GYNECOLOGIC ONCOLOGY GROUP
SUGGESTED PATIENT INFORMATION/INFORMED CONSENT

TITLE OF RESEARCH PROJECT: **GOG-0262**: A PHASE III TRIAL OF EVERY-3-WEEKS PACLITAXEL VERSUS DOSE DENSE WEEKLY PACLITAXEL IN COMBINATION WITH CARBOPLATIN WITH OR WITHOUT CONCURRENT AND CONSOLIDATION BEVACIZUMAB (NSC #704865, IND #113912) IN THE TREATMENT OF PRIMARY STAGE II, III OR IV EPITHELIAL OVARIAN, PERITONEAL OR FALLOPIAN TUBE CANCER and **ACRIN 6695**: PERFUSION CT IMAGING TO EVALUATE TREATMENT RESPONSE IN PATIENTS PARTICIPATING IN GOG-0262

PRINCIPAL INVESTIGATOR:

GENERAL

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 have also been told that you have the option not to participate. 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.

This study is being carried out under the sponsorship of the Gynecologic Oncology Group (GOG), an organization dedicated to clinical research in the field of gynecologic cancer and the American College of Radiology Imaging Network (ACRIN), an organization dedicated to using imaging in research. Both GOG and ACRIN are funded by the Federal Government through the National Cancer Institute (NCI).

You are being asked to take part in this study because you have ovarian, fallopian tube or primary peritoneal cancer and you have a target lesion that can be evaluated through imaging.

WHY IS THIS STUDY BEING DONE?

The American College of Radiology Imaging Network (ACRIN) is conducting an imaging study (ACRIN 6695) for patients participating in the GOG-0262 treatment study. You must agree to participate in the imaging component as well as the treatment component as described in this consent.

The current standard treatment for ovarian, fallopian tube, and primary peritoneal cancer is a combination of chemotherapy drugs, carboplatin and paclitaxel, given every three weeks. Recently, investigators have shown that giving paclitaxel every week can increase the length of time without disease; however, there was more anemia (low red blood cell count) associated with this treatment. In this study you and your doctor will choose whether you receive paclitaxel every week or every three weeks along with carboplatin. Both treatments will be given for six cycles.

Some patients will have primary surgery to remove as much disease as possible followed by the chemotherapy described above. Other patients will receive three cycles of chemotherapy as described above, then have surgery to remove as much disease as possible, followed by three additional cycles of chemotherapy. The decision about whether to have surgery before the chemotherapy or in the middle

of the chemotherapy (this is called interval cytoreduction) will be made by you and your doctor before you begin the study.

Bevacizumab (Avastin™), has recently been approved by the U.S. Food and Drug Administration (FDA) for use in combination with chemotherapy in patients with colon and lung cancer, but not for ovarian cancer. A recent study done by the GOG showed that women who received bevacizumab in addition to chemotherapy lived longer without their disease getting worse. Detailed review of the side effects of the treatment with chemotherapy and bevacizumab is still being done.

In this study, you will be able to choose whether or not to receive bevacizumab with your paclitaxel and carboplatin treatment. If you elect to receive bevacizumab, you will receive it every three weeks beginning with the second cycle of therapy and you will continue to receive bevacizumab alone every three weeks as long as there is no evidence that your tumor is growing or you experience unacceptable side effects.

Because you shouldn't have surgery while receiving bevacizumab, if you are going to have interval cytoreduction (surgery between chemotherapy cycles), and you chose to receive bevacizumab, you will only receive bevacizumab during cycles 2, 5 and 6 of the chemotherapy, and then you will continue to receive bevacizumab alone every three weeks as long as there is no evidence that your tumor is growing or you experience unacceptable side effects.

In addition to the standard of care CT or MRI scans and treatment, you will have perfusion CT scans in this study. The perfusion CT scans will be performed to see if these scans can be used to accurately predict how effective the drug therapies will be on ovarian, fallopian tube or primary peritoneal cancer. Perfusion CT scans may be able to show changes in and around your tumor from the drug treatment earlier than the standard of care CT or MRI scans.

The standard of care CT or MRI scans can measure the size of the tumor. However, the perfusion CT scans will be used to monitor the effects of both the chemotherapy and bevacizumab treatment (if given) on the blood flow to the tumor. If this study shows that perfusion CT scans can accurately predict effects of drug treatment, these results will allow investigators in the future to use perfusion CT scans to predict in advance whether a certain drug therapy is likely be successful for patients with ovarian, fallopian tube or primary peritoneal cancer.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

Approximately 75 people will take part in this study.

WHAT WILL HAPPEN IF I TAKE PART IN THIS RESEARCH STUDY?

Before you begin the study

To participate in this study, you will be asked to read and sign this consent form before you are enrolled to participate in this study and have any study procedures.

You will need to have the following exams, tests or procedures to find out if you can be in the study. Unless otherwise noted, 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.

- History and physical examination which may include pelvic examination.
- Blood tests to assess blood cell counts; liver and kidney function; blood mineral levels
- Urine test sample.
- A blood pregnancy test if you are capable of becoming pregnant
  - If you choose to receive bevacizumab, you will also have the following:
    - Due to issues related to safety with the drug bevacizumab and the research question to determine the effect of treatment on time without evidence of cancer growth, no major surgical procedure can be planned for the time you are on this study. This includes any non-emergency abdominal surgery while you remain without evidence of cancer growth, such as exploratory surgery to remove or diagnose cancer or reversal of a colostomy. You are encouraged to discuss this with your physician prior to enrolling on this study.
    - Blood pressure measurement
    - Urine test sample for urine protein measurement
    - A blood test to measure clotting time.
    - If you have any opening in the skin such as an incision made for your recent cancer surgery, an examination of the incision to make sure there is no evidence of infection or healing problem.

You will undergo the following procedures that are not part of regular cancer care and are being done only because you are in this study.

- You will have a perfusion CT scan at an imaging center selected by your study doctor;
- If you have not had a post-surgery CT scan before you join the trial, a CT scan may be performed the same day as the perfusion CT scan.

The first perfusion CT scan will take place within 14 days before you start your chemotherapy treatment. If you have had surgery, the first perfusion CT scan will take place at least two weeks after your surgery and within 14 days before you start your chemotherapy treatment. This first perfusion scan can be performed either on the same day as your standard of care CT (or MRI) scan, or will be scheduled for another day.

When you have the perfusion CT scan, an intravenous catheter will be inserted into your hand or arm. You will receive a dose of a contrast agent, also known as X-Ray dye, according to your body weight. You will be asked to remain still for the scan while a set of images are taken. It will take about 45 minutes.

During the study

If the 1st perfusion CT scan shows your tumor meets all of the requirements for the study, you will receive two (or three) more perfusion CT scans. If your tumor does not meet the requirements for the study you will remain on the GOG-0262 chemotherapy treatment study but will not have to return for the other perfusion CT scans.

If you are asked to return for the additional perfusion CT scans, the following will occur:

- The 2nd perfusion scan will be performed between days 18 and 21 after the start of your first cycle of chemotherapy. You may need to have a blood draw to check your kidney health before you have the 2nd perfusion scan, depending on when your kidneys were last checked. Your study doctor wants to check your kidney health to reduce your risk of a rare effect from the contrast agent, also known as X-ray dye. If you agree, you may be asked to have an additional perfusion scan at this time. The purpose of the additional perfusion CT scan is to determine if the measurements of blood flow in your tumor can be reproduced, that is whether the two scans taken the same day appear the same. You will have the additional perfusion CT scan approximately 15 minutes later. You do not need to stay on the scanner during the waiting period. These perfusion CT scan(s) may take place on the same day as your physical examination and routine blood tests.

    - Before you have the perfusion CT scan, an intravenous catheter will be inserted into your hand or arm. You will receive a dose of a contrast agent according to your body weight. You will be asked to remain still for the scan while a set of images are taken. It will take about 45 minutes.

    - If you have the additional perfusion CT scan, you will receive a smaller dose of the X-Ray dye according to your body weight. The additional perfusion CT scan will take about 25 minutes.

- The last perfusion CT scan will be performed between days 8 to 10 after the start of your second cycle of chemotherapy. You may need to have a blood draw to check your kidney health again before you have the last perfusion scan, depending on when your kidneys were last checked. The perfusion CT scan may take place on the same day as your routine blood tests and examination.

    - Before you have the perfusion CT scan, an intravenous catheter will be inserted into your hand or arm. You will receive a dose of a contrast agent according to your body weight. You will be asked to remain still for the scan while a set of images are taken. It will take about 45 minutes.

If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will need the following tests and procedures before beginning treatment, and periodically during treatment and after treatment is completed. They are part of regular cancer care.

- Periodic history and physical examination which may include pelvic examination.
- Electrocardiogram (EKG) to measure your heart function before beginning treatment.
- Chest x-ray or CT scan of the chest.
- Detectable tumor will be measured periodically by physical examination, CT scan, or MRI scan.

- Periodic blood testing for CA-125 level. CA-125 is a blood test that is generally performed for patients with your type of cancer to monitor the effectiveness of treatment.
- Periodic blood tests to assess blood cell counts; liver and kidney function; blood mineral levels.
- A hearing test, if you have a history of hearing loss prior to treatment and possibly during the study if your physician feels it is necessary.
  - If you choose to receive bevacizumab, you will also have the following:
    - Blood pressure measurement every week
    - Urine test sample for urine protein measurement every 6 weeks
    - If you are on a blood thinner medication, then periodic blood tests to measure clotting function
    - If you have any opening in the skin such as an incision made for your recent cancer surgery, you will undergo a weekly examination of the incision to make sure there is no evidence of infection or healing problem.

You will choose one of the study treatments described below.

If you are in group 1 (often called "Regimen I"), you will receive the following treatment every 21 days (a cycle) for 6 cycles: Paclitaxel into your vein over 3 hours, and Carboplatin into your vein over 30 minutes on Day 1. If you are going to have interval cytoreductive surgery, you will have it between cycles 3 and 4. If you choose to receive bevacizumab, you will receive it into your vein over 30-90 minutes on Day 1 (beginning on the second cycle). If you are going to have interval cytoreductive surgery, you will receive bevacizumab during cycles 2, 5 and 6. Then, after the first 6 cycles are finished, you will receive bevacizumab alone into your vein over 30-90 minutes every 21 days as long as there is no evidence that your tumor is growing and you are not experiencing any unacceptable side effects.

