Thte effect of acid reducing agents on the single dose pharmacokinetics of PQR309 and the absolute bioavailability, safety and tolerability of PQR309 following oral and intravenous administration in healthy subjects.

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

Summary

ID

NL-OMON43263

Source
ToetsingOnline

Brief title
Effect of acid reducing agents on PK of PQR309.

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Cancer

Research involving
Human

Sponsors and support

Primary sponsor: PIQUR Therapeutics AG
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: Cancer, PQR309

Outcome measures

Primary outcome

To assess the effect of acid reducing agents given either concomitantly or staggered on the pharmacokinetics (PK) of PQR309 following oral administration.

Secondary outcome

To derive primary and secondary PK parameters of PQR309 and their between subject variability after oral and intravenous (iv) administration in non-smokers and smokers.

To evaluate the effect of CYP1A2 inhibition on the PK parameters of PQR309 in smokers.

To evaluate the safety and tolerability of PQR309 following oral and iv administration of single doses in healthy volunteers in the absence and presence of acid reducing agents or a CYP1A2 inhibitor.

Study description

Background summary

PQR309 is a new investigational compound that may eventually be used for the treatment of cancer patients. The phosphoinositide 3-kinase

(PI3K)/AKT/mammalian target of rapamycin (mTOR) pathway is an intracellular signaling pathway important in regulating the cell cycle. Therefore, it is directly related to cell proliferation and cancer. PI3K and mTOR are proteins that can be inhibited by PQR309, which may result in an inhibition of tumor growth. PQR309 is not registered as a drug, but has been given to cancer patients before. The other compound that will be given in this study is ranitidine which is an approved drug and already available in the market under several dosages and formulations. Ranitidine is an acid reducing agent and is prescribed for the treatment of gastric and duodenal ulcers.

Study objective

The study will be performed in 3 groups, Group 1, 2 and 3. Group 1 will be performed in 12 healthy non smoking male volunteers. Group 2 will be performed in 12 healthy non smoking male volunteers and Group 3 will be performed in 14 healthy smoking male volunteers.

Study design

The actual study will consist of 3 treatment periods during which the volunteers will stay in the clinical research center in Groningen. The time interval between the different treatment periods is between 14 and 21 days. All volunteers will need to come to the clinical research center on Day -5 of Period 1, because on this day the order of all treatments will be randomly assigned to all volunteers (also called randomization). Dependent on the randomization of the treatments, they will need to come to the clinical research center for an ambulatory visit on Day -5 of 2 of the 3 periods or all 3 periods.During the study the volunteers will take ranitidine at home. They will receive instructions for home dosing and a diary in which they need to record the time of each administration of ranitidine. They will be contacted daily to check the administration of ranitidine.
The post-study screening will take place 21 - 28 days after administration of the study compound in Period 3. The appointment for the post-study screening will be made with you during the study. The participation to the entire study, from pre-study screening until the post-study screening, will be maximally 8 weeks.

Intervention

Group 1:
Treatment A: 80 mg PQR309 once
Treatment B: 300 mg ranitidine once a day for 4 days, 300 mg ranitidine once, 80 mg PQR309 once
Treatment C: 150 mg ranitidine twicel, per day for 4 days, 80 mg PQR309 once, 150 mg ranitidine once

Group 2:
Treatment D: 80 mg PQR309 once (capsul) and 100 mg caffein once
Treatment E: 20 mg PQR309 oncel (iv) and 100 mg caffein once
Treatment F: 300 mg ranitidine once per day for 4 days.80 mg PQR309 once (capsule), 300 mg ranitidine once

Group 3:
Treatment G: 80 mg PQR309 once (capsul) and 100 mg caffein once
Treatment H: 20 mg PQR309 once (iv) and 100 mg caffein once
Treatment I: 100 mg fluvoxamine once per day for 6 days, 80 mg PQR309 once (capsul), 100 mg caffein once,
100 mg fluvoxamine oncel, 100 mg fluvoxaminen once per day for 12 days, 50 mg fluvoxamine once a day for 2 days.

Study burden and risks

During the study various examinations are carried out that can be experienced more or less stressful. Blood sampling, indwelling canula, heart tracing.

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

healthy male subjects
18 - 65 years of age, inclusive
BMI 18.0 - 30.0 kilograms/meter2
non-smoking

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 90 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of this study

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-07-2016
Enrollment:	38
Type:	Actual

Ethics review

Approved WMO Date:	06-06-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-07-2016
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-09-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-09-2016
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2016-002178-11-NL
CCMO	NL58035.056.16