ISRCTN17354692 https://doi.org/10.1186/ISRCTN17354692

Secondary prevention of type 1 diabetes in children and adolescents aged 6 months - 18 years using oral Vitamin D (calcitriol and analogues)

Submission date
29/03/2020

Recruitment status
Recruiting

Registration date
05/05/2020

Overall study status
Ongoing

Last Edited
30/05/2023

Condition category
Nutritional, Metabolic, Endocrine

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Many people have blood sugar levels above the normal range, but not high enough to be diagnosed as having diabetes. This is sometimes known as pre-diabetes.
Celiac disease is a condition where the immune system attacks the body's own tissues when gluten is eaten.
Type 1 diabetes and celiac disease among with other autoimmune diseases may be prevented or regressed using the active hormone calcitriol or it's newer analogs.
Calcitriol is the active form of vitamin D, normally made in the kidney.
The aim of this study is to prove immunomodulating effects of timely administration of calcitriol and analogs for preventing, stopping progression, or succeeding in regression of prediabetes or subclinical Type-1 diabetes in children and adolescents.

Who can participate?
Patients aged six months to 18 years who have been identified as susceptible for type 1 diabetes or celiac disease.

What does the study involve?
Patients are assigned to oral calcitriol or paricalcitol at the highest individually tolerable doses and attend follow-up appointments every 3 - 6 months.

What are the possible benefits and risks of participating?
The main benefit will be to stop and revert seroconversion towards T1D-associated autoimmune targets, restore normal glucose metabolism and possibly acquire positive results regarding abs for celiac disease and hashimoto's thyroiditis as well.
The main risk is hypercalcemia-hypercalciuria and subsequent possible nephrocalcinosis. That is why all calcium metabolism parameters are carefully monitored with analogous titration of calcitriol/paricalcitol daily doses to prevent any adverse events.

Where is the study run from?
Pediatric Endocrine Clinics (Greece)

When is the study starting and how long is it expected to run for?
June 2010 to January 2030

Who is funding the study?
Pediatric Endocrine Clinics (Greece)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
9/2010

Study information

Scientific Title
Secondary PREvention of type 1 diabetes with oral CALcitriol and analogues in children and adolescents aged 6 months - 18 yrs

Acronym

PRECAL

Study objectives
The aim of this study is to prove immunomodulating effects of timely administration of calcitriol and analogs for preventing, stopping progression, or succeeding in regression of prediabetes or subclinical Type-1 diabetes in children and adolescents.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 05/01/2010, Athens Medical Center Ethics Committee (Pr. Andreas Fretzayas, Kifisias 58, 15125, Athens Medical Center, Greece, +302106862172, a.fretzayas@iatrikonet.gr), ref: 9 /2010

Study design
Interventional non-randomized

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Susceptibility for Type 1 Diabetes, Prediabetes Type 1, Newly diagnosed (subclinical) Type 1 Diabetes

Interventions
In all children aged six months - 18 yrs either at high risk of T1D (at least 1 positive T1D associated autoantibody: IAA, ICA, anti-GAD, anti-IA2) or a predisposing HLA subtype (A, DQ, DR) or diagnosed as prediabetic with an OGTT (using 1.75 gr/Kg oral glucose) showing glucose intolerance (Plasma Glucose > 140 mg/dl at 2hrs in the OGTT) in addition to the above criteria, or as having newly onset subclinical T1D with positive autoantobody(ies) and/or proven HLA susceptibility plus documented pathological OGTT (Glucose > 200 mg/dl at 2hrs) are initiated on oral calcitriol (0.25 mcg x1 up to 0.5 mcg x 3/day) or paricalcitol (1 mcg x 1 up to 24 mcg x 3 /day), as recommended, or MART-10 (when available and at the equivalent dose) while assuring optimal daily cholecalciferol supplementation to achieve 25OHD3 levels > 40-50 ng/ml.
Follow-up is every 3-6 months with Calcium metabolism: determination of Ca, P, parathyroid hormone (PTH), alkaline phosphatase (ALP) and total 25(OH)D3 levels, as well as the Ca /creatinine (Cr) ratio in a 2-h morning urine sample, Fasting Plasma Glucose, Insulin and c-peptide as well as HbA1c levels.
Individualisation of the highest safe dose of calcitriol/calcitriol analogue accepting a Ca plasma level as high as 11.5 mg/dl and a Ca/Cr 2-hour urine sample as high as 50%. Renal Ultrasound at those with hypercalciuria mandatory every six months. If negativation of auto-abs and regression of prediabetes is achieved, follow-up is extended every 6-12 months with a minimum of 1 year after the achievement of the primary endpoint.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Calcitriol, paricalcitol, MART-10

Primary outcome(s)
Measured at follow up every 3 - 6 months from entry into the study until end of study:
1. Type 1 Diabetes associated autoantibodies [Serum levels of islet cell autoantibodies (ICA), autoantibodies to glutamic acid decarboxylase (Gad 65) antigen (anti-GAD65), anti-insulin autoantibodies (IAA), and autoantibodies against protein tyrosine phosphatase IA2 (anti-IA2)] measured using ELISA kits
2. Glucose metabolism (HbA1c, Fasting Glucose, Insulin and c-peptide levels) measured using urine test
3. OGTT response measured using oral glucose tolerance test

Key secondary outcome(s))
Title and prevention or regression of celiac disease autoantibodies, thyroid autoantibodies and other autoimmune diseases if known and applicable measured using ELISA kits at follow up every 3 - 6 months from entry into the study until end of study

Completion date
31/12/2030

Eligibility

Key inclusion criteria
1. Age six months - 18 years
2. Positive HLA subtypes for T1D susceptibility
3. At least one positive T1D associated autoantibody
4. Positive HLA or autoantibodies for celiac disease

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
6 months

Upper age limit
18 years

Sex
All

Key exclusion criteria
Already clinically treated T1D on intensified insulin protocols

Date of first enrolment
01/06/2010

Date of final enrolment
01/01/2030

Locations

Countries of recruitment
Cyprus

Greece

Study participating centre
Pediatric Endocrine Clinics
58, Kifisias av
Athens
Greece
15125

Sponsor information

Organisation
Pediatric Endocrine Clinics

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Pediatric Endocrine Clinics

Results and Publications

Individual participant data (IPD) sharing plan

All data generated or analysed during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/09/2013	30/03/2020	Yes	No
Results article		11/05/2023	30/05/2023	Yes	No