Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of JNJ-40411813 as Adjunctive Therapy in Subjects with Focal Onset Seizures with Suboptimal Response to Levetiracetam or Brivaracetam

Summary

EudraCT number	2020-003698-24
Trial protocol	DE PL ES BE
Global end of trial date	07 February 2024

Results information

Result version number	v1 (current)
This version publication date	22 February 2025
First version publication date	22 February 2025

Trial information

Trial identification

Sponsor protocol code	40411813EPY2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04836559
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route 202, South Raritan, New Jersey, United States, 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	07 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 February 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the efficacy of up to 3 dose levels of adjunctive JNJ-40411813 compared to placebo based on the time to baseline monthly seizure count in subjects with focal onset seizures who were receiving levetiracetam or brivaracetam and up to 3 other anti-epileptic drugs (AEDs).

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 Practices and applicable regulatory requirements.

Background therapy:

Levetiracetam or Brivavrcetam

Evidence for comparator:

A placebo control was used to establish the change in seizure count and the change in safety endpoints that may occur in the absence of active treatment.

Actual start date of recruitment	18 May 2021
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	Belgium: 2
Country: Number of subjects enrolled	Germany: 7
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Korea, Republic of: 25
Country: Number of subjects enrolled	Poland: 37
Country: Number of subjects enrolled	Russian Federation: 9
Country: Number of subjects enrolled	Ukraine: 7
Country: Number of subjects enrolled	United States: 9
Worldwide total number of subjects	110
EEA total number of subjects	60

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)	108
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects with focal onset seizures receiving levetiracetam/brivaracetam and up to 3 other AEDs enrolled. Subjects stratified as treated with CYP3A4 enzyme inducing anti-epileptic drugs(EIAED[induced]) & without CYP3A4 EIAED(noninduced). Safety set (SAS):randomised subjects who received at least (>=)1 dose of JNJ-40411813/placebo.

Pre-assignment

Screening details:

PK set: randomised subjects who received >=1 dose of JNJ-40411813 and >=1 valid blood sample drawn for PK analysis, excluded samples with below lower limit of quantification/inconsistent date/time or samples with previous dose date/time incomplete/concentration <10ng/mL. Due to inclusion/exclusion criteria difference, PK count differed from SAS.

Period 1

Period 1 title	Double Blind Period (Day 1 to Day 85)
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	DB: Cohort 1: Placebo

Arm description:

During double-blind (DB) period, subjects were randomised to receive placebo matching to JNJ-40411813 (JNJ) tablet orally twice a day (BID) from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects were screened every 4 weeks for monthly seizure counts up to Week (W) 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment, or enter open-label extension (OLE) period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through Week 12 and had option to perform DB period end-of-study visit (last visit for last subject; Day 85) or entered OLE period. Subjects who continued treatment to end of DB period (Week 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (Week 14).

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

Dosage and administration details:

Subjects received placebo matching to JNJ-40411813 tablet orally BID from Day 1 up to Day 85.

Arm title	DB: Cohort 1: JNJ-40411813

Arm description:

During DB period, subjects randomised to receive JNJ 100 milligrams (mg) or 50 mg tablet orally BID from Day 1 to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects treated with EIAEDs (induced) received 100 mg JNJ, subjects not treated with EIAEDs (non-induced) received 50 mg JNJ. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy, perform end-of-study/early withdrawal visit, continued DB period or enter OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through W 12 and had option to perform DB period end-of-study (Day 85) or entered OLE period. Subjects who continued treatment to end of DB period (W 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (W 14).

Arm type	Experimental
Investigational medicinal product name	JNJ-40411813
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received JNJ-40411813 100 mg or 50 mg tablet orally BID from Day 1 to Day 85. Subjects treated with EIAEDs (induced) received 100 mg JNJ-40411813, subjects not treated with EIAEDs (non-induced) received 50 mg JNJ-40411813.

Arm title	DB: Cohort 2: Placebo

Arm description:

During DB period, subjects were randomised to receive placebo matching to JNJ tablet orally BID from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment, or enter OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through Week 12 and had option to perform DB period end-of-study visit (Day 85) or entered OLE period. Subjects who continued treatment to the end of the DB period (W 12) and were not elected to participate in the OLE were followed up for safety up to 2 weeks after the last dose (W 14).

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

Dosage and administration details:

Subjects received placebo matching to JNJ-40411813 tablet orally BID from Day 1 up to Day 85.

Arm title	DB: Cohort 2: JNJ-40411813

Arm description:

During DB period, subjects were randomised to receive JNJ200 mg or 100 mg tablet orally BID from Day 1 to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects treated with EIAEDs (induced) received 200 mg JNJ, subjects not treated with EIAEDs (non-induced) received 100 mg JNJ. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment or entered OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through W 12 and had option to perform DB period end-of-study visit(Day 85) or entered OLE period. Subjects who continued treatment to end of DB period (W 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (W 14).

Arm type	Experimental
Investigational medicinal product name	JNJ-40411813
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received JNJ-40411813 200 mg or 100 mg tablet orally BID from Day 1 to Day 85. Subjects treated with EIAEDs (induced) received 200 mg JNJ-40411813, subjects not treated with EIAEDs (non-induced) received 100 mg JNJ-40411813.

Number of subjects in period 1	DB: Cohort 1: Placebo	DB: Cohort 1: JNJ-40411813	DB: Cohort 2: Placebo
Started	20	40	9
Full Analysis Set	20	40	9
Subjects treated with EIAED	11 [1]	22 [2]	6 [3]
Subjects not treated with EIAED	9 [4]	18 [5]	3 [6]
Completed	18	35	7
Not completed	2	5	2
Consent withdrawn by subject	-	1	1
Adverse event, non-fatal	-	4	1
Randomized by Mistake With Study Treatment	-	-	-
Unspecified	1	-	-
Protocol deviation	1	-	-

Number of subjects in period 1	DB: Cohort 2: JNJ-40411813
Started	41
Full Analysis Set	40
Subjects treated with EIAED	24 [7]
Subjects not treated with EIAED	17 [8]
Completed	36
Not completed	5
Consent withdrawn by subject	3
Adverse event, non-fatal	1
Randomized by Mistake With Study Treatment	1
Unspecified	-
Protocol deviation	-

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: Only reported subjects were planned to be included in this milestone.

[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: Only reported subjects were planned to be included in this milestone.

[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: Only reported subjects were planned to be included in this milestone.

[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: Only reported subjects were planned to be included in this milestone.

[5] - 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: Only reported subjects were planned to be included in this milestone.

[6] - 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: Only reported subjects were planned to be included in this milestone.

[7] - 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: Only reported subjects were planned to be included in this milestone.

[8] - 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: Only reported subjects were planned to be included in this milestone.

Period 2

Period 2 title	OLE Period (Day 1 of OLE up to 2 years)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	OLE: Cohort 1: Placebo Followed by JNJ-40411813

Arm description:

During OLE period, cohort 1 subjects who had received placebo during the DB period received JNJ-40411813 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) from Day 1 of OLE up to 2 years. Induced subjects (with EIAEDs) received JNJ-40411813 100 mg BID, and non-induced subjects (without EIAEDs) received JNJ-40411813 50 mg BID. The dose could be increased at the second visit (Month 1) to 200 mg JNJ-40411813 BID for induced subjects (with EIAEDs) and 100 mg JNJ-40411813 BID for non-induced subjects (without EIAEDs).

Arm type	Experimental
Investigational medicinal product name	JNJ-40411813
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects JNJ-40411813 orally from Day 1 of OLE up to 2 years. Induced subjects (with EIAEDs) received JNJ-40411813 100 mg BID, and non-induced subjects (without EIAEDs) received JNJ-40411813 50 mg BID.

Arm title	OLE: Cohort 1: JNJ-40411813 Followed by JNJ-40411813

Arm description:

During OLE period, cohort 1 subjects who had received JNJ-40411813 during the DB period continued to receive JNJ-40411813 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) from Day 1 of OLE up to 2 years. Induced subjects (with EIAEDs) received JNJ-40411813 100 mg BID, and non-induced subjects (without EIAEDs) received JNJ-40411813 50 mg BID. The dose could be increased at the second visit (Month 1) to 200 mg JNJ-40411813 BID for induced subjects (with EIAEDs) and 100 mg JNJ-40411813 BID for non-induced subjects (without EIAEDs).

Arm type	Experimental
Investigational medicinal product name	JNJ-40411813
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received JNJ-40411813 orally from Day 1 of OLE up to 2 years. Induced subjects (with EIAEDs) received JNJ-40411813 100 mg BID, and non-induced subjects (without EIAEDs) received JNJ-40411813 50 mg BID.

Arm title	OLE: Cohort 2: Placebo Followed by JNJ-40411813

Arm description:

During the OLE period, cohort 2 subjects who had received placebo during the DB period received JNJ-40411813 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) from Day 1 of OLE up to 2 years. Subjects started with JNJ-40411813 100 mg BID. Induced subjects (with EIAEDs) had their dose increased to JNJ-40411813 200 mg BID on Day 8 of the OLE. Non-induced subjects (without EIAEDs) continued with JNJ-40411813 100 mg BID.

Arm type	Experimental
Investigational medicinal product name	JNJ-40411813
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received JNJ-40411813 orally from Day 1 of OLE up to 2 years. Subjects started with JNJ-40411813 100 mg BID. Induced subjects (with EIAEDs) had their dose increased to JNJ-40411813 200 mg BID on Day 8 of the OLE. Non-induced subjects (without EIAEDs) continued with JNJ-40411813 100 mg BID.

Arm title	OLE: Cohort 2: JNJ-40411813 Followed by JNJ-40411813

Arm description:

During OLE period, cohort 2 subjects who had received JNJ-40411813 during the DB period continued to receive JNJ-40411813 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) from Day 1 of OLE up to 2 years. Subjects started with JNJ-40411813 100 mg BID. Induced subjects (with EIAEDs) had their dose increased to JNJ-40411813 200 mg BID on Day 8 of the OLE. Non-induced subjects (without EIAEDs) continued with JNJ-40411813 100 mg BID.

