# Clinical trial of dabigatran on airway inflammation and coagulation in severe asthma.

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We hypothesize that in patients with severe corticosteroid dependent asthma Dabigatran etexilate will: 1. Reduce airway inflammation; 2. Improve asthma control and pulmonary function; 3. Reduce hypercoagulability in the airways.

| | |
|---|---|
| **Ethische beoordeling** | Positief advies |
| **Status** | Werving tijdelijk gestopt |
| **Type aandoening** | - |
| **Onderzoekstype** | Interventie onderzoek |

## Samenvatting

### ID

NL-OMON29666

**Bron**
Nationaal Trial Register

**Verkorte titel**
ARTDECO

**Aandoening**

asthma
dabigatran etexilate
airway inflammation
blood coagulation

### Ondersteuning

**Primaire sponsor:** Academic Medical Centre, Department of Respiratory Medicine, Meibergdreef 9, 1105 AZ, Amsterdam, the Netherlands
**Overige ondersteuning:** Netherlands Asthma Foundation

Academic Medical Centre, Department of Respiratory Medicine, Meibergdreef 9, 1105 AZ, Amsterdam, the Netherlands

## Onderzoeksproduct en/of interventie

## Uitkomstmaten

### Primaire uitkomstmaten

Primary end point will be: The change in sputum eosinophilia between baseline and after 12 weeks use of dabigatran etexilate.

# Toelichting onderzoek

### Achtergrond van het onderzoek

In many patients with severe refractory asthma airway inflammation is insufficiently suppressed by inhaled corticosteroids alone and these patients require chronic oral corticosteroids to maintain asthma control. High levels of glucocorticoids, either endogenous or exogenous, have been shown to induce hypercoagulability and an increased risk of venous thromboembolism. In addition, asthma itself has also been associated with a prothrombotic state, and preliminary data from our group have shown an increased risk of pulmonary embolism in patients with severe asthma that was associated with chronic oral corticosteroid use and frequent asthma exacerbations.

Anticoagulants, such as inhaled heparin and low molecular weight heparin have been shown to attenuate airway inflammation in patients with allergic asthma. Other anticoagulants showed similar, but weaker effects in in vitro studies and animal models of asthma.

These data suggest that the interaction between coagulation and inflammation is important in disease severity, therapy resistance and thromboembolic complications in patients with severe asthma. Although all anticoagulants have some antiinflammatory properties, dabigatran etexilate seem the most appropriate given its mode of action, safety profile and availability.

### Doel van het onderzoek

We hypothesize that in patients with severe corticosteroid dependent asthma Dabigatran etexilate will:

1. Reduce airway inflammation;

2. Improve asthma control and pulmonary function;

3. Reduce hypercoagulability in the airways.

**Onderzoeksopzet**

Baseline, 4, 8 and 12 weeks.

**Onderzoeksproduct en/of interventie**

Patients will be randomized to receive either 220mg of dabigatran etexilate or placebo control for 12 weeks.

# Contactpersonen

## Publiek

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## Wetenschappelijk

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# Deelname eisen

## Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age ≥ 18 years;

2. Non-smoking patients, or patients who stopped smoking more than 12 months ago and smoked 10 pack years or less;

3. Able to give written and dated informed consent prior to any study-specific procedures;

4. All patients have previous evidence of variable airways obstruction within the last 5 yrs, as documented by at least one of the following:

A. Reversibility in forced expiratory volume in one second (FEV1) of ≥9% predicted after 4 puffs of a 100 µg salbutamol dose-aerosol, administered via a spacer;

B. A mean diurnal variation in peak expiratory flow (PEF) ≥15% (highest PEF-lowest PEF) per mean PEF on ≥4 days per week for a minimum of 2 weeks;

C. An increase in FEV1 of ≥400 mL after a course of prednisolone 0.5 mg•kg−1•day−1 for 14 days;

D. A provocative concentration causing a 20% fall in FEV1 with histamine or methacholine <8 mg/mL.

5. On stable doses of oral and inhaled corticosteroids during the previous 4 weeks and during the study;

6. No other clinically significant abnormality on history and clinical examination;

7. Severe asthma according to the criteria of the International Consensus of the Innovative Medicine Initiative (IMI);

8. High- and ultrahigh dose of ICS (Fluticasone ≥1000 µg/day or equivalent drug) with continuous use of oral corticosteroids (≥5 mg/day);

9. Sputum eosinophil count ≥2 % of the total cell count.

## Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Women who are pregnant or lactating or who have a positive urine pregnancy test at screening;

2. Ongoing use of tobacco products of any kind or previous usage with a total pack year ≥ 10 years;

3. Use of omalizumab during the last 6 months before randomization;

4. Use of heparin, LMWH, NSAID or vitamin K antagonists;

5. Any bleeding diathesis;

6. History of acute intracranial disease or haemorrhagic stroke;

7. Major surgery, trauma, uncontrolled hypertension, or myocardial infarction in the past 3 months;

8. Gastrointestinal or urogenital bleeding, or ulcer disease in the past 6 months;

9. Severe liver disease;

10. Alanine or aspartate aminotransferase concentrations greater than two times the upper limit of the normal range in the past month;

11. Severe renal insuffi ciency (creatinine clearance less than 30 mL/min);

12. Active malignant disease;

13. Participation in any clinical investigational drug treatment protocol within the preceding 30 days;

14. Unwillingness or inability to coply with the study protocol for any other reason.

# Onderzoeksopzet

## Opzet

| | |
|---|---|
| Type: | Interventie onderzoek |
| Onderzoeksmodel: | Parallel |
| Toewijzing: | Gerandomiseerd |
| Blindering: | Dubbelblind |
| Controle: | Placebo |

## Deelname

Nederland

| | |
|---|---|
| Status: | Werving tijdelijk gestopt |
| (Verwachte) startdatum: | 15-03-2012 |
| Aantal proefpersonen: | 36 |
| Type: | Verwachte startdatum |

# Ethische beoordeling

Positief advies

| | |
|---|---|
| Datum: | 28-02-2012 |
| Soort: | Eerste indiening |

# Registraties

## Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

## Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

## In overige registers

| Register | ID |
|---|---|
| NTR-new | NL3168 |
| NTR-old | NTR3312 |
| Ander register | AF / EudraCT number : 3.2.11.021 / 2011-005406-30; |
| ISRCTN | ISRCTN wordt niet meer aangevraagd. |

# Resultaten

**Samenvatting resultaten**
N/A