Influencing Progression of Airway Disease in Primary Antibody Deficiency

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Objective: To show the protective value and to measure cost effectiveness of higher Ig dosing on progression of lung disease in PAD.

Ethical review	Not approved
Status	Will not start
Health condition type	Immunodeficiency syndromes
Study type	Observational invasive

Summary

ID

NL-OMON49108

Source
ToetsingOnline

Brief title
IPAD Trial

Condition

- Immunodeficiency syndromes

Synonym
Antibodydeficiencies, immune disorders

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMW,CSL Behring,Takeda

Intervention

Keyword: Dosing, Immunodeficiency, Immunoglobulines, Lungdisease

Outcome measures

Primary outcome

Main study parameters/endpoints: 1. Progression of lung disease, determined by computed tomography (CT) scanning and pulmonary function test

Secondary outcome

2. Number of respiratory infections 3. Days missed from school/work. 4. Cost savings 5. Quality of life.

Study description

Background summary

Rationale: Patients with Primary Antibody Deficiencies (PADs) frequently encounter chronic lung disease, caused by recurrent airway disease and/or interstitial lung disease. Chronic lung disease leads to absence from work and school and significant health costs. Patients with PAD are treated with immunoglobulin replacement therapy. Optimal dosing to prevent lung disease is unclear and different dosing regimens, all within prescription label, are used nationwide. We and others recently showed that higher immunoglobulin (Ig) trough levels were related to less airway infections and slower progression of airway disease. These findings need confirmation in a prospective randomized setting.

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Study objective

Objective: To show the protective value and to measure cost effectiveness of higher Ig dosing on progression of lung disease in PAD.

Study design

Study design: Multicenter, prospective randomized controlled trial, performed

by 3 academic centers in The Netherlands.

Intervention (if applicable): Two Ig dosing regimens (both in normal range) are compared: Control group: Ig dose 0.4-0.6 g/kg/L, vs intervention group: dose increase of 33% (relative to pre-study dose) will be administered for 2 years. CT scanning and pulmonary function tests will be performed at t=0 and 24 months.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The study compares two existing prophylaxis regimes for pulmonary disease in patients with primary antibody disease. Administration of medication and measurement of trough levels of medication follows routine medical guidelines for treatment and follow up. The extra procedures to which patients are subjected in this protocol are as follows: two CT scans of the lungs and two pulmonary function tests (t=0 and 24 months; 30 minutes per procedure). Futher, during routine venapunture moments, 5 extra blood samples will be taken, and 2 extra venapunctures will be taken apart from the routine samples. Finallly, three times the completion of a questionnaire set on quality of life and productivity losses (30 minutes per time in total). The extent of these extra procedures is considered to have low impact. Children will be part of the study. The study must be conducted in a pediatric population as well because children are especially at high risk for pulmonary disease.

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:
-Age 4-60 years
-Diagnosis of Primary Antibody Deficiency / Common Variable Immunodeficiency Disorder (see Appendix A).
-Indication for immunoglobulin replacement therapy and/or treated with immunoglobulin replacement therapy
-Current IgG dosing 0.4 - 0.6 gr / kg / 3-4 weeks
-Receiving treatment and follow up for PAD by one of the physicians in the participating centers
-Written informed consent
-Normal lung status, or mild to medium severe pulmonary disease (measured by pulmonary function test and on CT scan, scored by an independent radiologist based on the following criteria):
* Baseline AD score < 5 and ILD score < 7, or;
* Baseline AD score > 5 and/or ILD score > 7 without clinical diagnosis of severe respiratory insufficiency (defined as: saturations in room air <92% and / or oxygen dependency).
* Baseline pulmonary function (FEV1 and FVC >70% expected for age and body weight / length)

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded

from participation in this study:
-Age above 60 year
-Diagnosis of Combined Immunodeficiency (CID) disease at onset of study (see Appendix A). Explanation: Combined Immunodeficiency is featured by the occurrence of more viral infections and reactivations and thus less comparable to PAD.
-Severe pulmonary disease, determined by an independent radiologist:
* Baseline AD score > 5 and/or ILD score > 7, in combination with:
o Saccular bronchiectasis on CT scan, or;
o Clinical diagnosis of severe respiratory insufficiency (defined as: (defined as: saturations in room air <92%, and/ or oxygen dependency).
* Baseline pulmonary function (FEV1 and FVC >70% expected for age and body weight / length)

Study design

Design

Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	100
Type:	Anticipated

Ethics review

Not approved

Date:	28-01-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL74793.041.20