

Version 5/12/06

A Phase III Trial of Carboplatin and Paclitaxel Plus Placebo vs Carboplatin and Paclitaxel Plus Concurrent Bevacizumab Followed By Placebo, vs Carboplatin and Paclitaxel Plus Concurrent and Extended Bevacizumab, in Women with Newly Diagnosed, Previously Untreated, Stage III (Suboptimal), and All Stage IV, Epithelial Ovarian and Primary Peritoneal Cancer

Eligibility

- Patients must have histologic diagnosis of epithelial ovarian cancer or peritoneal primary carcinoma, FIGO stage III, with suboptimal (>1 cm maximal diameter any remaining lesion) residual disease, or FIGO stage IV following initial surgery and with appropriate tissue available for histologic evaluation (*see Section 3.11*).
- The following histological epithelial cell types are eligible: serous, endometrioid, mucinous or clear cell adenocarcinomas, undifferentiated, mixed epithelial, or transitional cell carcinomas, malignant Brenner's Tumor, or adenocarcinoma NOS.
- Patients must be entered between 1 and 12 weeks after initial surgery performed for the combined purpose of diagnosis, staging, and cytoreduction.
- Patients with measurable and non-measurable disease are eligible (*see Sections 8.11 and 8.12*). Patients may or may not have cancer-related symptoms.
- Patients must be 18 years of age or older; GOG Performance Status of 0, 1, or 2.
- Patients must **not** have a current diagnosis of borderline epithelial ovarian tumor (formerly LMP) or recurrent invasive epithelial ovarian cancer treated with surgery only (*see Section 3.21*).
- Patients must **not** have received prior RT to any portion of the abdominal cavity or pelvis. Prior RT for localized cancer of the breast, H&N, or skin is permitted as long as it ended > 3 years ago and the patient remains free of recurrent or metastatic disease.
- Patients must **not** have received prior chemotherapy for any abdominal or pelvic tumor. Prior adjuvant chemotherapy for breast cancer is permitted, as long as it ended > 3 years ago and the patient remains free of recurrent or metastatic disease.
- Patients must **not** have received any targeted therapy (including but not limited to vaccines, antibodies, TKIs) or hormonal therapy for their ovarian, peritoneal primary or fallopian tube carcinoma.
- Patient must **not** have received prior therapy with any anti-VEGF drug, including Bevacizumab.
- Patients must **not** have synchronous primary endometrial cancer, or a history of primary endometrial cancer unless a) stage ≤ I-B, b) no more than superficial myometrial invasion, without vascular or lymphatic invasion, and c) no poorly differentiated subtypes, including papillary serous, clear cell or other FIGO Grade 3 lesions.
- Except for non-melanoma skin cancer and other malignancies previously mentioned, patients must **not** have had evidence of other invasive malignancies within the past 5 years, or received treatment that contraindicates this protocol therapy.
- Patients must **not** have acute hepatitis or active infection that requires IV antibiotics.
- Patients must **not** have serious, non-healing wound, ulcer, or bone fracture (*see Section 3.28*).
- Patients must **not** have active bleeding or pathological conditions that carry high risk of bleeding.
- Patient must **not** have history or evidence of CNS disease, including primary brain tumor, uncontrolled seizures, brain mets, or history of CVA, TIA, or subarachnoid hemorrhage within 6 mos of study treatment.
- Patients must **not** have clinically significant cardiovascular disease (*see Section 3.31*).
- Patients must **not** have clinical symptoms or signs of GI obstruction *and* require parenteral nutrition and/or hydration.
- Patients must **not** have known hypersensitivity to Chinese hamster ovary cell products or other recombinant human or humanized antibodies.

THIS INFORMATION IS INTENDED TO BE USED AS A SCREENING TOOL ONLY AND SHOULD NOT BE USED IN PLACE OF THE PROTOCOL.

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Version 5/12/06

Eligibility, cont.

- Patients must **not** be pregnant or nursing; patients of childbearing potential must agree to use contraception during study therapy and for ≥ 6 months after completion of Bevacizumab therapy.
- Patients must **not** have had a major surgical procedure, open biopsy or significant traumatic injury within 28 days prior to Cycle 2; core biopsy within 7 days prior to Cycle 2; or be anticipating a major surgical procedure during the course of the study.

Schema

Arm I (standard chemotherapy)

Phase A Chemotherapy * day 1 every 21 days x 6 cycles
Placebo (for Bevacizumab) ** day 1 every 21 days beginning with cycle 2 x 5 cycles

Re-registration

Phase B Placebo (for Bevacizumab) ** day 1 every 21 days cycles 7 through 22 (06/26/06)

Arm II (concurrent bevacizumab)

Phase A Chemotherapy * day 1 every 21 days x 6 cycles
Bevacizumab ** day 1 every 21 days beginning with cycle 2 x 5 cycles

Re-registration

Phase B Placebo (for Bevacizumab) ** day 1 every 21 days cycles 7 through 22 (06/26/06)

Arm III (extended bevacizumab)

Phase A Chemotherapy * day 1 every 21 days x 6 cycles
Bevacizumab ** day 1 every 21 days beginning with cycle 2 x 5 cycles

Re-registration

Phase B Bevacizumab ** day 1 every 21 days cycles 7 through 22 (06/26/06)

*Paclitaxel 175mg/m² IV over 3 hours followed by Carboplatin AUC 6 IV over 30 minutes day 1 of cycles 1 through 6 only (Note: docetaxel 75mg/m² IV over 1 hour may be substituted for paclitaxel [see sections 2.65, 5.322, and 6.51])

**Bevacizumab / Placebo 15mg/kg IV day 1 of each cycle beginning with cycle 2

Required Laboratory / Tests

(Labs must be completed within 14 days prior to registration; Imaging and other studies within 28 days prior to registration)

- CBC, diff, BUN, Ca, PO4, Mg
- ANC ≥ 1,500/mm³
- Platelet count ≥ 100,000 /mm³
- Creatinine ≤ 1.5 x ULN
- SGOT, Alkaline Phosphatase ≤ 2.5 x ULN
- Bilirubin ≤ 1.5 x ULN
- PT/ INR ≤ 1.5 (or 2-3 if on stable dose of warfarin)
- PTT < 1.2 x ULN
- Urine Protein-Creatinine Ratio <1.0
- Serum CA-125 level within 28 days prior to initiating protocol therapy
- Serum pregnancy test if applicable
- Chest x-ray not necessary if chest CT or MRI done at baseline
- EKG
- Neurological function assessment ≤ CTCAE grade 1 neuropathy
- Audiogram if indicated by a history of hearing loss.
- CT or MRI for radiographic tumor measurement