Biomarkers of heterogeneity in type 1 diabetes: an integrated approach to clinical and metabolic phenotyping of individuals with established Type 1 diabetes

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

Summary

ID

NL-OMON47436

Source
ToetsingOnline

Brief title
Biomarkers in type 1 diabetes

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
insulin-dependent diabetes, type 1 diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Diabeter
Source(s) of monetary or material Support: JDRF Juvenile Diabetes Research Fund;New York USA

Intervention

Keyword: biomarkers, heterogeneity, precision medicine, type 1 diabetes

Outcome measures

Primary outcome

This biomarker research project intends to gain insight in the heterogeneity of

type 1 diabetes en and to gather knowledge on the cause, development and

treatment of the disease.

Secondary outcome

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Study description

Background summary

Type 1 diabetes is an autoimmune disease which is far more heterogeneous than previously assumed. This could explain why intervention studies aimed at inhibiting or curing the disease, have only had limited success. In intervention studies at the onset of the disease, patients of different ages and with different pathophysiological parameters are still combined in a study group, despite clear differences in the severity of clinical symptoms, levels of auto-immune markers, the severity of metabolic disturbance at onset, HbAc1 (high vs. low, reflecting a long vs. short preclinical phase), etc.. Although these studies did not show any overall benefit, beneficial effects could often be observed in subgroups of patients. For new studies, therefore, it is important to map the heterogeneity of type 1 diabetes. By a better staging and selection of patients, new, personalized therapies can be developed in the future. Previous studies showed examples of these heterogeneity in newly diagnosed type 1 diabetes patients, both in clinical and immunological parameters. These studies also showed an important role for hormones, such as glucagon, GLP-1 and pro-insulin, in influencing the duration of the remission

phase.
Through biomarker research, we want to study differences in hormonal, immune/inflammatory markers, metabolic markers and (epi)genetic factors in patients with long-standing (at least 5 years of) diabetes. In both participating centers, the UMCG and Diabeter, extensive clinical data on the entire treatment period of the patients are available. By this integrated approach of clinical and metabolic phenotyping, we want to gain insight in the clinical heterogeneity of type 1 diabetes.

Study objective

The aim of project is to map the heterogeneity of type 1 diabetes by identifying existing and new biomarkers. To this end, a group of 600 patients with at least 5 years of type 1 diabetes will be followed for a period of 3 years. By identifying clinically relevant biomarkers, the current staging and phenotyping of patients can be improved and clinical heterogeneity between groups of patients and the respective alterations during longstanding T1D can be compared. This is essential for successful intervention studies in the future and the development of new therapies, both for treatments that aim at reducing beta cell damage, and for treatments that focus on the improvement of glycemic control, reduction of complications and improvement of clinical outcome.

Study design

The study consists of the following parts:
1. Longitudinal and cross-sectional biomarker research on the heterogeneity of type 1 diabetes, which will be carried out for the next 3 years in 600 patients (minimum age 16 years) with at least 5 years of type 1 diabetes. The project focuses on hormonal, immune/inflammatory and metabolic markers.
2. Detailed test: Mixed Meal Tolerance Test (twice in 3 years) in a subgroup of 150 patients: 75 with a short diabetes duration (<15 years) and 75 with a long diabetes duration (>15 years). With this test, glucosemanagement (insuline, glucagon, GLP-1 etc.) can be measured and it can accurately be assessed whether somebody is capable of naturally producing insulin (again).

Study burden and risks

1. Blood sampling (combined with regular blood drawing for the standard yearly visit). Limited risk of pain, bruise. The volume taken is limited (114 ml in 3 years) and does not cause problems in (young) adults.
2. MMTT: same as for blood sampling. The insertion of an IV-line is not a risky procedure. Having the needle taped to the arm for 2,5 hours can be of minor discomfort to the patient. Also, being in a fasting state (from 12:00 midnight on the night before the test) can be uncomfortable. The raising blood glucose level after ingestion of the mixed meal might cause some discomfort in some

patients. The total amount of blood drawn for the MMTT is within reasonable limits (90 ml) and does not cause any problems.
3. The storage of data and body material (also including DNA) for future research can be considered as a potential risk. However, with the existing technical possibilities of protecting storage of data and body material, we consider this risk as minimal, especially since prof. Wolffenbuttel UMCG is involved in the *String-of-pearls initiative* (PSI) and LifeLines. The guidelines of the PSI and Lifelines will be followed to garantee confidential handling and responsible use of the data/body material.

Contacts

Public
Diabeter

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Scientific
Diabeter

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NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Type 1 diabetes determined by either autoantibodies or based on clinical and historical data, or both
2. At least 5 years of type 1 diabetes
3. Minimum age 16 years
4. Treated for type 1 diabetes at a diabetes center
5. Given informed consent by subject

Exclusion criteria

1. Non-type 1 diabetes
2. Patients with duration of type 1 diabetes below 5 years
3. Patients under the age of 16 years
4. Pregnancy or breastfeeding, until 3 months (12 weeks) after childbirth or breastfeeding
5. On experimental medication or participating in other studies with conflicting goals and schedules
6. Diseases or conditions that the investigator/physician believes to be a contraindication to participate
7. Unwilling to be informed on incidental findings

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-06-2016
Enrollment:	600

Type:	Actual

Ethics review

Approved WMO Date:	24-03-2016
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-08-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-01-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-07-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
CCMO	NL50314.042.15