

Study Title:

Open-Label Extension Study of Theophylline for Treatment of Pseudohypoparathyroidism

NCT number:

NCT04240821

Date:

31 December 2025

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Informed Consent Document for Research

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Version Date: 25 SEP 2023
PI: Ashley Shoemaker, MD, MSCI

This informed consent applies to ADULTS

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

Key Information:

The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:

This study will test whether an investigational drug (theophylline) is a safe and effective treatment for the symptoms of PHP. Theophylline is approved by the Food and Drug Administration (FDA), but is not approved as a treatment for pseudohypoparathyroidism. This study is a 24 month open label extension clinical trial. Patients that complete the Phase 2 Study of Theophylline for the Treatment of Pseudohypoparathyroidism randomized clinical trial will be eligible to screen and enroll in the extension study. Screening and enrollment will occur at the research visit 4 for the randomized clinical trial. Participants will be asked to come to VUMC for 5 onsite research visits over 24 months. Fasting is required for 8 hours prior to 4 of the research study visits. The maximum number of patients eligible for this study is 34.

The most common side effects of Theophylline are nausea, vomiting, headache, and insomnia. We may find a new medication to treat PHP with the information from this study.

Detailed Information:

The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this research study because you have the genetic disorder pseudohypoparathyroidism (PHP). People with PHP may have multiple medical problems, including resistance to multiple hormones and obesity.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study

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at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Side effects and risks that you can expect if you take part in this study:

Blood tests

Pain, redness, soreness, bruising, or infection may occur at the needle stick site. Rarely some people faint. The study doctor may put some cream (called EMLA) on your skin to numb the area so they will not feel the needle stick as much. The numbing cream may make your skin or the area have a change in skin color, but this is rare.

ECG

You may not like the sticky pads placed on your chest; they might irritate your skin. It might pull your skin when we take the pads off, similar to a Band-Aid being removed.

OGTT

You may not like the sugar drink.

Questionnaires

You may find it a bother to answer these questions. It is possible some information about you may be found out by others.

Theophylline

Common side effects

Caffeine-like effects such as nausea, vomiting, headache and insomnia are common with theophylline. Anti-nausea medications will be provided as needed.

Adverse reactions from an overdose

If the theophylline levels get too high, symptoms commonly include vomiting, nervousness, rapid heart rate and tremors. Rarely, patients can have electrolyte abnormalities, cardiac arrhythmias, seizures or low blood pressure. Death has been reported from an acute overdose of theophylline.

Side effects of theophylline are related to blood theophylline levels. It is very important that you take the prescribed dose of medication at the same time each day. It is also important that you have your blood levels checked as directed by the study staff. Other things that can change your theophylline levels include changes in your medications, fever, untreated hypothyroidism and interactions with food or alcohol.

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Please avoid alcohol while in this study. Contact the study staff if you have a fever for more than 2 days or if you have vomiting more than once in a day, a rapid heartbeat or shaking hands.

These medications may hurt an unborn child. If you are a female and are able to become pregnant, you will have a test to make sure that you are not pregnant before they receive treatment in this study.

Medication interactions

Other medications you take may interact with theophylline. It is very important that you tell the study doctor before you take any new medications or over-the-counter supplements. We will provide a letter for your regular doctors informing them about this study. The medicines in table 2 are most-likely to interact with theophylline. You may NOT take these medications while in the study.

Table 2: Drugs with clinically significant drug interactions with theophylline				
Adenosine	Diazepam	Halothane	Midazolam	Rifampin
Allopurinol	Disulfiram	Interferon alpha	Moricizine	St. Johns Wort
Aminoglutethimide	Enoxacin	Isoproterenol (IV)	Pancuronium	Sulfinpyrazone
Carbamazepine	Ephedrine	Ketamine	Pentoxifylline	Tacrine
Cimetidine	Erythromycin	Lithium	Phenobarbitol	Thiabendazole
Ciprofloxacin	Flurazepam	Lorazepam	Phenytoin	Ticlopidine
Clarithromycin	Fluvoxamine	Methotrexate	Propafone	Troleandomycin
		Mexiletine	Propranolol	Verapamil

Estrogen may increase the risk of a theophylline overdose. If you are a female taking estrogen or oral contraceptive pills ("birth control pills"), we will start with a lower dose of theophylline. If you need to stop OR start taking estrogen during this study, please contact the study doctor immediately.

