Clinical trial results:
A randomised, placebo-controlled, double-blind trial of the antidepressant efficacy of a novel CNS-penetrant P2X7 receptor antagonist, JNJ-54175446, in people with major depressive disorder, an incomplete response to monoaminergic antidepressant drugs, and a biomarker profile predictive of active P2X7 signalling.

Summary

EudraCT number	2018-001884-21
Trial protocol	GB
Global end of trial date	10 June 2022

Results information

Result version number	v1 (current)
This version publication date	12 November 2023
First version publication date	12 November 2023
Summary attachment (see zip file)	ATP_Final_StatsReport (ATP Final Stats Report V2.0.pdf)

Trial information

Trial identification

Sponsor protocol code	CCTU0251-ATP

Additional study identifiers

ISRCTN number	ISRCTN44411633
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IRAS ID: 248987

Notes:

Sponsors

Sponsor organisation name	Cambridgeshire and Peterborough NHS Foundation Trust and the University of Cambridge
Sponsor organisation address	Hills Road, Cambridge, United Kingdom, CB2 0QQ
Public contact	Professor Edward Bullmore, Cambridge University Hospital NHS Foundation Trust, +44 01223336583, sm822@medschl.cam.ac.uk
Scientific contact	Professor Edward Bullmore, Cambridge University Hospital NHS Foundation Trust, +44 0122336583, sm822@schl.cam.ac.uk

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	18 May 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 June 2022
Global end of trial reached?	Yes
Global end of trial date	10 June 2022
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The principal research objective is to evaluate whether a new anti-inflammatory drug, called JNJ-54175446, is effective in treating depressive symptoms in patients with major depressive disorder. This drug works by blocking a receptor called P2X7 which is known to cause brain inflammation in response to stress. We predict that blocking P2X7 will be beneficial for depressed patients who have not responded completely to standard anti-depressant drugs and who have blood test results at screening which indicate high levels of P2X7 activity.

Effectiveness will be measured using a standard clinical depression scale, called MADRS, after 8 weeks of treatment, and we will test the hypothesis that there is significantly greater improvement of depression in the patients treated with JNJ-54175446 compared to the patients treated with placebo.

Protection of trial subjects:

The trial has an Independent data monitoring committee (IDCM) and this is independent of the investigators, the trial team and the NIMA consortium. The roles, membership and frequency of meetings are described in the IDCM charter. Briefly the IDCM is responsible for reviewing all safety data including clinical laboratory data, adverse events and special reporting situations. The IDCM makes recommendations to the TSC. The IDCM meets annually

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 15
Worldwide total number of subjects	15
EEA total number of subjects	0

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)	15
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Potential trial participants are identified by any of the following:
their treating physician or by referral by their GP or local NHS consultants; databases that are part of the secondary care services; advertisements including media-based methods (local/national); Participant Identification centres (PICs); previous studies into depression;

Pre-assignment

Screening details:

Review of inclusion/exclusion criteria; physical measurements & physical examination; blood sampling; urine analysis; alcohol breath test; past and current antidepressant drug treatment & response; 12-lead ECG; supine vital signs; psychiatric examination; assessment of suicidality; concomitant therapy; review of trail restrictions

Pre-assignment period milestones

Number of subjects started	15
Number of subjects completed	15

Period 1

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

Blinding implementation details:

Trial participants, coordination and site staff including site pharmacists are blinded to the treatment during the duration of trial. Participants are assigned to one of two treatment groups (active drug or placebo) via a web-based randomisation system. Each participant is assigned a unique kit number held at the trial site. The trial statistician will be unblinded for the purpose of safety data reporting to IDMC.

Arms

Are arms mutually exclusive?	Yes
Arm title	Active product under investigation

Arm description:

Active product is a brain-penetrant P2X7 antagonist (JNJ-54175446) developed by Janssen Research and Development.

Arm type	Active comparator
Investigational medicinal product name	JNJ-54175445
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One 50 mg capsule to be taken once a day for 8 weeks

Arm title	Placebo arm

Arm description:

Matching placebo

Arm type	Placebo

Investigational medicinal product name	Matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

One placebo capsule to be taken once a day

Number of subjects in period 1	Active product under investigation	Placebo arm
Started	9	6
Completed	9	6

Period 2

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

Blinding implementation details:

Trial participants, principal investigators and other site staff including pharmacist were blinded to the treatment group during the duration of the trial. The physical appearance of the IMP is matched by the placebo and both were presented in identical packaging. Upon randomisations each participant is allocated to a kit number by the web-based randomisation systems (sealed envelope). The concealment codes were maintained within the web-based system.

