The effect of the acid-reducing drug esomeprazol on afatinib in lung cancer patients

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Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON22493

Bron
NTR

Verkorte titel
BIO-GIO study

Aandoening

NSCLC

non small cell lungcarcinoma

NKCLC

niet-kleincellig longcarcinoom

Ondersteuning

Primaire sponsor: Erasmus MC Rotterdam
Overige ondersteuning: Boehringer

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

To evaluate the area under the curve of afatinib compared to afatinib concomitantly used with esomeprazole and to afatinib used with esomeprazole 3 hours prior in patients with non-small cell lung cancer.

Toelichting onderzoek

Achtergrond van het onderzoek

In The Netherlands, afatinib is registered for the treatment of advanced lung cancer. A majority of the patients benefit of the therapy, with lower rates of cancer cell proliferation. Many cancer patients have gastric complaints such as reflux and have to use proton pump inhibitors, or get proton pump inhibitors prescribed to prefent gastric complaints. Concomitant use of afatinib with a proton pump inhibitor could lower afatinib bio-availability by increasing pH, and thus preventing absorbtion of afatinib in the intestinal tract. Nevertheless, to date, this interaction has never been studied.

Doel van het onderzoek

Acid-reducing drugs, such as PPIs, may profoundly decrease solubility and, as a result, (negatively) affect the bioavailability of afatinib. Since a PPI is often used concomitantly during afatinib therapy, this DDI confronts physicians, patients, and pharmacists with major challenges. So, it is highly relevant to study the effects of this DDI on afatinib bioavailability in real patients. In case a clinically relevant PK interaction is found, dosing adjustments could be made to guarantee adequate drug concentrations of afatinib. In this study we will also evaluate the influence of time of esomeprazole intake (3h before afatinib and concomitantly) so we could give an advice on time-depending dosing when a relevant DDI is found. On the other hand, when PPIs do not affect afatinib bioavailability, a DDI can be ruled out. Therefore, in this study we will evaluate the impact of esomeprazole during afatinib treatment in patients with NSCLC.

Onderzoeksopzet

Patients will be admitted to the hospital for a total of three days, during which pharmacokinetic blood withdrawals will be performed. Patients will be randomized into 2 sequence groups consisting of three phases. In 2 phases patients are also treated with esomeprazole for a total of 28 days.

Onderzoeksproduct en/of interventie

Esomeprazole 40mg once daily, in a total of 10 days. Afatinib is taken in accordance to standard of care. Esomeprazole will be taken concomitant and 3 hours prior afatanib intake, each period for 5 days.

Contactpersonen

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age ≥ 18 years

2. Histological or cytological confirmed diagnosis of EGFR-mutated NSCLC

3. WHO Performance Status ≤ 1

4. Able and willing to sign the Informed Consent Form prior to screening evaluations

5. No concurrent (over the counter) use of other acid reducing drugs (PPIs, H2As and/or antacids), other than esomeprazole 40mg once daily during the study.

6. No concurrent medication or supplements which can interact with esomeprazole or afatinib during the study period (such as PgP-inhibitors/inducers).

7. Abstain from grapefruit, grapefruit juice, herbal dietary supplements, cranberry juice, and herbal tea during the study period.

8. Adequate baseline patient characteristics (complete blood count, and serum biochemistry which involves sodium, calcium, potassium, creatinin, calculation of creatinin clearance (MDRD), AST, ALT, gamma-GT, lactate dehydrogenase (LDH), total bilirubin, albumin, glucose within two weeks prior to the study.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Pregnant or lactating patients.

2. Patients with known impaired drug absorption (e.g. gastrectomy and achlorhydria)

3. Known serious illness or medical unstable conditions that could interfere with this study; requiring treatment (e.g. infection, bleedings, uncontrolled hypertension despite optimal medical management, HIV, hepatitis, organ transplants, kidney, cardiac and respiratory diseases).

4. Unwillingness to abstain from acid beverages such as orange juice and cola in the morning during afatinib treatment in this study.

5. Patients who are clinical dependent of use of PPIs or other acid reducing drugs, e.g. due to elevated risk for gastro-intestinal bleeding.

Onderzoeksopzet

Opzet

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

Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-08-2017
Aantal proefpersonen:	28
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	17-07-2017
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	NL6336
NTR-old	NTR6652
Ander register	: MEC 2017-251

Resultaten