Clinical trial results:
A Twelve-Week, Double-Blind, Placebo-Controlled, Randomized, Parallel-Group, Multicenter Study of the Safety and Efficacy of JZP 110 [(R)-2-amino-3-phenylpropylcarbamate hydrochloride] in the Treatment of Excessive Sleepiness in Subjects with Obstructive Sleep Apnea (OSA)

Summary

EudraCT number	2014-005514-31
Trial protocol	DE NL
Global end of trial date	23 December 2016

Results information

Result version number	v1 (current)
This version publication date	07 January 2018
First version publication date	07 January 2018

Trial information

Trial identification

Sponsor protocol code	14-003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02348606
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Jazz Pharmaceuticals
Sponsor organisation address	3180 Porter Drive, Palo Alto, United States, 94304
Public contact	Clinical Trial Disclosure & Transparency, Jazz Pharmaceuticals Inc., 001 2158323661,
Scientific contact	Clinical Trial Disclosure & Transparency, Jazz Pharmaceuticals Inc., 001 2158323661,

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	03 March 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 December 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of JZP-110 administered once daily for up to 12 weeks in doses of 37.5, 75, 150, and 300 mg compared to placebo in the treatment of excessive sleepiness in adult subjects with OSA.

Protection of trial subjects:

Safety was assessed by the incidence of observed and reported adverse events (AEs), and changes in physical examination findings, electrocardiograms (ECGs), clinical laboratory tests, vital signs, 24-hour ABPM, 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	01 April 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	40 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	United States: 448
Worldwide total number of subjects	474
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)	391
From 65 to 84 years	83
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Note: 476 subjects were enrolled and randomized, however 2 subjects never received drug. This resulted in 474 subjects comprising the safety population.

Pre-assignment

Screening details:

During screening, subjects completed a medical exam. An overnight PSG assessment followed by MWT and 24-hour ABPM were conducted at baseline. After successful completion of the screening and baseline visits subjects were randomized in a 1:1:2:2:2 ratio to receive 37.5, 75, 150, or 300 mg JZP-110 or placebo.

Period 1

Period 1 title	Treatment Phase (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo condition.

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

Dosage and administration details:

Placebo administered orally, QD, for the 12 week treatment phase.

Arm title	37.5 mg JZP-110

Arm description:

37.5 mg JZP-110

Arm type	Experimental
Investigational medicinal product name	JZP-110
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

37.5 mg JZP-110 administered orally, QD, for the 12-week treatment phase.

Arm title	75 mg JZP-110

Arm description:

75 mg JZP-110

Arm type	Experimental

Investigational medicinal product name	JZP-110
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

75 mg JZP-110 administered orally, QD, for the 12-week treatment phase.

Arm title	150 mg JZP-110

Arm description:

150 mg JZP-110

Arm type	Experimental
Investigational medicinal product name	JZP-110
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to receive 150 mg JZP-110 initially received 75 mg JZP-110 from Day 1 through Day 3 of the treatment phase, and received 150 mg JZP-110 starting on Day 4, administered orally, QD.

Arm title	300 mg JZP-110

Arm description:

300 mg JZP-110

Arm type	Experimental
Investigational medicinal product name	JZP-110
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects randomized to receive 300 mg JZP-110 initially received 150 mg JZP-110 from Day 1 through Day 3 of the treatment phase and received 300 mg JZP-110 starting on Day 4, administered orally, QD.

Number of subjects in period 1	Placebo	37.5 mg JZP-110	75 mg JZP-110
Started	119	58	62
Completed	101	49	54
Not completed	18	9	8
Consent withdrawn by subject	4	2	2
Adverse event, non-fatal	4	3	2
Other reasons	6	3	4
Lost to follow-up	-	1	-
Treatment Noncompliant	2	-	-
Protocol deviation	2	-	-

Number of subjects in period 1	150 mg JZP-110	300 mg JZP-110
Started	117	118

Completed	106	94
Not completed	11	24
Consent withdrawn by subject	1	4
Adverse event, non-fatal	5	16
Other reasons	3	1
Lost to follow-up	-	2
Treatment Noncompliant	-	1
Protocol deviation	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo condition.	
Reporting group title	37.5 mg JZP-110
Reporting group description:	
37.5 mg JZP-110	
Reporting group title	75 mg JZP-110
Reporting group description:	
75 mg JZP-110	
Reporting group title	150 mg JZP-110
Reporting group description:	
150 mg JZP-110	
Reporting group title	300 mg JZP-110
Reporting group description:	
300 mg JZP-110	

Reporting group values	Placebo	37.5 mg JZP-110	75 mg JZP-110
Number of subjects	119	58	62
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 54.1 ± 11.41	 57.1 ± 10.19	 54.4 ± 11.46
Gender categorical Units: Subjects			
Female	42	19	27
Male	77	39	35

Reporting group values	150 mg JZP-110	300 mg JZP-110	Total
Number of subjects	117	118	474
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 52.7 ± 10.57	 53.2 ± 10.62	 -
Gender categorical Units: Subjects			
Female	45	44	177
Male	72	74	297

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description: Placebo condition.	
Reporting group title	37.5 mg JZP-110
Reporting group description: 37.5 mg JZP-110	
Reporting group title	75 mg JZP-110
Reporting group description: 75 mg JZP-110	
Reporting group title	150 mg JZP-110
Reporting group description: 150 mg JZP-110	
Reporting group title	300 mg JZP-110
Reporting group description: 300 mg JZP-110	

Primary: Change in Maintenance of Wakefulness Test (MWT) from Baseline to Week 12	
End point title	Change in Maintenance of Wakefulness Test (MWT) from Baseline to Week 12
End point description: Change in mean sleep latency time (in minutes) as determined from the first 4 trials of a 40-minute MWT from baseline to Week 12.	
End point type	Primary
End point timeframe: Baseline to Week 12	

End point values	Placebo	37.5 mg JZP-110	75 mg JZP-110	150 mg JZP-110
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	56	58	116
Units: minutes				
least squares mean (standard error)	0.21 (± 0.997)	4.74 (± 1.418)	9.08 (± 1.358)	10.96 (± 0.973)

End point values	300 mg JZP-110			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: minutes				
least squares mean (standard error)	12.99 (± 1.038)			

Statistical analyses

Statistical analysis title	Change in the MWT

Statistical analysis description:

A hierarchical testing procedure was used to make the following comparisons:

JZP-110 300 mg vs. Placebo: p <0.0001
JZP-110 150 mg vs. Placebo: p <0.0001
JZP-110 75 mg vs. Placebo: p <0.0001
JZP-110 37.5 mg vs. Placebo: p = .0086

Comparison groups	Placebo v 37.5 mg JZP-110 v 75 mg JZP-110 v 150 mg JZP-110 v 300 mg JZP-110
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	MMRM

Primary: Change in ESS Score from Baseline to Week 12

End point title	Change in ESS Score from Baseline to Week 12

End point description:

Change in ESS score from Baseline to Week 12. A negative change from baseline represents improvement in excessive sleepiness.

End point type	Primary

End point timeframe:

Baseline to Week 12

End point values	Placebo	37.5 mg JZP-110	75 mg JZP-110	150 mg JZP-110
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	56	58	116
Units: points on a scale				
least squares mean (standard error)	-3.3 (± 0.45)	-5.1 (± 0.64)	-5.0 (± 0.62)	-7.7 (± 0.44)

End point values	300 mg JZP-110			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: points on a scale				
least squares mean (standard error)	-7.9 (± 0.46)			

Statistical analyses

Statistical analysis title	Change in the ESS

Statistical analysis description:

A hierarchical testing procedure was used to make the following comparisons:

JZP-110 300 mg vs. Placebo: p <0.0001
JZP-110 150 mg vs. Placebo: p <0.0001
JZP-110 75 mg vs. Placebo: p = 0.0233
JZP-110 37.5 mg vs. Placebo: p = 0.0161

Comparison groups	Placebo v 37.5 mg JZP-110 v 75 mg JZP-110 v 150 mg JZP-110 v 300 mg JZP-110
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	MMRM

Secondary: Subjects Reported Improved on the Patient Global Impression of Change (PGIc) at Week 12

End point title	Subjects Reported Improved on the Patient Global Impression of Change (PGIc) at Week 12

End point description:

Percentage of subjects reported as improved (minimally, much, or very much) on the PGIc at Week 12.

This is the key secondary endpoint.

End point type	Secondary

End point timeframe:

Baseline to Week 12

End point values	Placebo	37.5 mg JZP-110	75 mg JZP-110	150 mg JZP-110
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	56	58	116
Units: percentage of subjects				
number (not applicable)	49.1	55.4	72.4	89.7

End point values	300 mg JZP-110			
Subject group type	Reporting group			
Number of subjects analysed	115			

Units: percentage of subjects				
number (not applicable)	88.7			

Statistical analyses

Statistical analysis title	Subjects Reported Improved on the PGIc at Week 12

Statistical analysis description:

A hierarchical testing procedure was used to make the following comparisons:

JZP-110 300 mg vs. Placebo: p <0.0001
JZP-110 150 mg vs. Placebo: p <0.0001
JZP-110 75 mg vs. Placebo: p = 0.0035
JZP-110 37.5 mg vs. Placebo: p = 0.4447

Comparison groups	Placebo v 37.5 mg JZP-110 v 75 mg JZP-110 v 150 mg JZP-110 v 300 mg JZP-110
Number of subjects included in analysis	459
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.05
Method	Chi-squared

Secondary: Change in Sleep Latency Time on each of the 5 MWT trials at Week 12

End point title	Change in Sleep Latency Time on each of the 5 MWT trials at Week 12

End point description:

Time course of efficacy in MWT: Change in sleep latency (in minutes) on each of the 5 MWT trials at week 12.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	37.5 mg JZP-110	75 mg JZP-110	150 mg JZP-110
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	56	58	116
Units: minutes				
least squares mean (standard error)				
Trial 1	-0.40 (± 1.327)	3.03 (± 1.881)	5.77 (± 1.808)	10.87 (± 1.284)
Trial 2	-0.44 (± 1.380)	6.93 (± 1.928)	9.47 (± 1.849)	11.91 (± 1.332)
Trial 3	0.58 (± 1.294)	3.59 (± 1.837)	11.32 (± 1.751)	11.50 (± 1.261)
Trial 4	1.29 (± 1.305)	6.11 (± 1.845)	9.04 (± 1.794)	8.93 (± 1.272)
Trial 5	0.18 (± 1.361)	3.57 (± 1.952)	7.75 (± 1.839)	8.05 (± 1.347)

End point values	300 mg JZP-110			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: minutes				
least squares mean (standard error)				
Trial 1	12.48 (± 1.401)			
Trial 2	14.94 (± 1.425)			
Trial 3	10.90 (± 1.340)			
Trial 4	11.94 (± 1.359)			
Trial 5	7.59 (± 1.432)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in the mean sleep latency time as determined from the first 4 trials of a 40-minute MWT from Baseline to Week 4

End point title	Change in the mean sleep latency time as determined from the first 4 trials of a 40-minute MWT from Baseline to Week 4

End point description:

Change in mean sleep latency time (in minutes) as determined from the first 4 trials of a 40-minute MWT from baseline to week 4.

End point type	Secondary

End point timeframe:

Baseline to Week 4

End point values	Placebo	37.5 mg JZP-110	75 mg JZP-110	150 mg JZP-110
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	56	58	116
Units: minutes				
least squares mean (standard error)	1.24 (± 0.942)	4.53 (± 1.360)	7.20 (± 1.307)	11.69 (± 0.932)

End point values	300 mg JZP-110			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: minutes				

least squares mean (standard error)	13.77 (± 0.976)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change in ESS Score from Baseline to Week 1, Week 4, and Week 8

End point title	Change in ESS Score from Baseline to Week 1, Week 4, and Week 8

End point description:

Change in ESS score from baseline to weeks 1, 4, and 8.

End point type	Secondary

End point timeframe:

Baseline to Weeks 1, 4, and 8

End point values	Placebo	37.5 mg JZP-110	75 mg JZP-110	150 mg JZP-110
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	56	58	116
Units: points on a scale				
least squares mean (standard error)				
Week 1	-2.6 (± 0.47)	-4.5 (± 0.66)	-4.4 (± 0.65)	-5.5 (± 0.46)
Week 4	-2.9 (± 0.45)	-4.7 (± 0.65)	-4.8 (± 0.63)	-6.1 (± 0.45)
Week 8	-3.8 (± 0.49)	-4.7 (± 0.70)	-6.3 (± 0.67)	-6.9 (± 0.48)

End point values	300 mg JZP-110			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: points on a scale				
least squares mean (standard error)				
Week 1	-6.6 (± 0.46)			
Week 4	-6.6 (± 0.46)			
Week 8	-7.7 (± 0.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Reported as Improved on the PGIc at Week 1,

Week 4, and Week 8

End point title	Percentage of Subjects Reported as Improved on the PGIc at Week 1, Week 4, and Week 8

End point description:

Percentage of subjects reported as improved (minimally, much, very much improved) on the PGIc at Weeks 1, 4, and 8.

End point type	Secondary

End point timeframe:

Weeks 1, 4, and 8

End point values	Placebo	37.5 mg JZP-110	75 mg JZP-110	150 mg JZP-110
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	56	58	116
Units: percentage of subjects				
number (not applicable)				
Week 1	47.4	58.9	65.5	78.3
Week 4	53.5	60.7	77.6	84.5
Week 8	57.0	57.1	79.3	88.8

End point values	300 mg JZP-110			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: percentage of subjects				
number (not applicable)				
Week 1	82.5			
Week 4	84.3			
Week 8	87.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects reported as improved on the CGIc at Week 12

End point title	Percentage of subjects reported as improved on the CGIc at Week 12

End point description:

Percentage of subjects reported as improved (minimally, much, very much) in CGIc at Week 12.

End point type	Secondary

End point timeframe:

Week 12

End point values	Placebo	37.5 mg JZP-110	75 mg JZP-110	150 mg JZP-110
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	56	58	116
Units: percentage of subjects				
number (not applicable)	49.1	58.9	70.7	90.5

End point values	300 mg JZP-110			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: percentage of subjects				
number (not applicable)	88.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Reported as Improved on the CGIc at Week 1, Week 4, and Week 8

End point title	Percentage of Subjects Reported as Improved on the CGIc at Week 1, Week 4, and Week 8

End point description:

Percentage of subjects reported as improved (minimally, much, very much) on the CGIc at Weeks 1, 4, and 8.

End point type	Secondary

End point timeframe:

Weeks 1, 4, and 8

End point values	Placebo	37.5 mg JZP-110	75 mg JZP-110	150 mg JZP-110
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	114	56	58	116
Units: percentage of subjects				
number (not applicable)				
Week 1	46.5	62.5	60.3	75.7
Week 4	52.6	60.7	77.6	85.2
Week 8	49.1	55.4	74.1	87.8

End point values	300 mg JZP-110			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: percentage of subjects				
number (not applicable)				
Week 1	82.6			
Week 4	81.7			
Week 8	87.8			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
The Safety Population consisted of all subjects who received at least 1 dose of study medication.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	37.5 mg JZP-110
Reporting group description: -	
Reporting group title	75 mg JZP-110
Reporting group description: -	
Reporting group title	150 mg JZP-110
Reporting group description: -	
Reporting group title	300 mg JZP-110
Reporting group description: -	

Serious adverse events	Placebo	37.5 mg JZP-110	75 mg JZP-110
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 119 (1.68%)	2 / 58 (3.45%)	0 / 62 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	1 / 119 (0.84%)	0 / 58 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Sciatica			
subjects affected / exposed	1 / 119 (0.84%)	0 / 58 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct obstruction			

subjects affected / exposed	0 / 119 (0.00%)	1 / 58 (1.72%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 119 (0.84%)	0 / 58 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 119 (0.84%)	0 / 58 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Streptococcal endocarditis			
subjects affected / exposed	0 / 119 (0.00%)	1 / 58 (1.72%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	0 / 119 (0.00%)	0 / 58 (0.00%)	0 / 62 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	150 mg JZP-110	300 mg JZP-110	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 117 (0.85%)	0 / 118 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Road traffic accident			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			

Sciatica			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct obstruction			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Streptococcal endocarditis			
subjects affected / exposed	0 / 117 (0.00%)	0 / 118 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 117 (0.85%)	0 / 118 (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	Placebo	37.5 mg JZP-110	75 mg JZP-110
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 119 (25.21%)	17 / 58 (29.31%)	21 / 62 (33.87%)
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 119 (8.40%)	4 / 58 (6.90%)	5 / 62 (8.06%)
occurrences (all)	13	4	5
General disorders and administration site conditions			
Feeling jittery			
subjects affected / exposed	0 / 119 (0.00%)	3 / 58 (5.17%)	3 / 62 (4.84%)
occurrences (all)	0	3	3
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	7 / 119 (5.88%)	3 / 58 (5.17%)	3 / 62 (4.84%)
occurrences (all)	7	3	3
Diarrhoea			
subjects affected / exposed	1 / 119 (0.84%)	1 / 58 (1.72%)	3 / 62 (4.84%)
occurrences (all)	2	1	3
Dry mouth			
subjects affected / exposed	2 / 119 (1.68%)	1 / 58 (1.72%)	1 / 62 (1.61%)
occurrences (all)	2	1	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 119 (0.00%)	3 / 58 (5.17%)	0 / 62 (0.00%)
occurrences (all)	0	5	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 119 (0.00%)	1 / 58 (1.72%)	2 / 62 (3.23%)
occurrences (all)	0	1	2
Insomnia			
subjects affected / exposed	2 / 119 (1.68%)	1 / 58 (1.72%)	0 / 62 (0.00%)
occurrences (all)	2	1	0
Irritability			
subjects affected / exposed	0 / 119 (0.00%)	3 / 58 (5.17%)	0 / 62 (0.00%)
occurrences (all)	0	3	0
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	8 / 119 (6.72%)	2 / 58 (3.45%)	1 / 62 (1.61%)
occurrences (all)	9	2	1
Sinusitis			
subjects affected / exposed	3 / 119 (2.52%)	1 / 58 (1.72%)	4 / 62 (6.45%)
occurrences (all)	3	2	4
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 119 (0.84%)	1 / 58 (1.72%)	3 / 62 (4.84%)
occurrences (all)	1	1	3

Non-serious adverse events	150 mg JZP-110	300 mg JZP-110	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 117 (35.04%)	60 / 118 (50.85%)	
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 117 (8.55%)	17 / 118 (14.41%)	
occurrences (all)	11	20	
General disorders and administration site conditions			
Feeling jittery			
subjects affected / exposed	1 / 117 (0.85%)	7 / 118 (5.93%)	
occurrences (all)	1	8	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	10 / 117 (8.55%)	12 / 118 (10.17%)	
occurrences (all)	11	16	
Diarrhoea			
subjects affected / exposed	5 / 117 (4.27%)	8 / 118 (6.78%)	
occurrences (all)	5	8	
Dry mouth			
subjects affected / exposed	5 / 117 (4.27%)	9 / 118 (7.63%)	
occurrences (all)	5	10	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 117 (0.85%)	0 / 118 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			

Anxiety			
subjects affected / exposed	6 / 117 (5.13%)	16 / 118 (13.56%)	
occurrences (all)	6	16	
Insomnia			
subjects affected / exposed	3 / 117 (2.56%)	11 / 118 (9.32%)	
occurrences (all)	3	12	
Irritability			
subjects affected / exposed	4 / 117 (3.42%)	1 / 118 (0.85%)	
occurrences (all)	4	1	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	7 / 117 (5.98%)	8 / 118 (6.78%)	
occurrences (all)	7	10	
Sinusitis			
subjects affected / exposed	0 / 117 (0.00%)	3 / 118 (2.54%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	9 / 117 (7.69%)	14 / 118 (11.86%)	
occurrences (all)	9	16	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 September 2015	This amendment made changes to the eligibility criteria.
08 February 2016	This amendment was made to further support enrollment of a representative patient sample, to clarify enrollment criteria, and to incorporate feedback from FDA about the proposed statistical analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported