Columbia University Medical Center Consent Form

Attached to Protocol: IRB-AAAB7145
Principal Investigator: James Reiffel (jar2)
IRB Protocol Title: Randomized Evaluation of Long term anticoagulant therapy comparing the efficacy and safety of 2 blinded doses of dabigatran etexilate with open label warfarin for the prevention of stroke and systemic embolism in patients with non-valvular atrial fibrillation:prospective, multi-centere, parallel-group, non-inferiority trial (protocol # 1160.26) Dated 12 September 2005

Consent Number: **CF-AAAC8335**
Participation Duration: 1 year
Anticipated Number of Subjects: 18,000

Contact

Contact	Title	Contact Type	Numbers
James Reiffel	Professor of Clinical medicine	Principal Investigator	Telephone: 212-305-5206 Pager: 917-899-2689
Maurita Baumeister	Nurse Practitioner	Study Coordinator	Telephone: 212-305-6167
HASAN GARAN	Director, Cardiac Electrophysiology	Co-Investigator	Telephone: (212)305-7646 Pager: 212 305-7646
Kathleen Hickey	Research Nurse Clinician	Study Coordinator	Telephone: 212-305-4944 Pager: 212 305-4944

Research Purpose
About 18,000 subjects will participate in this study at about 800 to 1000 research centers worldwide.

Your participation in this study will last at least one year but could last as long as three years or more. You will have at least 8 study visits but you could have as many as 15 visits, depending on when you entered the study relative to the study start. For example, subjects who enter at the very beginning of the enrollment period may be in the study for over 3 years, while subjects who enter near the end of the enrollment period may only be in the study for a year or so.

Before you agree to join this research study, it is important that you read and understand the following information about the study. This document describes the purpose, procedures, benefits, risks, discomforts, and precautions of the study. It also describes the alternative procedures that are available to you and your right to withdraw from the study at any time. No guarantees or assurances

can be made as to the results of the study. Please read this consent form carefully and ask as many questions as you like before deciding whether you want to take part in this study. Before you agree to take part in this study, you may take this information home and discuss the study with a friend, family member, your family doctor, or cardiologist.

If you are not completely truthful with your study doctor regarding your health history, you may harm yourself by taking part in this study.

The study is being conducted for Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI). Your study doctor is being paid by BIPI to conduct this study.

BACKGROUND AND PURPOSE OF STUDY

Atrial fibrillation is an irregular heartbeat that can cause blood clots to form in the heart. These clots, or pieces of these clots, can break away and block other blood vessels. If the clot blocks an artery (a type of blood vessel) in the brain it can cause a stroke. The chance of a stroke is increased if other diseases or conditions are present including coronary artery disease (CAD), high blood pressure, diabetes, heart failure, a previous heart attack, or a previous stroke including mini-strokes [transient ischemic attacks (TIAs)]. The risk of stroke is also increased for those over 75 years of age.

You are being asked to take part in a research study of an investigational drug, dabigatran etexilate, because you either have a history of chronic atrial fibrillation (AF) or have been newly diagnosed with AF, plus you have at least one other risk factor for stroke. An investigational drug is a drug that is not approved by the United States Food and Drug Administration (FDA). It is currently only available to subjects in research studies.

Patients with atrial fibrillation who are at a high risk of stroke may take a blood-thinning medication to reduce the risk of stroke. One example of such a product is warfarin which is sometimes sold under the brand name Coumadin. Frequent blood testing is required to maintain the right dose of warfarin. If the dose is too high, the blood may be too thin. This might lead to bleeding. If the dose is too low it may not be enough to prevent a stroke. In addition, the effectiveness of medications like warfarin is affected by certain other medications and foods, so the right dose can be difficult to maintain. The right dose is maintained by performing a blood test called an INR (or International Normalized Ratio) about once a month. The doctor uses the INR test result to determine how much warfarin to give to a patient.

Dabigatran etexilate is an investigational blood thinning medication. The purpose of this study is to evaluate how well this drug works (at two different doses) and how safe it is, compared to warfarin which is standard therapy for patients with atrial fibrillation. Warafin is an FDA Approved blood thinning medication commonly prescribed to people with atrial fibrillation. However, the warfarin tablets used in this study are not approved by the FDA for marketing/use in the United States, and therfore are also considered an investigational drug.

