

Neoadjuvant therapy trial for HER2/neu positive breast cancer

by David Ota, MD, FACS; and Heidi Nelson, MD, FACS

An important scientific theme of the American College of Surgeons Oncology Group (ACOSOG) is prospective evaluation of neoadjuvant therapies for resectable solid tumors. Previous ACOSOG articles in the *Bulletin* this year have described neoadjuvant aromatase therapy for postmenopausal ER + stage II and III breast cancer (Z1031, which appeared in the June issue), and neoadjuvant chemoradiation therapy followed by local excision for T2 rectal cancers (Z6041, which appeared in the August issue). ACOSOG Z1041 was activated in July 2007 and adds to the list of neoadjuvant trials.

Surgeons play an important role in the decision making of whether to initially operate or to consider neoadjuvant therapy before resection. ACOSOG is positioned to conduct such trials because of its surgeon orientation. Z1041 is a phase III randomized trial comparing neoadjuvant anthracycline-based chemotherapy sequentially followed by trastuzumab versus anthracycline-based chemotherapy and concomitant trastuzumab for HER2/neu positive breast cancer. A single institution trial demonstrated that the neoadjuvant chemotherapy and concomitant

trastuzumab regimen can result in >60 percent pathologic complete response rate in the resected primary tumor specimen for HER2/neu positive breast cancers.*

The goal of ACOSOG Z1041 is to confirm these findings in a multisite phase III clinical trial and to assess the toxicity of the neoadjuvant regimen. The primary objective of this trial is to compare the pathologic complete response rate between the two treatment regimens. Eligibility criteria include the following: (1) diagnosis of invasive adenocarcinoma by core needle biopsy, (2) breast cancer must be ≥ 2 cm by palpation, (3) breast cancer must be HER2/neu positive determined by fluorescence in situ hybridization (FISH) assay or 3+ immunohistochemistry, (4) left ventricular ejection fraction measured by multiple gated acquisition scan ≥ 55 , and (5) M1 disease patients are excluded.

This particular neoadjuvant regimen is of interest to breast

*Buzdar AU, Theriault RL, Hunt KK, et al. Significantly higher pathologic complete remission rate after neoadjuvant therapy with trastuzumab, paclitaxel, and epirubicin chemotherapy: Results of a randomized trial in human epidermal growth factor receptor 2-positive operable breast cancer. *J Clin Oncol.* 2005;23:3676-3685.

cancer surgeons. Such a high pathologic, complete response rate would demonstrate the efficacy of this treatment to induce tumor regression before surgery. A high response rate would also lead to a significant increase in lumpectomy and successful breast conservation therapy for many of these patients.

Z1041 has been activated and is on the ACOSOG Web site. ACOSOG considers this a high-priority trial and we are actively recruiting sites, surgeons, and medical oncologists to participate in this trial. If you are an ACOSOG breast surgeon, we urge you to go to the ACOSOG Web site and review the protocol. If you have questions regarding ACOSOG membership, contact Helen Harbett at 919/668-8836 or harbe011@notes.duke.edu. If you have questions regarding the Z1041 trial, contact Rosita Hester at 919/668-8827 or rosita.hester@duke.edu. ACOSOG very much needs your active participation and enrollment of patients into this trial.

Dr. Ota and Dr. Nelson are ACOSOG co-chairs.