPL554 versus 2.5 mg salbutamol
Comparison groups	2.5 mg salbutamol v 24 mg RPL554
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.59
Method	ANCOVA
Parameter estimate	LS Means Ratio
Point estimate	99.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	97.1
upper limit	101.69

Statistical analysis title	Peak FEV1 24 mg RPL554 versus 7.5 mg salbutamol
Comparison groups	7.5 mg salbutamol v 24 mg RPL554
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0702
Method	ANCOVA
Parameter estimate	LS Means Ratio
Point estimate	97.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	95.64
upper limit	100.18

Primary: Average FEV1

End point title	Average FEV1

End point description:

End point type	Primary

End point timeframe:

pre dose (-30 minutes and -15 minutes) and 10 minutes, 20 minutes, 30 minutes, 60 minutes, 90 minutes, 2 hours, 4 hours, 6 hours, 8 hours and 12 hours

End point values	0.4 mg RPL554	1.5 mg RPL554	6 mg RPL554	24 mg RPL554
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	27	26	27
Units: Litres				
arithmetic mean (full range (min-max))	3.189 (1.78 to 4.33)	3.284 (1.85 to 4.6)	3.318 (1.88 to 4.63)	3.492 (1.9 to 5.11)

End point values	Placebo	2.5 mg salbutamol	7.5 mg salbutamol	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	26	28	28	
Units: Litres				
arithmetic mean (full range (min-max))	2.986 (1.7 to 4.22)	3.375 (1.81 to 4.82)	3.443 (1.92 to 4.95)	

Statistical analyses

Statistical analysis title	Average FEV1 0.4 mg RPL554 versus placebo
Comparison groups	0.4 mg RPL554 v Placebo
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Geometric LS Means ratio
Point estimate	106.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	104.09
upper limit	109.34

Statistical analysis title	Average FEV1 1.5 mg RPL554 versus placebo

Comparison groups	Placebo v 1.5 mg RPL554
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Geometric LS Means ratio
Point estimate	107.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	105.03
upper limit	110.32

Statistical analysis title	Average FEV1 6 mg RPL554 versus placebo
Comparison groups	Placebo v 6 mg RPL554
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Geometric LS Means ratio
Point estimate	109.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	107.07
upper limit	112.47

Statistical analysis title	Average FEV1 24 mg RPL554 versus placebo
Comparison groups	Placebo v 24 mg RPL554
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Geometric LS Means ratio
Point estimate	113.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	110.65
upper limit	116.24

Statistical analysis title	Average FEV1 2.5 mg salbutamol versus placebo
Comparison groups	Placebo v 2.5 mg salbutamol
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Geometric LS Means ratio
Point estimate	111.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	108.46
upper limit	113.88

Statistical analysis title	Average FEV1 7.5 mg salbutamol versus p...
Comparison groups	Placebo v 7.5 mg salbutamol
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001
Method	ANCOVA
Parameter estimate	Geometric LS Means ratio
Point estimate	114.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	111.48
upper limit	117.02

Statistical analysis title	Average FEV1 6mg RPL554 versus 2.5 mg salbutamol
Comparison groups	2.5 mg salbutamol v 6 mg RPL554
Number of subjects included in analysis	54
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.3042
Method	ANCOVA
Parameter estimate	Geometric LS Means ratio
Point estimate	98.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	96.36
upper limit	101.17

Statistical analysis title	Average FEV1 24mg RPL554 versus 7.5 mg s...
Comparison groups	24 mg RPL554 v 7.5 mg salbutamol
Number of subjects included in analysis	55
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.5607
Method	ANCOVA
Parameter estimate	Geometric LS Means ratio
Point estimate	99.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	96.92
upper limit	101.72

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From informed consent to end of study visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	0.4 mg RPL554
Reporting group description: Single dose of 0.4 mg RPL554 administed using a nebuliser	
Reporting group title	1.5 mg RPL554
Reporting group description: Single dose of 1.5 mg RPL554 administered using a nebuliser	
Reporting group title	6 mg RPL554
Reporting group description: Single dose of 6 mg RPL554 administered using a nebuliser	
Reporting group title	24 mg RPL554
Reporting group description: Single dose of 24 mg RPL554 administered using a nebuliser	
Reporting group title	Placebo
Reporting group description: Single dose of placebo administered using a nebuliser	
Reporting group title	2.5 mg salbutamol
Reporting group description: Single dose of 2.5 mg salbutamol administered using a nebuliser	
Reporting group title	7.5 mg salbutamol
Reporting group description: Single dose of 7.5 mg salbutamol administered using a nebuliser	

Serious adverse events	0.4 mg RPL554	1.5 mg RPL554	6 mg RPL554
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 26 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	24 mg RPL554	Placebo	2.5 mg salbutamol
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 28 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	7.5 mg salbutamol		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 28 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	0.4 mg RPL554	1.5 mg RPL554	6 mg RPL554
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 26 (46.15%)	9 / 27 (33.33%)	10 / 26 (38.46%)
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 26 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	6 / 26 (23.08%)	4 / 27 (14.81%)	3 / 26 (11.54%)
occurrences (all)	6	4	3
Tremor			
subjects affected / exposed	0 / 26 (0.00%)	1 / 27 (3.70%)	1 / 26 (3.85%)
occurrences (all)	0	1	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 26 (3.85%)	0 / 27 (0.00%)	2 / 26 (7.69%)
occurrences (all)	1	0	2
Throat irritation			

subjects affected / exposed	0 / 26 (0.00%)	2 / 27 (7.41%)	0 / 26 (0.00%)
occurrences (all)	0	2	0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 26 (0.00%)	0 / 27 (0.00%)	0 / 26 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	24 mg RPL554	Placebo	2.5 mg salbutamol
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 27 (37.04%)	5 / 26 (19.23%)	10 / 28 (35.71%)
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	7 / 27 (25.93%)	1 / 26 (3.85%)	0 / 28 (0.00%)
occurrences (all)	8	1	0
Tremor			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	9 / 28 (32.14%)
occurrences (all)	0	1	9
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	1	0	0
Throat irritation			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	0 / 28 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypokalaemia			

subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (0.00%)	0 / 28 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	7.5 mg salbutamol		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 28 (57.14%)		
Cardiac disorders			
Palpitations			
subjects affected / exposed	7 / 28 (25.00%)		
occurrences (all)	7		
Tachycardia			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 28 (7.14%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	5 / 28 (17.86%)		
occurrences (all)	5		
Tremor			
subjects affected / exposed	12 / 28 (42.86%)		
occurrences (all)	12		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 28 (3.57%)		
occurrences (all)	1		
Throat irritation			
subjects affected / exposed	0 / 28 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	3 / 28 (10.71%)		
occurrences (all)	3		

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