An Open-label Single-arm Pharmacokinetic Trial, Investigating the Effect of CYP3A4 inhibitor Ritonavir on the Pharmacokinetics of Erlotinib (N19RER)

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The pharmacokinetics of erlotinib 150mg QD is comparable to the pharmacokinetics erlotinib 75mg + ritonavir 200mg QD.

Ethische beoordeling	Niet van toepassing
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22639

Bron
NTR

Verkorte titel
N19RER

Aandoening

Non-small cell lung cancer Niet-kleincellig longkanker

Ondersteuning

Primaire sponsor: The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL)
Overige ondersteuning: N/A

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Effect of the highly potent CYP3A4 inhibitor ritonavir on the pharmacokinetics (PK) of erlotinib, measured as AUC0-24h, AUCmean, Cmax and Cmin

Toelichting onderzoek

Achtergrond van het onderzoek

The standard therapy for non-small cell lung cancer (NSCLC) has been chemotherapy for decades. By identification of oncogenic driver mutations in NSCLC, the treatment of this malignancy has been improved. The most common oncogenic drivers are epidermal growth factor receptor (EGFR), anaplastic lymphoma kinase (ALK), ret proto-oncogene (RET) and receptor tyrosine kinase 1 (ROS1). These oncogenic drivers can be successfully treated by tyrosine kinase inhibitors (TKI). By identifying more (potential) driver genes, the increase in available TKI's and the possibility for multiple treatment lines, the amount of TKI use will keep rising in the coming years. Since the cost of this treatments will cover a large part of healthcare budget, new treatment strategies are needed to use TKI's as effectively as possible. Currently, the knowledge about alternative treatment schemas is limited.

Erlotinib is a tyrosine kinase inhibitor(TKI), which inhibits the (activated mutated) epidermal growth factor receptor (EGFR). Erlotinib has several indications in e.g. non-small cell lung cancer (NSCLC) as maintenance therapy and in pancreatic cancer. There is a link between erlotinib exposure and toxicity. The link between the amount of exposure to erlotinib and response is not yet established.

Erlotinib is predominantly (~70%) metabolized by cytochrome P450 3A4 (CYP3A4), with CYP1A2 being responsible for the other ~30%. Co-administration of the potent CYP-3A4 inhibitor ketoconazole increased the erlotinib exposure (AUC) and maximum concentration (Cmax) approximately by two-fold (mean ratio from 0.88 to 1.64, and 0.83 to 1.67, respectively), in healthy non-smoker males. Ciprofloxacin, an inhibitor of CYP3A4 and CYP1A2, co-administration resulted in an erlotinib AUC and Cmax increase of 39% and 17%, respectively. No previous studies investigated the possibility to lower the dose of a TKI by co-administrate a CYP3A4 inhibitor.

Based on the above, the aim of this study is to investigate whether it is possible to decrease the dose of erlotinib when it is co-administrated with CYP3A4 inhibitor ritonavir. Also, this study will provide data about the pharmacokinetics of erlotinib with a highly potent CYP3A4 inhibitor ritonavir, which can be used as future guidance on dosing instructions and adverse events expectations when in daily care erlotinib is given to patients using a highly potent CYP3A4 inhibitor.

Doel van het onderzoek

The pharmacokinetics of erlotinib 150mg QD is comparable to the pharmacokinetics erlotinib 75mg + ritonavir 200mg QD.

Onderzoeksopzet

First patient in: Q2 2019, last patient last visit: Q4 2019.

Onderzoeksproduct en/of interventie

Patients will be treated with erlotinib 75mg QD the first 7 days of the study and start with ritonavir on 9 until day 15. PK measerment will take place at day 1 and day 15.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

 1. Patients treated with single agent erlotinib 150mg QD for at least 4 weeks
 2. Age ≥ 18 years
 3. Accessible for repeated venipunctures
 4. Ability to understand the study and give signed informed consent prior to beginning of protocol specific procedures

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

 1. Concomitant use of medication(s) which could influence the pharmacokinetics of erlotinib within 14 days or five half-lives of the drug (whichever is shorter) before start of the study, consisting of (but not limited to) CYP3A4-inhibitors/inductors
 2. Active uncontrolled infection or severe cardiac dysfunction (such as New York Heart Association Class III or IV cardiac disease, myocardial infarction within the last 6 months, unstable arrhythmias, or unstable angina)
 3. Impaired hepatic function (total bilirubin > ULN or Child-Pugh A, B and C)
 4. Woman who are pregnant or breast feeding
 5. Progression on erlotinib at the latest regular response evaluation
 5. Current smokers

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-03-2019
Aantal proefpersonen:	10
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Toelichting
N/A

Ethische beoordeling

Niet van toepassing
Soort: Niet van toepassing

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	NL7542
CCMO	NL-nummer: 68511.031.19

Resultaten

Samenvatting resultaten
N/A