



Clinical trial results:

A Double-Blind, Placebo-Controlled, Randomized-Withdrawal, Multicenter Study of the Efficacy and Safety of JZP-258 in Subjects with Narcolepsy with Cataplexy

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2016-000426-20 |
| Trial protocol | GB CZ DE ES FR BE FI HR NL |
| Global end of trial date | 10 July 2019 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 23 July 2020 |
| First version publication date | 23 July 2020 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 15-006 |
|-----------------------|--------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Jazz Pharmaceuticals |
| Sponsor organisation address | 3180 Porter Drive, Palo Alto, California, United States, |
| Public contact | Director, Clinical Trial Disclosure & Transparency, Jazz Pharmaceuticals, ClinicalTrialDisclosure@JazzPharma.com |
| Scientific contact | Director, Clinical Trial Disclosure & Transparency, Jazz Pharmaceuticals, ClinicalTrialDisclosure@JazzPharma.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 | 10 July 2019 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 July 2019 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of JZP-258 in the treatment of cataplexy and excessive daytime sleepiness (EDS) in subjects with narcolepsy.

Protection of trial subjects:

Safety was assessed by the incidence of observed and reported adverse events (AEs), and changes in electrocardiograms (ECGs), clinical laboratory tests, vital signs, and the Columbia-Suicide Severity Rating Scale (C-SSRS). Safety was assessed throughout the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 14 March 2017 |
| 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 | United States: 79 |
| Country: Number of subjects enrolled | Netherlands: 1 |
| Country: Number of subjects enrolled | Poland: 12 |
| Country: Number of subjects enrolled | Spain: 36 |
| Country: Number of subjects enrolled | United Kingdom: 3 |
| Country: Number of subjects enrolled | Belgium: 9 |
| Country: Number of subjects enrolled | Czech Republic: 26 |
| Country: Number of subjects enrolled | Finland: 12 |
| Country: Number of subjects enrolled | France: 7 |
| Country: Number of subjects enrolled | Germany: 16 |
| Worldwide total number of subjects | 201 |
| EEA total number of subjects | 122 |

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) | 195 |
| From 65 to 84 years | 6 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects were evaluated for eligibility during the Screening Period (up to 30 days).

Period 1

| | |
|------------------------------|------------------------------------|
| Period 1 title | Open Label Treatment and Titration |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------|--------------------|
| Arm title | Open-label JZP-258 |
|------------------|--------------------|

Arm description:

All 201 subjects entered the Open Label Optimized Treatment and Titration Period (OL OTP) and received at least 1 dose of study drug. During the OL OTP (12 weeks), eligible subjects were transitioned to JZP-258 treatment based on their pre-treatment status.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | JZP-258 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

During the Open-label Treatment and Titration Period (12 weeks), eligible subjects were transitioned to JZP-258 (0.5 g/mL.) treatment based on their pretreatment status (Xyrem, Xyrem and a non-Xyrem antiepileptic, non-Xyrem antiepileptic only, or no antiepileptic).

| Number of subjects in period 1 | Open-label JZP-258 |
|--------------------------------|--------------------|
| Started | 201 |
| Completed | 155 |
| Not completed | 46 |
| Physician decision | 3 |
| Consent withdrawn by subject | 6 |
| Non-Compliance with Study Drug | 4 |
| Adverse event, non-fatal | 18 |
| Other | 1 |
| Sponsor Decision | 2 |
| Lost to follow-up | 3 |
| Lack of efficacy | 1 |
| Protocol deviation | 8 |

Period 2

| | |
|------------------------------|-----------------------------|
| Period 2 title | Stable Dose |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|-----------|--------------------|
| Arm title | Open-label JZP-258 |
|-----------|--------------------|

Arm description:

During the Stable Dose Period, subjects received open-label JZP-258 at the same unchanged dose that they received during the last 2 weeks of the Open Label Treatment and Titration Period.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | JZP-258 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Open-label JZP-258 (0.5 g/ mL) at the same unchanged dose as during the last 2 weeks of the Open Label Treatment and Titration Period.

| | |
|---|--------------------|
| Number of subjects in period 2^[1] | Open-label JZP-258 |
| Started | 149 |
| Completed | 144 |
| Not completed | 5 |
| Adverse event, non-fatal | 1 |
| Lost to follow-up | 1 |
| Protocol deviation | 3 |

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: Of the 201 subjects that entered the Open-label Treatment and Titration Period, 149 achieved a tolerable and efficacious dose of JZP-258 and entered the Stable Dose Period. Of those subjects, 136 were randomized.

