CONSENT TO TAKE PART IN RESEARCH

Simple Study Title: Exenatide for Smoking Cessation and Prevention of Weight Gain

Full Study Title: A Randomized Controlled Trial of Exenatide as an Adjunct to Nicotine Patch for Smoking Cessation and Prevention of Post-Cessation Weight Gain

Study Sponsor: National Institutes of Health, National Institute of Drug Abuse

Protocol No.: HSC-M5-21-0639

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You are invited to take part in this research study. This consent form has important information about this study to help you decide whether or not to take part in this study. Your decision to participate is voluntary. You may refuse to take part, or choose to stop taking part, at any time. A decision not to take part or to stop being a part of the research project will not change the services available to you from Dr. Luba Yammine or the research staff at the University of Texas Health Science Center at Houston (UTHealth).

The purpose of this study will examine whether a medication called exenatide (Bydureon) is useful as a treatment for people who want to quit smoking and prevent post-quit weight gain. Exenatide is not available for this purpose outside of study because it is experimental and not approved for this purpose. Exenatide is thought to influence certain chemicals in your brain that affect craving for both cigarettes and food.

If you choose to participate in this study, you will be asked to complete an intake evaluation at UTHealth Center for Neurobehavioral Research on Addiction (CNRA) to determine your eligibility for the study. This intake process will involve medical and psychiatric evaluations by trained clinical staff members. If you qualify for the study, you will begin 14 weeks of outpatient treatment at the Treatment Research Clinic of the CNRA. The treatment will focus on helping you stop smoking. Once a week, you will be given the study medication, extended-release exenatide, also known as Bydureon or placebo (an inactive substance like saline). You will also receive nicotine patches for daily use and individual smoking cessation counseling. Exenatide (Bydureon) is approved for the treatment of type 2 diabetes. It is an injectable medication that is given just under the surface of the skin. Medical staff at the CNRA will take your vital signs and check your blood sugar level using a finger-stick procedure. You will also be asked questions to learn about any changes in cigarette smoking, cravings for cigarettes and food, and how you are feeling in general. Following completion of the 14-week treatment, you will be asked to come in for two follow-up visits (week 15 and week 26). The total amount of time you will be in this study is 27 weeks.

There are potential risks involved with this study that are described in this document. Some known risks include potential medication side effects, injection-site reactions, or discomfort answering personal questions.

There are potential benefits from your participation in this study. The study could help you quit smoking cigarettes while controlling your weight, and the information gained from your participation may benefit others in the future.

If you do not want to be in the study, there are no other choices except not to take part in the study, but researchers will provide you with referrals to other treatment programs in the community.

If you are interested in participating, please continue to read below.
What is the purpose of this study?
The purpose of this study is to investigate a potential treatment for quitting smoking and preventing post-quit weight gain.

This study will involve administration of exenatide (Bydureon), which is approved by the Food and Drug Administration (FDA) for the treatment of diabetes but not approved for treating nicotine addiction or weight maintenance. Because of this, exenatide is considered an "experimental" drug in this study. The sponsor is paying for this study to be completed.

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.

Who is being asked to take part in this study?
You have been invited to join this research study because you have elevated blood sugar (prediabetes) or are overweight and you are a cigarette smoker who wants to stop smoking. The study will enroll a total of 216 participants at two locations: the University of Texas Health Science Center at Houston (UTHealth) Center for Neurobehavioral Research on Addiction (CNRA) and Baylor College of Medicine (BCM), Michael E. DeBakey VA Medical Center (MEDVAMC).

What will happen if I take part in this study?
If you agree to participate in this study, we will perform a screening procedure to determine your eligibility. The screening will involve answering questions regarding your demographic and health history, lifestyle habits, a urine test to confirm that you are a smoker and rule out illicit drug use, and providing a blood sample (about 2 tsp of blood) for laboratory analysis. You will have your medical and psychiatric history taken, and a physical exam will be performed. You will be asked for your name, address, phone number, email address, and date of birth. The screening visit will take about 2 hours.

If you are determined eligible to participate in this study, you will have to return for 14 weekly visits (with one week separating each two visits). In addition, you will have to return for follow-up visits at week 15 and week 26. Visits 1 (week 1) and 3 (week 3) will take about 1.5 hours. The rest of the visits will take 35-45 minutes. You should not consume alcohol prior to any study visit, nor are any illicit (illegal) drugs permitted during any time while on study. If you take any over-the-counter (OTC) or prescription medications, the study principal investigator (PI) will review them and discuss with you whether these are allowed while you are in the study.

