IRB NUMBER: 207102012815

LOYOLA UNIVERSITY CHICAGO
HEALTH SCIENCES DIVISION
MAYWOOD, ILLINOIS
DEPARTMENT OF OBSTETRICS & GYNECOLOGY
DIVISION OF FEMALE PELVIC MEDICAINE AND RECONSTRUCTIVE SURGERY

INFORMED CONSENT

Participant's Name: _____

Medical Record Number: _____

PROJECT TITLE: Mirabegron and Urinary Urgency Incontinence: The Clinical Response and the Female Urinary Microbiome

THE APPROVAL FOR THIS PROJECT EXPIRES ON 01/17/2019.

Participant Information

PRINCIPLES CONCERNING RESEARCH: You are being asked to take part in a research project. It is important that you read and understand the principles that apply to all individuals who agree to participate in the research project described below:

1. Taking part in the research is entirely voluntary.

2. We do not know if you will benefit from taking part in the research but the knowledge obtained may help others.

3. You may withdraw from the study at any time without anyone objecting and without penalty or loss of any benefits to which you are otherwise entitled.

4. If during your participation in the research project new information becomes available which would affect your being in the research project (such as better treatments or the side effects of the treatments), your doctor will discuss this new information with you and will help you make a decision about your continuing in the research.

The purpose of the research, how it is to be done, and what your part in the research will be is described below. Also described are the risks, inconveniences, discomforts and other important information which you need to make a decision about whether or not you wish to participate. You are urged to discuss any questions you have about this research with the staff members.

PURPOSE OF RESEARCH: You are being asked to participate in this study because you have been diagnosed with urgency incontinence or overactive bladder (OAB).

This purpose of this study is to see why so many patients with OAB symptoms have persistent symptoms while taking medications for OAB. We believe that bladder bacteria plays a role in women not responding to OAB treatment. Although it is not well known, most women have bacteria in their bladders. These bacteria live in the bladder without causing symptoms. When women get symptoms of overactive bladder, they only improve with medications about 50% of the time

Mirabegron is an FDA-approved medication for urgency incontinence. Mirabegron is a medication that works on receptors in the bladder wall muscle. When these receptors are filled and activated, the bladder actively relaxes and is less likely to develop overactive bladder contractions that result in urgency incontinence.

The purpose of this study is to see if women who respond to mirabegron have different bladder bacteria than women who do not respond. Our hope is that by studying the interaction between mirabegron and bladder bacteria we will better understand the cause of urgency incontinence.

This research is sponsored by Astellas Pharma US

Approximately 120 women with OAB people will participate in this research.

DESCRIPTION AND EXPLANATION OF PROCEDURES: If you agree to participate in this study, you will be asked to sign this consent document.

If you are currently are taking an anticholinergic medication for overactive bladder symptoms you will need to stop taking the medication for 2 weeks before you can start the study. Stopping the medication may temporarily worsen your overactive bladder symptoms.

Mirabegron is used for the treatment of overactive bladder. Stopping your current medication allows us to better understand how mirabegron (once you start taking it) is helping your symptoms.

You will be required to come to the clinic for 4 visits: baseline, 4 weeks, 8 weeks & 12 weeks total participation time will be 12 to 14 weeks.

At each visit your urine will be tested to see if you have a urinary tract infection. The urine sample will be collected by passing a catheter (a small rubber tube) through your urethra and into your bladder. This is called a catheterized urine samples. You will also need to complete 5 questionnaires (USIQ, PFDI, OABq and UDI-6, PGI-S, and PPBC). You will then be given mirabegron (Myrbetriq) to start treatment. This visit should take about 45-60 minutes.

We will collect urine at each visit and the urine will be sent to the research laboratory for special tests done on the bacteria in the urine. Since these are research tests and the meaning of the results not known, you and your doctor will not be notified of the results of any research tests done on your bacteria and your urine.

If you have an active urinary tract infection at 4 or 8 weeks or 12 weeks, we will collect a catheterized sample and then treat appropriately with antibiotics. This visit would be part of your usual care. One week after completion of antibiotic therapy, we will obtain another catheterized sample and complete the questionnaires.

You will take a daily 25 mg dose by mouth of Mirabegron. You will take this medication by mouth once a day for twelve weeks. If after **4** weeks you do not feel that your symptoms are adequately improved you will have the option of increasing the Mirabegron dose to 50 mg per day for the remaining **8** weeks of the study.

The data collected is being used solely for research purposes and will be given a study identification number in order to insure your privacy.

We will also review your medical record to collect additional information that is normally collected as part of your routine care. Again, no personal identifiers will be used in collecting this information. As above, your study identification number will be used.

A description of this clinical trial will be available at *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 website at any time.