Arm type	Experimental
Investigational medicinal product name	JNJ-40411813
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received JNJ-40411813 orally from Day 1 of OLE up to 2 years. Subjects started with JNJ-40411813 100 mg BID. Induced subjects (with EIAEDs) had their dose increased to JNJ-40411813 200 mg BID on Day 8 of the OLE. Non-induced subjects (without EIAEDs) continued with JNJ-40411813 100 mg BID.

Number of subjects in period 2[9]	OLE: Cohort 1: Placebo Followed by JNJ-40411813	OLE: Cohort 1: JNJ-40411813 Followed by JNJ-40411813	OLE: Cohort 2: Placebo Followed by JNJ-40411813
Started	12	23	7
OLE: subjects treated with EIAED	6	15	4
OLE: subjects not treated with EIAED	6	8	3
Completed	0	0	0
Not completed	12	23	7
Consent withdrawn by subject	4	2	-
No Longer Clinically Benefitting	-	-	-
Study Terminated by Sponsor	7	14	4
Lack of efficacy	1	7	3

Number of subjects in period 2[9]	OLE: Cohort 2: JNJ-40411813 Followed

	by JNJ-40411813
Started	31
OLE: subjects treated with EIAED	19
OLE: subjects not treated with EIAED	12
Completed	0
Not completed	31
Consent withdrawn by subject	2
No Longer Clinically Benefitting	1
Study Terminated by Sponsor	24
Lack of efficacy	4

Notes:

[9] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only reported subjects were planned to be included in this period.

Baseline characteristics

Reporting groups

Reporting group title	DB: Cohort 1: Placebo

Reporting group description:

During double-blind (DB) period, subjects were randomised to receive placebo matching to JNJ-40411813 (JNJ) tablet orally twice a day (BID) from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects were screened every 4 weeks for monthly seizure counts up to Week (W) 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment, or enter open-label extension (OLE) period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through Week 12 and had option to perform DB period end-of-study visit (last visit for last subject; Day 85) or entered OLE period. Subjects who continued treatment to end of DB period (Week 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (Week 14).

Reporting group title	DB: Cohort 1: JNJ-40411813

Reporting group description:

During DB period, subjects randomised to receive JNJ 100 milligrams (mg) or 50 mg tablet orally BID from Day 1 to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects treated with EIAEDs (induced) received 100 mg JNJ, subjects not treated with EIAEDs (non-induced) received 50 mg JNJ. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy, perform end-of-study/early withdrawal visit, continued DB period or enter OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through W 12 and had option to perform DB period end-of-study (Day 85) or entered OLE period. Subjects who continued treatment to end of DB period (W 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (W 14).

Reporting group title	DB: Cohort 2: Placebo

Reporting group description:

During DB period, subjects were randomised to receive placebo matching to JNJ tablet orally BID from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment, or enter OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through Week 12 and had option to perform DB period end-of-study visit (Day 85) or entered OLE period. Subjects who continued treatment to the end of the DB period (W 12) and were not elected to participate in the OLE were followed up for safety up to 2 weeks after the last dose (W 14).

Reporting group title	DB: Cohort 2: JNJ-40411813

Reporting group description:

During DB period, subjects were randomised to receive JNJ200 mg or 100 mg tablet orally BID from Day 1 to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects treated with EIAEDs (induced) received 200 mg JNJ, subjects not treated with EIAEDs (non-induced) received 100 mg JNJ. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment or entered OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through W 12 and had option to perform DB period end-of-study visit(Day 85) or entered OLE period. Subjects who continued treatment to end of DB period (W 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (W 14).

Reporting group values	DB: Cohort 1: Placebo	DB: Cohort 1: JNJ-40411813	DB: Cohort 2: Placebo
Number of subjects	20	40	9
Age Categorical Units: Subjects			

Age continuous Units: Years			
arithmetic mean	41.3	37.5	39.7
standard deviation	± 12.55	± 12.40	± 10.84
Gender categorical Units: Subjects			
Male	15	23	4
Female	5	17	5
Ethnicity Units: Subjects			
Hispanic or Latino	1	2	4
Not Hispanic or Latino	19	37	5
Unknown or Not Reported	0	1	0
Race Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	5	11	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	15	29	8
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	DB: Cohort 2: JNJ-40411813	Total	
Number of subjects	41	110	
Age Categorical Units: Subjects			

Age continuous Units: Years			
arithmetic mean	41.3		
standard deviation	± 11.47	-	
Gender categorical Units: Subjects			
Male	18	60	
Female	23	50	
Ethnicity Units: Subjects			
Hispanic or Latino	5	12	
Not Hispanic or Latino	36	97	
Unknown or Not Reported	0	1	
Race Units: Subjects			
American Indian or Alaska Native	1	2	
Asian	10	26	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	30	82	
More than one race	0	0	

Unknown or Not Reported	0	0	

End points reporting groups

Reporting group title	DB: Cohort 1: Placebo

Reporting group description:

During double-blind (DB) period, subjects were randomised to receive placebo matching to JNJ-40411813 (JNJ) tablet orally twice a day (BID) from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects were screened every 4 weeks for monthly seizure counts up to Week (W) 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment, or enter open-label extension (OLE) period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through Week 12 and had option to perform DB period end-of-study visit (last visit for last subject; Day 85) or entered OLE period. Subjects who continued treatment to end of DB period (Week 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (Week 14).

Reporting group title	DB: Cohort 1: JNJ-40411813

Reporting group description:

During DB period, subjects randomised to receive JNJ 100 milligrams (mg) or 50 mg tablet orally BID from Day 1 to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects treated with EIAEDs (induced) received 100 mg JNJ, subjects not treated with EIAEDs (non-induced) received 50 mg JNJ. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy, perform end-of-study/early withdrawal visit, continued DB period or enter OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through W 12 and had option to perform DB period end-of-study (Day 85) or entered OLE period. Subjects who continued treatment to end of DB period (W 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (W 14).

Reporting group title	DB: Cohort 2: Placebo

Reporting group description:

During DB period, subjects were randomised to receive placebo matching to JNJ tablet orally BID from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment, or enter OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through Week 12 and had option to perform DB period end-of-study visit (Day 85) or entered OLE period. Subjects who continued treatment to the end of the DB period (W 12) and were not elected to participate in the OLE were followed up for safety up to 2 weeks after the last dose (W 14).

Reporting group title	DB: Cohort 2: JNJ-40411813

Reporting group description:

During DB period, subjects were randomised to receive JNJ200 mg or 100 mg tablet orally BID from Day 1 to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects treated with EIAEDs (induced) received 200 mg JNJ, subjects not treated with EIAEDs (non-induced) received 100 mg JNJ. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment or entered OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through W 12 and had option to perform DB period end-of-study visit(Day 85) or entered OLE period. Subjects who continued treatment to end of DB period (W 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (W 14).

Reporting group title	OLE: Cohort 1: Placebo Followed by JNJ-40411813

Reporting group description:

During OLE period, cohort 1 subjects who had received placebo during the DB period received JNJ-40411813 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) from Day 1 of OLE up to 2 years. Induced subjects (with EIAEDs) received JNJ-40411813 100 mg BID, and non-induced subjects (without EIAEDs) received JNJ-40411813 50 mg BID. The dose could be increased at the second visit (Month 1) to 200 mg JNJ-40411813 BID for induced subjects (with EIAEDs) and 100 mg JNJ-40411813 BID for non-induced subjects (without EIAEDs).

Reporting group title	OLE: Cohort 1: JNJ-40411813 Followed by JNJ-40411813

Reporting group description:

During OLE period, cohort 1 subjects who had received JNJ-40411813 during the DB period continued to receive JNJ-40411813 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) from Day 1 of OLE up to 2 years. Induced subjects (with EIAEDs) received JNJ-40411813 100 mg BID, and non-induced subjects (without EIAEDs) received JNJ-40411813 50 mg BID. The dose could be increased at the second visit (Month 1) to 200 mg JNJ-40411813 BID for induced subjects (with EIAEDs) and 100 mg JNJ-40411813 BID for non-induced subjects (without EIAEDs).

Reporting group title	OLE: Cohort 2: Placebo Followed by JNJ-40411813

Reporting group description:

During the OLE period, cohort 2 subjects who had received placebo during the DB period received JNJ-40411813 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) from Day 1 of OLE up to 2 years. Subjects started with JNJ-40411813 100 mg BID. Induced subjects (with EIAEDs) had their dose increased to JNJ-40411813 200 mg BID on Day 8 of the OLE. Non-induced subjects (without EIAEDs) continued with JNJ-40411813 100 mg BID.

Reporting group title	OLE: Cohort 2: JNJ-40411813 Followed by JNJ-40411813

Reporting group description:

During OLE period, cohort 2 subjects who had received JNJ-40411813 during the DB period continued to receive JNJ-40411813 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) from Day 1 of OLE up to 2 years. Subjects started with JNJ-40411813 100 mg BID. Induced subjects (with EIAEDs) had their dose increased to JNJ-40411813 200 mg BID on Day 8 of the OLE. Non-induced subjects (without EIAEDs) continued with JNJ-40411813 100 mg BID.

Subject analysis set title	DB: Cohort 1: JNJ-40411813 Induced
Subject analysis set type	Safety analysis

Subject analysis set description:

During DB period, subjects treated with EIAEDs (induced) received 100 mg JNJ-40411813 tablet orally BID from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29 and 57. Subjects were screened every 4 weeks for monthly seizure counts up to Week 12. Subjects who had exceeded their pre-randomization monthly seizure count had the option to discontinue study drug due to lack of efficacy and perform the end-of-study/early withdrawal visit, continued DB treatment, or enter OLE period. Subjects who had not exceeded pre-randomization seizure count continued DB treatment period through W 12 and had option to perform end-of-study for DB period visit (last visit for last subject; Day 85) or enter OLE period. Subjects who continued treatment to the end of the DB period (W12) and were not elected to participate in the OLE were followed up for safety up to 2 weeks after the last dose (W 14).

Subject analysis set title	DB: Cohort 2: JNJ-40411813 Non-induced
Subject analysis set type	Safety analysis

Subject analysis set description:

During DB period, subjects not treated with EIAEDs (non-induced) received 100 mg JNJ-40411813 tablet orally BID from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had the option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment, or enter OLE period. Subjects who had not exceeded pre-randomization seizure count continued the DB treatment period through Week 12 and had option to perform the end-of-study for DB period visit (Day 85) or enter the OLE period. Subjects who continued treatment to the end of the DB period (W 12) and were not elected to participate in the OLE were followed up for safety up to 2 weeks after last dose (W 14).

