Pharmacokinetic study of minocycline in patients with nontuberculous mycobacterial disease

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Mycobacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON54666

Source
ToetsingOnline

Brief title
MINO-PK

Condition

- Mycobacterial infectious disorders

Synonym
infection caused by a nontuberculous mycobacteria, NTM disease

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: STIMAG subsidie 2022

Intervention

Keyword: M. avium complex, Minocycline, Nontuberculous mycobacteria, Pharmacokinetics

Outcome measures

Primary outcome

Total exposure (area under the concentration versus time curve from T=0 up to

24 hours, after a 5-day dosing periode of minocycline; AUC0-24h), pre-dose

concentration (Ctrough) and peak serum concentration (Cmax) of minocycline

before and after start of a rifampicin containing regimen

Secondary outcome

Pharmacokinetic parameters of rifampicin.

Study description

Background summary

NTM disease is emerging in the Netherlands, particularly among patients with underlying (pulmonary) diseases like COPD. Current treatment regimens of NTM disease are challenging, with frequent adverse events and poor cure rates (50-70%) after an average treatment duration of 6-18 months. The currently recommended treatment regimen for pulmonary disease caused by Mycobacterium avium complex, M. xenopi, M. kansasii and M. malmoense consists of rifampicin, combined with ethambutol, azithromycin, isoniazid and possibly clofazimine and/or amikacine. During recent studies in the hollow fiber model, we identified minocycline as an active drug against M. avium complex bacteria, but there is no pharmacokinetic data available for patients with M. avium complex disease. In addition, it has not been established to what extent rifampicin, frequently used in M. avium complex pulmonary disease and a strong inducer of metabolic enzymes and drug transporters, will decrease the exposure to minocycline. Pharmacokinetic data of minocycline in actual patients with NTM disease will allow us to propose an appropriate dose of minocycline when co-administered with or without rifampicin in the target population.

Study objective

The primary objective is to describe the pharmacokinetics of a 5-day dosing

period of minocycline in patients with NTM disease.
The secondary objective is to evaluate the effect of rifampicin on the pharmacokinetics of a 5-day dosing period of minocycline in patients with NTM disease.

Study design

This is an open label, one-arm, two-period, fixed-order pharmacokinetic study in patients with NTM disease.

Subjects will receive two oral administrations of a 5-day dosing period of 200 mg minocycline.The first dosing period is given before the start of rifampicin (as part of the antimycobacterial therapy). The rest of the antimycobacterial regimen (e.g. ethambutol, a macrolide, isoniazid, possibly with additional clofazimine and amikacine) can be started prior to or simultaneous with minocycline as part of standard care. Rifampicin will be started after the first 5-day minocycline dosing period, when PK sampling is completed.. The second administration of a 5-day dosing period of minocycline is given after 1 month (±1 week) of rifampicin treatment.

On the fifth day of both 5-day dosing periods, minocycline will be taken on an empty stomach (8-hour overnight fast continued until 4 hours after administration). Patients will be sampled at t=0 (before minocycline administration) and at t=1, 2, 3, 4, 6, 8 and 24, hours (after minocycline administration), to measure plasma concentrations of minocycline. Additionally, during the second study visit samples at t = 2, 4 and 6 hours (after minocycline and rifampicin administration) will be sampled for rifampicin plasma concentration measurements.
On both study visits blood samples will be taken to assess kidney and liver function; i.e. hemoglobin, serum creatinine, urea, ASAT,ALAT, γ-GT, alkaline phosphatase and LDH measurements. Weight and BMI will be assessed on both occasions.

Intervention

Patients will receive two 5-day dosing periods of 200 mg minocycline

Study burden and risks

The potential risk of this study is small because it consists of two short-lasting (5-day) dosing periods of the study product. Risks include:
1) the possible side effects of minocycline: angioedema, rash, urticaria (0.1-1%) and fever, eosinophilia, neutropenia and thrombocytopenia (rare). A typical side-effect is photosensitivity to sunlight after taking minocycline. Patients are informed in advance about these side effects. Furthermore, they are monitored for side effects and they can reach a doctor at any time.

2) The 5-day delay of rifampicin treatment; this is an acceptable risk in our view, because MAC lung infections are chronic infections that typically require at least 18 months of treatment. Hence, relatively few time is lost.
3) the frequent blood sampling can be considered a burden for patients. Where possible, a peripheral intravenous catheter will be used for blood sampling.
4) the extra time burden for participants.

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/ERS/IDSA diagnostic criteria for NTM disease are met.

- The subject is eligible to start the guideline-recommended rifampicin-based regimen according to the treating physician.

.- Age >= 18 years.

- Signed and dated patient informed consent

Exclusion criteria

- ATS/ERS/IDSA diagnostic criteria for NTM disease are met.

- The subject is eligible to start the guideline-recommended rifampicin-based regimen according to the treating physician.

- Age >= 18 years.

- Signed and dated patient informed consent

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-06-2023
Enrollment:	15
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	Minocycline
Generic name:	Minocycline

Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	07-04-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-04-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-05-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-06-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-01-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	10-01-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-06-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-02-2024
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
EudraCT	EUCTR2019-000938-20-NL
ClinicalTrials.gov	NCT05861258
CCMO	NL69313.091.19