# Heavy menstrual bleeding in premenopausal women treated with direct oral anticoagulants - a randomised controlled trial.

Published: 16-10-2019
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To evaluate management strategies in premenopausal women with heavy menstrual bleeding associated with factor Xa inhibitor therapy.

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Coagulopathies and bleeding diatheses (excl thrombocytopenic) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON55056

**Source**
ToetsingOnline

**Brief title**
MEDEA

### Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)

**Synonym**
heavy menstrual bleeding, Menorrhagia

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W,Boehringer Ingelheim

## Intervention

**Keyword:** Anticoagulants, Bleeding, DOACs, Menstrual

## Outcome measures

### Primary outcome

The difference in pictorial bleeding assessment chart (PBAC)-score, a validated score for assessing HMB, before randomisation (i.e. while on factor Xa treatment) compared to the PBAC-score after randomisation. The primary analysis is a comparison of the mean PBAC-score before randomization (i.e. while on factor Xa treatment) with the mean PBAC-score after the participant has switched to dabigatran.

### Secondary outcome

- Quality of life assessment, by means of the disease-specific menstrual bleeding questionnaire (MBQ) and a standardized 36-item short form survey (SF-36) for Quality-of-Life assessment
- Laboratory values, including haemoglobin and iron-status at baseline and end of study
- Any bleeding event other than heavy menstrual bleeding
- Any event requiring a change in anticoagulant treatment, i.e. a newly onset thromboembolic event while on anticoagulant treatment, interruption of anticoagulant treatment before minor or major surgical procedures

# Study description

### Background summary

Treatment with direct oral anticoagulants (DOACs), in particular factor Xa inhibitors, is associated with an increased risk of abnormal uterine bleeding, particularly heavy menstrual bleeding (HMB), in premenopausal women. It has been suggested that abnormal uterine bleeding, including HMB and intermenstrual bleeding, occurs less frequently during treatment with the thrombin inhibitor dabigatran. The association between the type of DOACs (factor Xa versus thrombin inhibitor) and HMB has not been fully elucidated and merely assumptions on possible mechanisms exist. Use of tranexamic acid during the menstrual period may be effective in patients with HMB, but prospective data regarding safety in patients with an indication for anticoagulant treatment are lacking. DOACs are prescribed increasingly and a direct comparison between dabigatran and a factor Xa inhibitor, as well as an evaluation of the effects of additional tranexamic acid in women with HMB is highly relevant for clinical practice.

### Study objective

To evaluate management strategies in premenopausal women with heavy menstrual bleeding associated with factor Xa inhibitor therapy.

### Study design

Randomised controlled trial.

### Intervention

Eligible patients will be randomised in a 1:1:1 ratio to switch to dabigatran, to continue treatment with the factor Xa inhibitor without intervention, or to continue treatment with the factor Xa inhibitor with the addition of 1 gram tranexamic acid three times a day during the first four days of the menstrual period.

### Study burden and risks

Study procedures will coincide with routine clinical care for anticoagulated patients with HMB and potentially eligible patients will undergo extensive evaluation of HMB as part of standard medical practice. Participants will be asked to fill out the PBAC-assessment and a menstrual bleeding questionnaire, which will be evaluated in a monthly telephone call for study follow-up. The risk and burden of these assessments are small.

## Contacts

### Public

Academisch Medisch Centrum

Meibergdreef 9
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NL
**Scientific**
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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)

## Inclusion criteria

- premenopausal women
- age *18 years
- anticoagulant treatment with a factor Xa inhibitor
- indication for anticoagulant treatment >3months after inclusion
- heavy menstrual bleeding and a PBAC-score >150
- use of adequate contraceptive methods during study participation (this is advised to any woman on factor Xa inhibitors during fertile ages, regardless of study participation)

## Exclusion criteria

- PBAC-score *150
- postmenopausal women; women >12 consecutive months of spontaneous amenorrhea
- concomitant use of hormonal therapy as a new intervention for HMB
- pregnancy or currently planning for pregnancy
- active malignancy or treatment with chemotherapy/radiotherapy

- cervical preneoplastic lesions
- contra indication for the registered products dabigatran or tranexamic acid
- any condition that, as judged by investigator, would place the subject at an increased risk of harm if she participated in the study

# Study design

## Design

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| Study phase: | 4 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |

**Primary purpose:** Treatment

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 13-02-2020 |
| Enrollment: | 110 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | Cyklokapron |
| Generic name: | Tranexamic Acid |
| Registration: | Yes - NL intended use |
| Product type: | Medicine |
| Brand name: | Pradaxa |
| Generic name: | Dabigatran etexilate |
| Registration: | Yes - NL intended use |

## Ethics review

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| Approved WMO Date: | 16-10-2019 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 12-11-2019 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 24-02-2020 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 05-03-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 18-03-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 23-03-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 28-05-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 24-06-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 01-07-2021 |

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| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 06-09-2021 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 15-01-2022 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |

# 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 |
|---|---|
| EudraCT | EUCTR2019-002138-35-NL |
| CCMO | NL70177.018.19 |