Subject analysis set title	DB: Cohort 2: JNJ-40411813 Induced
Subject analysis set type	Safety analysis

Subject analysis set description:

During DB period, subjects treated with EIAEDs (induced) received 200 mg JNJ-40411813 tablet orally BID from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had the option to discontinue the study treatment due to lack of efficacy and perform the end-of-study/early withdrawal visit, continue DB treatment, or enter the OLE period. Subjects who had not exceeded the pre-randomisation seizure count continued the DB treatment period through W 12 and had the option to perform the end-of-study for DB period visit (Day 85) or enter the OLE period. Subjects who continued treatment to the end of the DB period (W 12) and were not elected to participate in the OLE were followed up for safety up to 2 weeks after the last dose (W 14).

Subject analysis set title	DB: Cohorts 1 and 2: Placebo
Subject analysis set type	Safety analysis

Subject analysis set description:

During DB period, subjects were randomised to receive placebo matching to JNJ-40411813 tablet orally BID from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomization monthly seizure count had the option to discontinue the study treatment due to lack of efficacy and perform the end-of-study/early withdrawal visit, continue DB treatment, or enter the OLE period. Subjects who had not exceeded the pre-randomisation seizure count continued the DB treatment period through W 12 and had the option to perform the end-of-study for DB period visit (Day 85) or enter the OLE period. Subjects who continued treatment to the end of the DB period (W 12) and were not elected to participate in the OLE were followed up for safety up to 2 weeks after the last dose (W 14).

Subject analysis set title	DB: Cohorts (C) 1 and 2: JNJ-40411813
Subject analysis set type	Safety analysis

Subject analysis set description:

During DB period, subjects randomised to receive JNJ tablets orally BID from Day 1 to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects treated with EIAEDs received 100 mg (C 1) or 200 mg (C 2) JNJ. Subjects not treated with EIAEDs received 50 mg (C 1) or 100 mg (C 2) JNJ. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment or enter OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through W 12 and had option to perform end-of-study for DB period (Day 85) or enter OLE period. Subjects who continued treatment to end of DB period (W 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (W 14).

Subject analysis set title	OLE: Cohort 1: JNJ-40411813 Non-induced
Subject analysis set type	Safety analysis

Subject analysis set description:

During OLE period, cohort 1 non-induced subjects (without EIAEDs) received JNJ-40411813 50 mg BID along with previously prescribed AEDs (one of which must include levetiracetam or brivaracetam) from Day 1 of OLE up to 2 years. The dose could be increased at the second visit to 100 mg JNJ-40411813 BID.

Subject analysis set title	OLE: Cohort 1: JNJ-40411813 Induced
Subject analysis set type	Safety analysis

Subject analysis set description:

During OLE period, cohort 1 induced subjects (with EIAEDs) received JNJ-40411813 100 mg BID along with previously prescribed AEDs (one of which must include levetiracetam or brivaracetam) from Day 1 of OLE up to 2 years. The dose could be increased at the second visit to 200 mg JNJ-40411813 BID.

Subject analysis set title	OLE: Cohort 2: JNJ-40411813 Non-induced
Subject analysis set type	Safety analysis

Subject analysis set description:

During the OLE period, cohort 2 subjects started with JNJ-40411813 100 mg BID along with previously prescribed AEDs (one of which must include levetiracetam or brivaracetam) from Day 1 of OLE up to 2 years. Non-induced subjects (without EIAEDs) continued with JNJ-40411813 100 mg BID up to 2 years of OLE.

Subject analysis set title	OLE: Cohort 2: JNJ-40411813 Induced
Subject analysis set type	Safety analysis

Subject analysis set description:

During the OLE period, cohort 2 subjects started with JNJ-40411813 100 mg BID along with previously prescribed AEDs (one of which must include levetiracetam or brivaracetam) from Day 1 of OLE up to 2 years. Induced subjects (with EIAEDs) had their dose increased to JNJ-40411813 200 mg BID on Day 8 up to 2 years of OLE.

Subject analysis set title	OLE: Cohorts 1 and 2: Placebo Followed by JNJ-40411813
Subject analysis set type	Safety analysis

Subject analysis set description:

During OLE period, subjects who had received placebo during the DB period received JNJ-40411813 along with previously prescribed AEDs (one of which must include levetiracetam or brivaracetam) from Day 1 of OLE up to 2 years. Cohort 1: Induced subjects (with EIAEDs) started with JNJ-40411813 100 mg BID, which could be increased to 200 mg BID at the second visit. Non-induced subjects (without EIAEDs) started with JNJ-40411813 50 mg BID, which could be increased to 100 mg BID at the second visit. Cohort 2: All subjects started with JNJ-40411813 100 mg BID. Induced subjects (with EIAEDs) had their dose increased to 200 mg BID on Day 8 of the OLE, while non-induced subjects (without EIAEDs)

continued with 100 mg BID.

Subject analysis set title	OLE: Cohorts 1 and 2: JNJ-40411813 Followed by JNJ-40411813
Subject analysis set type	Safety analysis

Subject analysis set description:

During OLE period, subjects who had received JNJ-40411813 during the DB period continued to receive JNJ-40411813 along with previously prescribed AEDs (one of which must include levetiracetam or brivaracetam) from Day 1 of OLE up to 2 years. Cohort 1: Induced subjects(with EIAEDs) received JNJ-40411813 100 mg BID, which could be increased to 200 mg BID at the second visit. Non-induced subjects (without EIAEDs) received JNJ-40411813 50 mg BID, which could be increased to 100 mg BID at the second visit. Cohort 2: All subjects started with JNJ-40411813 100 mg BID. Induced subjects (with EIAEDs) had their dose increased to 200 mg BID on Day 8 of the OLE, while non-induced subjects (without EIAEDs) continued with 100 mg BID.

Subject analysis set title	DB: Cohort 1: JNJ-40411813 Non-induced
Subject analysis set type	Safety analysis

Subject analysis set description:

During DB period, subjects not treated with EIAEDs (non-induced) received 50 mg JNJ-40411813 tablet orally BID from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29 and 57. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study drug due to lack of efficacy and perform end-of-study/early withdrawal visit, continued DB treatment, or enterOLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB treatment period through W 12 and had option to perform end-of-study for DB period visit (Day 85) or enter OLE period. Subjects who continued treatment to the end of DB period (W 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after the last dose (W 14).

Primary: Cohort 1 and 2: Time to Baseline Monthly Seizure Count up to the End of the 12-Week Double-blind (DB) Treatment Period

End point title	Cohort 1 and 2: Time to Baseline Monthly Seizure Count up to the End of the 12-Week Double-blind (DB) Treatment Period

End point description:

Time (in days) to baseline monthly seizure count was defined as the number of days until the subjects cumulative seizure count during the DB period was equal to their baseline monthly seizure count. The baseline monthly seizure count was defined as the number of observable focal onset seizures occurred during the 8-week baseline period (Day -56 to -1), multiplied by 28/XBL, where XBL was the number of days comprising the subjects baseline period. Observable focal onset seizures included focal aware seizures with motor signs, focal impaired awareness seizures and focal to bilateral tonic-clonic seizures. Focal aware seizures without motor signs, myoclonic, or other generalised seizures was not counted towards baseline monthly seizure count. Cluster seizures were counted as a single seizure. Kaplan-Meier method was used for the analysis. Full analysis set (FAS) included all randomised subjects assigned to receive study intervention and had both baseline and postbaseline seizure data.

End point type	Primary

End point timeframe:

From DB period Day 1 up to Day 85

End point values	DB: Cohort 1: Placebo	DB: Cohort 1: JNJ-40411813	DB: Cohort 2: Placebo	DB: Cohort 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	9	40
Units: Days				
median (confidence interval 95%)	32 (28 to 37)	34 (27 to 48)	29 (22 to 69)	38 (28 to 48)

Statistical analyses

Statistical analysis title	Statistical analysis 2
Comparison groups	DB: Cohort 2: Placebo v DB: Cohort 2: JNJ-40411813
Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6306
Method	t-test, 1-sided
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.75

Statistical analysis title	Statistical analysis 1
Comparison groups	DB: Cohort 1: Placebo v DB: Cohort 1: JNJ-40411813
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3571
Method	t-test, 1-sided
Parameter estimate	Hazard ratio (HR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	1.38

Secondary: Cohort 1 and 2: Number of Subjects With Seizure Freedom at the End of OLE Period

End point title	Cohort 1 and 2: Number of Subjects With Seizure Freedom at the End of OLE Period

End point description:

Number of subjects with seizure freedom at the end of OLE period was reported. Seizure freedom was defined as having no seizures over the complete OLE study period. FASOLE analysis set included all FAS subjects who received at least 1 dose of study intervention in the OLE period.

End point type	Secondary

End point timeframe:

From OLE baseline (Day 1 of OLE) up to 24 months after start of OLE (the actual OLE starting time varied for each subject)

End point values	OLE: Cohort 1: Placebo Followed by JNJ-40411813	OLE: Cohort 1: JNJ-40411813 Followed by JNJ-40411813	OLE: Cohort 2: Placebo Followed by JNJ-40411813	OLE: Cohort 2: JNJ-40411813 Followed by JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	23	7	31
Units: Subjects	1	0	0	3

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and 2: Percent Reduction in the Open Label Extension (OLE) Period Monthly Seizure Rate

End point title	Cohort 1 and 2: Percent Reduction in the Open Label Extension (OLE) Period Monthly Seizure Rate

End point description:

The percent reduction in the OLE monthly seizure rate was defined as 100*(baseline monthly seizure count minus OLE monthly seizure count) divided by (baseline monthly seizure count). The OLE monthly seizure count was defined as the total number of observable focal onset seizures occurred during the OLE period, multiplied by 28/XOLE, where XOLE was the number of days comprising the OLE. A positive percentage change in the OLE monthly seizure count indicated improvement. Observable seizures included focal aware seizures with motor signs, focal impaired awareness seizures and focal to bilateral tonic-clonic seizures. Focal aware seizures without motor signs, myoclonic, or other generalised seizures was not counted towards baseline monthly seizure count. Cluster seizures were counted as a single seizure. Full analysis set: open-label extension (FASOLE) analysis set included all FAS subjects who received at least 1 dose of study intervention in the OLE period.

End point type	Secondary

End point timeframe:

From OLE baseline (Day 1 of OLE) up to 24 months after start of OLE (the actual OLE starting time varied for each subject)

End point values	OLE: Cohort 1: Placebo Followed by JNJ-40411813	OLE: Cohort 1: JNJ-40411813 Followed by JNJ-40411813	OLE: Cohort 2: Placebo Followed by JNJ-40411813	OLE: Cohort 2: JNJ-40411813 Followed by JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	23	7	31
Units: Percent change (reduction)				
median (inter-quartile range (Q1-Q3))	39.9 (14.3 to 64.1)	49.1 (-1.5 to 77.1)	29.1 (22.6 to 76.6)	52.1 (-3.7 to 85.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and 2: Number of Subjects With at Least 50 Percent (%) Reduction (Response) in the OLE Monthly Seizure Count

End point title	Cohort 1 and 2: Number of Subjects With at Least 50 Percent (%) Reduction (Response) in the OLE Monthly Seizure Count

End point description:

Number of subject having at least a 50% reduction in the monthly seizure rate (response) during the OLE study period was reported. FASOLE analysis set included all FAS subjects who received at least 1 dose of study intervention in the OLE period.

End point type	Secondary

End point timeframe:

From OLE baseline (Day 1 of OLE) up to 24 months after start of OLE (the actual OLE starting time varied for each subject)

End point values	OLE: Cohort 1: Placebo Followed by JNJ-40411813	OLE: Cohort 1: JNJ-40411813 Followed by JNJ-40411813	OLE: Cohort 2: Placebo Followed by JNJ-40411813	OLE: Cohort 2: JNJ-40411813 Followed by JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	23	7	31
Units: Subjects	5	11	3	16

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Cohort 1 and 2: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	OLE Period: Cohort 1 and 2: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point description:

Number of subjects with TEAEs and TESAEs were reported. Adverse event (AE) was any untoward medical occurrence in a clinical study subject administered a medicinal (investigational or non-investigational) product. AE does not necessarily have a causal relationship with the intervention. Serious AE: any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was a suspected transmission of any infectious agent via a medicinal product, or was medically important. TEAE/TESAE: any AE/SAE occurred at or after initial administration of study intervention(SI) through the day of last dose plus 5 days. TEAEs included serious and non-serious events. Safety open label extension (SAFOLE) analysis set: all randomised subjects who received at least 1 dose of study intervention in OLE period.

End point type	Secondary

End point timeframe:

From OLE baseline (Day 1 of OLE) up to 5 days after last dose of OLE period (5 days + 24 months after start of OLE) (the actual OLE starting time varied for each subject)

End point values	OLE: Cohort 1: Placebo Followed by JNJ-40411813	OLE: Cohort 1: JNJ-40411813 Followed by JNJ-40411813	OLE: Cohort 2: Placebo Followed by JNJ-40411813	OLE: Cohort 2: JNJ-40411813 Followed by JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	23	7	31
Units: Subjects				
TEAEs	6	16	6	17
TESAEs	0	5	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Cohort 1 and 2: Number of Subjects With Treatment-emergent (TE) Clinically Important Changes in Vital Signs (VS)

End point title	OLE Period: Cohort 1 and 2: Number of Subjects With Treatment-emergent (TE) Clinically Important Changes in Vital Signs (VS)

End point description:

TE clinically important changes in VS: pulse rate(PR) greater than (>)100 beats per min(bpm) and >30bpm increase from baseline(BL), PR less than (<)50 bpm and >20bpm decrease from BL, systolic blood pressure(SBP) >140millimetres of mercury(mmHg) and >40mmHg increase from BL, SBP <90mmHg and >30 mmHg decrease from BL), diastolic blood pressure(DBP) >90mmHg and >30mmHg increase from BL, DBP <50mmHg and >20mmHg decrease from BL, temperature >38degree Celsius(C) and greater than or equal to(>=)1degree C increase from BL. TE: post-BL value was above upper limit(UL), BL value was below UL(Normal/Low). Same applies to post-BL value below lower limit(LL) with BL value above LL(Normal/High). TEVS:VS occurred at/after initial administration of SI through last dose plus 5 days. Categories with at least 1 subject had data were reported. SAFOLE set. N(number of subjects analysed)=subjects with at least 1 post BL value for specified VS;n(number analysed)=subjects evaluable at specified parameter.

End point type	Secondary

End point timeframe:

From OLE baseline (Day 1 of OLE) up to 24 months + 5 days after start of OLE (the actual OLE starting time varied for each subject)

End point values	OLE: Cohort 1: Placebo Followed by JNJ-40411813	OLE: Cohort 1: JNJ-40411813 Followed by JNJ-40411813	OLE: Cohort 2: Placebo Followed by JNJ-40411813	OLE: Cohort 2: JNJ-40411813 Followed by JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[1]	1	0[2]	1
Units: Subjects				
PR>100bpm with >30bpm increase from BL n=0,1,0,1		1		1
SBP>140mmHg,with >40mmHg increase fromBLn=0,1,0,0		1		0
DBP>90mmHg,with >30mmHg increase from BLn=0,1,0,0		1		0

Notes:

[1] - There was no subjects with at least 1 postbaseline value for the specified vital sign parameters

[2] - There was no subjects with at least 1 postbaseline value for the specified vital sign parameters

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Cohort 1 and 2: Number of Subjects With Changes in Laboratory Assessments Recorded as TEAE

End point title	OLE Period: Cohort 1 and 2: Number of Subjects With Changes in Laboratory Assessments Recorded as TEAE

End point description:

Number of subjects with changes in laboratory assessments recorded as TEAE were reported. Laboratory assessments included clinical chemistry, hematology and urinalysis. Postbaseline abnormalities were compared with baseline values: if postbaseline value exceeding the upper limit (baseline below upper limit) or falling below the lower limit (baseline above lower limit) was considered treatment-emergent (TE); if baseline values were missing then any postbaseline abnormality was considered TE. SAFOLE analysis set included all randomised subjects who received at least 1 dose of study intervention in the OLE period. TEAE was defined as any AE occurring at or after the initial administration of study intervention through the day of last dose plus 5 days.

End point type	Secondary

End point timeframe:

From OLE baseline (Day 1 of OLE) up to 24 months + 5 days after start of OLE (the actual OLE starting time varied for each subject)

End point values	OLE: Cohort 1: Placebo Followed by JNJ-40411813	OLE: Cohort 1: JNJ-40411813 Followed by JNJ-40411813	OLE: Cohort 2: Placebo Followed by JNJ-40411813	OLE: Cohort 2: JNJ-40411813 Followed by JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	23	7	31
Units: Subjects				
Chemistry	2	4	0	2
Hematology	0	1	0	1
Urinalysis	0	2	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: DB Treatment Period: Cohort 1 and 2: Number of Subjects With Treatment-emergent Clinically Important Changes in Vital Signs

End point title	DB Treatment Period: Cohort 1 and 2: Number of Subjects With Treatment-emergent Clinically Important Changes in Vital Signs

End point description:

TE clinically important changes in VS: PR >100bpm and with >30bpm increase from BL, PR <50bpm and with >20bpm decrease from BL, SBP >140mmHg and with >40mmHg increase from BL, SBP <90mmHg and with >30mmHg decrease from BL, DBP >90mmHg and with >30mmHg increase from BL, DBP <50mmHg and with >20mmHg decrease from BL, and temperature >38degree C and with >=1degree C increase from BL. TE: post BL value was above UL and BL value was below UL (Normal/Low). Same applies to post BL value being below lower limit with baseline value being above lower limit (Normal/High). TEVS:VS occurred at/after initial administration of SI through last dose plus 5 days. Only categories in which at least 1 subject had data were reported. Safety analysis set: all randomised subjects who received at least 1 dose of JNJ-40411813 or placebo in DB period. N(number of subjects analysed)=subjects with at least 1 post-BL value for specified VS; (number analysed)=subjects evaluable at specified parameter.

End point type	Secondary

End point timeframe:

From DB period start (Day 1) up to 5 days after last dose of DB period (up to Day 90)

End point values	DB: Cohort 1: Placebo	DB: Cohort 1: JNJ-40411813	DB: Cohort 2: Placebo	DB: Cohort 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	1	1	0[3]	2
Units: Subjects				
PR >100bpm, >30bpm increase from BLn=0,1,0,2	0	1		2
SBP>140mmHg,with >40mmHg increase fromBLn=0,1,0,0	0	1		0
DBP>90mmHg,with >30mmHg increase from BLn=1,0,0,0	1	0		0

Notes:

[3] - There was no subjects with at least 1 postbaseline value for the specified vital sign parameters

Statistical analyses

No statistical analyses for this end point

Secondary: DB Treatment Period: Cohort 1 and 2: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point title	DB Treatment Period: Cohort 1 and 2: Number of Subjects With Treatment-emergent Adverse Events (TEAEs) and Treatment-emergent Serious Adverse Events (TESAEs)

End point description:

Number of subjects with TEAEs and TESAEs were reported. An AE was any untoward medical occurrence in a clinical study Subject administered a medicinal (investigational or non-investigational) product. An AE does not necessarily have a causal relationship with the intervention. A serious AE was defined as any untoward medical occurrence that at any dose resulted in death, was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, was a suspected transmission of any infectious agent via a medicinal product, or was medically important. TEAE/TESAE was defined as any AE/SAE occurring at or after the initial administration of study intervention through the day of last dose plus 5 days. TEAEs: serious and non-serious events. Safety analysis set (SAF): all randomised subjects who received at least 1 dose of JNJ-40411813 or placebo in DB period.

End point type	Secondary

End point timeframe:

From DB period start (Day 1) up to 5 days after last dose of DB period (up to Day 90)

End point values	DB: Cohort 1: Placebo	DB: Cohort 1: JNJ-40411813	DB: Cohort 2: Placebo	DB: Cohort 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	9	41
Units: Subjects				
TEAEs	7	22	8	24
TESAEs	0	1	1	2

Statistical analyses

No statistical analyses for this end point

Secondary: DB Treatment Period: Cohort 1 and 2: Number of Subjects With Treatment-emergent Clinically Important Changes in Electrocardiogram (ECG)

End point title	DB Treatment Period: Cohort 1 and 2: Number of Subjects With Treatment-emergent Clinically Important Changes in Electrocardiogram (ECG)

End point description:

ECG parameters analysed: heart rate, PR interval, RR interval, QRS interval, QT interval, and corrected QT (QTc) interval using following correction methods: Bazett's formula (QTcB), Fridericia's formula (QTcF). TE clinically important changes ECG values (relative to baseline) were heart rate (bpm): <45 and >100; PR interval (milllisecond [msec]): <120 and >200; QRS interval (msec): >120; QTc (msec): >470 in women and >450 in men. TE: post BL value was above UL and BL value was below the UL (Normal/Low). Same applies to post BL value being below the LL with BL value being above the LL (Normal/High). TE ECGs: clinically important ECGs which occurred as at or after initial administration of study intervention through last dose plus 5 days. Only categories in which at least 1 subject had data were reported. Safety analysis set. N (number of subjects analysed)=subjects with at least 1 post-BL value for specified parameter; n (number analysed)=subjects evaluable at specified parameter.

End point type	Secondary

End point timeframe:

From DB period start (Day 1) up to 5 days after last dose of DB period (up to Day 90)

End point values	DB: Cohort 1: Placebo	DB: Cohort 1: JNJ-40411813	DB: Cohort 2: Placebo	DB: Cohort 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	9	41
Units: Subjects				
PR Interval (<120) n= 19,40,9,40	1	2	0	2
PR Interval (>200) n= 19,40,9,40	0	2	1	2
QRS Duration (>120) n= 19,40,9,40	0	2	0	1
QTcB Interval (Female) (>470) n= 5,17,5,23	1	0	0	0
QTcB Interval (male) (>450) n= 14,23,4,17	0	1	0	2
QTcF Interval (male) (>450) n= 14,23,4,17	0	0	0	1
Heart Rate >100 n= 19, 40,9, 40	0	0	0	1

Statistical analyses

No statistical analyses for this end point

Secondary: DB Treatment Period: Cohort 1 and 2: Number of Subjects With Changes in Laboratory Assessments Recorded as TEAE

End point title	DB Treatment Period: Cohort 1 and 2: Number of Subjects With Changes in Laboratory Assessments Recorded as TEAE

End point description:

Number of subjects with changes in laboratory assessments recorded as TEAE were reported. Laboratory assessments included clinical chemistry, hematology and urinalysis. Postbaseline abnormalities were compared with baseline values: if postbaseline value exceeding the upper limit (with baseline below upper limit) or falling below the lower limit (with baseline above lower limit) was considered treatment-emergent (TE); if baseline values were missing then any postbaseline abnormality was considered TE. Safety analysis set included all randomised subjects who received at least 1 dose of JNJ-40411813 or placebo in the double-blind period. TEAE was defined as any AE occurring at or after the initial administration of study intervention through the day of last dose plus 5 days.

End point type	Secondary

End point timeframe:

From DB period start (Day 1) up to 5 days after last dose of DB period (up to Day 90)

End point values	DB: Cohort 1: Placebo	DB: Cohort 1: JNJ-40411813	DB: Cohort 2: Placebo	DB: Cohort 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	9	41
Units: Subjects				
Chemistry	0	1	0	1
Hematology	0	0	0	1
Urinalysis	0	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and 2: Percent Reduction in the Double-blind Period Monthly Seizure Rate

End point title	Cohort 1 and 2: Percent Reduction in the Double-blind Period Monthly Seizure Rate

End point description:

The percent reduction in the DB monthly seizure rate was defined as 100*(baseline monthly seizure count minus DB monthly seizure count) divided by (baseline monthly seizure count). The DB monthly seizure count was defined as the total number of observable focal onset seizures occurring during the 12-week DB period, multiplied by 28/XDB, where XDB was the number of days comprising the DB period. A positive percentage change in the double-blind monthly seizure count indicates improvement. Observable focal onset seizures included focal aware seizures with motor signs, focal impaired awareness seizures and focal to bilateral tonic-clonic seizures. Focal aware seizures without motor signs, myoclonic, or other generalised seizures was not counted towards baseline monthly seizure count. FAS included all randomised subjects assigned to receive study intervention and had both baseline and postbaseline seizure data.

End point type	Secondary

End point timeframe:

From DB period Day 1 up to Day 85

End point values	DB: Cohort 1: Placebo	DB: Cohort 1: JNJ-40411813	DB: Cohort 2: Placebo	DB: Cohort 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	9	40
Units: Percent change (reduction)				
median (inter-quartile range (Q1-Q3))	23.0 (7.7 to 37.7)	16.2 (-4.9 to 62.3)	10.1 (-1.3 to 28.2)	30.1 (-21.9 to 56.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and 2: Percentage of Subjects Who Achieved a More Than (>) 50 Percent (%) Reduction (Response) in Double-blind Monthly Seizure Count Relative to Baseline Monthly Seizure Count

End point title	Cohort 1 and 2: Percentage of Subjects Who Achieved a More Than (>) 50 Percent (%) Reduction (Response) in Double-blind Monthly Seizure Count Relative to Baseline Monthly Seizure Count

End point description:

Percentage of subjects who achieved a >50% reduction (response) in the DB monthly seizure count relative to baseline monthly seizure count during the DB period was reported. The baseline monthly seizure count was defined as the number of observable focal onset seizures occurred during the 8-week baseline period (Day -56 to -1), multiplied by 28/XBL, where XBL was the number of days comprising the subjects baseline period. Observable focal onset seizures included focal aware seizures with motor signs, focal impaired awareness seizures and focal to bilateral tonic-clonic seizures. Focal aware seizures without motor signs, myoclonic, or other generalized seizures was not counted towards baseline monthly seizure count. FAS included all randomised subjects assigned to receive study intervention and had both baseline and postbaseline seizure data.

End point type	Secondary

End point timeframe:

From DB period Day 1 up to Day 85

End point values	DB: Cohort 1: Placebo	DB: Cohort 1: JNJ-40411813	DB: Cohort 2: Placebo	DB: Cohort 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	9	40
Units: Percentage of Subjects				
number (not applicable)	15.0	32.5	22.2	30.0

Statistical analyses

No statistical analyses for this end point

Secondary: Cohort 1 and 2: Percentage of Subjects With Seizure Freedom During Double-blind Period

End point title	Cohort 1 and 2: Percentage of Subjects With Seizure Freedom During Double-blind Period

End point description:

Percentage of subjects with seizure freedom during DB period was reported. Seizure freedom was defined as having no seizures over the complete DB period. FAS included all randomised subjects assigned to receive study intervention and had both baseline and postbaseline seizure data.

End point type	Secondary

End point timeframe:

From DB period Day 1 up to Day 85

End point values	DB: Cohort 1: Placebo	DB: Cohort 1: JNJ-40411813	DB: Cohort 2: Placebo	DB: Cohort 2: JNJ-40411813
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	40	9	40
Units: Percentage of Subjects				
number (not applicable)	5.0	2.5	0.0	7.5

Statistical analyses

No statistical analyses for this end point

Secondary: DB Treatment Period: Cohort 1 and 2: Plasma Concentration of JNJ-40411813 and Its Metabolites: M30, M45 and M47

End point title	DB Treatment Period: Cohort 1 and 2: Plasma Concentration of JNJ-40411813 and Its Metabolites: M30, M45 and M47

End point description:

DB treatment period: Cohort 1 and 2: plasma concentration of JNJ-40411813 and its metabolites (M30, M45 and M47) were reported. The concentrations of JNJ-40411813 and its metabolites (M30, M45 and M47) were measured using a validated, specific, and sensitive liquid chromatography-mass spectrometry/mass spectrometry (LC-MS/MS) method. PK set: all randomised subjects who received at least 1 dose of JNJ-40411813 and had at least 1 valid blood sample drawn for PK analysis and excluded samples with below lower limit of quantification or samples with inconsistent date/time or samples with previous dose date/time incomplete or samples with concentration <10 ng/mL. Here, 'n' (number analysed) refers to number of subjects evaluable at each specified category. Data for this endpoint was not planned to be collected and analysed for Cohort 1 and 2 placebo arms.

End point type	Secondary

End point timeframe:

Day 1: 2 hours post-dose, Days 29: pre-dose and 1 hour post-dose, Day 57: pre-dose and Day 85: post-dose/Early withdrawal (EW)

End point values	DB: Cohort 1: JNJ-40411813 Induced	DB: Cohort 2: JNJ-40411813 Non-induced	DB: Cohort 2: JNJ-40411813 Induced	DB: Cohort 1: JNJ-40411813 Non-induced
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	22	17	22	18
Units: Nanograms per millilitre (ng/mL)				
arithmetic mean (standard deviation)				
JNJ: Day 1: 2 hours post-dose n=16,21,16,19	268 (± 139)	212 (± 113)	379 (± 192)	228 (± 116)
JNJ: Day 29: pre-dose n=15,18,15,19	356 (± 192)	506 (± 283)	797 (± 412)	272 (± 178)

