Clinical trial results:
A Phase 2a Randomized, Double-blind, Placebo-Controlled, Parallel-Group, Multi-center Study Investigating the Efficacy, Safety, Tolerability and Pharmacokinetics of JNJ-67953964 in Subjects with Major Depressive Disorder

Summary

EudraCT number	2019-000695-41
Trial protocol	GB
Global end of trial date	06 May 2020

Results information

Result version number	v1 (current)
This version publication date	21 May 2021
First version publication date	21 May 2021

Trial information

Trial identification

Sponsor protocol code	67953964MDD2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03559192
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route 202, Raritan, United States, NJ 08869
Public contact	Clinical Registry group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry group, Janssen Research & Development, LLC, 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	06 May 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 May 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to evaluate the efficacy of JNJ-67953964 (aticaprant) compared to placebo when administered as adjunctive treatment in subjects with major depressive disorder (MDD) partially responsive to selective serotonin reuptake inhibitor (SSRI) / serotonin-norepinephrine reuptake inhibitor (SNRI) treatment in terms of reduction of symptoms of depression, as assessed by the change from baseline on the Montgomery Asberg Depression Rating Scale (MADRS) in non-responders during the placebo lead-in period.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice (GCP) and applicable regulatory requirements. Safety was evaluated during the study through assessments: physical examination, neurological examination, vital signs, body weight, body temperature, clinical laboratory assessments, 12-lead electrocardiogram (ECG), urine drug screen, alcohol screening test, pregnancy testing, columbia suicide severity rating scale (C-SSRS) assessments, arizona sexual experiences scale (ASEX) assessment, karolinska sleepiness scale (KSS) assessment, and evaluation of adverse events (AEs) and concomitant medications.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 July 2018
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	Germany: 9
Country: Number of subjects enrolled	United Kingdom: 27
Country: Number of subjects enrolled	Moldova, Republic of: 29
Country: Number of subjects enrolled	Russian Federation: 47
Country: Number of subjects enrolled	Ukraine: 17
Country: Number of subjects enrolled	United States: 52
Worldwide total number of subjects	181
EEA total number of subjects	9

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)	181
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 181 subjects were enrolled in this study.

Period 1

Period 1 title	Lead-in Period (3 Weeks)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Arm title	Placebo

Arm description:

Subjects with major depressive disorder (MDD) who had inadequate response to selective serotonin reuptake inhibitor /serotonin-norepinephrine reuptake inhibitor (SSRI/SNRI) treatment received JNJ-67953964 matching placebo capsules (2*1 placebo capsules) once daily starting from Day 2 to 3 weeks in lead-in period in addition to SSRI/SNRI treatment.

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:

Matching placebo capsules (2*1 placebo capsules) were administered orally up to 3 weeks in lead-in period.

Number of subjects in period 1	Placebo
Started	181
Completed	169
Not completed	12
Consent withdrawn by subject	6
Adverse event, non-fatal	4
Serious Adverse Event, Non-Fatal	1
Protocol deviation	1

Period 2

Period 2 title	Double-Blind Treatment Period (6 Weeks)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects who were responders or non-responders to lead-in placebo group were re-randomized to receive JNJ-67953964 matching placebo capsules (2*1 placebo capsules) once daily during double-blind treatment period (up to 6 weeks after lead-in period) in addition to SSRI/SNRI treatment.

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:

Matching placebo capsules (2*1 placebo capsules) were administered orally up to 6 weeks after lead-in period.

Arm title	JNJ-67953964 10 milligrams (mg)

Arm description:

Subjects who were responders or non-responders to lead-in placebo group were re-randomized to receive 10 mg JNJ-67953964 capsules (2*5 mg JNJ-67953964 capsules) once daily during double-blind treatment period (up to 6 weeks after lead-in period) in addition to SSRI/SNRI treatment.

Arm type	Experimental
Investigational medicinal product name	JNJ-67953964
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

10 mg JNJ-67953964 capsules (2*5 mg JNJ-67953964 capsules) were administered orally up to 6 weeks after lead-in period.

