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

No registrations found.

Ethical review	Not applicable
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON22639

Source
NTR

Brief title
N19RER

Health condition

Non-small cell lung cancer Niet-kleincellig longkanker

Sponsors and support

Primary sponsor: The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital (NKI-AVL)
Source(s) of monetary or material Support: N/A

Intervention

Outcome measures

Primary outcome

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

Secondary outcome

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

Study description

Background summary

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.

Study objective

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

Study design

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

Intervention

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.

Contacts

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Eligibility criteria

Inclusion criteria

 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

Exclusion criteria

 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

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2019
Enrollment:	10
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Plan description
N/A

Ethics review

Not applicable
Application type: Not applicable

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	NL7542
CCMO	NL-nummer: 68511.031.19

Study results

Summary results
N/A