# Characterization of platelets and antibodies in adult patients with immune thrombocytopenia (ITP)

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The aim of this study is to characterize the in vitro properties of platelets and autoantibodies of adult patients with primary/chronic ITP, in order to gain insight in the molecular mechanisms underlying the disease. This may lead to development of...

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| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Platelet disorders |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON47599

**Source**
ToetsingOnline

**Brief title**
Research into the development of ITP

### Condition

- Platelet disorders
- Autoimmune disorders

**Synonym**
immune thrombocytopenia

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Erasmus MC, Universitair Medisch Centrum Rotterdam
**Source(s) of monetary or material Support:** European Hematology Association Research

Fellowship

## Intervention

**Keyword:** autoantibodies, immune, platelets, thrombocytopenia

## Outcome measures

### Primary outcome

One of the primary results will include platelet properties as described in the study design. Investigation will involve receptor expression on the thrombocytes and functional properties via aggregation tests.

The other primary result will be the characterization of patient autoantibodies, and successful isolation of mononuclear cells and subsequent selection of platelet-reactive B-cells.

### Secondary outcome

N/a

# Study description

### Background summary

Primary immune thrombocytopenia (ITP) is an acquired isolated thrombocytopenia (platelets/thrombocytes < 100 x 10^9/l), without a clear underlying disease. Possible causes of ITP include an increased breakdown of platelets mediated by autoantibodies, disruption of platelet production, or T-cell mediated processes. Incidence of ITP is approximately 50/1,000,000. The disease is equally common amongst men and women, except in women between 30-60 years, in which the disease is more prevalent compared to men of the same age. ITP is characterized according to the timespan of the disease in acute, persistent (3-12 months) or chronic ITP (> 12 months). Clinical features may vary considerably. Patients may not have any features, petechia, purpura or mucosal bleedings, but also life-threating gastrointestinal- or intracranial bleedings. Usually, clinical features only emerge in patients with platelet counts below

30 x 10^9/l, although the severity of the disease does not always correlate with the bleeding risk. Other causes for thrombocytopenia have to be excluded before ITP is diagnosed.

In part due to the poorly understood etiology of ITP and limited diagnostic tools, there is a large diversity in this patient population. This makes it very difficult to perform randomized trials. The Dutch guidelines on ITP are mostly based on international guidelines and expert opinions due to the limited number of randomized studies.

Setting up this study will generate more insight into the properties of platelets and autoantibodies of patients with ITP.

**Study objective**

The aim of this study is to characterize the in vitro properties of platelets and autoantibodies of adult patients with primary/chronic ITP, in order to gain insight in the molecular mechanisms underlying the disease. This may lead to development of new therapeutic options for ITP.

**Study design**

Inclusion:
Between twenty and thirty patients with primary or chronic ITP will be included in this study. Informed consent will be requested by the treating hematologist. Upon admission, patients will receive a unique study-number. Medical records (age, sex, ITP status, past and current treatment) will be collected and analysis of thrombocytes and autoantibodies will be performed by the primary researcher.

Blood draw:
Blood will be obtained during a singular event (during a routine venipuncture):
• 20 ml heparin blood
• 40 ml citrated blood
• 40-60 ml EDTA blood and/or
• 10 ml coagulation tube

Platelet properties
Receptor expression will be measured (including VWF receptor complex, P-selectin, annexin V, DC-SIGN and lectins) via flow cytometry (20 ml citrated blood). Platelet function will be determined by aggregation tests (20 ml citrated blood).

Autoantibody properties
Autoantibodies will be determined in plasma via MAIPA technique (40-60 ml EDTA blood and/or 10 ml coagulation tube), which is performed by Sanquin Research

Amsterdam (Diagnostic Test Code T924). For patients with a known platelet count <15*10^9/L, only a 10 ml coagulation tube is used. For patients between 15 and 30*10^9/L, 60 ml EDTA blood is used. For patients <30*10^9/L, 40 ml EDTA blood and a 10 ml coagulation tube is needed.

B-cells will be isolated to collect and characterize these antibodies (20 ml heparin blood). Ficoll separation will be used to isolate the mononuclear fraction. B-cells will be cultured and autoantibodies will be isolated.

**Study burden and risks**

Blood will be drawn in a singular event to perform the required experiments. This will be done during a routine venipuncture, which means patients will not have to visit the hospital multiple times. Hence, the burden on the patient(s) is minimal. There is also little risk involved in drawing the amount of additional blood as described in the protocol.

# Contacts

**Public**
Erasmus MC, Universitair Medisch Centrum Rotterdam

Wytemaweg 80
Rotterdam 3015 CN
NL
**Scientific**
Erasmus MC, Universitair Medisch Centrum Rotterdam

Wytemaweg 80
Rotterdam 3015 CN
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

Patients receiving corticosteroids, IVIG or TPO receptor agonists are allowed to participate. ;- Age minimal 18 years, both men and women
- Subjects with primary/chronic ITP (as defined by [Rodeghiero] with platelet numbers that have been below <30*10^9/L at one timepoint)
- Written informed consent
- WHO performance status <3

## Exclusion criteria

- Prior treatment with rituximab as this will interfere with B-cell isolation
- Use of anticoagulants (e.g. NSAIDs) affecting platelet function
- Inadequate renal and liver function, i.e. creatinine or bilirubin >2.5 x the upper normal value
- Severe cardiac dysfunction
- Severe pulmonary dysfunction
- Severe neurological or psychiatric disease
- Any psychological, familial, sociological and geographical condition potentially hampering compliance with the study protocol
- Concurrent severe and/or uncontrolled medical condition (e.g. uncontrolled diabetes, hypertension, cancer, etc.)
- Neutrophil count <1.5*10^9/L and hemoglobin level <6.2 mmol/L.
- Active bleeding (defined by grade 3 or 4 according to NCI CTCAE v3.0)
- Pregnant or lactating
- Systemic infections: active viral infections, including HIV
- Seriously immunocompromised patients
- Systemic autoimmune disorders (e.g. systemic lupus erythematosus, SLE)
- Current malignant disease
- Any experimental therapy within 30 days prior to blood draw

# Study design

## Design

**Study type:** Observational non invasive
Masking: Open (masking not used)

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| Control: | Uncontrolled |
| Primary purpose: | Basic science |

### Recruitment

NL

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| Recruitment status: | Completed |
| Start date (anticipated): | 12-10-2017 |
| Enrollment: | 30 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 04-09-2017 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |
| Approved WMO Date: | 24-07-2018 |
| Application type: | Amendment |
| 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 | NL61696.078.17 |