

A Randomized Phase III Trial of Neoadjuvant Therapy in Patients with Palpable and Operable Breast Cancer Evaluating the Effect on Pathologic Complete Response (pCR) of Adding Capecitabine or Gemcitabine to Docetaxel when Administered Before AC with or without Bevacizumab and Correlative Science Studies Attempting to Identify Predictors of High Likelihood for pCR with Each of the Regimens

STUDY SUMMARY: This prospective, randomized Phase III clinical trial will evaluate three neoadjuvant chemotherapy regimens given with or without bevacizumab for women with palpable and operable HER2-negative breast cancer diagnosed by core needle biopsy. Patients will initially receive one of the following docetaxel-based regimens:

- Docetaxel (100 mg/m² Day 1) +/- bevacizumab (15 mg/kg IV Day 1) every 3 weeks for 4 cycles
- Docetaxel (75 mg/m² Day 1) + capecitabine (825 mg/m² po BID Days 1-14) +/- bevacizumab (15 mg/kg IV Day 1) every 3 weeks for 4 cycles
- Docetaxel (75 mg/m² Day 1) + gemcitabine (1000 mg/m² IV Days 1 and 8) +/- bevacizumab (15 mg/kg IV Day 1) every 3 weeks for 4 cycles

The docetaxel-based regimens will be followed by doxorubicin 60 mg/m² and cyclophosphamide 600 mg/m² (AC) every 3 weeks for 4 cycles with or without bevacizumab 15 mg/kg given only with the initial 2 cycles of AC. Treatment groups randomized to receive bevacizumab will resume bevacizumab postoperatively at 15 mg/kg every 3 weeks for an additional 10 doses.

Patients will have assessments of clinical response between the chemotherapy regimens and following neoadjuvant therapy (before surgery). Following completion of neoadjuvant therapy, patients will undergo lumpectomy or mastectomy and axillary staging with the choice of surgical procedure at the physician's discretion. Use of tissue expanders is permitted; however, expansion is prohibited throughout bevacizumab therapy, and for at least 6 weeks after the last dose of bevacizumab. Postoperative RT will be given at the physician's discretion except for prohibiting use of partial breast irradiation techniques utilizing brachytherapy. Choice of hormonal therapy for patients with hormone receptor-positive tumors will be at the physician's discretion.

Collection of 4 core needle biopsy specimens submitted in RNAlater[®], formalin, and shipping medium for Precision Therapeutics, Inc. is a pre-entry requirement. A tumor block from any gross residual disease ≥ 1.0 cm at surgery is also required. If no gross residual disease is found at surgery or gross residual disease is < 1.0 cm, no submission is required. For patients who have consented, blood and serum specimens will be collected at baseline, and serum will be collected at 2 time points during preoperative therapy.

To determine the impact of bevacizumab on cardiac function, all patients will have evaluation of LVEF by MUGA scans or echocardiograms at baseline and following preoperative chemotherapy. LVEF assessment at 18 months is required for patients randomized to receive bevacizumab.

STUDY AIMS: The primary aims are to determine whether the addition of capecitabine or gemcitabine to docetaxel followed by AC will increase the rate of pCR in the breast and to determine whether the addition of bevacizumab to the docetaxel/anthracycline based regimens will increase the rate of pCR relative to the same docetaxel/anthracycline-based regimens without bevacizumab.

Secondary aims include determination of whether pCR in the breast and axillary nodes, clinical overall response (cOR), clinical complete response (cCR), and disease-free survival can be improved by the regimens. Secondary aims include determination of whether the addition of bevacizumab will increase surgical complication rates, toxicity, and adverse effects on cardiac function. Additionally, secondary aims include identifying gene expression profiles that can predict pCR and cOR, as well as to test the accuracy of an in vitro chemoresponse assay (ChemoFx[®], Precision Therapeutics, Inc.) as a predictor of pCR and cOR.

NSABP sites should call 1-800-477-7227 for more information about participating in Protocol B-40.

Investigators not aligned with the NSABP can enroll patients through the NCI Cancer Trials Support Unit (CTSU).

