Immunological analyses of Long-term Molecular and Cellular Responses to Hymenoptera Venom Immunotherapy Indolent Systemic Mastocytosis patients.

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

Summary

ID

NL-OMON48343

Source
ToetsingOnline

Brief title
VIT-ISM

Condition

- Allergic conditions
- Haematopoietic neoplasms (excl leukaemias and lymphomas)

Synonym
mast cell abundance, Mastocytosis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cellular response, Hymenoptera venom allergy, Indolent systemic mastocytosis, Venom immunotherapy

Outcome measures

Primary outcome

Primary outcome will be the change in fraction (fraction expressed as

percentage) of proliferating Th2-cells, defined by IL-4 expression and low

expression of CFSE, within the allergen-specific CD4+ T-cell population within

both patient groups, ISM and non-ISM after thirteen weeks and seven months of

VIT.

Secondary outcome

Changes in the profiles of gene expression and proteome of T- and B-cells are

secondary outcomes for ISM+ and ISM- patients.

Study description

Background summary

Hymenoptera venom allergy (HVA) is a immunoglobulin E (IgE) mediated reaction to insect stings, which may be severe and cause potentially life-threatening anaphylaxis. Venom immunotherapy (VIT) is highly effective in inducing peripheral tolerance against venom allergens, and provides a reliable and long-term clinical protection to future stings.

Some HVA patients suffer from underlying indolent systemic mastocytosis (ISM). In ISM patients HVA reactions are generally more severe and VIT is less effective. We hypothesize that the reduced effectiveness of VIT in ISM is either caused by the lack of an immunological alteration or that an

immunological alteration does occur, but is insufficient due to the mast cell abundance.

Study objective

The primary objective is to assess the adaptive T cell response to VIT in HVA patients with underlying ISM (ISM+) after treatment induction (at thirteen weeks) and upon reaching maintenance dose, after seven months, in comparison to the baseline condition at the start of treatment. Secondarily, this response will be compared to that of HVA patients without underlying ISM (ISM-) undergoing VIT.

Study design

Prospective cohort study, assessing the immunological T cell response to VIT of ISM+ and ISM- patients. Patients will be recruited at the UMCG, where peripheral blood mononuclear cells (PBMCs) will be isolated and cryopreserved. T cell cultures and analysis will be performed at the Swiss Institute of Allergy and Asthma Research (SIAF).

Study burden and risks

Participation in the study concerns the collection of three additional peripheral blood mononuclear cells (PBMCs) samples compared to standard care, at baseline, at thirteen weeks and at seven months of VIT treatment. No additional questionnaires or other interventions are required.
ISM+ patients receive their VIT in the outpatient clinic of the UMCG due to their increased risk of side-effects from VIT treatment. We will collect the PBMC samples during these visits. Therefore, no additional hospital visits are required for this patient group. ISM- patients receive VIT at the day-care in the UMCG until 13 weeks, when maintenance dose is reached. Afterwards treatment is continued at the general practioner. Study participation hence implies 1 additional hospital visits for these patients.

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

- A systemic reaction to an wasp sting, grade IV according to the Muller classification.
- Diagnostic confirmation by specific IgE levels against wasp venom.
- A conclusive bone marrow biopsy confirming or excluding the presence of mastocytosis or the presence of monoclonal mast cell disease.
- The patient has chosen VIT as treatment of HVA.

Exclusion criteria

- No (conclusive) bone marrow biopsy in patients with grade IV reactions.
- Contra-indications for VIT
- Minors (<18 years)
- Legally incapacitated patients

Study design

Design

Study type:	Observational invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	27-03-2019
Enrollment:	32
Type:	Actual

Ethics review

Approved WMO

Date:	01-02-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL67507.042.18