SINGLE-CENTER, OPEN-LABEL, RANDOMIZED, TWO-PARTS, TWO-WAY CROSSOVER STUDY TO INVESTIGATE THE EFFECTS ON HEART RATE, BLOOD PRESSURE, AND PHARMACOKINETIC INTERACTIONS OF ACT-128800 COMBINED WITH A CALCIUM-CHANNEL BLOCKER OR A BETA-BLOCKER IN HEALTHY SUBJECTS

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Primary:to investigate the effects on heart rate (HR) and rhythm of concomitant administration of the study drug with a calcium-channel blocker (CCB) or a beta-blocker (BB)Secondary:- to investigate the effects on blood pressure (BP) of concomitant...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON36345

Source
ToetsingOnline

Brief title
ACT-128800 DDI study

Condition

- Immune disorders NEC

Synonym
Immune disease

Research involving
Human

Sponsors and support

Primary sponsor: Actelion Pharmaceuticals
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: ACT-128800, immune diseases

Outcome measures

Primary outcome

Cardiodynamics (telemetry)

Pharmacokinetics

Safety

Secondary outcome

n.a.

Study description

Background summary

The drug to be given is a new, investigational compound that may eventually be used for the treatment of immune diseases. The study drug blocks the egress of lymphocytes from lymphoid organs and reduces the availability of circulating effector T-cells that can invade target organs and cause immune diseases.
This new compound is not registered as a drug but has been given to humans before.
In addition also atenolol (beta-blocker) or diltiazem (calcium-channel blocker)

will be given. These are registered drugs which are used for the treatment of hart-related diseases.
Atenolol is used for the treatment of high blood pressure, angina pectoris (pain on the chest) and for early intervention at suspicion of acute heart attack. Diltiazem is used for the treatment of angina pectoris and high blood pressure.

Study objective

Primary:
to investigate the effects on heart rate (HR) and rhythm of concomitant administration of the study drug with a calcium-channel blocker (CCB) or a beta-blocker (BB)

Secondary:
- to investigate the effects on blood pressure (BP) of concomitant administration of the study drug with a CCB or a BB
- to evaluate the safety and tolerability of concomitant administration of the study drug with a CCB or a BB
- to evaluate the effects of a CCB or a BB on the pharmacokinetics (PK) of the study drug
- to evaluate the effects of the study drug on the PK of a CCB or a BB

Study design

Design:
a randomized, open-label, two-part, two-period, two-way crossover study consisting of two groups of twelve healthy subjects, groups receive either CCB or BB treatment for six days followed by a single oral dose of the study drug in one period (design A1 and B1) and a single oral dose of the study drug in the other period (design A2 and B2) (at least 30% of each sex for each treatment), a wash-out of 7-10 Days between dosing; treatment scheme Part A: sequence 1: A1 A2, sequence 2: A2 A1, Part B: sequence 1: B1 B2, sequence 2: B2 B1

Procedures and assessments:
Screening and follow up:
clinical laboratory, physical examination, vital signs, ECG; at eligibility screening: medical history, drug screen, HBsAg, anti HCV, anti-HIV 1/2 and pregnancy test (females only); to be repeated upon each admission: vital signs, ECG, clinical laboratory, drug screen, pregnancy test (females only);
follow-up phone call to check on adverse events: 7 and 30 days after last study drug administration

Observation period:
one period in clinic from -18 h up to 24 h after drug administration on Day 6

(design A1 and B1)
one period in clinic from -18 h up to 24 h after drug administration on Day 1 (design A2 and B2)

Blood samples:
design A1 and B1:
for pharmacokinetics of atenolol or diltiazem: 24, 48, 72, 96, 97, 98, 99, 100, 101, 102, 103, 104, 106, 108, 110, 120, 121, 122, 123, 124, 125, 126, 127, 128, 130, 132, 134 and 144 h post-dose on Day 1
for pharmacokinetics of the study drug: pre-dose and 1, 2, 3, 4, 6, 10, 14 and 24 h post-dose on Day 6
design A2 and B2:
for pharmacokinetics of the study drug: pre-dose and 1, 2, 3, 4, 6, 10, 14 and 24 h post-dose

Telemetry
design A1 and B1:
interval from 96 * 108 and 120 - 132 h post dose on Day 1
design A2 and B2:
interval from pre-dose - 12 h post dose on Day 1

Safety assessments
design A1 and B1:
adverse events: throughout the study; vital signs and ECG: pre-dose and 1, 2, 3, 4, 24, 48, 72, 96, 97, 98, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, 110, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 134 and 144 h post-dose on Day 1; physical examination: at discharge; clinical laboratory: pre-dose and 96, 120 and 144(incl. pregnancy test (females only)) h post dose on Day 1
design A2 and B2:
adverse events: throughout the study; vital signs and ECG: pre-dose and 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14 and 24 h post dose; physical examination: at discharge; clinical laboratory: pre-dose and 1 and 24(incl. pregnancy test (females only)) h post dose

Bioanalysis:
analysis of plasma atenolol samples using a validated method by PRA
analysis of plasma diltiazem samples using a validated method by PRA
analysis of plasma study drug samples using a validated method by Sponsor

Intervention

Active substance: ACT-128800, atenolol, diltiazem extended release

Study burden and risks

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

Contacts

Public
Actelion Pharmaceuticals

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CH
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Actelion Pharmaceuticals

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Age: 18-60 years, inclusive (at screening)
BMI: 18.0-30.0 kg/m2, inclusive;Women of childbearing potential must:
- have a negative serum pregnancy test at screening and prior to first drug intake;
- agree to use two methods of contraception from the screening visit until 2 months after study drug discontinuation.;Systolic blood pressure 100*150 mmHg, diastolic blood pressure 50*90 mmHg measured on the right arm, and HR 55*95 bpm (inclusive)

Exclusion criteria

- Pregnant or lactating woman.
- Known hypersensitivity to any excipients of the study drug formulation
- Known hypersensitivity to atenolol or diltiazem or any of their excipients
- Veins unsuitable for i.v. puncture on either arm
- Treatment with another investigational drug within 3 months prior to screening.
- Excessive caffeine consumption, defined as > 800 mg per day at screening.
- Smoking or nicotine replacement therapy within the last month prior to screening.
- Any immunosuppressive treatment within 6 weeks before study drug administration.
- Previous treatment with any prescribed or over-the-counter medications (including herbal medicines such as St John*s Wort) within 2 weeks prior to screening or 5 half-lives of the drug, whichever is longer (except for contraceptives).
- Loss of 250 mL or more of blood within 3 months prior to screening.
- Positive hepatitis B surface antigen or hepatitis C antibody tests or positive results for HIV serology, at screening
- Any circumstances or conditions, which, in the opinion of the investigator, may affect the subject*s full participation in the study or compliance with the protocol.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-03-2011
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Atenolol Sandoz 50
Generic name:	Atenolol
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Cardizem LA
Generic name:	Diltiazem
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	28-01-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-02-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-04-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-04-2011
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	EUCTR2010-023248-33-NL
CCMO	NL35329.056.11