A 12 month, open label, parallel-cohort study to evaluate the efficacy, safety and tolerability of canakinumab in children with Kawasaki disease

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The objective of this study is:1. To evaluate the efficacy, safety and the tolerance of Canakinumab in 'IVIG-resistent' patients (cohort 1) and 'IVIG-naive' patients (cohort 2) with Kawasaki disease.2. To evaluate the incidence...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON52448

Source
ToetsingOnline

Brief title
Kawakinumab study

Condition

- Coronary artery disorders
- Aneurysms and artery dissections

Synonym
Acute vasculitis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Fonds Kind & Handicap, voorheen Stinafo (Stichting Nationaal Fonds "Het Gehandicapte Kind"),Fonds Kind & Handicap;voorheen Stinafo

Intervention

Keyword: Canakinumab, IVIG, Kawasaki disease, Pediatric patients

Outcome measures

Primary outcome

Determine how many patients will be fever-free after administration of

Canakinumab, in which fever-free is defined as a body temperature of <37.5

degrees Celsius after 48 hours.

Secondary outcome

1. Determine how many patients develop coronary artery aneurysms in week 6-8

and at 6 and 12 months after administration of the therapy.

2. The location, number of coronary artery aneurysms (CAA) and diameter.

3. Follow the development of CAA over time with echocardiography.

Study description

Background summary

Kawasaki disease (KD) is an IL-1 driven, acute febrile illness and systemic vasculitis predominantly affecting children younger than 5 years old. The disease clinically presents as acute systemic inflammation characterized by fever and bilateral non-exudative conjunctivitis, erythema of the lips and oral mucosa, edema of palms and soles often with sheet-like desquamation, rash, and cervical lymphadenopathy. Coronary arteries are especially susceptible to inflammatory cell infiltration and structural damage which results in coronary artery aneurysms (CAA) in about 15-25% of untreated KD (Kato, 1996).

These CAA*s -depending on the luminal diameter- have the tendency to continue

to exist and can lead to severe damage in time. Patients who had KD in childhood have an increased risk for myocardial infarction, arrhythmias and sudden death during adolescence and early adulthood. This increased risk is caused by coronary artery damage due to the formation of thrombosis in such an aneurysm and the long term effects of the inflammation such as plaque and arterial thickening which can cause obstruction of the normal blood flow.

The first choice of therapy for children with KD is a single infusion with intravenous immunoglobulins (IVIG); sometimes followed by a second administration of IVIG in the case of persistent fever. Whenever this second infusion with IVIG does not give the desired effect, immunomodulators can be chosen to treat KD patients resistant to IVIG (high dose corticosteroids, infliximab, methotrexate or cyclophosphamide).

In this research the drug Canakinumab is being researched. Canakinumab is an anti-human interleukin-1β (IL-1β) antibody and is registered by the Dutch government for the treatment of a.o. systemic juvenile idiopathic arthritis (sJIA), however Canakinumab is not registered as a treatment for KD, for this research is necessary.

Canakinumab has already shown to be effective in treating pediatric and adult patients with inherited auto-inflammatory conditions presumably derived from overproduction of IL-1-beta. We assume that overproduction of IL-1β is a key factor in KD. By inhibition of IL-1β we would combat the inflammatory response. With this research we want to investigate whether Canakinumab can also combat the acute symptoms of KD.

Study objective

The objective of this study is:
1. To evaluate the efficacy, safety and the tolerance of Canakinumab in 'IVIG-resistent' patients (cohort 1) and 'IVIG-naive' patients (cohort 2) with Kawasaki disease.

2. To evaluate the incidence of coronary aneurysms after administration of Canakinumab

Study design

Open label, monocenter, prospective intervention study

Intervention

Canakinumab will be administered once intraveneously (6 mg/kg)

Study burden and risks

The risk for side effects due to Canakinumab and the inconveniences of the procedures of the investigation (E9).

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Written informed consent, must be obtained by the legal guardian(s)
Female / male patients < 12 years
Active Kawasaki disease defined as:
1. fever >= 38.5°C for 4 days
2. four out of five of the following clinical crtiteria: (i) conjuctival infection, (ii) oral muscous membrane changes, (e.g. infected pharynx or strawberry tongue), (iii) erythema of hands or feet, (iv)polymorphous rash, (v) cervical lymphadenopathy
OR

IVIG-nonresponsiveness, defined as persistent fever 48 hours after IVIG

Exclusion criteria

a. Fever for 8 days or longer for IVIG-naive patients (cohort 2)
b. Treatment with biologicals (e.g. Anakinra, Etanercept, Infliximab, Tocilizumab, Adalimumab)
c. Every other study medication given 30 days prior to inclusion
d. Immunosuppressive drugs given within 3 months prior to inclusion
e. Known history of allergy to biologicals
f. Significant abnormalities on ECG, or symptoms compatible with myocaridal ischemia or infarction
which may jeopardize the participation to this study.
g. Every other decision of the prjnciple investigator regarding safety or otherwise that will preclude
inclusion.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-07-2022
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ilaris

Generic name:	Canakinumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	15-08-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-03-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-08-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-02-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-05-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2019-002783-27-NL
CCMO	NL68717.018.19