Anti-inflammatory effects of tiotropium in patients with stable COPD-A randomized controlled double-blind study

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This research proposal aims to assess the anti-inflammatory effects after 6 weeks treatment with tiotropium compared to placebo in patients with stable COPD.

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

Summary

ID

NL-OMON55417

Source
ToetsingOnline

Brief title
ANTIOFLAM study

Condition

- Bronchial disorders (excl neoplasms)

Synonym
Chronic obstructive pulmonary disease, COPD

Research involving
Human

Sponsors and support

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

Intervention

Keyword: anti-inflammatory effects, COPD, tiotropium

Outcome measures

Primary outcome

A decrease of the amount of interleukin-6 en interleukin-8 proteins in induced sputum will be the main parameter for assessing the anti-inflammatory effects of 6 week treatment with tiotropium in patients with stable COPD.

Secondary outcome

Additionally, changes in sputum cell differentials and other cytokine parameters (protein, mRNA,LTB4), blood cell differentials, CRP, and cytokine parameters, health related quality of life (CCQ, CAT) will be assessed as well as changes in post-bronchdilator FEV1.

Study description

Background summary

Acetylcholine is the primary parasympathetic neurotransmitter in the airways, and induces bronchoconstriction. Since the cholinergic tone appears to be the major reversible component of obstruction, muscarinic receptor antagonism and bronchodilation represent the primary goal of anticholinergic therapy in patients with COPD. Long-acting anticholinergic therapy is central in GOLD stage B-D, because of improvements in lung function, quality of life, and especially reduction of exacerbations. The elicited reduction in exacerbations with the LAMA tiotropium appears larger than that of the LABA salmeterol even when the bronchodilation is similar. These effects on exacerbation frequency suggest that tiotropium might exert anti-inflammatory effects in the airways next to bronchodilatory effects. This has been proven in animal models
Such an anti-inflammatory effect of anticholinergic intervention could be clinically relevant; however it has not been previously demonstrated in patients with COPD.
We hypothesize that tiotropium bromide reduces the ongoing inflammation in patients with COPD compared to placebo. We expect a decrease of the amount of

interleukine-6 en interleukine-8 proteins in induced sputum after treatment with tiotropium bromide

Study objective

This research proposal aims to assess the anti-inflammatory effects after 6 weeks treatment with tiotropium compared to placebo in patients with stable COPD.

Study design

This will be a parallel design randomized controlled double-blinded study.

Intervention

COPD patients will be randomized to the treatment group (Tiotropium Respimat) or to the placebo group.

Study burden and risks

It is not expected that subjects will receive any major individual benefit from participation in this study. The study also has no major risks. Minor risks for participants in this study are: 1) blood collection may cause bruising; 2) sputum induction can lead to transient bronchoconstriction; 3) Tiotropium Respimat may cause mild side effects, most notably dry mouth. It has been a major drug for this indication already for more than 10 years in most countries worldwide.

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

•Men or women, age >= 40 years
•post-bronchodilator FEV1 >= 0.8 Litres
•smoking history of > 10 pack years.
•Being in a stable phase of COPD, as judged by the investigator. No courses of systemic steroids last 4 weeks
•Post-bronchodilator FEV1 / FVC ratio < 70% and post-bronchodilator FEV1 < 80%pred.

Exclusion criteria

•Treatment with long-acting anticholinerigcs <4 weeks before the start of the study.
•Treatment with corticosteroids <4 weeks before the start of the study.
•Concomitant diagnosis of asthma.
•Females of childbearing potential without an efficient contraception unless they meet the following definition of post-menopausal: 12 months of natural (spontaneous) amenorrhea or 6 months of spontaneous amenorrhea with serum FSH >40 mIU/mL or the use of one or more of the following acceptable methods of contraception:
a) Surgical sterilization (e.g. bilateral tubal ligation, hysterectomy).
b) Hormonal contraception (implantable, patch, oral, injectable).
c) Barrier methods of contraception: condom or occlusive cap (diaphragm or cervical/vault caps) with spermicidal foam/gel/cream/suppository.
d) Continuous abstinence.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	19-08-2019
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tiotropium respimat 2.5 µg
Generic name:	tiotropium
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	01-11-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-12-2018
Application type:	First submission

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	25-03-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-04-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-12-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-01-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-05-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	28-09-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2018-002173-22-NL
CCMO	NL65946.042.18