A Double-Blind, Placebo-Controlled, Randomized, Multiple Ascending Oral Dose Study to Investigate The Safety, Tolerability, Pharmacokinetics And Pharmacodynamics of JNJ-26070109 In Healthy Subjects

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JNJ-2607019 is an investigational drug being developed for gastroesophageal reflux disease (GERD) to reduce the complaints of abdominal pain and heartburn in people with this disease. JNJ-26070109 inhibits the gastrin receptor in the stomach. The...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal conditions NEC
Study type	Interventional

Summary

ID

NL-OMON30846

Source
ToetsingOnline

Brief title
MAD (Multiple Ascending Dose) study

Condition

- Gastrointestinal conditions NEC

Synonym
abdominal pain and heartburn

Research involving

Human

Sponsors and support

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

Intervention

Keyword: dose escalation, pharmacodynamic, pharmacokinetic, safety

Outcome measures

Primary outcome

Safety and tolerability, pharmocokinetic and pharmacodynamic blood and urine tests, adverse events, safety laboratory parameters, vital signs, heart rate, ECG, alcohol breath test and continuously hearth rhythm (telemetry) . For Part 2 also a Helicobacter pylori breath test and intra-gastric pH measurements will be assessed for a period of 24 hours, on Day -1, Day 1, Day 7 and Day 14. and finished 24 hours after dosing.

Secondary outcome

Not applicable.

Study description

Background summary

The study has three objectives. Firstly, we will study the safety and tolerability of JNJ-26070109 after the administration of multiple doses of the drug. Secondly, we will investigate the maximum tolerated concentration of the drug in the body. Thirdly, we will study the speed at which the drug is absorbed in the body, as well as the degree of elimination of the drug after multiple doses.

Study objective

JNJ-2607019 is an investigational drug being developed for gastroesophageal reflux disease (GERD) to reduce the complaints of abdominal pain and heartburn in people with this disease. JNJ-26070109 inhibits the gastrin receptor in the stomach. The gastrin receptors are small particles in the stomach. When the gastrin receptor is triggered the stomach will produce acid. In people with GERD the acid in the stomach is the cause for the abdominal pain and heartburn. By blocking the gastrin receptor the acid production will decrease and the complaints of pain and heartburn will diminish.

Study design

This is a single center study in healthy male and female subjects, and consists of 3 parts.
Part One is a double-blind, randomized, placebo-controlled multiple ascending dose design. Subjects will participate in one of four (4) cohorts (n = 10) and will receive either JNJ 26070109 oral suspension (n = 7) or placebo (n = 3) daily for 14 consecutive days. Blinded data arising from the previous level(s), based on the concentrations of study drug in blood, safety and tolerability will be reviewed.
Dose escalations will continue if all these data are found acceptable.
It will continue until maximum tolerated dose (MTD) is reached per the dose limiting toxicity (DLT) described in Section (4.6.6). Each dose escalation will not exceed 3 fold of the previous dose and the dose will not exceed 1000 mg.
In Part Two of the study, based on safety, the concentration of study drug in blood and tolerability data of Part 1, two doses will be selected. 2 Satellite cohorts, each with 20 healthy male subjects, will be dosed in order to measure 24-hour intragastric pH as a pharmacodynamic endpoint. Each cohort in Part Two will receive one of these two doses of JNJ-26070109 (n=15 per cohort) or placebo (n=5 per cohort) daily for 14 consecutive days and will be evaluated in a similar fashion to Part One. Commencement of Part Two may occur in parallel with Part One but only after completion of the in-life phase in the 10 subjects in Part One at the same selected dose. The staggered start of subjects in Part Two by at least 2 weeks from Part One at the selected doses provides an added level of safety for any adverse effects that may be reported over the 14-day treatment period in Part One. The only difference in procedures and assessments for subjects enrolled in Part One and Part Two is that intragastric pH will be measured for 24 hours on Days -1 (day before dosing), 1, 7 and 14 in subjects in Part Two and a Helicobacter Pylori breath test will be taken.
Part Three, Upon completion of the dose escalation in males in Part One, a cohort of 10 healthy females not of childbearing potential will be dosed with JNJ-26070109 (n=7 per cohort) or placebo (n=3 per cohort) daily for 14 consecutive days and will be evaluated in a similar fashion to Part One. The dose and regimen of JNJ-26070109 will be no greater than the highest dose that has been shown to be tolerable in males.
The total duration per subject is 68 days at a maximum. The study will include a medical examination, one admission period of 20 days, one visit and finally a follow-up. The following assessments will be taken; physical exam, blood-and

urine sample collections, alcohol breath test, blood sample for DNA-assessment, vital signs, ECG*s and continuously hearth rhythm (telemetry) . For part 2, also intra gastric pH monitoring will be assessed for 24 hours at Day -1, Day 1, Day 7 and Day 14 and a Helicobacter pylori breath test will be taken.

Intervention

Every subject is only allowed to participate after randomization to one of the cohorts. Per treatment subjects will receive the study drug for 14 consecutive days.
Part 1:
Treatment A 50 mg JNJ-26070109 suspension or placebo qd
Treatment B 150 mg JNJ-26070109 suspension or placebo qd
Treatment C 400 mg JNJ-26070109 suspension or placebo qd
Treatment D 1000 mg JNJ-26070109 suspension or placebo qd
Part 2:
This part was initially designed to have 2 cohorts of 20 healthy male subjects each.
After completion of Part one and the first 10 subjects of Part two it was confirmed that JNJ-26070109 exposure on day 1 was up to 40% lowwer compaired with exposures observed in the SAD (C-2006-003) study at the higher dose level of 400 mg and 1000 mg suspension. The next three cohorts will receive JNJ-260720109 in hard gel capsule formulaion.
cohort 1 400 mg JNJ-26070109 suspension or plavebo qd
cohort 2 100 mg JNJ-26070109 in hard gel capsule formulation or placebo qd.
cohort 3 300 mg JNJ-26070109 in hard gel capsule formulation or placebo qd.
cohort 4 based on PK, pH and safety/tolerability data of previous 2 cohorts, a dose level which will no exeed 500 mg JNJ-26070109 in hard gel capsule formulation or placebo qd.
Part 3:
Upon completion of the dose escalation in males and dependent on the observed safety of the preceeding cohorts and PK-exposure data a cohort of 10 females may be dosed with JNJ-27070109 hard gel capsules or placebo qd.

Study burden and risks

The associated risks to this study are the occurrence of possibility side effects of the use of JNj-26070109. The burden of the subjects are the confinement period in the unit, venipuncture, the insertion of the cannula and connection of the telemetry equipment. For Part 2 also the insertion of the gastric tube. All subjects will be carefully monitored regarding possible adverse events by experienced study personnel and physicians

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

Female subjects must not be of childbearing potential, ie must be surgically sterile (> 6 months) or post-menopausal (no menses for > 2 years).
Subjects must have supine blood pressure (after resting for 5 min) between the range of 95 - 139 mm Hg systolic (inclusive), and 50 - 89 mm Hg diastolic (inclusive).
Subjects must be in good general health prior to study participation with no clinically relevant abnormalities as assessed by the investigator and determined by: medical history, physical examination, blood chemistry, complete blood count (CBC), UA, and ECG.
Male subjects must consent to utilize a medically acceptable method of contraception throughout the entire study period and for 3 months after the study is completed.
Subjects must be Helicobacter pylori negative at screening.

Exclusion criteria

Subjects with evidence of clinically significant hepatic, reproductive, gastrointestinal, renal, hematologic, pulmonary, neurologic, respiratory, endocrine/metabolic, or cardiovascular system abnormalities, psychiatric disorders, oncologic conditions or acute or chronic infection.
Subjects with past or current gastric or duodenal ulceration.
Subjects with history of lactose intolerance.
Subjects who have a history of having a first degree relative die from cardiac causes prior to the age of 40 years.
Subjects with significant history of heartburn or other symptoms of gastroesophageal reflux disease (GERD) or subjects who have used prescription, or non-prescription medications, for symptoms of heartburn or symptoms of GERD within 3 months prior to screening.
Subjects who have taken JNJ-26070109 previously in a clinical study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-04-2007
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO

Date:	14-02-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	23-02-2007
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-03-2007
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-10-2007
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-10-2007
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-10-2007
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2007-000265-38-NL
CCMO	NL16597.040.07