Influencing Progression of Airway Disease in Primary Antibody Deficiency

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This study has been transitioned to CTIS with ID 2024-513124-41-00 check the CTIS register for the current data. To show the protective value and to measure cost effectiveness of higher Ig dosing on progression of lung disease in PAD.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immunodeficiency syndromes
Study type	Interventional

Summary

ID

NL-OMON51878

Source
ToetsingOnline

Brief title
IPAD Trial

Condition

- Immunodeficiency syndromes
- Infections - pathogen unspecified

Synonym
immunodeficiency, PAD

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: airway disease, immunoglobulin, primary antibody deficiency

Outcome measures

Primary outcome

Difference in mean AD and ILD scores (as measured with CT scanning) between t=0 and t=2 years in patients with standard vs higher Ig replacement therapy dosing.

Secondary outcome

1. The incidence of symptomatic lower pulmonary infections in PAD patients with high Ig replacement therapy dosing versus standard Ig replacement therapy dosing.

2. Number of physician diagnosed lower respiratory tract infections in patients with high vs standard Ig replacement therapy dosing.

3. Number of hospital admissions and duration of hospital admissions for pulmonary complications (ao exacerbations of bronchiectasis)

4. Outcomes of pulmonary function tests (specifically: Total Lung Capacity (TLC), Forced Expiratory Volume after 1 second (FEV1), CO diffusion) on t=0 and t=2 years in all patients

5. Days missed from work / school in patients with high vs standard Ig replacement therapy dosing.

6. Total therapeutic and preventive costs

Study description

Background summary

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. Standard treatment for patients with PAD consists of 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.

Study objective

This study has been transitioned to CTIS with ID 2024-513124-41-00 check the CTIS register for the current data.

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

Study design

Multicenter, randomized controlled study performed by 3 academic centers in The Netherlands.

Intervention

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

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)

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
1. Age 8-60 years
2. Diagnosis of Primary Antibody Deficiency / Common Variable Immunodeficiency Disorder (see Appendix 1).
3. Indication for immunoglobulin replacement therapy and/or treated with

immunoglobulin replacement therapy
4. Current IgG dosing 0.25 - 0.6 gr / kg / 3-4 weeks
5. Receiving treatment and follow-up for PAD by a physician in one of the participating centers
6. Written informed consent

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
1. Diagnosis of Combined Immunodeficiency (CID) disease at onset of study (see Appendix 1). Explanation: Combined Immunodeficiency is featured by the occurrence of more viral infections and reactivations and thus less comparable to PAD.
2. Severe pulmonary disease, determined by an independent radiologist:
a. Baseline AD score > 7 and/or ILD score > 5, in combination with:
i. Saccular bronchiectasis on CT scan, or;
ii. Clinical diagnosis of severe respiratory insufficiency ((defined as: saturations in room air <92%, and/ or oxygen dependency).
b. Baseline pulmonary function (FEV1 and FVC) <70% expected for age and body weight / length)
3. Active smoker

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-08-2022
Enrollment:	100

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Normal immunoglobulines (im en sc)
Generic name:	Normal immunoglobulines (im en sc)
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Normal immunoglobulines (iv)
Generic name:	Normal immunoglobulines (iv)
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	08-12-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	24-12-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	28-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-01-2023
Application type:	Amendment
Review commission:	METC NedMec

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
EU-CTR	CTIS2024-513124-41-00
EudraCT	EUCTR2021-005001-26-NL
CCMO	NL79088.041.21