OPEN LABEL PHASE I STUDY TO INVESTIGATE THE EFFECT OF MULTIPLE DOSES OF KETOCONAZOLE ON THE SINGLE-DOSE PHARMACOKINETICS OF TASQUINIMOD IN HEALTHY SUBJECTS

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Primary:- To assess the effect of multiple doses of ketoconazole on the single-dose pharmacokinetics (PK) of tasquinimod.Secondary:- To assess the safety and tolerability of multiple doses of ketoconazole with single doses of tasquinimod.

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

Summary

ID

NL-OMON35292

Source
ToetsingOnline

Brief title
Ketoconazole * Tasquinimod Interaction Study

Condition

- Miscellaneous and site unspecified neoplasms benign
- Prostatic disorders (excl infections and inflammations)

Synonym
prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: PRA International EDS
Source(s) of monetary or material Support: sponsor van het onderzoek: Active Biotech

Intervention

Keyword: Interaction, Ketoconazole, Prostate cancer, Tasquinimod

Outcome measures

Primary outcome

Pharmacokinetics:

primary: maximum plasma concentration (Cmax), area under the concentration-time

curve (AUC) from time 0 to time t (AUC0-t), AUC from time 0 extrapolated to

infinity (AUC0-inf), and elimination half-life (t*) of tasquinimod

Safety:

AEs, vital signs, 12-lead ECG; clinical laboratory, physical examination

Secondary outcome

n/a

Study description

Background summary

Tasquinimod is a new, investigational compound that may eventually be used for the treatment of prostate cancer. In addition, Tasquinimod may be used for other indications in the future.
Ketoconazole is a registered drug for the treatment of infections caused by fungus or yeast that are not responding to local treatment. Ketoconazole inhibits the enzyme CYP3A4. Tasquinimod is broken down by this enzyme. Inhibition of the activity of CYP3A4 by ketoconazole may result in not breaking down of tasquinimod, leading to increased tasquinimod blood concentrations. This study will possibly clarify the potential effect of ketoconazole on the

concentrations of tasquinimod in the body.

Study objective

Primary:
- To assess the effect of multiple doses of ketoconazole on the single-dose pharmacokinetics (PK) of tasquinimod.

Secondary:
- To assess the safety and tolerability of multiple doses of ketoconazole with single doses of tasquinimod.

Study design

Design
This is an open-label, 2-period, fixed sequence, crossover, drug interaction study in healthy volunteers. Subjects will receive a single dose of tasquinimod alone on Day 1 of Period 1, followed by an assessment/washout period of at least 7 days. On Days 1 to 13 of Period 2, subjects will receive daily doses of ketoconazole in combination with a single dose of tasquinimod on Day 4.

Treatments
12 healthy male or female subjects will receive treatments in 2 periods as follows:
Period 1: single per oral dose of 0.5 mg tasquinimod administered on Day 1 followed by 7 days of assessment and washout.
Period 2: multiple per oral doses of 400 mg ketoconazole, administered once daily on Days 1-13, and given in combination with a single per oral dose of 0.5 mg tasquinimod on Day 4 (tasquinimod administered immediately after the ketoconazole dose)

Procedures and assessments
Screening:
medical history, demographic data (including body weight and height), clinical laboratory (including clinical chemistry, haematology and urinalysis), alcohol and drug screen, pregnancy test (females only), hepatitis B surface antigen (HBsAg), anti-hepatitis C virus (HCV) and anti-human immunodeficiency virus (HIV) *, vital signs (including supine and standing systolic and diastolic blood pressure, pulse rate, respiratory rate and body temperature measured with an ear thermometer), 12 lead electrocardiogram (ECG), physical examination, adverse events (AEs) from the signing of the informed consent form (ICF) and previous and concomitant medication

Follow-up:
clinical laboratory (including clinical chemistry, haematology and urinalysis), vital signs (including supine systolic and diastolic blood pressure, pulse

rate, respiratory rate and body temperature), 12-lead ECG, physical examination, pregnancy test (females only), AEs and concomitant medication

Each admission (Day -1 in each period):
drug and alcohol screen, pregnancy test (females only), clinical laboratory (including
clinical chemistry, haematology and urinalysis), vital signs (including supine systolic and diastolic blood pressure, pulse rate, respiratory rate and body temperature), 12-lead ECG, AEs and concomitant medication

Observation period: 2 periods in the clinic
Period 1: from the afternoon on Day -1 until the morning of Day 3, daily outpatient visit on Days 5 and 7 (Day 7 of Period 1 is the same day as Day -1 of Period 2)
Period 2: from the afternoon on Day -1 until the morning of Day 14 (a follow-up visit will occur 7 to 10 days after the Day 13 dose of ketoconazole)

Blood sampling:
for PK of tasquinimod in plasma: at pre-dose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, 48, 96, and 144/168 hours after administration of tasquinimod on Day 1 of Period 1 and at pre-dose, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 24, 36, 48, 72, 96, 120, 144, 168, 192, 216 and 240 hours after administration of tasquinimod on Day 4 of Period 2
for PK of ketoconazole in plasma: at pre-dose on Days 1, 2, 4, 5, 7 and 10 of Period 2

Safety assessments:
AEs recorded from the signing of the ICF until completion of the follow up visit; clinical laboratory (including clinical chemistry, haematology and urinalysis) and 12-lead ECG at screening, Day -1 of each period, 4 hours post-dose on Days 1 and 3 of Period 1 and Days 1, 3, 4 and 6 of Period 2, and at follow-up; vital signs (including supine systolic and diastolic blood pressure, pulse rate, respiratory rate and body temperature measured with an ear thermometer) at screening, Day -1 of each period, once daily within 2 and 4 hours after any dosing on in-clinic days (but in the morning around 11 am on Days 2 and 3 of Period 1 and Day 14 of Period 2 when there is no dosing), and at follow-up; physical examination at screening and at follow-up.

Intervention

Active substance: tasquinimod
Activity: anti-angiogenic
Strength: 0.5 mg
Dosage form: per oral capsule

Active substance: ketoconazole
Activity: antimycotic

Indication: mycotic infections
Strength: 200 mg/tablet; a dose of 400 mg will be administered
Dosage form: per oral tablets

Study burden and risks

Risks
Procedures:
Pain, light bleeding, heamotoma, possibly an infection

Medication:
Tasquinimod: muscle or joint pain, tiredness, dizziness and headache.

Ketoconazole:
The most common adverse effects of ketoconazole are nausea, vomiting, bloating, reduced appetite, diarrhea and abdominal pain. Sometimes adverse effects such as, headache, dizziness, photophobia, rash, itching and allergic reactions can occur. Finally, transient changes of certain laboratory blood values can occur (liver enzymes).

Contacts

Public
PRA International EDS

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Scientific
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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 and female volunteers
Age: 18-55 years, inclusive
BMI: 18.0 * 30.0 kg/m2, inclusive

Exclusion criteria

- Suffering from hepatitis B, cancer or HIV/AIDS
- In case of participation in another drug study within 60 days before the start of this study
- In case of donation of more than 50 ml of blood within 60 days prior to drug administration
- Donation of more than 1.5 L of blood (for men) / more than 1.0 L of blood (for women) in the 10 months preceding the start of the 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):	08-11-2011
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nizoral
Generic name:	Ketoconazole
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Tasquinimod
Generic name:	n/a

Ethics review

Approved WMO Date:	24-10-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-11-2011
Application type:	First submission
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	EUCTR2011-004511-23-NL
CCMO	NL38489.056.11