The effects of the proton pump inhibitor esomeprazole on the bioavailability of afatinib (Giotrif®) in patients with non-small cell lung cancer (NSCLC) 'the BIO-GIO study'

Published: 22-05-2017
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Primary objective: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.Secondary objective:1....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON45272

Source
ToetsingOnline

Brief title
BIO-GIO study

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
NSCLC or lungcancer

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Bedrijf farmaceutische industrie;namelijk Boehringer Ingelheim.,Boehringer Ingelheim

Intervention

Keyword: Afatinib, Esomeprazole

Outcome measures

Primary outcome

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.

Secondary outcome

1. Other pharmacokinetic outcomes (i.e. clearance, maximum concentration and

time to Cmax).

2. To evaluate the incidence and severity of side-effects of treatment with

afatinib in absence and presence of esomeprazole.

Study description

Background summary

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.

Study objective

Primary objective:
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.

Secondary objective:
1. Other pharmacokinetic outcomes (i.e. clearance, maximum concentration and time to Cmax).
2. To evaluate the incidence and severity of side-effects of treatment with afatinib in absence and presence of esomeprazole.

Study design

Open label three-period, randomized, cross-over pharmacokinetic study.

Intervention

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.

Study burden and risks

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. Patients do not benefit individually from this study. Major risks to be expected are side effects of esomeprazole or afatinib for which patients will be observed carefully.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

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.

Exclusion criteria

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.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	02-08-2017
Enrollment:	28
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Giotrif
Generic name:	Afatinib
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Nexium
Generic name:	Esomeprazole
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	22-05-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-07-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-05-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-05-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
EudraCT	EUCTR2017-001284-20-NL
CCMO	NL61424.078.17