Period 3

| | |
|------------------------------|------------------------------------|
| Period 3 title | Double Blind Randomized Withdrawal |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|---------|
| Arm title | JZP-258 |
|------------------|---------|

Arm description:

JZP-258 at the dose taken during the last 2 weeks of the Stable Dose Period.

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | JZP-258 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

JZP-258 (0.5 g/mL) at the dose taken during the last 2 weeks of the Stable Dose Period

| | |
|------------------|---------|
| Arm title | Placebo |
|------------------|---------|

Arm description:

A matching oral solution to JZP-258.

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

Dosage and administration details:

A matching oral solution to JZP-258.

| Number of subjects in period 3 ^[2] | JZP-258 | Placebo |
|--|---------|---------|
| | | |
| Started | 69 | 67 |
| Completed | 69 | 59 |
| Not completed | 0 | 8 |
| Randomized in error | - | 2 |
| Consent withdrawn by subject | - | 1 |
| Adverse event, non-fatal | - | 3 |
| Lack of efficacy | - | 2 |

Notes:

[2] - 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: After completing the Stable Dose Period, 136 subjects were randomized. Two subjects were randomized in error, but did not receive any dose of study drug in the DB RWP. Therefore, 134 subjects received at least 1 dose of study drug in the DB RWP.

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------------------------|
| Reporting group title | Open Label Treatment and Titration |
|-----------------------|------------------------------------|

Reporting group description: -

| Reporting group values | Open Label Treatment and Titration | Total | |
|--|------------------------------------|-------|--|
| Number of subjects | 201 | 201 | |
| 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) | 195 | 195 | |
| From 65-84 years | 6 | 6 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 122 | 122 | |
| Male | 79 | 79 | |

End points

End points reporting groups

| | |
|---|--------------------|
| Reporting group title | Open-label JZP-258 |
| Reporting group description: All 201 subjects entered the Open Label Optimized Treatment and Titration Period (OL OTTP) and received at least 1 dose of study drug. During the OL OTTP (12 weeks), eligible subjects were transitioned to JZP-258 treatment based on their pre-treatment status. | |
| Reporting group title | Open-label JZP-258 |
| Reporting group description: During the Stable Dose Period, subjects received open-label JZP-258 at the same unchanged dose that they received during the last 2 weeks of the Open Label Treatment and Titration Period. | |
| Reporting group title | JZP-258 |
| Reporting group description: JZP-258 at the dose taken during the last 2 weeks of the Stable Dose Period. | |
| Reporting group title | Placebo |
| Reporting group description: A matching oral solution to JZP-258. | |

Primary: Change in Average Weekly Number of Cataplexy Attacks

| | |
|---|--|
| End point title | Change in Average Weekly Number of Cataplexy Attacks |
| End point description: Subjects completed a daily Cataplexy Frequency Diary each night prior to bedtime. Subjects were to record the number of cataplexy attacks that they had each day. | |
| End point type | Primary |
| End point timeframe: From the two weeks of the Stable-Dose Period to the two weeks of the Double Blind Randomized Withdrawal Period. | |

| End point values | JZP-258 | Placebo | | |
|---------------------------------------|----------------------|----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 | 65 | | |
| Units: Number | | | | |
| median (inter-quartile range (Q1-Q3)) | 0.00 (-0.49 to 1.75) | 2.35 (0.00 to 11.61) | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Change in Weekly Number of Cataplexy Attacks |
| Comparison groups | JZP-258 v Placebo |

| | |
|---|-------------------|
| Number of subjects included in analysis | 134 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Rank-based ANCOVA |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.044 |
| upper limit | -1.5 |

Secondary: Change in Epworth Sleepiness Scale (ESS) Score

| | |
|---|--|
| End point title | Change in Epworth Sleepiness Scale (ESS) Score |
| End point description: This is the key secondary endpoint. The Epworth Sleepiness Scale (ESS) is a self-administered questionnaire with 8 questions asking the subject how likely they would be to doze off or fall asleep in different situations. | |
| End point type | Secondary |
| End point timeframe: From the end of the Stable Dose Period to the end of the Double Blind Randomized Withdrawal Period | |

| End point values | JZP-258 | Placebo | | |
|---------------------------------------|--------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 | 65 | | |
| Units: Point on Scale | | | | |
| median (inter-quartile range (Q1-Q3)) | 0.00 (-1.0 to 1.0) | 2.0 (0.00 to 5.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Patient Global Impression of Change (PGIc) for Narcolepsy Overall

| | |
|---|---|
| End point title | Patient Global Impression of Change (PGIc) for Narcolepsy Overall |
| End point description: At the end of the Double Blind Randomized Withdrawal Period, subjects rated the change in their condition on a 7-point scale ranging from 1 = "very much improved" to 7 = "very much worse" since the last visit. This endpoint measures the percentage of subjects with worsening PGIc scores for narcolepsy overall (defined as scores of Much Worse or Very Much Worse). | |
| End point type | Secondary |
| End point timeframe: At the end of the Double Blind Randomized Withdrawal Period. | |

| End point values | JZP-258 | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 69 | 65 | | |
| Units: subjects | | | | |
| number (not applicable) | 3 | 29 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Global Impression of Change (CGIc) for Narcolepsy Overall

| | |
|-----------------|--|
| End point title | Clinical Global Impression of Change (CGIc) for Narcolepsy Overall |
|-----------------|--|

End point description:

At the end of the Double Blind Randomized Withdrawal Period, Investigators rated their impression of any change in the severity of the subject's narcolepsy overall condition since the start of the Double Blind Randomized Withdrawal Period on a 7-point scale ranging from 1 = "very much improved" to 7 = "very much worse". This endpoint measures the percentage of subjects with worsening CGIc scores for narcolepsy overall, defined as scores of Much Worse or Very Much Worse.

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

End point timeframe:

At the end of the Double Blind Randomized Withdrawal Period.

| End point values | JZP-258 | Placebo | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 68 | 65 | | |
| Units: subjects | | | | |
| number (not applicable) | 4 | 39 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in 36-Item Short Form Health Survey Version 2 (SF-36v2) Scores

| | |
|-----------------|---|
| End point title | Change in 36-Item Short Form Health Survey Version 2 (SF-36v2) Scores |
|-----------------|---|

End point description:

The SF-36v2 is a multi-purpose, short-form health survey with 36 questions/ items. It yields an 8-scale profile of functional health and well-being scores as well as a psychometrically-based physical and mental overall component summary measures.

Two summary scores were derived using the SF-36v2. Physical Component Summary measures dimensions of functional health that are meaningful to respondents, including the impact of health and health-related changes on physical function, pain, and the ability to carry out daily roles. The Mental Component Summary component scale measures the impact of health and health-related changes on well-being, including vitality, social function, and emotional well-being.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At the end of the Double Blind Randomized Withdrawal Period. | |

| End point values | JZP-258 | Placebo | | |
|---------------------------------------|-----------------------|-----------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 67 | 65 | | |
| Units: Score | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Physical Component Summary | -0.03 (-2.07 to 2.41) | -1.92 (-3.46 to 1.73) | | |
| Mental Component Summary | 1.55 (-1.88 to 3.78) | -1.92 (-6.28 to 1.34) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change in EQ-5D-5L Crosswalk Index Score and Visual Analog Scale

| | |
|-----------------|--|
| End point title | Change in EQ-5D-5L Crosswalk Index Score and Visual Analog Scale |
|-----------------|--|

End point description:

