Pharmacokinetic evaluation and local tolerability of dry powder amikacin via the Cyclops® in patients with drug susceptible tuberculosis

Published: 04-10-2019
Last updated: 12-04-2024

The first main objective is to investigate the pharmacokinetic properties of dry powder amikacin at different dosages and compare the peak serum values to a single i.v. dose. The secondary main objective is to assess the local tolerability of dry…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Mycobacterial infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON55683

Source
ToetsingOnline

Brief title
Amika-01

Condition

- Mycobacterial infectious disorders

Synonym
Tuberculosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Amikacin, Dry powder, Inhalation, Tuberculosis

Outcome measures

Primary outcome

The following pharmacokinetic parameters will be calculated: actual dose (dose minus remainder in inhaler after inhalation), AUC0-24 (area under the curve from 0-24 h), Cmax (maximum serum concentration), Tmax (time to maximum serum concentration).

For local tolerability of the inhalation of dry powder amikacin the following procedures will be done. Both points need to have a positive result.

* Drop of FEV1 of >15 % (lung function measurement)

* Questioning/ registration adverse events

Secondary outcome

Inspiratory parameters during the inhalation maneuver. Following parameters will be calculated:

* dPmax (maximum pressure drop)

* Vi (inhaled volume)

* Ti (total inhalation time)

* PIF (peak inspiratory flow rate)

* MIF (mean inspiratory flow rate)

* FIR (average flow increase rate between 20% and 80% of PIF)

Study description

Background summary

Multidrug-resistant tuberculosis (MDR-TB) is defined as tuberculosis resistant to isoniazid and rifampicin. The incidence of MDR-TB worldwide is 3.9% for new cases and 21% for previously treated cases. However, the incidence of previously treated cases can rise to above 50% in eastern European countries.[1] With increasing frequency of MDR-TB (and even extensively drug-resistant types), morbidity and mortality due to TB fail to decline worldwide. Cornerstones of MDR-TB treatment are aminoglycosides, like amikacin, and fluoroquinolones. Amikacin is given intravenously for 6-8 months in the usual MDR-TB treatment. Since 2016 it can also be given for 4-6 months in the short-course treatment for MDR-TB. In many countries, this implicates long hospital admissions for the patients, as well as problems in venous access, often necessitating surgical insertion of venous access ports. Amikacin has the most potent effect when reaching a high peak serum concentration and this means that high doses have to be administered. Treatment with amikacin by inhalation would be a tremendous advantage due to the high local dose in the lungs, obtaining high local levels without the possible toxicity due to high serum levels.

Study objective

The first main objective is to investigate the pharmacokinetic properties of dry powder amikacin at different dosages and compare the peak serum values to a single i.v. dose.
The secondary main objective is to assess the local tolerability of dry powder amikacin via the Cyclops* at different dosages.

Study design

single center, active control, ascending dose response study

Study burden and risks

All participants included in this study are patients with DSTB, who are admitted at the Tuberculosis Center Beatrixoord. They will receive 3 different doses of amikacin using the DPI with (at least) one week in between doses, they will also receive one dose of intravenous amikacin. Before using the dry powder inhaler (DPI) they will receive instructions and their inspiratory flow will be tested. Before each test dose an indwelling canula will be inserted and before and after each test dose in total 9 blood samples will be collected. To investigate local tolerability, lung function tests will be performed and the

occurrence of adverse events will be scored.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Age above 18 years
* Diagnosed with DSTB, either by culture or molecular testing
* Obtained written informed consent

Exclusion criteria

* Pregnancy or breast feeding

* Subjects with known or suspected (by spontaneous reporting or by active questioning) renal, auditory, vestibular or neuromuscular dysfunction.
* History of adverse events on previous amikacin or other aminoglycoside use (by spontaneous reporting nor by active questioning)
* Concurrent use of aminoglycosides, cyclosporin, cisplatin, amfotericin B, cephalosporins, polymyxins and vancomycin

Study design

Design

Study type:	Observational invasive
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):	27-05-2020
Enrollment:	8
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Amikacin
Generic name:	Amikacin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	04-10-2019

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-02-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-04-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-08-2020
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)

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	EUCTR2018-001893-95-NL
CCMO	NL66924.042.18