



Clinical trial results:

Randomized, multi-center, double-blind, placebo-controlled, group-comparison study to investigate safety, tolerability and pharmacodynamics of BAY2253651 after administration of a single nasal dose in 60 subjects with obstructive sleep apnea and open exploratory evaluation of safety and local tolerability of repeated doses in patients

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2017-001851-29 |
| Trial protocol | GB |
| Global end of trial date | 23 May 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 04 June 2020 |
| First version publication date | 04 June 2020 |

Trial information

Trial identification

| | |
|-----------------------|------------------|
| Sponsor protocol code | BAY2253651/19038 |
|-----------------------|------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03603678 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Bayer AG |
| Sponsor organisation address | Kaiser Wilhelm Allee, Leverkusen, Germany, D-51368 |
| Public contact | Therapeutic Area Head, Bayer AG, clinical-trialscontact@bayer.com |
| Scientific contact | Therapeutic Area Head, Bayer AG, clinical-trialscontact@bayer.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 | 23 May 2019 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 23 May 2019 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To investigate changes of apnoea-hypopnoea-index (AHI) within 4 hours after a single dose administration of BAY2253651.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator:

Placebo

| | |
|---|----------------|
| Actual start date of recruitment | 13 August 2018 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Switzerland: 30 |
| Country: Number of subjects enrolled | United Kingdom: 4 |
| Worldwide total number of subjects | 34 |
| EEA total number of subjects | 4 |

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) | 17 |
| From 65 to 84 years | 17 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Study was conducted at two study centers in Switzerland and United Kingdom, between 13-Aug-2018 2018 (first subject first visit) and 23-May-2019 (study termination).

Pre-assignment

Screening details:

Overall, 168 subjects were screened at the two study centers in Switzerland and United Kingdom. 134 subjects failed screening. 34 subjects were randomized with recurring OSA of moderate to severe degree.

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Study Part A |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-------------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Part A single dose BAY2253651 |

Arm description:

Subjects received single dose 100 µg (500 µg/ml * 200 µl) BAY2253651 intranasally

| | |
|--|-----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | BAY2253651 |
| Investigational medicinal product code | BAY2253651 |
| Other name | |
| Pharmaceutical forms | Nasal spray, solution |
| Routes of administration | Nasal use |

Dosage and administration details:

Subjects received single dose 100 µg (500 µg/ml * 200 µl) BAY2253651 intranasally

| | |
|------------------|----------------------------|
| Arm title | Part A single dose Placebo |
|------------------|----------------------------|

Arm description:

Subjects received single dose matching Placebo

| | |
|--|-----------------------|
| Arm type | Placebo |
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Nasal spray, solution |
| Routes of administration | Nasal use |

Dosage and administration details:

Subjects received single dose matching Placebo

| Number of subjects in period 1 | Part A single dose BAY2253651 | Part A single dose Placebo |
|---|----------------------------------|-------------------------------|
| Started | 17 | 17 |
| Completed | 16 | 15 |
| Not completed | 1 | 2 |
| Criteria for analysis set not fulfilled | 1 | 2 |

Period 2

| | |
|------------------------------|----------------|
| Period 2 title | Study Part B |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

Single arm, open label

Arms

| | |
|--|---------------------------------|
| Arm title | Part B multiple dose BAY2253651 |
| Arm description: | |
| 5 days with repetitive once daily doses of 100µg intra-nasally before bed rest | |
| Arm type | Experimental |
| Investigational medicinal product name | BAY2253651 |
| Investigational medicinal product code | BAY2253651 |
| Other name | |
| Pharmaceutical forms | Nasal spray, solution |
| Routes of administration | Nasal use |

Dosage and administration details:

Subjects received multiple dose
100 µg (500 µg/ml * 200 µl)
BAY2253651 intranasally once
daily on 5 consecutive nights

| Number of subjects in period 2 ^[1] | Part B multiple dose BAY2253651 |
|--|------------------------------------|
| Started | 10 |
| Completed | 6 |
| Not completed | 4 |
| Criteria for analysis set not fulfilled | 4 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Per Protocol Set - Part B included subjects of the Per Protocol Set Part A who additionally had dosed him/herself on at least 4 of the 5 consecutive nights with 100µg BAY 2253651 intranasally only

Baseline characteristics

Reporting groups

| | |
|---|-------------------------------|
| Reporting group title | Part A single dose BAY2253651 |
| Reporting group description: | |
| Subjects received single dose 100 µg (500 µg/ml * 200 µl) BAY2253651 intranasally | |
| Reporting group title | Part A single dose Placebo |
| Reporting group description: | |
| Subjects received single dose matching Placebo | |

| Reporting group values | Part A single dose BAY2253651 | Part A single dose Placebo | Total |
|--|-------------------------------|----------------------------|-------|
| Number of subjects | 17 | 17 | 34 |
| 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) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 5 | 12 | 17 |
| From 65-84 years | 12 | 5 | 17 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous Units: years | | | |
| median | 59.0 | 70.0 | |
| full range (min-max) | 46.0 to 70.0 | 57.0 to 75.0 | - |
| Gender Categorical Units: Subjects | | | |
| Female | 3 | 9 | 12 |
| Male | 14 | 8 | 22 |

Subject analysis sets

| | |
|---|---|
| Subject analysis set title | Study part A: Per Protocol Set (PPS) - BAY2253651 |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| PPS included all subjects: | |
| <ul style="list-style-type: none"> received at least one dose of study drug had a valid AHI by PSG in a sleep laboratory on the third and fourth night of CPAP withdrawal and did not have an important deviation from the protocol or validity finding having an impact on the primary PD variable. | |
| Subject analysis set title | Study part A: Per Protocol Set (PPS) - Placebo |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| PPS included all subjects: | |
| <ul style="list-style-type: none"> received at least one dose of study drug had a valid AHI by PSG in a sleep laboratory on the third and fourth night of CPAP withdrawal | |

and

- did not have an important deviation from the protocol or validity finding having an impact on the primary PD variable.

| | |
|----------------------------|---|
| Subject analysis set title | Study part B: Per Protocol Set (PPS) - BAY2253651 |
| Subject analysis set type | Per protocol |

Subject analysis set description:

Per Protocol Set - Part B included all subjects of the Per Protocol Set who additionally:

- participated in part B and
- had dosed him/herself on at least 4 of the 5 consecutive nights with 100µg BAY 2253651 intranasally

| Reporting group values | Study part A: Per Protocol Set (PPS) - BAY2253651 | Study part A: Per Protocol Set (PPS) - Placebo | Study part B: Per Protocol Set (PPS) - BAY2253651 |
|--|---|--|---|
| Number of subjects | 16 | 15 | 6 |
| 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) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 11 | 4 | 4 |
| From 65-84 years | 5 | 11 | 2 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: years | | | |
| median | 58.6 | 68.2 | 63.0 |
| full range (min-max) | 46.0 to 70.0 | 57.0 to 75.0 | 54 to 75 |
| Gender Categorical | | | |
| Units: Subjects | | | |
| Female | 3 | 7 | 2 |
| Male | 13 | 8 | 4 |

End points

End points reporting groups

| | |
|---|---|
| Reporting group title | Part A single dose BAY2253651 |
| Reporting group description: | |
| Subjects received single dose 100 µg (500 µg/ml * 200 µl) BAY2253651 intranasally | |
| Reporting group title | Part A single dose Placebo |
| Reporting group description: | |
| Subjects received single dose matching Placebo | |
| Reporting group title | Part B multiple dose BAY2253651 |
| Reporting group description: | |
| 5 days with repetitive once daily doses of 100µg intra-nasally before bed rest | |
| Subject analysis set title | Study part A: Per Protocol Set (PPS) - BAY2253651 |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| PPS included all subjects: | |
| <ul style="list-style-type: none">received at least one dose of study drughad a valid AHI by PSG in a sleep laboratory on the third and fourth night of CPAP withdrawal anddid not have an important deviation from the protocol or validity finding having an impact on the primary PD variable. | |
| Subject analysis set title | Study part A: Per Protocol Set (PPS) - Placebo |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| PPS included all subjects: | |
| <ul style="list-style-type: none">received at least one dose of study drughad a valid AHI by PSG in a sleep laboratory on the third and fourth night of CPAP withdrawal anddid not have an important deviation from the protocol or validity finding having an impact on the primary PD variable. | |
| Subject analysis set title | Study part B: Per Protocol Set (PPS) - BAY2253651 |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| Per Protocol Set - Part B included all subjects of the Per Protocol Set who additionally: | |
| <ul style="list-style-type: none">participated in part B andhad dosed him/herself on at least 4 of the 5 consecutive nights with 100µg BAY 2253651 intranasally | |

Primary: The rate of the responders: changes of apnoea-hypopnoea-index (AHI)

| | |
|--|--|
| End point title | The rate of the responders: changes of apnoea-hypopnoea-index (AHI) ^[1] |
| End point description: | |
| A responder is defined by the reduction of the AHI (over 0-4h) from baseline by ≥ 50% after a single dose administration of BAY2253651 | |
| End point type | Primary |
| End point timeframe: | |
| Apnoea-hypopnoea-index (AHI) (over 0-4h) obtained by polysomnography (PSG) at Visits 1 and 2 | |

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: Descriptive statistics were done, no inferential statistical analyses were planned for this endpoint.

| End point values | Study part A: Per Protocol Set (PPS) - BAY2253651 | Study part A: Per Protocol Set (PPS) - Placebo | | |
|---|--|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 16 | 15 | | |
| Units: Percentage | | | | |
| number (not applicable) | | | | |
| Reduction of AHI (0-4h) from baseline by $\geq 50\%$ | 6.3 | 6.7 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number and severity of treatment emergent adverse events (TEAEs) - Part A

| | |
|---|---|
| End point title | Number and severity of treatment emergent adverse events (TEAEs) - Part A |
| End point description: SAF | |
| End point type | Secondary |
| End point timeframe: From the start of study medication administration up to 2 days after the end of treatment with study medication | |

| End point values | Part A single dose BAY2253651 | Part A single dose Placebo | | |
|--|-------------------------------------|-------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 17 | | |
| Units: Subjects | | | | |
| Any AE | 12 | 9 | | |
| Intensity for any AE: mild | 11 | 8 | | |
| Intensity for any AE: moderate | 1 | 0 | | |
| Any study drug related AE | 11 | 8 | | |
| Intensity for study drug related AE: mild | 11 | 7 | | |
| Intensity for study drug related AE: severe | 0 | 1 | | |
| Any AE related to protocol procedures | 1 | 1 | | |
| Any AE leading to discontinuation of study drug | 0 | 0 | | |
| Any SAE | 0 | 0 | | |
| Study drug related SAEs | 0 | 0 | | |
| SAE related to protocol procedures | 0 | 0 | | |
| SAE leading to discontinuation of study drug | 0 | 0 | | |
| AE with the outcome death | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number and severity of treatment emergent adverse events (TEAEs) - Part B

| | |
|-----------------|---|
| End point title | Number and severity of treatment emergent adverse events (TEAEs) - Part B |
|-----------------|---|

End point description:

SAF

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

End point timeframe:

From the start of study medication administration up to 2 days after the end of treatment with study medication

| | | | | |
|--|---------------------------------|--|--|--|
| End point values | Part B multiple dose BAY2253651 | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 6 | | | |
| Units: Subjects | | | | |
| Any AE | 5 | | | |
| Intensity for any AE: mild | 5 | | | |
| Any BAY 2253651 related AE | 5 | | | |
| Intensity for BAY 2253651 related AE: mild | 5 | | | |
| Any AE related to protocol procedures | 0 | | | |
| Any AE leading to discontinuation of BAY 2253651 | 0 | | | |
| Any SAE | 0 | | | |
| BAY 2253651 related SAEs | 0 | | | |
| SAE related to protocol procedures | 0 | | | |
| SAE leading to discontinuation of BAY 2253651 | 0 | | | |
| AE with the outcome death | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study treatment up to 2 days after end of treatment with study medication

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 22.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------|
| Reporting group title | BAY2253651 Part A |
|-----------------------|-------------------|

Reporting group description: -

| | |
|-----------------------|----------------|
| Reporting group title | Placebo Part A |
|-----------------------|----------------|

Reporting group description: -

| | |
|-----------------------|-------------------|
| Reporting group title | BAY2253651 Part B |
|-----------------------|-------------------|

Reporting group description: -

| Serious adverse events | BAY2253651 Part A | Placebo Part A | BAY2253651 Part B |
|---|-------------------|----------------|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 17 (0.00%) | 0 / 10 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | BAY2253651 Part A | Placebo Part A | BAY2253651 Part B |
|---|-------------------|-----------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 12 / 17 (70.59%) | 9 / 17 (52.94%) | 5 / 10 (50.00%) |
| Nervous system disorders | | | |
| Dysgeusia | | | |
| subjects affected / exposed | 7 / 17 (41.18%) | 2 / 17 (11.76%) | 3 / 10 (30.00%) |
| occurrences (all) | 7 | 2 | 3 |
| Head discomfort | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 17 (5.88%) | 0 / 10 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| General disorders and administration site conditions | | | |

| | | | |
|--|---------------------|----------------------|----------------------|
| Application site pain subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 17 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Thirst subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 17 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Eye disorders Visual impairment subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 17 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Gastrointestinal disorders Dry mouth subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 2 / 17 (11.76%) 2 | 2 / 10 (20.00%) 2 |
| Glossitis subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 17 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Glossodynia subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 17 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Toothache subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 17 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 17 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Dry throat subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 17 (5.88%) 1 | 1 / 10 (10.00%) 1 |
| Nasal congestion subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 17 (5.88%) 1 | 0 / 10 (0.00%) 0 |
| Nasal dryness subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 17 (5.88%) 1 | 0 / 10 (0.00%) 0 |

| | | | |
|--|----------------------|---------------------|----------------------|
| Throat irritation subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 17 (0.00%) 0 | 1 / 10 (10.00%) 1 |
| Throat tightness subjects affected / exposed occurrences (all) | 2 / 17 (11.76%) 2 | 0 / 17 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Intranasal paraesthesia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 17 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Laryngeal discomfort subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 17 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Pharyngeal hypoaesthesia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 17 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 17 (5.88%) 1 | 0 / 10 (0.00%) 0 |
| Pharyngeal paraesthesia subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 17 (5.88%) 1 | 0 / 10 (0.00%) 0 |
| Skin and subcutaneous tissue disorders Decubitus ulcer subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 17 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Skin discomfort subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 17 (5.88%) 1 | 0 / 10 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders Gouty arthritis subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 17 (0.00%) 0 | 0 / 10 (0.00%) 0 |
| Muscle spasms subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 17 (5.88%) 1 | 0 / 10 (0.00%) 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 06 August 2018 | Amendment 1, dated 06 Aug 2018 was issued to incorporate modifications requested by the British Competent Authority (MHRA). All changes were implemented prior to study start: <ul style="list-style-type: none">• Clarification of study inclusion criteria for adequate contraception• Inclusion of non-REM AHI for Polysomnography exploratory objectives and analysis• Standardization of blood pressure measurement• Updated Short Form Health Survey (SF-36, Version 2)• Removal of IxRS from drug accountability processes |
| 10 December 2018 | Amendment 2, dated 10 Dec 2018 was implemented to include the following modifications: <ul style="list-style-type: none">• Combining Visit 4 (Part A) and Visit 5 (Part B) study activities• Clarification of estimated AHI count procedures• Revised ODI screening range (Part A)• Manual adjustment of screening oximetry data• Repeat of non-evaluable CPAP assessments• Extension of screening phase from 6 to 12 weeks• Revised scheduling of assessments conducted at Screening Visit 2 and Visit 2• Addition of criteria for evaluating PSG assessment at Visit 2 |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date | Interruption | Restart date |
|-------------|-------------------|--------------|
| 23 May 2019 | Study termination | - |

Notes:

Limitations and caveats

None reported