STUDY TITLE:
The Effects of Mirtogenol® with Bimatoprost on Intraocular Pressure in Hispanics with Open-Angle Glaucoma: A Double-Blind, Randomized Controlled Trial

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SCHOOL OF PHARMACY
DEPARTMENT OF PHARMACEUTICAL PRACTICE

INFORMED CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY AND AUTHORIZATION FOR USE AND DISCLOSURE OF PROTECTED HEALTH INFORMATION

TITLE: The effects of Mirotgenol® with bimatoprost on intraocular pressure in Hispanics with open-angle glaucoma: a randomized, double-blind controlled study

PROTOCOL NUMBER: A4570119

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SPONSOR: Life Extension Clinical Research, Inc.

LOCATION: Office of Ophthalmology Dr. Marino Blasini

NUMBERS OF PHONES ASSOCIATED TO THE STUDY:
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Marino Blasini, M.D. 787-758-2525 x-1933, 787- 728- 2318

This consent form may contain words that you do not understand. Please ask the researcher or any study staff to explain any words or information you do not understand. You can take home a copy of this consent form to think about your participation in this study or to discuss it with your family or friends before making your decision

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I. INTRODUCTION AND KEY INFORMATION:

You have been invited to participate in a research study. This study is being conducted for the purpose of determining whether the Mirtogenol supplement has an additive effect on reducing intraocular pressure when combined with bimatoprost 0.1% in the Hispanic population with primary open-angle glaucoma. When you are invited to participate, you have the right to be informed about the study procedures so that you can decide whether you want to consent to participate. Before agreeing to participate in this study, please read this consent form carefully and ask any questions necessary to ensure that you understand the procedures including risks and benefits. Your participation is voluntary, and you do not have to be in the study if you do not want to. You can refuse to participate in the study, and nothing will happen. If you do not wish to continue participating in the study, you may stop at any time without penalty or loss of profits to which you are entitled.

II. STUDY PURPOSE:

The purpose of the study is to determine whether the supplement Mirtogenol has an additive effect on the reduction of intraocular pressure when combined with bimatoprost 0.1% in the Hispanic population with primary open angle glaucoma. Because current medications are not able to cure or stop glaucoma, new complementary alternatives that can slow down their progress and blindness are beneficial in preserving the patient's visual function and quality of life.

III. STUDY PARTICIPANTS:

An estimated 72 Hispanic participants with the following inclusion will be considered for the study:

1. Diagnosed with primary open-angle glaucoma (POAG)

2. ≥ 21 years old

3. Patient must be Hispanics (self-identified)

4. Using bimatoprost 0.01% (Lumigan®) only and with stable IOP ≤ of 21 mmHG

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The following shall be excluded:

1. < 21 year old,

2. Pregnant women or those who are planning to become pregnant in the next six(6) months (There is insufficient reliable information available about the safety of Mirtogenol® when used in medicinal amounts during pregnancy and lactation),

3. Women who are breastfeeding (There is insufficient reliable information available about the safety of Mirtogenol® when used in medicinal amounts during pregnancy and lactation),

4. Individuals with cardiovascular diseases that have required medical intervention in the past three (3) months,

5. Patients that required any kind of surgery, radiotherapy or chemotherapy in the past three (3) months,

6. Patients with advanced glaucoma with a cup to disk ratio > 0.9, previous glaucoma surgeries or other abnormalities of the eye that affect the visual pathway,

7. Patients with uveitis, diabetic retinopathy, macular edema or degenerative eye,

8. Patients with a history of adverse side effects of prostaglandin inhibitors,

9. Patients planning to undergo trabeculectomy or cataract surgery during the next six (6) months,

10. Patients using immunosuppressant therapy and anticoagulant,

11. Patients currently using Mirtogenol®.

The duration of the study will be one year. The expected duration of the subject's participation shall be 24 weeks.

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IV. PROCEDURES

Volunteers who are Hispanics aged 21 and over with primary open-angle glaucoma using the drug bimatoprost 0.01%, who are interested in the study and are able to consent will be asked to provide medical personal information. This information will help us determine if you can be part of the trial, reducing risks and possible errors in the results of the study.You will be randomly assigned to one of the study groups described below. Randomization means you may have the opportunity (possibility) to be assigned to a group. It is like tossing a coin. A computer will assign the group you will be in. Neither you, the researcher nor the study staff will choose the group in which you will participate. You will have an equal chance of being placed in any group. The groups are bimatoprost with Mirtogenol or bimatoprost with placebo. Bimatoprost 0.01% is a glaucoma treatment medicine. All participants will continue with bimatoprost 0.01% for the duration of the study as directed by their ophthalmologist. Mirtogenol is a supplement that contains a synergistic combination formula of 80 mg of standardized cranberry extract called Mirtoselect® and 40 mg of French maritime pine bark extract called Pycnogenol. Placebo is an inactive pill that has no treatment value. In clinical trials, experimental treatments are often compared with placebos to assess the treatment's effectiveness.

