The Anti-Interleukin-1 in Diabetes Action trial

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The aim of the Anti-Interleukin-1 in Diabetes Action trial (AIDA) study is to test the feasibility, safety/tolerability and potential efficacy of anti-IL-1 therapy in maintaining or enhancing beta-cell function in people with new-onset Type 1...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON32562

Source
ToetsingOnline

Brief title
AIDA

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
type 1 diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Steno Diabetes Center
Source(s) of monetary or material Support: AMGEN,JDRF (internationaal diabetes fonds)

Intervention

Keyword: Anakinra, Interleukin-1, Type 1 diabetes

Outcome measures

Primary outcome

The primary endpoint is beta-cell function assessed as C-peptide response to a standardized 2-h mixed-meal test.

Secondary outcome

Secondary endpoints include insulin requirement, percent insulin-free remission, and 2h glucose levels after the mixed meal test.

Study description

Background summary

The aim of the Anti-Interleukin-1 in Diabetes Action trial (AIDA) study is to test the feasibility, safety/tolerability and potential efficacy of anti-IL-1 therapy in maintaining or enhancing beta-cell function in people with new-onset Type 1 diabetes.

The hypothesis is that anti-IL-1 treatment as add-on therapy to conventional insulin therapy will preserve or enhance beta-cell function assessed as the 2 h-area under the curve (AUC) for C-peptide in response to standard mixed meal. For 20 years it has been recognized that the pro-inflammatory cytokine interleukin-1 is selec-tively cytotoxic to rodent and human beta-cells in vitro and anti-IL-1 therapies reduce diabetes incidence in animal prevention models. The following observations can be highlighted: 1) IL-1 alone or in combination with other inflammatory cytokines causes beta-cell destruction in rodent and human islets and in perfused pancreas via the MAPK and NFkB signalling pathways, 2) IL-1 given i.p. to non-diabetes prone animals causes transient insulinopenic diabetes 3) IL-1 is expressed early in NOD islets 4) anti-IL-1 intervention prevents diabetes development in models of Type 1 diabetes and islet graft destruction and 5) transgenic mice with knock-out of the IL-1 receptor reduces diabetes incidence by 30%. We recently reported that 13 w of IL-1 receptor antagonist therapy improved glycaemia and beta-cell function in Type 2 diabetes, a disorder in which glucose-induced beta-cell apoptosis may be

IL-1 dependent and the intervention is safe.

Study objective

The aim of the Anti-Interleukin-1 in Diabetes Action trial (AIDA) study is to test the feasibility, safety/tolerability and potential efficacy of anti-IL-1 therapy in maintaining or enhancing beta-cell function in people with new-onset Type 1 diabetes.

Study design

A randomized, placebo-controlled, double-masked, parallel-group, multi-centre trial of IL-1 antagonism in subjects with newly-diagnosed Type 1 diabetes. Patients are instructed to inject 100 mg human recombinant interleukin-1 receptor antagonist (anakinra, Kineret®, Amgen, CA) or placebo s.c. once daily for 2 years. Endpoints will be evaluated every three months, with an interim analysis after 6 months.

Intervention

The patients are instructed to administer anti-IL-1 therapy in the form of recombinant human non-glycosylated interleukin-1 receptor antagonist (anakinra) at a dose of 100 mg once daily or placebo by subcutaneous injection at the same time-point in the morning. There will be a mixed meal test at every hospital visit.

Study burden and risks

During the trial period the patient will visit the hospital six times. This will take approximately 3-4 hours. During the first visit the studie docter will take a history and a physical exam. We also take blood and do an urineanalysis. Hereafter a ECG and a fundusphoto will be performed. This all is to exclude any unknown diseases or diabetic complications. Then there will be a mixed meal test. The next visits there will be a short history taken and a physical exam. Also shall there be blood withdrawn and a mixed meal test. After the first return visit the patient will start using the studie medication. The patient has to inject the studiemedication s.c. every day at the same timepoint.

We think the burden on the patient will be relatively mild because the patient only has to come to hospital for six times in nine months. Also will the use of the studie medication in this group of patients not be a heavy burden because of they have to do a subcutanous injection a few times a day with their insulin therapy.

Anakinra has been shown to be a drug with few side effects. The adverse effects

of anti-IL-1 therapy have been reversible upon withdrawal.

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

Type 1 diabetes diagnosis <12 weeks
positive GAD antibodies
18-35 years old

Exclusion criteria

Severe liver or renal disease (creatinine > 100 µmol/L, ASAT/ALAT > 2* ULN, alkaline

phosphatase > 2 * ULN)
History of heart disease, signs of cardiac failure or abnormal ECG
Present or previous malignancy
Pregnancy or failure of fertile female to comply with contraceptional planning, or breast-feeding. (Safe contraceptive methods include birth control pills, IUD, and gestagen implants) .
Plans of pregnancy within 2 years.
Participation in other clinical intervention studies
Anti-inflammatory therapy (except aspirin £ 100 mg/d)
Active infections (CRP>30), history of recurrent infection or predisposition to infections
Neutropenia: ANC < 1.5*109/L, or anaemia: Haemoglobin < 8.0 g/dL
Immune-suppressive treatment or immune-deficiency
Presence at diagnosis of late diabetic complications
Concurrent vaccination with live vaccine. Known need for live vaccinations within 2 years.
Use of Etanercept within 6 months before screening or during the double-blinded study period
Hypersensitivity to E. coli-derived proteins, anakinra or any components of the product.

Study design

Design

Study phase:	2
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):	09-03-2009
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	kineret
Generic name:	anakinra
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	30-09-2008
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	13-10-2008
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2007-007146-34-NL
CCMO	NL23927.058.08