Clinical trial results:
A Multicenter, Double-Blind, Placebo-Controlled Study of JNJ-40411813 as Adjunctive Treatment to an Antidepressant in Adults with Major Depressive Disorder with Anxiety Symptoms

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2011-006121-26
Trial protocol	HU BG SK
Global end of trial date	25 November 2013

Results information

Result version number	v2 (current)
This version publication date	15 July 2016
First version publication date	13 August 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	40411813DAX2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01582815
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, Division of Janssen-Cilag Ltd
Sponsor organisation address	Turnhoutseweg 30, 2340 Beerse, Belgium,
Public contact	Clinical Registry Group, Janssen Research & Development, Division of Janssen-Cilag Ltd, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, Division of Janssen-Cilag Ltd, ClinicalTrialsEU@its.jnj.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	25 November 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy, as assessed by the change from baseline on a 6-item subscale derived from the Hamilton Anxiety Scale (HAM-A6), and to evaluate overall safety and tolerability of treatment with adjunctive JNJ-40411813 (a positive allosteric modulator of the metabotropic glutamate receptor 2) compared with placebo in subjects who have MDD with anxiety symptoms being treated with a selective serotonin reuptake inhibitor (SSRI) or serotonergic/noradrenergic reuptake inhibitor (SNRI).

Protection of trial subjects:

The safety assessments included monitoring adverse events (AEs) clinical laboratory assessments (for example hematology, serum chemistry and urinalysis), vital signs measurements (oral temperature, pulse rate, blood pressure), 12-lead electrocardiogram (ECG),and physical and neurologic examinations.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 August 2012
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	Bulgaria: 14
Country: Number of subjects enrolled	Hungary: 7
Country: Number of subjects enrolled	Moldova, Republic of: 7
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	Russian Federation: 42
Country: Number of subjects enrolled	Ukraine: 43
Worldwide total number of subjects	121
EEA total number of subjects	29

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)	121
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

121 subjects were enrolled and treated with JNJ-40411813 or Placebo in Period 1 of the study. Subjects who were randomly assigned to adjunctive treatment with placebo in Period 1 who did not respond to treatment were re-randomized to adjunctive placebo or JNJ-40411813 in Period 2. A subset of 22 subjects (of 121) were re-randomized in Period 2.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Period 1: Placebo

Arm description:

Participants received matching Placebo for 4 weeks during Period 1.

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

Dosage and administration details:

Matching Placebo orally twice daily for 4 weeks in Period 1.

Arm title	Period 1: JNJ-40411813

Arm description:

Participants received JNJ-40411813 orally for 4 weeks during Period 1.

Arm type	Experimental
Investigational medicinal product name	JNJ-40411813-AAA-Capsule
Investigational medicinal product code	JNJ-40411813-AAA
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

JNJ-40411813 titrated from 25 mg (G029) capsules twice daily (b.i.d) to 50 mg (G025) b.i.d and later flexibly dosed in the range of 50mg b.i.d. up to 150 mg b.i.d. orally for 4 weeks during Period 1.

Number of subjects in period 1[1]	Period 1: Placebo	Period 1: JNJ-40411813
Started	58	61
Completed	54	53
Not completed	4	8
Consent withdrawn by subject	1	4
Adverse event, non-fatal	3	1
Exclusion Criteria	-	1
Protocol deviation	-	2

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Not all the enrolled subjects were treated with study drugs. As baseline only included treated subjects, the worldwide number enrolled in the trial differs with the number of subjects reported in the baseline period

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	No
Arm title	Period 2: Placebo

Arm description:

Participants who got Placebo in Period 1 and were eligible for re-randomization received matching Placebo for 4 weeks during Period 2.

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

Dosage and administration details:

Matching Placebo orally twice daily for 4 weeks in Period 2.

Arm title	Period 2: JNJ-40411813

Arm description:

Participants who got Placebo in Period 1 and were eligible for re-randomization received JNJ-40411813 orally for 4 weeks during Period 2.

Arm type	Experimental
Investigational medicinal product name	JNJ-40411813-AAA-Capsule
Investigational medicinal product code	JNJ-40411813-AAA
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

JNJ-40411813 titrated from 25 mg (G029) capsules twice daily (b.i.d) to 50 mg (G025) b.i.d and later flexibly dosed in the range of 50mg b.i.d. up to 150 mg b.i.d. orally for 4 weeks during Period 2.

Number of subjects in period 2	Period 2: Placebo	Period 2: JNJ-40411813
Started	11	11
Completed	10	11
Not completed	1	0
Consent withdrawn by subject	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Period 1: Placebo
Reporting group description:	
Participants received matching Placebo for 4 weeks during Period 1.	
Reporting group title	Period 1: JNJ-40411813
Reporting group description:	
Participants received JNJ-40411813 orally for 4 weeks during Period 1.	