If you are in group 2 (often called "Regimen II"), you will receive the following treatment every 21 days (a cycle) for 6 cycles: Paclitaxel into your vein over 1 hour on Days 1, 8 and 15 (every week) and Carboplatin into your vein over 30 minutes on Day 1. If you are going to have interval cytoreductive surgery, you will have it between cycles 3 and 4. If you choose to receive bevacizumab, you will receive it into your vein over 30-90 minutes on Day 1 (beginning on the second cycle). If you are going to have interval cytoreductive surgery, you will receive bevacizumab during cycles 2, 5 and 6. Then, after the first 6 cycles are finished, you will receive bevacizumab alone into your vein over 30-90 minutes every 21 days as long as there is no evidence that your tumor is growing and you are not experiencing any unacceptable side effects.

In both regimens, prior to the day one paclitaxel therapy you will be asked to take an oral steroid medication (dexamethasone) six and 12 hours prior to the expected infusion time. This is given to prevent allergic reactions to the paclitaxel. You will also be given intravenous medication to block allergic reactions to paclitaxel, and drugs to prevent side effects including nausea and vomiting.

If you chose to receive bevacizumab, the bevacizumab is given slowly (over 90 minutes) the first time it is administered, but if tolerated well, it will only take thirty-sixty minutes for subsequent treatments.

Whichever group you are in, your doctor may decide to give you a drug called docetaxel instead of paclitaxel if you have an allergic reaction or severe numbness in your hands and feet when you are treated with paclitaxel. The docetaxel will be given into your vein every 21 days.

After your treatments are completed:

To monitor your well-being and the status of your cancer, you will undergo these tests and procedures that are part of regular cancer care, every three months for two years, then every six months for three years, then yearly:

- History and physical examination which will include pelvic examination.
- Blood tests to assess blood cell counts; liver and kidney function; blood mineral levels if your physician feels they are necessary for monitoring
- Hearing test, if your physician feels it is necessary for monitoring
- CA-125 blood tests
- CT or MRI scan, if previously detectable tumor was monitored using these methods or if your physician has concern about the possibility of cancer recurrence.
    - If you choose to receive bevacizumab, you will also have the following:
        - Blood pressure measurement
        - Urine test sample for urine protein level at the first follow-up visit and then only if your physician feels it is necessary.
        - Blood clotting function tests if your physician feels it is necessary.

Study Chart

You will receive paclitaxel (either weekly or every 21 days) and carboplatin every 21 days in this study. If you chose to receive bevacizumab, you will also receive bevacizumab (starting cycle 2) every 21 days. This 21-day period of time is called a cycle. You will receive paclitaxel and carboplatin for 6 cycles. If you chose to receive bevacizumab, then you will receive bevacizumab alone every 21 days as long as there is no evidence that your tumor is growing and you are not experiencing any unacceptable side effects.

Each cycle is numbered in order. The chart below shows what will happen to you during Cycle 1 and future treatment cycles as explained previously. The left-hand column shows the day in the cycle and the right-hand column tells you what to do on that day.

Cycle 1 (All Patients)

Day	**What you do**
Within 28 days before starting study	• History and physical examination, which may include a pelvic exam. • Electrocardiogram (EKG) to measure heart function • Audiogram (if there is a history of hearing loss) • A CT scan or MRI of abdomen and pelvis to measure tumor • For patients receiving Bevacizumab: • Blood pressure measurement

Within 14 days before starting treatment	• Get routine blood tests and urinalysis.
	• Get a pregnancy test if you could possibly become pregnant.
	• A perfusion CT scan (may be same day as the CT scan or MRI of abdomen and pelvis to measure tumor).
	• For patients receiving bevacizumab:
	  • Get blood tests to measure blood clotting function
	  Examination of incision if still partially open since abdominal surgery (for primary surgery patients only)

Day 1	• Pre-chemotherapy medications by IV (into your vein) or mouth to prevent allergic reactions • Go to your doctor's office or infusion center for treatment with IV paclitaxel and carboplatin chemotherapy. You will be there for approximately 2-4 hours.
Day 8	• Get routine blood tests. • Examination of incision if still partially open since abdominal surgery (for primary surgery patients only) • If you are in Regimen II, receive IV paclitaxel over 1 hour.
Day 15	• Get routine blood tests. • Examination of incision if still partially open since abdominal surgery (for primary surgery patients only) • If you are in Regimen II, receive IV paclitaxel over 1 hour.
Between Days 18 & 21	• Physical examination • Get routine blood tests. • Get your kidney health checked if it has not been done recently • Get a perfusion CT scan • Get another perfusion CT scan approximately 15 minutes following the first, if you agree and are asked to by your physician.
Day 22	• Begin Cycle 2 (Day 1 of Cycle 2, see next chart)

Cycles 2-6 (for patients who had primary surgery)

Day	**What you do**

Day 1	• Pre-chemotherapy medications by IV or mouth to prevent allergic reactions
	• Go to your doctor's office or infusion center for treatment.
	• Receive paclitaxel and carboplatin into your vein. You will be there for approximately 2 hours.
	• If you are receiving bevacizumab:
	  • Blood pressure measurement
	  • Examination of incision if still partially open since abdominal surgery
	  • Receive bevacizumab into your vein over 30-90 minutes

Day 8	• Get routine blood tests. • If you are in Regimen II, receive IV paclitaxel over 1 hour. • If you are receiving bevacizumab:

