Targeting antibiotics to pseudomonas aeruginosa in small airways (TAPAS) study in patients with cystic fibrosis: pharmacokinetics (PK)

No registrations found.

Ethical review	Positive opinion
Status	Other
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27081

Source
NTR

Brief title
TAPAS-PK study in patients with CF

Health condition

Cystic Fibrosis
Taaislijmziekte
Inhaled antibiotics
Inhalatie antibiotica
Pseudomonas aeruginosa

Sponsors and support

Primary sponsor: Erasmus MC, Rotterdam
Source(s) of monetary or material Support: fund = initiator = sponsor

Intervention

Outcome measures

Primary outcome

Primary endpoint: systemic bioavailability of inhaled tobramycin, defined as serum tobramycin AUC0-24hr.

Secondary outcome

 Maximum tobramycin serum level (Cmax);

 Time to maximum serum level (Tmax);

 Trough level of inhaled tobramycin (Ctrough; 24 hours post dose);

 Adverse events (coughing, bronchospasm).

Study description

Background summary

Small Airways Disease (SAD) plays an important role in the pathophysiology of cystic fibrosis (CF) lung disease. Chronic infection and airway inflammation lead to progressive structural tissue damage. Chronic infection with Pseudomonas aeruginosa (Pa) causes faster progression of CF lung disease. Inhaled tobramycin has proven to be effective in delaying lung function decline in chronic Pa infections. However, SAD is not improving with current inhaled therapy, either with standard jet-nebulizer or with dry powder inhaler. The newly introduced smart nebuliser Akita® is substantially more efficient to reach the small airways. Recently, the Akita® has been shown to improve SAD when delivering dornase alpha. Hence, the use of smart nebulisers like the Akita® for tobramycin inhalation therapy in CF patients chronically infected with Pa disease might significantly reduce SAD.
The bactericide efficacy of tobramycin is better with high peak levels. For intravenous use, tobramycin once daily is as effective as thrice daily and results in less toxicity. Inhaled tobramycin is dosed twice daily. Whether dosing once daily is as effective has never been studied. This would significantly reduce treatment burden. This grant application proposes a randomised study to investigate the pharmacokinetics and efficacy of inhaled tobramycin dosed once daily in patients with CF, ≥ 12 years, when using an Akita® compared with the PARI-LC® Plus. This will be conducted with a pharmacokinetic study in 10 patients to establish safety.

Study objective

Primary objective: To determine the safety of once daily inhalation of the recommended daily

dose of tobramycin with the Akita® and the PARI-LC® Plus nebulizer in patients with CF. Systemic absorption can be used as surrogate parameter for safety. Secondary objectives: To assess tolerability of inhalation of a double dose of tobramycin by registering adverse effects (coughing, bronchospasm). To compare pharmacokinetics of the recommended dose of inhaled tobramycin once daily with either the Akita® or PARI-LC® Plus to pharmacokinetic data from the literature about standard twice daily tobramycin inhalation with the PARI-LC® Plus.

Reaching a higher peak concentration by inhaling the double lung dose in one nebulisation session might be as effective, or perhaps even more effective for bacterial killing of Pseudomonas aeruginosa. Tobramycin inhalation targeted to the small airways with the Akita® nebulizer could contribute to better treatment of small airways disease in comparison with the conventional PARI-LC® Plus nebulizer. Both approaches will reduce the treatment burden and may improve adherence.

Study design

2 study visits

Intervention

Ten patients will be inhaling a double tobramycin dose twice at the outpatient clinic department in a cross-over setting: once with the Akita® nebulizer and the other time with the PARI-LC® Plus nebulizer.

Contacts

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Eligibility criteria

Inclusion criteria

 Age ≥ 18 years;

 FEV1 predicted ≥ 30%;

 Clinical diagnosis of CF and a positive sweat test or two CF-related mutations;

 Chronic PA colonization;

 Ability to breathe through a mouthpiece and to use the inhaler;

 Ability to perform lung function tests;

 Written informed consent.

Exclusion criteria

 Severe acute exacerbation of pulmonary infection (needing intravenous treatment);

 Patients receiving intravenous tobramycin treatment;

 Patients who are pregnant, planning to become pregnant or breastfeeding;

 Known impaired kidney function (estimated creatinine clearance < 60 ml/min);

 Known aminoglycoside hypersensitivity;

 Therapy (e.g. furosemide) or disease which may complicate evaluation of the study protocol, as judged by the investigator;

 Participation in another drug-investigating clinical study at the start or within 1 month prior to the start;

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Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Other
Start date (anticipated):	01-03-2014
Enrollment:	10
Type:	Unknown

Ethics review

Positive opinion

Date:	16-04-2014
Application type:	First submission

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
NTR-new	NL4394
NTR-old	NTR4525
Other	NL46747.098.13 : TAPAS-PK-2014

Study results