Reporting group values	Period 1: Placebo	Period 1: JNJ-40411813	Total
Number of subjects	58	61	119
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	58	61	119
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	44.8	44	
standard deviation	± 11.55	± 12.78	-
Title for Gender Units: subjects			
Female	12	18	30
Male	46	43	89

End points

End points reporting groups

Reporting group title	Period 1: Placebo
Reporting group description:	
Participants received matching Placebo for 4 weeks during Period 1.	
Reporting group title	Period 1: JNJ-40411813
Reporting group description:	
Participants received JNJ-40411813 orally for 4 weeks during Period 1.	
Reporting group title	Period 2: Placebo
Reporting group description:	
Participants who got Placebo in Period 1 and were eligible for re-randomization received matching Placebo for 4 weeks during Period 2.	
Reporting group title	Period 2: JNJ-40411813
Reporting group description:	
Participants who got Placebo in Period 1 and were eligible for re-randomization received JNJ-40411813 orally for 4 weeks during Period 2.	
Subject analysis set title	Period 1: Intent-to-treat (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
ITT population included the subjects receiving at least one dose of study medication during the Period 1, having both a baseline and at least one post-baseline primary efficacy assessment during the Period 1.	
Subject analysis set title	Period 2: Intent-to-treat (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
ITT population included Period 1 placebo subjects who were eligible for re-randomization, receiving at least one dose of study medication during the Period 2 and having both a baseline and at least one post-baseline primary efficacy assessment during the Period 2.	

Primary: Change from Baseline to Week 4 on the Hamilton Anxiety Rating scale (HAM-A6) Score

End point title	Change from Baseline to Week 4 on the Hamilton Anxiety Rating scale (HAM-A6) Score
End point description:	
The HAM-A6 is a 6-item subscale derived from the original Hamilton Anxiety scale (HAM-A). The rating scale measures the severity of anxiety symptomatology. Higher scores represent more severe anxiety symptoms.	
End point type	Primary
End point timeframe:	
Baseline and Week 4	

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[1]	11[2]	61[3]	11[4]
Units: units on a scale				
least squares mean (standard error)	-3.7 (± 0.33)	-3 (± 0.91)	-3.5 (± 0.33)	-4.5 (± 0.89)

Notes:

[1] - Period 1: ITT

[2] - Period 2: ITT

[3] - Period 1: ITT

[4] - Period 2: ITT

Statistical analyses

Statistical analysis title	Period 1 and 2 Combined: Placebo v JNJ-40411813

Statistical analysis description:

Based on MMRM model with treatment, time, pooled center, and time-by treatment interaction as factors, and baseline value (for respective period) as a covariate. This was the doubly randomized design: 119 subjects from Period 1 and 22 re-randomized subjects from Period 2 contributed to the JNJ-40411813 vs Placebo comparison. Statistics defined as a weighted combination of the test statistics from both periods, where weights satisfied pre-specified power optimality criterion was used.

Comparison groups	Period 1: Placebo v Period 1: JNJ-40411813
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.513 [5]
Method	Mixed models analysis

Notes:

[5] - One-sided p-value measured.

Secondary: Change from Baseline to Endpoint on the SIGH-A (Structured Interview Guide of the Hamilton Anxiety Scale 14-item HAM-A) Total Score

End point title	Change from Baseline to Endpoint on the SIGH-A (Structured Interview Guide of the Hamilton Anxiety Scale 14-item HAM-A) Total Score

End point description:

The (HAM-A) is a 14-item scale designed to measure anxiety in individuals. Each question reflects a symptom of anxiety and physical as well as mental symptoms are represented. The answers range from 0 which signifies a complete lack of that symptom to 4, which indicates a very severe show of anxiety with that symptom.

End point type	Secondary

End point timeframe:

Baseline and Week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[6]	11[7]	61[8]	11[9]
Units: units on a scale				
least squares mean (standard error)	-8.8 (± 0.78)	-7.4 (± 1.96)	-8.7 (± 0.78)	-8.8 (± 1.93)

Notes:

[6] - Period 1: ITT

[7] - Period 2: ITT

[8] - Period 1: ITT

[9] - Period 2: ITT

Statistical analyses

Statistical analysis title	Period 1 and 2 Combined: Placebo v JNJ-40411813

Statistical analysis description:

Based on MMRM model with treatment, time, pooled center, and time-by treatment interaction as factors, and baseline value (for respective period) as a covariate. This was the doubly randomized design: 119 subjects from Period 1 and 22 re-randomized subjects from Period 2 contributed to the JNJ-40411813 vs Placebo comparison. Statistics defined as a weighted combination of the test statistics from both periods, where weights satisfied pre-specified power optimality criterion was used.

Comparison groups	Period 1: Placebo v Period 1: JNJ-40411813
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.453 [10]
Method	Mixed models analysis

Notes:

[10] - One-sided p-value measured

Secondary: Number of Participants at Week 4 with greater than or equal to 50 percent improvement on the SIGH-A (Structured Interview Guide of the Hamilton Anxiety Scale 14-item HAM-A) Total Score

End point title	Number of Participants at Week 4 with greater than or equal to 50 percent improvement on the SIGH-A (Structured Interview Guide of the Hamilton Anxiety Scale 14-item HAM-A) Total Score

End point description:

The (HAM-A) is a 14-item scale designed to measure anxiety in individuals. Each question reflects a symptom of anxiety and physical as well as mental symptoms are represented. The answers range from 0 which signifies a complete lack of that symptom to 4, which indicates a very severe show of anxiety with that symptom.

End point type	Secondary

End point timeframe:

Week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[11]	11[12]	61[13]	11[14]
Units: participants				
number (not applicable)	16	3	16	4

Notes:

[11] - Period 1: ITT

[12] - Period 2: ITT

[13] - Period 1: ITT

[14] - Period 2: ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint on the Hamilton Depression Rating Scale (HDRS17) Total Score

End point title	Change from Baseline to Endpoint on the Hamilton Depression Rating Scale (HDRS17) Total Score

End point description:

The HDRS17 is a clinician-administered rating scale designed to assess the severity of symptoms in patients diagnosed with depression with a score range of 0 to 52. Questions are related to symptoms such as depressed mood, guilt feelings, suicide, sleep disturbances, anxiety levels and weight loss. The higher the score, the more severe the depression.

End point type	Secondary

End point timeframe:

Baseline and week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[15]	11[16]	61[17]	11[18]
Units: units on a scale				
least squares mean (standard error)	-9 (± 0.72)	-7 (± 1.62)	-9.4 (± 0.72)	-9.8 (± 1.6)

Notes:

[15] - Period 1: ITT

[16] - Period 2: ITT

[17] - Period 1: ITT

[18] - Period 2: ITT

Statistical analyses

Statistical analysis title	Period 1 and 2 Combined: Placebo v JNJ-40411813

Statistical analysis description:

Based on MMRM model with treatment, time, pooled center, and time-by treatment interaction as factors, and baseline value (for respective period) as a covariate. This was the doubly randomized design: 119 subjects from Period 1 and 22 re-randomized subjects from Period 2 contributed to the JNJ-40411813 vs Placebo comparison. Statistics defined as a weighted combination of the test statistics from both periods, where weights satisfied pre-specified power optimality criterion was used.

Comparison groups	Period 1: Placebo v Period 1: JNJ-40411813

Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.182 [19]
Method	Mixed models analysis

Notes:

[19] - One-sided p-value measured

Secondary: Number of Participants with Either Greater than or Equal to 50 Percent or Greater than or equal to 30 Percent Improvement on the HDRS17 Total Score at Week 4

End point title	Number of Participants with Either Greater than or Equal to 50 Percent or Greater than or equal to 30 Percent Improvement on the HDRS17 Total Score at Week 4

End point description:

The HDRS17 is a clinician-administered rating scale designed to assess the severity of symptoms in patients diagnosed with depression with a score range of 0 to 52. Questions are related to symptoms such as depressed mood, guilt feelings, suicide, sleep disturbances, anxiety levels and weight loss. The higher the score, the more severe the depression.

End point type	Secondary

End point timeframe:

Week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[20]	11[21]	61[22]	11[23]
Units: participants				
number (not applicable)				
Greater than or equal to 50 Percent Improvement	14	3	15	6
Greater than or equal to 30 Percent Improvemnet	34	5	37	9

Notes:

[20] - Period 1: ITT

[21] - Period 2: ITT

[22] - Period 1: ITT

[23] - Period 2: ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Remission Rates (HDRS 17 Total Score less than or equal to 7)

End point title	Number of Participants with Remission Rates (HDRS 17 Total Score less than or equal to 7)

End point description:

Remission is defined as HDRS 17 total score ≤ 7. The HDRS17 is a clinician-administered rating scale designed to assess the severity of symptoms in patients diagnosed with depression with a score range of 0 to 52. Questions are related to symptoms such as depressed mood, guilt feelings, suicide, sleep disturbances, anxiety levels and weight loss. The higher the score, the more severe the depression.

End point type	Secondary

End point timeframe:

Week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[24]	11[25]	61[26]	11[27]
Units: participants				
number (not applicable)	1	1	4	2

Notes:

[24] - Period 1: ITT

[25] - Period 2: ITT

[26] - Period 1: ITT

[27] - Period 2: ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in the Hamilton Depression Rating Scale (HDRS17) Anxiety/Somatization Factor Total Score

End point title	Change from Baseline to Endpoint in the Hamilton Depression Rating Scale (HDRS17) Anxiety/Somatization Factor Total Score

End point description:

The anxiety/somatization factor total score derived from HDRS scale. It includes six items from the original 17-item version: psychic anxiety, somatic anxiety, gastrointestinal somatic symptoms, general somatic symptoms, hypochondriasis, and insight. The scale measures the severity of anxious depression. The higher the score, the more severe anxiety symptoms.

End point type	Secondary

End point timeframe:

Baseline and Week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[28]	11[29]	61[30]	11[31]
Units: units on a scale				
least squares mean (standard error)	-3.1 (± 0.31)	-2.9 (± 0.61)	-3.5 (± 0.31)	-4 (± 0.59)

Notes:

[28] - Period 1: ITT

[29] - Period 2: ITT

[30] - Period 1: ITT

[31] - Period 2: ITT

Statistical analyses

Statistical analysis title	Period 1 and 2 Combined: Placebo v JNJ-40411813

Statistical analysis description:

Based on MMRM model with treatment, time, pooled center, and time-by treatment interaction as factors, and baseline value (for respective period) as a covariate. This was the doubly randomized design: 119 subjects from Period 1 and 22 re-randomized subjects from Period 2 contributed to the JNJ-40411813 vs Placebo comparison. Statistics defined as a weighted combination of the test statistics from both periods, where weights satisfied pre-specified power optimality criterion was used.

Comparison groups	Period 1: Placebo v Period 1: JNJ-40411813
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.099 [32]
Method	Mixed models analysis

Notes:

[32] - One-sided p-value measured

Secondary: Number of Participants Meeting Criteria for Anxious Depression at Week 4

End point title	Number of Participants Meeting Criteria for Anxious Depression at Week 4

End point description:

The anxiety/somatization factor total score derived from HDRS scale. It includes six items from the original 17-item version: psychic anxiety, somatic anxiety, gastrointestinal somatic symptoms, general somatic symptoms, hypochondriasis, and insight. The scale measures the severity of anxious depression. The higher the score, the more severe anxiety symptoms.

End point type	Secondary

End point timeframe:

Week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[33]	11[34]	61[35]	11[36]
Units: participants				
number (not applicable)	30	5	25	0

Notes:

[33] - Period 1: ITT

[34] - Period 2: ITT

[35] - Period 1: ITT

[36] - Period 2: ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint in the Hamilton Depression Rating Scale - 6-item (HAM-D6) Score

End point title	Change from Baseline to Endpoint in the Hamilton Depression Rating Scale - 6-item (HAM-D6) Score

End point description:

The HAM-D6 is a 6-item subscale derived from the Hamilton Depression Rating Scale (HDRS17). The

rating scale measures the severity of depressive symptomatology. Higher scores represent more severe depressive symptoms.

End point type	Secondary
End point timeframe:	
Baselien and Week 4	

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[37]	11[38]	61[39]	11[40]
Units: units on a scale				
least squares mean (standard error)	-4.3 (± 0.37)	-3.1 (± 0.84)	-4.6 (± 0.37)	-5.1 (± 0.83)

Notes:

[37] - Period 1: ITT

[38] - Period 2: ITT

[39] - Period 1: ITT

[40] - Period 2: ITT

Statistical analyses

Statistical analysis title	Period 1 and 2 Combined: Placebo v JNJ-40411813

Statistical analysis description:

Based on MMRM model with treatment, time, pooled center, and time-by treatment interaction as factors, and baseline value (for respective period) as a covariate. This was the doubly randomized design: 119 subjects from Period 1 and 22 re-randomized subjects from Period 2 contributed to the JNJ-40411813 vs Placebo comparison. Statistics defined as a weighted combination of the test statistics from both periods, where weights satisfied pre-specified power optimality criterion was used.

Comparison groups	Period 1: Placebo v Period 1: JNJ-40411813
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.133 [41]
Method	Mixed models analysis

Notes:

[41] - One-sided p-value measured

Secondary: Change from Baseline to Endpoint in the Inventory of Depressive Symptomatolgy -Clinician rated (IDS-C30) Total Score

End point title	Change from Baseline to Endpoint in the Inventory of Depressive Symptomatolgy -Clinician rated (IDS-C30) Total Score

End point description:

The IDS-C30 is a clinician administered 30 item depression specific severity rating scale designed to measure specific signs and symptoms of depression including melancholic, atypical and anxious features. Scores range from 0 to 84 with higher scores representing greater severity of depressive symptoms.

End point type	Secondary

End point timeframe:

Baseline and Week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[42]	11[43]	61[44]	11[45]
Units: units on a scale				
least squares mean (standard error)	-15 (± 1.23)	-10.4 (± 2.92)	-15.8 (± 1.23)	-15.1 (± 2.89)

Notes:

[42] - Period 1: ITT

[43] - Period 2: ITT

[44] - Period 1: ITT

[45] - Period 2: ITT

Statistical analyses

Statistical analysis title	Period 1 and 2 Combined: Placebo v JNJ-40411813

Statistical analysis description:

Based on MMRM model with treatment, time, pooled center, and time-by treatment interaction as factors, and baseline value (for respective period) as a covariate. This was the doubly randomized design: 119 subjects from Period 1 and 22 re-randomized subjects from Period 2 contributed to the JNJ-40411813 vs Placebo comparison. Statistics defined as a weighted combination of the test statistics from both periods, where weights satisfied pre-specified power optimality criterion was used.

Comparison groups	Period 1: Placebo v Period 1: JNJ-40411813
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.195 [46]
Method	Mixed models analysis

Notes:

[46] - One-sided p-value measured

Secondary: Change from Baseline to Endpoint in the Inventory of Depressive Symptomatology - Clinician-Rated (IDS-C30) Anxiety Subscale Score

End point title	Change from Baseline to Endpoint in the Inventory of Depressive Symptomatology - Clinician-Rated (IDS-C30) Anxiety Subscale Score

End point description:

The IDS-C30 is a clinician administered 30 item depression specific severity rating scale designed to measure specific signs and symptoms of depression including melancholic, atypical and anxious features. The anxiety subscale includes five anxiety symptoms: anxious mood, somatic complaints, sympathetic arousal, panic, and gastrointestinal symptoms. The rating scale measures the severity of anxiety symptomatology. Higher scores represent more severe anxiety symptoms.

End point type	Secondary

End point timeframe:

Baseline and Week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[47]	11[48]	61[49]	11[50]
Units: units on a scale				
least squares mean (standard error)	-2.6 (± 0.25)	-1.9 (± 0.65)	-2.8 (± 0.25)	-2.7 (± 0.64)

Notes:

[47] - Period 1: ITT

[48] - Period 2: ITT

[49] - Period 1: ITT

[50] - Period 2: ITT

Statistical analyses

Statistical analysis title	Period 1 and 2 Combined: Placebo v JNJ-40411813

Statistical analysis description:

Based on MMRM model with treatment, time, pooled center, and time-by treatment interaction as factors, and baseline value (for respective period) as a covariate. This was the doubly randomized design: 119 subjects from Period 1 and 22 re-randomized subjects from Period 2 contributed to the JNJ-40411813 vs Placebo comparison. Statistics defined as a weighted combination of the test statistics from both periods, where weights satisfied pre-specified power optimality criterion was used.

Comparison groups	Period 1: Placebo v Period 1: JNJ-40411813
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.174 [51]
Method	Mixed models analysis

Notes:

[51] - One-sided p-value measured

Secondary: Number of participants with Clinical Global Impression - Improvement (CGI-I) score

End point title	Number of participants with Clinical Global Impression - Improvement (CGI-I) score

End point description:

The CGI-I is a 7-point scale that requires the clinician to assess how much the patient's illness has improved or worsened relative to a baseline state at the beginning of the intervention and rated as: 1=very much improved; 2=much improved; 3=minimally improved; 4=no change; 5=minimally worse; 6=much worse; 7=very much worse.

End point type	Secondary

End point timeframe:

Week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[52]	11[53]	61[54]	11[55]
Units: participants				
number (not applicable)				
Minimally Worse	0	0	2	0
No Change	11	3	7	1
Minimally Improved	22	3	21	3
Much Improved	20	4	26	3
Very Much Improved	5	1	5	4

Notes:

[52] - Period 1: ITT

[53] - Period 2: ITT

[54] - Period 1: ITT

[55] - Period 2: ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Endpoint on the Perceived Stress Scale (PSS) Total Score

End point title	Change from Baseline to Endpoint on the Perceived Stress Scale (PSS) Total Score

End point description:

The PSS is a 10-item, self-reported unidimensional instrument developed to measure perceived stress in response to situations in a person's life. Prevalence of an item within the last month is measured on a 5 point scale, ranging from "never" to "very often". Higher scores reflect higher levels of perceived stress.

End point type	Secondary

End point timeframe:

Baseline and Week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[56]	10[57]	59[58]	11[59]
Units: units on a scale				
least squares mean (standard error)	-5.1 (± 0.64)	-4 (± 2)	-5.8 (± 0.63)	-7.1 (± 1.93)

Notes:

[56] - Period 1: ITT

[57] - ITT population with evaluable participants for this endpoint out of 11 (full Period 2 ITT).

[58] - ITT population with evaluable participants for this endpoint out of 61 (full Period 1 ITT).

[59] - Period 2: ITT

Statistical analyses

Statistical analysis title	Period 1 and 2 Combined: Placebo v JNJ-40411813

Statistical analysis description:

Based on ANCOVA model with treatment(placebo,JNJ-40411813) and pooled center as factors and

baseline value (for respective period) as a covariate. This was the doubly randomized design: 117 subjects from Period 1 and 21 re-randomized subjects from Period 2 contributed to the JNJ-40411813 vs Placebo comparison. Statistics defined as a weighted combination of the test statistics from both periods, where weights satisfied pre-specified power optimality criterion was used.

Comparison groups	Period 1: Placebo v Period 1: JNJ-40411813
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.124 [60]
Method	Mixed models analysis

Notes:

[60] - One-sided p-value measured

Secondary: Change From Baseline to Endpoint in the Profile of Moods Scale-Brief Form (POMS-BF)

End point title	Change From Baseline to Endpoint in the Profile of Moods Scale-Brief Form (POMS-BF)

End point description:

The POMS-BF is a 30 item, self-report inventory in which a series of mood states (such as "Tense" or "Worn out") are rated based on how well each item describes the respondent's mood during the past week, including today. Items are rated on a 5-point scale with response options of: "Not at all", "A little", "Moderately", "Quite a bit" or "Extremely" with a global score range of 0 to 120 or individual domain scores on Tension-Anxiety, Depression-Dejection, Anger-Hostility, Vigor-Activity, Fatigue-Inertia, and Confusion-Bewilderment. Total Mood Disturbance score is calculated by summing the domains scores for Tension- Anxiety, Depression-Dejection, Anger-Hostility, Fatigue-Inertia, and Confusion-Bewilderment, then subtracting the domain score for Vigor-Activity. A higher Total Mood Disturbance score indicates worse mood state.

End point type	Secondary

End point timeframe:

Baseline and week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[61]	10[62]	59[63]	11[64]
Units: units on a scale				
least squares mean (standard error)	-20 (± 2.08)	-14.7 (± 4.23)	-19.5 (± 2.04)	-18.8 (± 4.07)

Notes:

[61] - Period 1: ITT

[62] - ITT population with evaluable subjects for this endpoint out of 11 (full Period 2 ITT).

[63] - ITT population with evaluable participants for this endpoint out of 61 (full Period 1 ITT).

[64] - Period 2: ITT

Statistical analyses

Statistical analysis title	Period 1 and 2 Combined: Placebo v JNJ-40411813

Statistical analysis description:

Based on ANCOVA model with treatment (placebo,JNJ-40411813) and pooled center as factors and baseline value (for respective period) as a covariate. This was the doubly randomized design: 117 subjects from Period 1 and 21 re-randomized subjects from Period 2 contributed to the JNJ-40411813 vs Placebo comparison. Statistics defined as a weighted combination of the test statistics from both periods, where weights satisfied pre-specified power optimality criterion was used.

Comparison groups	Period 1: JNJ-40411813 v Period 1: Placebo
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.445 [65]
Method	Mixed models analysis

Notes:

[65] - One-sided p-value measured

Secondary: Change from Baseline to Endpoint on the Medical Outcomes Study-12-item Sleep Scale Acute - Revised (MOS Sleep-R)

End point title	Change from Baseline to Endpoint on the Medical Outcomes Study-12-item Sleep Scale Acute - Revised (MOS Sleep-R)

End point description:

The MOS Sleep-R is a self-reported scale containing 12 items addressing dimensions of sleep. It comprises six subscales: sleep disturbance, snoring, shortness of breath or headache, sleep adequacy, sleep somnolence, and sleep quantity. Items are answered on 5-point scales, where 1="all of the time," and 5="none of the time," 1 item (sleep latency) is answered on a 5 point scale from 1="0-15 minutes" to 5="more than 60 minutes." Score range of 0 to 100, where higher scores indicate fewer sleep-related problems. Duration of sleep is scored as the average number of hours slept per night. Here 'n' signifies number of participants who were analysed for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline and Week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[66]	11[67]	61[68]	11[69]
Units: units on a scale				
arithmetic mean (standard deviation)				
Shortness of Breath (n= 58, 59, 10, 11)	8.3 (± 12.68)	3.5 (± 13.66)	9.4 (± 11.94)	6.4 (± 14.3)
Sleep Adequacy (n= 58, 59, 10, 11)	9.5 (± 11.15)	8.2 (± 11.2)	8.9 (± 10.48)	7.5 (± 15.67)
Sleep Disturbance (n= 58, 59, 10, 11)	9.2 (± 8.83)	6 (± 8)	8.6 (± 10.44)	8.4 (± 9.82)
Snoring (n= 58, 59, 10, 11)	0.9 (± 4.29)	0.8 (± 2.4)	2.2 (± 5.48)	3.5 (± 7.87)
Somnolence (n= 58, 59, 10, 11)	6.3 (± 9.01)	9.3 (± 4.53)	6.9 (± 8.19)	3.9 (± 8.79)
Sleep Problems Index (6 items) (n= 58, 59, 10, 11)	11.9 (± 10.28)	7.8 (± 10.14)	10.9 (± 10.5)	8.5 (± 15.54)
Sleep Problems Index (9 items) (n= 58, 59, 10, 11)	10.9 (± 9.68)	8.4 (± 9.86)	10.8 (± 10.07)	9.2 (± 13.33)
Sleep Quantity (n= 58, 59, 10, 11)	1.1 (± 1.66)	0.3 (± 1.06)	0.9 (± 1.39)	0.6 (± 1.29)

Notes:

[66] - Period 1: ITT

[67] - Period 2: ITT

[68] - Period 1: ITT

[69] - Period 2: ITT

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 4 in the Work Limitations Questionnaire (WLQ)

End point title	Change from Baseline to Week 4 in the Work Limitations Questionnaire (WLQ)

End point description:

The WLQ is a 25-item questionnaire self-report rating scale developed to measure the on-the-job impact of chronic health problems and/or treatment ("work limitations"), with a recall period of the previous 2 weeks. It comprises four dimensions of limitations: handling time, physical, mental-interpersonal, and output demands. Patients respond to each item with options ranging from "Almost all of the time" to "none of the time", or "Does not apply to my job". The global score ranges from 0 to 100 with lower score indicating low level of work limitations. Here 'n' signifies number of participants who were analysed for this outcome measure.

End point type	Secondary

End point timeframe:

Baseline and Week 4

End point values	Period 1: Placebo	Period 2: Placebo	Period 1: JNJ-40411813	Period 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	58[70]	11[71]	61[72]	11[73]
Units: units on a scale				
arithmetic mean (standard deviation)				
Time Management (n= 42, 41, 8 , 10)	-20.6 (± 23.61)	-7.5 (± 23.6)	-17.9 (± 21.95)	-29.5 (± 23.27)
Physical Demands (n= 42, 44, 7, 10)	-14.6 (± 15.81)	-11.5 (± 17.76)	-14.7 (± 18.38)	-20.8 (± 18.63)
Mental-Interpersonal Demands (n= 42, 43, 8, 10)	-15.5 (± 19.6)	-13 (± 20.93)	-16.9 (± 18.34)	-23.3 (± 22.15)
Output Demands (n= 42, 43, 8, 10)	-17.6 (± 18.4)	-9.4 (± 20.26)	-18.2 (± 18.84)	-27 (± 23.12)
WLQ Productivity Loss Score (%) (n= 41, 40, 7, 10)	-4.2 (± 4.18)	-3.3 (± 5.11)	-3.9 (± 3.63)	-6.4 (± 5.16)

Notes:

[70] - Period 1: ITT

[71] - Period 2: ITT

[72] - Period 1: ITT

[73] - Period 2: ITT

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to Follow-up (2 weeks after the last dose of study drug administration)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Placebo / NA
Reporting group description:	
Participants receiving matching Placebo who dropped out before or at the end of Period 1.	
Reporting group title	JNJ-40411813 / JNJ-40411813
Reporting group description:	
Participants receiving JNJ-40411813 in Period 1, having at least one dose of JNJ-40411813 in Period 2.	
Reporting group title	Placebo / JNJ-40411813
Reporting group description:	
Participants receiving matching Placebo in Period 1, having at least one dose of JNJ-40411813 in Period 2.	
Reporting group title	JNJ-40411813 / NA
Reporting group description:	
Participants receiving JNJ-40411813 who dropped out before, or at the end of Period 1.	
Reporting group title	Placebo / Placebo
Reporting group description:	
Participants receiving matching Placebo in Period 1, having at least one dose of Placebo in Period 2.	

Serious adverse events	Placebo / NA	JNJ-40411813 / JNJ-40411813	Placebo / JNJ-40411813
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Serious adverse events	JNJ-40411813 / NA	Placebo / Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Placebo / NA	JNJ-40411813 / JNJ-40411813	Placebo / JNJ-40411813
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	29 / 53 (54.72%)	8 / 11 (72.73%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	2 / 53 (3.77%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Raynaud's Phenomenon			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Vascular Pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hyperthermia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Hypothermia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Irritability			
subjects affected / exposed	0 / 5 (0.00%)	2 / 53 (3.77%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Dysmenorrhoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Endometrial Hyperplasia			

subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Abnormal Dreams			
subjects affected / exposed	0 / 5 (0.00%)	2 / 53 (3.77%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Agitation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 5 (0.00%)	2 / 53 (3.77%)	0 / 11 (0.00%)
occurrences (all)	0	3	0
Libido Decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Restlessness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0

Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	1	0	0
Blood Pressure Increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Heart Rate Increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Urine Ketone Body Present			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Weight Decreased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Joint Dislocation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Sinus Bradycardia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Balance Disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Disturbance in Attention			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Dizziness Exertional			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Dizziness Postural			
subjects affected / exposed	1 / 5 (20.00%)	5 / 53 (9.43%)	1 / 11 (9.09%)
occurrences (all)	2	8	1
Headache			
subjects affected / exposed	0 / 5 (0.00%)	5 / 53 (9.43%)	1 / 11 (9.09%)
occurrences (all)	0	5	1
Somnolence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 5 (20.00%)	12 / 53 (22.64%)	3 / 11 (27.27%)
occurrences (all)	1	25	4
Eye disorders			
Accommodation Disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 5 (0.00%)	2 / 53 (3.77%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	0 / 5 (0.00%)	2 / 53 (3.77%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Dry Mouth			

subjects affected / exposed	0 / 5 (0.00%)	4 / 53 (7.55%)	0 / 11 (0.00%)
occurrences (all)	0	5	0
Dyspepsia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Faecal Incontinence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 5 (0.00%)	3 / 53 (5.66%)	0 / 11 (0.00%)
occurrences (all)	0	4	0
Vomiting			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	1 / 11 (9.09%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Urinary Incontinence			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Pain in Extremity			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 5 (0.00%)	2 / 53 (3.77%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Pharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Respiratory Tract Infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	1 / 11 (9.09%)
occurrences (all)	0	0	1

Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 5 (0.00%)	2 / 53 (3.77%)	0 / 11 (0.00%)
occurrences (all)	0	2	0
Rhinitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0
Viral Infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 53 (1.89%)	0 / 11 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 53 (0.00%)	0 / 11 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	JNJ-40411813 / NA	Placebo / Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 9 (33.33%)	20 / 43 (46.51%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Raynaud's Phenomenon			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Vascular Pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Hyperthermia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	

Hypothermia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Irritability			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Dysmenorrhoea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
Endometrial Hyperplasia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Abnormal Dreams			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Agitation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
Libido Decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	

Restlessness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 43 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Blood Lactate Dehydrogenase Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Blood Pressure Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Heart Rate Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Urine Ketone Body Present			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
Weight Decreased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Joint Dislocation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			

Palpitations			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
Sinus Bradycardia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Balance Disorder			
subjects affected / exposed	1 / 9 (11.11%)	0 / 43 (0.00%)	
occurrences (all)	1	0	
Disturbance in Attention			
subjects affected / exposed	1 / 9 (11.11%)	0 / 43 (0.00%)	
occurrences (all)	1	0	
Dizziness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Dizziness Exertional			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	2	
Dizziness Postural			
subjects affected / exposed	0 / 9 (0.00%)	2 / 43 (4.65%)	
occurrences (all)	0	2	
Headache			
subjects affected / exposed	0 / 9 (0.00%)	5 / 43 (11.63%)	
occurrences (all)	0	9	
Somnolence			
subjects affected / exposed	0 / 9 (0.00%)	2 / 43 (4.65%)	
occurrences (all)	0	2	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 9 (11.11%)	4 / 43 (9.30%)	
occurrences (all)	1	4	
Eye disorders			

Accommodation Disorder			
subjects affected / exposed	1 / 9 (11.11%)	0 / 43 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Abdominal Pain Upper			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Constipation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	3	
Dry Mouth			
subjects affected / exposed	0 / 9 (0.00%)	3 / 43 (6.98%)	
occurrences (all)	0	3	
Dyspepsia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Faecal Incontinence			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	0 / 9 (0.00%)	5 / 43 (11.63%)	
occurrences (all)	0	6	
Vomiting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			

Urinary Incontinence			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Pain in Extremity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Respiratory Tract Infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Rhinitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	
Viral Infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 43 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 9 (0.00%)	1 / 43 (2.33%)	
occurrences (all)	0	1	

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