GOG 0213: A Phase III Randomized Controlled Clinical Trial of Carboplatin and Paclitaxel (or Gemcitabine) Alone or in Combination with Bevacizumab (NSC #704865, IND #7921) Followed By Bevacizumab and Secondary Cytoreductive Surgery in Platinum-Sensitive, Recurrent Ovarian, Peritoneal Primary, and Fallopian Tube Cancer

Fast Facts

Eligibility Criteria

1. Patients enrolled after August 7, 2011 must be candidates for cytoreductive surgery and consent to have their surgical treatment determined by randomization.
2. Patients with the following histologic epithelial cell types are eligible: Serous adenocarcinoma, endometrioid adenocarcinoma, mucinous adenocarcinoma, undifferentiated carcinoma, clear cell adenocarcinoma, mixed epithelial carcinoma, transitional cell carcinoma, malignant Brenner's Tumor, or adenocarcinoma not otherwise specified (N.O.S.).
3. Patients must have had a complete response to front-line platinum-taxane therapy (at least three cycles).
   - 3.1. A complete response to front-line chemotherapy must include: negative physical exam, negative pelvic exam, normalization of CA125, if elevated at baseline. Although not required, any radiographic assessment of disease status (e.g. CT, MRI, PET/CT etc) obtained following the completion of primary therapy (defined in section 3.133) should be considered negative for disease.
   - 3.2. All patients must also had a treatment-free interval without clinical evidence of progressive disease lasting at least 6 months from completion of front-line chemotherapy (both platinum and taxanes). Front-line therapy may have included a biologic agent (i.e. bevacizumab). .
   - 3.3. Front-line treatment may include maintenance therapy following complete clinical or pathological response. However, maintenance cytotoxic chemotherapy must be discontinued for a minimum of 6 months prior to documentation of recurrent disease. Patients receiving maintenance biological therapy or hormonal therapy are ELIGIBLE provided their recurrence is documented more than 6 months from primary cytotoxic chemotherapy completion (includes maintenance chemotherapy) AND a minimum 4 weeks has elapsed since their last infusion of biological therapy.
4. Patients must have clinically evident recurrent disease.
   - 4.1. *Measurable disease* (RECIST) is defined as at least one lesion that can be accurately measured in at least one dimension (longest dimension to be recorded). Each lesion must be more than or equal to 20 rnm when measured by conventional techniques, MRI or CT, or more than or equal to 10 mm when measured by spiral CT.
5. Patients must have adequate:
   - 5.1. Bone marrow function: Absolute neutrophil count (ANC) greater than or equal to 1,500/mm^3, equivalent to Common Toxicity Criteria for Adverse Events v3.0 (CTCAE) Grade1.
   - 5.2. Platelets greater than or equal to 100,000/mm^3. (CTCAE Grade 0-1).
   - 5.3. Renal function: Creatinine (non-IDMS) ≤ 1.5 ULN, CTCAE Grade 1
   - 5.4. Hepatic function:
     - 5.4.1. Total bilirubin ≤ 1.5 ULN (CTCAE Grade 1).
     - 5.4.2. SGOT/AST and Alkaline Phosphatase ≤ 2.5 times the upper limit of normal in the absence of liver metastasis. SGOT/AST and Alkaline Phosphatase <5.0 times ULN in the presence of liver metastasis.
   - 5.5. Patients must have a urine protein-to-creatinine ratio (UPCR) < 1.0mg/dL. The UPCR has been found to correlate directly with the amount of protein excreted in a 24 hr urine collection. Specifically, a UPCR of 1.0 is equivalent to 1.0 gram of protein in a 24-hour urine collection. Obtain at least 4 ml of a random urine sample in a sterile container (does not have to be a 24 hour urine). Send the sample to the lab with a request for urine protein and creatinine levels [separate requests]. The lab will measure protein concentration (mg/dL) and creatinine concentration (mg/dL). The UPCR is derived as: protein concentration (mg/dL) / creatinine concentration (mg/dL).
6. Patients must have met the pre-entry requirements specified in Section 7.0.

7. Patients must have signed an approved informed consent and authorization permitting release of personal health information.
8. Patients must have a GOG Performance Status of 0, 1, or 2.
9. Patients must be at least 18 years old.