RISKS/DISCOMFORTS: It is possible that the study treatment you receive may not be effective in treating your overactive bladder symptoms.

If you are currently taking an anticholinergic medication for overactive bladder symptoms and stop taking it for the washout period of 2 weeks, there is the chance that your symptoms may temporarily worsen until you start taking mirabegron.

You may experience slight discomfort when the catheter (rubber tube) is placed into the opening of the bladder (urethra). There is a small risk (less than a 1% chance) of a urinary tract infection with the placement of the catheter (rubber tube) into the opening of the bladder (urethra).

The medication used for this study is Mybetriq (mirabegron). It is approved for the treatment of urge incontinence.

Uncommon side effects of mirabegron (1-5%) reported include:

- high blood pressure,
- difficulty emptying the bladder,
- fatigue

Rare events have been reported. These include:

- swelling,
- skin rash,
- allergic reactions (including very severe reactions that require hospitalization),
- headache,

- confusion,
- hallucinations,
- heart palpitations,
- changes in the electrical pattern of the heart

As mentioned above you will not be identified by name or by any other identifying information on the questionnaires. A study identification number will be listed on each questionnaire and data collection sheets.

REPRODUCTIVE AND SEXUAL ACTIVITY INFORMATION: The intervention in this study could affect a developing baby. Therefore, you cannot participate in this research project if you are pregnant or breast feeding.

If you are a woman of childbearing potential, a pregnancy test will be done to make certain that you are not pregnant before beginning the study. Women who are able to have children must use an effective method of preventing pregnancy while participating in this study.

In addition, as study medications may remain in the body for a period beyond their administration, you will be asked to continue to employ an effective method of preventing pregnancy for 4 weeks after you have finished taking the study medication. You are encouraged to discuss your preferred method with the study physician Dr. Mueller. She will answer any questions you have regarding effective methods of preventing pregnancy. It is important that you consult with your physician because some study medications may affect the effectiveness of various methods of preventing pregnancy.

If you become pregnant, suspect that you have become pregnant, notify Dr. Mueller immediately.

BENEFITS: We do not know if you will benefit from participating in this study. The information learned may help others in the future.

ALTERNATIVE TREATMENTS: You do not have to participate in this research project to receive care and treatment at Loyola University Medical Center.

You can choose the treatment, mirabegron in this project without participating in the project.

Your doctor has discussed other options with you along with their risks and benefits.

FINANCIAL INFORMATION: Some health plans will not pay the costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting treatment without being in this study. Depending on your health insurance, there may be a co-payment for the standard visits. You will be responsible for any usual out-of-pocket expenses such as co pays, coinsurance or deductibles.

As part of your normal clinical care, a catheterized urine culture will be obtained. The clinic will

also obtain a catheterized specimen for any urinary symptoms that suggest a urinary tract infection. This is part of the clinic routine of care and as such will be charged to your health insurance plan just as they would if you were not participating in a research study.

Costs for procedures not included in the standard care will be covered by the research study.

The medication used in this study will be provided at no cost to you. There will be no costs to you for participating in this research. You will be responsible for all other costs associated with your care.

Neither you nor your insurance provider will be billed for any procedures that are performed exclusively for this research study. Those procedures that are being performed for research purposes only include 4, 8, and 12 week catheterized urine culture, research tests done on the urine and expanded quantitative urine culture. The study will pay for the 4, 8, and 12 week office visits.

You will be given a parking sticker for the day of your visit.

RESEARCH RELATED INJURY: In the event that you are injured or have side effects as a result of participating in this research project, your doctor will take the necessary steps to treat the problem. There are no funds available from Loyola University Medical Center, Loyola University Health System or Loyola University Chicago to pay for the cost of care of the problem. You will be financially responsible for the cost of care of any problems. By signing this form, you are not giving up any legal rights to seek to obtain compensation of injury.

INFORMATION COLLECTED AND WHAT WILL HAPPEN TO IT: In order to meet the goals of the research study (see Purpose of Research section of this consent), we will collect information on you, your test results, and how you do from you and your Loyola University Medical Center (LUMC) medical records. The information will be collected by the Principal Investigator Dr. Wolfe, the study physician(s), the research nurses, data administrators and secretaries.

Information about you will be provided to Loyola University Chicago; Astellas Pharma US, the research sponsor; data collection and study verification agencies; and/or government regulatory agencies such as the Food and Drug Administration.

In this way, we will learn why so many patients with overactive bladder still have symptoms after treatment with Myrbetriq. We believe that bladder bacteria play a role in OAB symptom persistence.

