Dissection of the blood B cell compartment in affected and non-affected family members of patients with Common Variable Immunodeficiency (CVID).

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Investigation of the blood B cell compartment in family members of CVID patients (with and without a CVID family history) to identify or exclude B-cell defects and to improve our insight into a potential familial background of CVID.

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

Summary

ID

NL-OMON48185

Source
ToetsingOnline

Brief title
Blood B cell compartment in CVID families

Condition

- Immunodeficiency syndromes

Synonym
Common Variable Immunodeficiency

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: B cells, Blood, CVID, Flowcytometry

Outcome measures

Primary outcome

Disturbances in the composition of the blood B cell compartment with special attention for the absolute numbers and relative distribution of naive B cells, memory B cells, plasma cells and their various subsets.

Secondary outcome

How these aberrancies are distributed over the family members and whether the ab-errant B-cell and T-cell patterns are comparable between family members;

To select families eligible for a new study to investigate the genetic background and pathophysiology of CVID.

Study description

Background summary

Only in 10% of CVID patients a monogenetic disorder is identified and directly associated with the disease. However, in approximately 30% there is a positive family history. To understand the mechanism of disease of unexplained CVID it is important to investigate to what extend family members have an affected B cell compartment in relation to the index case. Recently, high dimensional and standardized flowcytometry studies (within the EuroFlow consortium) have demonstrated that absolutely no plasma cells are detectable in blood of CVID patients. In addition, major aberrancies are observed in the memory B cell compartment while the naïve B cell compartment might be normal or slightly

reduced. In part of the CVID patients also the T cell CD4+ compartment appears to be affected.
We hypothesize that in family members of CVID patients with a positive family history aberrancies in the blood B cell compartment can be found also in healthy family members. Since we expect that in more cases a familiar background might be present, we also expect to find aberrancies in the B cell compartment of family members of CVID patients where there is no positive family history. We want to verify this by an in-depth analysis of the B cell compartment. This in-depth analysis has been used to define CVID and other B cell deficiencies.

Study objective

Investigation of the blood B cell compartment in family members of CVID patients (with and without a CVID family history) to identify or exclude B-cell defects and to improve our insight into a potential familial background of CVID.

Study design

Pilot study to develop criteria for selection of families which have a higher chance for a monogenetic versus a polygenetic background of CVID (see for more information extensive description in the study protocol).

Study burden and risks

Only one time 9 mL of blood will be drawn from study participants. Since drawing blood is common practice in a clinical setting, there are no additional risks for participation of the study.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:;Inclusion criteria for the index case
- ESID-defined probable or possible CVID patients with or without positive family history for CVID according to the ESID registry (2014) criteria;Inclusion criteria for the family members
- Siblings (> 16 years of age), parents and grandparents
- Each participating family member will have to provide informed consent in order for the family to be eligible for inclusion.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- ESID-defined CVID patients having a known mono-genetic cause of CVID disease
- ESID-defined CVID patients having another mono-genetic disorder not obvious related to CVID
- ESID-defined CVID patients having a chromosomal defect
- Infections within 3 months prior to this study
- Surgeries within 6 months prior to this study
- Vaccinations within 3 months prior to this study
- Family members having significant disorders, including other immunodeficiency other than CVID, cancer, oral steroid therapy or any history of any comorbidity that, in the opinion of the investigator, might confound the results of the study

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-05-2019
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO

Date:	09-05-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL69477.091.19