JNJ: Day 29: 1 hour post-dose n=15,18,15,21	560 (± 281)	633 (± 289)	958 (± 465)	403 (± 285)
JNJ: Day 57: pre-dose n=15,15,11,12	360 (± 187)	516 (± 216)	687 (± 248)	276 (± 205)
JNJ:Day 85:post-dose/EW n=14,19,13,15	440 (± 343)	515 (± 267)	785 (± 394)	354 (± 385)
M30: Day 1: 2 hours post-dose n=14,20,14,16	21.5 (± 15.5)	12.6 (± 8.85)	24.8 (± 20.4)	20.8 (± 11.7)
M30: Day 29: pre-dose n=13,16,14,16	232 (± 109)	294 (± 119)	239 (± 100)	326 (± 116)
M30: Day 29: 1 hour post-dose n=13,18,14,18	221 (± 105)	275 (± 119)	220 (± 116)	295 (± 108)
M30: Day 57: pre-dose n=16,15,13,12	219 (± 108)	289 (± 135)	277 (± 111)	291 (± 150)
M30:Day 85:post-dose/EW n=15,19,12,14	191 (± 122)	248 (± 121)	274 (± 93.7)	299 (± 123)
M45: Day 1: 2 hours post-dose n=15,20,14,16	49.8 (± 31.0)	45.51 (± 21.6)	52.5 (± 22.5)	58.9 (± 24.2)
M45: Day 29: pre-dose n=13,16,14,16	65.4 (± 45.7)	122 (± 64.9)	76.3 (± 35.2)	107 (± 60.1)
M45: Day 29: 1 hour post-dose n=13,18,14,18	68.9 (± 36.3)	115 (± 56.0)	74.5 (± 28.4)	106 (± 54.8)
M45: Day 57: pre-dose n=15,15,13,12	63.6 (± 42.9)	113 (± 56.8)	76.0 (± 32.1)	103 (± 55.7)
M45: Day 85: post-dose/EW n=15,18,12,15	62.3 (± 41.6)	113 (± 64.2)	73.5 (± 40.1)	101 (± 57.9)
M47: Day 1: 2 hours post-dose n=15,20,14,16	34.7 (± 19.7)	19.4 (± 10.5)	36.8 (± 20.3)	25.8 (± 14.0)
M47: Day 29: pre-dose n=13,16,14,16	63.7 (± 31.7)	81.6 (± 41.5)	93.8 (± 42.9)	51.9 (± 36.1)
M47: Day 29: 1 hour post-dose n=13,18,14,18	69.7 (± 29.2)	77.3 (± 36.4)	90.1 (± 45.3)	53.5 (± 30.5)
M47: Day 57: pre-dose n=15,15,13,12	61.7 (± 26.2)	84.0 (± 41.7)	94.3 (± 30.1)	53.3 (± 47.5)
M47: Day 85: post-dose/EW n=15,19,11,14	60.2 (± 37.8)	97.4 (± 27.8)	100 (± 39.9)	52.9 (± 58.8)

Statistical analyses

No statistical analyses for this end point

Secondary: DB Treatment Period: Cohort 1 and 2: Plasma Concentration of AED: Levetiracetam

End point title	DB Treatment Period: Cohort 1 and 2: Plasma Concentration of AED: Levetiracetam

End point description:

DB treatment period: Cohort 1 and 2: plasma concentration of AED: levetiracetam were reported. The concentrations of levetiracetam were measured using a validated, specific, and sensitive LC-MS/MS method.PK set: all randomised subjects who received at least 1 dose of JNJ-40411813 and had at least 1 valid blood sample drawn for PK analysis and excluded samples with below lower limit of quantification or samples with inconsistent date/time or samples with previous dose date/time incomplete or samples with concentration <10 ng/mL. 'N' (number of subjects analysed)=number of subjects evaluable for this endpoint; 'n' (number analysed)=number of subjects evaluable at each specified category. Pooled levetiracetam data for placebo and JNJ-40411813 (irrespective of JNJ-40411813 dose regimen or treatment with or without EIAED) was planned to be collected and analysed in this endpoint.

End point type	Secondary

End point timeframe:

Day 1: pre-dose and 2 hours post-dose, Days 29: pre-dose and 1 hour post-dose, Day 57: pre-dose and Day 85: post-dose/Early withdrawal

End point values	DB: Cohorts 1 and 2: Placebo	DB: Cohorts (C) 1 and 2: JNJ-40411813		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	64		
Units: Nanograms per millilitre				
arithmetic mean (standard deviation)				
Day 1: pre-dose n=21,49	15119 (± 14805)	14453 (± 11397)		
Day 1: 2 hours post-dose n=26, 64	28279 (± 14058)	26244 (± 15009)		
Day 29: pre-dose n=20, 50	14204 (± 10679)	13016 (± 8605)		
Day 29: 1 hour post-dose n=23,54	29112 (± 18309)	25687 (± 17761)		
Day 57: pre-dose n=22, 42	14122 (± 10393)	14147 (± 8745)		
Day 85: post-dose/EW n=18, 47	22358 (± 16346)	20196 (± 16835)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Treatment Period: Cohort 1 and 2: Plasma Concentration of AED: Brivaracetam

End point title	DB Treatment Period: Cohort 1 and 2: Plasma Concentration of AED: Brivaracetam

End point description:

DB treatment period: Cohort 1 and 2: plasma concentration of AED: brivaracetam were reported. The concentrations of brivaracetam were measured using a validated, specific, and sensitive LC-MS/MS method.PK set: all randomised subjects who received at least 1 dose of JNJ-40411813 and had at least 1 valid blood sample drawn for PK analysis and excluded samples with below lower limit of quantification or samples with inconsistent date/time or samples with previous dose date/time incomplete or samples with concentration <10 ng/mL. 'N' (number of subjects analysed)=number of subjects evaluable for this endpoint; 'n' (number analysed)=number of subjects evaluable at each specified category. Pooled brivaracetam data for placebo and JNJ-40411813 (irrespective of JNJ-40411813 dose regimen or treatment with or without EIAED) was planned to be collected and analysed in this endpoint. Here, '99999' signifies that standard deviation could not be estimated for single subject.

End point type	Secondary

End point timeframe:

Day 1: pre-dose and 2 hours post-dose, Days 29: pre-dose and 1 hour post-dose, Day 57: pre-dose and Day 85: post-dose/Early withdrawal

End point values	DB: Cohorts 1 and 2: Placebo	DB: Cohorts (C) 1 and 2: JNJ-40411813		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2	13		
Units: Nanograms per millilitre				
arithmetic mean (standard deviation)				
Day 1: pre-dose n=2,11	798 (± 342)	977 (± 775)		
Day 1: 2 hours post-dose n=2,10	2560 (± 580)	2518 (± 1566)		

Day 29: pre-dose n=2,11	870 (± 170)	1121 (± 1027)		
Day 29: 1 hour post-dose n=2,13	3090 (± 198)	2587 (± 1207)		
Day 57: pre-dose n=1,8	1020 (± 99999)	858 (± 611)		
Day 85: post-dose/EW n=2,9	2036 (± 1829)	1674 (± 1621)		

Statistical analyses

No statistical analyses for this end point

Secondary: DB Treatment Period: Cohort 1 and 2: Plasma Concentration of AED: Carbamazepine

End point title	DB Treatment Period: Cohort 1 and 2: Plasma Concentration of AED: Carbamazepine

End point description:

DB treatment period: Cohort 1 and 2: plasma concentration of AED: carbamazepine were reported. The concentrations of carbamazepine were measured using a validated, specific, and sensitive LC-MS/MS method. PK set: all randomised subjects who received at least 1 dose of JNJ-40411813 and had at least 1 valid blood sample drawn for PK analysis and excluded samples with below lower limit of quantification or samples with inconsistent date/time or samples with previous dose date/time incomplete or samples with concentration <10 ng/mL. 'N' (number of subjects analysed)=number of subjects evaluable for this endpoint; 'n' (number analysed)=number of subjects evaluable at each specified category. Pooled carbamazepine data for placebo and JNJ-40411813 (irrespective of JNJ-40411813 dose regimen or treatment with or without EIAED) was planned to be collected and analysed in this endpoint.

End point type	Secondary

End point timeframe:

Pre-dose: Day 1, Days 29, and Day 57

End point values	DB: Cohorts 1 and 2: Placebo	DB: Cohorts (C) 1 and 2: JNJ-40411813		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	14		
Units: Nanograms per millilitre				
arithmetic mean (standard deviation)				
Day 1: pre-dose n=6,14	7562 (± 2709)	6976 (± 2139)		
Day 29: pre-dose n=5,10	7758 (± 1267)	6537 (± 2538)		
Day 57: pre-dose n=4,7	7555 (± 1790)	5621 (± 1053)		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Cohort 1 and 2: Plasma Concentration of JNJ-40411813 and Its Metabolites: M30, M45 and M47

End point title	OLE Period: Cohort 1 and 2: Plasma Concentration of JNJ-40411813 and Its Metabolites: M30, M45 and M47

End point description:

OLE period: Cohort 1 and 2: plasma concentration of JNJ-40411813 and its metabolites (M30, M45 and M47) were reported. The concentrations of JNJ-40411813 and its metabolites (M30, M45 and M47) were measured using a validated, specific, and sensitive LC-MS/MS method. PK set: all randomised subjects who received at least 1 dose of JNJ-40411813 and had at least 1 valid blood sample drawn for PK analysis and excluded samples with below lower limit of quantification or samples with inconsistent date/time or samples with previous dose date/time incomplete or samples with concentration <10 ng/mL. Here, 'n' (number analysed)=number of subjects evaluable at each specified category. Data for this endpoint was not planned to be reported for Cohort 1 and 2 placebo arms. Here, '9999' signifies that no subjects were available for analysis for the specified category.

End point type	Secondary

End point timeframe:

Cohort 1: OLE visit 2 (1st month), OLE visit 3 (2nd month); OLE visit 4 to 7 (up to 1 year); Cohort 2: OLE visit 2 (1st month), OLE visit 3 (2nd month); OLE visit 4 to 5 (up to 1 year)

