Autosomal Dominant Hypocalcemia Types 1 and 2 (ADH1/2) Disease Monitoring Study (DMS)

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Primary:• Determine the biochemical manifestations of ADH1/2 over timeSecondary:• Understand renal health of participants with ADH1/2 • Determine incidence of nephrocalcinosis and/or nephrolithiasis in ADH1/2 participants• Understand bone health in...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bone, calcium, magnesium and phosphorus metabolism disorders
Study type	Observational invasive

Summary

ID

NL-OMON53610

Source
ToetsingOnline

Brief title
ADH1DMP

Condition

- Bone, calcium, magnesium and phosphorus metabolism disorders

Synonym
Autosomal Dominant Hypocalcemia, discorder of calcium homeostasis

Research involving
Human

Sponsors and support

Primary sponsor: Calcilytix Therapeutics
Source(s) of monetary or material Support: Calcilytix Therapeutics

Intervention

Keyword: ADH1/2, Disease Monitoring Study

Outcome measures

Primary outcome

Retrospective and prospective assessment of mineral homeostasis over time, including blood calcium, phosphorus, magnesium, intact PTH (iPTH), 1,25-dihydroxyvitamin D and urine calcium, phosphorus, and magnesium handling

Secondary outcome

Retrospective and prospective assessment of renal health over time, including blood creatinine and estimated glomerular filtration rate (eGFR)

• Retrospective and prospective assessment of renal ultrasound to evaluate for nephrocalcinosis and nephrolithiasis

• Retrospective and prospective assessment of dual-energy X-ray absorptiometry (DXA) to evaluate bone mineral density and assessment of bone turnover markers

• SF-36 (participants >=16 years) and SF-10 (participants >= 6 years and < 16 years)

• Retrospective and prospective assessment of ADH1/2 treatment regimens

• ADH1/2 Questionnaires

• Baseline and prospective assessment of electrocardiogram (ECG) and cardiac symptoms

Study description

Background summary

Autosomal dominant hypocalcemia type 1 (ADH1) and autosomal dominant hypocalcemia type 2 (ADH2) are rare disorders of systemic calcium homeostasis. The Sponsor is conducting a research study to better understand the natural history of Autosomal Dominant Hypocalcemia Types 1 and 2 (ADH1/2). This means they want to better understand how ADH1/2 is diagnosed, the symptoms patients with ADH1/2 experience, how patients are treated and how ADH1/2 affects patients* lives. The purpose of this research study is to collect your medical history and to continue to collect medical information from you for up to 7 years. This study is a disease monitoring study, which means there is no active treatment or study medication provided to you. If you are currently receiving calcium and active vitamin D supplements by your medical doctor for ADH1 or ADH2, you will be allowed to continue those supplements while participating in this study.

Study objective

Primary:

• Determine the biochemical manifestations of ADH1/2 over time

Secondary:

• Understand renal health of participants with ADH1/2
• Determine incidence of nephrocalcinosis and/or nephrolithiasis in ADH1/2 participants
• Understand bone health in ADH1/2
• Understand impact of ADH1/2 on quality of life
• Understand ADH1/2 treatment regimens
• Determine the clinical manifestations and progression of ADH1/2 over time
• Understand cardiovascular manifestations, including symptoms, clinical events, or electrocardiogram (ECG) abnormalities referable to abnormalities of calcium handling

Study design

A global, multi-center, longitudinal, disease monitoring study in participants with ADH1/2 designed to characterize ADH1/2 disease presentation and progression through retrospective and prospective data collection. This study will provide a more comprehensive assessment of the natural history of ADH1/2 than has been performed to date. This is a disease monitoring study, as no investigational product is being administered, and any standard of care (SoC) treatment participants may receive will be as directed by their treating physicians. Demographic, biochemical, disease severity, and progression data will be collected in all participants. Eligible participants include children (birth to 17 years) and adults (18 - 90 years) with ADH1/2 as determined by an activating variant or variant of uncertain significance of CASR in ADH1 or

GNA11 in ADH2.

Study burden and risks

Some procedures performed during the study may carry risks. Should the patient have any questions regarding procedures or the risks associated with the tests, the patient's study doctor can provide more information.

Procedure Risk
Blood Draws • Discomfort due to swelling or bruising around the site where a needle was inserted
• Light-headedness and/or fainting
• Risk of infection at or around the site where a needle was inserted
ECG • The sticky pads placed on the patient's chest may cause skin irritation

DXA Scan • Risks involve exposure to the radiation of X-rays which can be harmful to pregnant and lactating mothers.
• The amount of radiation exposure during a DXA scan is low and not much higher than the patient's radiation exposure that occurs naturally in the environment. Should the patient have concerns about the amount of radiation he/she could receive in this trial, please speak with the patient's study doctor.

Renal Ultrasound • Most people don't experience any side effects. In rare instances, the patient may notice some mild tenderness over the areas that have been examined, but this should subside within a couple of hours.

Contacts

Public
Calcilytix Therapeutics

Owens Street Suite C-1200 1800
San Francisco CA 94158
NL
Scientific
Calcilytix Therapeutics

Owens Street Suite C-1200 1800
San Francisco CA 94158
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Participants from birth to age 90 years must meet all the following criteria for inclusion during screening:
1. Have a documented activating variant or variant of uncertain significance of the CASR gene for ADH1 or documented activating variant or variant of uncertain significance of the GNA11 gene for ADH2 associated with a clinical syndrome of hypoparathyroidism prior to enrollment. Note: Acceptable documentation includes CASR or GNA11 genetic analysis report. If no prior documented CASR or GNA11 gene variant or variant of uncertain significance, potential participants can undergo CASR and GNA11 gene variant analysis at Screening.
2. Be willing and able to provide informed consent or assent after the nature of the study has been explained, and prior to any research-related procedures
3. Be willing and able to provide access to prior medical records including imaging, biochemical, and diagnostic and medical history data, if available
4. Be willing and able to comply with the study visit schedule and study procedure

Exclusion criteria

Participants are excluded from the study if any of the following criteria apply:
1. Have serious medical or psychiatric comorbidity that, in the opinion of the Investigator, would present a concern for
participant safety or compromise the ability to provide consent or assent,

or comply with the study visit schedule and
study procedures
2. Enrollment in an ADH1/2 interventional clinical study at the time of DMS
Screening visit

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-04-2023
Enrollment:	3
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	26-09-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-02-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	18-01-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-12-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
CCMO	NL80300.078.22