

**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 Obstructive Sleep Apnea
Summary**

EudraCT number	2015-003930-28
Trial protocol	DE BE
Global end of trial date	28 May 2019

Results information

Result version number	v1 (current)
This version publication date	14 June 2020
First version publication date	14 June 2020

Trial information**Trial identification**

Sponsor protocol code	15-004
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02806895
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, Jazz Pharmaceuticals Inc., 001 2158323750, ClinicalTrialDisclosure@JazzPharma.com
Scientific contact	Grace Wang, MD, Jazz Pharmaceuticals Inc., 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	28 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 May 2019
Global end of trial reached?	Yes
Global end of trial date	28 May 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is 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	05 July 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: 34
Worldwide total number of subjects	34
EEA total number of subjects	34

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)	33
From 65 to 84 years	1
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	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

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
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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	34	34
JZP-110/Placebo	17 ^[1]	17 ^[2]
Placebo/JZP-110	17 ^[3]	17 ^[4]
Completed	33	33
Not completed	1	1
Sponsor decision	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
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Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	34	34	
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 (21-65 years)	34	34	
Age continuous			
Units: years			
median	51.6		
standard deviation	± 12.30	-	
Gender categorical			
Units: Subjects			
Female	4	4	
Male	30	30	

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	33 ^[1]	34		
Units: centimeter (cm)				
least squares mean (standard error)	19.92 (\pm 0.630)	18.83 (\pm 0.627)		

Notes:

[1] - One subject did not receive placebo resulting in 33 subjects in the placebo group.

Statistical analyses

Statistical analysis title	SDLP at 2 Hours Post-dose (Approximately at Tmax)
Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0062
Method	ANOVA

Secondary: SDLP at 6 Hours Post-dose

End point title	SDLP at 6 Hours Post-dose
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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
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End point timeframe:

6 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32 ^[2]	32 ^[3]		
Units: cm				
least squares mean (standard error)	20.04 (\pm 0.632)	19.24 (\pm 0.631)		

Notes:

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

[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
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Statistical analysis description:

The mean change in SDLP 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 32 for Placebo and 32 for JZP-110 not a total of 64 due to cross over design.

Comparison groups	Placebo v JZP-110
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Number of subjects included in analysis	64
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Analysis specification	Pre-specified
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Analysis type	superiority
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P-value	= 0.0432
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Method	ANOVA
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Secondary: Proportion of Subjects with Improved or Impaired Driving on JZP-110 Compared to Placebo at 2 Hours Post-dose

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

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33 ^[4]	34 ^[5]		
Units: distribution of change				
number (not applicable)	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 at 6 Hours Post-dose

End point title	Proportion of Subjects with Improved or Impaired Driving on JZP-110 Compared to Placebo at 6 Hours Post-dose
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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	33 ^[6]	34 ^[7]		
Units: distribution of change				
number (not applicable)	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
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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
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End point timeframe:

2 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33 ^[8]	34		
Units: kilometers/hour (km/hr)				
least squares mean (standard error)	2.55 (± 0.099)	2.62 (± 0.098)		

Notes:

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

Statistical analyses

Statistical analysis title	SDS 2 Hours Post-dose
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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 33 for Placebo and 34 for JZP-110 not a total of 67 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4116
Method	ANOVA

Secondary: SDS at 6 Hours Post-dose

End point title	SDS at 6 Hours Post-dose
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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
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End point timeframe:

6 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32 ^[9]	32 ^[10]		
Units: km/hr				
least squares mean (standard error)	2.84 (± 0.100)	2.73 (± 0.099)		

Notes:

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

[10] - 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
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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 32 for Placebo and 32 for JZP-110 not a total of 64 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1991
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
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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
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End point timeframe:

2 hour post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33 ^[11]	34		
Units: number of lapses				
least squares mean (standard error)	2.89 (± 0.566)	1.76 (± 0.558)		

Notes:

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

Statistical analyses

Statistical analysis title	Lapses in Driving Test at 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 33 for Placebo and 34 for JZP-110 not a total of 67 due to cross over design.	
Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0806
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	32 ^[12]	32 ^[13]		
Units: number of lapses				
least squares mean (standard error)	2.07 (± 0.573)	2.12 (± 0.573)		

Notes:

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

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

Statistical analyses

Statistical analysis title	Lapses in Driving Test at 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 32 for Placebo and 32 for JZP-110 not a total of 64 due to cross over design.	
Comparison groups	Placebo v JZP-110

Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9391
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
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End point description:

The PVT was administered at screening for practice only, and at pre-dose 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
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End point timeframe:

2 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33 ^[14]	34		
Units: RT > 500 msec				
least squares mean (standard error)	6.37 (± 2.111)	2.71 (± 2.077)		

Notes:

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

Statistical analyses

Statistical analysis title	PVT Number of Lapses at 2 Hours Post-dose
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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 33 for Placebo and 34 for JZP-110 not a total of 67 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2116
Method	ANOVA

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

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

The PVT was administered at screening for practice only, and at pre-dose 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 Reaction Time (RT) in milliseconds > 500 milliseconds (RT > 500 msec).

End point type	Secondary
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End point timeframe:

6 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33 ^[15]	33 ^[16]		
Units: RT > msec				
least squares mean (standard error)	7.73 (± 2.111)	3.60 (± 2.086)		

Notes:

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

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

Statistical analyses

Statistical analysis title	PVT Number of Lapses at 6 Hours Post-dose
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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 33 for Placebo and 33 for JZP-110 not a total of 66 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1604
Method	ANOVA

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

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

The PVT was administered at screening for practice only, and at pre-dose 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
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End point timeframe:

2 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33 ^[17]	34		
Units: msec				
least squares mean (standard error)	318.66 (\pm 19.307)	286.55 (\pm 19.004)		

Notes:

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

Statistical analyses

Statistical analysis title	PVT Mean Reaction Time at 2 Hours Post-dose
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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 33 for Placebo and 34 for JZP-110 not a total of 67 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2144
Method	ANOVA

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

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

The PVT was administered at screening for practice only, and at pre-dose 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
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End point timeframe:

6 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33 ^[18]	33 ^[19]		
Units: msec				
least squares mean (standard error)	341.37 (\pm 19.307)	286.88 (\pm 19.188)		

Notes:

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

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

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 33 for Placebo and 33 for JZP-110 not a total of 66 due to cross over design.	
Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0387
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 pre-dose 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	33 ^[20]	34		
Units: (1/RT(s))				
least squares mean (standard error)	3.59 (± 0.111)	3.69 (± 0.110)		

Notes:

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

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 33 for Placebo and 34 for JZP-110 not a total of 67 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3426
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 pre-dose 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	33 ^[21]	33 ^[22]		
Units: (1/RT(s))				
least squares mean (standard error)	3.59 (± 0.111)	3.75 (± 0.110)		

Notes:

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

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

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 33 for Placebo and 33 for JZP-110 not a total of 66 due to cross over design.	
Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1531
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
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End point description:

The PVT was administered at screening for practice only, and at pre-dose 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
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End point timeframe:

2 hours post-dose

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33 ^[23]	34		
Units: RT < 100 msec				
least squares mean (standard error)	2.40 (\pm 0.741)	1.82 (\pm 0.730)		

Notes:

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

Statistical analyses

Statistical analysis title	PVT Number of Errors of Commission at 2 Hours Post
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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 33 for Placebo and 34 for JZP-110 not a total of 67 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5603
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
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End point description:

The PVT was administered at screening for practice only, and at pre-dose 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	33 ^[24]	33 ^[25]		
Units: RT < 100 msec				
least squares mean (standard error)	2.46 (± 0.741)	1.76 (± 0.740)		

Notes:

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

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

Statistical analyses

Statistical analysis title	PVT Number of Errors of Commission at 6 Hours Post
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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 33 for Placebo and 33 for JZP-110 not a total of 66 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4851
Method	ANOVA

Secondary: Toronto Hospital Alert Test (THAT)

End point title	Toronto Hospital Alert Test (THAT)
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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
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End point timeframe:

post-treatment

End point values	Placebo	JZP-110		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33 ^[26]	34		
Units: score on a scale				
least squares mean (standard error)	23.94 (± 1.180)	27.52 (± 1.162)		

Notes:

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

Statistical analyses

Statistical analysis title	THAT
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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 33 for Placebo and 34 JZP-110 not a total of 67 due to cross over design.

Comparison groups	Placebo v JZP-110
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0241
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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

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

Reporting group title	JZP-110
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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 / 33 (0.00%)	0 / 34 (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	8 / 33 (24.24%)	15 / 34 (44.12%)	
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 33 (6.06%)	3 / 34 (8.82%)	
occurrences (all)	2	3	
Headache			

subjects affected / exposed occurrences (all)	4 / 33 (12.12%) 4	4 / 34 (11.76%) 4	
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	4 / 34 (11.76%) 4	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	4 / 34 (11.76%) 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