Fungal infections as complication of monoclonal antibody therapy directed against IL-17 mediated inflammation: estimating incidence and severity and identifying influence of immunogenetics to establish a guideline for screening, prevention and treatment.

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1. To estimate the incidence and severity of fungal infections during anti-Th17 mAb therapy2. To characterize the determinants (clinical, immunological, mycobiome/microbiomeand genetical) for developing fungal infections during anti-Th17mAb therapy…

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

Summary

ID

NL-OMON46165

Source
ToetsingOnline

Brief title
Fungal infections as complication of anti-Th17 mAB therapy.

Condition

- Immunodeficiency syndromes
- Fungal infectious disorders
- Epidermal and dermal conditions

Synonym
fungal infections, inflammatory skin disease

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: anti-Th17 mAb therapy, fungal infections, IL-17 pathway, psoriasis

Outcome measures

Primary outcome

1) Incidence and severity of fungal infections.

2) Function immune system.

3) Mycobiome/microbiome.

4) Gene polymorphisms at DNA level.

Secondary outcome

non applicable

Study description

Background summary

The incidence and severity of fungal infection and clinical treatment difficulties during the newly introduced anti-Th17 mAb therapy are yet largely unknown. It is envisaged that specific individual patients are particularly at risk to develop these complications, based on clinical, immunological, or genetic determinants influencing their Th17 anti-infective responses. Identification of such patients will lead to a personalized healthcare approach, aimed at better understanding of the potential risks, directed patient selection and monitoring of Th17-targeted mAb therapy, and may lead to better prevention and treatment of severe fungal infections in this patient

group.
This asks for a coordinated approach by experts in the field of Candida infections, fungal immunogenetics, and psoriasis immunotherapy, in an international collaboration with the drug manufacturers and the governmental adverse events registries.

Study objective

1. To estimate the incidence and severity of fungal infections during anti-Th17 mAb therapy
2. To characterize the determinants (clinical, immunological, mycobiome/microbiomeand genetical) for developing fungal infections during anti-Th17mAb therapy.

Study design

A case-control study will be performed in the Radboudumc. The duration of the study is 3 years. Participants will be recruited via the BioCAPTURE registry (Continuous Assessment of Psoriasis Treatment Use Registry with Biologics). This registry contains all patients on biological treatment in the Radboudumc and 10 regional hospitals in the Netherlands.

We will use several approaches to investigate the above-described objectives:
* Patient characteristics and patient history will be collected partly via the BioCAPTURE registry and partly via a questionnaire
* Venous blood will be taken to measure part of the function of the immune system and to look for gene polymorphisms at DNA level.
* A skin biopsy will be taken to measure another part of the function of the immune system namely the defensins in epithelial cells.
* Mycobiome/microbiome analysis will be performed on stool, oral, vaginal, and skin samples using 16s and 18s sequence analysis.

Study burden and risks

Burden:
- Venapuncture
- Skinbiopsy

Risks:
- There will be no risks other than local hematoma related to venous puncture.
- There will be a very small risk of minimal bleeding and infection after skinbiopsy

Benefit:

- There will be no direct benefits for the subjects enrolled in this study.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert grooteplein Zuid 10
Nijmegen 6525 GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert grooteplein Zuid 10
Nijmegen 6525 GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Diagnosis of psoriasis
* Age * 18 years
* Treatment with either a TNF-*-inhibitor for at least 1 year, ustekinumab for at least 1 year, secukinumab for at least 6 months, ixekizumab for at least 6 months or brodalumab for at least 6 months or planning to start treatment with an anti-Th17 mAb therapeutic agent
* Registration in the BioCAPTURE registry

Exclusion criteria

* Pregnancy
* Any active cancer treatment

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	15-10-2018
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	05-03-2018
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	NL61622.091.17