A Randomized, Double-Blind, Placebo-Controlled, Parallel Group Dose Ranging Study to Investigate the Safety and Efficacy of JNJ-16269110 in Overweight and Obese Subjects

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Ethical review	Approved WMO
Status	Pending
Health condition type	Appetite and general nutritional disorders
Study type	Interventional

Summary

ID

NL-OMON30928

Source
ToetsingOnline

Brief title
N/A

Condition

- Appetite and general nutritional disorders

Synonym
corpulence- obesity

Research involving
Human

Sponsors and support

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

Intervention

Keyword: efficacy, MTP-inhibitor, obesity, safety

Outcome measures

Primary outcome

The primary objective of the study is to find the appropriate, clinically relevant dosages (among the 5, 10, and 15 mg twice-daily dosages) of JNJ-16269110 by assessing mean changes in body weight from baseline to Week 12, compared to placebo

Secondary outcome

The secondary objectives are:

· To estimate the dose-response relationship between the different dosages of JNJ-16269110 and the decrease in body weight from baseline to Week 12

· To estimate the effect on weight loss of different JNJ-16269110 dosages versus placebo as expressed by mean percent change from baseline in body weight and in body mass index (BMI), and the percentage of subjects who lose at least 5% or 10% of their initial body weight

· To estimate changes in body composition using anthropometric measurements and by means of Dual X Ray Absorptiometry (DEXA [only at selected sites] to explore if weight loss is predominantly due to loss of fat mass

· To explore changes in obesity-associated comorbidities as assessed by glucose homeostasis, fasting lipid profile, and systolic and diastolic blood pressure

· To explore the effect of JNJ-16269110 on changes in levels of PYY, GLP 1, and oxyntomodulin

· To explore the impact of health status using the Impact of Weight on Quality of Life-Lite (IWQOL Lite) Questionnaire

· To explore patient-reported assessment of GI symptoms

· To assess safety and tolerability with specific emphasis on gastrointestinal (GI) adverse events, hepatic function, and absorption of lipid-soluble vitamins and essential fatty acids

· To assess pharmacokinetic (PK) exposure and to explore exposure-response relationships, and to develop a population PK model

Study description

Background summary

JNJ-16269110 is a novel microsomal triglyceride transfer protein (MTP) inhibitor that aims to limit the caloric intake in obese and overweight patients by reducing food consumption via enterically mediated neural and hormonal mechanisms.

Study objective

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The secondary objectives are:
· To estimate the dose-response relationship between the different dosages of JNJ-16269110 and the decrease in body weight from baseline to Week 12
· To estimate the effect on weight loss of different JNJ-16269110 dosages versus placebo as expressed by mean percent change from baseline in body weight and in body mass index (BMI), and the percentage of subjects who lose at least 5% or 10% of their initial body weight
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if weight loss is predominantly due to loss of fat mass
· To explore changes in obesity-associated comorbidities as assessed by glucose homeostasis, fasting lipid profile, and systolic and diastolic blood pressure
· To explore the effect of JNJ-16269110 on changes in levels of PYY, GLP 1, and oxyntomodulin
· To explore the impact of health status using the Impact of Weight on Quality of Life-Lite (IWQOL Lite) Questionnaire
· To explore patient-reported assessment of GI symptoms
· To assess safety and tolerability with specific emphasis on gastrointestinal (GI) adverse events, hepatic function, and absorption of lipid-soluble vitamins and essential fatty acids
· To assess pharmacokinetic (PK) exposure and to explore exposure-response relationships, and to develop a population PK model

Study design

This is a multicenter, randomized, double-blind, placebo- controlled, parallel-group, dose-ranging design with 4 treatment arms each consisting of 80 randomized overweight or obese subjects. A sufficient number of subjects will be enrolled into the run-in phase to randomize a total sample of 320 subjects in the double-blind treatment phase. Subjects will be stratified by study center and by a run in weight loss of less or equal to 2 kg or more than 2 kg. Subjects who discontinue from the study during the double-blind treatment phase will not be replaced.
The study will consist of 3 phases.
- In the pretreatment phase, after giving written informed consent, subjects will undergo screening evaluations, and be provided dietary counseling by a dietitian within 7 days before the start of the run-in period.
- Subjects who have successfully completed the screening period will enter the 4 week run-in period and start standardized nonpharmacologic therapy including an individualized 600-kcal deficit diet containing a maximum of 30% of calories derived from fat.
- Subjects who have completed the run-in period will enter the double-blind treatment phase. The double blind treatment phase is 12 weeks in duration and ends with an End-of-Treatment or Early Withdrawal Visit. In the posttreatment phase the subject is evaluated 14 days after the end of treatment.
Standardized nonpharmacologic therapy will be administered from Week *4 through the follow-up period. Subjects will be instructed not to start a diet or new exercise program other than the weight loss procedures that are part of this study.
Study visits are scheduled to occur every 14±3 days. The total study duration for each subject is approximately 19 weeks.
An extra 10 mL blood sample will be collected for pharmacogenomic analysis after that the patient has given consent for this.

Intervention

In the double-blind treatment phase of the study, all subjects will be randomly assigned to receive 1 of 4 treatments: JNJ-16269110, 5, 10, or 15 mg capsules, or matching placebo capsules twice daily.

Study burden and risks

Burden:
The study lasts approximately 19 weeks. During these 19 weeks, 11 visits are planned.
Blood will be drawn at 9 visits. A total of 340 ml blood will be drawn.
Approximately 50 % of the patiens will undergo a DEXA after written consent from the patient.
The patient will be asked to fill out 5 times a questionnaire about the impact of weight on quality of life.
The patient will be asked to fill out 6 times a questionnaire about gatro-intestinal symptoms
A physical examination will be performed 3 times (no internal examination)
Risks:
JNK16269110 can cause unwanted effects, called side effects. These are listed in the patient information.

Contacts

Public
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Nederland
Scientific
Janssen-Cilag

Postbus 90240
5000 LT Tilburg
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

· Men or women
· Between 18 and 65 years of age, inclusive
· Women must be:
· postmenopausal,
· or surgically incapable of childbearing
· or sexually abstinent
· Women of childbearing potential must be practicing an acceptable method of birth control and have had a negative urine pregnancy test at screening as well as at the baseline visit before receiving study drug, which will be followed immediately by a serum beta-human chorionic gonadotropin (b-hCG) test. · Must be obese or overweight at screening (start of run-in period), defined as:
· BMI *30 kg/m2 and <50 kg/m2 or
· BMI *27 kg/m2 and <50 kg/m2 in the presence of controlled hypertension and/or treated or untreated dyslipidemia. For subjects receiving antihypertensive and/or hypolipidemic medications, these should have been at a stable dosage for at least 2 months before the start of the run-in period. There should be no anticipated changes to antihypertensive or lipid-lowering medications during the course of the study.
· Controlled hypertension is defined as a diastolic blood pressure <100 mmHg and a systolic blood pressure <160 mmHg, in the presence of antihypertensive drug treatment.
· For subjects who are not on lipid-lowering drugs, dyslipidemia is defined as LDL-C *3.4 mmol/L (130 mg/dL), HDL C <1 mmol/L (40 mg/dL) for men or <1.3 mmol/L (50 mg/dL) for women, or triglycerides *1.7 mmol/L (150 mg/dL).
· If subjects are clinically diagnosed with dyslipidemia as a result of screening assessments, they can only continue in the run-in phase of the study if in the clinical judgment of the investigator initiation of lipid-lowering therapy is not required either immediately or during the course of the study.
· A stable weight, i.e., increasing or decreasing not more than 5 kg in the 3 months before the start of the run-in period.
· Consumption of breakfast and dinner on a daily basis
· Fasting plasma glucose24 <7.0 mmol/L (126 mg/dL) at screening

Exclusion criteria

· History of obesity with a known cause
· History of anorexia nervosa, bulimia, or binge-eating disorder

· An established diagnosis of diabetes mellitus or treatment with glucose-lowering prescription drugs at screening
· Prior exposure or known contraindication or hypersensitivity to JNJ 16269110
· History of weight-reducing diet or receiving any drugs to treat obesity within the 3 months prior to screening
· Treatment with any investigational drug or device within 1 month before the start of the run-in period
· History or evidence of liver disease
· History of HIV or presence of hepatitis C antibodies or positive hepatitis B serology
· History of clinically significant gastro-intestinal disease
· History of major gastro-intestinal surgery other than appendectomy or uncomplicated cholecystectomy.
· Previous gastric restrictive surgery or other surgical procedures to induce weight loss
· Liposuction within the last 3 months before screening
· Pregnant or nursing women, or women who plan to become pregnant during the study
· History of significant cardiovascular disease within 6 months of enrollment.
· History of clinically significant cardiac valvular disease, or congestive heart failure
· 12-lead ECG showing evidence of clinically significant heart rhythm or conduction abnormality at screening or baseline.
· An average of 3 seated readings where diastolic blood pressure *100 mmHg or a systolic blood pressure *160 mmHg at screening
· Thyroid-stimulating hormone (TSH) >1.5 times ULN at screening. Subjects on medication for hypothyroidism should have been on a stable dosage for at least 3 months before enrollment (the start of the run-in period).
· A significant change in smoking habits within 3 months of the start of the run-in period; subjects planning to alter smoking habits during the course of the study
· Malignancy or a history of a malignancy within 5 years before the start of the run-in period, other than basal cell carcinomas of the skin or in situ cervical carcinoma
· History or evidence of clinically significant abnormal values for hematology, coagulation, or clinical biochemistry.
· Increased liver function tests,
· ALT above 1.5 X ULN
· ALT above ULN but less than 1.5 X ULN with a concomitant increase of AST, bilirubin, alkaline phosphatase or LDH above 1.5 X ULN or GGT above 2x ULN at screening.
· Increased creatinine kinase (CK) above ULN in subjects who take lipid lowering agents and CK level above 2 x ULN in subjects who do not take lipid lowering agents at screening visit.
· Fasting TG >33.3 mmol/L (600 mg/dL) at screening.
· Evidence of renal impairment (serum creatinine >133 mmol/L (1.5 mg/dL) in men, >124 mmol/L (1.4 mg/dL) in women)
· History of drug or alcohol abuse within the previous 2 years
· Alcohol consumption exceeding 4 units per day for men or 3 units per day for women
· Receiving any excluded medication (see section 8)
· History of seizures or significant central nervous system-related disorders
· History of significant psychiatric disorder, including, schizophrenia, or psychosis (depressive disorders do not preclude participation in the trial)
· Current use of cannabinoids

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	25-10-2007
Enrollment:	52
Type:	Anticipated

Ethics review

Approved WMO Date:	25-09-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-11-2007
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-08-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2006-006772-38-NL
Other	N/A
CCMO	NL19366.018.07