Participants will take one (1) capsule of Mirtogenol or placebo orally daily in the morning with food. The expected duration of the subject's participation shall be 24 weeks, which includes five (5) medical visits in Dr. Marino Blasini's Ophthalmological Office. You will be tested to determine visual acuity, visual field, intraocular pressure, thickness of the cornea, and progression of glaucoma at the beginning and end of the study. At weeks 4 and 8, visual acuity, and intraocular pressure evaluations will be determined using the Goldmann Applanation Tonometry, this last test will be measured twice, with a waiting time of 10 minutes between measurements. At week 12, visual acuity, visual field and intraocular pressure will be performed. All tests are non-invasive and will last approximately thirty (30) minutes to one (1) hour. Each test will be measured in the morning. Any therapy deemed necessary for the patient's well-being will be administered at the discretion of the treating physician and documented.

V. RISK

Both bimatoprost 0.01% and Mirtogenol have been shown to have a good tolerability profile and a low incidence of side effects. The risks and discomfort that may result because of this study are mild and minimal. Mirtogenol contains bilberry and Pycnogenol which may interact with immunosuppressive therapies (Drugs used to lower your body’s immune respone), and

anticoagulant (Drug used to stop blood from clotting). If you begin the above therapies or medications during the study, consult your study researcher. Risks and discomforts that may result from Mirtogenol use are gastrointestinal discomfort, dizziness, headache and nausea.

The ophthalmic solution of bimatoprost can cause an increase in the pigmentation of the iris, periorbital tissue (eyelid) and eyelashes. After discontinuation of bimatoprost, iris pigmentation is likely to be permanent, while periorbital tissue pigmentation and eyelash changes may be reversible in some patients. Bimatoprost can cause longer length, thickness, and number of lashes. These changes in the eyelashes are usually reversible after discontinuation of treatment. Some adverse reactions with bimatoprost include conjunctival hyperemia, conjunctival edema, conjunctival hemorrhage, eye irritation, eye pain, eye itching, eyelid sprain, pruritus eyelids, blurred vision and reduced visual acuity.

All visual tests will be noninvasive, but applanation tonometry has a small chance of the cornea scratching (corneal abrasion). The scratch will usually heal in a few days. Your glaucoma may not improve or worsen while you are in this study. If the participant has any side effects, he or she should be reported to the study doctor. The probability is that you will suffer from these serious side effects is minimal and usually reversible once their use is discontinued. Throughout the duration of the study, you will be monitored by a glaucoma specialist and will receive medical care that will ensure your well-being and safety. If this occurs, you will be reviewed by a physician experienced in acute medical complications, using authorized treatments and with drugs approved by the Federal Drug Administration (FDA), at no cost.

Medications should be kept out of reach of children and people who cannot read or understand the label. If you become pregnant during this study, there may be other risks for you and your unknown fetus. If you are a woman and may become pregnant, you should use two (2) contraception throughout the study and for at least 4 weeks after you stop taking the study medication. One method should be an acceptable barrier method (diaphragm with spermicide gelatin, condoms, etc.). Not having a sexual relationship is an acceptable method of birth control; If you become pregnant for the duration of the study, you should stop taking your study medicine immediately and contact the study researcher.

VI. BENEFITS

Your intraocular pressure may improve because of your participation in this study. However, there is no guarantee of this. The information in this research study may lead to better treatment in the future for people with glaucoma.

VII. COSTS

There will be no charges or costs for you for your participation in this study.

VIII. COMPENSATION FOR YOUR PARTICIPATION

You will not receive any monetary stipend for participating in this study. You will receive ophthalmological evaluations during the duration of the study.

IX. ALTERNATIVE TO PARTICIPATE

Several FDA approved treatments are available such as the addition of another drug from another therapeutic class (beta-blocker, carbonic anhydrase inhibitor or sympathomimetic), that may be added to bimatoprost, laser trabeculoplasty or surgery for the treatment of glaucoma. However, for patients whose intraocular pressure is already at goal, these additional treatments are not normally recommended. You also have the option of not participating in this study and will not be penalized for your decision.

X. PRIVACY AND CONFIDENTIALITY

If you choose to participate in this study, the researcher and the study staff will obtain personal information about you. This may include information that could identify you, such as name, address, age, phone number, and email. The researcher can also obtain information about your health, including:

- Medical records of the past and present
- Research records on study visits
- Records of phone calls made as part of this investigation
- Information obtained during this research on:
    - Diseases transmitted such as HIV/AIDS, hepatitis infection or other sexually transmitted diseases
    - Other reported infectious diseases
    - Physical exams
    - Results from laboratory tests, x-rays and other tests
    - Journals, questionnaires and other instruments
    - Diagnosis and treatment of a mental health condition

• Records of any study medications you received
• Records about the study device
This information about you and your health that can identify you may be disclosed to others as part of this research study. These include:

