An open-label extension study of CACZ885H2357E1 on the treatment and prevention of gout flares in patients with frequent flares for whom NSAIDs and/ or colchicine are contraindicated, not tolerated or ineffective

Published: 28-07-2010
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Primary: Long term safety and tolerability.Secondary: Time to 1st flare, number and severity of flares, efficiacy in treating flares, effect on inflammatory markers, immunogenicity, PK.

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

Summary

ID

NL-OMON34238

Source
ToetsingOnline

Brief title
H2357E2

Condition

- Joint disorders

Synonym
Gout

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: acute gout, canakinumab

Outcome measures

Primary outcome

Adverse effects.

Secondary outcome

Time to 1st flare, number and severity of flares, efficiacy in treating flares,

effect on inflammatory markers, immunogenicity, PK.

Study description

Background summary

Gout is the most common form of inflammatory joint disease in men over the age of 40 years . It is estimated to affect 0.5-2.8% of men, with a lower rate of occurrence among women, who experience gout, primarily, after menopause. The most common clinical finding in these patients is a sudden onset of an acute gout flare (also referred to as acute gout attack), which is a severe arthritis (monoarticular/ oligoarticular/ polyarticular) in any joints in the body, predominantly seen in a peripheral joint in the leg.
Several lines of evidence suggest that gout inflammation is primarily IL-1β driven and therefore, inflammation in gout may be significantly attenuated with a selective blockade of IL-1β. In line with this, anakinra, an IL-1 receptor antagonist, significantly relieved the pain of acute gout flares in patients who could not tolerate or had failed standard anti-inflammatory therapies for gouty arthritis. Moreover, rilonacept (IL-1 trap), an IL-1 inhibitor decreased the disease activity and pain in patients with chronic active gout and also reduced the occurrence of new gout flares that are often seen during initiation of urate-lowering therapy.
Canakinumab (ACZ885) is a fully human monoclonal anti-human IL-1β antibody. It is designed to bind to human IL-1β and thus blocks the interaction of this cytokine with its receptors. This results in neutralized bioactivity of IL-1β,

but does not prevent the binding of the natural inhibitor, IL-1Ra, nor binding to IL-1α. Detailed background information on the chemistry, pharmacology, toxicology, preclinical and clinical data of canakinumab is also given in the Investigator*s Brochure. Results of a single-dose, 8-week Phase II study (CACZ885H2255) in gout patients that were refractory and/ or contraindicated to NSAIDs and/ or colchicine indicated that canakinumab at the selected dose of 150 mg subcutaneously (s.c.) was more effective in treating patient*s pain at the time of acute gout flares and also in preventing the occurrence of new gout flares as compared to triamcinolone acetonide 40 mg intramuscularly (i.m.). This is the 2nd follow-up study (open label, non-comparative), open to patients who have completed the study CACZ885H2357 (canakinumab vs triamcinolon acetonide, 12 weeks) and the 1st follow-up study (CACZ885H2357E1).

Study objective

Primary: Long term safety and tolerability.
Secondary: Time to 1st flare, number and severity of flares, efficiacy in treating flares, effect on inflammatory markers, immunogenicity, PK.

Study design

Multicenter open label, non-comparative phase III study.
Patients who have successfully completed the preceding studies CACZ885H2357 and CACZ885H2357E1 of who have experienced too many flares in the preceding study may participate. In case of a new flare, they will be treated with a single dose of canakinumab 150 mg subcutaneously.
Study duration 1 year.
Pain killer to be used if needed: paracetamolmol (max. 3 g daily) or codeïne (max. 180 mg daily) , s.n. prednisolon.
150-200 patients.

Intervention

Treatment with canakinumab in case of gout flare.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: 4 visits in 1 year (NB 1st visit = last visit of preceding study).
All visits: fasting, blood tests (approx 20 ml/visit, total volume: 85 ml) and questionnaires (VAS, Likert scale, global evaluation, gout questionnaire, EQ-5D, HAQ-DI or SF-36, work-productivity questionnaire); estimated completion time 15-20 minutes per visit. In case of flare and study drug administration 7 visits in 3 months and 80 mls of blood extra.
In addition: Physical examination (4x), ECG (2x), pregnancy test (2x), diary (use of pain killers, symptoms).

In selected centres: Doppler examination joints (4x).

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

• Successful completion of preceding study CACZ885H2357E1 or 9 flares during that study.

Exclusion criteria

• Pregnancy and lactation.
• No contraception or insufficiently safe contraception method (women of childbearing potential)

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	10-11-2010
Enrollment:	1
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	28-07-2010
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

Approved WMO

Date:	09-08-2010
Application type:	First submission
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

Approved WMO Date:	31-08-2010
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	28-01-2011
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	24-02-2011
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	31-05-2011
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)
Approved WMO Date:	14-06-2011
Application type:	Amendment
Review commission:	RTPO, Regionale Toetsingscie Patientgebonden Onderzoek (Leeuwarden)

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
Other	clinicaltrials.gov, regsitratienummer n.n.b.
EudraCT	EUCTR2010-020060-38-NL
CCMO	NL33130.099.10