Meets 2018 Common Rule Requirements

Walter Reed National Military Medical Center
CONSENT TO PARTICIPATE IN RESEARCH
Title: Urinary Tract Infection Prophylaxis In Intradetrusor OnabotulinumtoxinA Procedures: A Randomized Controlled Trial
Principal Investigator: MAJ Jordan Gisseman, MD

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

Please take time to carefully review this information. 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 potential participation in this research study. You do not have to take part in this study. Participation is voluntary. You may also leave the research study at any time without penalization.

1. KEY INFORMATION:

OnabotulinumtoxinA (Botox®) has been shown in multiple studies to be effective for treating overactive bladder (OAB) symptoms that do not get better with behavioral changes or medications. OnabotulinumtoxinA is marketed in the United States and is FDA approved for the treatment for OAB. OnabotulinumtoxinA has also been shown to be effective for the treatment of interstitial cystitis/bladder pain syndrome (IC/BPS). This study will follow the same instructions for which it is FDA approved. Urinary tract infection (UTI) is a common event following onabotulinumtoxinA injections. To prevent this, patients are given a course of antibiotics, however the research is not conclusive about the best antibiotic to use, or best duration of treatment, and there is data to suggest that a single dose of antibiotic may be as effective as a longer course. Concerns with using more antibiotic than needed include antibiotic side effects, developing other infections after using the antibiotic, and development of bacteria with resistance to antibiotics. This study will compare using a single dose of 100mg of nitrofurantoin given at the time of bladder onabotulinumtoxinA injection with a 3-day twice daily course of 100mg of nitrofurantoin. Consent for this study will be obtained and participation in this study is voluntary. Participation in this study will require follow-up for up to 45 days following the procedure. Research activities that differ from standard of care for this procedure will include completing a questionnaire prior to the injection of onabotulinumtoxinA into the bladder as well as completing a questionnaire at 30-45 days after the injection. Possible risks of participating in the study include the possibility of a higher risk of UTI with a single dose of antibiotic versus the higher risk of side effects with the 3-day course of antibiotic, which most commonly include nausea or headache, but also include a very small risk of anaphylaxis. Alternatives for treatment if you decline to participate in the study are receiving the standard antibiotic regimen for the clinic, which is a 3-day course of nitrofurantoin or trimethoprim-sulfamethoxazole based on any allergies you may have.

Your decision will not affect your future care at Walter Reed National Military Medical Center. 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 in all sections of the consent form, including the risks and possible benefits to you.

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

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 OAB or IC/BPS and either have failed other treatments or declined other treatments and desire injection of onabotulinumtoxinA into the bladder to treat your symptoms. The purpose of this research study is to learn if using a single dose of nitrofurantoin at the time of the procedure will result in a similar reduction in post procedure UTIs compared to the standard 3-day regimen of nitrofurantoin. The study will help to determine whether nitrofurantoin can be used to reduce potential side effects from unnecessary antibiotics. The duration of participation begins with your procedure and ends with a follow up phone call 30-45 days later.

There will be about 100 people taking part in the study at WRNMMC over a period of 1-2 years. Enrollment will be stopped once complete data is collected for 100 participants. During the study, you will have 1 visit with the Urogynecology Division at WRNMMC and a follow up phone call 30-45 days later. 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?

Prior to treatment with bladder onabotulinumtoxinA you will also be asked to complete a demographic sheet that asks basic information about you i.e. age, medical history, etc. You will also be asked to give a urine sample one week prior to the procedure to ensure you do not have a UTI. If your urine is concerning for a UTI you will be treated, and your procedure may have to be delayed until after treatment is completed.

You will be randomly assigned to one of two groups. Randomization is a process like flipping a coin and means you will have a chance of being assigned to either of the groups. The assignments will be made randomly by a computer prior to beginning the study and placed in numbered envelopes. The day of the procedure an envelope will be opened to reveal your assignment to either the single dose of nitrofurantoin or the 3-day twice daily nitrofurantoin group, you will be informed of your assignment, and you will be given a dose of 100mg of nitrofurantoin prior to the procedure. You will then receive bladder onabotulinumtoxinA injections in accordance with the FDA approval for route, dosage, and subject population. If assigned to the 3-day twice daily group then you will additionally be given a prescription at your

pharmacy of choice for 5 additional tablets of nitrofurantoin, the first to be taken the evening of the procedure and then twice daily for the remaining 4 tablets.

Your physician will place an order for a urine culture in case you feel like you are developing a UTI with symptoms. Common symptoms that suggest a UTI include urethral burning, increased urinary frequency, or increased urinary urgency, however testing is needed to confirm this diagnosis. If you develop any of these symptoms then you can proceed directly to any military lab to leave a sample. You should also contact the clinic team at that time to inform us of your symptoms and treatment will be initiated if a UTI is found.

You will have your final contact with the study team at 30-45 days after the procedure by phone. At that time, you will be asked about any UTI symptoms, diagnoses, side effects, and any antibiotics you may have received from any other clinic during the study period, and your chart will be reviewed for urine test results. If you indicate that you were treated at a non-DOD facility then we will attempt to obtain records from your visit and lab results. If we are unable to get in contact with you for follow up, we will review your chart for any indication you were diagnosed with a UTI, including but not limited to lab results, visits with a physician, or prescriptions for antibiotics.

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

If you choose to take part in this study, there is a possibility of an increased risk of UTI. UTI happens in 20-30% of patients after onabotulinumtoxinA injections with variable doses of antibiotics. Being randomized to receive one dose of antibiotics may or may not increase that risk of UTI.

You may also have an allergic reaction to the antibiotic given regardless of duration of course. If you believe that you are having an allergic reaction that is not life-threatening such as nausea or a headache, please inform the clinic if you feel that these side effects are bad enough to discontinue the medication. Based on our discussion with you we may instruct you to stop taking the medication. If you believe you are having a life-threatening allergic reaction, such as trouble breathing, then please go to the nearest emergency room or call 911 immediately.

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.

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 a lower risk of side effects from antibiotics (headache, upset stomach, and development of antibiotic resistant bacteria), as well as the convenience of needing to take only one dose of antibiotic.

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

You may choose not to participate in this study. If you desire to receive onabotulinumtoxinA injections outside of the study then you will receive the clinic standard 3-day antibiotic course. Other options for treatment of OAB and IC/BPS are also available.

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

Jordan Gisseman, MD
MAJ, MC, USA
Phone: 301-400-2468

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. LOCATION OF THE RESEARCH:

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

13. DISCLOSURE OF FINANCIAL INTERESTS AND OTHER PERSONAL ARRANGEMENTS:

None

14. 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 Divisiono, 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 participant identification with the study numbers. This will be the only link to participant 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.

15. LONG TERM USE OF DATA

Data will not be saved for future research

16. 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.

17. 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 this research study that may relate to your decision to continue participation.

18. 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 onabotulinumtoxinA 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 Divisions 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 OAB symptoms or symptoms of UTI 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 he 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.

19. 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.

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: MAJ Jordan Gisseman, MD
Phone: 301-400-2468
Mailing Address:
Department of Gynecologic Surgery and Obstetrics/Urogynecology Division
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

By signing below, I agree that I have been provided time to read the information describing the research study in the consent form. The content and meaning of this information has been explained to me. I have been provided with the opportunity to ask questions. I voluntarily consent to participate in this study.

By signing this form, I have not given up any of my legal rights as a research 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