Arms

Are arms mutually exclusive?	Yes
Arm title	Active

Arm description:

Participants in the active arm were given JNJ-54175446 (a brain-penetrant P2X7 antagonist.

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

Dosage and administration details:

One 50 mg capsule taken orally daily

Arm title	Placebo arm

Arm description:

Matching placebo had the same appearance and packaging as the active product. It was taken orally once daily as a capsule.

Arm type	Placebo

Investigational medicinal product name	Matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Other use

Dosage and administration details:

One capsule of matching placebo was taken orally once daily.

Number of subjects in period 2	Active	Placebo arm
Started	9	6
Completed	9	6

Baseline characteristics

Reporting groups	
Reporting group title	Active product under investigation
Reporting group description:	
Active product is a brain-penetrant P2X7 antagonist (JNJ-54175446) developed by Janssen Research and Development.	
Reporting group title	Placebo arm
Reporting group description:	
Matching placebo	

Reporting group values	Active product under investigation	Placebo arm	Total
Number of subjects	9	6	15
Age categorical Units: Subjects			
Adults (18 to 60)	9	6	15
Age continuous Units: years			
arithmetic mean	37.2	47.5	
standard deviation	± 13.6	± 14.8	-
Gender categorical Units: Subjects			
Female	8	3	11
Male	1	3	4
Marital status Units: Subjects			
Single	3	3	6
Divorced/Widowed/Separated	2	2	4
Married/in partnership	4	1	5
Occupation Units: Subjects			
Full time	7	4	11
Part time	0	1	1
Not employed	2	1	3
Education Units: Subjects			
School	2	3	5
Postgraduate	2	2	4
College/University	5	1	6
BMI Units: number			
arithmetic mean	30.8	29.7	
standard deviation	± 3.14	± 1.97	-

Subject analysis sets	
Subject analysis set title	Efficacy
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Efficacy analysis is performed based on the intent-to-treat (ITT) analysis set, which will include all randomised participants who receive at least 1 dose of IMP and have both the baseline and and at least 1 post-baseline measurement. Baseline is defined as the last scheduled evaluation done before the IMP administration

Reporting group values	Efficacy		
Number of subjects	15		
Age categorical Units: Subjects			
Adults (18 to 60)	15		
Age continuous Units: years			
arithmetic mean	41.3		
standard deviation	± 14.6		
Gender categorical Units: Subjects			
Female	11		
Male	4		
Marital status Units: Subjects			
Single	6		
Divorced/Widowed/Separated	4		
Married/in partnership	5		
Occupation Units: Subjects			
Full time	11		
Part time	1		
Not employed	3		
Education Units: Subjects			
School	5		
Postgraduate	4		
College/University	6		
BMI Units: number			
arithmetic mean	30.4		
standard deviation	± 2.71		

End points

End points reporting groups

Reporting group title	Active product under investigation
Reporting group description:	
Active product is a brain-penetrant P2X7 antagonist (JNJ-54175446) developed by Janssen Research and Development.	
Reporting group title	Placebo arm
Reporting group description:	
Matching placebo	
Reporting group title	Active
Reporting group description:	
Participants in the active arm were given JNJ-54175446 (a brain-penetrant P2X7 antagonist.	
Reporting group title	Placebo arm
Reporting group description:	
Matching placebo had the same appearance and packaging as the active product. It was taken orally once daily as a capsule.	
Subject analysis set title	Efficacy
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Efficacy analysis is performed based on the intent-to-treat (ITT) analysis set, which will include all randomised participants who receive at least 1 dose of IMP and have both the baseline and and at least 1 post-baseline measurement. Baseline is defined as the last scheduled evaluation done before the IMP administration	

Primary: MADRS score

End point title	MADRS score[1]
End point description:	
The Montgomery Asberg Depression Rating Scale (MADRS) is a researcher-rated scale designed to measure depression severity and detects changes due to antidepressant treatment. The test consists of 10 items, each of which is scored from 0 (item not present or normal) to 6 (severe or continuous presence of the symptoms), for a total score of 60. Higher scores represent a more severe conditions.	
End point type	Primary
End point timeframe:	
MADRS score is taken at baseline and end of treatment at week 8. The primary endpoint will be the difference between the MADRS score taken at baseline and at end of treatment at week 8.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Due to the small number of participants recruited to the trial prior to its premature termination, no statistical analysis was possible.

