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

No registrations found.

Ethical review	Positive opinion
Status	Suspended
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON29666

Source
Nationaal Trial Register

Brief title
ARTDECO

Health condition

asthma
dabigatran etexilate
airway inflammation
blood coagulation

Sponsors and support

Primary sponsor: Academic Medical Centre, Department of Respiratory Medicine, Meibergdreef 9, 1105 AZ, Amsterdam, the Netherlands
Source(s) of monetary or material Support: Netherlands Asthma Foundation

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

Intervention

Outcome measures

Primary outcome

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

Secondary outcome

Secondary endpoints will be:

1. Changes in markers of hemostasis and inflammation in blood, induced sputum and exhaled breath;

2. Changes in spirometry and asthma control questionaire (ACQ).

Study description

Background summary

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.

Study objective

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.

Study design

Baseline, 4, 8 and 12 weeks.

Intervention

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

Contacts

Public
Academic Medical Centre
Dept. of Respiratory Medicine (F5-144)
Meibergdreef 9
C.J. Majoor
Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5664356
Scientific
Academic Medical Centre
Dept. of Respiratory Medicine (F5-144)
Meibergdreef 9
C.J. Majoor
Amsterdam 1105 AZ
The Netherlands
+31 (0)20 5664356

Eligibility criteria

Inclusion criteria

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.

Exclusion criteria

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.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Suspended
Start date (anticipated):	15-03-2012
Enrollment:	36

Type:	Anticipated

Ethics review

Positive opinion Date:	28-02-2012
Application type:	First submission

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
NTR-new	NL3168
NTR-old	NTR3312
Other	AF / EudraCT number : 3.2.11.021 / 2011-005406-30;
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results
N/A