Ineligibility Criteria

1. Patients who have received more than one previous regimen of chemotherapy (maintenance is not considered a second regimen).
2. Patients receiving concurrent immunotherapy, or radiotherapy.
3. Patients who have received prior radiotherapy to any portion of the abdominal cavity or pelvis are excluded.
4. Patients whom have already undergone secondary cytoreduction for recurrent disease are excluded.
5. Patients with a prior histologic diagnosis of borderline, low malignant potential (grade 0) epithelial carcinoma that was surgically resected and who subsequently developed an unrelated, new invasive epithelial ovarian or peritoneal primary cancer are eligible provided that they meet the criteria listed in Section 3.12.
6. Patients who require parenteral hydration or nutrition and have evidence of partial bowel obstruction or perforation.
7. Patients who have received prior chemotherapy for any abdominal or pelvic tumor (other than ovarian, fallopian tube, and primary peritoneal) are excluded.
8. Patients with synchronous primary endometrial cancer, or a past history of primary endometrial cancer, are excluded, unless all of the following conditions are met: Stage not greater than I-B; no more than superficial myometrial invasion, without vascular or lymphatic invasion; no poorly differentiated subtypes, including papillary serous, clear cell or other FIGO Grade 3 lesions.
9. Patients with uncontrolled infection.
10. Patients with concurrent severe medical problems unrelated to the malignancy that would significantly limit full compliance with the study or expose the patient to extreme risk or decreased life expectancy.
11. Patients with ≥ grade 2 peripheral neuropathy
12. Patients with a history of allergic reactions to carboplatin and/or paclitaxel or chemically similar compounds. Patients with allergic (hypersensitivity) reactions to these chemotherapeutic agents are **NOT** excluded **IF** they were successfully retreated following a desensitization program or protocol.
13. Patients with known hypersensitivity to Chinese hamster ovary cell products or other recombinant human or humanized antibodies.
14. Patients of childbearing potential, not practicing adequate contraception, patients who are pregnant or patients who are nursing are not eligible for this trial. To date, no fetal studies in animal or humans have been performed. The possibility of harm to a fetus is likely. Bevacizumab specifically inhibits VEGF, which is responsible for the formation of new blood vessels during development, and antibodies can cross the placenta. Therefore, bevacizumab should not be administered to pregnant women. In addition, there are unknown immediate and long-term consequences of chemotherapy administration to these women. In addition, surgical exploration as mandated by randomization during pregnancy may cause imminent mortal consequences. Further, it is not known whether bevacizumab is excreted in human milk. Because many drugs are excreted in human milk, bevacizumab should not be administered to nursing women. Subjects will be apprised of the large potential risk to a developing fetus.
15. Patients with other invasive malignancies, with the exception of non-melanoma Skin cancer, who had (or have) any evidence of the other cancer present within the last 5 years or whose previous cancer treatment contraindicates this protocol therapy.
16. Patients with active bleeding or pathologic conditions that carry high risk of bleeding such as a known bleeding disorder, coagulopathy, or tumor involving major vessels.
17. Patients with a history or evidence upon physical examination of CNS disease, including primary brain tumor, seizures not controlled with standard medical therapy, any brain metastases or a history of stroke within 5 years of the first date of treatment on this study.
18. Patients with clinically significant cardiovascular disease. This includes:
    - 18.1 Patients with significant cardiac conduction abnormalities, i.e. PR interval >0.24 sec or 2nd or 3rd degree AV block.

18.2 Uncontrolled hypertension, defined as systolic > 150 mm Hg or diastolic > 90 mm Hg.
18.3 Myocardial infarction, cardiac arrhythmia or unstable angina < 6 months prior to registration.
18.4 New York Heart Association (NYHA) Grade II or greater congestive heart failure.
18.5 Serious cardiac arrhythmia requiring medication.
18.6 Grade II or greater peripheral vascular disease (exception: episodes of ischemia <24 hrs. in duration, that are managed non-surgically and without permanent deficit).
18.7 History of CVA within six months.

19. Patients who have had a major surgical procedure, open biopsy, dental extractions or other dental surgery/procedure that results in an open wound, or significant traumatic injury within 28 days prior to the first date of treatment on this study, or anticipation of need for major surgical procedure during the course of the study; patients with placement of vascular access device or core biopsy within 7 days prior to the first date of treatment on this study.
    19.1 Patients undergoing pre-treatment secondary cytoreduction will undergo therapy with bevacizumab on cycle #2 (See Section 5.234).
    19.2 Patients undergoing pre-treatment surgery for purposes other than cytoreduction may also participate provided they meet eligibility in Section 3.1. Patients randomized to arms containing bevacizumab must wait a minimum 28 days since that procedure to begin protocol treatment. Patients who undergo an uncomplicated port placement must wait a minimum of 7 days to begin protocol treatment.
20. All patients must be informed of the investigational nature of this study and give written informed consent according to institutional and federal guidelines.

Pre-Study Parameters

1. H&P, Blood Pressure
2. CBC with differential, CMP including creatinine, bilirubin, AST, alkaline phospahtase, calcium, phosphate, magnesium
3. CA-125
4. PT/PTT/INR
5. UPC ratio
6. EKG
7. Audiogram (for patients with a history of hearing loss)
8. Radiographic tumor measurement – CT(with IV and oral contrast) or MRI (with gadolinium) of at least abdomen and pelvis to establish post-surgical baseline extent of residual disease. PET-CT imaging alone cannot be used to establish post-operative residuum unless also performed with CT or MRI as described.
9. CXR (not req'd if CT or MRI of chest already completed)
10. Incision check

Treatment

SCHEMA beginning 8/29/2011(08/29/11) (12/19/11) (10/01/12)