



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 | Subject, Investigator, Monitor, 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 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

| 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 occurrences (all) | 0 / 26 (0.00%) 0 | 2 / 27 (7.41%) 2 | 0 / 26 (0.00%) 0 |
| Metabolism and nutrition disorders Hypokalaemia subjects affected / exposed occurrences (all) | 0 / 26 (0.00%) 0 | 0 / 27 (0.00%) 0 | 0 / 26 (0.00%) 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 occurrences (all) Tachycardia subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 1 / 27 (3.70%) 1 | 0 / 26 (0.00%) 0 0 / 26 (0.00%) 0 | 0 / 28 (0.00%) 0 0 / 28 (0.00%) 0 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Tremor subjects affected / exposed occurrences (all) | 0 / 27 (0.00%) 0 7 / 27 (25.93%) 8 0 / 27 (0.00%) 0 | 0 / 26 (0.00%) 0 1 / 26 (3.85%) 1 1 / 26 (3.85%) 1 | 0 / 28 (0.00%) 0 0 / 28 (0.00%) 0 9 / 28 (32.14%) 9 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Throat irritation subjects affected / exposed occurrences (all) | 1 / 27 (3.70%) 1 0 / 27 (0.00%) 0 | 0 / 26 (0.00%) 0 1 / 26 (3.85%) 1 | 0 / 28 (0.00%) 0 0 / 28 (0.00%) 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