CONSENT FORM AND AUTHORIZATION FOR DISCLOSURE OF PROTECTED HEALTH INFORMATION

STUDY TITLE: IS LESS MORE? DOES DECREASING ONABOTULINUMTOXINA SITES IN THE BLADDER INCREASE PATIENT SATISFACTION WHILE MAINTAINING EFFICACY?

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Research Locations:
William Beaumont Hospital - Royal Oak & Comprehensive Urology – Royal Oak

INTRODUCTION

Why is this study being done?

You are being asked to participate in a research study. The purpose of research is to look at the nature of disease and try to develop improved methods to diagnose and treat disease. The doctor or clinician in charge of the study believes you meet the initial requirements to take part in the study. Before agreeing to participate, it is important for you to read and understand the following explanation of the research procedures. This Consent and Authorization form describes the purpose, procedures, benefits, risks and discomforts of the study. It also describes the alternatives available to you, and your right to withdraw (quit) from the study at any time.

Please read this information carefully and ask as many questions as you like before deciding whether or not you would like to take part in this research study.

Overactive bladder (OAB) causes the sudden need to urinate. It has a negative impact on health-related quality of life. In the body, certain chemicals travel from nerve cells to muscle cells to make the bladder contract so that you can urinate. With OAB, these muscles contract uncontrollably and you frequently feel like you must empty your bladder. OnabotulinumtoxinA injected into the bladder works on the nerves and bladder muscle, blocking the signals that trigger OAB.

The goal of this study is to determine if three injection sites of onabotulinumtoxinA is just as effective as the common practice of ten injection sites. This study is also being done to determine if less injection sites has fewer complications and leads to better patient satisfaction and tolerability, because this procedure is performed in the doctor's office while you are awake.

A total of 192 patients will take part in this study at Beaumont.

How long will I be in the study?
If you decide to take part in this study, your participation is expected to last up to 12 months. You may not take part in this study if you are currently enrolled in another related research study which could alter or influence the study results.

DESCRIPTION OF THE STUDY
What will happen if I take part in the research study?
You are being asked to take part in this research study because you have been diagnosed with overactive bladder and your doctor has recommended onabotulinumtoxinA injections as a treatment.

If you agree to take part in this study you will be randomly assigned to the three-injection group or the ten-injection group. Randomization is like "the flip of a coin." The study team will know which group you are in, but you will not. This is called "blinding." Blinding is done to ensure that the results are not affected by a placebo effect (the power of suggestion).

Screening Evaluation/Visit 1
The study will be explained to you in detail, and you will have as much time as you need to ask questions. You will be asked to read and sign this Consent and Authorization form before any study-related procedures are performed. The following tests and procedures will be done to determine if you qualify to participate in this study:

- Review demographic information (birth date, gender etc.)
- Review of your medical and surgical history, review of medications you are currently taking and medications that you have taken in the past
- Collection of urine samples for laboratory tests. These tests include:
    - A urine pregnancy test for all women of childbearing potential. The result of the pregnancy test must be negative for you to participate in this study.
    - Urinalysis and/or urine culture
- Complete questionnaires about your urinary symptoms
- Receive a 3-day voiding (urination) diary to complete before Visit 2 – you will be instructed on how to complete the diary

Enrollment and Treatment/Visit 2
You must bring the completed voiding (urination) diary with you to this visit. If you meet the eligibility criteria, you will be enrolled in the study and randomized into the three-injection group or the ten-injection group. If you do not meet the eligibility criteria, you will not be able to participate in this study. The following assessment and procedures will be conducted:

- Review of medications you are currently taking and medications that you have taken in the past
- Evaluation of any new medical events that have occurred since your last visit
- Collection of urine samples for laboratory tests. These tests include:

  - A urine pregnancy test for all women of childbearing potential. The result of the pregnancy test must be negative for you to participate in this study and to receive onabotulinumtoxinA.
  - Urinalysis and/or urine culture
- The study doctor may order an antibiotic (medication to prevent urinary tract infection) to take by mouth before and after the procedure.
- Cystoscopy (a cystoscope is a long thin tube with a camera that the study doctor can see through). The cystoscope is inserted through your urethra (tube that transmits urine from the bladder to the exterior of the body during urination) and into your bladder. This procedure will allow your study doctor to see what your urethra and your bladder looks like.
- Injection of onabotulinumtoxinA into your bladder. The doctor will use a needle to inject the medication into your bladder. You will be given local anesthesia (numbing medicine) to decrease the discomfort of the procedure.
- Complete study questionnaire
- Evaluation of any side effects
- Receive a 3-day voiding (urination) diary to complete before Visit 3 – you will be instructed on how to complete the diary

2 Week Follow-up/Visit 3 through 12 Month Follow-up/Visit 7

- Review any medications you are taking and any adverse events you may have experienced.
- Collection of urine sample for urinalysis and pregnancy (at visits 4, 5, 6, 7), if applicable
- Post void residual (at visits 3 or 2 weeks after a repeat injection).
- Complete questionnaires about your urinary symptoms
- Receive a 3-day voiding (urination) diary to complete before your next visit – you will be instructed on how to complete the diary

- Visit 4, 5, 6, and 7 may be conducted by phone and mail if necessary.

Unscheduled visits

- Unscheduled visits may be necessary for repeating questionnaires and voiding diaries when a UTI is confirmed.

Below is a table describing what will occur at each study visit:

	Screening	**Enrollment/ Treatment**	**2 Week Follow -up**	**3 Month Follow -up**	**6 Month Follow -up**	**9 Month Follow -up**	**12 Month Follow -up**
	Visit 1	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**	**Visit 6**	**Visit 7**
Consent	x						
Medical History	x						
Questionnaires	x	x	x	x	x	x	x
3-Day Voiding Diary	x		x	x	x	x	x
Urine sample	x	x	x	x	x	x	x
BTX injection		x					
Post void residual			x				
Repeat BTX injection				x	x	x	

Repeat injections will be offered at the clinician's discretion. Participants will be eligible for repeat injections 3 month after initial injection.

Depending on your symptoms, you may request another injection at, or any time after, Visit 4 (3 Month Follow-up). This will be discussed with your doctor. If you have a repeat injection you would then have a 2 Week Follow-up visit and follow the above schedule.

FDA Clinical Trial Information

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.

PARTICIPANT RESPONSIBILITIES

You will be asked to note any side effects or medical problems you may experience while you are taking part in this study. For any illnesses or injuries, you should contact the study doctor immediately at the number listed in this Consent and Authorization form or in an emergency call 911 (or go to the nearest hospital emergency room).

RISKS, SIDE EFFECTS AND DISCOMFORTS

Ask your doctor what the standard of care risks are as well as the study risks. In this study the risks listed below are the same risks if you are not participating in this study.
What side effects or risks can I expect from being in the study?

Risks of onabotulinumtoxinA:

Most frequent (occurring more than 10% of the time)

- Weakness of the bladder muscle resulting in difficulty in urination or an inability to urinate or empty the bladder (urinary retention) for an extended period (less than a month in most cases, but could be longer). A catheter may need to be inserted into the bladder to drain all the urine.

Less frequent (occurring more than 1%, but less than 10% of the time)

- Constipation

Rare (occurring less than 1% of the time)

- Generalized weakness

Risks of the injection procedure:

As with any injection, participants may experience local pain/soreness, bleeding, bruising, infection, and/or swelling. Some people feel faint or pass-out when being injected with medications.

Most frequent (occurring more than 10% of the time)

- Urinary tract infection

Less frequent (occurring more than 1%, but less than 10% of the time)

- Blood in the urine
- Difficulty or painful urination

Rare (occurring less than 1% of the time)

- Temporary bleeding at the injection site resulting in a blood clot in the bladder tissue
- Urosepsis (an infection that occurs when the urinary tract infection spreads to the bloodstream)

The following side effects have not been observed previously with onabotulinumtoxinA injections but could possibly happen:

Less frequent (occurring more than 1%, but less than 10% of the time

- permanent tissue damage from repeated injections
- accidental bladder wall puncture resulting in onabotulinumtoxinA introduction into abdominal space or near-by structures
- injury from the cystoscope (long thin tube with a camera that the study doctor can see through) resulting in temporary urethral swelling, urethral injury, blockage of urine flow, or overstretching of the bladder
- increased blood pressure
- headache
- decreased heart rate

Rare (occurring less than 1% of the time):

- local pain/soreness
- bleeding
- bruising
- infection
- swelling
- feeling faint or passing out when being injected

Risks of Cystoscopy

Less frequent (occurring more than 1% but less than 10% of the time):

- discomfort or pain
- cramps
- infection
- painful or difficult urination

Rare (occurring less than 1% of the time):

- bleeding (blood in urine)
- inability to pass urine after the procedure
- trauma
- urinary tract infection
- puncture of the bladder
- temporary swelling or injury to the urethra
- overstretching of the bladder
- a change in urinary frequency
- urgency (the sudden urge to urinate), including urgency resulting in episodes of incontinence (the accidental leakage of urine)

Risks of Antibiotic (Medicine to Prevent Infection)

Less frequent (occurring more than 1% but less than 10% of the time):

- Diarrhea
- Nausea and vomiting
- Stomach cramping

Rare (occurring less than 1% of the time):

- Headache
- Itching
- Rash
- Allergic reaction

If you are required to stop taking a medication for overactive bladder you may experience an increase in your urinary symptoms (urinary urgency, frequency, and/or urge urinary incontinence).

There is a rare risk of breach of confidentiality (release of information which personally identifies you).

Pregnancy Warning

If you are a woman who is pregnant or becomes pregnant during the research study, there could be harmful effects to you or your unborn child. It is important you not be pregnant or breast-feeding during your study participation. If you are a woman of childbearing potential you must have a negative pregnancy test before entering the study.

BENEFITS

What are the benefits of taking part in this study?

There may be no direct benefit to you from taking part in this study. However, we hope to show that participants in the three-injection group have fewer complications, less pain, better tolerance of the procedure and greater patient satisfaction. Information gained from the results of this study may be of benefit to others in the future, with a similar medical condition.

ALTERNATIVE OPTIONS

What are my choices other than taking part in this study?

You do not have to take part in this study to receive treatment for your condition. Conservative adjustments you can make at home to help with the condition include avoidance of caffeine, carbonated beverages, and alcohol, which are known to be irritants to the bladder.

Alternative treatments that are available to treat overactive bladder include numerous oral medications that act by their effects on the nerves that supply the bladder. When taken on a regular basis, they may help to relieve symptoms of overactive bladder. These may cause side effects such as dry mouth and constipation.

Neuromodulation devices, which stimulate and regulate the nerves that supply the bladder, can also be utilized for treatment. This type of therapy can be provided in office based setting treatments or by surgically implanted devices that provide similar therapy. This may decrease urgency and frequency and help with urinary incontinence. Risks associated with this treatment include uncomfortable stimulation, migration of device leads, infection, and ineffective nerve stimulation.

ECONOMIC CONSIDERATIONS

What are the costs of taking part in this study?

All procedures are routine and you would have had them done even if you were not taking part in this study. They will be billed to your health insurance company and/or group health plans as usual (for example, urine laboratory tests (7), cystoscopy (1-5), and the onabotulinumtoxinA 100U vial (1-5).

If these routine care costs are <u>not</u> covered by your health insurance/group health plan, the cost will be your responsibility.

COMPENSATION

What happens if I am injured because I took part in this study?

Your involvement in this study is voluntary. The possible risks and side effects which might occur during the course of the research study have been described in this Consent and Authorization form.

A research injury is any physical injury or illness caused by the medications, devices, or procedures required by the study which are administered, used, or performed appropriately.

These medications, devices, or procedures are different from the medical treatment you would have received if you had not taken part in the study.

Should you experience a research injury, there are no designated funds provided for subsequent medical care or compensation by either the study doctor/clinician or Beaumont.

What are my rights if I take part in this study?
You are not giving up any of your legal rights by signing this form.

CONFIDENTIALITY, DISCLOSURE AND USE OF YOUR INFORMATION
Will my medical information be kept private?
We will keep your personal health information as confidential as possible. It is not likely your information will be given to others without your permission. In order for this research study to take place, you must also authorize the researchers to access and use some of your protected health information (PHI). PHI is information which could identify you as an individual such as name, address, date of birth, etc. By signing this Consent and Authorization Form, you give Beaumont permission to use and/or disclose (release) your health information related to this research. Your medical and billing records collected for the purpose of the study will remain confidential, but may be disclosed (released) or used by the following and/or their representatives:

- The investigators (study doctor/clinician, research staff)
- Beaumont and its' parent, Beaumont Health and affiliated hospitals
- The Food and Drug Administration
- Other governmental regulatory agencies (domestic and/or foreign)
- Your health insurance company and/or group health plans and their intermediaries (companies contracted to process claims) may also have access to your medical and billing records of the study.

The purpose for this disclosure (release) or use is, for example, to assure compliance with the study protocol, to evaluate the effectiveness of the study, and/or to provide protection to you as a research study participant. The disclosure and use of your information will continue after your involvement in the study has ended. There is no expiration date for the use of your medical and billing records from the study. Any information about you disclosed to the parties identified above may be re-disclosed by them; however, such re-disclosure is not under the protections of this Consent and Authorization.

You will not be identified in any publication or other release of study results, data, and other information (such as in professional writings, at professional meetings, and/or advertising or other promotional materials).

If you decide to withdraw your authorization for the researchers to access and use your protected health information before the end of the study, you will be withdrawn from the research study. However, where the study relied on your Consent and Authorization for the time you participated in the study, your Consent and Authorization cannot be withdrawn and the information already collected may still be used and disclosed as you previously authorized.

STOPPING STUDY PARTICIPATION

What if I decide to stop taking part in the study?

Taking part in this research study is completely voluntary. You may choose not to take part or to stop being in the study (withdraw) at any time without penalty or loss of benefits to which you are otherwise entitled, or without jeopardizing your medical care by your doctor at Beaumont. However, if you do not agree to sign this Consent and Authorization form, you will not be able to take part in this study.

If you decide to withdraw from the study you will need to notify the study doctor/clinician of your decision to stop taking part in the study. Written notification is preferred. This notice may be sent to Larry T. Sirls, MD at William Beaumont Hospital, 3535 West 13 Mile Road, Suite 438, Royal Oak, MI 48073.

Your participation in this study may be stopped by the study doctor/clinician or study sponsor, without your consent, for any reason, which will be explained to you. Examples include:

- The study procedures appear to be medically harmful to you.
- You fail to follow directions for participating in the study.
- It is discovered you do not meet the study requirements.
- The study is canceled.
- It is determined to be in your best interest (for example, your disease has progressed despite treatment).

If your study doctor/clinician stops your participation, or you decide not to continue, you may be asked to have a final study visit or examination, in order for you to be discontinued from the study in a safe and orderly manner.

CONTACTS

Who can answer my questions about the study?

You may talk to the study doctor/clinicians about any questions or concerns regarding your study participation, or you think you may have suffered a research-related injury. The doctor/clinician in charge of the study, Larry Sirls, MD may be reached at: 248-336-0123 to answer your questions.

Your contact person is Erica Zagaja, RN. You may contact her at (248) 551-0642.

If you have questions regarding your rights as a research participant, or have problems, concerns, complaints, want information or would like to offer input, you may contact the Institutional Review Board Chairperson at (248) 551-0662. The Institutional Review Board is charged with the oversight of all human participant research conducted at Beaumont facilities.

STATEMENT OF VOLUNTARY PARTICIPATION

I have read the above, have asked questions and have received answers about this study to my satisfaction. I understand what I have read and willingly give my consent to participate in

IS LESS MORE? DOES DECREASING ONABOTULINUMTOXINA SITES IN THE BLADDER INCREASE PATIENT SATISFACTION WHILE MAINTAINING EFFICACY?

I understand I will receive a signed copy of this document and will be promptly informed of any new findings regarding this study. I further authorize the use or disclosure of my health and personal information contained in records as described above.

_____
RESEARCH PARTICIPANT NAME (PLEASE PRINT)

_____ _____ _____
RESEARCH PARTICIPANT SIGNATURE DATE TIME

ALTERNATIVE SIGNATURE (for use only when participant is a minor, cognitively impaired or critically ill**)**
AS THE PERSONAL/LEGAL REPRESENTATIVE OF THE STUDY PARTICIPANT, PLEASE PRINT PARTICIPANTS NAME ON THIS LINE_____, AND CHECK ONE OF THE BOXES BELOW AS THE BASIS FOR YOUR AUTHORITY TO SIGN THIS CONSENT AND AUTHORIZATION:

☐ COURT-APPOINTED GUARDIAN
*COURT LETTER IS REQUIRED

☐ DURABLE POWER OF ATTORNEY
*ATTORNEY LETTER MUST BE PRESENT & VERIFIED BY 2 PHYSICIANS

☐ NEXT OF KIN

_____ _____
NAME (PLEASE PRINT) RELATIONSHIP TO PARTICIPANT

_____ _____ _____
SIGNATURE DATE TIME

☐ WITNESS TO ENTIRE CONSENT PROCESS AND SIGNATURE ARE REQUIRED IF THE PARTICIPANT IS VISUALLY IMPAIRED, ILLITERATE OR NON-ENGLISH SPEAKING ONLY

_____
WITNESS NAME (PLEASE PRINT)

_____ _____ _____
WITNESS SIGNATURE DATE TIME

AUTHORIZED CONSENT PROVIDER STATEMENT:

I have explained this study and have offered the study participant an opportunity for any further discussion or clarification.

_____ _____ _____
NAME (PLEASE PRINT) CREDENTIALS PHONE NUMBER

_____ _____ _____
SIGNATURE DATE TIME