Information on Research

STUDY PROCEDURES

This study is broken up into four parts: Screening, Randomization, Treatment, and Final Follow-Up.

There will be a Screening Visit (Visit 1) to determine if you qualify to take part in this study. If you qualify for the study, you will have a Randomization Visit (Visit 2) either that same day, or sometime within the next 14 days. Once randomized, you will be given study medication (study medication is either dabigatran or warfarin). You will take this medication every day for the duration of your participation in the trial. While you are taking the study medication, you will return for at least six more Treatment Visits; however, you may have more visits depending on when you entered the study. The follow-up Period will include a final study visit that is completed after you have completed your participation in the trial as dictated by your individual visit schedule.

Once randomized, you are in the trial regardless of a temporary or permanent discontinuation of study medication at any time in the trial. You always have the possibility of restarting medication again should your study doctor recommend you doing so and you continue to agree. Even if your study drug is permanently discontinued, you will be asked to continue the trial visit schedule approximately one visit every 3-4 months to understand how you are doing. If you are not able to continue the protocol-specified visit schedule, an alternate reduced schedule of visits and/or telephone contacts will be arranged.

In addition to the study visits, all (warfarin and dabigatran) subjects will also be sent for blood tests. These will be once a month to measure your liver function for the first year you are on this study, and every four months if you are on the study for longer than one year.

STUDY PROCEDURES
Visit 1 (Screening)
Reading and signing this consent form is required before you can participate or before any study-related procedures are performed. If you sign this consent form, the following screening tests and procedures will be performed to determine if you qualify:
Check your eligibility for participating in this study.
Review of your medical history, any current medications you are taking or have taken within the past month.
Physical examination.
Vital signs (blood pressure and heart rate).
Electrocardiogram (ECG - measures the electrical activity of the heart).
Collection of about 1 tablespoon of blood samples for routine "safety" laboratory tests.
Collection of about 2 tablespoons of blood samples for tests which look at factors which may influence your risk for AF-related events.
Blood pregnancy test (about 1 teaspoon) if you are a woman who is able to have a child. Results must be negative for you to participate in the study.
If you have a history of hepatitis B and/or C, additional hepatitis B and/or C blood testing may be required. Positive hepatitis results may be reportable to local health authorities according to local state laws.
This visit will last about an hour. All other visits will last about 45 minutes.

If you do not meet the screening requirements, you will not be entered in the study and no further follow-up is required.

Visit 2 (Randomization)
If you qualify, you will have Visit 2. Visit 2 can be done the same day as your Screening Visit or you can return within 14 days. The following
Visit 2 tests and procedures will be performed:

Review of any changes in how you have been feeling since your last study visit (including any medications that you may have taken).
Vital signs (blood pressure and heart rate).
Collection of an urine sample for a pregancy test (women of child bearing potential only). Results of the pregancy test must be negative for you to continue participation in the study.
You will be asked specific questions about any possible signs of a stroke,mini-stroke,and abnormal bleeding.

Dispensing Study Medication
If you continue to qualify at Visit 2, you will be randomly assigned by chance (like drawing numbers from a hat) to 1 of the following 3 study treatment groups:
1. Dabigatran etexilate 110 mg (one capsule twice daily)
2. Dabigatran etexilate 150 mg (one capsule twice daily)
3. Warfarin (tablets), dose based on INR blood test results (once daily)

You will have a 67% (2 out of 3) chance of receiving dabigatran etexilate and a 33% (1 out of 3) chance of receiving warfarin.
The assignment to either warfarin or Dabigatran etexilate treatment is open-label which means that you and the study doctor/study staff and you will know whether you are taking warfarin or dabigtran etexilate.

Dabigatran etexilate dosage is double-blind which means that neither you nor the study doctor/study staff will know which of two doses of dabigatran etexilate that you are receiving. However, this information will be available in case of an emergency.

Once randomized, you will be given active study medication (study medication is either dabigatran or warfarin), both of which are blood thinners that will be used instead of you previous blood thinner medication.If you are assigned to the warfarin treatment group, you will only take warfarin that will be provided by the study doctor. You and the study doctor/study staff will know that you are taking warfarin.

If you are assigned to dabigatran etexilate and you have NOT been on a blood thinning medication you will start the study medication on the day of randomization.

All patients will have an INR drawn prior to treatment assignment. If you are on any medications that are not allowed during the study, such as other blood thinners, you will be asked to stop taking those medications only. The exact timing of when you stop your blood thinning medications will depend on

your last INR and the next possible visit with your study doctor. You will continue on all of your other medications as directed by your primary M.D. If you are assigned to dabigatran etexilate your INR must be less than 2.0 before you can start taking dabigatran. If you are assigned to dabigatran and your INR is 2.0-2.1, your study doctor may have you start dabigatran within a few days of randomization without rechecking your INR.

If you are a assigned to the warfarin study group, you will start taking study warfarin, when your INR is less than 3.0. If your INR is too high to receive the study medication on the day of randomization, it will be monitored until you can receive study medication.

If necessary, your regular blood thinning medication may be stopped for a period of 1-3 days before you start your assigned study medication. During this period of withdrawal from warfarin, if your INR falls below 2.0, you are at a slightly increased risk of stroke. Patients may have their PT/INR done earlier as per the principal M.D. investigator's clinical judgment. Drawing an earlier PT/INR is not precluded in this investigation and will be based your medical history, prior stroke history and other risk factors.

Visit 3
Two weeks after you begin your study medication, you will be contacted by the study staff for a "telephone visit" that will last about ten minutes. You will not come to the clinic for this visit.

During this telephone call, you will be asked:
About any changes in how you have been feeling since your last study visit (including any medications that you may have taken).
Specific questions about any possible signs of a stroke, mini-stroke, or abnormal bleeding.

Visits 4-14 (Treatment)
Visit 4 will occur one month after you have started your study medication. Visit 5 will occur three months after you started your medication. Visits 6, 7 and 8 will occur every three months after that. If the study continues past 12 months of treatment, Visits 9 through 14 will occur every 4 months.

Some or all of the following tests and procedures will be performed at each study visit:
Collection of a urine sample for a pregancy test (in women of child bearing potential only). Results must be negative to continue participation in the study at all visits.
Review of any changes in how you have been feeling since your last study visit (including any medications that you may have taken) (all visits).
You will be asked specific questions about any possible signs of a stroke,mini-stroke or abnormal bleeding (all visits).
You will receive a three month supply of study medication at Visits 2, 5, 6, and 7 and a four month supply at each visit thereafter.
The study staff will count your remaining study medication at every visit to make sure that you are taking it right.
Collection of 1 ½ tablespoons of blood samples for safety laboratory tests at Visits 5, 6 and 8 and yearly thereafter.

Subjects assigned to dabigatran etexilate will have blood sampling (1 tablespoon) after 1 month of treatment to determine levels of dabigatran etexilate. If you are assigned to take the dabigatran etexilate, you will be instructed not to take your morning dose of dabigatran etexilate prior to this visit. At visit 4 two blood samples will be collected, (one before and one after you take you study medication in front of the with the study staff). This visit will last at least two hours.
Vital signs (blood pressure and heart rate) (all visits).
ECG (measures the electrical activity of the heart) (Visits 8, 11, and 14).

In addition:

All subjects (warfarin and dabigatran) will have monthly blood tests (about 2 teaspoons of blood will be drawn at each visit) for the first year in the study to measure liver function. If at anytime during the study your liver function blood tests rise above a certain level, you will be asked to return for additional blood tests until the test results are at the proper level. The study doctor may also do additional tests to determine the cause of this increase.
If the study staff thinks at any time that you may have had a stroke or a mini-stroke, you will be seen by a neurologist (doctor who specializes in brain disorders) for further testing. This testing will include a complete medical exam and either a CT scan or MR (tests that show images of the brain).
If you are assigned to the warfarin treatment group, you will have an INR test done at least every 4 weeks or more frequently as needed. Your INR measures how quickly your blood is able to clot(your response to warfarin) and can be affected by anyi things including travel, the kinds of food you eat, changes in your diet, the environment, your general health, and other medications you are taking. The dose of warfarin will be adjusted for you based on the results of the INR test.

Final Follow-Up Visit
You will return to the clinic for a final visit after you have completed your participation in the study as dictated by your individual visit schedule (visit 14/36 months or earlier, depending on when you began the study). The following tests and procedures will be performed:
Collection of a urine sample for a pregancy test (women of child bearing potential only)
Review of any changes in how you have been feeling since your last study visit (including any medications that you may have taken).
Physical examination.
Vital signs (blood pressure and heart rate).
Electrocardiogram (ECG - measures the electrical activity of the heart).
Collection of about 1 ½ tablespoons of blood samples for safety laboratory tests.
You will be asked specific questions about any possible signs of a stroke, mini-stroke or abnormal bleeding.
The study staff will count your remaining study medication. You must return all your study medication and bottles at this visit.

This visit should last about an hour. If anything abnormal shows up at this visit, the study doctor will follow up with you until he is satisfied with your condition.

SUBJECT RESPONSIBILITIES

It is very important to come for every study visit and to bring your supply of study drug with you to each study visit, including the empty bottles. Do not throw the study medication in the trash or flush it in the toilet and do not discard any bottles.

You should store your study drug in the bottle that was given to you. Keep the bottle at room temperature, out of direct sunlight, and keep the lid tightly closed (since the drug is sensitive to moisture in the air). Do not expose the drug to high heat (above 86 degrees for dabigatran etexilate and above 77 degrees for warfarin). The drug should be stored away from the reach of children or those who are not able to read and understand the label. You should take your study drug as instructed, and at the same time(s) every day. Do not take the drug out of the bottle until it is time for your next dose.

If you are taking dabigatran etexilate, the capsules (one in the morning and one at night) should be taken with a glass of water (at least 4 ounces) and swallowed whole. Do not chew, crush, open, or break the capsules. You can take them with or without food.

If you are assigned to take dabigatran etexilate you should not skip any doses, but if you do, you may still take the dose until 6 hours prior to the next scheduled dose. If it is within 6 hours of your next scheduled dose, you should not take the dose. Instead wait for your next scheduled dose. Contact the study doctor or study staff to ensure that you take your medications correctly. Do not take two doses at one time.

If you are taking warfarin, the tablet(s) should be taken with a glass of water (at least 4 ounces) and not chew ,crush or split. You should only take the number of tablets instructed by your study doctor. The study doctor will base your dose on your INR test results. If you are assigned to take warfarin you should not skip any doses, but if you do, you should take it as soon as possible on the same day. If you remember the next day, do not take your missed dose; only take the regularly scheduled dose. Contact the study doctor or study staff to ensure that you take your medication correctly. Do not take two doses at one time.

If you were on warfarin before you started this study, it is important not to take your original prescription of warfarin (also called Coumadin) while on this study medication. Please use only the warfarin that was given to you by the study doctor or study staff.

You should not take any medications, including prescriptions, over-the-counter medications or herbal products, unless the study doctor or staff tell you that it is OK. This is especially important if you are taking blood thinning medication, since so many medications like aspirin or products that contain aspirin, corticosteroids or any medication that could alter blood clotting, and herbal products can interfere with the way the drug works.

If you experience any unusual symptoms, it is very important for you to contact your study doctor as soon as possible at the telephone number listed on Page 1 of this consent form.

Risks

RISKS, SIDE EFFECTS AND/OR DISCOMFORTS

Your participation in this research study may involve risks that are currently unforeseen (unable to predict) or unknown. Known risks, side effects, and/or discomforts are listed below. Some of these side effects may need medical attention if they occur.

Dabigatran Etexilate

To date, excluding the patients enrolled in this trial approximately 7000 subjects have received dabigatran etexilate. Side effects that have occurred include the following:

Most Common:

Bleeding, such as

Hematoma (skin swelling containing clotted blood).

Blood in the urine.

Bruising.

Longer bleeding time.

Throwing up or spitting up blood.

Bleeding of the gums, around the eyes, nose bleed, stomach or intestines, or rectum.

Major bleeding may occur but is rare. Major bleeding includes fatal and life-threatening bleeding, bleeding into a vital organ (such as the stomach or brain), bleeding requiring transfusion or surgery or resulting in a larger loss of blood. Gastrointestinal bleeding can indicate the presence of an underlying bleeding condition which may require further study. In a previous research study of dabigatran in subjects with atrial fibrillation the risk of serious bleeding was significantly higher when high doses of dabigatran (higher than those used in this study) were taken together with aspirin. As with all blood thinning medications, there is a risk of bleeding which may be as minor as skin bruising or could be as severe as life-thretening major organ (stomach or brain) bleeding. Bleeding caused by blood thinning medications is generally associated with higher doses or accidental use of restricted medications. There is currently no medication or specific treatment available to reverse the blood thinning effects of dabigatran, should an emergency arise. However,standard therapy for bleeding (such as transfusion of blood products) will be instituted as determined by your study doctor should the need arise. There is also a risk that dabigatran will not be effective. If dabigatran is not effective, you may be at increased risk of having a stroke while in this study.

Bleeding events have occurred with increasing frequency with higher doses of dabigatran etexilate. Therefore, the doses of dabigatran etexilate used in this study have been carefully chosen to offer the best likelihood of preventing blood clots with the least chance of causing bleeding problems or other side effects. The highest dose of dabigatran etexilate in this study causes bleeding at approximately the same rate as warfarin, the comparator agent.

Less Common:

Increases in liver function tests. (Liver function tests will be an important part of your laboratory work-up and will be monitored carefully by your study doctor.)

Gastric (stomach) upset or dyspepsia (indigestion).

Rare:

Anemia
Gastric (stomach) or duodenal (intestine) ulcer associated with bleeding and black tarry stool as a result of blood in the intestine.
Warfarin

Major Risk:
Warfarin can cause major or fatal bleeding. Bleeding is more likely to occur during the starting period and with higher dose (resulting in a higher INR).

Risk factors for bleeding are:

INR greater than 4.0
age 65 or over
highly variable INRs
history of gastrointestinal bleeding (bleeding in the stomach or intestine)
hypertension (high blood pressure)
cerebrovascular disease (brain and circulatory system)
serious heart disease
anemia (decreased number of red blood cells). Symptoms of anemia include tiredness and weakness.
Malignancy (cancer)
trauma
renal insufficiency
concomitant drugs (other medicines you may be taking)
long duration of warfarin therapy

Major bleeding, if warfarin therapy is well controlled through frequent blood testing, is rare.
Gastrointestinal bleeding, even if warfarin therapy is well controlled, can indicate the presence of an underlying bleeding condition which may require further study.

Side Effects Causing Discontinuation of Warfarin:
Bleeding under the skin (black and blue bruising)
Fever
Hypersensitivity/Allergic reactions
Nausea
Vomiting
Swelling of the pancreas
Bleeding around the heart and lungs.
Bleeding from the nose
Fatal or nonfatal bleeding from any tissue or organ.

Other Known Side Effects:
Low white blood cell count (increased risk of infection) when infected ulcers in the mouth and intestinal tract are present

Diarrhea
Vomiting
Fatigue
Sleepiness
Weakness
Pain
Headache
Dizziness
Abnormal taste
Intolerance to cold
Paresthesia (numbness, tingling)
Itching
Dermatitis
Chest pain
Abdominal pain including cramping
Loss of consciousness
Syncope (fainting)
Stomach and intestinal irritation (gas, cramping and bloating)
"Purple toes syndrome" (painful, blue-purple colored toes)
Skin rashes
Jaundice (yellowing of the skin and whites of the eyes) and liver problems
Hepatitis (inflammation of the liver)
Cholestatic hepatic injury (liver injury due to bile duct obstruction)
Elevated liver enzymes
Formation of very small clots of cholesterol in the blood (microembolization)
Kidney problems with extra water buildup and protein found in the urine
Mouth ulcers
Hair loss
Hypotension (low blood pressure)
Vasculitis (inflammation of the arteries)
Edema (swelling)
Anemia (decreased number of red blood cells). Symptoms of anemia include tiredness and weakness.

Rare Events:
Skin necrosis (death of skin) within a few days of starting warfarin.
Tracheal/bronchial calcification.
Hypersensitivity reactions to galactose.

Blood Draw
A total of 13 tablespoons of blood may be collected throughout the three-year course of this study. Possible side effects from a blood draw include fainting (rare) and pain, swelling, bruising, or bleeding where the needle is inserted. There is also a slight possibility of infection where the needle is inserted.

Blood Pressure Measurements
The blood pressure cuff may cause some mild discomfort, bruising, or red spots on the arm.

ECGs
Skin irritation from the ECG electrodes is a possible risk. Pain when the electrodes are removed, especially from a hairy chest, is also a possible risk.

