# Molecular phenotyping of Mast Cells in Indolent Systemic Mastocytosis using Single Cell RNA-sequencing

Published: 17-01-2019
Last updated: 12-04-2024

To investigate which molecular mast cell phenotypes (as defined by the expressed genes and gene-networks) in bone marrow resident mast cells and their progenitors are associated with the presence or absence of ISM.

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Allergic conditions |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON48390

**Source**
ToetsingOnline

**Brief title**
MC-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:** Mastocytosis, single cell RNA sequencing

## Outcome measures

### Primary outcome

Differences in gene expression and gene-networks in bone marrow resident mast cells and their progenitors between ISM and non-ISM patients identified by single-cell RNA sequencing.

### Secondary outcome

Differences in gene expression and gene-networks in bone marrow resident mast cells and their progenitors between clinical subtypes of ISM, as identified by single-cell RNA sequencing.

Differences in gene expression and gene-networks of other cell types in unpurified bone marrow aspirate that might be the result of the presence of mast cells (or their progenitors) carrying the somatic cKIT mutation.

# Study description

### Background summary

Systemic mastocytosis is a disorder characterized by the pathological clonal proliferation of mast cells as a result of a somatic point mutation of the proto-oncogene c-KIT.(1,2) Indolent systemic mastocytosis (ISM) is the most prevalent type.(2) Accumulation and degranulation of mast cells in various tissues results in a wide clinical spectrum of mast cell activation complaints, e.g. drowsiness, flushing, typical gastro-intestinal complaints, fatigue. Other frequent manifestations are osteoporosis and hymenoptera venom allergy (HVA).(3)

How the c-KIT mutation affects mast cell phenotype unknown, as well as why some patients mainly show symptoms related to mast cell accumulation and others mainly to mast cell degranulation. Increased insight in mast cell heterogeneity

between ISM and non-ISM patients will be key to design novel therapeutic treatment options. Furthermore, the underlying pathophysiology for the variation in clinical presentation within the ISM population is unknown. We hypothesize that, as ISM patients show no other bone marrow alterations than mast cell abundance, clinical differences of subtypes may be traced back to differences in mast cell (progenitor) phenotypes. Identification of such differences within the ISM may help us in developing an optimized, personalized treatment.

### Study objective

To investigate which molecular mast cell phenotypes (as defined by the expressed genes and gene-networks) in bone marrow resident mast cells and their progenitors are associated with the presence or absence of ISM.

### Study design

Single-center, cross-sectional study, using single cell RNA sequencing (scRNA-seq).

### Study burden and risks

This observational study has no specific beneficial health effects for any of the participating subjects. The performed bone marrow biopsy is part of standard care. The study requires the withdrawal of an additional sample of 10mL. This entails no additional risks compared to the standard care. This method of inclusion enables us to include both ISM and non-ISM patients without the requirement of additional invasive procedures or hospital visits.

## 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 clinical suspicion of ISM, based on a constellation of clinical complaints, including drowsiness, gastro-intestinal complaints, myalgia and fatigue, or manifestations such as urticaria pigmentosa, osteoporosis or anaphylaxis.
- Eligible for a bone marrow biopsy
- Legally capacitated adults

-The second eligible patient group concerns patient enrolled in the avapritinib study (research register number 201800849, METc 2018.635). These patients with a confirmed diagnosis of ISM willl undergo a bone marrow biopsy as part of the study protocol of the avapritinib study. Therefore, also in this patient population no additional invasive procedures are required, hence the additional burden of the current study remains restricted to the withdrawal of the additional sample.

## Exclusion criteria

Lidocaine hypersensitivity.

# Study design

## Design

Study type: Observational invasive

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

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 26-03-2019 |
| Enrollment: | 40 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 17-01-2019 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 03-07-2019 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 13-08-2019 |
| Application type: | Amendment |
| 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 | NL67451.042.18 |