A Phase 1, Randomized, Double-Blind, Placebo-Controlled, Sequential Single Dose Escalation Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics and Effect of Food on Pharmacokinetics of CAL-120 in Healthy Male Subjects

Published: 15-03-2011
Last updated: 27-04-2024

Primary:to evaluate the safety and tolerability of single dose administration of the study drug in healthy male subjectsto determine the pharmacokinetic parameters following single dose administration of the study drug in healthy male subjectso...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON35937

Source
ToetsingOnline

Brief title
CAL-120 SAD study

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
cancer, solid tumors

Research involving
Human

Sponsors and support

Primary sponsor: Gilead Sciences (former Calistoga Pharmaceuticals, Inc.)
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: CAL-120, Solid tumors

Outcome measures

Primary outcome

Safety, tolerability

Pharmacokinetics

Secondary outcome

Pharmacodynamics (by platelet aggregation and basophil activation , as well as

the effect of food)

Study description

Background summary

The drug to be given CAL-120 is a new, investigational compound that may eventually be used for the treatment of solid tumors. A solid tumor is an abnormal growth of cells, with cancer of the lung, breast, colorectum, stomach and prostate being the most common types. The large number of cancer deaths and poor survival for many cancer types highlight the urgent need for new therapies. The enzyme (protein) PI3K has an important role in the growth and survival of cells. This enzyme (PI3K) can be inhibited by CAL-120, which will inhibit the growth of the tumor. Studies in animals with tumors have shown inhibition of solid tumors. Therefore, CAL-120 is a potential new agent for the treatment of solid tumors.
This is the first time that this compound is being given to humans. Similar drugs with the same method of action have been given to humans before.

In part 3 of the study, ketoconazole will also be administered. Ketoconazole is

a registered antifungal drug and is used to prevent and treat fungal skin infections.*

Study objective

Primary:
to evaluate the safety and tolerability of single dose administration of the study drug in healthy male subjects
to determine the pharmacokinetic parameters following single dose administration of the study drug in healthy male subjects
o evaluate the effects of CYP3A4 inhibition with ketoconazole on the PK profile of
CAL-120 in healthy male subjects

Secundary:
to assess pharmacodynamic effects on platelet aggregation and basophil activation , as well as the effect of food following single dose administration of the study drug in healthy male subjects

Study design

Design:
Part 1 (single ascending dose)
- a randomized, double blind, placebo controlled, sequential single dose escalation study with 7 groups of 8 healthy male subjects, each receiving a single oral dose of the study drug or placebo (six verum and two placebo) as a capsule.

Part 2 (food effects)
- A randomized, open-label, food effect study with 1 group of 12 healthy male subjects, each receiving a single oral dose of the study drug as a capsule on two occasions, once in a fasting state and one in a fed state.

Part 3 (drug-drug interaction)
- An open-label study with 1 group of 12 healthy male subjects, each receiving a single oral dose of ketoconazole once per day for 5 days administered in the fasting state. On the day of the last ketoconazole dose, the subjects will also receive a single dose of CAL-120 administered in a fasting state.

Procedures and assessments:
Screening and follow up:
clinical laboratory, vital signs, physical examination, ECG; at eligibility screening: medical history, height, weight, drug screen, HBsAg, anti HCV, anti-HIV 1/2; follow-up at discharge on Day 4 (Part 1) or on Day 8 (Part 2 and Part 3); drug screen, vital signs, haematology and clinical chemistry to be

repeated upon admission

Part 1
-Observation period:one period in clinic from -17 h up to 72 h after drug administration on Day 1

-Blood sampling:
for pharmacokinetics of CAL-120 in plasma: pre-dose and 15, 30 min, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, 48 and 72 h post-dose on Day 1
for pharmacodynamics of CAL-120 in blood: pre-dose and 1, 2,4, 8, 24, 48, and 72 h post-dose on Day 1
for genotyping: pre-dose on Day 1

-Urine sampling:
pharmacokinetics of CAL-120 and creatinine: pre-dose, and intervals at 0-4, 4-8, 8-12 and 12-24 post dose on Day 1.

-Safety assessments:
adverse events: throughout the study;
vital signs: pre-dose and 1, 2, 3, 4, 6, 8,12, 24, 48, and 72h post-dose on Day 1;
ECG: predose, 1, 2, 3, 4, 6 8, 12, 24, and 72h post-dose on Day 1;
telemetry: from 30 min pre-dose until 6h post-dose on Day 1.
Clinical lab (including coagulation) 24h post dose on Day 1

Part 2
-Observation period:
one period in clinic from -17 h before drug administration on Day 1 up to 72 h after drug administration on Day 5

-Blood sampling:
for pharmacokinetics of CAL-120 in plasma: pre-dose and 15, 30 min, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, 48 and 72 h post-dose on Days 1 and 5
for pharmacodynamics of CAL-120 in blood: pre-dose and, 2,4, 8, 24, 48, and 72 h post-dose on Days 1 and 5

-Urine sampling:
pharmacokinetics of CAL-120 and creatinine: pre-dose, and intervals at 0-4, 4-8, 8-12 and 12-24 post dose on Days 1 and 5

-Safety assessments:
adverse events: throughout the study;
vital signs: once on Days 1-8;
ECG: once on Days 1 and 8;
Clinical lab (including coagulation) 24, 72h post dose on Days 1 and 5

-Bioanalysis

analysis of plasma and urine CAL-120 samples using a validated method by PRA
whole blood FACS assay * ex vivo stimulation of basophil activation using a validated method by PRA
whole blood FACS assay * ex vivo stimulation of platelet activation using a validated method by PRA

Part 3:
Observation period:
one period in clinic from -17 h before drug administration on Day 1 up to 72 h after drug administration on Day 5

Blood sampling:
for pharmacokinetics of CAL-120 in plasma: pre-dose and 15, 30 min, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, 48 and 72 h post-dose on Day 5
for pharmacodynamics of CAL-120 in blood: pre-dose and, 2,4, 8, 24, 48, and 72 h post-dose on Day 5

Urine sampling:
pharmacokinetics of CAL-120 and creatinine: pre-dose, and intervals at 0-4, 4-8, 8-12 and 12-24 post dose on Day 5

Safety assessments:
adverse events: throughout the study; vital signs: once on Days 1-8; ECG: once on Days 5 and 8; clinical lab (including coagulation) 24, 72h post dose on Day 5

Bioanalysis:
analysis of plasma and urine CAL-120 samples using a validated method by PRA
whole blood FACS assay * ex vivo stimulation of basophil activation using a validated method by PRA
whole blood FACS assay * ex vivo stimulation of platelet activation using a validated method by PRA

Intervention

Active substance: CAL-120
Activity: PI3-kinase inhibitor
Dosage form: capsule

Active substance: Ketoconazol
Activity: CYP3A4 inhibitor
Dosage form: tablet

Study burden and risks

Procedures: pain, light bleeding, heamatoma, possibly an infection.

Contacts

Public
Gilead Sciences (former Calistoga Pharmaceuticals, Inc.)

199 East Blaine Street
Seattle, WA 98102
US
Scientific
Gilead Sciences (former Calistoga Pharmaceuticals, Inc.)

199 East Blaine Street
Seattle, WA 98102
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy male
Age between 18 and 65 years, inclusive.
BMI between 18 and 30 kg/m2, inclusive.
Non smoking or smoking a maximum of 5 cigarettes per day

Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of the study. In case of donating any blood or significant loss of blood within 60 days of the start of drug dosing.

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):	28-03-2011
Enrollment:	68
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nizoral
Generic name:	Ketoconazole
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	15-03-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-03-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	13-05-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-05-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-10-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-10-2011
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	EUCTR2011-000605-44-NL

Register	ID
CCMO	NL35886.056.11

Study results

Date completed:	17-11-2011
Actual enrolment:	80