Study Title: Antidepressant Response in the Treatment of Depressive Symptoms and Frailty Characteristics in Older Adults

Document Date: 10/18/2016

NCT: 01973283

New York State Psychiatric Institute – Columbia University Department of Psychiatry

ANTIDEPRESSANT RESPONSE IN THE TREATMENT OF DEPRESSIVE SYMPTOMS AND FRAILTY CHARACTERISTICS IN OLDER ADULTS:

PATIENT CONSENT COVER SHEET:

The following outline is meant to serve as a guide to help you learn about this research study and decide whether or not you want to take part. It does not replace the consent form that you will be asked to read and sign. The consent includes much more information that will help you make a decision about participating in this study. Read the consent form carefully, ask questions, and take your time or speak to others if you want to before you make your choice. Remember, even if you agree to take part in research you can change your mind at any time.

- Purpose: To examine the effect of antidepressant medication on treating depressive symptoms and the symptoms of frailty over 12-months (participants who enroll in Dr. Rutherford's 8-week trial entitled, "Antidepressant response in late life depression" [IRB 6836] will be followed for 10 months after the completion of that study).
- Participants: You have been asked to participate in this study because at the time of your initial evaluation you reported clinically significant depressive symptoms and one or more characteristics consistent with the frailty syndrome including exhaustion, decreased energy, weight loss, decreased grip strength, and slow/unsteady gait.
- Initial Treatment: You will be treated with either the medication escitalopram (trade name Lexapro) or duloxetine (trade name Cymbalta) for eight weeks.
    - Although the Food and Drug Administration approved these medications for the treatment of depression, these medications have not been tested to treat frailty.
    - Please discuss the side effects of the medications that are covered in the consent form with the study physician before you decide to participate in this study.
- Assessment: You will undergo two 90-minute evaluations (at baseline prior to treatment and again at Week 8) to assess your memory, day-to-day functioning, physical activity, and mobility.
- Acute treatment: After the baseline assessment you will begin treatment and come to the clinic every week for the next 8 weeks to monitor your progress and side effects.
- Following Acute Treatment: After you finish the 8-week trial, you will receive continued treatment in our clinic for 10 additional months. Whether you entered the study after completion of Dr. Rutherford's 8-week trial or completed the initial 8-week trial as part of this study, you can remain on the treatment that got you better or discuss alternative treatment approaches with your study physician including different medications or psychotherapy. Given the cost of certain medications, we may ask to use your insurance if applicable to cover the cost during the continued treatment phase. If there is a co-pay involved, the study will reimburse the cost of the co-pay to you. Two 90-minute assessments identical to those conducted at baseline and Week 8 will be conducted 6-months and 12-months after initial initiation of treatment.
- Early Discontinuation: You may stop your participation in the study at any time for any reason. Your doctor may take you out of the study if 1) Staying in the study would be harmful to you, 2) You need treatment not allowed in the study, or 3) You do not follow study procedures.
- If you are removed from the study or after you complete the 12-month study, you will be treated in the clinic at no cost to you for at least three months or, if you prefer, the clinic staff will refer you elsewhere for continued treatment.

New York State Psychiatric Institute – Columbia University Department of Psychiatry

ANTIDEPRESSANT RESPONSE IN THE TREATMENT OF DEPRESSIVE SYMPTOMS AND FRAILTY CHARACTERISTICS IN OLDER ADULTS: PATIENT CONSENT FORM

PURPOSE AND OVERVIEW

You are being asked to participate in a study being conducted at the New York State Psychiatric Institute to examine the effect of antidepressant medication on treating depressive symptoms and the symptoms of the syndrome of frailty. You have been asked to participate in this study because you have reported during your initial evaluation clinically significant depressive symptoms and one or more characteristics consistent with the frailty syndrome including exhaustion, decreased energy, weight loss, decreased grip strength, and slow/unsteady gait. For the treatment of your symptoms, you will initially be given either the medication escitalopram (trade name Lexapro) or duloxetine (trade name Cymbalta). Although escitalopram and duloxetine have been shown to be effective in and are approved for the treatment of depression by the Food and Drug Administration, these medications have not been tested in the treatment of frailty. As part of this study, you will be asked to take a number of tests that assess your memory, physical activity levels, and your day-to-day functioning. All procedures will take place at the New York State Psychiatric Institute. The purpose of this study is to determine the effect of antidepressant medication on treating depressive symptoms and the characteristics of frailty.

If you are entering this study after completing Dr. Rutherford's 8-week placebo-controlled trial entitled, "Antidepressant response in late life depression" (IRB 6836) and you responded to this treatment, you can remain on this treatment. If you did not respond to treatment, you can discuss alternative treatment approaches with your study physician. If you responded to placebo treatment, you can choose to remain off antidepressant treatment and be monitored in this study or start antidepressant treatment.

VOLUNTARY

Participation in this research study is voluntary. If you decide not to participate, or if you later decide to stop participating, you will not lose any benefits to which you are otherwise entitled. A decision not to participate or withdraw your participation will not affect your current or future treatment at the New York State Psychiatric Institute or Columbia University.

ALTERNATIVE TO STUDY PARTICIPATION

You do not have to participate in this study to receive treatment for your depressive symptoms. Many other available antidepressant medications have also been shown to be effective in the treatment of depressive symptoms. Additionally, some with your symptoms may respond to psychotherapy (cognitive-behavioral or problem-solving therapies).

STUDY PROCEDURES

Stopping your current antidepressant if you are taking one

If you are not responding to an antidepressant medication that you have taken for at least 6 weeks, you will be asked to stop taking the antidepressant medication you are

currently on before beginning the study medication (this is called a washout period). Your study doctor will speak with you about the length of the washout period, which differs depending on which drug you are taking. For example, washout periods for drugs such as sertraline (trade name: Zoloft) or Duloxetine (trade name: Cymbalta) are typically 1-week in duration; antidepressant medications such as Fluoxetine (trade name: Prozac) can take up to 4 weeks in duration. Weekly visits will be required for washout periods lasting more than one week to evaluate your health and to check for increased symptoms during the washout period. You are asked to contact the study team or your study doctor as soon as possible if these symptoms cause you any concern.

Cognitive and Function Testing

You will be asked to take a number of tests that measure cognition and day-to-day functioning (e.g., memory, attention, and other thought processes and physical, social, and instrumental activities of daily living) at your baseline visit prior to starting the study medication, 8 weeks, 6-months, and 12-months following starting study medication. These tests are either paper-and-pencil or measure your physical mobility and take about 90 minutes to complete at both the baseline and Week 8 study visits. Prior to each of these visits, you will be asked to wear a watch that assesses the level of your physical activity throughout the day and return this watch one week later when you arrive in clinic for your next visit. During Weeks 1-7, a study physician will follow-up with you weekly during clinic visits to provide clinical management and assess your weekly depressive symptoms, overall severity and improvement, and side effect profiles.

For individuals who enter this study after completing Dr. Rutherford's study, you will be asked to take these tests at 6-months and 12-months following the initiation of study medication in Dr. Rutherford's study; you will have completed baseline and Week 8 assessments as part of that study.

Treatment

During the initial 8-week study, you will be given either escitalopram (Lexapro) or duloxetine (Cymbalta). You will be asked to come to the clinic every week for visits with the study doctors. The baseline and Week 8 evaluation sessions will each last about 2 hours total (including the 90 minutes for testing described in the previous section). All other visits will last less than 1 hour.

If you have not taken an adequate dose of escitalopram for treatment of your current depressive symptoms, you will be started on escitalopram 10 mg daily for the first four weeks and, if necessary, increased to 20 mg daily by Week 4. This dose range is the same as doses used in regular clinical practice. The dose will be adjusted based on your clinical response and side effects, i.e., if side effects prove to be a problem, the dose will be reduced. If you show a consistent and good response before the maximum dose is reached, you will be maintained on the dose to which you responded, i.e., less than the maximum dose of 20 mg daily**.** If the study doctor feels that during the course of escitalopram treatment your condition worsens significantly, or intolerable side effects occur, the escitalopram will be discontinued and you will be treated in the clinic as clinically indicated with other medications. The dosing and side effects of duloxetine are explained in this consent form and your study doctor will review these with you.

If you have not responded to an adequate trial of the medication escitalopram given within the last year, you will be given the medication duloxetine as your initial treatment in this study. Duloxetine has been approved by the FDA for the treatment of depression and is in

widespread clinical use. Duloxetine will be given as a single dose, starting at 30 mg daily for the first week followed by increasing doses up to a maximum of 90 mg daily during the 8-week study. If you respond to duloxetine during the study, the dose increases will be stopped and you will be maintained on the effective dose (unless worsening again occurs, in which case the dose may again be increased). If you develop problematic side effects during the trial, the dose may be reduced after you discuss the side effects with your doctor. If your doctor finds that during the medication trial your condition worsens significantly, or intolerable side effects occur, the duloxetine will be discontinued and you will be treated in the clinic as clinically indicated with other medications.

If you respond to either escitalopram or duloxetine, you will be maintained on this treatment regimen and followed monthly for a total of 12-months of treatment. If you do not respond to acute phase trial, you will be treated in the clinic for a total of 12-months of treatment as clinically indicated with other medications. Given the cost of certain medications, we may ask to use your insurance if applicable to cover the cost during this continued treatment phase. If the use of your insurance requires a co-pay, the study will reimburse the cost of the co-pay to you.

