Phentermine/tOpiramate to eND Obesity and Uric Acid Stones Trial (POuND OUT)

ClinicalTrials.gov ID NCT04621929

University of Florida

Consent Form

Approved 04/06/2021

UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this Research Study?

Phentermine/tOpiramate to eND Obesity and Uric acid stones Trial (POuND OUT)

3. Whom do you call if you have questions about this Research Study (the "Study Team")?

Study Coordinator:	John Marks, 352-273-5618
Principal Investigator:	Benjamin Canales, MD (352) 273-6815
Other research staff:	Muna Canales, MD (352) 273-8821

4. Who is paying for this Research Study?

The sponsor of this study is the National Institutes of Health and the Department of Urology, University of Florida.

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at

(352) 273-9600. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

a) In general, what is the purpose of the research, how long will you be involved?

This study will investigate if treatment with the drugs phentermine and topiramate will decrease uric acid kidney stone formation in obese/diabetic patients. You will be randomly assigned to receive weight loss counselling/medications OR weight loss counselling alone in conjunction with the same treatments for your weight and kidney stones that you are receiving now. Your participation in this study would last approximately 18 months.

b) What is involved with your participation, and what are the procedures to be followed in the research?

Your participation in the study will be a total of eight (8) encounters over a period of 18 months, five of which are face to face visits.

Encounter 1 consisted of a consent and a telephone screening. You will now proceed to encounter #2 since you met the initial entry criteria for participating in this study

Encounter 2: Complete informed consent and randomization. Baseline on-site visit to collect study data, DEXA and CT scans, 24-hour urine, complete a mental health questionnaire and blood sample collection.

Encounter 3: One-month follow up phone call to review study medications and check for any subject concerns.

Encounter 4: Three-month on-site study visit to collect required study data and samples.

Encounter 5: Six-month on-site study visit to collect study data and samples.

Encounter 6: Twelve-month on-site study visit to collect study data samples.

Encounter 7: Seventeen-month phone call to remind subjects to complete study urine collection and to begin study medication taper.

Encounter 8: Eighteen-month on-site visit to collect end-of-study data, samples, and complete final DEXA and CT scans.

c) What are the likely risks or discomforts to you?

If you are randomly assigned to the experimental drug treatments, you will be asked to stop any alkalinizing medications you may currently be taking (potassium citrate, sodium bicarbonate) and take a combination of two drugs: phentermine and topiramate. **Phentermine:** Phentermine hydrochloride is a drug approved by the US Food and Drug Administration (FDA) in 1959 as an appetite

suppressant for short-term weight loss. Like other stimulants, side effects include hypertension and central nervous system stimulation. **Topiramate:** Topiramate was approved by the FDA for the treatment of epilepsy (1996) and migraine headaches (2004). In migraine studies, side effects occurred in were generally mild to include an abnormal prickly sensation, fatigue, weight loss, problems with concentration, dry mouth, changes in the sense of taste and nausea. Less common side effects included the development of kidney stones (primarily calcium phosphate stones due to highly alkaline urine), glaucoma, seeing images after removed from sight (palinopsia), Stevens–Johnson syndrome (flu-like symptoms with a painful rash and/or blisters), tremor, and twitches or sudden muscle contractions. A combination of these two medications,marketed as the drug called Qsymia®, was FDA approved in 2012 for weight lossin individuals with obesity. It is currently the most effective weight loss drug on the market.

This research study involves exposure to radiation from CT and DEXA scans. The radiation you will receive from these procedures exposes a part of your body to a higher level of radiation than the rest of your body. The effects of radiation add up over your lifetime. Repeated exposures may increase your risk of injury or disease. When deciding to enter this study you should consider previous and future potential exposures. More information is provided below.

d) What are the likely benefits to you or to others from the research?

You may not have direct health benefits from participating in this study. Those taking the study medication may lose more weight than those in the control group. However, you may experience some weight loss and improvement in your uric acid kidney stone disease regardless of which group you are in by following the guidelines presented by the study dietician.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

Should you choose to participate in this study or not, your treatment for kidney stones, diabetes, and being overweight will continue.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care, even if you do not participate in this Research Study?

Your treatment for weight loss and/or kidney stones includes:

- A recommended diet low in uric acid (purine), such as limited intake of animal protein (meat), bread, and beer
- Prescribing xanthine oxidase inhibitor medications that can lower serum uric acid levels, such as allopurinol (Aloprim, Lopurin, Zyloprim) and febuxostat (Uloric).

- Prescribing medications that alkalinize the urine and make it more basic (raise urine pH), such as sodium bicarbonate (baking soda), potassium citrate (Uro-Cit K; Poly-Citra K), or other citrate containing compounds (Bicitra)

You will remain on these treatments if you do not participate in the study or are randomized to the control group. If you are randomly selected for the study medications, you will stop taking medications that alkalinize the urine (raise the urine pH), such as sodium bicarbonate (baking soda), potassium citrate (Uro-Cit K; Poly-Citra K), or other citrate containing compounds (Bicitra).

7. What will be done only because you are in this Research Study?

You will be enrolled into either a control group (those not taking the study medication) or the intervention group (those taking the medication). Both groups will receive diet counseling by the study dietician. Since we will not know which group you will be in until you are randomized (like flipping a coin) you must be willing to participate in both groups in order to enroll in this study. **Unless otherwise stated both groups will complete the same study procedures.**

Encounter #1: consisted of a consent and a telephone screening. You will now proceed to encounter #2 since you met the initial entry criteria for participating in this study.

Encounter #2: This baseline, on-site, face to face visit will involve signing an additional informed consent (study participation) and confirmation of entry criteria. For all face to face visits we will collect medical history and body measurements (height/weight, waist and hip circumference), vital signs, and dietary history (dietician visit 1). We will also draw 2 vials of blood (less than a tablespoon). The first vial is to check how well your kidneys are working and fluid balances in your blood. This is referred to as a “Basic Metabolic Panel (BMP)”. The second vial is to measure your Hemoglobin A1c level (HbA1c). In addition, you will also complete a PHQ-9 questionnaire which is used to measure signs and severity of depression. A body composition DEXA scan will be scheduled. If you are female and of child-bearing age, you will be asked to take a pregnancy test before a CT or DEXA scan regardless of which group you are in and at each face to face visit only for those taking the study medication. If you are randomized to the intervention group, the study medication will be dispensed. Completion of all procedures for this visit should take approximately 2.5 hours.

Encounter #3: This 1-month follow-up phone call only for those taking the study medication (intervention group). We will review medication compliance/ reconciliation as well as record any adverse events. The phone call should take approximately 30 minutes.

Encounter #4: This 3-month, on-site, face to face visit. will involve: The collection of body measurements, vital signs, dietary history/ (dietician visit#2), pregnancy test

only for those taking the study medication, blood draw and completion of the PHQ-9 questionnaire. If you are taking the study medication (intervention group) we will adjust your medication dose accordingly: f total body weight loss is>5% and urine pH>6.5 (24 hr urine month 3), you will stay on the same dose. Medications for months 4, 5, 6 will be dispensed.

If total body weight loss is <5%, phentermine dose will be increased to 37.5 mg and you will remain on this dose through study duration. If urine pH<6.5 (24 hr urine month 3), topiramate dose will be increased to 150 mg daily. Medications will be adjusted appropriately for months 4, 5, 6. This visit should take approximately 1 hour.

Encounter #5: This 6-month, face to face, on-site visit will involve: The collection of body measurements, vital signs, dietary history (dietician visit#3), PHQ-9 questionnaire, and blood draw. For those taking the study drug medication compliance/ reconciliation, and adverse events will be collected and pregnancy test if necessary. This visit should take approximately 1 hour.

Encounter #6: This 12-month, face to face, on-site visit will involve: The collection of body measurements, vital signs, the PHQ-9 questionnaire and blood draw. For those taking study drug, medication compliance/reconciliation, adverse events, and pregnancy test if necessary. This visit should take approximately 1 hour.

Encounter #7: This 17-month phone call is to remind subjects to collect their fifth 24-hr urine. For those taking study drug, study coordinator will also remind participants to begin a 9-day topiramate drug taper as soon as collection is completed and to collect a final 24-hour urine sample 3 weeks after drug washout. This phone visit should take approximately 30 minutes.

Encounter #8: This is the 18-month, face to face, end-of study visit. We will collect: body measurements, vital signs, dietary history/dietician (visit # 4), blood draw, and PHQ-9 questionnaire. A body composition DEXA scan will be scheduled and pregnancy test if necessary. Should it be necessary, an end-of-study non-contrast CT scan of the abdomen will also be scheduled (if none performed for standard of care). This visit should take approximately 2.5 hours. For those taking study drug final drug reconciliation and adverse events will be recorded.

Once this research study is completed, any information that could identify you might be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If you have any questions now or at any time during this Research Study, please contact one of the Research Team members listed in question 3 of this form.

8. What identifiable health information will be collected about you and how will it be used?

The Research Team will collect the following from you:

- Demographic information, results of physical exams including medical history and medications, blood tests, lab results, x-rays, (DEXA scan and/or CT scan), questionnaire responses, other diagnostic and medical procedures, and social security number for study participation payment purposes.

The Research Team may collect this information from other healthcare providers, such as laboratories, which are a part of this research, as well as healthcare providers that are not part of this research (other doctors, hospitals or clinics). Other professionals at the University of Florida or Shands Hospital who provide study-related care, and the University of Florida Institutional Review Board (IRB), may also collect your health information.

