A first in human sequential dose-escalation study investigating safety, tolerability, pharmacokinetics and pharmacodynamics of single oral doses of NS11821 in healthy male subjects

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1. To investigate the safety and tolerability of single oral doses of NS11821 in healthy male subjects and estimate a maximum tolerated dose.2. To investigate the pharmacokinetics (PK) of single ascending oral doses of NS11821.

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

Summary

ID

NL-OMON33125

Source
ToetsingOnline

Brief title
NS11821 First In Man Study

Condition

- Anxiety disorders and symptoms

Synonym
anxiety, anxiety disorder

Research involving
Human

Sponsors and support

Primary sponsor: Neurosearch
Source(s) of monetary or material Support: NeuroSearch

Intervention

Keyword: NS11821, Pharmacodynamics, Pharmacokinetics, safety

Outcome measures

Primary outcome

Safety parameters

1. Adverse events.

2. Vital signs (supine and orthostatic blood pressure, heart rate, body

temperature, respiratory rate).

3. Electro-cardiogram (ECG).

4. Safety laboratory assays (clinical chemistry, haematology, and

urine-analysis).

Pharmacokinetics:

1. Plasma concentration of NS11821.

2. Urine concentration of NS11821.

Secondary outcome

Pharmacodynamics:

Saccadic eye movements: peak velocity, reaction time, inaccuracy.

Smooth pursuit.

Visual analogue scales (VAS) according to Bond and Lader: alertness, mood and

calmness.

VAS Bowdle: item *feeling high*, and composite factors *internal perception*

and *external perception*.

Body sway.

Adaptive tracking (tracking performance).

Power spectral changes in ph-EEG.

Cognitive function (Cognition (Visual Verbal Learning Test)).

Tapping.

Pharmacokinetics:

Plasma and urine concentration NS11821 metabolites.

Study description

Background summary

NS11821 is a new investigational drug that is being developed for the treatment of anxiety disorders. This drug is not yet registered and in this study will be administered to humans for the first time. Due to its more selective action in the brain, this compound is expected to cause less side effects than the current drugs in the market, such as lorazepam.

Study objective

1. To investigate the safety and tolerability of single oral doses of NS11821 in healthy male subjects and estimate a maximum tolerated dose.
2. To investigate the pharmacokinetics (PK) of single ascending oral doses of NS11821.

Study design

This is a single-dose, parallel, double blind, placebo-controlled, randomized, dose-escalation study in healthy male subjects.

Intervention

Three ascending single oral doses (i.e. 10, 30, and 50 mg) are planned with a dose escalation factor of approximately 2. However, based on safety, pharmacokinetic or pharmacodynamic findings, further decisions can be dose escalation, dose de-escalation, or dose repetition. It may also be possible to terminate the study prematurely. After the first three dose levels the scientific review committee will review all data and may decide to either continue or discontinue the study. An additional 2 cohorts may be rectuited. The maximum dose of NS11821 is 150mg.

Study burden and risks

Screening: medical history taking, physical examination, venapuntion (haematology, chemistry, virology), drugs screening.

Studyday: repeated performance of several tests, insertion of intravenous catheter for repeated blood sampling,
ECG.

Follow-up: physical examination, ECG

Restrictions: during the study period, restriction will be applied to living pattern and the use of alcohol, tobacco,
cafeine, recreational drugs and medication.

Side-effects: as this study is with a new drug, not all of the side effects are known. It is possible that unexpected side effects occur during the study.

Contacts

Public
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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. Voluntary provision of written informed consent prior to any study procedure, indicative of understanding the purpose of the study and willing to participate in the study and comply with the study procedures and restrictions.
2. Male.
3. Aged 18-45 years (both inclusive).

Exclusion criteria

1. Subject is unhealthy according to medical history, physical examination, ECG, blood pressure and heart rate, and laboratory profile of blood and urine. A volunteer with a clinical abnormality may be included only if the investigator or his designee considers that the abnormality will not introduce additional risk factor for the subject's health, or interfere with the study objectives.
2. Presence or history of clinical significant psychiatric diseases, as judged by the investigator.
3. Any clinically relevant acute or chronic diseases which according to the investigator could interfere with the subject*s safety during the trial, or expose them to undue risk, or which could interfere with the study objectives.
4. Presence or history of clinical significant diseases of the renal, hepatic, gastrointestinal, cardiovascular, musculoskeletal system or presence of history of clinical significant immunological, endocrine, metabolic diseases, or other condition known to interfere with the absorption, distribution, metabolism or excretion of drugs, as judged by the investigator.
5. Presence or history of clinically significant allergy or known hypersensitivity to any component of the investigational product.
6. Has a Body Mass Index (BMI) < 18 or > 30 kg/m2.
7. Has positive serology for HIV-1, HIV-2, hepatitis B (surface antigen), and/or hepatitis C.
8. Has planned medical treatments (including dental care) from screening to follow-up visit.

9. Use of prescribed medication or over-the-counter (OTC) medication within two weeks prior to dosing, except for paracetamol.
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C:\Documents and Settings\Default.WSIMAGE.001\Desktop\CHDR0907_pro_00.doc - 22-06-2009 Page 20 of 142
10. Enrolment in any investigational study or intake of an investigational drug within 3 months prior to the start of the study or more than 4 times a year.
11. Current regular user of any illicit drugs or history of drug or alcohol abuse. Subjects who have a positive drug screen at screening and/or pre-dose or subjects who have a positive alcohol breath test at pre-dose will be excluded.
12. Donation of blood/plasma outside limits of Sanquin Blood Supply Foundation guidelines.
13. Previous randomization in this study.
14. Has any barrier (language, mental incapacity, etc.) that could interfere with the psychomotor or cognitive tests.
15. Unlikely to co-operate in the study, and/or has poor compliance anticipated by the investigator. Or not consistently reachable in case of emergency.
16. Daily consumption of xanthine-containing products more than 6 units. Unwilling or unable to refrain from consumption of xanthine-containing foods or drinks from 2 days prior to admission and during the stay in the research unit. One caffeine unit is contained in the following items: one cup of coffee, two cans of cola, one glass of tea, * cup of energy drink (e.g. Red Bull) or three chocolate bars.
17. Unwilling or unable to refrain from intensive physical exercise from screening until the follow-up visit.
18. Unwilling or unable to refrain from products containing alcohol from 2 days before admission and during the stay in the research unit.
19. Unwilling or unable to refrain from products containing grapefruit from 2 days before admission and during the stay in the research unit.
20. Smokes more than 5 cigarettes (or equivalent as judged by the investigator) a day, or unwilling or unable to refrain from smoking from 24 hours before admission and during the stay in the research unit.
21. Unwilling to abstain from having unprotected sexual intercourse or donating sperm during the study and for 3 months after study.
22. Is unsuitable, in the opinion of the investigator, to participate in the study for any other reason.

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:	Recruitment stopped
Start date (anticipated):	12-08-2009
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	not known yet
Generic name:	not known yet

Ethics review

Approved WMO Date:	07-07-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	04-08-2009
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	14-10-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	19-03-2010
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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
EudraCT	EUCTR2009-012373-35-NL
CCMO	NL28807.058.09