End point values	Active product under investigation	Placebo arm	Efficacy	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	0[2]	0[3]	0[4]	
Units: MADRS Score				
number (not applicable)				
MADRS score				

Notes:

[2] - Due to the small number of participants recruited, no analysis was possible

[3] - Due to the small number of participants recruited, no analysis was possible

[4] - Due to the small number of participants recruited, no analysis was possible

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical and cognitive

End point title	Clinical and cognitive

End point description:

Clinical and cognitive endpoints will be measured during site clinic visits at baseline and then at Weeks 4 (Visit 2) and 8 (Visit 3) after start of treatment. The secondary endpoints will include the following:
-Clinician interviews including clinician reported scales of depressive symptom severity (PHQ-9, MADRS and MINI) and Columbia Suicidal Severity Rating Scale
-Participant reported outcome assessments (SHAPS, QIDS-SR16, GAD-7, Chalder Fatigue Questionnaire, Perceived Stress Scale, Beck's Depression Inventory, Childhood Trauma Questionnaire
-Cognitive function (Emotional Test Battery (ETB), Continuous performance test
-Fatigue/activity (real-life ambulatory monitoring of sleep-wake cycles and physical activity
-Brain structural imaging (structural and functional MRI)

End point type	Secondary

End point timeframe:

Baseline, week 4 and week 8

End point values	Active product under investigation	Placebo arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	6		
Units: clinician scales				
number (not applicable)				
clinical scales	9	6		
PROMs	9	6		
MRI images	9	6		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs will be reported by the participant for the duration of their study participation: from the point of consent until study termination (ie. the patient has completed the last follow-up visit, 7 or 14 days after last dose of IMP or has withdrawn early).

Adverse event reporting additional description:

For JNJ-54175446, there are no expected AEs/SAEs of special interest to follow.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Placebo
Reporting group description: -	
Reporting group title	Active

Reporting group description: -

Serious adverse events	Placebo	Active	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 9 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo	Active	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	8 / 9 (88.89%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast neoplasm	Additional description: Breast neoplasm		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Cervix carcinoma stage I	Additional description: Cervix carcinoma stage I		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Vascular disorders			

Hot flush	Additional description: Hot flush		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Chest pain	Additional description: Chest pain		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Fatigue	Additional description: Fatigue		
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Illness	Additional description: Illness		
subjects affected / exposed	0 / 6 (0.00%)	3 / 9 (33.33%)	
occurrences (all)	0	3	
Malaise	Additional description: Malaise		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Pain	Additional description: Pain		
subjects affected / exposed	1 / 6 (16.67%)	2 / 9 (22.22%)	
occurrences (all)	3	2	
Reproductive system and breast disorders			
Testicular pain	Additional description: Testicular pain		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Hypocapnia	Additional description: Hypocapnia		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Nasal congestion	Additional description: Nasal congestion		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain	Additional description: Oropharyngeal pain		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			

Anxiety	Additional description: Anxiety		
subjects affected / exposed	2 / 6 (33.33%)	0 / 9 (0.00%)	
occurrences (all)	3	0	
Depressed mood	Additional description: Depressed mood		
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Intrusive thoughts	Additional description: Intrusive thoughts		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Panic attack	Additional description: Panic attack		
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	3	
Sleep disorder	Additional description: Sleep disorder		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Sleep terror	Additional description: Sleep terror		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood bilirubin increased	Additional description: Blood bilirubin increased		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Blood creatinine decreased	Additional description: Blood creatinine decreased		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Blood phosphorus increased	Additional description: Blood phosphorus increased		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
Blood sodium decreased	Additional description: Blood sodium decreased		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Blood uric acid increased	Additional description: Blood uric acid increased		
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Blood cholesterol increased	Additional description: Blood cholesterol increased		

subjects affected / exposed	3 / 6 (50.00%)	3 / 9 (33.33%)	
occurrences (all)	7	4	
Blood calcium decreased	Additional description: Blood calcium decreased		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased	Additional description: Blood creatine phosphokinase increased		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Carbon dioxide decreased	Additional description: Carbon dioxide decreased		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
C-reactive protein increased	Additional description: C-reactive protein increased		
subjects affected / exposed	1 / 6 (16.67%)	2 / 9 (22.22%)	
occurrences (all)	1	3	
Eosinophil count abnormal	Additional description: Eosinophil count abnormal		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Heart rate abnormal	Additional description: Heart rate abnormal		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Monocyte count abnormal	Additional description: Monocyte count abnormal		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Platelet count increased	Additional description: Platelet count increased		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
pH urine increased	Additional description: pH urine increased		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Red blood cell count decreased	Additional description: Red blood cell count decreased		

subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Staphylococcus test positive	Additional description: Staphylococcus test positive		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Urine analysis abnormal	Additional description: Urine analysis abnormal		
subjects affected / exposed	0 / 6 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
White blood cell count decreased	Additional description: White blood cell count decreased		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Burn oesophageal	Additional description: Burn oesophageal		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Burns second degree	Additional description: Burns second degree		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Concussion	Additional description: Concussion		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Post procedural haematoma	Additional description: Post procedural haematoma		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Thermal burn	Additional description: Thermal burn		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
Nervous system disorders			
Headache	Additional description: Headache		
subjects affected / exposed	2 / 6 (33.33%)	3 / 9 (33.33%)	
occurrences (all)	4	5	
Migraine	Additional description: Migraine		
subjects affected / exposed	2 / 6 (33.33%)	0 / 9 (0.00%)	
occurrences (all)	3	0	
Persistent postural-perceptual dizziness	Additional description: Persistent postural-perceptual dizziness		

subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
Syncope	Additional description: Syncope		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Taste disorder	Additional description: Taste disorder		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Constipation	Additional description: Constipation		
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Nausea	Additional description: Nausea		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Toothache	Additional description: Toothache		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne	Additional description: Acne		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Night sweats	Additional description: Night sweats		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Rash	Additional description: Rash		
subjects affected / exposed	1 / 6 (16.67%)	1 / 9 (11.11%)	
occurrences (all)	2	2	
Renal and urinary disorders			

Pollakiuria	Additional description: Pollakiuria		
subjects affected / exposed	0 / 6 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Myalgia	Additional description: Myalgia		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Infections and infestations			
COVID-19	Additional description: COVID-19		
subjects affected / exposed	1 / 6 (16.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection	Additional description: Viral upper respiratory tract infection		
subjects affected / exposed	1 / 6 (16.67%)	2 / 9 (22.22%)	
occurrences (all)	1	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 February 2019	Amendment 1 (protocol version change from 1.0 to 1.1): Update on exclusion criteria, cardiac withdrawal criteria, list of prohibited medications and SAE timelines
26 July 2019	Amendment 2.0 (from protocol version 1.1 to version 2.0): Clarifications in some eligibility and exclusion criteria, addition of findings of BIODEP study and literature and updates to other sections of protocol.
11 December 2019	Amendment 3: (protocol version 3.0) Modification of exclusion criteria and biomarker objectives, updates to other sections of protocol
11 June 2020	Amendment 4: (protocol version 4.0) Change of depression severity assessment in eligibility, change in secondary outcome measures, addition of verbal consent, addition and changes to some questionnaires, updates to other sections of protocol.
24 August 2020	Amendment 5 (protocol version 5.0) Changes relating to management of participants due to COVID-19
20 October 2020	Amendment 6 (protocol version 5.1) Clarifications on the collection of saliva samples and that COVID-19 positive patients should be withdrawn from treatment
09 March 2021	Amendment 7 (from protocol version 5.1 to version 6.0): Updates on screening window and clinic visits, addition of exclusion criterion, updates in prohibited concomitant therapy, secondary endpoints and timing of telephone contacts.
10 December 2021	Amendment 8 (protocol version 6.1) Change in time windows for MRIs before visit 1 and visit 3, update in schedule of events table to remove MADRS from visit 4.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date

10 June 2022	The trial was terminated early due to the IMP supplier, Janssen, no longer supporting the trial. The IMP (JNJ-54175446) was supplied by Janssen to the distributor in bulk rather than in bottles for distribution to each trial site. Th cost of bottling the IMP by the distributor was considered too expensive by Janssen and they decided to withdraw their support for the trial. As the available supply of IMP at each site expired on 12 June 2022 with no ability to extend the expiry date, the trial had to terminate prematurely having recruited only 15 participants.	-

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

As the trial terminated prematurely with only 15 out of the planned 142 participants recruited, there are no sufficient data to conduct a statistical analysis and evaluate safety and efficacy of the IMP.

Notes: