A Randomized, Placebocontrolled, Double blind, Single Ascending Dose Study to Investigate Safety and Tolerability, Pharmacokinetics and Pharmacodynamics of JNJ-61393215 in Healthy Subjects

Published: 01-07-2016
Last updated: 25-03-2025

The primary objectives of this study in healthy subjects are:- To investigate the safety and tolerability of JNJ-61393215 versus placebo after single oral dose administration under fasted (ascending dose levels) and fed condition.- To characterize...

Ethical review	Approved WMO
Status	Completed
Health condition type	Anxiety disorders and symptoms
Study type	Interventional

Summary

ID

NL-OMON43169

Source
ToetsingOnline

Brief title
Study to Investigate JNJ-61393215 in Healthy Subjects

Condition

- Anxiety disorders and symptoms

Synonym
anxiety, mood disorders and substance abuse, panic

Research involving

Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: JNJ-61393215, pharmacodynamics, pharmacokinetics

Outcome measures

Primary outcome

Safety

- Adverse events

- Clinical laboratory tests

- ECG

- Telemetry

- Vital signs

- Physical & neurological examination

Pharmacokinetic parameters

Cmax, Clast, Tmax, Tlast, AUClast, Lambda, T1/2, CL/F, CLCR

Secondary outcome

Pharmacodynamic parameters

Cortisol & prolactin

Biomarkers

Study description

Background summary

JNJ-61393215 is a novel, selective, high affinity/potent orexin-1 receptor (OX1R) antagonist and is a potential first in class therapy for the treatment of panic, anxiety, mood disorders and substance abuse. The role of OX1Rs in complex emotional behavior is emerging. There is evidence for the overactivation of the OX1R pathway in hyper-arousal states (for example panic attacks), and consequently a selective OX1R antagonist might normalize overexcited networks without inducing sedation.
This will be the first study with JNJ-61393215 in humans; no clinical data are currently available.

Study objective

The primary objectives of this study in healthy subjects are:
- To investigate the safety and tolerability of JNJ-61393215 versus placebo after single oral dose administration under fasted (ascending dose levels) and fed condition.
- To characterize the pharmacokinetics of JNJ-61393125 in plasma, cerebrospinal fluid (CSF) and urine after single oral dose administration.
- To investigate the effect of food (high fat/high calorie) on the pharmacokinetics of JNJ-61393215 following single oral dose administration.
Additional primary objectives (if cohorts with one day of twice daily [b.i.d] dosing are needed based upon the pharmacokinetic [PK] data from preceding cohorts):
- To investigate the safety and tolerability of JNJ-61393215 versus placebo after 1 day of b.i.d. dosing.
- To characterize the pharmacokinetics of JNJ-61393215 in plasma after 1 day of b.i.d. dosing

The secondary objective of this study in healthy subjects is:
- To characterize the effect of JNJ-61393215 on alertness/sedation and cognition.

Study design

The study will consist of 3 parts with approximately 10 cohorts scheduled in total:

1) Part 1 (8 cohorts) is a double-blind single ascending dose part in young healthy male subjects; some cohorts of Part 1 might have 1 day of b.i.d. dosing, based upon the PK data from previous cohorts;
2) Part 2 (1 cohort) is an open-label single dose part in healthy elderly male

and female subjects including continuous CSF sampling to assess brain penetration of JNJ-61393215;
3) Part 3 (1 cohort) is a double-blind part to assess the effect of food on the bioavailability of JNJ-61393215 in young healthy male subjects.

Intervention

JNJ-61393215 or placebo

Study burden and risks

This will be the first study with JNJ-61393215 in humans. To date, no clinical data is available. The administration of JNJ-61393215 to humans is supported by nonclinical data.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

1. Subjects must have a body mass index (BMI) between 18 and 30 kg/m2, inclusive (BMI = weight/height2).
2. Subject must be healthy on the basis of physical examination, medical history, vital signs, and 12-lead ECG [incl. QTcF <= 450 msec for males and <= 470 msec for females] performed at screening and admission to the clinical unit. Minor abnormalities in ECG, which are not considered to be of clinical significance by the investigator, are acceptable. The presence of Left Bundle Branch Block (LBBB), AV Block (second degree or higher), or a permanent pacemaker or implantable cardioverter defibrillator [ICD] will lead to exclusion.
3. Subjects must be healthy on the basis of clinical laboratory tests performed at screening. If the results of the serum chemistry panel, hematology or urinalysis are outside the normal reference ranges, the subject may be included only if the investigator judges the abnormalities to be not clinically significant. This determination must be recorded in the subject's source documents and initialed by the investigator.
4. A man who is sexually active with a woman of childbearing potential and has not had a vasectomy must agree to use a barrier method of birth control e.g., either condom with spermicidal foam/gel/film/cream/suppository or partner with occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/film/cream/suppository during the study and for 3 months after receiving the last dose of study drug. All men must also not donate sperm during the study and for 3 months after receiving the last dose of study drug. In addition, their female partner should also use an appropriate method of birth control for at least the same duration.
5. Subjects must be willing to adhere to the prohibitions and restrictions specified in this protocol
6. Each subject must sign an informed consent form (ICF) indicating that he or she understands the purpose of and procedures required for the study and are willing to participate in the study.;Specific Inclusion Criteria;Part 1 and 3:
7. Healthy male subjects between 18 and 54 years of age, inclusive.
Part 2:
8. Healthy male and female subjects between 55 and 75 years of age, inclusive. Note: equal gender representation is preferred if feasible
9. Subject must be healthy and medically stable on the basis of clinical laboratory tests (at screening) and physical and neurological examination (at screening and at admission to the clinical unit). If the subject is medically stable with medication, inclusion can be allowed on a case by case basis with written agreement of the sponsor*s responsible safety physician.
10. Women must not be of childbearing potential (i.e., must be postmenopausal with amenorrhea for at least 12 months); permanently sterilized (e.g., tubal occlusion, hysterectomy, bilateral salpingectomy); or otherwise be incapable of pregnancy

Exclusion criteria

1. Subject has a history of or current liver or renal insufficiency; significant cardiac, vascular,

pulmonary, gastrointestinal, endocrine, neurologic, hematologic (including coagulation disorders), rheumatologic, psychiatric, or metabolic disturbances, any inflammatory illness or any other illness. Minor deviations, which are not considered to be of clinical significance to both the investigator and to the Janssen Safety Responsible Physician, are acceptable.
2. Subject has estimated glomerular filtration rate (eGFR) <60 mL/min/1.73m2 at screening (provided by the local laboratory).
3. Subject has a heart rate < 50 bpm at screening or at admission to the clinical unit.
4. Subject has a history of hepatitis B surface antigen (HBsAg) or hepatitis C antibody (anti-HCV) positive, or other clinically active liver disease, or tests positive for HBsAg or anti-HCV at screening.
5. Subject has Left Bundle Branch Block (LBBB), AV Block (second degree or higher), or a permanent pacemaker or implantable cardioverter defibrillator [ICD].
6. Subject has a history of human immunodeficiency virus (HIV) antibody positive, or tests positive for HIV at screening.
7. Subject has a history of malignancy within 5 years before screening (exceptions are squamous and basal cell carcinomas of the skin and carcinoma in situ of the cervix, or malignancy that in the opinion of the investigator, with written concurrence with the sponsor's medical monitor, is considered cured with minimal risk of recurrence).
8. Subject has a history of at least mild drug or alcohol use disorder according to Diagnostic and Statistical Manual of Mental Disorders (latest edition) criteria within 6 months before screening or has a positive test result(s) for alcohol and/or drugs of abuse (including: opiates (including methadone), cocaine, amphetamines, methamphetamines, cannabinoids, barbiturates, and benzodiazepines) at screening or admission to the clinical unit.
9. Subject drinks, on average, more than 8 cups of tea/coffee/cocoa/cola/caffeinated beverages (e.g., energy drink) per day.
10. Subject has a clinically significant acute illness within 7 days prior to study drug administration.
11. Subject smokes cigarettes (or equivalent) and/or has used nicotine based products within 3 months prior to study drug administration.
12. Subject is a man who plans to father a child while enrolled in this study or within 90 days after the last dose of study drug.
13. Subject has a history of clinically significant drug and/or food allergies.
14. Subject has known allergies, hypersensitivity, or intolerance to orexin-1*s excipients (refer to Investigator's Brochure).
15. Subject has taken any disallowed therapies before the planned first dose of study drug, as noted in Section 8, Prestudy and Concomitant Therapy.
16. Subject has received an investigational drug (including vaccines) or used an investigational medical device within 90 days prior to study drug administration or is currently enrolled in an investigational study.
17. Subject has had major surgery, (e.g., requiring general anesthesia) within 8 weeks before screening, or will not have fully recovered from surgery, or has surgery planned during the time the subject is expected to participate in the study or within 4 weeks after the last dose of study drug administration. Note: Subjects with planned surgical procedures to be conducted under local anesthesia may participate.
18. Subject has donated one or more units (approximately 450 mL) of blood or acute loss of an equivalent amount of blood within 90 days prior to study drug administration.
19. Subject has any condition for which, in the opinion of the investigator, participation would

not be in the best interest of the subject (e.g., compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.
20. Subject has psychological and/or emotional problems, which would render the informed consent invalid, or limit the ability of the subject to comply with the study requirements.
21. Vulnerable subjects (e.g., a person kept in detention or a person under guardianship).
22. Subject is unable to read and understand the consent forms, complete study-related procedures, and/or communicate with the study staff.
23. Subject is an employee of the investigator or study site, with direct involvement in the proposed study or other studies under the direction of that investigator or study site, as well as family members of the employees or the investigator.
24. Subject has been previously dosed with JNJ-61393215. Note: In case of b.i.d. dosing, subjects dosed with JNJ-61393215 in the morning can be
dosed again with JNJ-61393215 for the second dose in the evening.;Specific Exclusion Criteria:;Part 2 only:
25. Subject has a clinically significant abnormality on neurological examination at screening or admission which, in the opinion of the investigator, is not appropriate and reasonable for the population under study.
26. Subject has a relevant history of lower back pain or scoliosis and/or major (lumbar) back surgery (microdiscectomy is allowed) in the opinion of the investigator.
27. Subject is allergic to local anesthetics and/or iodine.
28. Subject has taken aspirin (even low dose) within 5 days prior to lumbar puncture and spinal catheter insertion.
29. Subject has taken Low Molecular Weight Heparin (LMWH) within 12 hours prior to spinal catheter insertion.
30. Subject has taken any anticoagulant treatment (besides LMWH described above) or any antiplatelet drug within 1 week or 2 times the half-life, whichever is longest, prior to lumbar puncture and spinal catheter insertion.
31. Subject has a topical infection or local dermatological condition at the puncture site prior to lumbar puncture (pre-puncture Day 1).
32. Subject has signs of increased intracranial pressure based on fundoscopy at screening.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	11-07-2016
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	01-07-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-07-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-10-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
Other	CR108182
EudraCT	EUCTR2016-000822-20-NL
CCMO	NL58044.056.16

Study results

Date completed: 09-11-2016

Results posted: 10-05-2019

URL result
URL
Type
int
Naam
M2.2 Samenvatting voor de leek
URL

Internal documents
File