MRI (if needed to determine if a stroke has occurred)
MRI (magnetic resonance imaging) uses a large magnet, radio waves, and computer equipment to produce pictures, or images, of the human body. There are risks with an MRI if you are pregnant, or have one of the following: an artificial heart valve, metal plate, pin or other metallic objects in your body (including gun shot or shrapnel). While taking an MRI, you will have to lie still on your back in the MRI scanner which is a tight space. This may make you anxious. The MRI scan does not cause any pain and does not expose you to x-ray radiation.
CT Scan (if needed to determine if a stroke has occurred)
CT Scans involve exposure to radiation. Although the amount of radiation exposure is higher than a typical x-ray, the risk of harmful effects from a single exam is very small. The dye that is injected into a vein for the scan is usually well tolerated. Some people feel dizzy or queasy or get a headache with it or notice a cold feeling near the injection site. There is a rare chance of having an allergic reaction to the dye that very rarely can be serious and life threatening.

Pregnancy Risks
If you are a woman who is pregnant, planning to become pregnant, or are nursing an infant or child you will not be able to take part in this study. If you are a woman who is able to have a child, you must be using an acceptable method of birth control now and during the study. You should discuss with your study doctor if the method of birth control you are using is medically acceptable. You must have a negative pregnancy test prior to treatment and you must not become pregnant while in the study. A pregnancy test will be done at visit 1 on all women who are able to have children to make sure that no pregnant women are accidentally enrolled into the study.

The effects of dabigatran etexilate on an embryo, fetus (unborn baby), or nursing infant are not known. If you should become pregnant during this study, you must notify your study doctor immediately. Whichever study drug you are on will be stopped. The effects of Dabigatran Etexilate on a human embryo (unborn baby) or nursing infant are not known. In animal studues, pregnant rats and rabbits experienced toxicity due to the pharmacodynamic effect of dabigatran etexilate. If you should become pregnant during this study, you must notify your study immediately. Whichever study drug you are on will be stopped.

Warfarin is not to be used in women who are or may become pregnant because it can cause blood to pass through the placenta and may cause fatal bleeding to the fetus. There have been reports of birth defects in children born to mothers who have been treated with warfarin during pregnancy.

Spontaneous abortion and stillbirth are known to occur and a higher risk of death of the fetus is linked to the use of warfarin. Low birth weight and growth retardation have also been reported.

If you become pregnant while taking warfarin, your doctor will again discuss with you the potential risks to the fetus.
Unforeseen Risks
Since the study medication is investigational (experimental) when taken alone or in combination with other medications, there may be other risks that are unknown. All medications have a potential risk of an allergic reaction, which, if not treated promptly, could become life threatening. Your condition may worsen, remain the same, or not improve as a result of participating in this research study.

Benefits

Possible benefits include a decreased risk of having a stroke, and the knowledge gained from the medical care and laboratory tests you will receive while you take part in this study. There is, however, no guarantee that you will receive any benefit from taking part of this study. However, the knowlegde gained may contribute information about the study medication that may benefit other patients in the future.

Alternative Procedures

The alternative to study participation is not to participate in this study and to receive the existing standard of care as prescribed by your primary health care provider. You do not have to participate in this study to receive treatment for your condition. There are warfarin products available in various dosage strengths in the United States for the prevention of stroke and blood clots in patients who have moderate to high-risk atrial fibrillation.

Confidentiality

Your medical records will be treated as confidentially as possible under local, state and federal laws. Information from this study will be submitted to the sponsor. "Sponsor" includes any persons or companies which are contracted by the sponsor to have access to the research information during and after the study. The results of this research will be shared with the sponsor.
Absolute confidentiality cannot be guaranteed. However, all information produced by your participation will not be identified by your name. If the study results are published in medical or scientific journals, you will not be identified by your name.
The information will also be given to the U.S. Food and Drug Administration (FDA). It may be given to governmental agencies in other countries where the study medication may be considered for approval. Medical records which identify you and the consent form signed by you will be looked at and/or copied for research or regulatory purposes by:
the sponsor;
the FDA;
Department of Health and Human Services (DHHS) agencies;
Governmental agencies in other countries; and
The Columbia University IRB (the committee that has reviewed this research project to help ensure that the rights and welfare of the volunteers are protected and that the study is carried out in an ethical manner).

Research Related Injuries

Injuries

During the study, if you experience any medical problems, suffer a research-related injury, or have questions about the study, please contact the study doctor listed on Page 1 of this consent form. If you seek emergency care, or hospitalization is required, please tell the healthcare provider that you are part of a research study being run by the study doctor listed on Page 1 of this form.

Compensation

Medical treatment and/or care will be provided to any person who has an injury as a result of the study medication or study procedures that would not have been conducted but for participation in the study. If medical care is required, however, you must agree to cooperate in obtaining any proceeds from other insurance or third party coverage you may have that cover the cost of such care. The sponsor will reimburse you for those medical expenses not covered by a third party payor. No other type of compensation, such as lost wages or payment for discomfort due to injury suffered, as a result of this study will be provided. You do not, however, give up any legal rights as a research subject by signing this form. There will be no charge to you for your participation in this study. The study medication, study-related procedures, and study visits will be provided at no charge to you or your insurance company.

To reimburse you for your time, travel expenses, parking, etc. during the study, you will be paid for a total of up to $200 for participating in this study. You will be reimbursed for actual expenses incurred.

Travel reimbursement is based on receipts.

Additional Costs

The study medication, study visits, and all study related procedures will be provided to you without any associated additional costs.

Voluntary Participation

Taking part in this research study is voluntary and you may refuse to take part in this study without any effect on your future medical care.

If you agree to participate in the study, you may discontinue taking your study drug or you may withdraw your consent to participate in the study at any time and for any reason. You may take either of these actions without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. For your safety to not discontinue taking study medication without first speaking with your study doctor. The study doctor or sponsor may remove you from the study without your consent for any of the following reasons: if it appears to be medically harmful to you, if you fail to follow directions for participating in the study, if it is discovered that you do not meet the study requirements, at the discretion of the study doctor, if the study is canceled, or for administrative reasons (including competitive enrollment which means that the target number of subjects have entered the treatment phase).

If you discontinue taking your study medication (regardless of whether this is your choice or is decided by the study doctor) before the end of the study, you will be asked to continue the trial schedule approximately one visit every 34 months. If you are unable to follow this schedule, a reduced schedule of visits and/or telephone follow-ups will be arranged. If you however choose to withdraw consent your participation in the study will end. You will have you study medication stopped and be asked to complete study -ending tests and procedures as listed for the Final Visit. You must return all remaining study medication and bottles.

You may be asked to return for follow-up visit(s) if there are any abnormal findings. These study visits are for your safety and to assess any unknown long-term effects of the study medication. Your continued followup visits can aid in quickly identifying any safety issues associated with the study medication, and are strongly recommended, as well as help understand how you are doing. The study staff is required, by law, to respect your wishes to not continue participation in this study. They can not dispense any additional study medication to you after you have chosen to withdraw from this study. For your safety, do not discontinue taking study medication without first speaking with your doctor.

Additional Information

NEW FINDINGS

If any new information or findings are learned about this study or the study medication that may affect your willingness to stay in this study, you will be told as soon as possible.

EMERGENCY CONTACT AND IRB CONTACT

During the study, if you experience any medical problems, suffer a research-related injury, or have questions about the study, please contact the study doctor listed on Page 1 of this consent form. If you seek emergency care, or hospitalization is required, please tell the healthcare provider that you are part of a research study being run by the study doctor listed on Page 1 of this form.

If you have any questions about your rights as a research subject, or complaints regarding this research study, you should call or write:

The Columbia University IRB
722 West 168 Street
4th floor Room 426
New York, NY 10032
212 305-5883

PRIMARY CARE PHYSICIAN/SPECIALIST NOTIFICATION OPTION

Please indicate below whether you want us to notify your primary care physician or your specialist of your participation in this study.

_____Yes, I want the study doctor to inform my primary care physician /specialist of my participation in this study.

_____No, I do not want the study doctor to inform my primary care physician /specialist of my participation in this study.

_____I do not have a primary care physician/specialist.

_____The study doctor is my primary care physician/specialist.

Consent
I have read and understand the above information. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I have volunteered to sign this form. I agree to join this study, until I decide otherwise. I will receive a copy of this signed and dated consent form.

Signature

Principal Investigator
Print Name_____Signature_____Date & Time_____

Study Participant
Print Name_____Signature_____Date & Time_____