Open-label phase I study to investigate the effect of multiple doses of tasquinimod on the single-dose pharmacodynamics and pharmacokinetics of warfarin in healthy subjects

Published: 26-09-2011
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Primary: To assess the effect of multiple doses of tasqinimod on the single-dose pharmacodynamics (PD) of warfarin. Secondary: To assess the effect of multiple doses of tasqinimod on the single-dose pharmacokinetics (PK) of warfarin. To assess the...

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

Summary

ID

NL-OMON35250

Source
ToetsingOnline

Brief title
Tasquinimod - Warfarin 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: Active Biotech
Source(s) of monetary or material Support: sponsor van het onderzoek: Active Biotech

Intervention

Keyword: Interaction, Prostate cancer, Tasquinimod, Warfarin

Outcome measures

Primary outcome

Pharmacodynamics: international normalised ratio (INR) values: area under the

INR effect curve (AUEC) from time 0 to 144 h (AUEC0-144), baseline corrected

AUEC (AUECcorr0-144), maximum INR value (INRmax), and maximum increase in INR

Secondary outcome

Pharmacokinetics: maximum plasma concentration (Cmax), area under the

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

time 0 extrapolated to infinity (AUC0-inf) of R warfarin and S-warfarin

Safety: AEs, vital signs, 12-lead ECG, clinical laboratory, physical

examination

Study description

Background summary

Tasquinimod is a new, investigational compound that may eventually be used for the treatment of prostate cancer. Warfarin is a drug for treatment and prevention of harmful blood clots and is likely to be a concomitant medication in patients with prostate cancer, This study is conducted to determine whether

tasquinimod may influence the pharmacokinetics and thereby also the effects of warfarin. This study is performed to learn more about the nature of this interaction to aid in the design of future studies.

Study objective

Primary:
To assess the effect of multiple doses of tasqinimod on the single-dose pharmacodynamics (PD) of warfarin.

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

Study design

Design
This is an open-label, fixed-sequence crossover study in healthy volunteers. Subjects will receive a single dose of warfarin alone on Day 1 of Period 1 followed by 7 days of assessment and washout. Subjects will then receive tasquinimod on Days 1 to 14 in Period 2 and a single dose of warfarin on Day 9. All subjects will receive the same treatment.

Treatments
All 15 subjects will be administered the following treatments in 2 study periods:
Period 1: a single oral dose of 25 mg warfarin on Day 1 followed by 7 days for assessment and washout
Period 2: multiple oral doses of 0.5 mg tasquinimod once daily on Days 1 to 14 and a single oral dose of 25 mg warfarin on Day 9

Procedures and assessments
Screening: medical history, demographic data (including body weight and height), clinical laboratory (including clinical chemistry, haematology, coagulation 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) 1/2, vital signs (including supine 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), previous and concomitant medication; genotyping: for cytochrome P (CYP) 450 2C9

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 measured with an ear thermometer), 12-lead ECG, physical examination, pregnancy test (females only), AEs and concomitant medication

Each admission: drug and alcohol screen, pregnancy test (females only), 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 visits through Day 7 (Day 7 of Period 1 is also Day -1 of Period 2)
Period 2: from the afternoon on Day -1 until the morning of Day 15 (a follow-up visit will occur 7 to 10 days after the Day 14 dose of tasquinimod)

Blood sampling:
for pharmacodynamics: samples for international normalised ratio (INR): 2 samples at least 10 min apart in the hour pre-dose (warfarin) and 8, 24, 36, 48, 72, 96, 120, and 144 h after warfarin doses on Day 1 of Period 1 and Day 9 of Period 2;
for pharmacokinetics of R-warfarin and S-warfarin in plasma: pre-dose and 1, 2, 4, 6, 8, 12, 24, 36, 48, 72, 96, 120 and 144 h after administration of warfarin on Day 1 of Period 1 and Day 9 of Period 2
for pharmacokinetics of tasquinimod in plasma: in Period 2, pre-dose (tasquinimod) on Days 1, 3, 5, 6 and 14 and, on Days 8 and 9, pre-dose and 2, 4, 8, 12, and 24 h after the tasquinimod doses (analysis optional; to be determined after treatment completion)
for genotyping of CYP2C9: once after start of dosing (preferably on Day 1)

Safety assessments:
AEs and concomitant medications: recorded from the time the ICF is signed until completion of the final visit; clinical laboratory (including clinical chemistry, haematology and urinalysis): screening, 4 h post-dose (warfarin) on Days 1 and 3 in Period 1, 4 h post-dose on Days 1, 3, 9, and 11 in 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, once daily 2 to 4 h after any dosing on in clinic days, and at follow-up; 12 lead ECG: screening, 4 h post-dose (warfarin) on Days 1 and 3 in Period 1, 4 h post-dose on Days 1, 3, 9, and 11 in Period 2, and at follow-up; physical examination: at screening, Day 3 of Period 1, Day 10 of Period 2, and at follow-up

Intervention

Study medication
Active substance: tasquinimod

Activity: anti-angiogenic
Indication: not applicable
Strength: 0.5 mg
Dosage form: oral capsule

Active substance: warfarin
Activity: anticoagulant
Indication: not applicable
Strength: 25 mg
Dosage form: oral tablet

Treatment
All 15 subjects will be administered the following treatments in 2 study periods:
Period 1: a single oral dose of 25 mg warfarin on Day 1 followed by 7 days for assessment and washout
Period 2: multiple oral doses of 0.5 mg tasquinimod once daily on Days 1 to 14 and a single oral dose of 25 mg warfarin on Day 9

Study burden and risks

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

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

Warfarin:
The most prominent adverse effect of warfarin use is an increased risk of haemorrhage (bleeding).

Contacts

Public
Active Biotech

Scheelevägen 22
Lund
SE
Scientific
Active Biotech

Scheelevägen 22

Lund
SE

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):	01-11-2011
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Coumardin
Generic name:	warfarin
Product type:	Medicine
Brand name:	Tasquinimod
Generic name:	not applicable

Ethics review

Approved WMO

Date:	26-09-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	07-10-2011
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	EUCTR2011-004510-42-NL
CCMO	NL38032.056.11