A Multicenter, Open-Label Study of doxercalciferol capsules for the Treatment of Secondary Hyperparathyroidisms (SHPT) in Stage 3 or Stage 4 Chronic kidney Disease (CKD) Patients

Published: 03-10-2007
Last updated: 09-05-2024

Primary Objective: To evaluate the safety and tolerability of Hectorol Capsules during 52 weeks of treatment in patients with Stage 3 or Stage 4 CKDSecondary Objective: To evaluate the efficacy of Hectorol Capsules during 52 weeks of treatment in...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Renal disorders (excl nephropathies)
Study type	Interventional

Summary

ID

NL-OMON31066

Source
ToetsingOnline

Brief title
Doxercalciferol for Treatment of Sec Hyperparathyreoidisms in CKD

Condition

- Renal disorders (excl nephropathies)

Synonym
Secondary Hyperparathyroidism in stage 3 or 4 Chronic kidney Disease: parathyroid working too hard in addition to a moderate to severe disturbed kidney function

Research involving
Human

Sponsors and support

Primary sponsor: Genzyme
Source(s) of monetary or material Support: Farmaceutisch industrie.

Intervention

Keyword: Chronic kidney Disease, Doxercalciferol, Open Label, Secundaire hyperparathyroïdie

Outcome measures

Primary outcome

Safety Endpoints:

• Incidence of adverse events and serious adverse events.

• Changes in physical examination findings, vital signs, or laboratory

evaluations.

Efficacy Endpoint:

The efficacy endpoint will be the proportion of patients meeting the iPTH

target range (defined as iPTH less than or equal to 70 pg/mL (7.7 pmol/L) for

Stage 3 patients and iPTH less than or equal to 110 pg/mL (12.1 pmol/L) for

Stage 4 patients) during the Treatment Period.

Secondary outcome

Not applicable.

Study description

Background summary

Hectorol has been marketed in the US since 1999 with no new safety concerns being identified in CKD 3, 4 or 5 patients with any of the available formulations.
However there remains limited data on long term safety. To date, clinical trials with Hectorol have treated patients up to 24 weeks5. This open-label, single-arm study will evaluate the safety and tolerability of Hectorol over a 52-week treatment period.

Study objective

Primary Objective: To evaluate the safety and tolerability of Hectorol Capsules during 52 weeks of treatment in patients with Stage 3 or Stage 4 CKD
Secondary Objective: To evaluate the efficacy of Hectorol Capsules during 52 weeks of treatment in patients with Stage 3 or Stage 4 CKD.

Study design

This is a Phase 3, multicenter, open-label study in patients with Stage 3 or 4 CKD. The study consists of a washout Period of u to 5 weeks duration followed by a 52-weeks treatment period.

Schematic

Period: (Washout Period) (----------Treatment Period----------)

[----------]X[----------]

Week: Screening -1 0 2 4 6 8 10 12 16 20 24 28 36 44 52
Enroll

Washout Period
At Screening, the study will be described to the patient and a signed Informed Consent will be obtained. The eligibility criteria will be reviewed.

All patients will be assessed for medical history and concomitant medications. A physical examination will be performed and vital signs will be measured. The following laboratory assessments will be performed: serum pregnancy (if applicable), serum chemistry profile, hematology, urinalysis, intact parathyroid hormone (iPTH), corrected serum calcium, phosphorus, albumin, calcium x phosphorus product (CaxP), and estimated glomerular filtration rate (GFR).

Patients taking active vitamin D (alfacalcidiol, calcitriol, or paricalcitol) or calcimimetic therapy will be instructed to discontinue this therapy and the Week-1 will be scheduled in 28 to 35 days.

Patients not prescribed an active vitamin D therapy or calcimimetic and currently on a stable renal diet and/or phosphate binder therapy (if needed) will be asked to return for Week -1 Visit 7 (+/- 5days) days later.

At the Week -1 visit, all subjects must be washed out of any active vitamin D or calcimimetic therapy for at minimum 28 days. The subject*s eligibility criteria will be confirmed. The following laboratory assessments will be performed: iPTH, corrected serum calcium, phosphorus, albumin, calcium x phosphorus product, spot urine calcium/creatinine ratio and spot urine protein/creatinine ratio.

Treatment Period
At Week 0, eligible patients will be enrolled. A physical examination will be performed and vital signs will be collected. The following laboratory assessments will be performed at the baseline Week 0 Visit: serum pregnancy (if applicable), serum chemistry profile, hematology, urinalysis, iPTH, corrected serum calcium, phosphorus, albumin, CaxP and a storage sample will be collected.

During the following 52-week Treatment Period study visits will occur every two weeks for the first 12 weeks, then monthly until week 28 and bi-monthly thereafter.

Patients will be dispensed study drug and asked to consume the assigned doxercalciferol dose daily. The dose of study drug will be titrated as necessary to maintain the iPTH level within the K/DOQI target range: for Stage 3 patients, 35-70 pg/mL (3.85 - 7.7 pmol/L); for Stage 4 patients, 70-110 pg/mL (7.7 - 12.1 pmol/L).

At all Treatment Period Visits the following blood analyses will be conducted: iPTH, corrected serum calcium, phosphorus, albumin, and CaP. Additionally at Weeks 24 serum pregnancy (if applicable), serum chemistry profile, hematology, and urinalysis panel will be conducted. At Week 52 or the Early Termination Visit, the following additional laboratory assessments will be performed: serum pregnancy (if applicable), serum chemistry profile, hematology, urinalysis. A physical examination will be performed and vital signs will be collected.

Adverse events (AEs) and concomitant medications will be collected from the time of Informed Consent through week 52. Any SAE regardless of relationship to treatment, occuring within 30 days of study completion or termination will be collected.

Dose/route/regimen: see protocol summary (page 6 of the protocol).

Intervention

Ongcontrolled open-label study: all participating patients receive doxercalciferol.

Study burden and risks

If a patient is treated for secundary hyperparathyroidism at the moment the investigator does inform the patient about the study, there is a possible need for a wash-out period of 5 weeks maximum to be able to participate in the study. Altough washout periods of up to 8 weeks have been safely employed in many similar studies without any observed harmful effects, a wash-out period is a potential risk.

Doxercalciferol may be less effective and/or may be less tolerated or there may be an increased risk of side effects than the patient's treatment before the wash-out period.

Doxercalciferol may cause all, some or none of the side effects described below. In addition, there is always a risk of side effects occurring which are unusual or which are currently unknown.

The most important side effects (harmful effects) of doxercalciferol can be calcium and/or phosphate levels in the blood which are too high or a parathyroid hormone level in the blood which is too low. Too much calcium in the blood during a prolonged period of time may result in hardening of soft tissues, including the heart and the arteries, and too much phosphate in the blood during a prolonged period of time may make the symptoms of hyperparathyroidism worse. If the parathyroid hormone level in the blood continues to be too low, this may lead to adynamic bone disease.

In view of the way doxercalciferol works, the drug may not be used in combination with drugs that contain magnesium or aluminium, like binders based on magnesium or aluminium. If you are using these drugs, you will be asked to stop using them during the clinical study.

The risks associated with blood withdrawal from a vein in your arm are pain, bruising and, in rare cases, infection at the injection site in your arm. Some people may experience a slight light-headedness, nausea or fainting.

Contacts

Public
Genzyme

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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

1. Male or female, aged 18 years or older.
2. CKD Stage 3 or 4, defined as GFR from the abbreviated Modification of Diet in Renal Disease (MDRD) equation between 30 and 59 mL/min/1.73m2 for CKD Stage 3 or between 15 and 29 mL/min/1.73m2 for CKD Stage 4 at the Screening Visit
3. iPTH > 70 pg/mL (7.7 pmol/L) for CKD Stage 3 patients or > 110 pg/mL (12.1 pmol/L) for CKD Stage 4 patients but < 700 pg/mL (77 pmol/L) at Week -1.
4. In the opinion of the Investigator, the patient is willing and able to maintain compliance with phosphate binder therapy (if applicable) throughout the study duration.
5. Willing and able to stop any prior active vitamin D therapy (e.g. alfacalcidiol, calcitriol, or paricalcitol) and/or calcimimetic for 28 days prior to Week -1 and maintain this throughout the study.
6. Willing and able to sign and date an Informed Consent form unless the patient has a legally authorized representative. If the patient has a legally authorized representative, the legally authorized representative must sign and date the Informed Consent.
7. The patient, if of childbearing potential, must be willing to use an effective contraceptive method throughout the study, which includes barrier methods, hormones, or IUDs.
8. A level of understanding and willingness to cooperate with all visits and procedures as described by the study personnel.

Exclusion criteria

1. Corrected serum calcium > 10.0 mg/dL (2.5 mmol/L) at Week -1.
2. Serum phosphorus > 5.0 mg/dL (1.61 mmol/L) at Week -1.
3. In the opinion of the Investigator, the patient currently has poorly controlled diabetes mellitus, poorly controlled hypertension, active vasculitis, HIV infection, or any other clinically significant, unstable medical condition.
4. Abnormal liver function as measured by ALT/AST greater than three times the upper limit of normal (ULN) at the Screening Visit.
5. Deemed by the Investigator to have rapidly deteriorating renal function.
6. Spot urine calcium/creatinine ratio greater than 0.2 at Week -1.
7. Current malabsorption, severe chronic diarrhea, or ileostomy.
8. Any evidence of active malignancy except for basal cell carcinoma of the skin. A history of malignancy is not an exclusion.
9. Allergic reaction to a drug which, in the opinion of the Investigator, suggests an increased potential for hypersensitivity to a Vitamin D therapy.
10. Active ethanol or drug abuse, excluding tobacco use.
11. Current use of aluminum or magnesium based binders.
12. Pregnant or breast-feeding women.
13. Anticipated dialysis or planned renal transplant less than 12 months from Week 0.
14. Treatment with an investigational drug during 30 days preceding the start of screening.
15. Prior renal transplant

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2007
Enrollment:	35
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Hectorol
Generic name:	doxercalciferol

Ethics review

Approved WMO Date:	03-10-2007
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	21-11-2007
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2007-001043-22-NL
CCMO	NL19634.068.07