A PHASE 1, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, ALTERNATING PANEL, SINGLE ASCENDING DOSE STUDY EVALUATING THE SAFETY, TOLERABILITY AND PHARMACOKINETICS OF JTK-656 AND THE EFFECT OF FOOD ON THE PHARMACOKINETICS OF JTK-656 IN HEALTHY MALE SUBJECTS

Published: 24-06-2008
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Primary :To investigate the safety and tolerability of ascending single oral doses of JTK-656 administered to healthy male subjectsSecondary:To determine the pharmacokinetics (PK) of ascending single oral doses of JTK-656 administered to healthy...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immunodeficiency syndromes
Study type	Interventional

Summary

ID

NL-OMON32420

Source
ToetsingOnline

Brief title
JTK-656 single ascending dose and food effect study

Condition

- Immunodeficiency syndromes

Synonym
immune deficiency infections

Research involving
Human

Sponsors and support

Primary sponsor: Japan Tobacco Inc.
Source(s) of monetary or material Support: Sponsor van dit onderzoek

Intervention

Keyword: HIV, JTK-656, Single ascending dose

Outcome measures

Primary outcome

Criteria for evaluation

Pharmacokinetics :Plasma JTK-656

concentrations, PK parameters

Safety :AEs, vital signs,

ECG-parameters, laboratory parameters, physical examination and weight

Exploratory lipid profile assessments :HDL2-cholesterol and HDL3-cholesterol

Statistical methods

Pharmacokinetic parameters :Analysis of variance (ANOVA) on

Cmax and AUC to explore the food effect, statistical analysis on

dose-normalized Cmax, AUClast and AUCinf to assess dose proportionality, other

parameters descriptive statistics

Safety parameters :Descriptive statistics,

frequency tables

Exploratory lipid profile parameters :Descriptive statistics

Secondary outcome

N.v.t.

Study description

Background summary

A randomized, double-blind, placebo-controlled, alternating panel, single ascending dose study with four panels of nine subjects each. Subjects will receive three single oral doses (Panels A, B and C) or two single oral doses (Panel D) of JTK-656 or placebo. The subjects will receive medication under fasting conditions, except in one period of Panel C where the medication will be taken after an FDA high-fat breakfast. At each dose level, 6 subjects will receive active drug and 3 subjects will receive placebo in a randomized fashion. Subjects in Panels A and B will receive placebo once in the study and active treatment twice. Subjects in Panel C will receive the same treatment twice, once under fasting conditions and once after an FDA high-fat breakfast. In Panels C and D, 6 subjects will receive placebo at least once and 3 subjects will receive active treatment only. There will be a wash-out of at least ten days between administrations within a panel.

Study objective

Primary :To investigate the safety and tolerability of ascending single oral doses of JTK-656 administered to healthy male subjects

Secondary:To determine the pharmacokinetics (PK) of ascending single oral doses of JTK-656 administered to healthy male subjects (Part 2 only)
To determine the effect of food on the PK of JTK-656 administered under fed and fasted conditions to healthy male subjects (Part 2, Panel C)

Study design

Part 1 (Period 1 of Panels A and B; Period 2 of Panel A)

Procedures and assessments

Screening and follow-up:Clinical laboratory, vital signs, physical examination, 12-lead electrocardiogram (ECG), weight and previous and concomitant medication; at eligibility screening only: height, medical history, alcohol and drug screen, cotinine test, hepatitis B surface antigen (HBsAg), anti hepatitis C virus (HCV) and anti-human immunodeficiency virus (HIV) 1/2; at follow-up only: adverse events (AEs)

Each admission :Alcohol and drug screen, cotinine test, vital signs, clinical laboratory, brief physical examination, AEs and previous and concomitant medication
Observation period :Each period in clinic from -17 h up to 24 h after drug administration and an ambulatory visit on Day 8 (+/- 1 day) for follow-up

Safety assessments :AEs: throughout the study and specifically at pre-dose and 1, 2, 4, 8, 12 and 24 h post dose; weight: pre-dose; vital signs: pre-dose and 1, 2, 3, 4, 6, 8, 12 and 24 h post-dose; 12-lead ECG: pre-dose and 1, 4 and 24 h post-dose; clinical laboratory: pre dose and 24 h post-dose

Exploratory lipid profile assessments:HDL2-cholesterol and HDL3-cholesterol: pre dose and 24 h post-dose
Bioanalysis:Analysis of serum exploratory lipid profile assessment samples (HDL2-cholesterol and HDL3 cholesterol) by the contracted laboratory

Part 2 (Period 1 of Panels C and D; Period 2 of Panels B, C and D; Period 3 of Panels A, B, and C)

Procedures and assessments

Screening and follow-up:Clinical laboratory, vital signs, physical examination, 12-lead ECG, weight and previous and concomitant medication; at eligibility screening only: height, medical history, alcohol and drug screen, cotinine test, HBsAg, anti HCV, anti-HIV 1/2; at follow-up only: AEs

Each admission :Alcohol and drug screen, cotinine test, vital signs, clinical laboratory, brief physical examination, AEs and previous and concomitant medication

Observation period :Each period in clinic from -17 h up to 48 h after drug administration and an ambulatory visit on Day 8 (+/- 1 day) for follow-up
Blood sampling :For PK of JTK-656: pre-dose and 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36 and 48 h post dose and at follow-up

Safety assessments :AEs: throughout the study and specifically at pre-dose and 1, 2, 4, 8, 12, 24, 36 and 48 h post-dose; weight: pre-dose; vital signs: pre-dose and 1, 2, 3, 4, 6, 8, 12, 24 and 48 h post dose; 12-lead ECG: pre-dose and 1, 4, 24 and 48 h post-dose; clinical laboratory: pre dose and 24 and 48 h post-dose

Exploratory lipid profile assessments:HDL2-cholesterol and HDL3-cholesterol: pre-dose and 24 and 48 h post-dose
Bioanalysis:Analysis of plasma JTK-656 samples using a validated high performance LC-MS/MS method by Sponsor
:Analysis of serum exploratory lipid profile assessment samples (HDL2-cholesterol and HDL3 cholesterol) by the contracted laboratory

Intervention

Study Medication
Active substance :JTK-656
Activity :HIV integrase inhibitor
Indication :HIV-1 infection
Strength :0.3 mg/2 g PEG400, 1.5 mg/2 g PEG400 and 7.5 mg/2 g PEG400 (Part 1) and 25 and 200 mg (Part 2)
Dosage form :Oral solution (Part 1) and tablet (Part 2)
Batch number :To be included in the clinical study report

Treatments

Part 1

Panel A : Period 1: a single oral dose of 0.3 mg JTK-656 or placebo in the fasted state
Period 2: a single oral dose of 7.5 mg JTK-656 or placebo in the fasted state

Panel B : Period 1: a single oral dose of 1.5 mg JTK-656 or placebo in the fasted state

Part 2

Panel A : Period 3: a single oral dose of 75 mg JTK-656 or placebo in the fasted state

Panel B : Period 2: a single oral dose of 25 mg JTK-656 or placebo in the fasted state
Period 3: a single oral dose of 200 mg JTK-656 or placebo in the fasted state

Panel C : One Period: a single oral dose of 400 mg JTK-656 or placebo in the fasted state
One Period: a single oral dose of 400 mg JTK-656 or placebo in the fed state
One Period: a single oral dose of 800 mg JTK-656 or placebo in the fasted state

Panel D : Period 1: a single oral dose of 1200 mg JTK-656 or placebo in the fasted state
Period 2: a single oral dose of 1600 mg JTK-656 or placebo in the fasted state

Study burden and risks

Procedures: insertion of the dwelling canula/venapuncture: some pain, bruise, light bleeding.

JTK-656:
adverse events in animal studies: vomiting, changes and increase of levels of blood lipids at high doses.

Contacts

Public
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Japan
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

Healthy volunteers
Male
18 and 55 years of age
Body Mass Index: 19 - 28 kg/m2, inclusive, at the screening visit

Exclusion criteria

Clinically relevant medical history
Hypersensitivity to any component of the JTK-656 formulation

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):	01-08-2008
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	JTK-656

Ethics review

Approved WMO Date:	24-06-2008
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-07-2008
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-09-2008
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-09-2008
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-09-2008
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-10-2008
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	EUCTR2008-003565-87-NL
CCMO	NL23782.056.08