NRG-GY006
Amendment #2
Version date: 11/29/2017

NCI Community Onocology Research Program-Kansas City (NCORP-KC)

Study Title for Study Participants: Testing the addition of a new anti-cancer drug, triapine, to the usual chemotherapy treatment (cisplatin) during radiation therapy for advanced-stage cervical and vaginal cancers.

Official Study Title for Internet Search on http://www.ClinicalTrials.gov:
Protocol NRG-GY006: A Randomized phase II trial of radiation therapy and cisplatin alone or in combination with intravenous triapine in women with newly diagnosed bulky stage IB2, or stage II, IIIB, or IVA cancer of the uterine cervix or stage II-IVA vaginal cancer.

This study is being carried out under the sponsorship of NRG Oncology, an organization dedicated to clinical research in the field of gynecologic cancer. NRG Oncology is funded by the Federal Government through the National Cancer Institute (NCI).

What is the usual approach to my cervical or vaginal cancer?

You are being asked to take part in this research study because you have newly diagnosed cervical or vaginal cancer for which surgical treatment is not possible. People who are not in a study are usually treated with radiation therapy with weekly Food and Drug Administration (FDA)-approved chemotherapy Sometimes, combinations of these are used and your doctor can explain which may be best for you. These treatments can reduce symptoms and may stop the tumor from growing for several months or more. For patients who receive the usual approach for this cancer, about 65 out of 100 are free of cancer at five years.

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

If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer but you may want to receive comfort care to relieve your symptoms.

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

Why is this study being done?

The purpose of this study is to compare any good or bad effects of adding triapine to the usual cisplatin chemotherapy and radiation therapy, compared to using cisplatin chemotherapy and radiation therapy alone. Triapine is an experimental drug being tested in the treatment of cervical cancer to improve the effects of standard

radiotherapy with concurrent chemotherapy. The addition of triapine to the usual chemotherapy and radiation therapy could shrink your tumor and increase the length of time till the cancer returns, but it could also cause side effects. This study will allow the researchers to know whether this different approach is better, the same, or worse than the usual approach.

What are the study groups?

This study has two study groups.

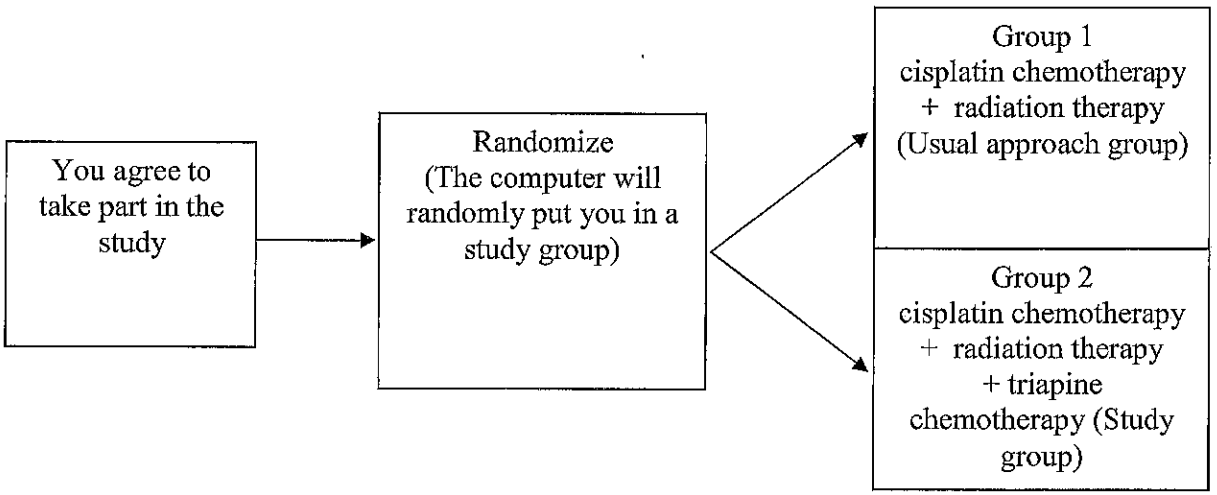
- Group 1 will get the usual cisplatin chemotherapy and radiation therapy used for this type of cancer.
- Group 2 will get the usual cisplatin chemotherapy and radiation therapy used for this type of cancer plus an investigational study drug called triapine three times per week.