End point values	OLE: Cohort 1: JNJ-40411813 Non-induced	OLE: Cohort 1: JNJ-40411813 Induced	OLE: Cohort 2: JNJ-40411813 Non-induced	OLE: Cohort 2: JNJ-40411813 Induced
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	8	15	11	16
Units: Nanograms per millilitre				
arithmetic mean (standard deviation)				
JNJ-40411813: OLE visit 2 n=8,14,11,16	272 (± 233)	372 (± 241)	524 (± 149)	930 (± 370)
JNJ-40411813: OLE visit 3 n=8,13,8,14	280 (± 217)	333 (± 157)	515 (± 172)	993 (± 361)
JNJ-40411813: OLE visit 4 n=6,12,4,11	311 (± 207)	392 (± 288)	539 (± 147)	921 (± 464)
JNJ-40411813: OLE visit 5 n=5,11,2,2	285 (± 241)	315 (± 197)	532 (± 105)	1610 (± 255)
JNJ-40411813: OLE visit 6 n=4, 10,0,0	442 (± 493)	349 (± 214)	9999 (± 9999)	9999 (± 9999)
JNJ-40411813: OLE visit 7 n=4,7,0,0	330 (± 252)	385 (± 269)	9999 (± 9999)	9999 (± 9999)
M30: OLE visit 2 n=7,14,10,15	298 (± 91.3)	225 (± 136)	316 (± 129)	249 (± 94.9)
M30: OLE visit 3 n=8,14,8,14	293 (± 135)	224 (± 172)	356 (± 113)	234 (± 73.7)
M30: OLE visit 4 n=6,12,4,11	265 (± 120)	263 (± 161)	333 (± 125)	251 (± 54.6)
M30: OLE visit 5 n=5,11,2,2	301 (± 154)	259 (± 169)	349 (± 223)	274 (± 65.1)
M30: OLE visit 6 n=4,10,0,0	286 (± 91.8)	236 (± 141)	9999 (± 9999)	9999 (± 9999)
M30: OLE visit 7 n=4,7,0,0	364 (± 64.7)	265 (± 115)	9999 (± 9999)	9999 (± 9999)
M45: OLE visit 2 n=7,14,10,15	85.3 (± 37.8)	57.7 (± 29.2)	101 (± 34.9)	87.4 (± 27.8)
M45: OLE visit 3 n=8,13,8,14	93.8 (± 41.2)	56.0 (± 28.0)	101 (± 54.5)	85.5 (± 29.0)
M45: OLE visit 4 n=6,12,4,11	81.1 (± 40.9)	64.0 (± 32.4)	112 (± 77.0)	84.0 (± 30.7)
M45: OLE visit 5 n=5,11,2,2	75.7 (± 45.2)	65.7 (± 38.0)	89.2 (± 9.69)	91.7 (± 6.22)
M45: OLE visit 6 n=4,10, 0,0	72.1 (± 49.8)	61.6 (± 41.9)	9999 (± 9999)	9999 (± 9999)
M45: OLE visit 7 n=4,7,0,0	71.8 (± 51.9)	59.3 (± 28.4)	9999 (± 9999)	9999 (± 9999)
M47: OLE visit 2 n=7,14,10,15	59.3 (± 71.0)	58.0 (± 31.4)	98.9 (± 34.6)	107 (± 30.8)
M47: OLE visit 3 n=8,13,8,14	52.8 (± 58.2)	58.7 (± 24.5)	81.7 (± 28.6)	122 (± 45.4)
M47: OLE visit 4 n=6,12,4,11	59.1 (± 66.0)	65.6 (± 34.1)	80.3 (± 12.4)	118 (± 47.1)
M47: OLE visit 5 n=5,11,2,2	62.8 (± 79.1)	57.6 (± 25.1)	78.0 (± 13.9)	157 (± 58.0)
M47: OLE visit 6 n=4,10,0,0	70.1 (± 90.8)	66.9 (± 44.9)	9999 (± 9999)	9999 (± 9999)
M47: OLE visit 7 n=4,7,0,0	70.3 (± 80.7)	69.8 (± 30.4)	9999 (± 9999)	9999 (± 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Cohort 1 and 2: Plasma Concentration of AED: Levetiracetam

End point title	OLE Period: Cohort 1 and 2: Plasma Concentration of AED: Levetiracetam

End point description:

OLE period: Cohort 1 and 2: plasma concentration of AED: levetiracetam were reported. The concentrations of levetiracetam were measured using a validated, specific, and sensitive LC-MS/MS method. PK set: all randomised subjects who received at least 1 dose of JNJ-40411813 and had at least 1 valid blood sample drawn for PK analysis and excluded samples with below lower limit of quantification or samples with inconsistent date/time or samples with previous dose date/time incomplete or samples with concentration <10 ng/mL. Here, 'N' (number of subjects analysed) refers to number of subjects evaluable for this endpoints; 'n' (number analysed) refers to number of subjects evaluable at each specified category. Pooled levetiracetam data for placebo and JNJ-40411813 (irrespective of JNJ-40411813 dose regimen or treatment with or without EIAED) was planned to be collected and analysed in this endpoints.

End point type	Secondary

End point timeframe:

OLE visit 2: 1st month; OLE visit 3: 2nd month

End point values	OLE: Cohorts 1 and 2: Placebo Followed by JNJ-40411813	OLE: Cohorts 1 and 2: JNJ-40411813 Followed by JNJ-40411813		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	9	33		
Units: Nanograms per millilitre				
arithmetic mean (standard deviation)				
OLE visit 2 n=9,33	11376 (± 4043)	14342 (± 8150)		
OLE visit 3 n=8,27	12118 (± 7351)	12484 (± 6907)		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Cohort 1 and 2: Plasma Concentration of AED: Brivaracetam

End point title	OLE Period: Cohort 1 and 2: Plasma Concentration of AED: Brivaracetam

End point description:

OLE period: Cohort 1 and 2: plasma concentration of AED: brivaracetam were reported. The concentrations of brivaracetam were measured using a validated, specific, and sensitive LC-MS/MS method. PK set: all randomised subjects who received at least 1 dose of JNJ-40411813 and had at least 1 valid blood sample drawn for PK analysis and excluded samples with below lower limit of quantification or samples with inconsistent date/time or samples with previous dose date/time incomplete or samples with concentration <10 ng/mL. Here, 'N' (number of subjects analysed) refers to number of subjects evaluable for this endpoint; 'n' (number analysed) = number of subjects evaluable at each specified category. Pooled brivaracetam data for placebo and JNJ-40411813 (irrespective of JNJ-40411813 dose regimen or treatment with or without EIAED) was planned to be collected and analysed in this endpoint. Here, '99999 signifies that standard deviation could not be estimated for single subject.

End point type	Secondary

End point timeframe:

OLE visit 2: 1st month; OLE visit 3: 2nd month

End point values	OLE: Cohorts 1 and 2: Placebo Followed by JNJ-40411813	OLE: Cohorts 1 and 2: JNJ-40411813 Followed by JNJ-40411813		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1	9		
Units: Nanograms per millilitre				
arithmetic mean (standard deviation)				
OLE visit 2 n=1,9	1030 (± 99999)	810 (± 665)		
OLE visit 3 n=1,5	1010 (± 99999)	694 (± 746)		

Statistical analyses

No statistical analyses for this end point

Secondary: OLE Period: Plasma Concentration of AED: Carbamazepine

End point title	OLE Period: Plasma Concentration of AED: Carbamazepine

End point description:

OLE period: Cohort 1 and 2: plasma concentration of AED: carbamazepine were reported. The concentrations of carbamazepine were measured using a validated, specific, and sensitive LC-MS/MS method. PK set: all randomised subjects who received at least 1 dose of JNJ-40411813 and had at least 1 valid blood sample drawn for PK analysis and excluded samples with below lower limit of quantification or samples with inconsistent date/time or samples with previous dose date/time incomplete or samples with concentration <10 ng/mL. Here, 'N' (number of subjects analysed) refers to the number of subjects evaluable for this endpoint. Pooled carbamazepine data for placebo and JNJ-40411813 (irrespective of JNJ-40411813 dose regimen or treatment with or without EIAED) was planned to be collected and analysed in this endpoint. Here, '99999' signifies that standard deviation could not be estimated for single subject.

End point type	Secondary

End point timeframe:

OLE visit 2: 1st month; OLE visit 3: 2nd month

End point values	OLE: Cohorts 1 and 2: Placebo Followed by JNJ-40411813	OLE: Cohorts 1 and 2: JNJ-40411813 Followed by JNJ-40411813		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1	8		
Units: Nanograms per millilitre				
arithmetic mean (standard deviation)				

OLE visit 2	5970 (± 99999)	5806 (± 1289)		
OLE visit 3	5780 (± 99999)	6952 (± 2784)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

DB arms: From DB period start (Day 1) up to 5 days after last dose of DB period (up to Day 90); OLE arms: From OLE baseline (Day 1 of OLE) up to 24 months after start of OLE (the actual OLE starting time varied for each participant)

Adverse event reporting additional description:

DB period: SAF included all randomized participants who received at least 1 dose of JNJ-40411813 or placebo in the DB period. OLE period: SAFOLE analysis set included all randomized participants who received at least 1 dose of study intervention in the OLE period.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	DB: Cohort 1: Placebo

Reporting group description:

During double-blind (DB) period, subjects were randomised to receive placebo matching to JNJ-40411813 (JNJ) tablet orally twice a day (BID) from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects were screened every 4 weeks for monthly seizure counts up to Week (W) 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment, or enter open-label extension (OLE) period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through Week 12 and had option to perform DB period end-of-study visit (last visit for last subject; Day 85) or enter OLE period. Subjects who continued treatment to end of DB period (Week 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (Week 14).

Reporting group title	DB: Cohort 2: Placebo

Reporting group description:

During DB period, subjects were randomised to receive placebo matching to JNJ tablet orally BID from Day 1 up to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment, or enter OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through Week 12 and had option to perform DB period end-of-study visit (Day 85) or enter OLE period. Subjects who continued treatment to the end of the DB period (W 12) and were not elected to participate in the OLE were followed up for safety up to 2 weeks after the last dose (W 14).

Reporting group title	OLE: Cohort 2: JNJ-40411813 Followed by JNJ-40411813

Reporting group description:

During OLE period, cohort 2 subjects who had received JNJ-40411813 during the DB period continued to receive JNJ-40411813 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) from Day 1 of OLE up to 2 years. Subjects started with JNJ-40411813 100 mg BID. Induced subjects (with EIAEDs) had their dose increased to JNJ-40411813 200 mg BID on Day 8 of the OLE. Non-induced subjects (without EIAEDs) continued with JNJ-40411813 100 mg BID.

Reporting group title	OLE: Cohort 1: Placebo Followed by JNJ-40411813

Reporting group description:

During OLE period, cohort 1 subjects who had received placebo during the DB period received JNJ-40411813 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) from Day 1 of OLE up to 2 years. Induced subjects (with EIAEDs) received JNJ-40411813 100 mg BID, and non-induced subjects (without EIAEDs) received JNJ-40411813 50 mg BID. The dose could be increased at the second visit (Month 1) to 200 mg JNJ-40411813 BID for induced subjects (with EIAEDs) and 100 mg JNJ-40411813 BID for non-induced subjects (without EIAEDs).

