



Clinical trial results:

An open-label extension of BPS-MR-PAH-203 in pulmonary arterial hypertension (PAH) patients

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2009-014453-32 |
| Trial protocol | BE IE DE CZ |
| Global end of trial date | 26 November 2013 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 31 January 2020 |
| First version publication date | 31 January 2020 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | BPS-MR-PAH-204 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00990314 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Lung Biotechnology PBC |
| Sponsor organisation address | 1040 Spring Street, Silver Spring, United States, 20910 |
| Public contact | Lung Biotechnology PBC Study Director, Lung Biotechnology PBC, +1 3016089292, |
| Scientific contact | Lung Biotechnology PBC Study Director, Lung Biotechnology PBC, +1 3016089292, |

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 | 27 May 2015 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 26 November 2013 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

This is an open-label study for patients who participated in the BPS-MR-PAH-203 study and have volunteered to continue treatment for PAH with Beraprost Sodium Modified Release (BPS-MR) tablets.

Protection of trial subjects:

The study was conducted in accordance with U.S. 21 CFR Parts 50, 56, and 312 and in accordance with the Declaration of Helsinki.

Background therapy:

Patients on background therapy (ERA alone, PDE-5 inhibitor alone, and ERA and PDE-5 inhibitor) were combined for the analysis.

Evidence for comparator: -

| | |
|---|-------------|
| Actual start date of recruitment | 05 May 2010 |
| 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: 4 |
| Country: Number of subjects enrolled | Czech Republic: 3 |
| Country: Number of subjects enrolled | Romania: 9 |
| Country: Number of subjects enrolled | United States: 15 |
| Worldwide total number of subjects | 31 |
| EEA total number of subjects | 16 |

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) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 27 |

| | |
|---------------------|---|
| From 65 to 84 years | 4 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This was an open-label study for subjects who participated in the BPS-MR-PAH-203 study and volunteered to continue treatment for PAH with BPS-MR tablets.

Pre-assignment

Screening details:

A Protocol Amendment was to include an optional arm investigating Beraprost Sodium Modified Release Tablets administered four times daily (QID), however, no subjects were enrolled into this arm.

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

| | |
|-----------|------------------|
| Arm title | Beraprost Sodium |
|-----------|------------------|

Arm description:

Beraprost Sodium Modified Release Tablet, 60 micrograms(mcg), twice a day dosing

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Beraprost Sodium Modified Release Tablet |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Modified-release tablet |
| Routes of administration | Oral use |

Dosage and administration details:

60 mcg twice a day

| Number of subjects in period 1 | Beraprost Sodium |
|--------------------------------|------------------|
| Started | 31 |
| Completed | 19 |
| Not completed | 12 |
| Adverse event, serious fatal | 2 |
| Consent withdrawn by subject | 3 |
| Non-Compliance | 1 |
| Physician decision | 3 |
| Adverse event, non-fatal | 2 |
| Lack of efficacy | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Beraprost Sodium |
|-----------------------|------------------|

Reporting group description:

Beraprost Sodium Modified Release Tablet, 60 micrograms(mcg), twice a day dosing

| Reporting group values | Beraprost Sodium | Total | |
|---|------------------|-------|--|
| Number of subjects | 31 | 31 | |
| Age categorical | | | |
| Baseline characteristics were defined at the baseline visit of the lead-in study, BPS-MR-PAH-203. | | | |
| 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) | 27 | 27 | |
| From 65-84 years | 4 | 4 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Baseline characteristics were defined at the baseline visit of the lead-in study, BPS-MR-PAH-203. | | | |
| Units: years | | | |
| arithmetic mean | 46.5 | | |
| standard deviation | ± 14.16 | - | |
| Sex: Female, Male | | | |
| Baseline characteristics were defined at the baseline visit of the lead-in study, BPS-MR-PAH-203. | | | |
| Units: Subjects | | | |
| Female | 26 | 26 | |
| Male | 5 | 5 | |
| Race (NIH/OMB) | | | |
| Baseline characteristics were defined at the baseline visit of the lead-in study, BPS-MR-PAH-203. | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 1 | 1 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 0 | |
| White | 30 | 30 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 0 | 0 | |
| Ethnicity (NIH/OMB) | | | |
| Baseline characteristics were defined at the baseline visit of the lead-in study, BPS-MR-PAH-203. | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 4 | 4 | |
| Not Hispanic or Latino | 27 | 27 | |
| Unknown or Not Reported | 0 | 0 | |

| | | | |
|---|--------|---|--|
| Six-Minute Walk Distance | | | |
| Area used for the Six Minute Walk Test (6MWT) was 30 meters in length. Rest periods were allowed if patient could no longer continue. If patient needed to rest, he could stand or sit and then begin again when rested but the clock continued to run. For purposes of the 6MWT, if patient was assessed at Baseline w/ oxygen therapy, all 6MWT were conducted in the same manner. All efficacy results are descriptive; no statistical analysis was conducted. Baseline characteristics were defined at the baseline visit of the lead-in study, BPS-MR-PAH-203. | | | |
| Units: meters | | | |
| arithmetic mean | 360.7 | | |
| standard deviation | ± 78.0 | - | |
| Borg Dyspnea Score | | | |
| Modified 0–10 Borg scale consists of 11-point rating level of dyspnea during the 6MWT. Scores range from 0 (best) and 10 (worst) with spacing of verbal descriptors of severity corresponding to specific numbers. Number or verbal descriptor to reflect presumed ratio properties of sensation/intensity. Only subjects w/ both a measurement at baseline and given visit are presented. Efficacy results are descriptive; no statistical analysis conducted. Baseline characteristics were defined at the baseline visit of the lead-in study, BPS-MR-PAH-203. | | | |
| Units: score | | | |
| arithmetic mean | 3.2 | | |
| standard deviation | ± 1.97 | - | |

End points

End points reporting groups

| | |
|--|------------------|
| Reporting group title | Beraprost Sodium |
| Reporting group description: | |
| Beraprost Sodium Modified Release Tablet, 60 micrograms(mcg), twice a day dosing | |

Primary: Number of Subjects Reporting at Least One Treatment-Emergent Adverse Event (TEAE)

| | |
|-----------------|--|
| End point title | Number of Subjects Reporting at Least One Treatment-Emergent Adverse Event (TEAE) ^[1] |
|-----------------|--|

End point description:

A treatment-emergent adverse event (TEAE) is defined as an event not present prior to the initiation of the treatment or any event already present that worsens in either intensity or frequency following exposure to the treatment. AEs occurring more than 3 days after the last day study drug was taken in the study was not included in the statistical analyses or summaries (except for subjects with adverse events leading to study drug withdrawn). Only TEAEs that occurred during the treatment period of the BPS-MR-PAH-204 study were summarized. Any adverse event starting prior to the first dose of study drug was excluded from the summary analyses and only presented in the data listings. All efficacy results are descriptive; no statistical analysis was conducted

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to 42 months

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | Beraprost Sodium | | | |
|-----------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 31 | | | |
| Units: subjects | 27 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of reported Treatment-Emergent Adverse Events

| | |
|-----------------|---|
| End point title | Number of reported Treatment-Emergent Adverse Events ^[2] |
|-----------------|---|

End point description:

A treatment-emergent adverse event (TEAE) is defined as an event not present prior to the initiation of the treatment or any event already present that worsens in either intensity or frequency following exposure to the treatment. AEs occurring more than 3 days after the last day study drug was taken in the study was not included in the statistical analyses or summaries (except for subjects with adverse events leading to study drug withdrawn). Only TEAEs that occurred during the treatment period of the BPS-MR-PAH-204 study were summarized. Any adverse event starting prior to the first dose of study drug was excluded from the summary analyses and only presented in the data listings. All efficacy results are descriptive; no statistical analysis was conducted.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Up to 42 months

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: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| | | | | |
|-----------------------------|------------------|--|--|--|
| End point values | Beraprost Sodium | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 31 | | | |
| Units: TEAEs | 230 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Six-Minute-Walk Distance (6MWD)

| | |
|---|---|
| End point title | Change in Six-Minute-Walk Distance (6MWD) |
| End point description: | |
| Area used for the Six Minute Walk Test (6MWT) was pre-measured at 30 meters in length. Rest periods were allowed if patient could no longer continue. If patient needed to rest, he/she could stand or sit and then begin again when rested but the clock continued to run. At the end of 6 minutes, the tester called "stop" while stopping the watch and then measured the distance walked. For purposes of the 6MWT, if patient was assessed at Baseline using oxygen therapy, all future 6MWT were conducted in the same manner. All efficacy results are descriptive; no statistical analysis was conducted. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline and 42 months | |

| | | | | |
|--------------------------------------|----------------------|--|--|--|
| End point values | Beraprost Sodium | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 22 | | | |
| Units: meters | | | | |
| arithmetic mean (standard deviation) | 24.09 (\pm 81.01) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Borg Dyspnea Score

| | |
|---|------------------------------|
| End point title | Change in Borg Dyspnea Score |
| End point description: | |
| The modified 0–10 category-ratio Borg scale consists of an 11-point scale rating the maximum level of | |

dyspnea experienced during the 6MWT. Scores range from 0 (for the best condition) and 10 (for the worst condition) with nonlinear spacing of verbal descriptors of severity corresponding to specific numbers. The participant chose the number or the verbal descriptor to reflect presumed ratio properties of sensation or symptom intensity. Baseline was defined as the last non-missing evaluation preceding the first dose of study drug in study BPS-MR-PAH-203. Only subjects with both a measurement at baseline and at the given visit are presented. All efficacy results are descriptive; no statistical analysis was conducted.

| | |
|------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline and 42 months | |

| | | | | |
|--------------------------------------|------------------|--|--|--|
| End point values | Beraprost Sodium | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 22 | | | |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | 0.86 (± 1.89) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects that experienced Clinical Worsening

| | |
|---|--|
| End point title | Number of subjects that experienced Clinical Worsening |
| End point description: | |
| Number of subjects that experienced Clinical Worsening in the opinion of the Investigator. Clinical Worsening was defined as any of these events following the Baseline visit: Death, Transplantation or atrial septostomy, Clinical deterioration as defined by: Hospitalization as a result of PAH symptoms or Initiation of any new PAH specific therapy (e.g. ERA, PDE-5 inhibitor, prostanoid). All efficacy results are descriptive; no statistical analysis was conducted. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to 42 months | |

| | | | | |
|---|------------------|--|--|--|
| End point values | Beraprost Sodium | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 31 | | | |
| Units: subjects | | | | |
| Death | 1 | | | |
| Hospitalization As A Result of PAH Symptoms | 2 | | | |
| New PAH Therapies | 4 | | | |
| Transplantation or atrial septostomy | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects With a Change in WHO Functional Class

| | |
|-----------------|--|
| End point title | Number of subjects With a Change in WHO Functional Class |
|-----------------|--|

End point description:

Change from Baseline in participant clinical status was recorded according to the World Health Organization (WHO) Functional Class. A change from lower to higher functional class (i.e. 'III to IV' or 'II to III') was considered as a deterioration. A change from higher to lower functional class (i.e. 'III to II' or 'II to I') was considered as an improvement. All efficacy results are descriptive; no statistical analysis was conducted.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline and 42 months

| End point values | Beraprost Sodium | | | |
|---|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 25 | | | |
| Units: subjects | | | | |
| Improved: Change from Class II to Class I | 2 | | | |
| Improved: Change from Class III to Class II | 7 | | | |
| Deteriorated: Change from Class II to Class III | 5 | | | |
| Deteriorated: Change from Class III to Class IV | 1 | | | |
| No Change in Class | 10 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline to 30 days after study treatment discontinuation, up to 42 months.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Beraprost Sodium |
|-----------------------|------------------|

Reporting group description:

Beraprost Sodium Modified Release Tablet, 60 micrograms(mcg), twice a day dosing

| Serious adverse events | Beraprost Sodium | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 31 (35.48%) | | |
| number of deaths (all causes) | 2 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Extremity necrosis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| Right ventricular failure | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Atrial flutter | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 2 | | |
| General disorders and administration site conditions | | | |
| Edema peripheral | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Enterocolitis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Worsening pulmonary arterial hypertension | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Varicella | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| | | | |
|---|------------------|--|--|
| Non-serious adverse events | Beraprost Sodium | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 26 / 31 (83.87%) | | |
| Investigations | | | |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Carbon dioxide decreased | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Neutrophil count increased | | | |

| | | | |
|-------------------------------------|------------------|--|--|
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Urine analysis abnormal | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| White blood cell count increased | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Brain natriuretic peptide increased | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | | |
| occurrences (all) | 6 | | |
| Hypotension | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences (all) | 3 | | |
| Hot flush | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 4 / 31 (12.90%) | | |
| occurrences (all) | 5 | | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 10 / 31 (32.26%) | | |
| occurrences (all) | 22 | | |
| Dizziness | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | | |
| occurrences (all) | 8 | | |
| Somnolence | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Syncope | | | |

| | | | |
|---|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 2 / 31 (6.45%) 2 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | | |
| occurrences (all) | 5 | | |
| Chest Pain | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Oedema | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Gastrointestinal disorders | | | |
| Nausea | | | |
| subjects affected / exposed | 9 / 31 (29.03%) | | |
| occurrences (all) | 9 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 7 / 31 (22.58%) | | |
| occurrences (all) | 13 | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences (all) | 3 | | |
| Cough | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 3 | | |
| Epistaxis | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |

| | | | |
|--|---|--|--|
| Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) | 2 / 31 (6.45%) 2 | | |
| Musculoskeletal and connective tissue disorders Back Pain subjects affected / exposed occurrences (all) | 2 / 31 (6.45%) 2 | | |
| Infections and infestations Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Tooth abscess subjects affected / exposed occurrences (all) | 4 / 31 (12.90%) 5 2 / 31 (6.45%) 3 3 / 31 (9.68%) 3 2 / 31 (6.45%) 2 | | |
| Metabolism and nutrition disorders Hypercholesterolaemia subjects affected / exposed occurrences (all) Hypokalaemia subjects affected / exposed occurrences (all) | 3 / 31 (9.68%) 3 2 / 31 (6.45%) 3 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 13 October 2011 | Amendment 1 dated 13 October 2011 (USA, Belgium, Romania): Revised to extend the calendar end date to allow ongoing subjects to continue to receive BPS-MR until 31 December 2013 or Lung LLC discontinues the project. A further administrative revision was applied to reflect the change of the Sponsor name from Lung Rx to Lung LLC. |
| 25 June 2012 | Amendment 2 dated 25 June 2012 (USA, Belgium, Romania): Revised to include an optional substudy investigating the safety, tolerability, and pharmacokinetics of BPS-MR tablets administered four times daily (QID). An additional revision was applied to extend the calendar end date to allow ongoing subjects to receive BPS-MR until 31 December 2014 or Lung LLC discontinues the project. Revisions were made to update the status of recently completed studies |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported