Official Title: A Randomized Clinical Trial of 100 Units of Intradetrusor Onabotulinum Toxin A for Refractory Overactive Bladder - Is 10 Injections Less Painful Than 20 Injections?
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Wake Forest®
School of Medicine

Department of Urology

A Randomized Clinical Trial of 100 Units of Intradetrusor Onabotulinum Toxin A for Refractory Overactive Bladder - Is 10 Injections less Painful than 20 Injections?

Informed Consent Form to Participate in Research
Catherine Matthews, MD Principal Investigator

Summary

You are invited to participate in a research study. The purpose of this research is to help determine if 100 units of Botox ® distributed in 10 injections to treat refractory overactive bladder is less painful than 20 injections. You are invited to be in this study because you have decided to undergo treatment of your overactive bladder with Botox ®. Your participation in this research will involve 4 visits and last about 3 months.

Participation in this study will involve you receiving the current United States Food and Drug Administration (FDA) recommended dose of Botox ® which is 100 units. However, you will either receive this dose in 10 injections or 20 injections based on randomization. All research studies involve some risks. A risk to this study that you should be aware of is the risk of urinary tract infections, urinary retention, and that this therapy may not work for you. These risks apply whether or not you participate in the study. You may or may not receive benefit by participating in this study. .

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include receiving Botox 100 units in the amount of injections determined by your provider's standard practice. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is Catherine Matthews, MD, the principle investigator of this study and Whitney Smith, MD, co-investigator. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study her contact information is: [redacted].

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at [redacted] or the Research Subject Advocate at Wake Forest at [redacted].

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you have refractory overactive bladder. Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to help determine if 10 injections of Botox ® 100 units is less painful than 20 injections of Botox ® 100 units based on effectiveness in reducing urge incontinence episodes. We will also assess the pain of procedure and adverse outcomes of 20 injections versus 10 injections.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

40 people will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

At your first visit, you will have a baseline post void residual (the amount of urine left in your bladder after you have emptied it in the restroom) measured by a bladder scanner (a portable ultrasound machine that will determine how much urine is left in your bladder), urinalysis (a urine sample test looking for abnormal conditions such as infection or blood in the urine), fill out a form to determine if you are eligible to participate in the study), complete a 3 day bladder diary at home as a part of standard procedure; that is you return a completed diary which was provided to you during your last visit and before deciding upon participation in this study, and complete a questionnaire regarding how bothersome your overactive bladder is to you.

At your second visit, you will undergo injections of Botox ® into your bladder through a cystoscope (an instrument used to visualize the inside of the bladder). Prior to doing this, again we will use the urinalysis to see if you have a urinary tract infection. At this visit you will be randomized to receive either 10 injections or 20 injections of a total 100 Units of Botox ® which is the dose recommended by the FDA. You will also fill out a form asking you to rate the pain of procedure.

At your third visit 2 weeks after your procedure, you will have your post void residual and urinalysis checked. You will fill out 3 forms to assess your level of bother from overactive bladder, how is it affecting your quality of life, and if you have had any complications such as urinary tract infection or urinary retention. You will be provided a 3 day bladder diary, which you will start updating 3 days in advance to complete before the last (4^{th}) visit. You will be requested to bring the completed diary during your 4^{th} (last) visit.

At your fourth visit 12 weeks after your procedure, you will have your post void residual and urinalysis checked. You will fill out 3 forms to assess your level of bother from overactive bladder, how is it affecting your quality of life, and if you have had any complications such as urinary tract infection or urinary retention. You will be required to complete a 3 day bladder diary at home, and you will fill out a form for the completion of the study.

You will be randomized into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in any group.

You will either fall in a group of study patients who receives 10 injections, or 20 injections. Study team opens an envelope before the procedure, which will have information whether you will be receiving 10 injections or 20. You will not be informed the group you are in to avoid any effect on your selection for the post procedural pain rate. During the procedure, one provider will count up to 20. If you are in a group of subjects receiving 10 injections, then you will not receive an injection at either an odd or even count from 1 to 20. You will also not be able to view the procedure on the monitor – the display will be turned in a way where only the provider and study staff will be able to see.

How Long Will I Be in the Study?

You will be in the study for about 12 weeks.

You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. Currently, there are no serious consequences for withdrawing early from the study.

What Are the Risks of the Study?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the procedures and drug we are studying include:

This study is comparing two approved methods for treating your condition. You will be randomly assigned to one of the two groups. It is possible that one treatment group may have a better response than the other. Therefore there is a risk that you may be assigned to a group that does not perform as well as its comparison.

The risks associated with this study are the risks associated with this procedure in general. There is a risk that you may not be able to empty your bladder completely requiring the use of catheterization, urinary tract infection requiring a course of antibiotics, allergic reactions, and

difficulty breathing and swallowing. Allergic reactions and difficulty breathing and swallowing are rare. The risk that you may require a catheter to empty your bladder or have a urinary tract infection is approximately 5%. These reactions are not permanent. There is also the potential that this treatment may not be effective for you. These risks are the same if you chose to participate in this study or not.

In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

Reproductive Risks and other Issues to Participating in Research

Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), Depo Provera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

Pregnant women are excluded from participation in this study. Because some methods of birth control are not 100% reliable, a pregnancy test is required at least 10 days from your last normal menstrual period, if you are a sexually active woman of childbearing potential.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You may or may not receive benefit from taking part in this research study. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, you have these options:

You could be treated with Botox ® 100 units even if you do not take part in the study. The number of injections administered will be determined by your individual provider.

If you chose not to use Botox ® 100 units all together, the other options for treating refractory

overactive bladder include sacral neuromodulation or percutaneous tibial nerve stimulation.

WHAT ARE THE COSTS?

All study costs will be paid for by the study. Costs for your regular medical care, which are not related to this study, which include BOTOX injections, will be your own responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

WILL YOU BE PAID FOR PARTICIPATING?

You will receive no payment or other compensation for taking part in this study.

The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Wake Forest Baptist Health Department of Urology. The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these

medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted].

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Drs. Catherine Matthews (principle investigator) or Whitney Smith (research study co-investigator) at [redacted], 24 hours a day and 7 days a week.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:** postvoid residual measurement, urinalysis, bother and quality of life questionnaires pertaining to overactive bladder, pain of procedure, bladder diaries, and adverse reactions to Botox ®.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

Monitors, auditors, IRB or other regulatory agencies will be granted direct access to the participant's original medical record for verification of clinical trial procedures or data, without violating confidentiality of the participant and to the extent permitted by other applicable laws.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept for at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed or it will be de-identified. Any research information entered into your medical record will be kept for as long as your medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Drs. Catherine Matthews or Whitney Smith that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Dr. Catherine Matthews and Whitney Smith
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

If you choose to participate in this study, your medical record at Wake Forest University Baptist

Medical Center will indicate that you are enrolled in a clinical trial. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

A description of this clinical trial will be available on http://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

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study

investigator, Whitney Smith, MD or Catherine Matthews, MD at [redacted] (24 hours a day, 7 days a week).

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted] or the Research Subject Advocate at [redacted].

You will be given a copy of this signed consent form.

SIGNATURES

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature: _____ Date: _____Time:_____ am pm

Person Obtaining Consent (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm