Pharmacokinetics and immunological aspects in nasal polyp patients treated with biologics: a pilot study

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Primary objective:To investigate the dose - (clinical) response relationship and therapeutic window of biologics in the treatment of CRSwNP.Secondary objectives:- To investigate the effect of biologics on the sensibilisation pattern of specific IgE...

Ethical review	Approved WMO
Status	Pending
Health condition type	Allergic conditions
Study type	Observational invasive

Summary

ID

NL-OMON51449

Source
ToetsingOnline

Brief title
Biologics in nasal polyp patients

Condition

- Allergic conditions
- Upper respiratory tract disorders (excl infections)

Synonym
chronic rhinosinusitis with nasal polyps; nasal polyps

Research involving
Human

Sponsors and support

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

Intervention

Keyword: biologics, chronic rhinosinusitis with nasal polyps, immune system, pharmacokinetics

Outcome measures

Primary outcome

To investigate the dose - response relationship and therapeutic window of biologics in the treatment of CRSwNP. Response refers to clinical outcome, as measured by the SNOT22 questionnaire.

Secondary outcome

1. To investigate the effect of biologics on the sensibilisation pattern of specific IgE and its relationship with (clinical) treatment outcome.

2. To investigate the effect of biologics on type 2 T helper and regulatory T cells, and its relationship with (clinical) treatment outcome.

Study description

Background summary

Chronic rhinosinusitis with nasal polyps is an inflammatory disease of the upper airways. Common complaints are nasal congestion, rhinorrhea, postnasal drip, a loss of smell, headaches and involvement of the lower airways. Until recently, treatment options were limited to local and oral steroids, and surgery when medical treatment was insufficient. Due to the chronic and sometimes recalcitrant nature of the disease, result outcomes can be very disappointing. Since 2020, we are able to prescribe biologics for this disease, with excellent results. At the moment these biologics include dupilumab, omalizumab and mepolizumab, which respectively suppress IL4R signalling, IgE mediated allergy and IL-5 function. Resulting modulation of type 2 helper T cell driven immune response, allergic response and eosinophilic granulocyte function may contribute to efficacy of treatment. In most patients, polyps shrink fast and even smell can return already a few days after the first injection. The outcome is far better than we could achieve in the past. Downside is the high costs of the treatment, which has led to defining

inclusion criteria for the initiation of biologics. These include age >= 18, a history of previous (extensive) sinus surgery, and 3 out of 5 of the following criteria: signs of eosinophily, anosmia, SNOT22 questionnaire >= 40 (symptom score, part of the attachments), a chronic need for oral steroids, and the use of inhalation corticosteroids.
As this is a relatively new treatment within patients with chronic rhinosinusitis with nasal polyps, there is no extensive knowledge of its underlying immunological mechanisms and their potential contribution to efficacy of treatment as indicated above. In this pilot study, we aim to investigate the effects of biologics on the immunologic and allergic response associated with CRSwNP and correlate them with subjective patients outcome. We also plan to investigate dose-response relationship between serum levels of biologics and efficacy of treatment in order to determine an optimal therapeutic window of biologic treatment.

Study objective

Primary objective:
To investigate the dose - (clinical) response relationship and therapeutic window of biologics in the treatment of CRSwNP.

Secondary objectives:
- To investigate the effect of biologics on the sensibilisation pattern of specific IgE and its relationship with (clinical) treatment outcome.
- To investigate the effect of biologics on type 2 T helper and regulatory T cells, and its relationship with (clinical) treatment outcome.

Study design

This pilot study will take approximately 3 years to complete: 2 years of inclusion, last blood withdrawal is 12 months after final inclusion. It will be an observational cohort study, in which the following data will be gathered:
- the completion of the SNOT22 questionnaire(5) and Asthma Control Test(6) (in case of asthma or the use of inhalation corticosteroids)
- smelling test
- fiberendoscopic evaluations of the nose
- blood test: eosinophils and total IgE
All of the above procedures are currently part of the standard diagnostic procedures in the treatment of CRSwNP patient. For study purposes, during the regular blood testing (time points: before treatment, and at 1, 3, 6 and 12 months after initiation of treatment; extra blood sampling will be done when clinically required, i.e. when eosinophils are increased), we will take an extra 3 tubes of blood.

Study burden and risks

The results of this study are not directly beneficial to the subject, although this may be so in the future, depending results. The risks associated with participation can be considered negligible and the burden minimal, as patients are not subjected to any additional activities outside the regular standard of care.

Contacts

Public
Erasmus MC, Universitair Medisch Centrum Rotterdam

Doctor Molewaterplein 40
Rotterdam 3015GD
NL
Scientific
Erasmus MC, Universitair Medisch Centrum Rotterdam

Doctor Molewaterplein 40
Rotterdam 3015GD
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- 18 years or above
- eligible for treatment with biologics: criteria include:
* previous extensive surgery
* AND at least 3 out of 5 of the following items:
* SNOT22 score above 39

* anosmia
* a chronic need for oral steroids
* the use of inhalation corticosteroids
* signs of eosinophily (blood eosinophils >= 0.25x10^9 / L or >=10 eosinophils per high-power field in histology)

Exclusion criteria

- Age < 18 years
- Mentally not competent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	06-06-2022
Enrollment:	30
Type:	Anticipated

Ethics review

Approved WMO

Date:	21-04-2022
Application type:	First submission
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	NL79596.078.21