The information we will collect and send includes:

__X__ DEMOGRAPHIC INFORMATION (e.g., name, address, phone number,)

__X__ MEDICAL RECORD (including, but not limited to, history and physical exam notes, progress notes, consultation reports, laboratory test results, AND/OR operative reports)

We will collect and provide this information about you for as long as you are in the study, Once the information is disclosed outside of LUMC, it may no longer be protected by federal privacy laws. This authorization does not expire.

It is possible that the sponsor, Astellas Pharma US, , research nurses, data collection and/or study verification agencies, data administrators or staff, or the Food and Drug Administration will come to LUMC and view the medical record (see above for description of content) and the research records. They may take notes or copy pages of the medical record. This is done to verify the accuracy of the information LUMC is sending to them.

The results of this research study may be published in a journal for the purpose of advancing medical knowledge. You will not be identified by name or by any other identifying information in any publication or report about this research.

Consent for LUMC to use and disclose your medical information is required in order for you to participate in the study.

WITHDRAWAL OF CONSENT: Your consent to use and disclose your medical information for the purpose of this research study is completely voluntary. You can withdraw your consent for LUMC to use and disclose your information and your consent to participate in this study at any time without affecting your ability to receive care and treatment at LUMC unrelated to the research study. Withdrawal means that all study procedures and follow-up will stop and we will not send any more information about you to the sponsor of this research or its designees. However, information already used and disclosed to the research sponsor prior to the time of your withdrawal from this study may continue to be used and disclosed by LUMC and the sponsor.

For your safety, we may ask that you return to clinic one more time for follow-up. We will also ask that you return any unused study medication. If you withdraw from the study, you will need to contact your physician(s) to discuss what other options may be available.

If you withdraw from the study, we will ask that you sign the form attached to this consent and send it to or give it to the study staff. Your withdrawal from the study will not have any effect on any actions by LUMC taken before the attached form is received by LUMC.

Your study doctor, the Institutional Review Board, the regulatory authorities, or the sponsor, Astellas Pharma US, may terminate the study at any time with or without your consent.

Your study doctor may choose to take you out of the study because of unexpected or serious side effects, treatment non-compliance, or because you are not taking the medication as you were instructed. You may also be removed from the study if your study doctor feels that you are not benefiting from the study treatment.

CONSENT

I have fully explained to _____ the nature and purpose of the above-described procedure and the risks that are involved in its performance. I have answered and will answer all questions to the best of my ability. I may be reached at 708-216-2067.

_____Date:____/_____/____
Signature

Alan Wolfe, Ph.D., is the principal investigator for this study. Elizabeth Mueller, M.D., is the clinical principal investigator for this research project. Dr. Mueller can answer any questions you have about the treatments, procedures and side effects or complications that can be associated with the study. Alan Wolfe, Ph.D., can answer any questions you may have about the relationship between bacteria in the bladder and response to treatments. Alan Wolfe, Ph.D., can be reached at: 708- 216-5814. Dr. Mueller can be reached at: 708-216-2170.

If you ever feel that you have been injured by participating in this study or if you have any questions concerning your rights as a research participant, you may contact either Kenneth Micetich, MD, Chair of the Institutional Review Board for the Protection of Human Subjects-Loyola University Chicago Health Sciences Division, at 708-216-2633 or the Director of the Human Research Subjects Protection Program at 708-216-4608.

Although you have the right to revoke this authorization, you accept that such revocation will not apply to any uses and disclosures of your information that are described in the Loyola University Health System Notice of Privacy Practices or otherwise allowable under any Federal or State laws.

You will receive a signed copy of this informed consent document.

You have been fully informed of the above-described research program with its possible benefits and risks. Your signature below indicates that you are willing to participate in this research study and agree to the use and disclosure of information about you as described above. You do not give up any of your legal rights by signing this consent document.

_____Date:____/_____/____
Signature: Participant

_____Date:____/_____/____
Signature: Witness

PROJECT TITLE: Mirabegron and Urinary Urgency Incontinence: The Clinical Response and the Female Urinary Microbiome

REVOCATION OF AUTHORIZATION TO
RELEASE PROTECTED HEALTH INFORMATION (PHI)

I, _____, hereby revoke my consent to participate in the study titled, "Mirabegron and Urinary Urgency Incontinence: The Clinical Response and the Female Urinary Microbiome", at Loyola University Medical Center ("LUMC"). I also revoke my consent to release information I provided to LUMC that allowed LUMC to use and disclose my medical information to Astellas Pharma US as outlined on the consent form, which I signed on ____/_____/____ (INSERT DATE CONSENT WAS SIGNED ORIGINALLY). I understand that this revocation does not apply to any action LUMC has taken in reliance on the consent I signed earlier.

_____Date:____/_____/____
Signature: Participant

Please return this form to:

Dr. Alan Wolfe
Loyola University Medical Center
2160 South First Avenue
Maywood, Illinois 60153