Pulmonary NTM disease: A regimen of ethambutol and azithromycin with as adjunctive rifampicin vs clofazimine.

Published: 05-10-2015
Last updated: 19-04-2024

To determine the effectiveness of the currently recommended treatment regimens.

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

Summary

ID

NL-OMON45792

Source
ToetsingOnline

Brief title
PERC

Condition

- Respiratory tract infections

Synonym
MAC-PD, pulmonary infection with M.avium complex

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Grotendeels pragmatisch (1e geldstroom);3e geldstroom Insmed,Insmed; deel van salaris promovendus,Novartis doneert clofazimine

Intervention

Keyword: Clofazimine, M.avium complex, Non tuberculous mycobacteria, Rifampicine

Outcome measures

Primary outcome

The primary endpoint is the percentage of patients that has converted to negative sputum cultures after 6 months of antibiotic treatment.

Secondary outcome

1. Sputum culture conversion at 1, 2 and 4 months (which treatment arm shows the fastest conversion).

2. The differences in radiological outcome.

3. The percentage of patients having adverse events related to study drugs and the percentage of patients that deviate from protocol.

4. Differences in patient-reported health status after 6 months of treatment (St. George's Respiratory Questionnaire (SGRQ)

5. Difference in lung function parameters: FEV1 (L), FVC (L), IC (L), FRC (L), TLC (L), 6 minute walking distance (6MWD).

6. Area under the time-concentration curve (AUC) and peak serum concentration (Cmax) at 1 month and 4 months for clofazimine, rifampicin, ethambutol and azithromycin.

7. Correlation between pharmacokinetics and adverse events

8. Correlation between pharmacokinetics and pharmacodynamics (culture conversion) after 1,2,4,6 months of treatment.

Study description

Background summary

Pulmonary disease caused by Mycobacterium avium complex is emerging in the Netherlands, particularly among patients with chronic obstructive pulmonary disease. Since very few clinical trials have been performed, the optimal antibiotic treatment for these infections is unknown. Different treatment recommendations have been issued, none of which have been compared in clinical trials.

Study objective

To determine the effectiveness of the currently recommended treatment regimens.

Study design

Open label randomized clinical trial. In this study we compare two regimens that are being used in daily clinical practice (rifampicine-ethambutol-azithromycin and clofazimine-ethambutol-azithromycin). Patients will have a follow up of 6 months during this trial.

Intervention

One group receives the regimen recommended by the American Thoracic Society (azithromycin, rifampicin and ethambutol) and one group receives the regimen recommended by Canadian investigators (azithromycin, clofazimine and ethambutol).

Study burden and risks

The diagnostic interventions in the study groups proposed are part of normal clinical practice. The antibiotics used in the treatment arms have shown efficacy in a clinical trial and case series, the antibiotics are thus used for a known indication.

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

- ATS diagnostic criteria for nodular bronchiectatic or fibro-cavitary MAC-PD met, i.e. symptomatic, fibro-cavitary lesions, bronchiectasis or nodules seen on X-ray or (HR)CT scan of the lungs and *2 positive cultures of the same M. avium complex species (Griffith et al., 2007).
- At least one of the positive cultures must be done in the last 4 months before inclusion.
- Age > 18 years.
- Signed and dated patient informed consent.
- Patients can be included in spite of previous treatment if treatment was conform ATS-guidelines and they did not receive any treatment in the last 2 months.

Exclusion criteria

- Extensive cavitary MAC-PD defined as cavitary lesions in two or more lobes with the smallest cavity having a diameter >3 centimetre, measured from Computed Tomography (CT) images or when physician deems it favourable to treat the patient with additional amikacine
- Macrolide-resistant MAC strain isolated at the time of diagnosis.
- A relevant medical history or current condition that might interfere with drug absorption, distribution, metabolism or excretion.

- Use of concomitant drugs that interfere with the pharmacokinetics of the study drugs.
- HIV infected.
- Diagnosed with cystic fibrosis.
- Pregnant or breastfeeding or inadequate contraceptive measures (if applicable).
- ALAT > 3 times the upper limit of normal.
- ASAT > 3 times the upper limit of normal.
- An abnormal serum creatinine level (defined as a level that is higher than the upper limit of normal).
- Active pulmonary malignancy (primary or metastatic) or any other malignancy requiring chemotherapy or radiotherapy within 1 year before screening or anticipated during the study period.
- - Use of drugs for co-morbid conditions that have interactions with any of the drugs in the study and that cannot be safely exchanged for an alternative drug for which such interactions are not known to occur; this is only applicable if these others drugs lower one of study drugs or cause safety issues; such as medication that causes QTc interval prolongation; such as bedaquiline, antidepressants, antiarrhythmics or fluoroquinolones, voriconazole, protease inhibitors
- Active alcohol abuse.
- Hypersensitivity to one of the study drugs.
- Patients with previous failure of treatment for MAC-PD, defined as persistent culture positivity despite >6 months of guideline-recommended treatment.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-04-2016
Enrollment:	124

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Azithromycin Teva
Generic name:	Azithromycin
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Lamprene
Generic name:	Clofazimine
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Myambutol
Generic name:	Ethambutol
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Rifadin
Generic name:	Rifampicin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	05-10-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-01-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-01-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	08-03-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
Other	2015-003786-28
EudraCT	EUCTR2015-003786-28-NL
CCMO	NL54916.091.15