Primary Immunodeficiencies: immunological and genetic background in relation to clinical complications

Published: 19-06-2013
Last updated: 01-05-2024

Project aims1. To provide a more precise overview of prevalence, presenting symptoms, referral routes, clinical complications and evolution during follow-up of PIDs in The Netherlands by registration and analysis of prospective patient data derived...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Immunodeficiency syndromes
Study type	Observational invasive

Summary

ID

NL-OMON55725

Source
ToetsingOnline

Brief title
Research into causes and disease course of primary immunodeficiencies

Condition

- Immunodeficiency syndromes
- Mood disorders and disturbances NEC

Synonym
immune disorders, primary immune deficiencies

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: VIDI grant M van der

Burg;ErasmusMC,Baxter,Zie onderzoeks protocol: "subsidising party"

Intervention

Keyword: Follow up, Genetics, Pathogenesis, Primary Immunodeficiency

Outcome measures

Primary outcome

Ad 1. prospective follow up study.

- Survival data

- Occurrence of complications, predominantly in the pulmonary, gastro

intestinal, hematological tracts, as well as the occurrence of malignancies

- These data will be related to clinical and laboratory phenotype

Ad 2. improved diagnostics.

- Genetic and associated functional defects causative of primary

immunodeficiencies.

Secondary outcome

Ad 1. prospective follow up study.

- Quality of life parameters

- Enhanced understanding of the healthy (mucosal) immune system

Ad 2. improved diagnostics.

- No secondary study outcome parameters.

Study description

Background summary

Background.
Primary immunodeficiencies (PIDs) are rare diseases that affect the immune system. Major issues for these diseases are
1. The lack of detailed knowledge of the (natural) course of disease in PID;
2. The need for improved diagnostics. This project will address both issues.

Study objective

Project aims
1. To provide a more precise overview of prevalence, presenting symptoms, referral routes, clinical complications and evolution during follow-up of PIDs in The Netherlands by registration and analysis of prospective patient data derived from (structured) routine patient care
2.To discover new genetic and immunophenotypic causes of PID by advanced genetic analysis and by functional characterization of novel genetic causes of PID. To implement improved diagnostic techniques to diagnose (genetic) causes of PID and to collaborate in this respect with other consortia which are active in or outside of the field of PID research.

Study design

Methods:
The study consist of a prospective follow up study in N=1000-1500 patients, combined with a cross sectional study for genetic causes of PID in a subset of N=200 patients. For certain aspects of the study, healthy family or houshold members and/or friends of patients will be included (up to N=200).

Ad 1. Prospective follow up study. Data derived from routine patient care (yearly follow up visits) will be entered into a database and analysed on a yearly basis. In this part of the study, 600 patients will participate. Data entered include medical history, physical examination, laboratory values, radiological findings, and results from microbiological evaluation. Apart from these data derived from routine medical care, patients will be asked to complete a yearly questionnaire on quality of life issues. Data will be coded and protected according to privacy guidelines.

Ad 2. Improved diagnostics. PID patients who lack a genetic diagnosis will be entered in this part of the study. DNA and RNA will be analysed using next generation sequencing. One part of the study will use a targeted array for all known PID genes. Another part will use whole exome sequencing. The technique used will depend on clinical presentation, the availability of affected family members, and the descriptive diagnosis. Results from genetic analyses will be combined with those of functional- and phenotypical analyses.

Study burden and risks

Ad 1. Prospective follow up study.
- Minimal burden: for patients an annual questionnair (30 minutes), healthy controls are asked to fill out a questionnaire (15 minutes) once. Parents of patients < 12 years can be asked to fill out a daily symptom record taking up a approixmately 1 minute per day with a maximum of 7 extra questions once per month. Controls > 18 years will be asked to donate blood (max. 20mL) once and controls of IgA deficient patients < 18 years will be asked to donate blood (max. 8 ml) once. Both groups are asked to donate noninvasive samples such as saliva, faeces, skin and/or oro-/nasopharyngeal swabs (up to max. 5 times annually in patients).

Ad 2. Improved diagnostics.
- The donation of extra blood during a venapuncture for standard (normal) diagnostics (once). Alternative: the donation of a small amount of salive for dna extraction.
- In some patients: the donation of a maximum of 4 extra blood samples per year for a maximum of 5 years during venapunctures meant for standard care.

These are all considered minimal burdens associated with participation.

There are no direct benefits associated with participation.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Patients: a diagnosis of a clinically relevant primary immunodeficiency or a strong suspicion of a diagnosis of primary immunodeficiency
Healthy controls: healthy family or household members and/or friends of patients
Both groups: informed consent

Exclusion criteria

No consent

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:	Recruiting
Start date (anticipated):	22-08-2013
Enrollment:	1500
Type:	Actual

Ethics review

Approved WMO Date:	19-06-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-11-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-06-2016
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-02-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-02-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-05-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	25-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-09-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-06-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-08-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-07-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-06-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL40331.078.12