If you have entered this study following the completion of Dr. Rutherford's 8-week antidepressant trial and you responded to your study medication (escitalopram or duloxetine) or placebo, you will be maintained on this treatment regimen and followed monthly for a total of 12-months of treatment. If you do not respond to treatment in Dr. Rutherford's study, you will be treated in the clinic for a total of 12-months as clinically indicated with other medications.

As part of this study, the initiation of new psychotherapy will be delayed. You will be asked to not start any new psychotherapy during the initial phase of treatment (lasting 8 weeks). Following the completion of this initial phase of treatment, if you prefer you will then be able to begin new psychotherapy.

If you have entered this study following the completion of Dr. Rutherford's 8-week antidepressant trial and you responded to your study medication or placebo, if you prefer you will then be able to begin new psychotherapy.

The assessment procedures for this study include interviews that will be conducted by a psychiatrist, psychologist, and social worker, as well as a research coordinator. If you find any questions during the interviews upsetting, you do not have to answer them.

Although an initial blood work-up for standard laboratory tests was already conducted as part of your initial clinic evaluation, follow-up blood work for standard laboratory tests will be done at Week 8, 6-months, and 12-months of this study. The total amount of blood taken at each visit will be about 20 cc, which is equivalent to about one and a half tablespoons. In total, no more than 100 cc of blood will be drawn for the 12-month study.

If you have entered this study following the completion of Dr. Rutherford's 8-week antidepressant trial, blood work will be conducted at the beginning of this study, 6-months and 12-months after the start of initial study medication.

Treatment at the end of the study

After you complete the 12-month study, you will be treated in the clinic at no cost to you for at least three months or, if you prefer, the clinic staff will refer you elsewhere for continued treatment.

Stopping the study

Your doctor may stop your participation in the study at any time for any reason. You may be taken out of the study if:

1. Staying in the study would be harmful to you;
2. You need treatment not allowed in the study;
3. You do not follow study procedures.

If you are removed from the study, you will be treated in the clinic at no cost to you for at least three months or, if you prefer, the clinic staff will refer you elsewhere for continued treatment.

RISKS

Escitalopram (Lexapro) Risks

It is possible that you may experience side effects from the medication escitalopram. The side effects most commonly reported are: headache, nausea, sexual difficulties (decreased sexual ability or desire, ejaculatory delay), somnolence (sleepiness), insomnia (difficulty falling or staying asleep), diarrhea, increased sweating, dry mouth, fatigue, dizziness, constipation, and decreased appetite.

Since escitalopram may have the potential to impair judgment, thinking, or motor skills, it is stressed that you should not drive or operate complicated machinery until you are reasonably certain that the medications do not produce these effects in you.

Rare side effects that occur with escitalopram also occur with other antidepressants, including serious allergic reactions. If these or other side effects prove to be a problem, your doctor will take necessary action in consultation with you, which may include lowering the dose or stopping the medication.

It is also important that you do not abruptly stop taking the medication without first discussing this with the doctor. Stopping these medications suddenly may be followed by withdrawal symptoms or by a return of the depressive feelings. You have to be cautious about drinking alcohol. Any alcohol that you do drink will have a greater impact, that is, one drink will feel like two. You must not take monoamine oxidase inhibitor drugs (MAOIs: including Nardil, Parnate) during your treatment with escitalopram. This is important because serious reactions including death have been reported when MAOIs have been taken along with other antidepressant medications.

Duloxetine (Cymbalta) Risks

You may experience side effects while taking duloxetine, the most common of which is nausea. For most people, the nausea is mild to moderate, and usually subsides within one to two weeks. Other common side effects are dry mouth, constipation, decreased appetite, fatigue, sleepiness, and increased sweating. If these or other side effects are intolerable, the medication dose will be lowered or stopped completely.

Rare side effects can occur in susceptible patients, including serious allergic reactions. If you experience an allergic reaction to duloxetine, such as rash, hives, or itching, you must notify your study doctor immediately. Long-term use of duloxetine is associated with osteoporosis/osteopenia. You have to be cautious about drinking alcohol. Any alcohol that you do drink will have a greater impact, that is, one drink will feel like two. You must not take monoamine oxidase inhibitor drugs (MAOIs: including Nardil, Parnate) during your treatment with duloxetine. This is important because serious reactions including death have been reported when MAOIs have been taken along with other antidepressant medications.

Medication is being dispensed in non-childproof packages and extra precautions need to be taken to keep the medication away from children.

Other Study Risks

If you require medications for sleep disturbance during the course of your participation, you may be prescribed lorazepam (up to 2 mg daily) or its equivalent, zolpidem (up to 10 mg), or trazodone (up to 150 mg). These medications have been used to successfully treat sleep disturbances.

It is possible that you may experience side effects from these medications. The side effects most commonly associated with lorazepam include sedation, somnolence, and falls. The side effects most commonly associated with zolpidem include fatigue and drowsiness, along with headache or muscle aches. The side effects most commonly associated with trazodone include dizziness, drowsiness, headache, and nausea.

It is possible that the study medicine may have no beneficial effect, and as a result you may feel that your depressive symptoms are getting worse. During the washout period, your depressive symptoms will not be treated with active medication and may become worse, stay the same, or improve. There is the possibility that when the antidepressant medication is discontinued your depressive symptoms may worsen and you may experience increasing symptoms of depression such as low mood, sleep and appetite disturbance, low energy and interest, and the possibility of suicidal feelings. You should inform your doctor immediately if this occurs.

Possible side effects that may be associated with obtaining a 1-2 tablespoon blood sample include pain, fainting, bruising, light-headedness, and, on rare occasions, infection. Precautions will be taken to avoid these difficulties. It also may be upsetting to answer some of the questions about how you are managing in your day-to-day life or to answer the pencil-and-paper tests of your memory. You can however stop these assessments at any point.

BENEFITS

No benefits can be guaranteed to you as a result of your participation in this study. The treatment offered in this study however may help improve your depressive symptoms. If you have entered this study following the completion of Dr. Rutherford's 8-week antidepressant trial, you will have access to an additional 10 months of antidepressant treatment (10 months of treatment in this study plus three months of additional treatment following the end of this study as compared to the three months of additional treatment offered at the end of Dr. Rutherford's study).

CONFIDENTIALITY

Your name and other personal identifying information will be stored in an electronically secure database at New York State Psychiatric Institute. All records of participating subjects will be kept in a locked room with access provided only to research staff including the research coordinator, data entry person, and the Principal Investigator, Dr. Brown. Records will be available to research staff, and to Federal, State and Institutional regulatory personnel (who may review records as part of routine audits). Each person participating in the study receives a coded number and only the researchers have access to the master list identifying names and numbers. All data collected will be kept confidential and used for professional purposes only (such as data entry and analysis for the presentation of results in scientific journals or at scientific conferences). Access to data stored in computers is restricted by security measures (passwords). Only the research coordinator, data entry person, and the Principal Investigator, Dr. Brown, have access. If you entered this study following completion of Dr. Rutherford's 8-week trial, data from that study corresponding to data collected as part

of this study will be shared between Principal Investigators, coordinators, and data entry people. Publications using this data will be done in a manner that fully protects the subject's anonymity. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

COMPENSATION AND ECONOMIC CONSIDERATIONS

You will not have to pay for any of the medications, medical examinations, or laboratory tests that are required for this study.

IN CASE OF INJURY

Compensation for Research Related Injuries: Federal regulations require that the investigators inform you about this institute's policy with regards to compensation and payment for treatment of research-related injuries.

In case of injury, New York State Psychiatric Institute will provide short term emergency medical treatment, which has been determined to be necessary by New York State Psychiatric Institute's doctors, and which is within the capability of New York State Psychiatric Institute to provide. In addition, we will provide assistance in arranging follow up care in such instances.

New York State Psychiatric Institute and Research Foundation for Mental Hygiene do not provide compensation or payment for treatment of research related injuries. However, you should be aware that you do not give up your legal right to seek such compensation through the court by participating in this research.

QUESTIONS

You will be notified of significant new findings that may relate to your willingness to continue to participate as a study informant. You have been given a copy of this consent to keep.

Your participation is voluntary, and you can discontinue the evaluation at any time.

You are free to contact the Principal Investigator, Dr. Patrick Brown (646-774-8666) with any questions you may have about this study.

If you have any questions about your rights as a research participant, want to provide feedback, or have a complaint, you may call the NYSPI Institutional Review Board (IRB). (An IRB is a committee that protects the rights of participants in research studies). You may call the IRB Main Office at (646) 774-7155 during regular office hours.

DOCUMENTATION OF CONSENT

I have read the above and voluntarily agree to participate in the research study described above.

Print name: _____

Signed: _____

Date: _____

I have discussed the proposed research with this participant including the risks, benefits, and alternatives to participation (including the alternative of not participating in the research). The participant has had an opportunity to ask questions and in my opinion is capable of freely consenting to participate in this research.

Print name: _____
Person Designated to Obtain Consent

Signed: _____

Date: _____