Risks that are not known:

Because this treatment is investigational, meaning non-FDA approved, there may be risks that we do not know about at this time.

Good effects that might result from this study:

The benefits to science and humankind that might result from this study:
We may find a new treatment for PHP.

The benefits you might get from being in this study:

You will receive information on your metabolism and body composition. If any hormone lab results are abnormal, you will be referred to your primary care doctor or endocrinologist for treatment.

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Procedures to be followed:

You should not participate in strenuous exercise or drink caffeine or alcohol in the 3 days prior to study visits. An overview of the study is provided in table 1.

STUDY VISIT 1 DAY 0 (Theophylline Extension Study)/VISIT 4 (WEEK 52 final visit of randomized clinical trial)

You will arrive at the Clinical Research Center before 5pm the night before the visit and will complete the study procedures for study visit 4 of Phase 2 Study of Theophylline for the Treatment of Pseudohypoparathyroidism. The study doctor will determine if you are eligible to participate in the Theophylline Extension Study. If you decide to take part in this study, first, you will sign this form to give your consent.

You will be sent home with a supply of study drug. The drug will be a capsule, tablet or liquid. The capsule will be taken by mouth once a day with your evening meal. The tablet will be taken by mouth twice a day. If you are unable to swallow a capsule or tablet, a liquid medication will be provided. The liquid medication is taken by mouth every 6 hours.

PHONE CALL and LOCAL LABS

Three to five days after your visit, we will call you over the phone to learn about any illnesses or new symptoms. You will also have a blood sample taken at a local lab. If you take the capsule or tablet, the blood sample will be drawn 12 hours after the last medication dose. If you take the liquid medication, the blood sample will be drawn 2 hours after the last medication dose. We will mail you a new supply of study drug after this lab draw.

We will call you again after 4 weeks to again ask about any illnesses or new symptoms. You will also have a blood sample taken at a local lab. If you take the capsule or tablet, the blood sample will be drawn 12 hours after the last medication dose. If you take the liquid medication, the blood sample will be drawn 2 hours after the last medication dose. We may adjust your medication dose based on the lab results.

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Table 1: Summary of Study Procedures						
	Randomized Clinical Trial Visit 4 Extension Study Visit 1 Day 0	Visit 2 Month 3	Visit 3 Month 6	Visit 4 Month 12	Visit 5 Month 18	Visit 6 Month 24
Overnight stay	X					
Physical exam	X	X	X	X	X	X
AE's	X	X	X	X	X	X
Vital Signs	X	X	X	X	X	X
Blood draw	X	X	X	X	X	X
OGTT	X			X		X
Safety Labs	X	X	X	X	X	X
Fasting Labs	X		X	X	X	X
Parathyroid Hormone Level PTH		X				
Hormone Replacement Therapy (HRT) Dose Adjustments		X	X	X	X	X
Metabolism test (REE)	X					
Bone age x-ray	X			X		X
Dual-energy x-ray absorptiometry (DXA)	X					X
6-minute walk	X			X		X
Questionnaires	X			X		X
Depression Screen	X		X	X	X	X
Electrocardiogram (ECG)	X	X		X	X	X
Drug dispensing	X	X	X	X	X	
Local blood draw	X					
Phone call	X (3-5 days and 4 weeks after the visit)					

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Theophylline Level	X (3-5 days and 4 weeks after the visit)	X	X	X	X	X
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VISIT 2 (Month 3)

You will arrive to the CRC by 8am.

