Influence of macrolide maintenance therapy and bacterial colonisation on exacerbation frequency and progression of COPD, a randomized double-blind placebo-controlled trial

Published: 29-10-2009
Last updated: 04-05-2024

To assess whether maintenance treatment with macrolide antibiotics in COPD patients with three or more exacerbations in the previous year can decrease the exacerbation rate in the year of treatment.

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

Summary

ID

NL-OMON36440

Source
ToetsingOnline

Brief title
COLUMBUS trial

Condition

- Bronchial disorders (excl neoplasms)

Synonym
chronic bronchitis, emphysema

Research involving
Human

Sponsors and support

Primary sponsor: Amphia Ziekenhuis
Source(s) of monetary or material Support: Stichting Solong.

Intervention

Keyword: bacterial colonisation, COPD, disease progression, macrolide

Outcome measures

Primary outcome

Reduction in the number of exacerbations in the year of treatment.

Secondary outcome

- Measurement of lungfunction parameters: FEV1 (L), FVC (L), IC(L), 6 minute walking test.

- BODE-index.

- Disease specific quality of life measured by St. George*s Respiratory Questionnaire (SGRQ).

- Generic health status measured by the 12-Item Short Form Health Survey (SF-12).

- Assessment of presence of type D personality by DS-14 questionnaire.

- Indication of anxiety and depression by Hospital Anxiety Depression Scale (HADS).

- Microbiology: Sputum specimens will be cultured. Polymerase chain reaction (PCR) in sputum and serology in serum for atypical and viral microorganisms will be performed. A rectal swab will be performed to to assess the effect of maintenance antibiotics on the intestinal flora via ISpro. Faeces samples will be collected to assess and characterize antibiotic resistancy patterns via

metagenomic sequencing. When sputum is not obtained, a throat swab will be performed.

- Measurement of inflammatory markers in serum.

- Difference in treatment effect between subjects with and without steroid maintenance therapy as hypothesis-generating secondary analysis.

- Decrease in percentage of clinical versus outpatient department exacerbations.

- Adverse events of treatment.

- Length of hospital stay.

- Time till next exacerbation.

Study description

Background summary

Chronic obstructive pulmonary disease (COPD) is characterized by progressive development of airflow limitation that is poorly reversible. Because of a poor understanding of COPD pathogenesis, treatment is mostly symptomatic and new therapeutic strategies are limited. There is a direct relationship between the severity of the disease and the intensity of the inflammatory response. One of the hypothesis for persistent airway inflammation, besides smoking, is that the presence of recurrent infections is responsible for this condition. Macrolide antibiotics have a bacteriostatic as well as anti-inflammatory properties. There is consistent evidence that macrolide therapy reduces infective exacerbations, decreases the requirement for additional antibiotics and improves nutritional measures in patients with cystic fibrosis, which is also a chronic inflammatory pulmonary disease. Until now, the number of studies investigating macrolide therapy in COPD is clearly extremely limited, but the positive benefit seen in other chronic inflammatory pulmonary diseases suggests that macrolide therapy can also have beneficial effects in patients with COPD.

Study objective

To assess whether maintenance treatment with macrolide antibiotics in COPD patients with three or more exacerbations in the previous year can decrease the exacerbation rate in the year of treatment.

Study design

The study will be conducted as a prospective randomized double-blind placebo-controlled trial.

Intervention

Subjects will be randomized to receive either Azithromycin 500mg 3 times a week or placebo 3 times a week.

Study burden and risks

The study participants will come to the outpatient department 5 times in 1 year. During all 5 visits a few questionnaires will be taken, blood and sputum samples will be taken, a lung function test and a 6 minute walking test will be done. Each of these visits will take about 1,5 to 2 hours.
Also the study participants will have to take either azithromycin or placebo 3 times a week during 1 year.
The burden of the tests is not very high. The tests are standard test which take place daily. For the rectal swabs and faeces samples the study participants have to give additional consent as these are not routine tests.
The risks for the study subjects are explained in the patient information folder.

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

COPD patients who have had 3 or more exacerbations in the previous year, which have been treated with antibiotics and/or corticosteroids.

Exclusion criteria

Use of antibiotics or a course of high doses of systemic steroids defined as more than 10 mg of prednisone a day within a month prior to involvement in the study.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-05-2010

Enrollment:	92
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Azitrocin, Ultreon, Azadose, Sumamed, Azacleus, Nuzaca, Toraseptol, Vinzam, Zentavion
Generic name:	Azithromycin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	29-10-2009
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	03-12-2009
Application type:	First submission
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	31-08-2010
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	27-10-2010
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)
Approved WMO Date:	10-11-2011
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)

Approved WMO Date:	24-11-2011
Application type:	Amendment
Review commission:	TWOR: Toetsingscommissie Wetenschappelijk Onderzoek Rotterdam e.o. (Rotterdam)

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	EUCTR2009-015857-19-NL
ClinicalTrials.gov	NCT00985244
CCMO	NL29500.101.09

Study results

Date completed:	18-06-2013
Actual enrolment:	92