If you are enrolled to Group 2, you will receive Triapine three times a week for five weeks (day 1, 3, 5, 8, 10, 12, 15, 17, 19, 22, 24, 26, 29, 31, and 33), beginning on day 1 of the radiation treatment. Triapine will need to be given through a tube inserted into a vein near your arm (IV) that allows the drug to be given directly into the vein each time you receive the drug. The infusion will last about two hours and it will begin about 90 minutes after your radiation ends. You will receive dexamethasone by IV prior to your triapine infusion to help reduce the side effects you might experience with triapine.

You may receive the chemotherapy drug cisplatin by IV over 1 ½ hours, given once a week for 5 weeks (day 2, 9, 16, 23, 30, 37 [day 37 may not be given]), beginning on day 2. Fluids and medications will be given by IV before and after the cisplatin treatment. In total, the cisplatin treatment may take up to 6 hours.

You will receive radiation therapy (external radiation from a machine that targets the cancer cells) daily Monday through Friday for 5-6 weeks, beginning on day 1 (a Monday). Weekends and holidays are excluded. During or following the external radiation therapy, you may also receive intracavitary radiation (internal radiation from a radioactive source placed into your uterus and vagina) for a specified period of time (sometimes given as an outpatient treatment or requiring 1 or 2 nights in the hospital depending on the technique used). This intracavitary radiation is part of the standard of care for your type of cancer. Some patients have both external and internal radiation therapy, either one after the other or at the same time.

A computer will by chance assign you to treatment groups in the study. This is called randomization. This is done by chance because no one knows if one study group is better or worse than the others. Another way to find out what will happen to you during this study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



How long will I be in this study?

You will receive the cisplatin chemotherapy and radiation therapy or triapine given with cisplatin chemotherapy and radiation therapy for up to eight weeks. After you finish either therapy, your doctor will continue to watch you for side effects and follow your condition every three months for the first two years and then every six months for the next three years after completion of your treatment.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual approach for your cancer. However, there are some extra tests and procedures that you will need to have if you agree to take part in this section of the study. We will use them to carefully monitor the effects of the study treatment, including preventing and manging side effects.

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will need the following extra exams, tests, and procedures. They are not part of the usual approach for your type of cancer or are being done more frequently because you are in this study.

During the study:

- a PET/CT scan at three months after radiation therapy completion to measure tumor response. The 3 month PET/CT scan will be done at no cost to the patient.
- The insurance coverage information for the tests and other parts of the study is listed in a later section, "What are the Costs?".

What possible risks can I expect from taking part in this study?

If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss
- The study drug/study approach may not be better, and could possibly be worse, than the usual approach for your cancer.
- The study drug, chemotherapy drug and radiation therapy used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health. There is also a risk that you could have side effects from the study approach that adds the study drug (triapine) to the usual chemotherapy and radiation therapy treatment.
- Every day, people are naturally exposed to low levels of radiation that come from the sun and the environment. This type of radiation is called "background radiation". The PET/CT scan that you will receive in this study will expose you to extra radiation that is equal to about 5 year's worth of background radiation. Most of the time, this low amount of extra radiation is not harmful to you. However, scientists believe that if you get extra radiation that is more than about 30 year's worth of background radiation, there is a chance of having a harmful side effect, including causing a new cancer. It is estimated that this could occur in about 1 out of every 1000 people who get a very large amount of extra radiation.
- There is also the risk that you could have side effects from the study drug, chemotherapy, and radiation therapy.

