Update #6
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NCI Community Oncology Research Program – Kansas City (NCORP-KC)

A221101,
A Phase III Randomized, Double-Blind Placebo Controlled Study of Armodafinil (Nuvigil®) To Reduce Cancer-Related Fatigue in Patients with High Grade Glioma

This is an important form. Please read it carefully. It tells you what you need to know about this research study. If you agree to take part in this study, you need to sign this form. Your signature means that you have been told about the study and what the risks are. Your signature on this form also means that you want to take part in this study.

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this study because you are experiencing fatigue that is related to your cancer. Cancer related fatigue is a very common symptom in people with cancer..

Why is this study being done?

The purpose of this study is to:

- See if taking the study agent, armodafinil, at a dose of 150mg or 250mg, will improve problems with fatigue in patients who have been diagnosed with cancer and are experiencing fatigue.
- See the effects (good and bad) of taking Armodafinil compared to placebo (an inactive agent) on cancer related fatigue.

In this study, you will take either the study agent, armodafinil, or the placebo (inactive agent). You will not take both.

Armodafinil (Nuvigil®) is a medicine that is currently FDA approved to promote wakefulness in people who have sleep disorders. However, it is not been studied in people with cancer related fatigue.

How many people will take part in the study?

About 330 people will take part in this study.

What will happen if I take part in this research study?

Before you begin the study...

You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Medical history (questions about your health and any medications you are taking), including weight and rating of how well you perform activities of daily living.
- General **neurological** examination
- Pregnancy test, if you have not already had one done and your doctor thinks this is needed (if you are a female and able to become pregnant)

During the study...

You will have already had radiation therapy or surgery for your cancer.

Before you start taking the study agent, armodafinil or placebo, you will complete a booklet of questionnaires. This booklet contains 6 brief questionnaires about the fatigue related symptoms you may be experiencing, and should take a total of 20-25 minutes to complete.

You will also be asked to complete a cognitive test (memory and concentration skills test). This will be done three times; once before you start taking the study agent, once at 4 weeks and once again at the end of the 8 week period, when you are finished taking the study agent. This is to see how the study agent is affecting your memory and concentration. For the test, you will be asked some questions about your memory and concentration by someone with specialized training in this area. This testing will be done at your doctor's office, and will take about 20-30 minutes to complete.

You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the study groups. Neither you nor your doctor can choose the group you will be in. You will have a one in three chance of being placed in any group.

If you are in group 1, you will take a dose of the armodafinil (150 mg) by mouth, every day in the morning. You will take this every day for 8 weeks.

If you are in group 2, you will take a dose of the placebo pill (inactive ingredient) by mouth, every day in the morning. You will take this every day for 8 weeks.

If you are in group 3, you will take a dose of the armodafinil (250 mg) by mouth, every day in the morning. You will take this every day for 8 weeks.

If you miss taking a tablet in the morning, you can take the tablet that day as long as you take it at least 12 hours before the next dose.

You will also complete a booklet of questionnaires at the end of weeks 4 and 8. This booklet contains the same 6 brief questionnaires about the fatigue, memory, and concentration that you completed before you started taking the study agent/placebo. This should take a total of 20-25 minutes to complete (as described above).

Someone from the study team will call you at the end of week 4 and week 8 and to see how you are doing and answer questions.

When I am finished taking the study agent/placebo…

You will complete the booklet of questionnaires (end of week 8) regarding your fatigue related symptoms, and undergo cognitive (memory and concentration skills) testing (as described above).

How long will I be in the study?

You will be asked to take the study agent or placebo for 8 weeks.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the study agent, armodafinil, can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen.

Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the study agent. In some cases, side effects can be serious, long lasting, or may never go away.
You should talk to your study doctor about any side effects that you have while taking part in the study.

Risks and side effects related to the study agent, armodafinil, include those which are:

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving armodafinil, from 4 to 20 may have:
• Headache • Trouble sleeping • Nausea • Dizziness • Anxiety • Diarrhea

RARE In 100 people receiving armodafinil, 3 or fewer may have:
• Upper abdominal pain • Fatigue • Rash • Agitation, attention disturbance, or nervousness • Decreased appetite, anorexia • Constipation • Shortness of breath • Excessive sweating • Flu-like symptoms • Pain • Numbness and tingling • Frequent urination • Fever • Thirst • Tremor or shakiness • Dry mouth • Vomiting • High blood pressure

RARE, AND SERIOUS In 100 people receiving armodafinil, 3 or fewer may have:
• Severe headaches • Severe allergic reaction • Increased heart rate • Irregular heart beat • Depression • Increased risk of suicidal thoughts • Stevens-Johnson Syndrome (see below)

Stevens-Johnson syndrome is a rare, serious disorder in which your skin and mucous membranes react severely to a medication or infection. Often, Stevens-Johnson syndrome begins with flu-like symptoms, followed by a painful red or purplish rash that spreads and blisters, eventually causing the top layer of your skin to die and shed. Stevens-Johnson syndrome is an emergency medical condition that usually requires hospitalization. Recovery after Stevens-Johnson syndrome can take weeks to months, depending on the severity of your condition. If you develop Stevens-Johnson syndrome and your doctor determines that it might have been caused by the study medication, you'll need to discontinue it.

Armodafinil has not been shown to produce impaired judgment, thinking or affect motor skills but due to the action of the medication, you should use caution when operating automobile or other hazardous machinery.

Reproductive risks: You should not become pregnant or father a baby while on this study because the drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. While doctors hope armodafinil will be helpful against cancer related fatigue, there is no proof of this yet. We do know that the information from this study will help doctors learn more about treatment for cancer related fatigue. This information could help future cancer patients.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- Getting treatment or care for your cancer related fatigue without being in a study
- Taking part in another study
- Getting no treatment

Talk to your doctor about your choices before you decide if you will take part in this study.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- Alliance Researchers
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people
- The Cancer Trials Support Unit (CTSU), a service sponsored by the NCI to provide greater access to cancer trials

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.

What are the costs of taking part in this study?

You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your cancer in this study. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

You will not need to pay for tests and procedures which are done just for this research study. This test is:

- Cognitive test

The study agents, armodafinil and placebo, will be supplied at no cost to you.

Even though it probably won't happen, it is possible that the manufacturer may not continue to provide the armodafinil for some reason. If this would occur, other possible options are:

- You might be able to get the armodafinil from the manufacturer or your pharmacy but you or your insurance company may have to pay for it.
- If there is no armodafinil available at all, no one will be able to get more and the study would close.
- If a problem with getting armodafinil occurs, your study doctor will talk to you about these options.

You will not be paid for taking part in this study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://cancer.gov/clinicaltrials/understanding/insurance-coverage . You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, _____ *[investigator's name(s)]*, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at _____ *[telephone number]*.

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

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Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor _____ *[name(s)]* at _____ *[telephone number]*.

For questions about your rights while taking part in this study, call the NCI Community Oncology Research Program – Kansas City Institutional Review Board (a group of people who review the research to protect your rights) at 913-948-5588

Where can I get more information?

You may also visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at 1-800-4-CANCER (1-800-422-6237).

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 study results. You can search this Web site at any time.

Release

By signing this form you authorize NCORP - KC to access and obtain information that is required for the study. This may include your medical records, labs, radiologic films and reports and pathology specimens. This authorization to disclose your medical records shall not expire, even upon death, unless specifically revoked in writing by you.

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Signature

I have been given a copy of all 9 pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

Printed Name of Participant

Signature of Participant **Date**

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent **Date**

Approval Date 6/14/2018 to 6/13/2019

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