	• Blood pressure measurement • Examination of incision if still partially open since abdominal surgery
Between Days 8 and 10	• Get your kidney health checked if it has not been done recently • Get a perfusion CT scan (Cycle 2)
Day 15	• Get routine blood tests. • If you are in Regimen II, receive IV paclitaxel over 1 hour. • If you are receiving bevacizumab: • Blood pressure measurement • Examination of incision if still partially open since abdominal surgery
Between Days 15 and 21	• CT or MRI scan (Cycle 3 and Cycle 6)
Between Days 18 and 21	• History and physical examination • Routine blood tests. • Routine urine test (cycles 2, 4 and 6)
Day 22	• Begin next cycle (Day 1 of next Cycle)

Cycle 2 (for patients who will have interval cytoreductive surgery)

Day	**What you do**
Day 1	• Pre-chemotherapy medications by IV or mouth to prevent allergic reactions • Go to your doctor's office or infusion center for treatment. • Receive paclitaxel and carboplatin into your vein. You will be there for approximately 2 hours. • If you are receiving bevacizumab: • Blood pressure measurement • Receive bevacizumab into your vein over 30-90 minutes

Day 8	• Get routine blood tests. • If you are in Regimen II, receive IV paclitaxel over 1 hour. • If you are receiving bevacizumab: • Blood pressure measurement
Between Days 8 and 10	• Get your kidney health checked if it has not been done recently • Get a perfusion CT scan (Cycle 2)
Day 15	• Get routine blood tests. • If you are in Regimen II, receive IV paclitaxel over 1 hour. • If you are receiving bevacizumab: • Blood pressure measurement
Between Days 18 and 21	• History and physical examination • Routine blood tests. • Routine urine test
Day 22	• Begin next cycle (Day 1 of next Cycle)

Cycles 3 and 4 (for patients who will have interval cytoreductive surgery)

Day	What you do
Day 1	• Pre-chemotherapy medications by IV or mouth to prevent allergic reactions • Go to your doctor's office or infusion center for treatment. • Receive paclitaxel and carboplatin into your vein. You will be there for approximately 2 hours. • Examination of incision if still partially open since abdominal surgery (cycle 4)
Day 8	• Get routine blood tests. (for primary surgery patients only) • Examination of incision if still partially open since abdominal surgery (cycle 4) • If you are in Regimen II, receive IV paclitaxel over 1 hour.
Day 15	• Get routine blood tests. • Examination of incision if still partially open since abdominal surgery (cycle 4) • If you are in Regimen II, receive IV paclitaxel over 1 hour.
Between Days 15 and 21	• CT or MRI scan (Cycle 3 and Cycle 6) • Have interval cytoreductive surgery (cycle 3)
Between Days 18 and 21	• History and physical examination • Routine blood tests. • Routine urine test (cycle 4)
Day 22	• Begin next cycle (Day 1 of next Cycle)

Cycles 5 and 6 (for patients who will have interval cytoreductive surgery)

Day	What you do

Day 1	• Pre-chemotherapy medications by IV or mouth to prevent allergic reactions
	• Go to your doctor's office or infusion center for treatment.
	• Receive paclitaxel and carboplatin into your vein. You will be there for approximately 2 hours.
	• If you are receiving bevacizumab:
	  ◦ Blood pressure measurement
	  ◦ Examination of incision if still partially open since abdominal surgery
	  ◦ Receive bevacizumab into your vein over 30-90 minutes

Day 8	• Get routine blood tests.
	• If you are in Regimen II, receive IV paclitaxel over 1 hour.
	• If you are receiving bevacizumab:
	  ◦ Blood pressure measurement
	  ◦ Examination of incision if still partially open since abdominal surgery

Day 15	• Get routine blood tests. • If you are in Regimen II, receive IV paclitaxel over 1 hour.

	• If you are receiving bevacizumab:
	  • Blood pressure measurement
	  • Examination of incision if still partially open since abdominal surgery

Between Days 15 and 21	• CT or MRI scan (Cycle 3 and Cycle 6)
Between Days 18 and 21	• History and physical examination • Routine blood tests. • Routine urine test (cycle 6)
Day 22	• Begin next cycle (Day 1 of next Cycle)

Cycles 7 and up (only for patients who chose to receive bevacizumab)