Here are important points about chemotherapy and radiation therapy side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects of triapine that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Risk Profile for Triapine®

COMMON, SOME MAY BE SERIOUS In 100 people receiving Triapine®, more than 20 and up to 100 may have:
• Anemia which may cause tiredness, or may require blood transfusion • Nausea, vomiting • Tiredness, fever • Bruising, bleeding • Infection, especially when white blood cell count is low

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Triapine®, from 4 to 20 may have:
• Skin changes which may appear blue or purple • Pain • Constipation, diarrhea, heartburn • Sores in mouth which may cause difficulty swallowing • Chills • Swelling and redness at the site of the medication injection • Change in the heart rhythm • Weight loss, loss of appetite • Dehydration • Dizziness, headache • Changes in taste • Cough, shortness of breath • Hair loss, rash • Flushing • High blood pressure which may cause blurred vision • Low blood pressure which may cause feeling faint

RARE, AND SERIOUS In 100 people receiving Triapine®, 3 or fewer may have:
• Heart failure which may cause shortness of breath, swelling of ankles, and tiredness • Swelling of the lungs which may cause shortness of breath

Possible Side Effects of Cisplatin

COMMON, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, more than 20 and up to 100 may have:
• Nausea, vomiting, • Infection, especially when white blood cell count is low • Anemia which may cause tiredness, or may require blood transfusions • Bruising, bleeding • Kidney damage which may cause swelling, may require dialysis • Hearing loss including ringing in ears

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Cisplatin, from 4 to 20 may have:
• Hair loss • Change in taste • Diarrhea • Allergic reaction which may cause rash, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Confusion • Difficulty with balance • Numbness and tingling of the arms and legs • Blurred vision or changes in ability to see colors (especially blue or yellow)

RARE, AND SERIOUS In 100 people receiving Cisplatin, 3 or fewer may have:
• Cancer of bone marrow later in life caused by chemotherapy • Seizure

Possible Side Effects of Research Radiation Therapy

COMMON, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, more than 20 and up to 100 may have:
• Reddening, tanning, or peeling of the skin • Mild pain • Hair loss • Tiredness • Diarrhea, nausea • Anemia, which may cause tiredness, or may require transfusion • Infection, especially when white blood cell count is low

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving radiation therapy, from 4 to 20 may have:
• Thickening and numbness of the skin • Sores or ulcers on the skin or near the cancer location • Permanent hair loss • Bleeding from the skin • Sores in mouth which may cause difficulty swallowing

RARE, AND SERIOUS In 100 people receiving radiation therapy, 3 or fewer may have:
• Damage to internal organs • Abnormal opening in internal organs which may cause pain and bleeding

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive Risks: Treatment with chemotherapy or radiation may involve unknown risks to an unborn child and it is not known whether taking this drug now may have effects on any future children that you may have. If you are pregnant or breast feeding, you cannot take part in this study. You will be given a pregnancy test before you begin the study to make sure that you are not pregnant. If there is a chance you could become pregnant during this study, you should not participate in the study or you must use a highly effective means of birth control while you are taking part. If you become or are found to be pregnant while taking part in this study, you must tell your study doctor immediately so that management of the pregnancy and the possibility of stopping treatment can be discussed. You should practice highly effective means of birth control for six months after treatment as the chemotherapy or radiation may involve unknown risks to the unborn child and it is not known whether taking this drug now can have effects on any future children that you may have in this time period. 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.

What possible benefits can I expect from taking part in this study?

It is not possible to know at this time if the study drug(s)/study approach is better than the usual approach so this study may or may not help you. This study will help researchers learn things that will help people in the future

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

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

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest;
- If new information becomes available;
- If you do not follow the study rules;
- If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights while in this study, call the NCI Community Onocology Research Program-Kansas City (NCORP-KC) Institutional Review Board at 913-948-5588.

What are the costs of taking part in this study?

The triapine drug will be supplied at no charge by the National Cancer Institute (NCI) in the U.S. while you take part in this study. The cost of getting the triapine ready and giving it to you is not paid by the study sponsor so you or your insurance company may have to pay for this. It is possible that the triapine may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

The NCI has provided funding to NRG oncology to help cover the cost of the PET/CT scan done at three months after radiation therapy completion to measure tumor response.

You will not be paid for taking part in this study. The institution receives payment that covers some but not all of the costs of the study.

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

If you are injured or hurt as a result of taking part in this study and need medical treatment, please tell your study doctor. The cost of medical treatment for injury will not be paid for by the study sponsor. Your insurance company may not be willing to pay for study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a study.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information and/or information about your specimen(s)

from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- NRG Oncology and any drug company supporting the study;
- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.

The National Institutes of Health (NIH) has issued NRG Oncology a Certificate of Confidentiality, which protects NRG Oncology from being forced to disclose personal information about you in response to a subpoena or other request in a federal or state legal proceeding.

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Where can I get more information?

You may 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 the results. You can search this Web site at any time.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ (insert name of study doctor[s]) at _____ (insert telephone number).

ADDITIONAL STUDIES SECTION:

This section is about optional studies you can choose to take part in.

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will be added to your medical records and you and your study doctor will know the results.

You may be billed for these optional studies. You can still take part in the main study even if you say NO to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Circle your choice of YES or NO for each of the following studies.

Optional Sample Collections for Laboratory Studies

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

If you choose to take part in this study and are selected to be in Group 2, the study doctor for the main study would like to collect blood for research on whether you develop methemoglobinemia (the presence of a protein, methemoglobin, in the blood).

What is involved?

If you agree to take part, here is what will happen next:

1) About one teaspoon of blood will be collected five times from a vein in your arm – before your first treatment and 1, 3, 5, and 24 hours after your first treatment. You will then be required to return the next day for one additional blood draw. Treatment is given over two hours, so you may be in clinic up to 7 hours after the start of treatment to allow for these blood draws. If you are noted to have an elevation of methemoglobinemia to greater than 6% on the 5 hour sample, you will need to be observed with repeat hourly blood draws until this value has decreased to below 6%.
2) Your samples and some related health information will be sent to a researcher for use in the study described above. Some of your health information may be placed in central databases that may be public, along with information from many other people. Information that could directly identify you will not be included.

What are the possible risks?

1) The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
2) There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
3) There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
4) In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of health information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information

about inherited traits that might affect you or your blood relatives could possibly be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

How will information about me be kept private?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1) Researchers to whom NRG Oncology sends your sample and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
2) Information that identifies you will not be given to anyone, unless required by law.
3) If research results are published, your name and other personal information will not be used.

What are the possible benefits?

You will not benefit from taking part.

The researchers, using the samples and related health information from you and others in this study, might make discoveries that could help people in the future.

Are there any costs or payments?

The optional blood draws described above for testing for methemoglobinemia will be billed to your insurance and may result in additional expenses. This is not paid for by the study. You will not be paid for taking part in this study. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

What if I change my mind?

If you decide you no longer want your samples to be used, you can call the study doctor, _____, at _____ who will let the researchers know. Then, any sample that remains will no longer be used and related health information will no longer be collected. Samples or related information that have already been given to or used by researchers will not be returned.

What if I have more questions?

If you have questions about the use of your samples for research, contact the study doctor, _____, at _____.

Please circle your answer to show whether or not you would like to take part in each option:

SAMPLES FOR THE LABORATORY STUDIES:

I agree to have my specimen(s) collected and I agree that my specimen sample(s) and related information may be used for the laboratory study(ies) described above.

YES NO

THIS IS THE END OF THE SECTION ABOUT OPTIONAL STUDIES.

Release

By signing this form you authorize NCORP-KC to access and obtain inforatmion that is required for the study. This may include your medial 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.

You will get a copy of this form. If you want more information about this study, ask your study doctor.

My Signature Agreeing to Take Part in the Main Study

I have read this consent form or had it read to me. I have discussed it with the study doctor and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study and any additional studies where I circled 'yes'.

Participant _____

Participant's signature_____

Date of signature_____

Person obtaining consent _____

Signature of person obtaining consent _____

Date of signature_____