The EQ-5D-5L is a standardized instrument for use as a measure of health outcome that includes a descriptive system consisting of 5 dimensions (mobility, self-care, usual activities, pain/ discomfort, and anxiety/ depression). The EQ-5D-5L includes five levels of severity for each of the 5 dimensions of the descriptive system (1= no problems, 2= slight problems, 3= moderate problems, 4= severe problems, and 5= extreme problems) that reflect increasing levels of difficulty. Subjects completed the EQ-5D-5L at the end of the OL SDP and the end of the DB RWP by selecting the most appropriate level in each of the 5 dimensions.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At the end of the Double Blind Randomized Withdrawal Period. | |

| End point values | JZP-258 | Placebo | | |
|---------------------------------------|----------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 68 ^[1] | 65 | | |
| Units: score | | | | |
| median (inter-quartile range (Q1-Q3)) | | | | |
| Crosswalk index | 0.00 (-0.01 to 0.03) | 0.00 (-0.05 to 0.03) | | |
| VAS Score | 0.00 (0.00 to 5.00) | -5.00 (-10.00 to 5.00) | | |

Notes:

[1] - There were 68 JZP-258 subjects included in the Crosswalk Index, and 69 in the VAS Score.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Safety data are summarized for all subjects who received at least 1 dose of study medication across all periods.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 19.1 |

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | JZP-258 |
|-----------------------|---------|

Reporting group description: -

| | |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events | JZP-258 | Placebo | |
|---|-----------------|----------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 5 / 201 (2.49%) | 2 / 65 (3.08%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| Muscle enzyme increased | | | |
| subjects affected / exposed | 0 / 201 (0.00%) | 1 / 65 (1.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Invasive ductal breast carcinoma | | | |
| subjects affected / exposed | 1 / 201 (0.50%) | 0 / 65 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 1 / 201 (0.50%) | 0 / 65 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |

| | | | |
|---|-----------------|----------------|--|
| Peripheral nerve paresis | | | |
| subjects affected / exposed | 1 / 201 (0.50%) | 0 / 65 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Bile duct stone | | | |
| subjects affected / exposed | 1 / 201 (0.50%) | 0 / 65 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 201 (0.50%) | 0 / 65 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hallucination | | | |
| subjects affected / exposed | 1 / 201 (0.50%) | 0 / 65 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 201 (0.00%) | 1 / 65 (1.54%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral cardiomyopathy | | | |
| subjects affected / exposed | 1 / 201 (0.50%) | 0 / 65 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | JZP-258 | Placebo | |
|---|--------------------|------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 108 / 201 (53.73%) | 12 / 65 (18.46%) | |
| Nervous system disorders | | | |

| | | | |
|--|-------------------------|---------------------|--|
| Cataplexy subjects affected / exposed occurrences (all) | 21 / 201 (10.45%) 23 | 5 / 65 (7.69%) 6 | |
| Dizziness subjects affected / exposed occurrences (all) | 23 / 201 (11.44%) 34 | 0 / 65 (0.00%) 0 | |
| Headache subjects affected / exposed occurrences (all) | 45 / 201 (22.39%) 85 | 1 / 65 (1.54%) 1 | |
| Somnolence subjects affected / exposed occurrences (all) | 5 / 201 (2.49%) 5 | 6 / 65 (9.23%) 6 | |
| Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) | 13 / 201 (6.47%) 16 | 0 / 65 (0.00%) 0 | |
| Nausea subjects affected / exposed occurrences (all) | 27 / 201 (13.43%) 32 | 0 / 65 (0.00%) 0 | |
| Infections and infestations Influenza subjects affected / exposed occurrences (all) | 17 / 201 (8.46%) 21 | 1 / 65 (1.54%) 1 | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 19 / 201 (9.45%) 21 | 2 / 65 (3.08%) 2 | |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 11 / 201 (5.47%) 16 | 0 / 65 (0.00%) 0 | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 15 / 201 (7.46%) 16 | 1 / 65 (1.54%) 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 05 August 2016 | Clinical Protocol Amendment 1.0 |
| 07 November 2016 | Updates to the efficacy population and statistical methodology. |
| 10 April 2017 | Updates to the efficacy population. |
| 15 December 2017 | Addition of a 6-month OLE. |
| 15 May 2018 | Addition of a planned interim analysis in order to ensure the availability of study results at the earliest possible date in order to provide a low sodium treatment option alternative. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported