Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Crossover On-Road Driving Study Assessing the Effect of JZP-110 on Driving Performance in Subjects with Excessive Sleepiness Due to Narcolepsy

Summary

EudraCT number	2015-003931-36
Trial protocol	NL DE
Global end of trial date	19 May 2019

Results information

Result version number	v1 (current)
This version publication date	17 June 2020
First version publication date	17 June 2020

Trial information

Trial identification

Sponsor protocol code	15-005

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02806908
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Jazz Pharmaceuticals Inc.
Sponsor organisation address	3170 Porter Drive, Palo Alto, United States, 94304
Public contact	Director, Disclosure & Transparency, Director, Disclosure & Transparency, 001 2158323750, ClinicalTrialDisclosure@JazzPharma.com
Scientific contact	Grace Wang, MD, Director, Disclosure & Transparency, 001 2158323750, 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	19 May 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 May 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

1. To evaluate the effect of JZP-110 on driving performance

Protection of trial subjects:

All subjects were to provide written informed consent, in accordance with local IEC/IRB requirements, before the performance of any study-related procedures.

Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	01 February 2016
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	Netherlands: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The screening phase involved a standard medical screening visit. Following screening, subjects entered the crossover treatment phase.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	No
Arm title	Placebo

Arm description:

Subjects received a single oral daily dose of placebo for 7 days in treatment period 1 or treatment period 2 in a counterbalanced order.

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

Dosage and administration details:

Subjects received a single oral daily dose of placebo for 7 days in Treatment Period 1 or Treatment Period 2 in a counterbalanced order.

Arm title	JZP-110

Arm description:

Subjects received a single oral daily dose of JZP-110 (150 mg/day for 3 days) then JZP-110 (300 mg/day for 4 days) during Treatment Period 1 or Treatment Period 2 in a counterbalanced order.

Arm type	Experimental
Investigational medicinal product name	solriamfetol
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single oral daily dose of JZP-110 (150 mg/day for 3 days) then JZP-110 (300 mg/day for 4 days) during Treatment Period 1 or Treatment Period 2 in a counterbalanced order.

Number of subjects in period 1	Placebo	JZP-110
Started	24	24
JZP-110/Placebo	11 [1]	11 [2]
Placebo/JZP-110	13 [3]	13 [4]
Completed	22	22
Not completed	2	2
Consent withdrawn by subject	1	1
Adverse event, non-fatal	1	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This was a crossover study where all subjects received placebo and JZP-110 in a counterbalanced order between treatment sequence 1 and treatment sequence 2. System error as system automatically doubles the enrollment.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This was a crossover study where all subjects received placebo and JZP-110 in a counterbalanced order between treatment sequence 1 and treatment sequence 2. System error as system automatically doubles the enrollment.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This was a crossover study where all subjects received placebo and JZP-110 in a counterbalanced order between treatment sequence 1 and treatment sequence 2. System error as system automatically doubles the enrollment.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: This was a crossover study where all subjects received placebo and JZP-110 in a counterbalanced order between treatment sequence 1 and treatment sequence 2. System error as system automatically doubles the enrollment.

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	24	24	
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	40.4		
standard deviation	± 11.84	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	13	13	

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received a single oral daily dose of placebo for 7 days in treatment period 1 or treatment period 2 in a counterbalanced order.	
Reporting group title	JZP-110
Reporting group description:	
Subjects received a single oral daily dose of JZP-110 (150 mg/day for 3 days) then JZP-110 (300 mg/day for 4 days) during Treatment Period 1 or Treatment Period 2 in a counterbalanced order.	

Primary: Standard Deviation of Lateral Position (SDLP) at 2 Hours Post-dose (Approximately at Tmax)

End point title	Standard Deviation of Lateral Position (SDLP) at 2 Hours Post-dose (Approximately at Tmax)
End point description:	
Subjects were instructed to drive with steady lateral position between the delineated boundaries of the slower (right) traffic lane, while maintaining a constant speed of 95 kilometers (km) per hour (hr). Deviation was measured by the vehicle's speed and lateral distance to the left lane line and was continuously recorded. Individual improvement was defined as a decrease in SDLP below the negative value of threshold; individual impairment was defined as an increase in SDLP above the threshold or failure to complete the driving test due to sleepiness or subjects related safety concerns.	
End point type	Primary
End point timeframe:	
2 hours post-dose	

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[1]	22[2]		
Units: centimeter (cm)				
median (full range (min-max))	20.46 (14.4 to 28.6)	19.08 (13.2 to 25.0)		

Notes:

[1] - The modified intent to treat (mITT) population consisted of 22 subjects.

[2] - The modified intent to treat (mITT) population consisted of 22 subjects.

Statistical analyses

Statistical analysis title	SDLP at 2 Hours Post-dose (Approximately at Tmax)
Statistical analysis description:	
The normality assumption, was not satisfied, therefore the Wilcoxon signed-rank test was used to compare the pairwise treatment differences for SDLP at 6 hours postdose. Total subjects in this analysis set was 22 for Placebo and 22 for JZP-110 not a total of 44 due to cross over design.	
Comparison groups	Placebo v JZP-110

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0022
Method	Wilcoxon signed-rank test

Secondary: SDLP at 6 Hours Post-dose

End point title	SDLP at 6 Hours Post-dose

End point description:

Subjects were instructed to drive with steady lateral position between the delineated boundaries of the slower (right) traffic lane, while maintaining a constant speed of 95 kilometers (km) per hour (hr). Deviation was measured by the vehicle's speed and lateral distance to the left lane line and was continuously recorded. Individual improvement was defined as a decrease in SDLP below the negative value of threshold; individual impairment was defined as an increase in SDLP above the threshold or failure to complete the driving test due to sleepiness or subjects related safety concerns.

End point type	Secondary

End point timeframe:

6 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[3]	22		
Units: cm				
median (full range (min-max))	19.78 (14.6 to 38.9)	19.59 (13.0 to 26.9)		

Notes:

[3] - Subjects in the mITT population missing an assessment for an endpoint were excluded in the analysis.

Statistical analyses

Statistical analysis title	SDLP at 6 Hours Post-dose

Statistical analysis description:

The normality assumption, was not satisfied, therefore the Wilcoxon signed-rank test was used to compare the pairwise treatment differences for SDLP at 6 hours postdose. Total subjects in this analysis set was 22 for Placebo and 22 for JZP-110 not a total of 44 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0416
Method	Wilcoxon signed-rank test

Secondary: Proportion of Subjects With Improved or Impaired Driving on JZP-110 Compared to Placebo 2 Hours Post-dose

End point title	Proportion of Subjects With Improved or Impaired Driving on JZP-110 Compared to Placebo 2 Hours Post-dose

End point description:

Improvement was defined as a decrease in SDLP comparing JZP-110 and placebo below the threshold and impairment was defined as an increase in SDLP above the threshold or failure to complete the driving test due to sleepiness or subjects related safety concerns. The maximum McNemar's statistic was used as the test statistic.

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[4]	22[5]		
Units: Number	0	0		

Notes:

[4] - The distribution of the change in driving performance (JZP-110/Placebo) could not be concluded.

[5] - The distribution of the change in driving performance (JZP-110/Placebo) could not be concluded.

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of Subjects with Improved or Impaired Driving on JZP-110 Compared to Placebo 6 Hours Post-dose

End point title	Proportion of Subjects with Improved or Impaired Driving on JZP-110 Compared to Placebo 6 Hours Post-dose

End point description:

Improvement was defined as a decrease in SDLP comparing JZP-110 and placebo below the threshold and impairment was defined as an increase in SDLP above the threshold or failure to complete the driving test due to sleepiness or subjects related safety concerns. The maximum McNemar’s statistic was used as the test statistic.

End point type	Secondary

End point timeframe:

6 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22[6]	22[7]		
Units: Number	0	0		

Notes:

[6] - The distribution of the change in driving performance (JZP-110/Placebo) could not be concluded.

[7] - The distribution of the change in driving performance (JZP-110/Placebo) could not be concluded.

Statistical analyses

No statistical analyses for this end point

Secondary: Standard Deviation of Speed (SDS) at 2 Hours Post-dose

End point title	Standard Deviation of Speed (SDS) at 2 Hours Post-dose

End point description:

Mean SDS was a common measure of the driver's ability to maintain a constant driving speed. Variations in driving speed were recorded and analyzed.

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: kilometers/hour (km/hr)				
least squares mean (standard error)	2.97 (± 0.151)	2.76 (± 0.151)		

Statistical analyses

Statistical analysis title	SDS 2 Hours Post-dose

Statistical analysis description:

The Driving Performance parameter was analyzed using a repeated mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), driving performance test (2 hours post-dose), treatment period, treatment sequence and treatment by driving performance test interaction as fixed effects and subject as a random effect. Total subjects in this analysis set was 22 for Placebo and 22 for JZP-110 not a total of 44 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1141
Method	ANOVA

Secondary: SDS at 6 Hours Post-dose

End point title	SDS at 6 Hours Post-dose

End point description:

Mean SDS was a common measure of the driver's ability to maintain a constant driving speed. Variations in driving speed were recorded and analyzed.

End point type	Secondary

End point timeframe:

6 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[8]	22		
Units: km/hr				
least squares mean (standard error)	3.18 (± 0.153)	3.08 (± 0.151)		

Notes:

[8] - Subjects in the mITT population missing an assessment for an endpoint were excluded in the analysis.

Statistical analyses

Statistical analysis title	SDS 6 Hours Post-dose

Statistical analysis description:

The Driving Performance parameter was analyzed using a repeated mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), driving performance test (6 hours post-dose), treatment period, treatment sequence and treatment by driving performance test interaction as fixed effects and subject as a random effect. Total subjects in this analysis set was 21 for Placebo and 22 for JZP-110 not a total of 43 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4441
Method	ANOVA

Secondary: Number of Lapses in Driving Test at 2 Hours Post-dose

End point title	Number of Lapses in Driving Test at 2 Hours Post-dose

End point description:

Number of driving lapses (also known as lane drift, was defined as deviations > 100 cm from the mean lateral position and from the absolute lateral position for 8 seconds. Driving performance will be assessed using a standardized on-road driving test on Day 7 (Visit 4) and on Day 14 (Visit 5). A practice driving test was done during the screening period to familiarize the subject with the vehicle and test scenario, assess if the subject could adequately operate the manual transmission vehicle, and determine if any safety concerns existed that excluded the subject from participating in the study.

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: number of lapses				
least squares mean (standard error)	3.26 (± 0.834)	2.27 (± 0.834)		

Statistical analyses

Statistical analysis title	Total Number of Lapses in Driving Test at 2 Hours

Statistical analysis description:

The Driving Performance parameter was analyzed using a repeated mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), driving performance test (2 hours post-dose), treatment period, treatment sequence and treatment by driving performance test interaction as fixed effects and subject as a random effect. Total subjects in this analysis set was 22 for Placebo and 22 for JZP-110 not a total of 44 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3423
Method	ANOVA

Secondary: Number of Lapses in Driving Test at 6 Hours Post-dose

End point title	Number of Lapses in Driving Test at 6 Hours Post-dose

End point description:

Number of driving lapses (also known as lane drift, was defined as deviations > 100 cm from the mean lateral position and from the absolute lateral position for 8 seconds. Driving performance will be assessed using a standardized on-road driving test on Day 7 (Visit 4) and on Day 14 (Visit 5). A practice driving test was done during the screening period to familiarize the subject with the vehicle and test scenario, assess if the subject could adequately operate the manual transmission vehicle, and determine if any safety concerns existed that excluded the subject from participating in the study.

End point type	Secondary

End point timeframe:

6 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21[9]	22		
Units: number of lapses				
least squares mean (standard error)	3.72 (± 0.844)	3.64 (± 0.834)		

Notes:

[9] - Subjects in the mITT population missing an assessment for an endpoint were excluded in the analysis.

Statistical analyses

Statistical analysis title	Total Number of Lapses in Driving Test at 6 Hours

Statistical analysis description:

The Driving Performance parameter was analyzed using a repeated mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), driving performance test (6 hours post-dose), treatment period, treatment sequence and treatment by driving performance test interaction as fixed effects and subject as a random effect. Total subjects in this analysis set was 21 for Placebo and 22 for JZP-110 not a total of 43 due to cross over design.

Comparison groups	Placebo v JZP-110

Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9384
Method	ANOVA

Secondary: Psychomotor Vigilance Test (PVT) Number of Lapses at 2 Hours Post-dose

End point title	Psychomotor Vigilance Test (PVT) Number of Lapses at 2 Hours Post-dose

End point description:

The PVT was administered at screening for practice only, and at predose and within 30 minutes before each driving test on Days 7 and 14
(Visits 4 and 5, respectively). The test was administered over 10 minutes with visual stimuli appearing randomly at variable intervals of 2 to 10
seconds. Subjects were instructed to respond to the appearance of a visual stimulus on a computer screen by pushing a response button as
quickly as possible. Lapses were measured as (RT > 500 msec).

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: RT>500 msec				
least squares mean (standard error)	7.47 (± 2.357)	3.04 (± 2.357)		

Statistical analyses

Statistical analysis title	PVT Number of Lapses at 2 Hours Post-dose

Statistical analysis description:

PVT was analyzed using a repeated mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), PVT test (2 hours post-dose), treatment period, treatment sequence and treatment by PVT test interaction as fixed effects and subject as a random effect. Number of errors of commission: number of responses without a stimulus, or false starts Inverse reaction time. Total subjects was 22 for Placebo and 22 for JZP-110 not a total of 44 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0939
Method	ANOVA

Secondary: PVT Number of Lapses at 6 Hours Post-dose

End point title	PVT Number of Lapses at 6 Hours Post-dose

End point description:

The PVT was administered at screening for practice only, and at predose and within 30 minutes before each driving test on Days 7 and 14
(Visits 4 and 5, respectively). The test was administered over 10 minutes with visual stimuli appearing randomly at variable intervals of 2 to 10
seconds. Subjects were instructed to respond to the appearance of a visual stimulus on a computer screen by pushing a response button as
quickly as possible. Lapses were measured as (RT > 500 msec).

End point type	Secondary

End point timeframe:

6 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: RT > 500 msec				
least squares mean (standard error)	9.88 (± 2.357)	3.81 (± 2.357)		

Statistical analyses

Statistical analysis title	PVT Number of Lapses at 6 Hours Post-dose

Statistical analysis description:

PVT was analyzed using a repeated mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), PVT test (6 hours post-dose), treatment period, treatment sequence and treatment by PVT test interaction as fixed effects and subject as a random effect. Number of errors of commission: number of responses without a stimulus, or false starts Inverse reaction time. Total subjects was 22 for Placebo and 22 for JZP-110 not a total of 44 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0246
Method	ANOVA

Secondary: PVT Mean Reaction Time at 2 Hours Post-dose

End point title	PVT Mean Reaction Time at 2 Hours Post-dose

End point description:

The PVT was administered at screening for practice only, and at predose and within 30 minutes before each driving test on Days 7 and 14
(Visits 4 and 5, respectively). The test was administered over 10 minutes with visual stimuli appearing randomly at variable intervals of 2 to 10
seconds. Subjects were instructed to respond to the appearance of a visual stimulus on a computer screen by pushing a response button as
quickly as possible. Mean RT is measured in msec.

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: msec				
least squares mean (standard error)	633.30 (± 162.286)	311.74 (± 162.286)		

Statistical analyses

Statistical analysis title	PVT Mean Reaction Time at 2 Hours Post-dose

Statistical analysis description:

PVT was analyzed using a repeated mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), PVT test (2 hours post-dose), treatment period, treatment sequence and treatment by PVT test interaction as fixed effects and subject as a random effect. Inverse reaction time: Each RT (ms) was divided by 1,000 and reciprocally transformed. The transformed values were then averaged. Total subjects was 22 for Placebo and 22 for JZP-110 not a total of 44 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1475
Method	ANOVA

Secondary: PVT Mean Reaction Time at 6 Hours Post-dose

End point title	PVT Mean Reaction Time at 6 Hours Post-dose

End point description:

The PVT was administered at screening for practice only, and at predose and within 30 minutes before each driving test on Days 7 and 14
(Visits 4 and 5, respectively). The test was administered over 10 minutes with visual stimuli appearing randomly at variable intervals of 2 to 10
seconds. Subjects were instructed to respond to the appearance of a visual stimulus on a computer screen by pushing a response button as
quickly as possible. Mean RT is measured In msec.

End point type	Secondary

End point timeframe:

6 hours post dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: msec				
least squares mean (standard error)	628.26 (± 162.286)	309.81 (± 162.286)		

Statistical analyses

Statistical analysis title	PVT Mean Reaction Time at 6 Hours Post-dose

Statistical analysis description:

PVT was analyzed using a repeated mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), PVT test (6 hours post-dose), treatment period, treatment sequence and treatment by PVT test interaction as fixed effects and subject as a random effect. Inverse reaction time: Each RT (ms) was divided by 1,000 and reciprocally transformed. The transformed values were then averaged. Total subjects was 22 for Placebo and 22 for JZP-110 not a total of 44 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1513
Method	ANOVA

Secondary: PVT Inverse Reaction Time at 2 Hours Post-dose

End point title	PVT Inverse Reaction Time at 2 Hours Post-dose

End point description:

The PVT was administered at screening for practice only, and at predose and within 30 minutes before each driving test on Days 7 and 14
(Visits 4 and 5, respectively). The test was administered over 10 minutes with visual stimuli appearing randomly at variable intervals of 2 to 10
seconds. Subjects were instructed to respond to the appearance of a visual stimulus on a computer screen by pushing a response button as
quickly as possible. Inverse reaction time was expressed as 1/reaction time in msec.

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: (1/RT(s))				
least squares mean (standard error)	3.36 (± 0.136)	3.82 (± 0.136)		

Statistical analyses

Statistical analysis title	PVT Inverse Reaction Time at 2 Hours Post-dose

Statistical analysis description:

PVT was analyzed using a repeated mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), PVT test (2 hours post-dose), treatment period, treatment sequence and treatment by PVT test interaction as fixed effects and subject as a random effect. Inverse reaction time: Each RT (ms) was divided by 1,000 and reciprocally transformed. The transformed values were then averaged. Total subjects was 22 for Placebo and 22 for JZP-110 not a total of 44 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	ANOVA

Secondary: PVT Inverse Reaction Time at 6 Hours Post-dose

End point title	PVT Inverse Reaction Time at 6 Hours Post-dose

End point description:

The PVT was administered at screening for practice only, and at predose and within 30 minutes before each driving test on Days 7 and 14
(Visits 4 and 5, respectively). The test was administered over 10 minutes with visual stimuli appearing randomly at variable intervals of 2 to 10
seconds. Subjects were instructed to respond to the appearance of a visual stimulus on a computer screen by pushing a response button as
quickly as possible. Inverse reaction time was expressed as 1/reaction time in msec.

End point type	Secondary

End point timeframe:

6 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: (1/RT(s))				
least squares mean (standard error)	3.34 (± 0.136)	3.77 (± 0.136)		

Statistical analyses

Statistical analysis title	PVT Inverse Reaction Time at 6 Hours Post-dose

Statistical analysis description:

PVT was analyzed using a repeated mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), PVT test (6 hours post-dose), treatment period, treatment sequence and treatment by PVT test interaction as fixed effects and subject as a random effect. Inverse reaction time: Each RT (ms) was divided by 1,000 and reciprocally transformed. The transformed values were then averaged. Total subjects was 22 for Placebo and 22 for JZP-110 not a total of 44 due to cross over design.

Comparison groups	Placebo v JZP-110

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0005
Method	ANOVA

Secondary: PVT Number of Errors of Commission at 2 Hours Post-dose

End point title	PVT Number of Errors of Commission at 2 Hours Post-dose

End point description:

The PVT was administered at screening for practice only, and at predose and within 30 minutes before each driving test on Days 7 and 14
(Visits 4 and 5, respectively). The test was administered over 10 minutes with visual stimuli appearing randomly at variable intervals of 2 to 10
seconds. Subjects were instructed to respond to the appearance of a visual stimulus on a computer screen by pushing a response button as
quickly as possible. Errors of commission were measured as the number of responses without a stimulus or false starts with (RT < 100 msec).

End point type	Secondary

End point timeframe:

2 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: RT < 100 msec				
least squares mean (standard error)	1.65 (± 0.439)	1.26 (± 0.439)		

Statistical analyses

Statistical analysis title	PVT Number of Errors of Commission at 2 Hours Post

Statistical analysis description:

PVT was analyzed using a repeated mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), PVT test (2 hours post-dose), treatment period, treatment sequence and treatment by PVT test interaction as fixed effects and subject as a random effect. Number of errors of commission: number of responses without a stimulus, or false starts Inverse reaction time. Total subjects was 22 for Placebo and 22 for JZP-110 not a total of 44 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4774
Method	ANOVA

Secondary: PVT Number of Errors of Commission at 6 Hours Post-dose

End point title	PVT Number of Errors of Commission at 6 Hours Post-dose

End point description:

The PVT was administered at screening for practice only, and at predose and within 30 minutes before each driving test on Days 7 and 14
(Visits 4 and 5, respectively). The test was administered over 10 minutes with visual stimuli appearing randomly at variable intervals of 2 to 10
seconds. Subjects were instructed to respond to the appearance of a visual stimulus on a computer screen by pushing a response button as
quickly as possible. Errors of commission were measured as the number of responses without a stimulus or false starts with (RT < 100 msec).

End point type	Secondary

End point timeframe:

6 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: RT < 100 msec				
least squares mean (standard error)	1.92 (± 0.439)	1.45 (± 0.439)		

Statistical analyses

Statistical analysis title	PVT Number of Errors of Commission at 6 Hours Post

Statistical analysis description:

PVT was analyzed using a repeated mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), PVT test (6 hours post-dose), treatment period, treatment sequence and treatment by PVT test interaction as fixed effects and subject as a random effect. Number of errors of commission: number of responses without a stimulus, or false starts Inverse reaction time. Total subjects was 22 for Placebo and 22 for JZP-110 not a total of 44 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3801
Method	ANOVA

Secondary: Toronto Hospital Alert Test (THAT)

End point title	Toronto Hospital Alert Test (THAT)

End point description:

The Toronto Hospital Alert Test (THAT) is a 10-item self-report questionnaire designed to measure perceived alertness in the preceding
week. The THAT was administered at baseline and the end of each treatment period. The total score of THAT can range between 0 to 50
where the higher score indicates greater alertness.

End point type	Secondary

End point timeframe:

post treatment

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	22		
Units: score on a scale				
least squares mean (standard error)	26.83 (± 1.400)	33.97 (± 1.397)		

Statistical analyses

Statistical analysis title	THAT

Statistical analysis description:

THAT was analyzed using a mixed effect ANOVA model. The model included treatment (JZP-110 and placebo), treatment period, treatment sequence as fixed effects and subject as a random effect. Total subjects in this analysis set was 22 for Placebo and 22 JZP-110 not a total of 44 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	ANOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from the time written informed consent was obtained until the final study visit or early termination.

Adverse event reporting additional description:

The Safety Population consisted of all subjects who received at least 1 dose of study medication. A treatment-emergent AE (TEAE), was defined as an AE that either began after first study drug dose or worsened after the first dose. When determining the percent of subjects who experienced an AE, multiple increases in severity were counted as one AE.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects received a single oral daily dose of placebo for 7 days

Reporting group title	JZP-110

Reporting group description:

Subjects received a single oral daily dose of JZP-110 (150 mg/day for 3 days) then JZP-110 (300 mg/day for 4 days)

Serious adverse events	Placebo	JZP-110	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	0 / 23 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Placebo	JZP-110	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 23 (26.09%)	17 / 23 (73.91%)	
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 23 (0.00%)	2 / 23 (8.70%)	
occurrences (all)	0	2	
Nervous system disorders			

Headache			
subjects affected / exposed	3 / 23 (13.04%)	4 / 23 (17.39%)	
occurrences (all)	3	4	
Somnolence			
subjects affected / exposed	2 / 23 (8.70%)	3 / 23 (13.04%)	
occurrences (all)	2	3	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 23 (4.35%)	2 / 23 (8.70%)	
occurrences (all)	1	2	
Psychiatric disorders			
Sleep disorder			
subjects affected / exposed	1 / 23 (4.35%)	3 / 23 (13.04%)	
occurrences (all)	1	3	
Agitation			
subjects affected / exposed	0 / 23 (0.00%)	3 / 23 (13.04%)	
occurrences (all)	0	3	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 23 (4.35%)	4 / 23 (17.39%)	
occurrences (all)	1	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported