

Walter Reed National Military Medical Center
CONSENT TO PARTICIPATE IN RESEARCH

Principal Investigator: LCDR Angela DiCarlo-Meacham, MD

Contact Information: 301-400-2468

OnabotulinumtoxinA (Botox) has been shown in multiple studies to be effective for treating overactive bladder symptoms that do not get better with behavioral changes or medications. Botox is marketed in the US and is FDA approved for the indication of treatment for overactive bladder. This study will follow the route, dosage and subject population for which it is FDA approved. The standard way that onabotulinumtoxinA is given to patients for treating overactive bladder is with a series of 20 injections into the bladder with 100 units or 30 injections with 200 units for neurogenic overactive bladder. Idiopathic overactive bladder occurs in patients for an unknown reason. Neurogenic overactive bladder occurs due to an injury to the brain or spinal cord. This is often done under local anesthetic in the office. A small amount of research shows that injecting the same amount of onabotulinumtoxinA with fewer injections may work similarly to the 20 injections. The purpose of this study is to compare the standard technique with a technique using only five injections to see whether the results are similar for treating overactive bladder symptoms. Consent for this study will be obtained and participation in this study is voluntary. Participation in this study will require follow-up for 6-9 months following the procedure for injection of onabotulinumtoxinA into the bladder. Research activities that differ from standard of care for this procedure will include completing a series of questionnaires prior to the injection of onabotulinumtoxinA into the bladder as well as completing those same questionnaires at 4-12 weeks and 6-9 months following the procedure. Foreseeable risks of participating in the study include decreased effectiveness of the treatment to help symptoms of overactive bladder as well as risk of the procedure itself which include urinary tract infection, difficulty urinating temporarily, need to use a catheter temporarily and weakness or flu-like symptoms from the injection of onabotulinumtoxinA. The investigators think that giving the same dose in fewer injections will not be less effective than the standard way and think it is possible it may have fewer side effects when given in fewer injections, thus benefits of participating are potentially lower risks of infection and difficulty urinating with equal effectiveness of the treatment. Additionally, the procedure may be more comfortable with fewer injections needed. At the end of the study, participants' information or biospecimens will not be used or distributed for future research studies even if identifiers are removed. Alternatives for treatment if you decline to participate in the study are undergoing onabotulinumtoxinA injection into the bladder per standard of care with 20 injections or a number of other treatments for overactive bladder to include behavioral therapies, medications or neuromodulation.

- 1. PROTOCOL TITLE:** Standard injections vs reduced injections for intravesical onabotulinumtoxinA treatment for idiopathic and neurogenic overactive bladder: a randomized study



You may be eligible to take part in this research study. This form gives you important information about the study.

Please take time to review this information carefully. You should talk to the researchers about the research study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or your personal physician) about your participation in this study. If you decide to take part in this research study, you will be asked to sign this document. Before you sign this document, be sure you understand what the research study is about, including the risks and possible benefits to you.

Please tell these researchers if you are taking part in another research study.

You do not have to take part if you do not want to. You may also leave the research study at any time. If you choose not to take part in this research study or if you leave the study before it is finished, there will be no penalty.

Your decision will not affect your future care at Walter Reed National Military Medical Center

2. WHAT IS THE PURPOSE AND DURATION OF THIS RESEARCH AND WHO WILL TAKE PART?

You are being asked to take part in this research study because you have bothersome overactive bladder and either have failed other treatments or declined other treatments and desire injection of onabotulinumtoxinA (Botox) into the bladder to treat your symptoms. The purpose of this research study is to learn about whether a fewer number of injections (five) with the same overall dose of Botox provides similar results as the standard twenty or thirty injections. Additionally, the difference in urinary tract infections and difficulty emptying the bladder following the procedure will be studied. The duration of participation per visit is 30-60 minutes per visit with a follow-up period of 6-9 months from the date of Botox injection.

Up to 184 people will be taking part in the study at WRNMMC over a period of 2 years or longer. Enrollment will be stopped once complete data is collected for 64 patients in each group or when a total of 184 patients are enrolled, whichever occurs first.

During the study, you will have about 2-3 visits with the Urogynecology or Urology department at WRNMMC. You may also need to return more times as needed if you develop any concerns related to the study treatment.

The participant may receive relevant clinical information through his/her healthcare provider. Research data will not be shared with the participant.

3. WHAT WILL HAPPEN IF YOU DECIDE TO BE IN THIS RESEARCH?

You will: Prior to treatment with bladder Botox, you will be asked to complete three questionnaires to assess your symptoms of overactive bladder and their impact on your quality of life. You will also be asked to complete a demographic sheet that asks more questions regarding



your overactive bladder symptoms as well as basic information about you i.e. age, medical history, etc. All of these forms should not take more than 10-15 minutes to complete total.

You will then receive bladder Botox injections according to the study protocol using either the standard technique or the study technique. The technique that is used for your procedure will depend on which group you are assigned as is discussed later here. Following the procedure, you will be asked to rate your post-procedure pain level on a scale of 0-10 using a visual pain scale with 0 being no pain and 10 being worst possible pain.

You will follow-up in the Urogynecology of Urology clinic 4-12 weeks following the procedure and will repeat the questionnaires again. You will also undergo an ultrasound of the bladder after you void to see how well you are able to empty your bladder. If you are experiencing symptoms concerning for a urinary tract infection, we will obtain a catheterized urine specimen to send to the lab to look for signs of an infection. If an infection is found, you will be treated with antibiotics and a culture will be obtained to ensure the appropriate antibiotics are being given. If you are found to have an infection at your 4-12 week follow-up, you will be asked to delay completing the questionnaires until the infection has been treated.

You will then be contacted 6-9 months following Botox treatment and will be asked to complete the questionnaires a final time. This can be done either by phone, via email or in person depending on your preference.

If at any time following the treatment, you find that your symptoms are not well controlled, you can follow-up in the Urology or Urogynecology clinic for further evaluation and discussion on treatment options. You may be offered repeat Botox injection but it cannot be done prior to 12 weeks after the initial injection. Repeat Botox is standard of care when the symptoms of overactive bladder come back after treatment.

For your Botox treatment, you will be randomly assigned to one of 2 groups (standard or study technique). Randomization is a process like flipping a coin and means you will have a chance of being assigned either of the groups.

Group A- Patients will be receiving the standard technique for Botox injection into the bladder. A dose of 100 units of Botox will be mixed into 10mL of sterile injectable saline (if you have idiopathic overactive bladder) or 200 units in 30mL of sterile injectable saline (if you have neurogenic overactive bladder). If you have idiopathic overactive bladder, the Botox will be administered with 20 small injections of 0.5mL spaced approximately 1cm apart along the back wall of the bladder above the bladder base. If you have neurogenic overactive bladder, the Botox will be administered with 30 small injections of 1mL spaced approximately 1cm apart along the back wall of the bladder above the bladder base. This is the technique described in the Botox package instructions.

Group B- Patients will receive the study technique for injection of Botox into the bladder. A dose of 100 units (for idiopathic overactive bladder) or 200 units (for neurogenic overactive bladder) of Botox will be mixed into 10mL of sterile injectable saline. The Botox will then be injected with 5 injections of 2mL for each site with two rows of two injections with a fifth site in the



middle to form an “X” configuration. The injections will be above the bladder base with the injections on either side being in line with the openings of the ureters (tubes that connect the kidneys to the bladder).

4. WHAT ARE THE RISKS OR DISCOMFORTS FROM BEING IN THIS RESEARCH?

If you choose to take part in this study, there is a risk of:

Risk of Botox treatment for overactive bladder include anxiety and/or pain associated with the procedure. For most patients, this procedure is done in the office under local anesthesia and some patients find the procedure to be painful. Additionally, there is a risk of urinary tract infection following the procedure with a risk ranging from 20-30% on average. Urinary retention, or the inability to empty the bladder normally, occurs in 25% of patients with 5% of those needing to temporarily catheterize themselves. Other common side effects from bladder Botox is lower abdominal pain temporarily following the procedure and blood tinged urine for a couple days following the procedure. Rare risks are allergic reactions to the medication and generalized muscle weakness.

Although efforts are made to protect your research study records, there is always a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.

It is not known whether Botox can cause birth defects or other problems in an unborn child.

If you are a FEMALE ABLE TO BECOME PREGNANT and you want to take part in this study, you should know that Botox injection into the bladder might be harmful to (1) an unborn child if you are pregnant; or (2) an infant if you are breast-feeding. You will take a pregnancy test before you can participate in this study. You should not get pregnant or breastfeed while in this study. The only completely reliable methods of birth control are not having sex or surgical removal of the uterus. Other methods, such as the use of condoms, a diaphragm or cervical cap, birth control pills, IUD, or sperm killing products are not totally effective in preventing pregnancy.

If you become pregnant or feel you might be pregnant, contact your personal physician and the principal investigator of this study listed in the Contact Information section at the end of this document.

There may also be other risks of taking part in this study that we do not yet know about.

5. WHAT ARE THE POSSIBLE BENEFITS FROM THIS RESEARCH?:



The possible benefits to you as a research participant in this research study are less pain or discomfort during the procedure and possibly a lower likelihood of developing a urinary tract infection or urinary retention following the procedure if you receive the study technique. However, there is no guarantee that you will benefit from being in this research.

6. WHAT ARE THE ALTERNATIVES TO TAKING PART IN THIS RESEARCH?

There may be other options for treating overactive bladder. Alternative treatments and/or procedures that may be available to you include: physical therapy, behavioral modifications, oral medications and sacral neuromodulation. These should have all been discussed with you prior to the decision to proceed with Botox. You should talk with your personal physician (if applicable) about these options.

Choosing not to take part in this research study is also an option.

The medication involved in this research study may also be available through your personal physician without taking part in this study.

7. IS THERE COMPENSATION FOR YOUR PARTICIPATION IN THIS RESEARCH?

No, you will not receive any compensation for participating in this study.

8. ARE THERE COSTS FOR PARTICIPATING IN THIS RESEARCH?

No, there are no costs to you for taking part in this research study.

9. WHO IS CONDUCTING THIS RESEARCH?

Division of Urogynecology at Walter Reed National Military Medical Center

10. STUDY SPONSOR (the organizations or persons who oversee the study and are responsible for analyzing the study data):

Department of Defense

As the sponsor of this research, the Department of Defense may have access to your research data in accordance with DoDI 3216.02.

11. SOURCE OF FUNDING:

None



12. PRINCIPAL INVESTIGATOR (the person(s) responsible for the scientific and technical direction of the study):

Angela DiCarlo-Meacham, MD
LCDR, MC, USN

13. LOCATION OF THE RESEARCH:

Urogynecology and Urology clinics, Building 9
Walter Reed National Military Medical Center
Bethesda, MD

14. DISCLOSURE OF FINANCIAL INTERESTS AND OTHER PERSONAL ARRANGEMENTS:

None

15. WHO WILL SEE MY INFORMATION (PRIVACY) AND HOW WILL IT BE PROTECTED (CONFIDENTIALITY)?

Records of your participation in this research study may only be disclosed in accordance with state and federal law, including the Federal Privacy Act, 5 U.S.C.552a, and its implementing regulations. DD Form 2005, Privacy Act Statement - Military Health Records, contains the Privacy Act Statement for the records. A copy of DD Form 2005 can be given to you upon request, or you can read on-line at:

<http://www.dtic.mil/whs/directives/infomgt/forms/eforms/dd2005.pdf>.

The research team will keep your research records. These records may be looked at by staff from the Urogynecology department, the Institutional Review Board (IRB), and the DoD Higher Level Review as part of their duties. These duties include making sure that the research participants are protected. Confidentiality of your records will be protected to the extent possible under existing regulations and laws but cannot be guaranteed.

Procedures to protect the confidentiality of the data in this study include but are not limited to: All participants will be assigned a study number and all data collected will be identified by the study number only. A master list will be kept that links patient identification with the study numbers. This will be the only link to patient identification and will be kept on a department share drive and will be password protected on a CAC enabled computer. Only members of the research team will be given access to the password. Study data will be collected on data sheets which will be stored in a locked file cabinet of a locked office when not in use. These records may be looked at by staff from the Walter Reed (WRNMMC) Department of Research Programs, the Walter Reed (WRNMMC) Institutional Review Board (IRB), the DoD Higher Level Review, and other organizations, such as the Food and Drug Administration (FDA) as part of their duties.



Researchers will make every effort to protect your privacy and confidentiality; however, there are risks of breach of information security and information loss.

If applicable, 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 results. You can search this Web site at any time.

By signing this document, you give your permission for information gained from your participation in this research study to be published in literature, discussed for educational purposes, and used generally to further science. You will not be personally identified; all information will be presented as anonymous data.

Complete confidentiality cannot be promised for military personnel, because information regarding your health may be required to be reported to appropriate medical or command authorities to ensure the proper execution of the military mission, including evaluation of fitness for duty.

The principal investigator and the research team will have access to your records and agree to safeguard your protected health information by using and disclosing it only as permitted by you in this consent or as directed by state and federal law.

16. WHAT HAPPENS IF YOU ARE INJURED AS A RESULT OF THIS RESEARCH?

If you think that you have a research-related injury, notify your Principal Investigator immediately at 301-400-2468.

If you are injured because of your participation in this research and you are a DoD healthcare beneficiary (e.g., active duty military, dependent of active duty military, retiree), you are authorized space-available medical care for your injury within the DoD healthcare system, as long as you remain a DoD healthcare beneficiary. This care includes, but is not limited to, free medical care at DoD hospitals or DoD clinics.

If you are injured because of your participation in this research and you are not a DoD healthcare beneficiary, you are authorized space-available medical care for your injury at a DoD hospital or an DoD clinic; medical care charges for care at a DoD hospital or a DoD clinic will be waived for your research-related injury. If you obtain care for research-related injuries outside of a DoD or DoD hospital or clinic, you will not be reimbursed for those medical expenses.

For DoD healthcare beneficiaries and non-DoD healthcare beneficiaries: Transportation to and from hospitals or clinics will not be provided or paid for by DoD. Unless you are covered by TRICARE, no DoD reimbursement is available if you incur medical expenses to treat research-related injuries. No compensation is available for research-related injuries. You are not waiving any legal rights.



17. WHAT HAPPENS IF I WITHDRAW FROM THIS RESEARCH?

You may withdraw your consent at any time and stop participating in this research study without affecting your eligibility for care or any other benefits to which you are entitled. Should you choose to withdraw, you must notify a member of the research team as soon as possible once you decide to withdraw from the research. Any information already collected from you will still be used in the final analysis to maintain the integrity of the research. All data that is collected will be coded, which minimizes the risk for breach of confidentiality. Some of the data collected from participants that withdraw contain important data points that the investigators would like to use for analysis. However, any further information will not be collected once you withdraw. If you desire to have all your data withdrawn from the study and analysis, that request will be honored.

If you wish to **withdraw** from the study, please notify the PI via phone, email, letter, or in person. If you wish to have **all of your data withdrawn from the study**, please notify the PI in writing.

Should you change your mind after withdrawal and desire to again participate in the research, you will be welcome to do so provided you are within the appropriate windows following the Botox procedure to complete the study questionnaires. Regardless of when you choose to withdraw from the study, you are encouraged to follow-up with either the Urogynecology or Urology departments at WRNMMC for further treatment of symptoms or if you have any concerns regarding the treatment you received. If you do not follow these procedures, you may experience unwanted phone calls or emails if you no longer desire to participate in the study but do not notify us of that. You may also experience recurrence of overactive bladder symptoms or symptoms of urinary tract infection or urinary retention that will go untreated if you choose not to come back for follow-up.

If you are receiving treatment as part of this research study, you will no longer be eligible for such research-related treatment. Contact your personal physician to discuss medical treatment for your condition.

Please note that withdrawing your consent to participate in this research does not fully revoke your HIPAA Authorization Form to use/disclose your protected health information. To make that revocation, please send a letter to the principal investigator as discussed in the HIPAA Authorization Form.

The principal investigator of this research study may terminate your participation in this research study at any time if she determines this to be in your best interest, if you are unable to comply with the procedures required, or if you no longer meet eligibility criteria.

18. VOLUNTARY PARTICIPATION:



The decision to take part in this research study is completely voluntary on your part. You will be informed if significant new findings develop during the course of this research study that may relate to your decision to continue participation.

19. INCIDENTAL FINDINGS

There is a possibility that while reviewing your test results we may see an abnormality that we did not expect to see in this study. This is what is called an "incidental finding."

We will let you know if we see such an incidental finding. Depending on the type of incidental finding, we may contact you by phone. In the case of a potential serious emergency, the researcher will inform you right away.

You do not have an option to decline receiving information about an incidental finding. A qualified person (usually a member of the research team) will talk to you if there is an incidental finding.

We will also give information about this incidental finding to your primary doctor or we will refer you to an appropriate doctor for further evaluation.

- An incidental finding may cause you to feel anxious
- Since an incidental finding will be part of your medical record, you could face greater difficulty in getting health or life insurance

The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility. If you are a DoD beneficiary, you will have access to care through standard Military Health System and TRICARE procedures.

20. CONTACT INFORMATION:

Principal Investigator (PI)

The Principal Investigator or a member of the research staff will be available to answer any questions throughout this study.

Principal Investigator: Angela DiCarlo-Meacham, MD

Phone: 301-400-2468

Mailing Address: Department of Obstetrics and Gynecology/Division of Female Pelvic Medicine and Reconstructive Surgery
8901 Wisconsin Ave
Bethesda, MD 20889

Institutional Review Board (IRB) Office



If you have any questions about your rights as a research participant or if you have concerns or complaints about the research study, please contact the IRB Office at:

301-295-8239

Walter Reed National Military Medical Center
Department of Research Programs
Building 17B
8901 Wisconsin Ave
Bethesda, MD 20889

Participants with research related injuries may contact the Staff Judge Advocate at 301-295-2215

IF THERE IS ANY PORTION OF THIS DOCUMENT THAT YOU DO NOT UNDERSTAND, ASK THE INVESTIGATOR BEFORE SIGNING. YOU MAY CONSULT WITH YOUR PERSONAL PHYSICIAN OR LEGAL ADVISOR, IF YOU WISH.

A signed and dated copy of this document will be given to you.

SIGNATURE OF PARTICIPANT

Printed Name of Participant

Signature of Participant

Date/Time

SIGNATURE OF INDIVIDUAL ADMINISTERING CONSENT

(Can only be signed by an investigator or staff approved to administer consent)

Printed Name of Administering Individual

Signature of Administering Individual

Date/Time