A first-in-human, randomized, double-blind, placebo-controlled, single ascending dose and multiple ascending dose study to investigate the safety, tolerability, pharmacokinetics (including food effect), pharmacodynamics and proof of concept of CKD-506 in healthy subjects and inflammatory bowel disease patients

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

Summary

ID

NL-OMON45538

Source
ToetsingOnline

Brief title
CKD-506 Phase 1 SAD/MAD/FE/POC study

Condition

- Gastrointestinal inflammatory conditions
- Joint disorders

Synonym
inflammatory bowel disease, rheumatoid arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Chong Kun Dang Pharmaceutical Corp.
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: inflammatory bowel disease, rheumatoid arthritis

Outcome measures

Primary outcome

- To assess the safety and tolerability of single and multiple ascending oral

doses of CKD-506 in healthy subjects (SAD and MAD parts)

- To assess the PK profile of single and multiple ascending oral doses of

CKD-506 in healthy subjects (SAD and MAD parts)

- To assess the effect of food on the absorption and PK profile of CKD-506

following a single oral dose of CKD-506 in healthy subjects (FE part)

- To assess the effect of IBD on the absorption and PK profile of CKD-506

following multiple oral doses of CKD-506 in IBD patients (POC part)

Secondary outcome

- To evaluate the biological activity (PD) of single and multiple ascending

doses of CKD-506 in healthy human subjects (SAD and MAD parts)

- To evaluate the effect of food on the safety and tolerability of CKD-506

following a single oral dose of CKD-506 in healthy subjects (FE part)

- To evaluate the effect of IBD on the safety and tolerability of CKD-506

following multiple oral doses of CKD-506 in IBD patients (POC part)

- To evaluate the biological activity (PD) of multiple oral doses of CKD-506 in

IBD patients (POC part)

Study description

Background summary

CKD-506 is a new investigational compound that may eventually be used for the treatment of inflammatory bowel disease (IBD) and rheumatoid arthritis (RA), both inflammatory diseases. IBD is a chronic inflammatory disorder of the gastrointestinal tract of which 2 main forms can be distinguished, namely Crohn*s disease (CD) and ulcerative colitis (UC). Rheumatoid arthritis is a long-lasting auto-immune disorder that primarily affects the joints. Inflammation is characterized by increased blood supply and activation of defense mechanisms, resulting in redness, swelling, heat and pain. The study compound that will be researched in this study, CKD-506, inhibits a protein (HDAC6) that is involved in abnormal immune responses seen in this type of conditions. This is the first time that CKD-506 is being given to humans.

Study objective

The purpose of the study is to investigate how safe CKD-506 is and how well CKD-506 is tolerated (all study parts). It will also be investigated how quickly and to what extent CKD-506 is absorbed by and eliminated from the body (this is called pharmacokinetics) (all study parts). Further, the effect of food on CKD-506 pharmacokinetics will be investigated (FE part only). In addition, the effect of the compound on certain proteins in your blood will be investigated (this is called pharmacodynamics) (all study parts).

Study design

SAD Part: (Groups 1, 2, 3, 5 and 6):
The study will consist of 1 period during which the volunteer will stay in the clinical research center for 4 days (3 nights).
The volunteer will receive a single dose of CKD-506 or placebo as oral capsules on Day 1 with 340 milliliters of water.

SAD + FE Part: (Group 4):
The study will consist of 2 periods during which the volunteer will stay in the clinical research center for 4 days (3 nights) each period.
The volunteer will receive a single dose of CKD-506 or placebo as oral capsules on Day 1 with 340 milliliters of water.

MAD Part: (Groups 7, 8 en 9):
The actual study will consist of 1 period during which the volunteer will stay in the clinical research center for 17 days (16 nights).
On Days 1 to 14, every day the volunteer will receive a dose of CKD-506 or placebo as oral capsules with 340 milliliters of water.

Intervention

Groups 1, 2, 3, 4 (only the first period), 5 and 6:
The SAD part of the study will consist of 1 study period (except for Group 4, see below) during which you will receive either CKD-506 or placebo once under fasted conditions. CKD-506 and placebo will be given in the form of oral capsules.

Group 4 (only the second period):
When the volunteer is participating in Group 4, he/she are also participating in the FE study part and will therefore participate in 2 study periods. In the first period the volunteer will receive CKD-506 or placebo under fasted conditions, whereas in the second period the volunteer will receive CKD-506 or placebo after a breakfast. When the volunteer receives CKD-506 in the first period, he/she will also receive CKD-506 in the second period. Likewise, when the volunteer receives placebo in the first period, he/she will also receive placebo in the second period.

Groups 7, 8 and 9:
The MAD part of the study will consist of 1 study period during which the volunteer will receive either CKD-506 or placebo once every day for a period of 14 days. CKD-506 and placebo will be given in the form of oral capsules.

Study burden and risks

All potential drugs cause adverse effects; the extent to which this occurs differs. As CKD-506 will be administered to man for the first time in this study, adverse effects of CKD-506 in man have not been reported to date.

Animal studies have previously been conducted with CKD-506. Myelosuppression was observed in monkeys that received CKD-506 at a very high dose of 70 milligrams per kilogram body weight per day every day for 4 weeks. Myelosuppression means that bone marrow activity is decreased, which results in decreased numbers of red and white blood cells and platelets. Lymphoid atrophy

(decrease of thymus weight and lymph follicles of the spleen and mesenteric lymph nodes) was also observed in monkeys at the same dose of CKD-506. Further, decreased values were seen in blood for total cholesterol, high-density lipoprotein, low-density lipoprotein, protein and albumin. Also the coagulation parameter activated partial thromboplastin time was prolonged; this may result in bleeding.

With very high doses of 200 milligrams CKD-506 per kilogram body weight per day every day for 4 weeks in rats, also myelosuppression was observed. Further, anemia, lymphoid atrophy, degeneration and decrease in immature sperm cells, decreased protein in blood, and decreased body weight gain and food consumption was observed at this CKD-506 dose level in rats.

In animals, no effects were observed on the respiratory system or central nervous system (up to 1000 milligrams CKD-506 per kilogram per day in rats), or the cardiovascular system (up to 200 milligrams CKD-506 per kilogram per day in monkeys.

Clinical studies have been conducted with other compounds that inhibit the same family of proteins (HDAC proteins). These studies show that these compounds are well tolerated. The side effects observed were nausea, vomiting and fatigue. Also, transient and reversible low levels of platelets and neutrophils (a type of white blood cell) were noted as well as anemia, and changes in liver enzymes.

Clinical studies have also been conducted with Ricolinostat, which is a HDAC6 inhibitor, similar to CKD-506. The most common side effects were mild cases of fatigue, diarrhea and low levels of neutrophils.

Procedures: pain, minor bleeding, possible infection

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

healthy male or female volunteers, IBD patients
18-55 years, inclusive
BMI: 18.0-32.0 kg/m2, inclusive
non-smoking

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating or losing more than 100 milliliters of blood in the 60 days prior the start of this study.

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):	01-09-2016
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO Date:	28-07-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-09-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-02-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-03-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-07-2017
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	EUCTR2016-002816-42-NL
CCMO	NL58682.056.16