UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

Please read this form, which describes the study in some detail. A member of the research team will describe this study to you and answer all of your questions. Your participation is voluntary. If you choose to participate, you can change your mind at any time and withdraw from the study. You will not be penalized in any way or lose any benefits to which you would otherwise be entitled if you choose not to participate in this study or to withdraw. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study?

Improving Treatment Personalization of Pulmonary Hypertension Associated with Diastolic Heart Failure

3. Who do you call if you have questions about this research study?

Principal Investigator: Julio Duarte, Pharm.D., Ph.D.
Assistant Professor, UF College of Pharmacy
352-273-8132
juliod@cop.ufl.edu

Other research staff: Evan Waters
Clinical Research Coordinator
352-294-5885
waterse@ufl.edu

4. Who is paying for this research study?

The sponsor of this study is the United States National Institutes of Health.

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research, how long will you be involved?

This study is testing a new treatment for pulmonary hypertension associated with a specific type of heart failure (left diastolic heart failure).

b) What is involved with your participation, and what are the procedures to be followed in the research?

Participation in this study will involve taking an oral nebivolol tablet once daily for four months, and at least four study visits to test your response and check for any potential adverse effects using vital signs, laboratory tests, electrocardiogram, cardiac catheterization and echocardiogram.

c) What are the likely risks or discomforts to you?

While not common, risks could include adverse effects from the study medication or study procedures.

d) What are the likely benefits to you or to others from the research?

You many not benefit directly from this research, but if nebivolol benefits patients with this type of pulmonary hypertension, it may be studied further as a potential treatment for this disease.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

There are no established treatments for this type of pulmonary hypertension, so your physician will continue to treat your heart failure and monitor your disease.

Additional and more detailed information is provided within the remainder of this Informed Consent form, please read before deciding if you wish to participate in this study.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this research study)?

No treatments exist for this disease. Your doctor will continue to treat your heart failure and monitor your pulmonary hypertension.

7. What will be done only because you are in this research study?

You will have approximately 3 tablespoons of blood taken at each study visit, a total of 4 times. The blood will be taken from your arm. The total amount of blood taken for the whole study will be about 12 tablespoons. The blood will be used to test your liver function, your genetics, your blood cell counts, proteins that are associated with heart failure, and to check electrolytes in your blood.

Visit 1: You will be asked to provide a blood sample and a brief medical history, including questions about certain medications you take. Vital signs (such as blood pressure, pulse, temperature, and breathing rate) will be measured, an electronic tracing of your heart (EKG) will be done, and you will be given a breathing questionnaire and a 6-minute walk test. You will then be asked to take oral nebivolol 2.5 mg once daily for one month (or 5 mg if you are already on a similar heart medication). If you are currently taking a similar heart medication, you will stop that medication the day before you start nebivolol.

Visit 1A (if needed): Either the same day as visit 1 or within a few days, you will be asked to undergo a transthoracic echocardiogram (measurement using sound waves to look at the heart) and a right heart catheterization (pressure measurements of your heart done with a catheter inserted into your arm or leg vein until it reaches your heart) for research purposes if you have not undergone one within 3 months of enrollment. These measurements are needed to assess the degree of your heart failure and pulmonary hypertension.

One week after your visit, you will be called to check for any potential problems.

If you were started on 2.5 mg of nebivolol, you will be called to check for any potential problems or side effects two weeks after your visit. If you have no problems, and a study physician decides you are tolerating the medication well, you will be asked to increase your nebivolol dose to 5 mg. If you were already taking 5 mg, this call will not be needed.

Visit 2 (4 weeks): Your vital signs will be checked, a blood sample will be obtained, and an EKG will be performed to check for unwanted side effects. If a study physician decides that you tolerate the study medication well, you will receive a dose increase to 5 mg daily for another 2 weeks (or 10 mg if you were previously taking 5 mg).

One week after your visit, you will be called to check for any potential problems.

Visit 3 (8 weeks): Your vital signs will be checked, a blood sample will be obtained, and an EKG will be performed to check for unwanted side effects. If a study physician decides that you tolerate the study medication well, you will receive a dose increase to 10 mg daily for the remaining 12 weeks, if you were not already taking 10 mg. If any dose increase is not tolerated, you will be asked to revert to your previously tolerated dose.

One week after your visit, you will be called to check for any potential problems.

Visit 4 (18 weeks): Your vital signs will be checked, a blood sample will be obtained, and an EKG will be performed to check for unwanted side effects. (EKG) You will also be asked to undergo another right heart catheterization, heart ultrasound, breathing questionnaire, and a 6-minute walk test. After the final measurements are taken, it will be up to your physician if you will continue nebivolol. The right heart catheterization can occur either the same day or within a few days of your study visit.

Tests done only for research purposes will not be evaluated or used to diagnose or treat any of your medical problems. This/these test(s) may need to be repeated if required for your medical care in the future.

Once this research study is completed, any information that could identify you will be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative

If you have any questions now or at any time during the study, please contact one of the research team members listed in question 3 of this form.

8. How long will you be in this research study?

Completion of the research study will take approximately 4 months.

9. How many people are expected to take part in this research study?

Up to 60 subjects may be involved in this research.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

10. What are the possible discomforts and risks from taking part in this research study?

Risk of side effects from nebivolol include headache, nausea, fatigue, diarrhea, very slow heart rate, difficulty breathing, decrease in blood pressure, and dizziness. Please keep the study drug out of the reach of children or others who may not be able to read or understand the directions on the label. Do not let anyone else take the study drug besides you.

The risks of taking blood include pain, a bruise at the point where the blood is taken, redness and swelling of the vein, and a rare risk of fainting and infection.

Transthoracic echocardiogram: There are no risks associated with this procedure.

Right heart catheterization (you may have this procedure done once or twice): pain, bruising, swelling, and rare risk of: infection, blood vessel or heart valve damage, internal bleeding, lung collapse, blood clots, irregular heart rhythms, and excessive fluid surrounding the heart.

6-minute walk distance: You may experience fatigue during walk.

The risks of genetic testing include those related to confidentiality surrounding the genetic information, and the chance that the genetic information could in some way expose you to increased risk regarding employment or that future life, health, disability or long term care insurance providers could potentially use this genetic information to deny, limit or raise rates for insurance coverage. To protect you from this risk, your DNA will not be stored with any of your identifying information and the results of your genetic testing will not be given to you and it will not become part of your medical record. If you signed a separate consent form for banking, your left over DNA and study records will be stored for future unknown research in the UF Center for Pharmacogenomics Tissue and Data Bank. If you do not sign the consent form for banking, your leftover DNA and study records will be used until the end of this study and then destroyed. None of your personal health information or any identifying information will be stored with your DNA and study records. If your DNA or study recorders are shared with other researchers, none of your personal identifying information will be shared.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Additional information

can be obtained at: http://irb.ufl.edu/gina.html or call 1-800-669-3362. If you think this law has been violated, it will be up to you to pursue any compensation from the offending insurance company and/or employer.

Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information, such a release could upset or embarrass you, or possibly affect your insurability or employability. Questions 17-21 in this form discuss what information about you will be collected, used, protected, and shared.

This study may include risks that are unknown at this time.

Participation in more than one research study or project may further increase the risks to you. If you are already enrolled in another research study, please inform one of the research team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

Throughout the study, the researchers will notify you of new information that may become available and might affect your decision to remain in the study.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the research team members listed in question 3 in this form.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You have been informed that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. That is, if you give written consent for the release of information, we cannot withhold that information and we cannot hold responsibility for how that person may use your information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances. If we learn about child abuse, elder abuse, or intent to harm yourself or others, we will report that information to appropriate authorities.

11a. What are the potential benefits to you for taking part in this research study?

You may not directly benefit from participating in this study. Based on experience with nebivolol in patients with similar conditions, researchers believe it may be of benefit to subjects with your condition by reducing blood pressure in your lungs and improving your heart function. However, because individuals respond differently to therapy, no one can know in advance if it will be helpful in your particular case.

11b. How could others possibly benefit from this study?

If this study shows that nebivolol benefits patients with your condition, it may be studied further as a treatment for this disease.

11c. How could the researchers benefit from this study?

In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator listed in question 3 of this form may benefit if the results of this study are presented at scientific meetings or in scientific journals.

12. What other choices do you have if you do not want to be in this study?

Participation in this study is voluntary. Your doctor will continue to monitor you and try to optimize your heart failure medications, as there are no other accepted treatments for this disease.

13a. Can you withdraw from this study?

You are free to withdraw your consent and to stop participating in this study at any time. If you do withdraw your consent, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you decide to withdraw your consent to participate in this study for any reason, please contact one of the research team members listed in question 3 of this form. They will tell you how to stop your participation safely.

If you have any questions regarding your rights as a research subject, please call the Institutional Review Board (IRB) office at (352) 273-9600.

13b. If you withdraw, can information about you still be used and/or collected?

If you discontinue participation in the study (withdraw), the information about you collected up until the time you withdraw can still be used.

13c. Can the Principal Investigator withdraw you from this study?

You may be withdrawn from the study without your consent for the following reasons:

- You no longer meet study eligibility criteria
- You do not follow the study procedures

- You experience a severe side effect from the study medication or any study procedures
- The study investigators believe it is in your best interest

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

14. If you choose to take part in this research study, will it cost you anything?

Study Drug

Nebivolol, the study drug, will be provided at no cost to you while you are participating in this study.

Study Services

The Sponsor will pay for all medical services required as part of your participation in this study as described above in the question "What Will Be Done Only Because You Are In This Research Study". If you receive a bill for these services, please contact Dr. Julio Duarte at (352) 273-8132.

Items/Services Not Paid for by the Sponsor

All other medical services you receive would have been provided to you even if you were not in this study. These services will be billed to you or your insurance company in the usual manner. You will be responsible for paying any deductible, co-insurance, co-payments, for those services, and for any non-covered or out-of-network services.

15. Will you be paid for taking part in this study?

You will receive cash in the amount below for completion of each study event as follows:

Visit 1 = $50
1st right heart catheterization (if needed) = $200
Visit 2 = $40
Visit 3 = $40
2nd right heart catheterization = $200
Visit 4 = $50
TOTAL = $580

If you are paid more than $75 for taking part in this study, your name and social security number will be reported to the appropriate University employees for purposes of making and recording the payment as required by law. You are responsible for paying income taxes on any payments provided by the study. If the payments total $600 or more or you are a nonresident alien, payment will be processed through the

University of Florida Accounts Payable department and the University must report the amount you received to the Internal Revenue Service (IRS). The IRS is not provided with the study name or its purpose. If you have questions about the collection and use of your Social Security Number, please visit: http://privacy.ufl.edu/SSNPrivacy.html.

Your payment for participation in this research study is handled through the University of Florida's Human Subject Payment (HSP) Program. Your information which will include your name, address, date of birth, and SSN (depending on amount of money you are paid) is protected. Access to the (HSP) Program site is limited to certain staff with the assigned security role. You will be randomly assigned a specific identification (ID) number to protect your identity.

The study team will provide you with an informational form called the Prepaid Card Facts document. If you have any problems regarding your payment call the HSP Office (352) 392-9057.

16. What if you are injured because of the study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact one of the research team members listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this study.

17. How will your health information be collected, used and shared?

If you agree to participate in this study, the Principal Investigator will create, collect, and use private information about you and your health. This information is called protected health information or PHI. In order to do this, the Principal Investigator needs your authorization. The following section describes what PHI will be collected, used and shared, how it will be collected, used, and shared, who will collect, use or

share it, who will have access to it, how it will be secured, and what your rights are to revoke this authorization.

Your protected health information may be collected, used, and shared with others to determine if you can participate in the study, and then as part of your participation in the study. This information can be gathered from you or your past, current or future health records, from procedures such as physical examinations, x-rays, blood or urine tests or from other procedures or tests. This information will be created by receiving study treatments or participating in study procedures, or from your study visits and telephone calls. More specifically, the following information may be collected, used, and shared with others:

- Demographic information
- Medical information and measurements as they relate to your heart and lungs
- Genetic information
- Medical and laboratory information as they relate to your response to nebivolol
- Social Security Number for participant payment purposes

This information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices.

Some of the information collected could be included in a "limited data set" to be used for other research purposes. If so, the limited data set will only include information that does not directly identify you. For example, the limited data set cannot include your name, address, telephone number, social security number, photographs, or other codes that link you to the information in the limited data set. If limited data sets are created and used, agreements between the parties creating and receiving the limited data set are required in order to protect your identity and confidentiality and privacy.

18. For what study-related purposes will your protected health information be collected, used, and shared with others?

Your PHI may be collected, used, and shared with others to make sure you can participate in the research, through your participation in the research, and to evaluate the results of the research study. More specifically, your PHI may be collected, used, and shared with others for the following study-related purpose(s):

- Research involving nebivolol response and heart or lung diseases

Once this information is collected, it becomes part of the research record for this study.

19. Who will be allowed to collect, use, and share your protected health information?

Only certain people have the legal right to collect, use and share your research records, and they will protect the privacy and security of these records to the extent the law allows. These people include:

- the study Principal Investigator (listed in question 3 of this form) and research staff associated with this project.
- other professionals at the University of Florida or Shands Hospital that provide study-related treatment or procedures.
- the University of Florida Institutional Review Board (IRB; an IRB is a group of people who are responsible for looking after the rights and welfare of people taking part in research).

20. Once collected or used, who may your protected health information be shared with?

Your PHI may be shared with:

- the study sponsor (listed in Question 4 of this form).
- United States governmental agencies who are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections .
- Government agencies who are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments.

Otherwise, your research records will not be released without your permission unless required by law or a court order. It is possible that once this information is shared with authorized persons, it could be shared by the persons or agencies who receive it and it would no longer be protected by the federal medical privacy law.

21. If you agree to take part in this research study, how long will your protected health information be used and shared with others?

Your PHI will be used and shared with others until completion of the study.

You are not required to sign this consent and authorization or allow researchers to collect, use and share your PHI. Your refusal to sign will not affect your treatment, payment, enrollment, or eligibility for any benefits outside this research study. However, you cannot participate in this research unless you allow the collection, use and sharing of your protected health information by signing this consent and authorization.

You have the right to review and copy your protected health information. However, we can make this available only after the study is finished.

You can revoke your authorization at any time before, during, or after your participation in this study. If you revoke it, no new information will be collected about you. However, information that was already collected may still be used and shared with others if the researchers have relied on it to complete the research. You can revoke your authorization by giving a written request with your signature on it to the Principal Investigator.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent and Authorization	Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described in sections 17-21 above. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing	Date