A blood sample will be taken. If you take the capsule or tablet, the blood sample will be drawn 12 hours after the last medication dose. If you take the liquid medication, the blood sample will be drawn 2 hours after the last medication dose. We may adjust your medication dose based on the lab results. We will also test hormone levels and liver function. We may adjust your hormone medication dose based on the lab results. If you are female and able to have children, a blood pregnancy test will be performed.

You will have a physical exam and vital signs will be measured, like at a doctor's visit for a "check-up".

We will ask you to report any illnesses or symptoms since your last phone call.

You will have an electrocardiogram (ECG). This will tell us about the electrical activity in your heart. We will place sticky electrodes on your chest, but the ECG will not hurt.

We will provide you with a new supply of study drug. You will be asked to return your old medication containers and any leftover medication.

VISIT 3 (Month 6)

You will arrive to the CRC by 8am. You should not have anything to eat or drink, other than water for 8 hours before the visit.

A blood sample will be taken. If you take the capsule tablet, the blood sample will be drawn 12 hours after the last medication dose. If you take the liquid medication, the blood sample will be drawn 2 hours after the last medication dose. We may adjust your medication dose based on the lab results. We will also test hormone levels and liver function. We may adjust your hormone medication dose based on the lab results. If you are female and able to have children, a blood pregnancy test will be performed.

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You will then be allowed to eat breakfast.

You will have a physical exam and vital signs will be measured, like at a doctor's visit for a "check-up".

We will ask you to report any illnesses or symptoms since your last phone call. During the visit you will be asked to complete a depression screen. If the study doctor is worried that you may be depressed or suicidal, we will refer you to a mental health provider and the study visit will end.

will provide you with a new supply of study drug. You will be asked to return your old medication containers and any leftover medication.

VISIT 4 (Month 12)

You will arrive to the CRC by 8am. You should not have anything to eat or drink, other than water for 8 hours before the visit.

A blood sample will be taken. If you take the capsule or tablet, the blood sample will be drawn 12 hours after the last medication dose. If you take the liquid medication, the blood sample will be drawn 2 hours after the last medication dose. We may adjust your medication dose based on the lab results. We will also test hormone levels and liver function. We may adjust your hormone medication dose based on the lab results. If you are female and able to have children, a blood pregnancy test will be performed.

You will have an oral glucose tolerance test (OGTT). An intravenous catheter (IV) will be placed in a vein in your arm so that we can take blood samples. You will drink a sugar drink. We will take blood samples from the IV over the next 2 hours. The blood samples will be used to test hormone levels and blood sugar levels. After two hours, the test is finished and the IV will be removed. After the test, you will be allowed to eat breakfast.

You will have a physical exam and vital signs will be measured, like at a doctor's visit for a "check-up".

You and your parents will complete several surveys. These surveys will ask questions about what kind of foods you like, how hungry you are, your mood and your development as a child. If the

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study doctor is worried that you may be depressed or suicidal, we will refer you to a mental health provider and the study visit will end.

You will do an exercise test where you are asked to walk up and down a hallway as many times as you can in 6 minutes. If you become too tired, you are allowed to rest during the test. This walking test will be repeated one more time during the visit.

You will have an electrocardiogram (ECG). This will tell us about the electrical activity in your heart. We will place sticky electrodes on your chest, but the ECG will not hurt.

You will have a bone age x-ray of your left hand, fingers and wrist to determine the approximate age of your skeletal system.

We will provide you with a new supply of study drug. You will be asked to return your old medication containers and any leftover medication.

VISIT 5 (Month 18)

You will arrive to the CRC by 8am. You should not have anything to eat or drink, other than water for 8 hours before the visit.

A blood sample will be taken. If you take the capsule or tablet, the blood sample will be drawn 12 hours after the last medication dose. If you take the liquid medication, the blood sample will be drawn 2 hours after the last medication dose. We may adjust your medication dose based on the lab results. We will also test hormone levels and liver function. We may adjust your hormone medication dose based on the lab results. If you are female and able to have children, a blood pregnancy test will be performed.

You will then be allowed to eat breakfast.

You will have a physical exam and vital signs will be measured, like at a doctor's visit for a "check-up".

You will have an electrocardiogram (ECG). This will tell us about the electrical activity in your heart. We will place sticky electrodes on your chest, but the ECG will not hurt.

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We will ask you to report any illnesses or symptoms since your last phone call. During the visit you will be asked to complete a depression screen. If the study doctor is worried that you may be depressed or suicidal, we will refer you to a mental health provider and the study visit will end.

We will provide you with a new supply of study drug. You will be asked to return your old medication containers and any leftover medication.

VISIT 6 (Month 24)

You will arrive to the CRC by 8am. You should not have anything to eat or drink, other than water for 8 hours before the visit.

We will repeat the study procedures from VISIT 4.

A whole body dual-energy x-ray absorptiometry (DXA) scan will be done. This is an x-ray that measures how strong your bones are and your body composition. You will lie on a table while the x-ray is done. The test takes about 10 minutes.

You will be asked to return your old medication containers and any leftover medication. This is the end of the study.

Payments for your time spent taking part in this study or expenses:

We may ask you for your Social Security number and address before you are compensated for taking part in this study. You will receive \$50/visit (up to \$250 total) for completing the study visits 2, 3, 4, 5, and 6. Checks will be mailed to your home address 2-4 weeks after the study. If you live more than 50 miles from Vanderbilt University, we will provide travel assistance. Eligible expenses include plane tickets for the patient and one parent or car mileage (50 cents per mile). If you live more than 100 miles from Vanderbilt, we will provide a hotel room the night before study visits as needed.

Costs to you if you take part in this study:

There is no cost to you for taking part in this study.

Payment in case you are injured because of this research study:

If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

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There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:

If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact Dr. Ashley Shoemaker at 615-343-8116. If you cannot reach the research staff, please page the study doctor at (615) 831-6167.

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the VUMC Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:

You will be taken out of the study if you are found not to meet the inclusion/exclusion criteria.

What will happen if you decide to stop being in this study?

If you decide to stop being part of the study, you should tell your study doctor. Deciding to not be part of the study will not change your regular medical care in any way.

Clinical Trials Registry:

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

Confidentiality:

Study results will be kept in a password protected research database. Only Dr. Shoemaker and her study staff will have access to the information that identifies you as being in this study. Paper records will be kept in a locked office. The results of some tests run on your samples may not be recorded in your medical records and you and your regular doctor may not be told of the results.

Vanderbilt may share your information, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Dr. Shoemaker and her staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

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This study may have some support from the National Institutes of Health (NIH). If so, your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Privacy:

Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit as a result of the tests done on your samples. These tests may help us or other researchers learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Study Results:

Study results will be shared with participants via published manuscript and via Dr. Shoemaker's PHP research group Facebook page.

Authorization to Use/Disclose Protected Health Information

All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is, or has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Dr. Ashley Shoemaker and her study team may share the results of your study and/or non-study linked laboratory results, x-rays and DEXA scan, as well as parts of your medical record, to the groups named below. These groups may include people from the Federal Government Office for Human Research Protections, the Vanderbilt University Institutional Review Board and the Food and Drug Administration. Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

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The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact Dr. Ashley Shoemaker in writing and let her know that you withdraw your consent. Her mailing address is – Village at Vanderbilt, 1500 21st Ave South, Suite 1514, Nashville, TN 37212. At that time, we will stop getting any more data about you. But, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

What information is being collected, used, or shared?

To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?

The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt, for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

Do you have to sign this Authorization?

You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?

Your Authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

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What if you change your mind?

You may change your mind and cancel this Authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let them know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this consent form and the research study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this study.

Date

Signature of patient/volunteer

Consent obtained by:

Date

Signature

Printed Name and Title

Time: _____

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