A phase 1, double blind (3rd party open), randomized, placebo controlled, crossover single dose escalation study to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of PF-06372865 in healthy subjects

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON40275

Source
ToetsingOnline

Brief title
A study to investigate the effects of PF-0637286 in healthy volunteers

Condition

- Neurological disorders NEC

Synonym
Chronic pain

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer
Source(s) of monetary or material Support: Pharmaceutical company

Intervention

Keyword: First In Human, Partial GABA-A agonist

Outcome measures

Primary outcome

Safety: Adverse events, vital signs measurements, 12-lead ECGs, physical examination findings and clinical safety laboratory measurements.

Pharmacokinetics: Cmax, Tmax, AUClast, AUC24, AUCinf,, CL/F, Vz/F, t1/2.

Pharmacodynamics (Neurocart assessments):

* Saccadic Eye Movements (saccadic reaction time, saccadic peak velocity (deg/sec), and saccadic inaccuracy).

* Body Sway (antero-posterior sway (mm/2min)).

* Smooth Pursuit (percentage of time the eyes of the subjects are in smooth pursuit of the target (%)).

* Bond and Lader VAS (alertness, calmness, mood subscales (mm)).

* Adaptive Tracking (%).

* Visual Verbal Learning Test (immediate recall (number correct, incorrect, and double words), delayed recall (number correct, incorrect, and double words), and delayed recognition (number correct and incorrect words; average and SD of reaction time for correct and incorrect words (sec)).

* Pharmaco-EEG (alpha, beta, delta, and theta power).

Secondary outcome

- The effect of food on PF-06372865 pharmacokinetic parameters may be

investigated.

- The pharmacokinetics of PF-06372865 administered as a tablet may be

investigated.

Study description

Background summary

PF-06372865 is a subtype-selective GABAA positive allosteric modulator that is being developed for the treatment of chronic pain conditions. This is a first-in-human study for PF-06372865, a partial GABA-A agonist which exerts functional selectivity for the alpha 2/3/5 subunits over the alpha 1 subunit.

Study objective

The objective of the first two cohorts of this study is to explore the safety, tolerability, pharmacokinetics, and pharmacodynamics of PF-06372865 after a single dose across a wide exposure range up to the maximum tolerated dose or the maximum predefined PK exposure limits based on the toxicology and toxicokinetic data, whichever is lower.

Study design

This is a double blind, 3rd party open (ie, subject blind, investigator blind and sponsor open), randomized, placebo-controlled, ascending single oral dose, 2 cohort, interleaving design, with placebo substitution, crossover study of PF-06372865. In addition, a third cohort may be run to further explore the pharmacodynamics of PF-06372865.

Intervention

- PF-06372865
- Placebo
- Lorazepam
- PF-06372865 + lorazepam

Study burden and risks

No exceptional severe adverse drug reactions are expected and burden/inconvenience for the subjects are considered relatively mild. Safety margins from results in preclinical research are conservatevely stablished.

Contacts

Public
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GB
Scientific
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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. Healthy male and/or female subjects of non-childbearing potential between the ages of 18 and 55 years, inclusive (Healthy is defined as no clinically relevant abnormalities identified by a detailed medical history, full physical examination, including blood pressure and pulse rate measurement, 12-lead ECG, and clinical laboratory tests).;Female subjects of non-

childbearing potential must meet at least one of the following criteria:
a. Achieved postmenopausal status, defined as: cessation of regular menses for at least 12 consecutive months with no alternative pathological or physiological cause; and have a serum FSH level within the laboratory*s reference range for postmenopausal females.
b. Have undergone a documented hysterectomy and/or bilateral oophorectomy.
c. Have medically confirmed ovarian failure.;All other female subjects (including females with tubal ligations and females that do NOT have a documented hysterectomy, bilateral oophorectomy and/or ovarian failure) will be considered to be of childbearing potential.;2. Body Mass Index (BMI) of 17.5 to 30.5 kg/m2; and a total body weight >50 kg (110 lbs).;3. Evidence of a personally signed and dated informed consent document indicating that the subject has been informed of all pertinent aspects of the study.;4. Subjects who are willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures.

Exclusion criteria

1. Evidence or history of clinically significant haematological, renal, endocrine, pulmonary, gastrointestinal, cardiovascular, hepatic, psychiatric, neurologic, or allergic disease (including drug allergies, but excluding untreated, asymptomatic, seasonal allergies at time of dosing).;2. Subjects with history of sleep apnea.;3. Any condition possibly affecting drug absorption (eg, gastrectomy).;4. A positive urine drug screen.;5. History of regular alcohol consumption exceeding 14 drinks/week for females or 21 drinks/week for males (1 drink = 5 ounces (150 mL) of wine or 12 ounces (360 mL) of beer or 1.5 ounces (45 mL) of hard liquor) within 6 months of Screening.;6. Treatment with another investigational drug within 3 months prior to screening or having participated in more than 4 investigational drug studies within 1 year prior to screening.;7. Screening supine blood pressure >=140 mm Hg (systolic) or >=90 mm Hg (diastolic), following at least 5 minutes of rest. If BP is >=140 mm Hg (systolic) or >=90 mm Hg (diastolic), the BP should be repeated two more times and the average of the three BP values should be used to determine the subject*s eligibility.;8. 12-lead ECG demonstrating QTcF >450 msec or a QRS interval >120 msec at Screening. If QTcF exceeds 450 msec, or QRS exceeds 120 msec, the ECG should be repeated two more times and the average of the three QTcF values should be used to determine the subject*s eligibility.;9. Males who are unwilling or unable to use a highly effective method of contraception as outlined in this protocol for the duration of the study and for at least 90 days after the last dose of investigational product.;10. Use of prescription or nonprescription drugs and dietary supplements within 7 days or 5 half-lives (whichever is longer) prior to the first dose of study drug. As an exception, acetaminophen/paracetamol may be used at doses of =<1 g/day. Limited use of non-prescription medications that are not believed to affect subject safety or the overall results of the study may be permitted on a case-by-case basis following approval by the sponsor.;11. Herbal supplements and hormone replacement therapy within 28 days prior to the first dose of study drug.;12. Blood donation (excluding plasma donations) of approximately 1 pint (500 mL) or more within 56 days prior to dosing.;13. Unwilling or unable to comply with the Lifestyle Guidelines described in this protocol.;14. Other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may

interfere with the interpretation of study results and, in the judgment of the investigator, would make the subject inappropriate for entry into this study.;15. Subjects who are investigational site staff members directly involved in the conduct of the study and their family members, site staff members otherwise supervised by the Investigator, or subjects who are Pfizer employees directly involved in the conduct of the study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-10-2013
Enrollment:	45
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N/A
Generic name:	Lorazepam
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	07-10-2013
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-10-2013
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-01-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-01-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-05-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-06-2014
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
EudraCT	EUCTR2013-003182-34-NL
CCMO	NL46185.056.13