A randomised controlled trial of Dabigatran Etexilate on airway inflammation and coagulation in severe corticosteroid dependent asthma.

Published: 13-12-2011
Last updated: 01-05-2024

To investigate the effect of dabigatran etexilate on airway inflammation, hemostasis and asthma control in patients with severe asthma.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bronchial disorders (excl neoplasms)
Study type	Interventional

Summary

ID

NL-OMON39442

Source
ToetsingOnline

Brief title
ARTDECO

Condition

- Bronchial disorders (excl neoplasms)

Synonym
severe asthma, Severe refractory asthma

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: collectebusfondsen

Intervention

Keyword: Asthma, Blood Coagulation, Dabigatran etexilate, Inflammation

Outcome measures

Primary outcome

Primary endpoint will be the change from baseline in percentage of eosinophils in induced sputum as a marker of anti-inflammatory activity after 3 months treatment with dabigatran etexilate.

Secondary outcome

Secondary endpoints will be changes from baseline in asthma control, lung function, exhaled nitric oxide, and changes in markers of hemostasis and inflammation in blood and induced sputum.

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. 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

To investigate the effect of dabigatran etexilate on airway inflammation, hemostasis and asthma control in patients with severe asthma.

Study design

a single-center, randomized, parallel, double-blind, placebo-controlled trial

Intervention

Patients will be randomized to receive dabigatran etexilate (once daily 220 mg orally) or identical placebo for 12 weeks.

Study burden and risks

For patients with severe, refractory asthma, there are hardly any therapeutic options except oral corticosteroids that are associated with serious long-term side effects. This study will investigate whether anticoagulant treatment may have beneficial effects in these patients in terms of reduction of the procoagulant and inflammatory state, and better asthma control (by ACQ). Adverse effects of anticoagulants are well documented and limited with a prophylactic dose. Dabigatran etexilate is a new oral thrombininhibitor with a similar bleeding risk as that of low molecular weight heparins. Since a prophylactic dose will be administered in the present study, we believe that the potential benefits of participating in this study largely outweigh the potential risks of this treatment for patients with severe refractory asthma.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Age >= 18 years
• Non-smoking patients, or patients who stopped smoking more than 12 months ago and KCO >= 90% pred.
• Able to give written and dated informed consent prior to any study-specific procedures
• All patients have previous evidence of variable airways obstruction within the last 5 yrs, as documented by at least one of the following:
*- 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.
*- 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.
*- An increase in FEV1 of >=400 mL after a course of prednisolone 0.5 mg•kg*1•day*1 for 14 days.
*- A provocative concentration causing a 20% fall in FEV1 with histamine or methacholine <8 mg/mL.
• On stable doses of oral and inhaled corticosteroids during the previous 4 weeks and during the study.
• No other clinically significant abnormality on history and clinical examination
• Severe asthma according to the criteria of the International Consensus of the Innovative Medicine Initiative (IMI)
• High- and ultrahigh dose of ICS (Fluticasone >=1000 µg/day or equivalent drug) with continuous use of oral corticosteroids (>=5 mg/day).
• Sputum eosinophil count > 3% of the total cell count.

Exclusion criteria

• Women who are pregnant or lactating or who have a positive urine pregnancy test at screening
• Ongoing use of tobacco products of any kind.
• Ex-smoking patients with reduced diffusion capacity: KCO < 90% pred.
• Use of omalizumab during the last 6 months before randomization
• Use of heparin, LMWH, NSAID or vitamin K antagonists.
• Any bleeding diathesis
• History of acute intracranial disease or haemorrhagic stroke
• Major surgery, trauma, uncontrolled hypertension, or myocardial infarction in the past 3 months
• Gastrointestinal or urogenital bleeding, or ulcer disease in the past 6 months
• Severe liver disease
• Alanine or aspartate aminotransferase concentrations greater than two times the upper limit of
the normal range in the past month
• Severe renal insufficiency (creatinine clearance less than 30 mL/min)
• Active malignant disease
• Participation in any clinical investigational drug treatment protocol within the preceding 30 days
• Unwillingness or inability to comply 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
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-07-2012
Enrollment:	36
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Pradaxa
Generic name:	Dabigatran etexilate
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	13-12-2011
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-01-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-03-2013
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	EUCTR2011-005406-30-NL
CCMO	NL38698.018.11