

Comprehensive Cancer Center of Wake Forest University
CCOP Research Base Protocol # 83403

**A Phase II Study of Single Agent Depsipeptide (FK228) in Recurrent, Platinum Sensitive
Adeno-Carcinoma of the Ovary or Peritoneum**

WAKE FOREST UNIVERSITY CONSENT FORM

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You may or may not receive any benefit from being part of the study. There may also be risks associated with being part of research studies. Clinical trials include only patients who choose to take part. Ask your study doctor or the study staff to explain any words or information that you do not understand. Please take your time to make your decision. Discuss it with your friends and family. Ask for the NCI booklet "Taking Part in Clinical Trials: What Cancer Patients Need To Know."

You are being asked to take part in this study because you have a cancer of the ovary or peritoneum, which has returned after completion of the initial therapy.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to find out what effects (good and bad) depsipeptide, an investigational agent, has on you and your ovarian / peritoneal cancer. An investigational agent is a new medication, of which we do not know the value at this time.

There are several medications, which are useful for the treatment of your cancer such as liposomal doxorubicin, topotecan, gemcitabine and others. We think that depsipeptide may be a good medication in this situation as well. We do not know at this time, what the effect on ovarian cancer is. The medication is not yet approved for treatment of ovarian cancer. We hope that this study will determine how effective depsipeptide is for the treatment of ovarian cancer.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 50 people will take part in this study. About 10 patients will be treated at Wake Forest University.

WHAT IS INVOLVED IN THE STUDY?

If you take part in this study, you will have the following tests and procedures:

- 1) Before starting the medication, you will be asked about your medical history, you will undergo a complete physical examination as well as blood tests (3 tablespoons of blood will be drawn from a vein). Your cancer will be evaluated by x-rays. All these tests would also be necessary, if you would get the standard of care treatments and will be done, even if you do not participate in a study.

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- 2) One treatment course will consist of three treatments. Before each treatment, you will be asked about how you feel, you will undergo a short examination and a blood sample will be drawn (2 teaspoons). This would also be done, if you would get standard of care weekly treatments. One week after the third treatment another blood sample will be drawn (2 teaspoons). This is not usually done during standard of care therapy. Blood can be drawn at Baptist Hospital, at a hospital or clinic closer to where you live or sometimes by home health personnel.
- 3) Your EKG will be checked:
 - o Prior to registration
 - o Prior to an immediately following 1st administration of study drug
 - o Prior to 2nd administration of study drug
 - o Prior to 3rd administration of study drug

Later your EKG will only be checked if you develop problems with your heart.

- 4) Before every other course, your cancer will be re-evaluated with x-rays. During standard of care therapy this would also be done every other or every third course.
- 5) Procedures solely done for research purposes include the blood draw 1 week before the next treatment and 2 tablespoons of blood drawn before every course. No further procedures are necessary for this part of the research.
- 6) The total amount of blood drawn for research purposes depends on how long you benefit from the study medication.
- 7) To learn more about the way Depsipeptide affects cancer cells we also would like to examine small sections from your original tumor removed from your pelvis. These sections will be cut from previously preserved tissue. No additional procedures are necessary. In addition we would like to examine a blood sample (one teaspoon) prior to each treatment. This will be drawn at the same time, as the other necessary samples. These studies are **optional**. You may be eligible for this study even if you do not wish to have these extra tests done.

HOW LONG WILL I BE IN THE STUDY?

We think you will be in the study for as long as you benefit from the treatment.

Even after you have stopped taking the study medication, we will continue to follow you for 5 years, to ensure, that all side effects are detected, even if they appear after the treatment is discontinued. However, no additional clinic visits will be scheduled because you were in the study.

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The researcher may decide to take you off this study if it is in your medical best interest, funding is stopped, supply of agent(s) is insufficient, your condition worsens, or new information becomes available.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first and learn about any potential health or safety consequences. If you withdraw suddenly, we need to make sure, that your blood counts do not drop too much and therefore have to continue and check blood samples. The same would be done after any chemotherapy treatment.

WHAT ARE THE RISKS OF THE STUDY?

While on the study, you are at risk for side effects as described below. You should discuss these with the researcher and/or your regular doctor. There also may be other side effects that we cannot predict. Other agents will be given to make side effects less serious and uncomfortable. Many side effects go away shortly after depsiptide is stopped, but in some cases side effects can be serious or long-lasting or permanent.

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The following kinds of side effects may occur related to the experimental drug depsipeptide:

	Common Happens to 21-100 out of every 100	Occasional Happens to 5-20 out of every 100	Rare Happens to <5 out of every 100
Immediate: Within 1-2 days of receiving drug	Nausea, vomiting, loss of appetite	Changes and irregularities in heart rhythm	
Prompt: Within 2-3 weeks, prior to next course	Decrease in the numbers of red and white blood cells and platelets made in the bone marrow. A low number of platelets in the blood may increase the risk of bleeding. Abnormal levels of liver enzymes	High level of enzymes in the blood that may indicate muscle stress or damage, tiredness	Low level of calcium salts in the blood, low levels of albumin (a protein), high levels of uric acid, decreased hemoglobin (oxygen-carrying substance in red blood cells), decreased infection- fighting cells, weight loss, decreased phosphates in the blood, build up of fluid surrounding the lungs, tumor lysis syndrome*

* Tumor lysis syndrome can occur when cancer cells die rapidly as a result of anti-cancer treatment. This syndrome causes metabolic abnormalities that can lead to kidney failure. Patients with this syndrome are treated with medications to increase their urine output.

Risks and side effects related to the depsipeptide we are studying include:

Risks of Infection: When the white blood cells are low, there is an increased risk of infection. In such cases, patients may need antibiotics if they become ill or develop a fever. If red blood cell counts drop too low, a blood transfusion may be needed. If platelet counts are very low, a platelet transfusion may be needed.

Risks of Blood Transfusions: Blood products come from voluntary donors who are carefully selected and tested, but there are still some risks to blood transfusion. These risks are uncommon and are usually mild, but may be severe or life threatening. Occasional risks include fever,

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allergic reactions, and the formation of antibodies (formed by the body to fight infections). Less common risks include infections with viruses, such as hepatitis, and fluid overload. Very rare risks are serious incompatibility reactions and infections including HIV, the virus that causes AIDS. The alternative to volunteer donor blood is directed donor blood donated by a family member or friend, if appropriate for your disease.

Risk of Pharmacokinetic Studies: If an intravenous catheter is required, there is a risk of pain, bruising, or bleeding at the site. After placement, the line may be infected which may require hospitalization, antibiotics, and possibly removal and/or replacement.

Risk of Heart Damage: Treatment with depsipeptide may result in damage or stress to the heart and irregular heart rhythms that may or may not be permanent. Researchers will be closely monitoring your heart function. Modifications to therapy will be made if there are symptoms of heart injury.

Risk of Warfarin Interaction: Treatment with depsipeptide and warfarin may result in possible interactions between these two medications and may cause potential bleeding tendencies.

Very rarely, you may develop unpredictable complications including death.

Reproductive Risks: Because the agents used in this study can affect an unborn baby, you should not become pregnant while on this study. You should not nurse your baby while on this study. Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while participating in this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, Norplant, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and a spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

Pregnant women are excluded from participation in this study. If you are a woman of childbearing potential a negative pregnancy test is required within 1 week of registration to check for possible early pregnancy prior to starting treatment.

You may experience discomfort, bruising and/or bleeding where the needle is inserted. Occasionally some people become dizzy lightheaded or feel faint. Infection may occur on rare occasions.

For more information about risks and side effects, ask the researcher.

There may also be other side effects we cannot predict. You should tell the research staff about all medications, vitamins and supplements you take and any medical conditions you have. This

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may help avoid side effects, interactions and other risks.

WHAT ARE THE BENEFITS OF TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you. We hope the information learned from this study will benefit other patients with cancer of the ovary or peritoneum in the future. The benefit of participation in this study may be that your tumor gets smaller and that you may have less discomfort. Of course, because individuals respond differently to therapy, no one can know in advance if it will be helpful in your case.

WHAT OTHER TREATMENT OPTIONS ARE AVAILABLE?

Instead of being in this study, you have these options: further chemotherapy with carboplatin, cisplatin, paclitaxel, docetaxel, liposomal doxorubicin, topotecan, gemcitabine or other drugs. All these drugs have been used with success in ovarian cancer. But there is no way we can predict for sure, which medication will be the best for your tumor. You could also elect not to receive any further treatment and be followed with best supportive care only.

Please talk to your regular doctor about these and other options. You may also ask for the Patient information sheets from the National Cancer Institute or call toll free at 1-800-4-CANCER.

WHAT ABOUT CONFIDENTIALITY?

By taking part in this research study, your personal health information, as well as information that directly identifies you, may be used and disclosed. Information that identifies you includes, but is not limited to, such things as your name, address, telephone number, and date of birth. Your personal health information includes all information about you which is collected or created during the study for research purposes. It also includes your personal health information that is related to this study and that is maintained in your medical records at this institution and at other places such as other hospitals and clinics where you may have received medical care. Examples of your personal health information include your health history, your family health history, how you respond to study activities or procedures, laboratory and other test results, medical images, and information from study visits, phone calls, surveys, and physical examinations.

Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

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Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the institutional review board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study.

If this research study involves the treatment or diagnosis of a medical condition, then information collected or created as part of the study may be placed in your medical record and discussed with individuals caring for you who are not part of the study. This will help in providing you with appropriate medical care. In addition, all or part of your research related health information may be used or disclosed for treatment, payment, or healthcare operations purposes related to providing you with medical care.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

When you sign this consent and authorization form you authorize or give permission for the use of your health information as described in the consent form. This authorization does not have an expiration date. You can revoke or take away your authorization to use and disclose your health information at any time. You do this by sending a written notice to the investigator in charge of the study at the following address:

Brigitte Miller, M.D.
Department of Gynecologic Oncology
Wake Forest University School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27157

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If you withdraw your authorization you will not be able to be in this study. If you withdraw your authorization, no new health information that identifies you will be gathered after that date. Your health information that has already been gathered may still be used and disclosed to others. This would be done if it were necessary for the research to be reliable. You will not have access to your health information that is included in the research study records until the end of the study.

WHAT ARE THE COSTS?

The Division of Cancer Treatment and Diagnosis, NCI, will provide you with depsipeptide free of charge while you are being treated on this study. Every effort will be made to ensure adequate supplies of the sponsored/supplied agent(s), free of charge, for all participants. If the drug becomes commercially available for this indication, there is a remote possibility that you may be asked to purchase subsequent supplies. Your physician will discuss this with you should this situation arise.

Taking part in this study may lead to added costs to you or your insurance company. Please ask about any expected added costs or insurance problems. Research only studies will not be charged to the patient. We can give you an estimate of what the added cost may be based on your particular situation and insurance coverage.

You or your insurance company will be billed for continuing medical care and/or hospitalization.

WILL YOU BE PAID FOR PARTICIPATING?

You will receive no payment or other compensation for taking part in this study.

The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

WHO IS SPONSORING THE STUDY?

This study is being sponsored by the National Cancer Institute and Wake Forest University Research Base. The sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

You should notify the study doctor as soon as you believe you have experienced any study related illness, adverse event, or injury.

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Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of \$25,000. Endurance Specialty Insurance Ltd. provides the insurance policy for this coverage. It provides a maximum of \$25,000 coverage for each claim, and is limited to a total of \$250,000 for all claims in any one year. The Wake Forest University School of Medicine, and The North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at (336) 716-3467.

You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should contact the study investigator, BRIGITTE MILLER MD at (336) 716 6673 or (336) 716 2011.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to which you are entitled.

If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is no longer in your best interest, your condition worsens, new knowledge becomes available, you had an unexpected reaction, you failed to follow instructions or because the entire study has been stopped.

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing the data from this research throughout the study. We will tell you about the new information from this study or other studies that may affect your health, welfare, or willingness to stay in this study.

IMPORTANT INFORMATION REGARDING THE STORAGE OF YOUR TISSUE SAMPLES

If you agree to participate in this study, we will need to draw blood from you. This blood will be kept and may be used in future research to learn more about other diseases. These blood samples will be obtained before you begin treatment and throughout the treatment course.

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Your blood sample will be stored with a unique identifier and will not include any identifiable information about you such as your name, address, phone number, social security number, medical record number or any of the identifiers outlined in the HIPAA Privacy Rule regulations.

The research that may be done with your blood sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research done with your blood sample will not be given to you or your doctor. These results will not be put in your health records. The research using your blood sample will not affect your care. Your blood sample will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of this research.

Sometimes blood samples used for genetic research may provide information about diseases that are passed on in families. Even if your blood sample is used for this kind of research, the results will not be told to you or members of your family, and will not be put in your health records.

The choice to let your blood sample be kept for future use is up to you. No matter what you decide to do, it will not affect your care in this study. If you decide now that your blood sample can be kept for research, you can change your mind at any time. Just contact your study investigator, Dr. Brigitte Miller (336-716-6673), and let her know that you do not want your blood sample used and it will no longer be used for research. Otherwise, the blood sample may be kept until it is used up or it is destroyed.

In the future, people who do research may need to know more about your health. While the study investigator may give reports about your health, he/she will NOT be given your name, address, phone number, or any other identifying information about who you are, unless you agree to being contacted in the future.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact Brigitte Miller, M.D. at (336) 716-6673 or (336) 716-2011.

For questions about your rights as a research participant, contact the Review Board of your hospital or call Wake Forest University Health Sciences Institutional Review Board (which is a group of people who review the research to protect your rights) at (336) 716-4542.

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WHERE CAN I GET MORE INFORMATION?

You may call the Cancer Information Service at:
1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

Visit the NCI's Web Sites
cancerTrials: comprehensive clinical trials information
http://www.cancer.gov/clinical_trials/

CancerNet™: accurate cancer information including PDQ
http://www.cancer.gov/cancer_information/

You will get a copy of this form. You can also request a copy of the protocol (full study plan).

SIGNATURE

I agree to take part in this study.

Participant _____ Date _____

Person Administering Consent _____ Date _____

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ADDENDUM TO INFORMED CONSENT TEMPLATE

I agree to allow the use of blood samples, other body fluids, and tissues obtained during testing, operative procedures, or other standard medical practices for further research purposes. Please read each sentence below and think about your choice, then initial the answer, that is right for you. If you have any questions, talk to your doctor or nurse.

a. I agree to the use of my specimens for research and teaching purposes related to Ovarian Cancer.

_____ Yes _____ No

b. I agree to be re-contacted in the future to discuss whether I will give permission for my specimens to be used for genetic research.

_____ Yes _____ No

c. I agree to allow my specimens to be used for research unrelated to Ovarian Cancer.

_____ Yes _____ No

d. My tissue and blood specimens may be used for research to learn more about the effects of Depsipeptide. _____ Yes _____ No Initials _____

e. My tissue and blood specimens may be used for research to learn more about cancer. _____ Yes _____ No Initials _____

f. My tissue and blood specimens may be used for research to learn more about other diseases. _____ Yes _____ No Initials _____

g. The clinical information collected in this study as part of my participation may be used for future research that uses my specimens. _____ Yes _____ No Initials _____

h. Someone from the Wake Forest University Research Base may contact me in the future to take part in more research. _____ Yes _____ No Initials _____

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SIGNATURE

Participant _____ Date _____

Person Administering Consent _____ Date _____

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