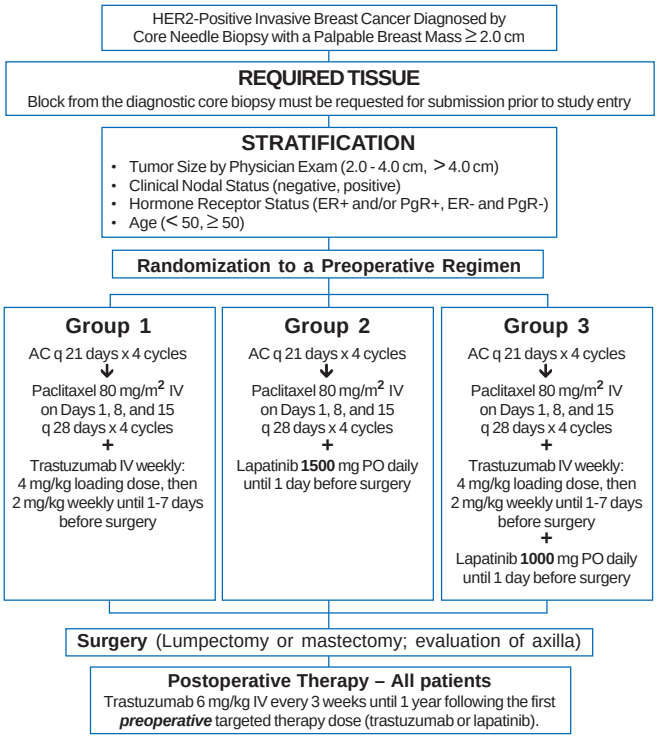
Open to Accrual: NSABP Protocol B-41

A Randomized Phase III Trial of Neoadjuvant Therapy for Patients with Palpable and Operable HER2-Positive Breast Cancer Comparing the Combination of Trastuzumab Plus Lapatinib to Trastuzumab and to Lapatinib Administered with Weekly Paclitaxel Following AC Accompanied by Correlative Science Studies to Identify Predictors of Pathologic Complete Response

STUDY SUMMARY: The neoadjuvant lapatinib trial is a Phase III randomized trial for women with palpable and operable HER2-positive breast cancer. All patients will receive standard doses of AC every 3 weeks for 4 cycles followed by weekly paclitaxel (80 mg/m^2 IV) on Days 1, 8, and 15 every 28 days for 4 cycles. Concurrently with paclitaxel, Group 1 patients will receive trastuzumab (2 mg/kg IV) weekly until surgery; Group 2 patients will receive lapatinib (1500 mg by mouth) daily until surgery; and Group 3 patients will receive trastuzumab (2 mg/kg IV) weekly plus lapatinib (1000 mg by mouth) daily until surgery.

Following completion of neoadjuvant therapy, patients will undergo lumpectomy or mastectomy. Axillary staging following neoadjuvant therapy will be required, but the choice of the procedure will be at the physician's discretion. All patients will receive postoperative trastuzumab (6 mg/kg) every 3 weeks continuing until 1 year after administration of the first preoperative targeted therapy (trastuzumab and/or lapatinib) dose.



Postoperative radiation therapy will be given at the physician's discretion with the exception of the use of partial breast irradiation techniques, which are prohibited. The type and duration of hormonal therapy for patients with hormone receptor-positive tumors will also be at the physician's discretion.

Pathology specimens will be collected and used to identify gene expression profiles that can predict pathologic complete response rates. Submission of a tumor block from the diagnostic core biopsy specimen is required for participation in B-41. Tumor block(s) from any gross residual disease ≥ 1.0 cm at the time of surgery is also required. For patients who have agreed, blood and serum specimens will be collected at baseline and serum will be collected after completion of chemotherapy (before surgery).

To monitor the cardiac function of patients receiving anti-HER2 therapy following AC, all patients will have evaluation of left ventricular ejection fraction by MUGA scans or echocardiograms performed at baseline, after the last dose of AC (before trastuzumab and/or lapatinib are initiated), after the last dose of paclitaxel (before surgery), and at 9 months following study entry.

STUDY AIMS: The primary aims of the study are to determine whether the regimen of AC→weekly paclitaxel (WP) plus trastuzumab and lapatinib yields a greater rate of pCR in the breast than the regimen of AC→WP plus trastuzumab and to determine whether the regimen of AC→WP plus lapatinib yields a greater rate of pCR in the breast than the regimen of AC→WP plus trastuzumab.

A secondary aim for this study is determining whether AC followed by WP plus trastuzumab and lapatinib yields a greater rate of pCR in the breast than AC followed by WP plus lapatinib. Secondary aims also include corresponding comparisons of rates of pCR in the breast and nodes; clinical overall response rates; clinical complete response rates; recurrence-free interval; overall survival; and evaluation of cardiac and non-cardiac toxicities of each treatment regimen.

Investigators interested in participating in Protocol B-41 should call 1-800-477-7227 for more information. Patients cannot be enrolled through the NCI Cancer Trials Support Unit (CTSU).