IgG4:IgG mRNA ratio as disease activity marker in vasculitis

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Aim 1: Confirm the hypothesis that the IgG4 qPCR test score correlates with disease activity in vasculitis as observed in the pilot study. Aim 2: Study IgG4-expressing B-cells from blood of vasculitis patients to understand their role in the...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON46036

Source
ToetsingOnline

Brief title
IgG4 and vasculitis

Condition

- Autoimmune disorders
- Vascular disorders NEC

Synonym
blood vessel inflammation, Vasculitis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: VENI beurs,PI budget

Intervention

Keyword: Disease activity marker, IgG4, Quantitative polymerase chain reaction, Vasculitis

Outcome measures

Primary outcome

Primary: completion of inclusions and sampling (section 5.1)

Arm A: 120-140 participants

This arm consists of one inclusion visit and an additional visit within 12

months in case of change of disease activity.

Arm B: 60-80 participants

This arm consists of 5-7 visits and will consist of individuals that have de

novo or established disease at inclusion.

Secondary outcome

nvt

Study description

Background summary

Vasculitis is a heterogeneous group of inflammatory diseases that primarily affects blood vessels. The pathogenesis of the inflammation is largely unknown. The vascular inflammation impairs blood flow which causes hypoxia, necrosis and organ failure with devastating consequences. The fluctuating course of primary vasculitides together with difficulties in reliable assessment of disease activity on the individual patient level leads to periods of over- and undertreatment with associated side-effects, morbidity and mortality. Clinical scores (such as BVAS-v3 (1)) assume that a physician is certain that symptoms are attributable to vasculitis which is often not the case. Notably, the differentiation of active vasculitis and infection may be difficult. As a result, patients regularly need to undergo intensive additional investigations. Specific and sensitive of current biomarkers are lacking in vasculitis (2): the

ones that serve as diagnostic biomarkers (e.g. ANCA) do not serve very well as disease activity markers. Thus, from the current clinical perspective, there is a pressing need for specific biomarkers that sensitively reflect disease activity. In addition, more understanding of the pathogenesis of these diseases is needed to further improve clinical care and treatment regimes.
We recently completed a pilot study that indicated that a qPCR test which indirectly measures the presence of immunoglobulin-G4 positive B-cells and plasmacells (Hereafter: IgG4+ cells) might be a good disease activity marker in vasculitis. Historically, IgG4 is regarded as an immunomodulator (e.g. in controlling allergies), but recent work on IgG4-RD and pemphigus also raised the hypothesis that IgG4 might be pro-inflammatory (3). Multiple studies have implicated IgG4 in the pathogenesis of vasculitis, in particular ANCA-associated vasculitis (4-9), while clinically, there is overlap between large vessel vasculitis and IgG4-RD (10). However, so far, the presence of IgG4+ mRNA has not been tested as a disease activity marker in vasculitis.

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Study objective

Aim 1:
Confirm the hypothesis that the IgG4 qPCR test score correlates with disease

activity in vasculitis as observed in the pilot study.
Aim 2:
Study IgG4-expressing B-cells from blood of vasculitis patients to understand their role in the pathogenesis
Aim 3:
By conducting the studies under aim 1 and 2 we will build a unique cohort which contains detailed clinical data and blood samples. These will be used for the current project, but will also help in addressing future questions in vasculitis. To this end we will store serum, PBMCs and RNA from blood at each time point. If biopsies are performed, RNA from these samples will be added following patient consent.

Study design

Longitudinal observational study with two arms. We will collect clinical information and blood to study biomarkers. If left-over tissue is present from standard diagnostic tests, this will also be analysed for biomarkers.
- Arm A (120-140 patients): 2 visits within 1 year
- Arm B (60-80 patients): Visits every 6 months for 2 years and extra visit in case of suspected new disease activity

Study burden and risks

Patients will be seen for blood withdrawals related to the study. 2 to 5-7 times 77ml is the average (depending on the study arm).

There are hardly any risks to blood withdrawals (<1% chance of infection/bleeding).

For biopsy materials that we will receive from the pathology department after diagnostic routine analysis, there will be no prior research related actions.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Subjects must be older than 18 years of age
- They must have a form of the following vasculitides:
* Granulomatosis with polyangiitis
* Eosinophilic Granulomatosis with Polyangiitis
* Giant Cell Arteritis
* Takayasu Arteritis
- OR polymyalgia rheumatica

Exclusion criteria

• (Previous) presence of (concomitant) auto-immune disease
• Under any administrative or legal supervision.
• Conditions/situations such as:
o Patients with conditions/concomitant diseases making them non evaluable for the primary endpoint
o Impossibility to meet specific protocol requirements (e.g. blood sampling)
o Patient is the Investigator or any sub-investigator, research assistant, pharmacist, study coordinator, other staff or relative thereof directly involved in the conduct of the protocol
o Uncooperative or any condition that could make the patient potentially non-compliant to the study procedures

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-05-2019
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	06-12-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-07-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL66034.018.18