9. With whom will this health information be shared?

This health information may be shared with:

- The study sponsor (listed in question 4).
- The medical staff that take care of you and any laboratories, pharmacies or others who are part of this research study.
- The data safety monitoring board or others who monitor the data and safety of the study.
- United States governmental agencies which are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections;
- Government agencies which are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments.
- The IRB that reviewed this Research Study and ensures your rights as a Study Subject are protected

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by the federal privacy law.

10. How long will you be in this Research Study?

Approximately 18 months.

This Authorization to use and share your health information expires at the end of the study, unless you revoke it (take it back) sooner.

11. How many people are expected to take part in this Research Study?

Up to 40 people will be enrolled in this part of the study.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

12. What are the possible discomforts and risks from taking part in this Research Study?

Medications: If you are randomly assigned for the experimental drug treatments, you will be asked to stop any alkalinizing medications you may currently be taking (potassium citrate, sodium bicarbonate) and take a combination of two drugs, phentermine and topiramate. **Phentermine:** Phentermine hydrochloride is a drug approved by the US Food and Drug Administration (FDA) in 1959 as an appetite suppressant for short-term weight loss. Like other stimulants, side effects include hypertension and central nervous system stimulation. **Topiramate:** Topiramate was approved by the FDA for the treatment of epilepsy (1996) and migraine headaches (2004). In migraine studies, side effects occurred in were generally mild to include an abnormal prickly sensation, fatigue, weight loss, problems with concentration, dry mouth, changes in the sense of taste and nausea. Less common side effects include the development of kidney stones (primarily calcium phosphate due to alkaline urine), glaucoma, seeing images after removed from sight (palinopsia), Stevens–Johnson syndrome (flu-like symptoms with a painful rash and/or blisters), tremor, and twitches or sudden muscle contractions. A combination of these two medications, marketed as the drug called Qsymia®, was FDA approved in 2012 for weight loss in individuals with obesity. It is currently the most effective weight loss drug on the market.

You cannot participate in this study if you are pregnant, as topiramate can cause fetal toxicity. If you are a woman of child-bearing age, you will be asked to take a pregnancy test prior to enrollment and at every face to face visit. You will also be asked to use barrier contraception throughout the study. If you find out that you are pregnant while on the study, contact the Investigators in Section 3 immediately.

Blood draws: The risks of drawing blood from a vein include discomfort at the site of puncture, possible bruising and swelling around the puncture site, rarely an infection, and, uncommonly, faintness from the procedure.

Imaging: You will have two different forms of imaging in this study: a DEXA scan and a CT scan. The first set will occur at the beginning of the study. The second set will occur at the end of study. For both tests, you will be asked to remove any metal objects or jewelry from the region being scanned, and you will need to change into a hospital gown.

- DEXA Scan: A DEXA is a type of xray used to measure bone strength. During this test, xray pictures of your body will determine how much of your weight is compartmentalized as fat mass, lean mass, and bone mineral content. You will lie flat on a table and a machine will take pictures of different areas of the body. This test will last about 15 minutes. You should not have this test if you may be pregnant. If you are female of child-bearing age, you should have a urine pregnancy test to ensure you are not pregnant.
- Non-contrast computed tomography (CT) scan: This diagnostic test uses xrays to produce images of internal body parts and your kidney stones. The average test time is about 20 minutes. You may be asked to hold still during this time. You also may be asked to hold your breath for a portion of the images. A technologist will monitor you throughout the scan and will be communicating with you intermittantly during the test. You should not have this test if you may be pregnant. If you are female of child-bearing age, you should have a urine pregnancy test to ensure you are not pregnant.
- Discomfort and Risks: Both imaging procedures require you to lie on your back, so you may experience discomfort based on your positioning. Both DEXA and CT scan use low levels of ionizing radiation. It is the smallest dose possible to gather the information needed and is not likely to adversely affect you or your disease. However, the effects of radiation can add up over a lifetime. It is possible that having several of these tests may add to your cancer risk. When deciding to enter this study, think about your past and future contact with radiation. Examples of contact with radiation include x-rays taken for any reason or radiation therapy for cancer treatment. Because of its ability to give high kidney stone resolution, CT scan is the standard of care test for acid stones. In some clinical cases, there are alternatives to having CT scans, such as having a plain xray or an ultrasound. However, uric acid stones are radiolucent (“invisible”) and difficult to see by plain xray or ultrasound. These exams should assist your physician with your kidney stone diagnosis and aid in future kidney prevention.
- This research study involves exposure to radiation from CT and DEXA scans. The radiation you will receive from these procedures exposes a part of your body to a higher level of radiation than the rest of your body. The typical radiation exposure from an abdominal/pelvis CT scan is about 10 mSv (1000 millirem) which is equal to about 3.4 years of natural background radiation exposure. You will also receive two DEXA scans during this study. The radiation exposure from the DEXA scans is equal to about 0.05 mSv (5 millirem), which is comparable to about 5 to 6 days of natural background radiation.
- The effects of radiation add up over your lifetime. Repeated exposures may increase your risk of injury or disease. When deciding to enter this study you should consider previous and future potential exposures.”

This Research Study may also include risks that are unknown at this time.

Please note, participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform one of the Research Team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

During the study, the Research Team will notify you of new information that may become available and might affect your decision to remain in the study.

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by University policy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the Research Team members listed in question 3 in this form.

13a. What are the potential benefits to you for taking part in this Research Study?

You may not have direct health benefits from participating in this study. Those taking the study medication may lose more weight than those in the control group. However, you may experience some weight loss and improvement in your uric acid kidney stone disease regardless of which group you are in by following the guidelines presented by the dietician.

13b. How could others possibly benefit from this Research Study?

The results of this study may help to provide better treatment options to patients with uric acid kidney stones.

13c. How could the Research Team members benefit from this Research Study?

In general, presenting research results helps the career of a researcher. Therefore, the Research Team listed in question 3 of this form may benefit if the results of this Research Study are presented at scientific meetings or in scientific journals.

13d. Will you be allowed to see the research information collected about you for this Research Study?

You may not be allowed to see the research information collected about you for this Research Study, including the research information in your medical record, until after the study is completed. When this Research Study is over, you will be allowed to see any research information collected and placed in your medical record.

14. What other choices do you have if you do not want to be in this study?

Your participation in this study is completely voluntary. If you do not want to participate, do not sign this document. Your care will not change in any way whether you decide to participate or not.

You may also refuse to authorize the use of your health information, but if you refuse, you may not be allowed to be in this research study or receive any research-related treatment that is only available in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

15a. Can you withdraw from this study?

You may withdraw your consent and stop participating in this Research Study at any time. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. If you decide to withdraw your consent to participate in this Research Study for any reason, please contact the Research Team listed in question 3 of this form. They will tell you how to safely stop your participation.

You can also change your mind and take back this Authorization at any time by sending a written notice to the Research Team listed in question 3 of this form to let them know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study. No additional health information about you will be collected or disclosed to the Research Team. However, if you take back this Authorization, you may not be able to continue in this study. Please discuss this with a member of the Research Team listed in question #3.

15b. Can the Principal Investigator withdraw you from this Research Study?

You may be withdrawn from this Research Study without your consent for the following reasons:

- To protect a participant from excessive risk or risk with a demonstrated lack of benefits (e.g., a participant experiences serious medication side-effects without the anticipated therapeutic effects)
- To maintain the integrity of the data (e.g., a participant is not following study procedures or may be deliberately providing false information)

Whenever an investigator terminates a subject's participation in research, the investigator must explain to the participant the reasons for the termination and, as appropriate, other treatment options available to the participant.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

16. If you choose to take part in this Research Study, will it cost you anything?

There will be no additional costs to you or your health plan as a result of your participation in this study. The sponsor will pay for all health care costs related to your participation, including all required study items, services and procedures described in this consent form. However, if you feel you have received a bill related to this study, please contact the Principal Investigator listed in question 3 on this form.
If you receive any healthcare at UF Health that is not related to this study, this care will be billed as usual.

17. Will you be paid for taking part in this Research Study?

You will be compensated for each of the study visits you complete based on the table noted below:

Encounter Number	Timing	Compensation
2	First Visit	$100
4	3 months	$100
5	6 months	$150
6	12 months	$200
8	18 months	$300

If you are paid more than $75 for taking part in this study, your name and social security number will be reported to the appropriate University employees for purposes of making and recording the payment as required by law. You are responsible for paying income taxes on any payments provided by the study. Payments to nonresident aliens must be processed through the University of Florida Payroll and Tax Services department. If the payments total $600 or more in a calendar year, the University must report the amount you received to the Internal Revenue Service (IRS). The IRS is not provided with the study name or its purpose. If you have questions about the collection and use of your Social Security Number, please visit: http://privacy.ufl.edu/SSNPrivacy.html

Your payment for participation in this research study is handled through the University of Florida's Human Subject Payment (HSP) Program. Your information which will include your name, address, date of birth, and SSN (depending on amount of money you are paid) is protected. Access to the (HSP) Program site is limited to certain staff with the assigned security role. You will be randomly assigned a specific identification (ID) number to protect your identity.

If you have any problems regarding your payment contact the study coordinator.

18. What if you are injured while in this Research Study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is routinely offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact the Principal Investigator listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this study.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this Research Study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent and Authorization Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing Date