The effect of anagrelide and hydroxyurea on platelet function in patients with Essential Thrombocytosis.
An observational in vitro and ex vivo study on the dynamic conditions of platelet function and (systemic) coagulation activation.

Published: 24-11-2011
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1. To compare the platelet function between healthy controls and patients with ET under both static and dynamic conditions. 2. To study the effects of anagrelide and hydroxyurea on platelet function. 3. To study the intrinsic platelet activation...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Platelet disorders
Study type	Observational invasive

Summary

ID

NL-OMON35998

Source
ToetsingOnline

Brief title
The effect of anagrelide and hydroxyurea on platelet function.

Condition

- Platelet disorders

Synonym
Thrombocythemia or primary thrombocytosis (no laymen's term)

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Shire,Shire plc.

Intervention

Keyword: anagrelide, essential thrombocytosis, hydroxyurea, platelet function

Outcome measures

Primary outcome

The primary study parameters of this study are;

1. Platelet reactivity (FACS analysis - static conditions)

2. Platelet aggregate formation (perfusion model - dynamic conditions)

Secondary outcome

The secondary study parameters of this study are;

1. The effect of in vitro addition of anagrelide, BCH4426 (the metabolite of

anagrelide) and hydroxyurea on the platelet reactivity.

2. Markers of systemic platelet activation

- Soluble P-selectin (sPsel)

- Soluble CD-40 ligand (sCD40L)

- Regulated upon Activation, Normal T cell Expressed and Secreted (RANTES)

- Neutrophil Activating Protein-2 (CXCL7)

- Microparticles

- Von Willebrand Factor (vWF)

3. Markers of systemic coagulation activation

- Prothrombin fragment 1+2

- Thrombin-Antithrombin (TAT)-complexes

- Fibrine monomers

- D-dimers

4. Platelet-monocyte complex formation

Study description

Background summary

The pathogenesis of thrombosis in Essential Thrombocytosis (ET) is not fully understood. The clinical manifestations of ET varies from asymptomatic to life threatening thrombosis. Cytoreductive therapy with hydroxyurea or anagrelide has shown to reduce platelet count, but the effect on platelet function has not been delineated. We aim to study the effects of ET on platelet function and the multifactorial thrombotic environment and evaluate the effect of cytoreductive therapy. A better understanding of this effect might benefit treatment options or risk assessment of thrombosis and bleeding in the future.

Study objective

1. To compare the platelet function between healthy controls and patients with ET under both static and dynamic conditions.
2. To study the effects of anagrelide and hydroxyurea on platelet function.
3. To study the intrinsic platelet activation routes in ET and the effects of cytoreductive therapy on these routes.

Study design

Monocenter observational study; cross sectional for group 1, 2, 3 and 4 and a prospective cohort study for group 5 and 6.

Study burden and risks

This study will contribute to the knowledge of platelet function in ET and the effect of cytoreductive therapy on this function. Improved insights may lead to improved treatment strategies and a better risk assessment of thrombosis and bleeding.
The results of this study will not be directly beneficial for the participating patients. Adverse events are not expected to occur in this study. One to three visits to the hospital (according to the study group) is requested when participating and a total amount of 35.5-106.5ml of blood is donated

respectively. The risk of venapuncture is considered to be very low.

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

- Essential Thrombocytosis, diagnostic criteria met by the WHO criteria.
- According to the studied patient group, included patients will either use no cytoreductive therapy, or already use hydroxyurea or anagrelide. Or they will start treatment with hydroxyurea or anagrelide within two months.
- Age18 years or older

Exclusion criteria

- Use of medication that is known to influence platelet function (other than acetylsalicylic acid), s.a. clopidogrel, dipyridamole and NSAIDs (Non-Steroidal Anti-Inflammatory Drugs) within 14 days prior to inclusion and during follow up.

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:	Recruitment stopped
Start date (anticipated):	01-11-2012
Enrollment:	62
Type:	Actual

Ethics review

Approved WMO

Date:	24-11-2011
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL35936.041.11