As part of this study you will receive a medication called exenatide (Bydureon) or you will receive placebo (an inactive substance like saline). You will not know which medication you will receive. You will receive exenatide or placebo by injection at each of your clinic visit during weeks 1-14. Regardless of whether you receive exenatide or placebo, you will also receive nicotine replacement therapy (nicotine patches) for daily use and weekly smoking cessation counseling during weeks 1-14. Your target quit date will be two weeks after the start of the study (after you have received two doses of the exenatide or placebo). You should do your best to entirely abstain from smoking after your target quit date; however, if you relapse, you will still be able to continue the study and try to quit later during the study. Your smoking status will be biochemically verified during each visit using breath test.

This treatment portion of the study will take 14 weeks in total, requiring you to come in once a week for a total of 14 visits. The following will occur during each study visit (weeks 1-14):

- Your blood pressure, heart rate, respiratory rate, weight, smoking status (using self-report and breath test), fingerstick stick blood sugar levels, health status, and overall wellbeing will be assessed.
- You will be asked to complete several questionnaires.
- You will receive exenatide or placebo. Exenatide/placebo is administered subcutaneously (in the fatty tissue) in the back of your arm, stomach or thigh area. The medication can be administered with or without food.
- You will receive a 1-week supply of nicotine replacement therapy (nicotine patches) for the upcoming week and individual smoking cessation counseling. Smoking cessation counseling will address preparation for quitting, identification of high-risk situations for smoking, support before and after the quit date, management of withdrawal symptoms, and keeping or resetting a quit date.
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If you are a woman of childbearing potential, you will be asked to complete a urine pregnancy test every two weeks.

In addition to the procedures described above, during week 1 and week 3 visits, the study staff will record your brain activity using an encephalogram (EEG, please see the details below).

Following the treatment completion, you will be required to return to clinic two times (follow-up visits), at week 15 and at week 26, for the assessment of smoking status (using self-report and breath test), weight and waist circumference and completion of several questionnaires. In addition, a blood sample (about 2 tsp of blood) for laboratory analysis will be collected during the week 15 and week 26 follow-up visits.

EEG. EEG will be conducted during week 1 and week 3 visits. To record your EEG, a net-like cap will be placed on your scalp. While you are wearing the cap, you will be asked to look at a series of pictures on a screen in front of you, and you may or may not be asked to perform a decision-making task. You may be offered a small snack (such as a granola bar, crackers, or similar) before the EEG, in which case, the study staff will ask you about any food allergies you may have. The pictures will include images of people, nature scenes, artwork, food and/or nicotine related content, and images that may be disturbing (such as mutilated bodies or nude people). You will be shown examples of these pictures before you start this part of the visit. After you complete the EEG, you may be asked to view and rate a set of pictures that are similar to the ones you viewed during the EEG. These pictures are images that have been used in other studies. Obtaining ratings from many people will help to validate these pictures for use in this type of research. You may also be asked to complete a short computer task called Mouse Tracking. For this task, you will use a computer mouse to click on pictures and objects on the screen. This will take about 10 minutes to complete. Finally, you will be asked to complete a short survey to provide feedback about the study session. This should take about 5 minutes to complete. A camera will be used to monitor you during the session. No videos or images will be recorded during the session.

How long will you be in the study?
If you agree to take part, your participation will last for about 27 weeks (17 visits total) and will involve 1 visit for the screening procedures, 14 weekly clinic visits (weeks 1-14) during the treatment part of the study, and 2 follow-up visits (week 15 and week 26).

What choices do you have other than this study?
You may select other options than being in this research study. The research staff will be happy to discuss these other options with you if you choose not to take part in this study.

What are the risks of taking part in this study?
There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks of exenatide: Extended-release exenatide (Bydureon) has the following Black Box Warning:

Risk of Thyroid C-Cell Tumors
- Exenatide extended-release (Bydureon) causes thyroid C-cell tumors at clinically relevant exposures in rats. It is unknown whether Bydureon causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC) in humans, as human relevance could not be determined by clinical or nonclinical studies.
- Bydureon is contraindicated in patients with a personal or family history of MTC or in patients with multiple endocrine neoplasia type 2.

There is a risk that you could have side effects from the study medication (Bydureon).

Common side effects associated with exenatide (Bydureon) include nausea, diarrhea, injection site nodule (a bump at the injection site), constipation, headache, dyspepsia (indigestion), vomiting, and injection site reaction. A regular reaction site reaction consists of swelling and discomfort at the injection site. A severe injection site reaction (described below) is more serious and consists of damage to the tissue.
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The risk of low blood sugar (hypoglycemia) with the use of exenatide is low. However, the risk of getting low blood sugar may be higher if exenatide is combined with another medicine that can cause low blood sugar (i.e. insulin). Upon the study entry and during the course of the study, the investigators will ask you about all medications that you are taking. Signs and symptoms of low blood sugar include dizziness or lightheadedness, sweating, confusion or drowsiness, headache, blurred vision, slurred speech, Shakiness, fast heartbeat, anxiety, irritability, mood changes, hunger, weakness, or feeling jittery.

Other serious reactions include hypersensitivity reaction (an exaggerated reaction to the medicine), anaphylaxis (life threatening allergic reaction), nephrotoxicity (poisonous effect on the kidneys), pancreatitis (inflammation in the pancreas), decreased platelet count (i.e. reduced number of platelets in your blood) and severe injection site reaction (severe pain, swelling, blisters, or a dark scab). In studies of patients without diabetes, the most common side effect of exenatide treatment was nausea. Overall, the side effects of exenatide are similar among patients with and without diabetes.

You will be asked if you have been experiencing various symptoms such as nausea, indigestion, stomach pain, diarrhea, changes in urination, weakness and other symptoms. Certain symptoms may prompt further evaluation by medical personnel and collection of blood samples for laboratory analysis. You will also meet with a study doctor at each injection visit and be checked for any symptoms or side effects.

**Pregnancy:** Exenatide (Bydureon) may harm your unborn baby. If you are a woman of childbearing potential (being able to become pregnant), due to the possible risks to a fetus, you may not participate in this study unless you are not pregnant and, with the investigator’s knowledge and approval, you are using a medically acceptable form of birth control (contraception). Examples of reliable forms of birth control include the Pill, Norplant, Depo-Provera, and consistent and correct use of condoms. You must agree to give urine samples to test for pregnancy (at no charge to you) before entering the study and during the study.

Other potential risks include -

**Risks of nicotine replacement therapy:** Nicotine patches is an OTC product with a proven safety record. Common side effects associated with nicotine patches include skin irritation, itchiness, rapid heartbeat, dizziness, and nausea.

**Risks of blood collection:** The risks of inserting a needle into a vein may involve pain from insertion of the needle; lightheadedness; fainting; hematoma (like a bruise) at the site of the needle insertion; inflammation of the vein; clotting of the vein; rarely, infection where the needle enters the skin, or rarely, an allergic reaction to the tape applied afterwards.

**Risks of subcutaneous injection:** The risks of subcutaneous injection may include pain from insertion of the needle, injection site reaction (i.e., abscess, cellulitis, or necrosis) with or without a nodule, or rarely, an allergic reaction to the tape applied afterwards.

**EEG:** Having an EEG may lead to skin irritation where the sensors are placed on the scalp. In addition, questionnaires may contain questions that are sensitive in nature. You may refuse to answer any questions that makes you feel uncomfortable. In the unlikely event that you become distressed from viewing certain images during the study or remain distressed after the study, mental health professionals are available for you to meet with.

**Confidentiality:** There is a risk of loss of confidentiality. In order to maintain confidentiality, all information you will provide in this study will not be provided to anyone outside the research group unless you give us written permission to do so. The only exceptions to this are reports of child abuse, elder abuse, or if you have serious thoughts to harm yourself or others.

**Unknown Risks:** There may be some risks that the study doctors do not yet know about.

**What are the benefits to taking part in this study?**

The benefits of participating in this study may be smoking cessation and prevention of post-cessation weight gain. However, you may receive no direct benefit from participating.

The study may help the study doctors learn things that may help others in the future.

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Can you stop taking part in this study?
Your participation in this study is voluntary. You may decide to stop taking part in the study at any time. To withdraw from the study, please contact Dr. Luba Yammine at 713-486-2800.

Your doctor or the sponsor can stop the study at any time. Your doctor or the sponsor may stop your participation in the study if your condition worsens, the study is stopped, the study medication is no longer available, you do not meet all the requirements of the study, or the study is not in your best interest. If your participation in the study is stopped, your doctor will discuss other options for your treatment.

If you stop participating in this study, the information already collected about you will still be used in the data analysis. However, no further information will be collected without your permission.

While taking part in this study, the study team will notify you of new information that may become available and could affect your willingness to stay in the study.

What happens if you are injured during the study?
In the event of injury resulting from this research, UTHealth is not able to offer financial compensation nor to absorb the costs of medical treatment. However, necessary facilities, emergency treatment, and professional services will be available to you, just as they are to the general community. You or your insurance company will be billed for any treatment. You should report any such injury to Luba Yammine at 713-486-2800 and to the Committee for the Protection of Human Subjects at 713-500-7943. You will not give up any of your legal rights by signing this consent form.

What are the costs of taking part in this study?
There are no costs to you to participate in this study. If you receive a bill that you believe is related to your taking part in this research study, please contact Dr. Yammine at 713-486-2800 with any questions.

Will you receive compensation for taking part in this study?
You will receive compensation for participating in this study as follows:
- Screening = $20
- Week 1-4 visits = $10/visit
- Week 5-8 visits = $15/visit
- Week 9-12 visits = $20/visit
- Week 13-14 visits = $25/visit
- Week 15 follow-up visit = $30
- Week 26 follow-up visit = $50
- EEG sessions (week 1 and week 3) = $20/session
- Return of used/unused nicotine patches (weeks 2-15) = $5/weekly return
- Additional coverage as needed for transportation-related expenses (e.g., bus, parking).

The total amount of compensation, including the screen, 14 treatment visits, follow-up visits at weeks 15 and 26, nicotine patch returns, and two EEG sessions will be $440.00.

You will be compensated with cash or a cash equivalent (reloadable debit card or gift cards), following the completion of each study visit. All information is stored in a secure fashion and will be deleted from the system once the study has been completed.

If you receive payment for taking part in this study, please be informed that you will be asked to complete a copy W-9 form that will be forwarded to the accounting department as a requirement by the Internal Revenue Service. You will also be issued a 1099-Misc form from this study for tax reporting purposes.
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The University of Texas Health Science Center at Houston owns any data collected and the use of the data, results, treatments, or inventions that can be made from the research. The University's ownership includes the right to license or transfer the use or ownership to other parties including without limitation, commercial entities contracting with UTHealth. There are no plans to compensate you for any patents or discoveries that may result from your participation in this research study. You will not be paid for any use of your data, samples, or results.

How will privacy and confidentiality be protected?
Your privacy is important and your participation in this study will be kept confidential. However, absolute confidentiality cannot be guaranteed.

If you sign this document, you give permission to UTHealth to use and disclose (release) your health information. The health information that we may use or disclose for this research includes medical history and psychological testing information obtained at intake screening. Please understand that health information used and disclosed may include information relating to HIV infection, drug abuse, alcohol abuse, behavioral health, and psychiatric care.

Personal identifiers such as your name and medical record number will be removed from the information and samples collected in this study. After we remove all identifiers, the information or samples may be used for future research or shared with other researchers without your additional informed consent.

Please understand that research study data will be sent to the sponsor of this research study, National Institutes of Health (NIH). The data that will be sent to the sponsor will not include your name but may include your initials, date of birth, date of study visits, and date of study procedures.

People who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect your health information and may share your information with others without your permission, if permitted by laws governing them. You will not be personally identified in any reports or publications that may result from this study. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

Representatives of the organizations listed below will see your name and other personal identifiers when they review your research records and medical records for the purposes of verifying study data:

- Representatives of UTHealth
- Representatives from the U.S. Food and Drug Administration (FDA)
- Representatives from the National Institute on Drug Abuse (NIDA)
- Members of Data and Safety Monitoring Boards (an independent group of experts that reviews this study's data to make sure participants are safe and the research data is reliable)
- Companies engaged with UTHealth for the commercialization of the results of the research study

Please note that you do not have to sign this Authorization, but if you do not, you may not participate in this research study. UTHealth may not withhold treatment or refuse treating you if you do not sign this Authorization.

You may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must contact Dr. Luba Yammine in writing at 1941 East Road, Houston, TX. 77054.

This Authorization will expire 15 years after the end of the study.

Certificate of Confidentiality:
To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.
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The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, medical care provider, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality does not prevent the researchers from disclosing, without your consent, information that they are required by law to disclose to government authorities. For example, researchers must comply with laws requiring the reporting of suspected child abuse and neglect and communicable diseases.

Whom can you contact if you have questions about the study?

If you have questions at any time about this research study, please feel free to contact the principal investigator, Dr. Luba Yammine at 713-486-2800, as they will be glad to answer your questions. You can contact the study team to discuss problems, report injuries, voice concerns, obtain information in addition to asking questions about the research.

The Committee for Protection of Human Subjects at the University of Texas Health Science Center has reviewed this research study. You may contact them for any questions about your rights as a research subject, and to discuss any concerns, comments, or complaints about taking part in a research study at (713) 500-7943.

SIGNATURES

Sign below only if you understand the information given to you about the research and you choose to take part in this research study. Make sure that all your questions have been answered. If you decide to take part in this research study, a copy of this signed consent form will be given to you.

Printed Name of Subject ___________________________ Signature of Subject ___________________________ Date ________ Time ________

Printed Name of Person Obtaining Informed Consent ___________________________ Signature of Person Obtaining Informed Consent ___________________________ Date ________ Time ________

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