

# Lapatinib-paclitaxel combo shows promise in IBC

**M**ore than 75% of women with inflammatory breast cancer (IBC) have a clinical response when treated with lapatinib (Tykerb) followed by the combination of lapatinib and paclitaxel as neoadjuvant therapy, researchers from the M. D. Anderson Cancer Center in Houston reported. In addition, 17% of HER2/*neu*-positive patients do not have any evidence of residual tumor at the time of surgery.

Introducing the phase II trial, Massimo Cristofanilli, MD, said, "We are proud of this opportunity because this is the first multicenter, multinational clinical trial ever performed in patients with IBC testing a targeted therapy in this disease." Furthermore, he added, M. D. Anderson has just opened a clinic dedicated to IBC, allegedly the first one in the world.

Women with treatment-naïve IBC were divided into two cohorts. The 30 patients in cohort A had tumors overexpressing HER-2/*neu* (also called ErbB2), defined as 2+ or 3+; the 5 patients in cohort B had tumors that were positive for epidermal growth factor receptor (EGFR; also called ErbB1), defined as any positivity, but did not overexpress HER2/*neu*. After an initial biopsy, the patients were treated daily with lapatinib—an oral small molecule that is a dual inhibitor of the HER2 and EGFR tyrosine kinases—for 2 weeks. Following a second biopsy, they received treatment with both daily lapatinib and weekly paclitaxel for 12 weeks; then surgery; and finally adjuvant radiation therapy, chemotherapy, and hormonal therapy.

### PCR: a strong prognostic factor

With lapatinib monotherapy, the rate of clinical response (50% reduction in tumor size) was 30% in cohort A and 0% in cohort B; with neoadju-

vant therapy overall, the rate was 77% in cohort A and 80% in cohort B. At the time of surgery, the corresponding rates of pathologic complete response (PCR; the trial's primary endpoint) were 17% and 0% among evaluable patients; two of the three patients with this outcome had been among those with a clinical response to lapatinib monotherapy. For comparison, Dr. Cristofanilli added, the PCR rate achieved with standard anthracycline and taxane neoadjuvant chemotherapy is about 10%–15%.

"The PCR after completion of neoadjuvant chemotherapy is a very strong prognostic factor and the strongest that we know so far," he noted.

Preliminary safety data showed that the most common adverse effects of the combination neoadjuvant therapy rated as grade 3 or higher were diarrhea (60%), fatigue (20%),

and asthenia (20%). All patients but one were able to complete treatment with minimal dose reductions, and none of the patients died as a result of treatment.

The trial's findings, although preliminary, suggest that neoadjuvant lapatinib is active in HER2/*neu*-positive IBC and has predictable and manageable toxicity, Dr. Cristofanilli said. Moreover, high expression of IBC-related genes appears to predict a good response to this agent. "We strongly believe that these exciting preliminary data provide new hope for patients with IBC," he concluded.

Cristofanilli M. A phase II combination study of lapatinib and paclitaxel as a neoadjuvant therapy in patients with newly diagnosed inflammatory breast cancer (IBC). Paper presented at the 29<sup>th</sup> Annual Meeting of the San Antonio Breast Cancer Symposium; December 14–17, 2006; San Antonio, Tex. Abstract 1.