Reporting group title	OLE: Cohort 1: JNJ-40411813 Followed by JNJ-40411813

Reporting group description:

During OLE period, cohort 1 subjects who had received JNJ-40411813 during the DB period continued to receive JNJ-40411813 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam)

from Day 1 of OLE up to 2 years. Induced subjects (with EIAEDs) received JNJ-40411813 100 mg BID, and non-induced subjects (without EIAEDs) received JNJ-40411813 50 mg BID. The dose could be increased at the second visit (Month 1) to 200 mg JNJ-40411813 BID for induced subjects (with EIAEDs) and 100 mg JNJ-40411813 BID for non-induced subjects (without EIAEDs).

Reporting group title	OLE: Cohort 2: Placebo Followed by JNJ-40411813

Reporting group description:

During the OLE period, cohort 2 subjects who had received placebo during the DB period received JNJ-40411813 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) from Day 1 of OLE up to 2 years. Subjects started with JNJ-40411813 100 mg BID. Induced subjects (with EIAEDs) had their dose increased to JNJ-40411813 200 mg BID on Day 8 of the OLE. Non-induced subjects (without EIAEDs) continued with JNJ-40411813 100 mg BID.

Reporting group title	DB: Cohort 1: JNJ-40411813

Reporting group description:

During DB period, subjects randomised to receive JNJ 100 milligrams (mg) or 50 mg tablet orally BID from Day 1 to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects treated with EIAEDs (induced) received 100 mg JNJ, subjects not treated with EIAEDs (non-induced) received 50 mg JNJ. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy, perform end-of-study/early withdrawal visit, continued DB period or enter OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through W 12 and had option to perform DB period end-of-study (Day 85) or enter OLE period. Subjects who continued treatment to end of DB period (W 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (W 14).

Reporting group title	DB: Cohort 2: JNJ-40411813

Reporting group description:

During DB period, subjects were randomised to receive JNJ200 mg or 100 mg tablet orally BID from Day 1 to Day 85 along with previously prescribed AEDs (1 must be levetiracetam/brivaracetam) on Days 1, 29, and 57. Subjects treated with EIAEDs (induced) received 200 mg JNJ, subjects not treated with EIAEDs (non-induced) received 100 mg JNJ. Subjects were screened every 4 weeks for monthly seizure counts up to W 12. Subjects who had exceeded their pre-randomisation monthly seizure count had option to discontinue study treatment due to lack of efficacy and perform end-of-study/early withdrawal visit, continue DB treatment or enter OLE period. Subjects who had not exceeded pre-randomisation seizure count continued DB period through W 12 and had option to perform DB period end-of-study visit (Day 85) or enter OLE period. Subjects who continued treatment to end of DB period (W 12) and were not elected to participate in OLE were followed up for safety up to 2 weeks after last dose (W 14).

Serious adverse events	DB: Cohort 1: Placebo	DB: Cohort 2: Placebo	OLE: Cohort 2: JNJ-40411813 Followed by JNJ-40411813
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	1 / 31 (3.23%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pituitary Tumour Benign			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Cervical Vertebral Fracture			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb Traumatic Amputation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head Injury			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 31 (3.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Change in Seizure Presentation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status Epilepticus			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary Mass			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OLE: Cohort 1: Placebo Followed by JNJ-40411813	OLE: Cohort 1: JNJ-40411813 Followed by JNJ-40411813	OLE: Cohort 2: Placebo Followed by JNJ-40411813
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	5 / 23 (21.74%)	0 / 7 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pituitary Tumour Benign			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Cervical Vertebral Fracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Limb Traumatic Amputation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head Injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Change in Seizure Presentation			
subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status Epilepticus			
subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pulmonary Mass			
subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DB: Cohort 1: JNJ-40411813	DB: Cohort 2: JNJ-40411813	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 40 (2.50%)	2 / 41 (4.88%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pituitary Tumour Benign			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Cervical Vertebral Fracture			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb Traumatic Amputation			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head Injury			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Change in Seizure Presentation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status Epilepticus			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary Mass			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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	DB: Cohort 1: Placebo	DB: Cohort 2: Placebo	OLE: Cohort 2: JNJ-40411813 Followed by JNJ-40411813
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 20 (35.00%)	7 / 9 (77.78%)	12 / 31 (38.71%)
Vascular disorders			

Hypertension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	3 / 31 (9.68%)
occurrences (all)	0	0	3
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Gait Disturbance			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Choking			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Wheezing			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	1 / 31 (3.23%)
occurrences (all)	0	1	1
Suicidal Ideation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Investigations			
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Blood Chloride Increased			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod Bite			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Head Injury			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Ligament Sprain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Wound			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Dizziness Postural			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Dysarthria			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Somnolence			

subjects affected / exposed	2 / 20 (10.00%)	1 / 9 (11.11%)	1 / 31 (3.23%)
occurrences (all)	2	1	1
Seizure			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Memory Impairment			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	2 / 31 (6.45%)
occurrences (all)	1	0	6
Tremor			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Vision Blurred			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Vomiting			

subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	1 / 31 (3.23%)
occurrences (all)	0	1	2
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 20 (0.00%)	1 / 9 (11.11%)	0 / 31 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Muscle Contracture			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0
Joint Swelling			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	1 / 31 (3.23%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 9 (0.00%)	2 / 31 (6.45%)
occurrences (all)	2	0	3
Respiratory Tract Infection Viral			
subjects affected / exposed	1 / 20 (5.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	1	0	0

Metabolism and nutrition disorders			
Hypernatraemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 9 (0.00%)	0 / 31 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	OLE: Cohort 1: Placebo Followed by JNJ-40411813	OLE: Cohort 1: JNJ-40411813 Followed by JNJ-40411813	OLE: Cohort 2: Placebo Followed by JNJ-40411813
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 12 (50.00%)	12 / 23 (52.17%)	6 / 7 (85.71%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 12 (8.33%)	3 / 23 (13.04%)	0 / 7 (0.00%)
occurrences (all)	1	3	0
Malaise			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gait Disturbance			
subjects affected / exposed	1 / 12 (8.33%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Choking			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Suicidal Ideation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Investigations			
Aspartate Aminotransferase Increased			
subjects affected / exposed	1 / 12 (8.33%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	1 / 12 (8.33%)	2 / 23 (8.70%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
Blood Chloride Increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Arthropod Bite			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Head Injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Ligament Sprain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Wound			
subjects affected / exposed	1 / 12 (8.33%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	3 / 7 (42.86%)
occurrences (all)	0	0	3
Dizziness Postural			

subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Dysarthria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Somnolence			
subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	2 / 7 (28.57%)
occurrences (all)	0	1	2
Seizure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Memory Impairment			
subjects affected / exposed	1 / 12 (8.33%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 12 (8.33%)	3 / 23 (13.04%)	0 / 7 (0.00%)
occurrences (all)	1	3	0
Tremor			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Eye disorders			
Vision Blurred			
subjects affected / exposed	1 / 12 (8.33%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Diplopia			

subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	1 / 23 (4.35%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Muscle Contracture			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Joint Swelling			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Infections and infestations			
Covid-19			
subjects affected / exposed	2 / 12 (16.67%)	3 / 23 (13.04%)	0 / 7 (0.00%)
occurrences (all)	2	3	0
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	4 / 23 (17.39%)	0 / 7 (0.00%)
occurrences (all)	0	6	0
Respiratory Tract Infection Viral			
subjects affected / exposed	0 / 12 (0.00%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypernatraemia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 23 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	DB: Cohort 1: JNJ-40411813	DB: Cohort 2: JNJ-40411813	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 40 (40.00%)	19 / 41 (46.34%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 40 (5.00%)	1 / 41 (2.44%)	
occurrences (all)	2	1	
Malaise			
subjects affected / exposed	2 / 40 (5.00%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Gait Disturbance			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	
occurrences (all)	4	0	
Respiratory, thoracic and mediastinal disorders			
Choking			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Wheezing			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	
occurrences (all)	0	1	
Suicidal Ideation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Investigations			
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	
occurrences (all)	0	1	
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Blood Chloride Increased			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Arthropod Bite			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Contusion			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Head Injury			
subjects affected / exposed	1 / 40 (2.50%)	1 / 41 (2.44%)	
occurrences (all)	1	1	
Fall			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Ligament Sprain			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	

Wound			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 40 (2.50%)	2 / 41 (4.88%)	
occurrences (all)	1	3	
Dizziness Postural			
subjects affected / exposed	1 / 40 (2.50%)	3 / 41 (7.32%)	
occurrences (all)	1	3	
Dysarthria			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Syncope			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Somnolence			
subjects affected / exposed	3 / 40 (7.50%)	3 / 41 (7.32%)	
occurrences (all)	3	3	
Seizure			
subjects affected / exposed	2 / 40 (5.00%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Migraine			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Memory Impairment			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Headache			
subjects affected / exposed	2 / 40 (5.00%)	4 / 41 (9.76%)	
occurrences (all)	10	4	
Tremor			
subjects affected / exposed	2 / 40 (5.00%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	0 / 40 (0.00%)	5 / 41 (12.20%)	
occurrences (all)	0	8	
Eye disorders			
Vision Blurred			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Diplopia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	
occurrences (all)	5	0	
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal Reflux Disease			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	3 / 40 (7.50%)	0 / 41 (0.00%)	
occurrences (all)	5	0	
Diarrhoea			
subjects affected / exposed	2 / 40 (5.00%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Constipation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Abdominal Pain Upper			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	

Musculoskeletal and connective tissue disorders			
Muscle Contracture			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Joint Swelling			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Covid-19			
subjects affected / exposed	2 / 40 (5.00%)	0 / 41 (0.00%)	
occurrences (all)	2	0	
Nasopharyngitis			
subjects affected / exposed	2 / 40 (5.00%)	1 / 41 (2.44%)	
occurrences (all)	2	1	
Respiratory Tract Infection Viral			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypernatraemia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 January 2021	The overall reason for this amendment was to implement several different corrections.
07 April 2022	The overall reason for this amendment was to add an open-label extension (OLE) treatment period after completion of the double-blind treatment period.
12 July 2022	The overall reason for this amendment was to allow for starting enrolment in the double-blind treatment phase of the second cohort as soon as enrolment of 60 in the first cohort has been completed so that there was no pause in recruitment, provided that no safety concerns were observed during the continuous safety monitoring of ongoing subjects.
16 November 2022	The overall reason for this amendment was to provide instructions for up-titration in the induced patients in Cohort 2 and to allow for dose increases in the Open Label Extension Part of the study and to implement several different corrections and clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported