A Multicenter single-arm Extension Study to Describe the Long-term Safety of AMG 416 in the Treatment of Secondary Hyperparathyroidism in Subjects With Chronic Kidney Disease on Hemodialysis.

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Primary: characterize the long-term safety and tolerability of AMG 416 in the treatment of secondary hyperparathyroidism (SHPT) in subjects with chronic kidney disease (CKD) on hemodialysis.Secondary: to characterize intact parathyroid hormone (iPTH...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Parathyroid gland disorders
Study type	Interventional

Summary

ID

NL-OMON41088

Source
ToetsingOnline

Brief title
AMG 416 in the Treatment of SHTP in Subj. With Chronic Kidney Disease on HD

Condition

- Parathyroid gland disorders
- Renal disorders (excl nephropathies)

Synonym
Patients with Chronic Kidney Disease on Hemodialysis and Secondary Hyperparathyroidism

Research involving
Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Amgen B.V.

Intervention

Keyword: AMG 416, Open label, Phase 3, Secondary hyperparathyroidism in subjects With chronic kidney disease on hemodialysis

Outcome measures

Primary outcome

To characterize the long-term safety and tolerability of AMG 416 in the

treatment of secondary hyperparathyroidism (SHPT) in subjects with chronic

kidney disease (CKD) on hemodialysis.

Secondary outcome

To characterize intact parathyroid hormone (iPTH), total serum albumin

corrected calcium (cCa), and serum phosphorous (P) values in the treatment of

SHPT in subjects with CKD who are on hemodialysis, who are being treated with

AMG 416.

Study description

Background summary

SHPT is characterized by persistently elevated PTH levels and occurs commonly among patients with CKD largely as an adaptive response to maintain mineral homeostasis. Among patients managed with dialysis, SHPT is associated with important disturbances in calcium and phosphorus metabolism including hyperphosphatemia, pathological changes in bone described collectively as renal osteodystrophy, soft-tissue and vascular calcification, left ventricular hypertrophy, and cardiovascular events. The importance of managing SHPT is

highlighted by recommendations provided in clinical practice guidelines such as the Kidney Disease Outcomes Quality Initiative (KDOQI) from the National Kidney Foundation (NKF) and the Kidney Disease Improving Global Outcomes (KDIGO) initiative (KDIGO, 2009; K/DOQI, 2003). The effect of AMG 416 to lower the serum levels of iPTH, calcium, and phosphorus among subjects with SHPT receiving hemodialysis was demonstrated initially in early phase clinical trials that included a randomized, double-blind, placebo-controlled, single ascending dose (SAD) study and a randomized, double-blind, placebo-controlled multiple ascending dose (MAD) study. The efficacy and safety of AMG 416 in this patient population was evaluated further in a phase 2, open-label, 12-week, dose titration study and in a subsequent, ongoing 40-week open-label extension study.
Additional information about the long-term safety and tolerability of AMG 416 in the management of SHPT among patients receiving hemodialysis would be beneficial to the overall understanding of the AMG 416 program. The study is descriptive and no formal hypothesis will be tested. The study will characterize the ongoing management of SHPT among subjects receiving hemodialysis and the ability of AMG 416 to maintain plasma iPTH levels within the KDIGO recommended range in subjects previously treated with AMG 416.

Study objective

Primary: characterize the long-term safety and tolerability of AMG 416 in the treatment of secondary hyperparathyroidism (SHPT) in subjects with chronic kidney disease (CKD) on hemodialysis.
Secondary: to characterize intact parathyroid hormone (iPTH), total serum albumin corrected calcium (cCa), and serum phosphorous (P) values in the treatment of SHPT in subjects with CKD who are on hemodialysis, who are being treated with AMG 416.

Study design

This is a phase 3, interventional, open-label, single-arm extension study, designed to assess the long-term safety and tolerability of AMG 416.
The overall study design is described by a study schema at the end of the protocol synopsis section in the protocol. Also see section "aanvullende informatie".

Intervention

Subjects entering from open-label parent studies AMG 416 Study 20120231 or 20120334 will receive a starting dose of AMG 416 thrice weekly (TIW) with intravenous (IV) administration after hemodialysis identical to the last dose received in the parent study. Subjects entering from randomized, double-blind parent Study 20120360, will receive a starting dose of 2.5 mg AMG 416 TIW administered IV after hemodialysis. All subjects will continue to receive AMG

416 until approximately 2.5 years after the first subject enrolls. All subjects will continue to receive background standard of care (other than cinacalcet) as mandated by individual Investigator. See Section 6 of the protocol.
Procedures: For subjects from open-label parent studies: After providing written informed consent, subjects from parent studies AMG 416 20120231 and 20120334 enter a screening period of up to 30 days which is concurrent with the last 30 days of investigational product while
in the parent study. Subjects are enrolled into the current study without immediately undergoing the 30-day washout period from the parent study. These subjects will defer the 30-day washout of study drug from the parent study, until the end of the current study. In the current study, subjects will continue receiving AMG 416 at the same dose as in the parent study. This dose may be 0 mg if investigational product was on suspension at the end of the open-label parent study. Every effort must be made to ensure there is no interruption in dosing between the end of the parent study and the start of the current study. Subjects are defined as enrolled on the day of their next hemodialysis session after receiving the last dose in the parent study, contingent upon providing written informed consent and meeting all eligibility criteria. For those subjects with recently suspended AMG 416 dosing however, dosing with AMG 416 must not resume until all dose resumption criteria have been met (see Sections 6.2.2.4 * 6.2.2.7 in the protocol).
For subjects from a double-blind parent study: After providing written informed consent, subjects from AMG 416 parent Study 20120360 enter a screening period of up to 30 days. The screening period in the current study should be concurrent with the mandatory 30-day washout of investigational product at the conclusion of treatment in Study 20120360, as described in the protocol for Study 20120360. All subjects will start at a dose of 2.5 mg of AMG 416 upon meeting all dosing conditions as described in Section 6.2.2.2 of the protocol.
For subjects from all parent studies: dose titration of AMG 416 is at the discretion of the Investigator and will be based upon the values of the site*s contracted laboratory provider iPTH and Ca (cCa, total Ca, or ionized Ca), with the frequency of these laboratory draws at the discretion of each individual Investigator, per standard of care for subjects receiving treatment with a calcimimetic agent. At a minimum however, calcium and albumin must be measured monthly. Doses of AMG 416 should in general be adjusted to maintain iPTH levels above the Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines of 2x the ULN, but no greater than 9x the ULN, with the ULN based on the reference range of the assay used at the individual site. Guidance for titration of AMG 416 dose has been provided based on trends in iPTH within this range. See Section 6.2.2.3 in the protocol.
Concomitant therapy with active vitamin D analogues, calcium supplements, and phosphate binders may be adjusted as needed throughout the study, based on Investigator clinical judgment. Dialysate calcium concentration may be adjusted as needed throughout the study, but must be maintained * 2.25 mEq/L. The site*s contracted provider for standard of care laboratory values for subjects receiving treatment with a calcimimetic agent will be used to determine AMG 416 dose titration throughout the study. Additional blood samples must be obtained

for pregnancy testing for women of childbearing potential (WOCBP) and for antidrug antibodies (ADA). Subjects will be followed for safety throughout the treatment period, and for 30 days after the last dose of AMG 416.
The treatment period will continue for approximately 2.5 years after the first subject enrolls in the study. Dosing of AMG 416 is to be directed by the Investigator, using his/her best medical judgment. Dosing with AMG 416 may be modified or suspended, based on protocol guidance for the predialysis contracted provider laboratory iPTH or Ca (cCa, total Ca, or ionized Ca) symptomatic hypocalcemia, or other drug-related advers events.
For a full list of study procedures, including the timing of each procedure, please refer to Section 7 and the Schedule of Assessments (Table 3) in the protocol.

Study burden and risks

A treatment regimen for SHPT that includes standard of care and AMG 416 will increase the proportion of subjects who will have a reduction in iPTH. SHPT is characterized by persistently elevated PTH levels and occurs commonly among patients with CKD largely as an adaptive response to maintain mineral homeostasis. Among patients managed with dialysis, SHPT is associated with important disturbances in calcium and phosphorus metabolism including hyperphosphatemia, pathological changes in bone described collectively as renal osteodystrophy, soft-tissue and vascular calcification, left ventricular hypertrophy, and cardiovascular events.

Four clinical studies have been completed to date. Most adverse events (AE) were mild or moderate in severity. The incidence of nausea, vomiting and diarrhea were similar in the AMG 416- and placebo-treated subjects. Serious adverse events (SAEs) have been reported; none were considered related to study drug. Administration of foreign proteins poses a small risk of developing antibody-mediated hypersensitivity reactions, including anaphylaxis. Such reactions are often related to release of cytokines or vasoactive amines. Symptoms may include fever, chills, rigor/shakes, hypotension, respiratory distress, rash/urticaria, and arthralgias and myalgias. However, AMG 416 is a small peptide produced by chemical synthesis that is unlikely to be immunogenic. The overall clinical safety findings to date suggest that AMG 416 is well-tolerated. Furthermore, the burden for the patient is relatively low as they do not have to have extra visits during the treatment phase. AMG 416 provides the opportunity for hemodialysis patients with SHPT to increase compliance over an oral calcimimetic and have one less oral regimen to manage as AMG 416 is dosed 3 times a week, concurrent with hemodialysis and administered by the dialysis site staff. For patients the long term safety of AMG 416 is important information.

Contacts

Public
Amgen

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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

-Subject has provided informed consent prior to initiation of any study-specific activities/procedures.
-Subject has completed treatment in Study 20120231 (also known as KAI-4169-008) or Study 20120360, or has participated in Study 20120334 (also known as KAI-4169-005-01).
-Female subjects who are:
* post menopausal (post menopausal is defined as no menses for the previous 1 year and over the age of 50 years)
* surgically sterilized
* have a medical condition that prevents pregnancy
* remain abstinent
* or are willing to use an acceptable method of effective contraception during

the study and for 3 months after the last dose
Women of child-bearing potential (WOCBP) must have a negative serum pregnancy test within 2 weeks prior to the first dose of AMG 416 in the current study.
-Subject must be receiving hemodialysis 3 or 4 times weekly for at least 3 months.

Exclusion criteria

-Currently receiving treatment in another investigational device or drug study (other than in one of the designated parent studies).
-Other investigational procedures while participating in this study are excluded.
-Subject has known sensitivity to any of the products or components to be administered during dosing.
-Subject has been prescribed cinacalcet by the primary nephrologist between the conclusion of the parent study and the start of dosing with AMG 416 in the current study.
-Subject has any illness that, in the judgment of the Investigator, might confound the results of the study or pose additional risk to the subject.
-Subject is receiving dialysis prescription dialysate calcium concentration < 2.25 mEq/L
-Subject is pregnant or nursing.
-History or evidence of any other clinically significant disorder, condition or disease (with the exception of those outlined above) that, in the judgment of the Investigator would pose a risk to subject safety or interfere with the study evaluation, procedures, or completion.

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):	13-03-2015

Enrollment:	4
Type:	Actual

Ethics review

Approved WMO Date:	30-09-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-11-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-02-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-12-2015
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	EUCTR2013-004136-30-NL
ClinicalTrials.gov	NCT02102204
CCMO	NL49763.056.14