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

Gepubliceerd: 16-04-2014 Laatst bijgewerkt: 18-08-2022

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....

Ethische beoordeling	Positief advies
Status	Anders
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON27081

Bron
NTR

Verkorte titel
TAPAS-PK study in patients with CF

Aandoening

Cystic Fibrosis
Taaislijmziekte
Inhaled antibiotics
Inhalatie antibiotica
Pseudomonas aeruginosa

Ondersteuning

Primaire sponsor: Erasmus MC, Rotterdam
Overige ondersteuning: fund = initiator = sponsor

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

2 study visits

Onderzoeksproduct en/of interventie

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.

Contactpersonen

Publiek

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

 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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

 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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 Inability to follow instructions of the investigator.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Cross-over
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Anders
(Verwachte) startdatum:	01-03-2014
Aantal proefpersonen:	10
Type:	Onbekend

Ethische beoordeling

Positief advies

Datum:	16-04-2014
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL4394
NTR-old	NTR4525
Ander register	NL46747.098.13 : TAPAS-PK-2014

Resultaten