Bronchiectasis and long term Azithromycin (AZM) Treatment: a randomised placebo-controlled trial studying disease modifying effects of immunomodulating treatment

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Primary objectives1. Does prolonged antibiotic treatment with AZM reduce the number of bacterial exacerbations in patients with bronchiectasis?2. Does treatment with AZM increase lung function parameters (Δ FEV1, Δ FVC)?...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON30795

Source
ToetsingOnline

Brief title
The BAT trial: AZM versus placebo in bronchiectasis

Condition

- Respiratory tract infections

Synonym
BRONCHIECTASIS, CHRONIC BRONCHITIS

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Centrum Alkmaar
Source(s) of monetary or material Support: Subsidie van het Foreest Instituut;MCA;Alkmaar

Intervention

Keyword: Antibiotic Prophylaxis, Azithromycin, Bronchiectasis, Inflammation, Macrolide, randomized controlled trial (RCT)

Outcome measures

Primary outcome

Reduction in number exacerbations.

Definition of exacerbation: increase in dyspnoea, coughing, and sputum

production for which a course of prednisolone and/or antibiotic is needed.

Change in lung function parameters measured by spirometry: FEV1 (L), FVC (L).

Secondary outcome

Symptomscore. A number of symptoms will be measured on a Visual Analogue Scale

(LRTI-VAS) (Appendix 2)

Bacterial coloniation. Sputum samples will be cultures. The isolated bacteria

will be quantified.

Inflammatory markers.

Sputum: MPO, ECO, elastase, IL-1-α of IL-1β, IL-6, IL-8, TNF-α, MMP*s.

Serum: CRP, procalcitonine, Il-6, IL-8, TNF-α.

Quality of life.

Change in quality of life will be measured by St. George*s Respiratory

Questionnaire (SGRQ).

Study description

Background summary

Rationale: Patients with bronchiectasis often experience lower respiratory tract infections with progression of symptoms and decline in quality of life. Macrolides, as has been shown in panbronchiolitis and cystic fibrosis, may break or weaken the link between infection and inflammation resulting in an improvement of symptoms. Also the number of exacerbations may lowered.
Objective: A reduction in number of infective exacerbations and improvement in longfunction by AZT treatment are the primary objectives. Secondary objectives that will be evaluated are: symptoms score, quality of life, inflammatory parameters, bacterial colonisation, and adverse events.
Study design: Randomised double blind multicenter study in the Netherlands. Patients will be stratified for colonisation with P.aeruginosa.
Study population: Patients with bronchiectasis demonstrated by HR-CT scan or bronchography.
Intervention: Patients receive AZT 500 mg p.o. every other day or placebo.
Main study parameters/endpoints: Reduction in number exacerbations, definied as increase symptoms such as dyspnoea, coughing, and sputum production for which a course of prednisolone and/or antibiotic is needed. Change in lung function parameters (FEV1, FVC) measured by spirometry is the other primairy endpoint.
Nature and extent of the burden and risks associated with participation, benefit and group relatedness: The risk of participating in this study is low. Laboratory, radiographic examinations, and pulmonary function tests are commonly used as diagnostic procedures during outpatients visits and during exacerbations. Adverse effects in maintance treatment with AZT are usually mild and mainly gastrointestinal. Sometimes rash and abnormal liver function tests are observed. A better quality of life will probably the beneficial effect of long term treatment with AZT. This will be achieved by a reduction in respiratory and non-respiratory symptoms and number of exacerbations

Study objective

Primary objectives
1. Does prolonged antibiotic treatment with AZM reduce the number of bacterial exacerbations in patients with bronchiectasis?

2. Does treatment with AZM increase lung function parameters (Δ FEV1, Δ FVC)?

Secondary objectives
1. Is there any improvement in symptom score during treatment with AZM?
2. What is the effect of AZM on bacterial colonisation?
3. Does treament with AZM reduce inflammatory parameters?
4. Does treatment with AZM change the quality of life?
5. Is there any differences in adverse events between AZM en placebo treatment?

Study design

Randomised double blind multicenter study in the Netherlands. Patients will be stratified for colonisation with P.aeruginosa.

Intervention

AZM tablet 500 mg every other day versus placebo 500mg

Study burden and risks

Minimal risk: chance of mild adverse effects
Some extra visits to outpatient ward

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

•Patients aged 18 >= years
•Bronchiectasis diagnosed by plain bronchography or high resolution computer tomography.
•Minimal 4 lower respiratory tract infection (LRTI) treated with oral/IV antibiotics in the year preceeding the study inclusion.
•The presence of chronic respiratory symptoms such as cough, dyspnoea, expectoration of sputum.
•Three sputum cultures with either P.aeruginosa or H. influenzae in the preceeding year.
•Informed consent.

Exclusion criteria

•Previous (>= 6 weeks) prolonged macrolide therapy.
•Pregnant or lactating women.
•Allergy to macrolides.
•Intolerance to macrolides.
•Liver disease (alanine transaminase and/or aspartate transaminase levels 2 or more times the upper limit of normal).
•Use of antibiotics within 14 days of screening.
•Use of orale or IV corticosteroids (>= 30 mg prednisolone/daily) within 30 days of screening.
•Initiation of tobramycin/colimycin solution for inhalation, recombinant human DNAase inhalation solution, or high dose ibuprofen within 30 dagen of screening.
•Other research medication started 2 months prior to inclusion.

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:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-04-2008
Enrollment:	90
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Zithromax
Generic name:	azithromycin
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	07-02-2007
Application type:	First submission
Review commission:	METC Noord-Holland (Alkmaar)

Approved WMO

Date:	24-04-2007
Application type:	First submission
Review commission:	METC Noord-Holland (Alkmaar)

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	EUCTR2007-000001-30-NL
ClinicalTrials.gov	NCT00415350
CCMO	NL16025.094.07