• The U.S. Food and Drug Administration (FDA)
• Department of Health and Human Services (DHHS) Agencies
• Government agencies to which certain diseases (reportable diseases) must be informed about you and your health that could identify you may be given to others to conduct this research study. Records will be protected in accordance with the regulations of the Health Insurance Portability and Accountability Act (HIPAA). The information can also be used to meet the requirements of reports made to government agencies. The results of this research may be published in scientific journals or presented at medical and professional meetings, but their identity will not be disclosed. The information can be reviewed by the Institutional Review Committee (IRB) of the Medical Sciences Campus of the University of Puerto Rico (UPR RCM IRB). UPR RCM IRB is a group of people who conduct independent reviews of research as required by regulations. Your health information will be kept as confidential as possible under the law.

This authorization will be effective until the end of the study. You may cancel this authorization at any time by sending a written notice to the principal investigator at the following address:

Dr. Jorge R Miranda-Massari
School of Pharmacy. Medical Sciences Campus.
University of Puerto Rico.
Office 322. Third Floor, Pharmacy School Building.
PO Box 36 5067. PR 00936-5067

If you cancel this authorization, the principal Investigator will no longer use or disclose your personal health information under the authorization for this study, unless he/she needs to use or disclose some of your information to preserve the scientific integrity of the study. The information submitted before you cancel this authorization can still be used by the associates.
The Authorization for the Use and Disclosure of Protected Health Information for research purposes is entirely voluntary. However, if you do not sign this document you will not be able to participate in this study. If you cancel this authorization in the future, you will not be able to continue participating in this study.

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STUDY REGISTRATION in ClinicalTrials.gov

A description of this clinical trial will be available in http://www.ClinicalTrials.gov, as required by United States law. This website will not include identifying information. At most, it will include a summary of the results. You can search this website at any time. The website may include IRB-approved consent to recruit study participants.

COLLECTION OF IDENTIFIABLE PRIVATE INFORMATION

Personal identifiers from the information collected in the study will be removed, after such information is deleted, the information could be used for future research studies or distributed to another researcher for future without the additional informed consent of the participant or the Authorized Legal Representative (LAR), if this may be a possibility.

XI. COMPENSATION IN THE EVENT OF DAMAGE

In the event of a physical and/or mental injury as a result of this research study, you will receive cost-free medical treatment at the University Hospital or any other hospital at the University of Puerto Rico. The University of Puerto Rico has no plans to provide compensation of any type directly to you. However, by signing this consent form, you do not waive any legal rights.

XII. PARTICIPATION AND VOLUNTEER RETURN

Your participation in this study is voluntary. You may decide not to participate, or you may leave the study at any time. Your decision does not result against any penalty or loss of profits to which you are entitled. You are informed of any new information discovered during this study that may be in your health, well-being or willingness to participate in this study. Your participation in this study may be withdrawn at any time by the study physician, Dr. Marino Blasini without your consent. If necessary, your participation in this study may be withdraw at any time by the researcher without your consent, if circumstance arise that warrant it.

XIV. QUESTIONS

If you have any questions about this study or your participation in this study or if at any time you feel that there has been an injury or a reaction from the study contact:

Dr. Jorge R Miranda-Massari
School of Pharmacy. Medical Sciences Campus.
University of Puerto Rico.
Office 322. Third Floor, Pharmacy School Building.

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PO Box 36 5067. PR 00936-5067
Tel. 787-758-2525 ext. 5320, Cel. 787-646-0720

If you have questions about your rights as a study participant, please contact:

Office for the Protection of Human Research Participants (OPPHI)
University of Puerto Rico
Medical Sciences Campus
Phone: 787-758-2525 Ext. 2510 to 2515
Email: opphi.rcm@upr.edu

Do not sign this consent unless you have had the opportunity to make and receive satisfactory responses for all your questions. If you agree to participate in this study, you will receive a copy of this informed consent with the IRB seal of approval on each sheet for their records.

XV. CONSENT AND SIGNATURE

The information provided in this consent has been read or read to me, if applicable. All my questions about the study and my participation in it have been answered. My signature below means that I freely consent to participate in this research study. I authorize the use and disclosure of my health information to entities prior to entries in this consent for the purposes described above. By signing this consent, none of my legal rights are waived.

_____
Participant's Name

_____ _____
Participant's Signature Date

_____
Name of person who makes the discussion of consent

_____
Signature of person who makes the discussion of consent

_____

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Date

**********Impartial Witness **********

If this consent form (addendum) is read to the subject because the subject (or legally authorized representative) is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement: I confirm that the information in the informed consent (annex) and any other written information was explained accurately and apparently understood by the participant (or the legally representative authorized by the participant). The participant (or the participant's legally authorized representative) freely agrees to participate in the research study.

_____
Signature of Impartial Witness

_____ _____
Name of Impartial Witness Date