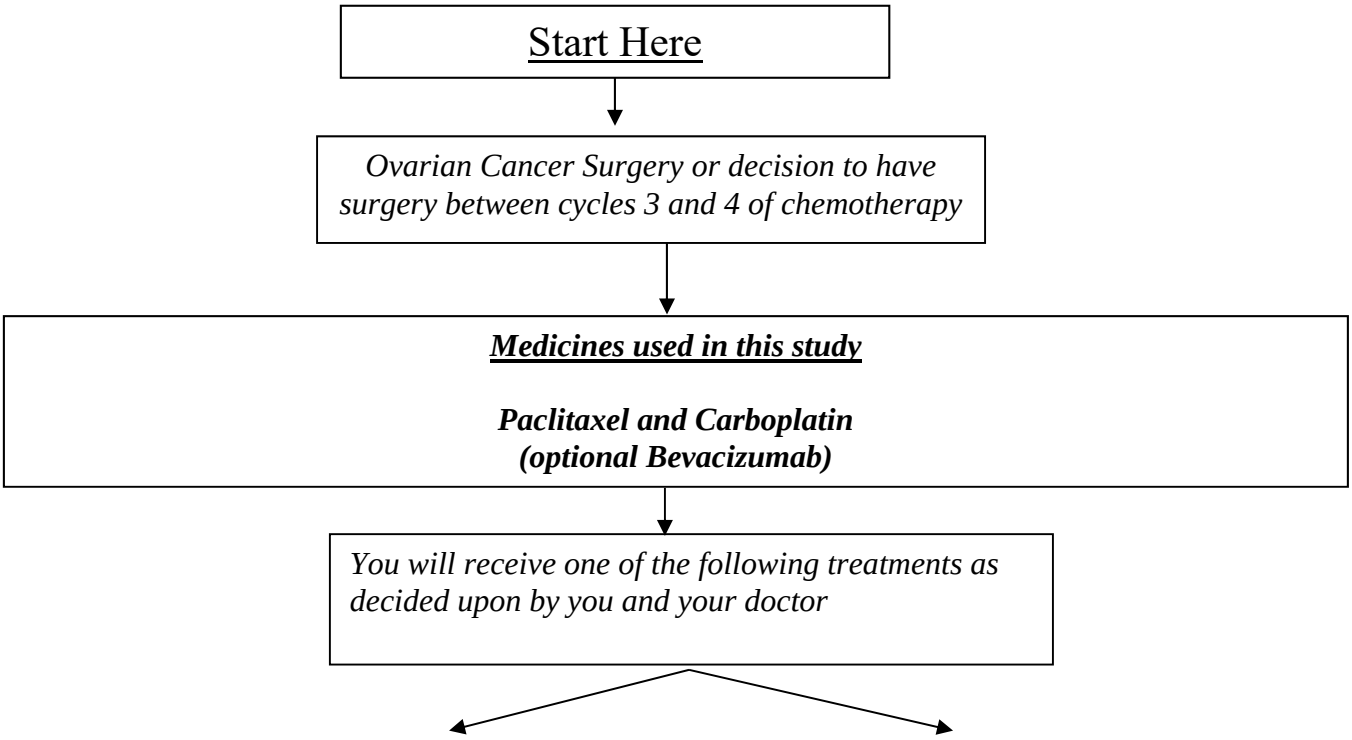
Day	**What you do**
Day 1	• Blood pressure measurement • Go to your doctor's office or infusion center for treatment with IV bevacizumab. You will be there for approximately 1-2 hours.
Day 8	• Get routine blood tests. • Blood pressure measurement (to be arranged at home or doctor's office) • Examination of incision if still partially open since abdominal surgery
Day 15	• Get routine blood tests. • Blood pressure measurement (to be arranged at home or doctor's office) • Examination of incision if still partially open since abdominal surgery
Between Days 15 and 21	• CT or MRI scan (every 3 months)
Between Days 18 and 21	• History and physical examination (every other cycle) • Blood pressure measurement • Routine blood tests (every other cycle) • Routine urine test (every other cycle)
Day 22	• Begin next cycle (Day 1 of next Cycle)

After Completion of Treatment (ALL REGIMENS)

Timing	**What you do**
Every 3 months, 8 times, then every 6 months, 6 times, then every year	• History and physical examination • Assessment of side effects • CA-125 blood test • If you are receiving bevacizumab: • Blood pressure measurement
If physician feels there is a possibility of cancer re-growth	• CT or MRI scan

Study Plan

Another way to find out what will happen to you during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.



Group 1

Paclitaxel and Carboplatin by vein every 21 days for 6 cycles*
If you chose to receive bevacizumab, you will receive it by vein every 21 days beginning with cycle 2 until your tumor regrows or you experience unacceptable side effects*
*If you decided to have interval cytoreductive surgery, you will receive it between cycles 3 and 4 and you will not receive bevacizumab during cycles 3 and 4

A cycle is 21 days

You will have a perfusion CT scan within 14 days before beginning chemotherapy and then again (once or twice) between days 18 and 21 after the start of cycle 1, and then again between days 8 and 10 of cycle 2 of chemotherapy.

Group 2

Paclitaxel by vein every week and Carboplatin by vein every 21 days for 6 cycles*

If you chose to receive bevacizumab, you will receive it by vein every 21 days beginning with cycle 2 until your tumor regrows or you experience unacceptable side effects*

*If you decided to have interval cytoreductive surgery, you will receive it between cycles 3 and 4 and you will not receive bevacizumab during cycles 3 and 4

A cycle is 21 days

You will have a perfusion CT scan within 14 days before beginning chemotherapy and then again (once or twice) between days 18 and 21 days after the start of cycle 1, and then again between days 8 and 10 of cycle 2 of chemotherapy.

HOW LONG WILL I BE IN THE STUDY?

The perfusion CT scanning portion of the study will last approximately eight to ten weeks. You will complete the imaging portion of the study (perfusion CT scans) before the start of your third cycle of chemotherapy.

You will be asked to take paclitaxel and carboplatin for approximately five months. If you decided to have interval cytoreductive surgery, you will have it done approximately 9 weeks after starting chemotherapy. If you chose to receive bevacizumab, you will receive bevacizumab starting cycle 2 every 21 days as long as there is evidence that your tumor is not growing and you are not experiencing any unacceptable side effects. If you decided to have interval cytoreductive surgery, you will not receive bevacizumab during cycles 3 and 4.

After you are finished your study treatment, the study doctor will ask you to visit the office for follow-up exams every three months for the first two years and then every six months for the next three years after completion of your treatment. At the end of this five-year period we would like to keep track of your medical condition for the rest of your life by calling you once a year to see how you are doing. Keeping in touch with you and checking on your condition every year helps us look at the long-term effects of the study.

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 side effects/risks from the paclitaxel, carboplatin and bevacizumab 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 thinks it is best for you; 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 paclitaxel, carboplatin and bevacizumab**.** In some cases, side effects can be serious because they can be long lasting, may never go away, may result in hospitalization, or may be life-threatening**.** There is also a risk of death.

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 Perfusion CT

Two different types of risks are associated with the perfusion CT scans in the study: radiation from the X-ray used in the perfusion CT and possible reactions to the contrast agent, also known as X-Ray dye.

Radiation (X-Ray) Risks

Radiation dose is measured in units called milliSieverts (mSv). With each of the perfusion CT scans, you will receive a dose of 15 mSv (or 30 mSv with the additional scan at 2nd time point). In this study, you will receive from 1 to 4 perfusion scans with exposure from 15 mSv to 60 mSv. As a comparison, the average person in the United States receives a dose of about 3.0 mSv of radiation per year as a result of daily life. There is no direct evidence that the amount of radiation delivered by a standard CT scan causes cancer. However, much higher radiation doses (greater than 50 times than a standard CT) have been linked to increased risk for cancer 20 or more years in the future. Skin reddening (erythema) has been reported with repeated perfusion CT scans but this event is considered extremely unlikely in this study.

Risks Associated with the Contrast Agent or X-Ray Dye

These reactions occur in less than 3 out of 100 patients. In particular, the more severe reactions occur in approximately 1 in 2,000 patients who receive X-ray dye. If these reactions occur, you will be treated immediately and your participation in the perfusion CT portion of the study will be stopped. You will remain on the GOG-0262 chemotherapy treatment study but will not have to return for the other perfusion CT scans.

Risks Associated With Intravenous (IV) Catheter Placement

Likely

- Minor discomfort;
- Bruising;
- Pain at the injection site.

Rare

- Fainting;
- Bleeding;
- Infection.

Risks Associated with the Contrast Agent or X-Ray Dye

Unlikely

- Nausea/vomiting;
- Warm sensation or a flushed feeling;
- Skin rashes or hives.

Rare, but Serious

- Swelling of the mouth and throat;
- Temporary damage to the kidney.

Risks and side effects related to **Paclitaxel (Taxol®)** include those which are:

Likely

- Low white blood cell counts - this may make you more open to infection
- Low platelet count - this may make you bruise more easily and bleed longer if injured
- Low red blood cell count which may cause tiredness, shortness of breath or fatigue
- Mild to severe allergic reaction which may be life-threatening with hives, wheezing (difficulty breathing) and change in blood pressure (low or high)
- Numbness and pain of the hands and feet that sometimes worsens with additional treatment and may not disappear after the drug is stopped. This may lead to difficulty walking, buttoning clothes, etc. (may be serious)
- Hair loss
- Muscle weakness and muscle loss
- Muscle and joint aches
- Nausea and/or vomiting
- Diarrhea
- Sores in the mouth or throat (that can lead to difficulty swallowing and dehydration)

Less likely

- Low blood pressure
- Irregular heartbeats
- Fever
- Fatigue, weakness
- Swelling, accumulation of fluid
- Elevation in liver function blood tests
- Confusion; mood changes
- Skin tissue irritation, swelling or discoloration around the injection site
- Skin tissue damage if some of the drug leaks from the vein while it is being given
- Changes in taste
- Rash

Rare but serious

- Elevation of serum creatinine in kidneys (may be reversible or can lead to kidney damage)
- Inflammation of the colon, pancreas or lungs (may be serious)
- Liver failure
- Seizures
- A slowing of the heart rate (a slow pulse is not harmful; however, if you should develop any other irregularities in heart rate during treatment, an EKG and other tests may be required.)
- Heart attack
- Blood clots
- Blockage in the intestines
- Opening in the bowel wall

If you experience a severe allergic reaction to IV paclitaxel that cannot be overcome with standard anti-allergy medications, or numbness or tingling in your hands or feet which would cause discontinuation of paclitaxel, then the drug docetaxel (Taxotere) will be substituted for paclitaxel. Docetaxel has been found to be as effective in patients with ovarian and primary peritoneal cancer as paclitaxel. Docetaxel is from the same chemical family as paclitaxel and generally has the same type of side effects as paclitaxel with some important differences. When compared to paclitaxel, docetaxel has been found to cause less tingling and numbness in the hands and feet but has been found to cause lower white blood cell counts and higher risk of infection and a chance of severe fluid retention (see below). It has also been found that some patients who experience allergic reactions to paclitaxel do not demonstrate allergic reactions to docetaxel.

Risks and side effects related to **Docetaxel (Taxotere)** include those which are:

Likely:

- Low white blood cell counts - this may make you more open to infection
- Low platelet count - this may make you bruise more easily and bleed longer if injured
- Low red blood cell count which may cause tiredness, shortness of breath or fatigue
- Mild to severe allergic reaction which may be life-threatening with hives, wheezing and low blood pressure
- Numbness and pain of the hands and feet that sometimes worsens with additional treatment and may not disappear after the drug is stopped. This may lead to difficulty walking, buttoning clothes, etc.
- Hair loss
- Muscle weakness and muscle loss; muscle and joint aches
- shortness of breath
- skin irritation(including hives and itching if allergic reactions)
- low or high blood pressure
- nausea and/or vomiting
- diarrhea
- mouth and throat sores
- fatigue
- excessive tearing of the eyes
- chills; fever
- Fluid retention, in the form of weight gain, poorly tolerated swelling of the legs, arms, tissues beneath the skin, sometimes fluid collections in the chest causing shortness of breath and strain on the heart, and sometimes fluid collections in the abdomen (ascites) which can cause abdominal discomfort, distention and indigestion.
- Nail changes (e.g. discoloration, fungal infection, bleeding under the nail, etc.)

Less likely, but serious:

- A slowing of the heart rate (a slow pulse is not harmful; however if you should develop any other irregularities in heart rate during treatment, an EKG and other tests may be required.)
- Irregular heartbeats
- Heart attack
- Sores in the mouth or throat (that can lead to difficulty swallowing and dehydration)

- Lightheadedness
- Headaches
- Kidney damage
- An increase in triglycerides (a blood lipid) levels which could increase risk of hardening of the arteries
- Liver damage
- Confusion; mood changes
- Skin tissue damage if some of the drug leaks from the vein while it is being given
- Changes in taste
- Irritation and swelling of the skin in an area previously treated with radiation therapy
- Rash
- Inflammation of the colon, pancreas or lungs
- Blurred vision or other changes in eyesight such as sensation of flashing lights or spots
- Infection and/or bleeding complications as a result of decreased blood counts

Rare, but serious:

- Liver failure
- Swelling of the Brain
- Seizures
- severe allergic reaction resulting in development of a rash, difficulty breathing , and low blood pressure
- Acute leukemia

Risks and side effects related to **Carboplatin** include those which are:

Likely:

- Low white blood cell counts - this may make you more open to infection
- Low platelet count - this may make you bruise more easily and bleed longer if injured
- Low red blood cell count which may cause tiredness, shortness of breath or fatigue
- Tiredness
- Loss of appetite and weight loss
- Diarrhea, constipation, nausea and vomiting, and abdominal pain
- Complete hair loss
- Skin rash
- Changes in taste
- Changes in electrolytes in the blood such as magnesium and potassium

Less likely, but serious:

- Numbness or tingling in fingers or toes
- Ringing in the ears and hearing loss
- Allergic reactions
- Chills and fever with aches and pains
- Decrease in kidney or liver function
- Sores in mouth and throat (that can lead to difficulty swallowing and dehydration)

- Altered vision

Rare, but serious:

- Seizures
- Secondary cancers such as acute leukemia
- Kidney failure requiring dialysis
- Deafness
- Death

Risks and side effects related to **Bevacizumab** include those which are:

COMMON, SOME MAY BE SERIOUS In 100 people receiving bevacizumab (rhuMAb VEGF), more than 20 and up to 100 may have:
• High blood pressure which may cause headaches, dizziness, blurred vision

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving bevacizumab (rhuMAb VEGF), from 4 to 20 may have:
• Anemia which may require blood transfusion • Low white cell count that may increase the risk of infection • Infection, including collection of pus in the belly or rectum • Abnormal heartbeat which may cause palpitations or fainting • Pain in the belly, rectum, chest, joints, muscles, or tumor • Low appetite, constipation, diarrhea, heartburn, nausea, vomiting, or dehydration • Bleeding from multiple sites including the vagina or nose • Internal bleeding which may cause black tarry stool, blood in vomit, coughing up blood, or blood in urine • Blockage of internal organs which may cause vomiting or inability to pass stool • Sores in the mouth • Allergic reaction during or after infusion of bevacizumab which may cause fever, chills, rash, itching, hives, low blood pressure, wheezing, shortness of breath, swelling of the face or throat • Delay in healing of wounds or spontaneous opening of wounds • Weight loss, tiredness, or dizziness • Muscle weakness • Damage to the jawbone which may cause loss of teeth • Headache • Numbness, tingling, or pain in the fingers or toes • Hoarseness, stuffy nose, or cough • Dry skin • Swelling and redness of the skin • Blood clot in limbs or lungs which may cause swelling, pain, shortness of breath • Leakage of protein in the urine, which can rarely lead to damage to the kidney

RARE, AND SERIOUS In 100 people receiving bevacizumab (rhuMAb VEGF), 3 or fewer may have:
• Clots in the arteries, causing stroke (which may cause paralysis or weakness) or heart attack (which may cause chest pain or shortness of breath). This risk is significantly increased in patients who are elderly or with history of diabetes • Heart failure which may cause shortness of breath, swelling of ankles, and tiredness • Bowel perforation (a tear in the bowel) that can cause pain or bleeding and require surgery to repair • A tear or hole (fistula) in internal organs such as the nose, throat, lungs, esophagus, rectum, or vagina. These conditions may cause serious infections or bleeding and require surgery to repair • Sores in the throat • Flesh-eating bacteria syndrome, an infection in the deep layers of skin • Damage to organs (bone, lungs, others) which may cause loss of motion • Bleeding in the tumor, brain, belly, or lungs which may cause confusion, blood in stool or coughing up blood • Brain damage which may cause headache, seizure, blindness (also known as Reversible Posterior Leukoencephalopathy Syndrome) • Kidney damage which may require dialysis • Redness, pain or peeling of palms and soles

Additional Notes on Possible Side Effects for Bevacizumab:

- Risk in children or adolescents: abnormal bone changes which may interfere with growth.
- Risk in pre-menopausal women: more likely to develop menopause when taking bevacizumab.

Bevacizumab is approved for human use against other cancers. It is considered an experimental drug when used in this study. Possible side effects of bevacizumab listed above are based on studies of bevacizumab in humans. These side effects may be a minor inconvenience or could be severe enough to be life threatening or fatal. In addition, there is always the risk that you could experience other presently unknown side effects. You will be watched closely for any side effects and if serious side effects occur the drug will be stopped and you will be treated appropriately.

Reproductive risks:

Because possible exposure to radiation can harm an unborn baby, you will need to inform your study doctor or research staff if you are pregnant or suspect that you may be pregnant. If you are pregnant, you will not be able to participate in this study. If you are unsure, you will need to have a negative pregnancy result per the usual standard of care prior to enrolling and/or prior to imaging in this trial.

You should not become pregnant while on this study because the drug(s) in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. **It is important you understand that if you could become pregnant, 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. If you are capable of becoming pregnant, a pregnancy test will be required before starting the study. You should notify your health care team immediately if you think you have become pregnant while participating 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 treatment with paclitaxel every week will be more useful against cancer compared to treatment with paclitaxel every 21 days, there is no proof of this yet. The information from this study 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 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.

WHAT ABOUT CONFIDENTIALITY?

Efforts will be made to keep your personal information confidential, and GOG procedures include removing your name and other identifying information from data collected during the Study, in order to protect your privacy. However, we cannot guarantee total confidentiality. Portions of your medical records will be sent to the Montana Cancer Consortium, GOG Administrative Office, the GOG Statistical and Data Center, and possibly to the GOG Tissue Bank and ACRIN headquarters, to be reviewed and analyzed by physicians and other Study personnel. Your records may be accessed by GOG representatives, by the Cancer Trials Support Unit (CTSU), a service sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials, and by the NCI for research, quality assurance, and data analysis purposes.

In addition, your records may be reviewed by the Food and Drug Administration (FDA), or other agencies of the Department of Health and Human Services (DHHS) for research or regulatory purposes. Also, information from the Study may be given to government agencies in other countries where the study drug may be considered for approval.

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.

Authorized representatives of the Pharmaceutical Collaborator, the manufacturer of bevacizumab, may also see your records.

Under NCI policy, data from this Study may be provided to another researcher at some future time for use in an approved research project. If this occurs, the researcher must agree to keep individual patient information confidential.

When the research results are published or discussed in conferences, no information will be included that reveals your identity. The National Institutes of Health (NIH) has issued GOG a Certificate of Confidentiality, which protects GOG 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.

WHAT ARE THE COSTS OF TAKING PART IN THIS STUDY?

You and/or your health plan/insurance company will need to pay for all of the costs of treating your cancer in this study, including the cost of managing the side effects of therapy. 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. You will be responsible for paying any deductibles, coinsurance, and co-payments as required under the terms of your insurance plan(s).

You will not be charged for any of the perfusion CT scans.

The NCI will supply the bevicizumab at no charge while you take part in this study. The NCI does not cover the cost of getting the bevacizumab ready and giving it to you, so you or your insurance company may have to pay for this.

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

- You might be able to get the bevacizumab from the manufacturer or your pharmacy but you or your insurance company may have to pay for it.

- If there is no bevacizumab available at all, no one will be able to get more and the study would close.

If a problem with getting bevacizumab occurs, you study doctor will talk to you about these options.

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.

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, if you feel that you have been injured because of taking part in this study. Contact information for your study doctor is listed on the consent cover page.

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.

No funds have been set aside to compensate you in the event of injury.

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.

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 information for your study doctor is listed on the consent cover page.

For questions about your rights while in this study, you may contact the Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

If you agree, you will be asked to have an additional perfusion scan at this time for a subset of patients. The purpose of the additional perfusion CT scan is to determine if the measurements of blood flow in your tumor was repeatable. You will have the additional scan approximately 15 minutes after the 2nd perfusion scan. You do not need to stay on the scanner during the waiting period.

- If you have the additional perfusion CT scan, you will receive another small dose of the X-Ray dye for your body weight. This additional perfusion CT scan will take about 25 minutes.

If selected, do you agree to have the additional reproducibility perfusion CT scan?

Yes No Patient initials _____

WHERE CAN I GET MORE INFORMATION?

You may call the National Cancer Institute's Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI Web site at http://cancer.gov/

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

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

Signature:

This study has been explained to me, and I have been told what my enrollment in the study involves. I have read all pages of this consent and have had my questions answered to my satisfaction at this time. I consent to participate in this study and any additional studies where I circled 'yes'. I understand that by signing this form I have not given up any of my legal rights. I will be given a copy of this consent form. I may also request a copy of the protocol (full study plan).

Participant Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)
(Required for initial consent only)