Number of subjects in period 2	Placebo	JNJ-67953964 10 milligrams (mg)
Started	84	85
Placebo Lead-in Responders	22 [1]	23 [2]
Placebo Lead-In Non-Responder	62 [3]	62 [4]
Completed	81	80
Not completed	3	5
Consent withdrawn by subject	1	-
Adverse event, non-fatal	-	1
Other	1	1

Non-compliance with study drug	-	1
Serious Adverse Event-Non Fatal	1	-
Protocol deviation	-	1
Lack of efficacy	-	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: Out of 84 subjects in Placebo arm, 22 were Placebo Lead-in Responders and 62 were Placebo Lead-In Non-Responders. For JNJ-67953964 arm, out of 85 subjects: 23 were Placebo Lead-in Responders and 62 were Placebo Lead-In Non-responders.

[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: Out of 84 subjects in Placebo arm, 22 were Placebo Lead-in Responders and 62 were Placebo Lead-In Non-Responders. For JNJ-67953964 arm, out of 85 subjects: 23 were Placebo Lead-in Responders and 62 were Placebo Lead-In Non-responders.

[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: Out of 84 subjects in Placebo arm, 22 were Placebo Lead-in Responders and 62 were Placebo Lead-In Non-Responders. For JNJ-67953964 arm, out of 85 subjects: 23 were Placebo Lead-in Responders and 62 were Placebo Lead-In Non-responders.

[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: Out of 84 subjects in Placebo arm, 22 were Placebo Lead-in Responders and 62 were Placebo Lead-In Non-Responders. For JNJ-67953964 arm, out of 85 subjects: 23 were Placebo Lead-in Responders and 62 were Placebo Lead-In Non-responders.

Period 3

Period 3 title	Withdrawal Period (2 Weeks)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Arm title	Placebo

Arm description:

Subjects who completed the double-blind treatment period continued to receive JNJ-67953964 matching placebo capsules (2*1 placebo capsules) once daily during the withdrawal period for up to 2 weeks.

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:

Matching placebo capsules (2*1 placebo capsules) were administered orally up to 2 weeks in withdrawal period.

Number of subjects in period 3	Placebo
Started	161
Completed	160
Not completed	1
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Subjects with major depressive disorder (MDD) who had inadequate response to selective serotonin reuptake inhibitor /serotonin-norepinephrine reuptake inhibitor (SSRI/SNRI) treatment received JNJ-67953964 matching placebo capsules (2*1 placebo capsules) once daily starting from Day 2 to 3 weeks in lead-in period in addition to SSRI/SNRI treatment.	

Reporting group values	Placebo	Total	
Number of subjects	181	181	
Title for AgeCategorical Units: subjects			
Adults (18-64 years)	181	181	
Title for AgeContinuous Units: years			
arithmetic mean	42.5		
standard deviation	± 12.91	-	
Title for Gender Units: subjects			
Female	131	131	
Male	50	50	

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects with major depressive disorder (MDD) who had inadequate response to selective serotonin reuptake inhibitor /serotonin-norepinephrine reuptake inhibitor (SSRI/SNRI) treatment received JNJ-67953964 matching placebo capsules (2*1 placebo capsules) once daily starting from Day 2 to 3 weeks in lead-in period in addition to SSRI/SNRI treatment.

Reporting group title	Placebo

Reporting group description:

Subjects who were responders or non-responders to lead-in placebo group were re-randomized to receive JNJ-67953964 matching placebo capsules (2*1 placebo capsules) once daily during double-blind treatment period (up to 6 weeks after lead-in period) in addition to SSRI/SNRI treatment.

Reporting group title	JNJ-67953964 10 milligrams (mg)

Reporting group description:

Subjects who were responders or non-responders to lead-in placebo group were re-randomized to receive 10 mg JNJ-67953964 capsules (2*5 mg JNJ-67953964 capsules) once daily during double-blind treatment period (up to 6 weeks after lead-in period) in addition to SSRI/SNRI treatment.

Reporting group title	Placebo

Reporting group description:

Subjects who completed the double-blind treatment period continued to receive JNJ-67953964 matching placebo capsules (2*1 placebo capsules) once daily during the withdrawal period for up to 2 weeks.

Primary: Change from Treatment Baseline in Montgomery Asberg Depression Rating Scale (MADRS) Total Score at Treatment Week 6 in Non-Responders during Placebo Lead-in Period

End point title	Change from Treatment Baseline in Montgomery Asberg Depression Rating Scale (MADRS) Total Score at Treatment Week 6 in Non-Responders during Placebo Lead-in Period

End point description:

The MADRS is a clinician-rated scale designed to measure depression severity and detects changes due to antidepressant treatment. The scale consists of 10 items, each of which is scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms), summed for a total possible score of 60. Higher scores represent a more severe condition. The MADRS evaluates apparent sadness, reported sadness, inner tension, sleep appetite, concentration, lassitude, inability to feel (interest level), pessimistic thoughts, and suicidal thoughts. Negative change from baseline indicates improvement. The enriched intent-to-treat (eITT) analysis set included all enrolled lead-in placebo non-responders who were randomized into a treatment period, received at least 1 dose of study medication, and had at least 1 post-baseline MADRS assessment during the treatment period. Here 'N' (number of subjects analyzed) includes the number of subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Treatment Baseline and Treatment Week 6

End point values	Placebo	JNJ-67953964 10 milligrams (mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: score on a scale				
least squares mean (standard error)	-8.0 (± 0.92)	-10.1 (± 0.93)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v JNJ-67953964 10 milligrams (mg)
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0443
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-2.1
Confidence interval	
level	Other: 80 %
sides	1-sided
upper limit	-1.09
Variability estimate	Standard error of the mean
Dispersion value	1.25

Secondary: Change from Treatment Baseline in Montgomery Asberg Depression Rating Scale (MADRS) Total Score at Treatment Week 6 in Both Responders and Non-Responders during Placebo Lead-in Period

End point title	Change from Treatment Baseline in Montgomery Asberg Depression Rating Scale (MADRS) Total Score at Treatment Week 6 in Both Responders and Non-Responders during Placebo Lead-in Period

End point description:

The MADRS is a clinician-rated scale designed to measure depression severity and detects changes due to antidepressant treatment. The scale consists of 10 items, each of which is scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms), summed for a total possible score of 60. Higher scores represent a more severe condition. The MADRS evaluates apparent sadness, reported sadness, inner tension, sleep appetite, concentration, lassitude, inability to feel (interest level), pessimistic thoughts, and suicidal thoughts. Negative change from baseline indicates improvement. The full intent-to-treat (fITT) analysis set included all enrolled subjects who were randomized into a treatment period, received at least 1 dose of study medication, and had at least 1 post-treatment baseline assessment of MADRS during the treatment period. Here 'N' (number of subjects analyzed) includes the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Treatment Baseline and Treatment Week 6

End point values	Placebo	JNJ-67953964 10 milligrams (mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	81	77		
Units: score on a scale				
least squares mean (standard error)	-6.5 (± 0.78)	-9.6 (± 0.79)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v JNJ-67953964 10 milligrams (mg)
Number of subjects included in analysis	158
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0017
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Point estimate	-3.1
Confidence interval	
level	Other: 80 %
sides	1-sided
upper limit	-2.21
Variability estimate	Standard error of the mean
Dispersion value	1.05

Secondary: Number of Subjects with Treatment-emergent Adverse Events (TEAEs) during Treatment Period

End point title	Number of Subjects with Treatment-emergent Adverse Events (TEAEs) during Treatment Period

End point description:

An AE can be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal (investigational or non investigational) product, whether or not related to that medicinal (investigational or non investigational) product. TEAEs were AEs with onset during the treatment phase that has worsened since baseline. The full safety analysis set included all enrolled subjects who received at least 1 dose of study medication in the treatment period.

End point type	Secondary

End point timeframe:

Up to Week 9

End point values	Placebo	JNJ-67953964 10 milligrams (mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	84	85		
Units: Subjects	30	40		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Treatment Baseline in Snaith-Hamilton Pleasure Scale (SHAPS) Total Score at Treatment Week 6

End point title	Change from Treatment Baseline in Snaith-Hamilton Pleasure Scale (SHAPS) Total Score at Treatment Week 6

End point description:

The SHAPS is a self-reported 14-item, instrument, developed for the assessment of hedonic capacity. Subjects score whether they experience pleasure in performing a list of activities or experiences. Subjects can rate the answers as 1-4 where 1 indicates "Definitely agree", 2 indicates "Agree", 3 indicates "Disagree" and 4 indicates "Definitely disagree". The subject's item responses are summed to provide a total score ranging from 14 to 56. A higher total SHAPS score indicates higher levels of current anhedonia. Negative change from baseline indicates improvement. The eITT analysis set included all enrolled lead-in placebo non-responders who were randomized into a treatment period, received at least 1 dose of study medication, and had at least 1 post-baseline MADRS assessment during the treatment period. Here 'N' (number of subjects analyzed) includes the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Treatment Baseline and Treatment Week 6

End point values	Placebo	JNJ-67953964 10 milligrams (mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: scores on a scale				
least squares mean (standard error)	-3.7 (± 0.64)	-4.4 (± 0.64)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Comparison groups	Placebo v JNJ-67953964 10 milligrams (mg)

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4188
Method	Mixed models analysis
Parameter estimate	Least Squares Mean Difference
Confidence interval	
level	Other: 80 %
sides	1-sided
upper limit	0.41
Variability estimate	Standard error of the mean
Dispersion value	0.87

Secondary: Change from Treatment Baseline in Clinical Global Impression - Severity (CGI-S) Total Score at Treatment Week 6

End point title	Change from Treatment Baseline in Clinical Global Impression - Severity (CGI-S) Total Score at Treatment Week 6

End point description:

CGI-S provides an overall clinician-determined summary measure of severity of subject's illness that considers all available information, including knowledge of subject's history, psychosocial circumstances, symptoms, behavior, and impact of symptoms on subject's ability to function. CGI-S evaluates severity of psychopathology on scale of 0 to 7. Subject is assessed on severity of mental illness at time of rating according to: 0=not assessed; 1=normal (not at all ill); 2=borderline mentally ill; 3=mildly ill; 4=moderately ill; 5=markedly ill; 6=severely ill; 7=among most extremely ill patients. Negative change in score indicates improvement. eITT analysis set included all enrolled lead-in placebo non-responders who were randomized into a treatment period, received at least 1 dose of study medication, had at least 1 post-baseline MADRS assessment during treatment period. Here 'N' (number of subjects analyzed) includes number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Treatment Baseline and Treatment Week 6

End point values	Placebo	JNJ-67953964 10 milligrams (mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: Scores on a scale				
arithmetic mean (standard deviation)	-0.76 (± 0.858)	-0.92 (± 1.039)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Treatment Baseline in Symptoms of Major Depressive Disorder Scale (SMDDS) Total Score at Treatment Week 6

End point title	Change from Treatment Baseline in Symptoms of Major

	Depressive Disorder Scale (SMDDS) Total Score at Treatment Week 6

End point description:

The SMDDS is a 16-item patient reported outcome (PRO) measure. Each item was rated by the subject according to a 5-point Likert scale. Subjects respond to each question using a rating scale between 0 ("Not at all" or "Never") to 4 ("Extremely" or "Always"). The total score ranges from 0 to 60. The SMDDS uses a 7-day recall period and verbal rating scales. Higher score indicates more severe depressive symptomatology. Negative change from baseline indicates improvement. The eITT analysis set included all enrolled lead-in placebo non-responders who were randomized into a treatment period, received at least 1 dose of study medication, and had at least 1 post-baseline MADRS assessment during the treatment period. Here 'N' (number of subjects analyzed) includes the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Treatment Baseline and Treatment Week 6

End point values	Placebo	JNJ-67953964 10 milligrams (mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: Scores on a scale				
arithmetic mean (standard deviation)	-8.49 (± 9.567)	-8.03 (± 9.957)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Self-Assessment of Treatment Experience (SATE) Score at Treatment Week 6

End point title	Number of Subjects with Self-Assessment of Treatment Experience (SATE) Score at Treatment Week 6

End point description:

SATE questionnaire is a 1- or 2-item self-reported scale designed to provide additional information regarding subject’s subjective experience while taking treatment. This was internal Janssen questionnaire and questions were asked to subject weekly by the Q1.6-app. For rating overall depression, subject selected one option out of Improved, not changed or got worse; for depression improvement, subject selected one option out of slightly improved, much improved, very much improved and for depression worsen subject selected slightly worse, much worse, very much worse. The eITT analysis set included all enrolled lead-in placebo non-responders who were randomized into a treatment period, received at least 1 dose of study medication, and had at least 1 post-baseline MADRS assessment during the treatment period. Here 'n' (number analyzed) included all subjects evaluable for specified categories.

End point type	Secondary

End point timeframe:

Week 6

End point values	Placebo	JNJ-67953964 10 milligrams (mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	60		
Units: subjects				
Overall Depression (Got worse) (n= 40, 30)	1	0		
Overall Depression (Not changed) (n= 40, 30)	12	9		
Overall Depression (Improved) (n= 40, 30)	27	21		
Depression Worsened (Slightly worse) (n= 1, 0)	1	0		
Depression Worsened (Much worse) (n= 1, 0)	0	0		
Depression Worsened (Very much worse) (n=1,0)	0	0		
Depression Slightly improved (n=27, 21)	13	15		
Depression Much improved (n=27, 21)	11	6		
Depression Very Much Improved (n=27, 21)	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Treatment Baseline in Hamilton Anxiety Scale 6 (HAM-A6) Total Score at Treatment Week 6

End point title	Change from Treatment Baseline in Hamilton Anxiety Scale 6 (HAM-A6) Total Score at Treatment Week 6

End point description:

HAM-A scale assesses severity of different anxiety-related symptoms with a score range of 0 to 52. Higher score indicated severity in anxiety symptoms. Each of the 14 items is rated by clinician on a 5-point scale ranging from 0 (not present) to 4 (maximum degree). HAM-A6 is a uni-dimensional, 6-item subscale derived from HAM-A. HAM-A6 comprises of five psychic anxiety symptoms: anxious mood, psychic tension, fears, intellectual disturbances, and anxious behaviour observed at the interview, as well as one somatic item, muscular tension. HAM-A6 Subscale Score ranges from 0 to 24, with higher scores indicating greater severity of core symptoms. eITT analysis set included all enrolled lead-in placebo non-responders who were randomized into a treatment period, received at least 1 dose of study medication, and had at least 1 post-baseline MADRS assessment during the treatment period. Here 'N' (number of subjects analyzed) includes number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Treatment Baseline and Treatment Week 6

End point values	Placebo	JNJ-67953964 10 milligrams (mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: scores on a scale				
arithmetic mean (standard deviation)	-2.19 (± 2.837)	-2.73 (± 2.651)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Treatment Baseline in Structured Interview Guide for the Hamilton Anxiety Rating Scale (SIGH-A) Score at Treatment Week 6

End point title	Change from Treatment Baseline in Structured Interview Guide for the Hamilton Anxiety Rating Scale (SIGH-A) Score at Treatment Week 6

End point description:

SIGH-A is a 14-item scale to measure severity of different anxiety-related symptoms in subjects. Each of the 14 items is rated by the clinician on a 5-point scale ranging from 0 (not present) to 4 (maximum degree) with a total score range of 0 to 56 where higher score indicates worsening. The eITT analysis set included all enrolled lead-in placebo non-responders who were randomized into a treatment period, received at least 1 dose of study medication, and had at least 1 post-baseline MADRS assessment during the treatment period. Here 'N' (number of subjects analyzed) includes the number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Treatment Baseline and Treatment Week 6

End point values	Placebo	JNJ-67953964 10 milligrams (mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	59	59		
Units: scores on a scale				
arithmetic mean (standard deviation)	-5.37 (± 6.549)	-5.85 (± 5.369)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of JNJ-67953964

End point title	Maximum Plasma Concentration (Cmax) of JNJ-67953964

End point description:

Cmax is defined as maximum plasma concentration of JNJ-67953964. eITT population included all enrolled lead-in placebo non-responders who were randomized into a treatment period, received at least 1 dose of study medication, and had at least 1 post-baseline MADRS assessment during the treatment

period. Here 'N' (number of subjects analyzed) includes the number of subjects evaluable for this endpoint. Here 'n' (number analyzed) included all subjects evaluable for specified time point categories.

End point type	Secondary

End point timeframe:

Week 1, 3 and 6

End point values	JNJ-67953964 10 milligrams (mg)			
Subject group type	Reporting group			
Number of subjects analysed	58			
Units: nanograms per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
Week 1 (n=58)	32.7 (± 10.9)			
Week 3 (n=58)	33.5 (± 11.1)			
Week 6 (n=56)	34.3 (± 11.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Week 9

Adverse event reporting additional description:

Safety analysis set included all enrolled subjects who received at least 1 dose of study drug in treatment period. As planned, AEs were collected only during double blind treatment phase when study drug JNJ-67953964 was administered to randomized subjects. No AEs collected during Lead-in and Withdrawal period as subjects received only placebo.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Placebo

Reporting group description:

Subjects who were responders or non-responders to lead-in placebo group were re-randomized to receive JNJ-67953964 matching placebo capsules (2*1 placebo capsules) once daily during double blind treatment period (up to 6 weeks after lead-in period) in addition to SSRI/SNRI treatment.

Reporting group title	JNJ-67953964 10 milligrams (mg)

Reporting group description:

Subjects who were responders or non-responders to lead-in placebo group were re-randomized to receive 10 mg JNJ-67953964 capsules (2*5 mg JNJ-67953964 capsules) once daily during double-blind treatment period (up to 6 weeks after lead-in period) in addition to SSRI/SNRI treatment.

Serious adverse events	Placebo	JNJ-67953964 10 milligrams (mg)	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Hepatobiliary disorders			
Cholecystitis Acute			
subjects affected / exposed	1 / 84 (1.19%)	0 / 85 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	JNJ-67953964 10 milligrams (mg)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 84 (10.71%)	23 / 85 (27.06%)	

Nervous system disorders Headache subjects affected / exposed occurrences (all)	 6 / 84 (7.14%) 6	 10 / 85 (11.76%) 11	
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	 2 / 84 (2.38%) 2	 7 / 85 (8.24%) 7	
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	 0 / 84 (0.00%) 0	 5 / 85 (5.88%) 5	
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 2 / 84 (2.38%) 2	 5 / 85 (5.88%) 5	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 June 2018	Amendment INT-1 was substantial amendment and the overall reason for the amendment was to harmonize with procedures of some vendors, to update dosing instructions, and to correct typographical errors.
26 February 2019	Amendment INT-2 was substantial amendment and the overall reason for the amendment was to add the EudraCT number, to change inclusion criterion on female sterilization, to change exclusion criteria on concomitant medication (due to reconsideration of current clinical practices), and to implement a few changes requested by clinical sites.
28 August 2019	Amendment INT-3 was substantial amendment and the overall reason for the amendment was to harmonize aspects of local amendments (GBR-1 and GER-1) into one common protocol, to include corrections already documented in note-to-files, and to include some administrative corrections.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported