

Correlation of Oncotype DX Recurrence Scores with Pathologic Response following Neoadjuvant Ixabepilone and Cyclophosphamide in Patients with HER2-Negative Breast Cancer

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Background: Ixabepilone (Ixa) is active in taxane-refractory metastatic breast cancer as well as in the neoadjuvant setting where Ixa yielded a pathologic complete response (pCR) rate of 18%. In this study, we evaluated Ixa in combination with cyclophosphamide (Cyc) as neoadjuvant treatment for HER2-negative breast cancer. The primary endpoint was pathologic complete response (pCR) rate, defined as no residual cancer in breast or lymph nodes. Responses were correlated with Oncotype DX recurrence scores.

Methods: Eligible women had localized breast cancer that was HER2-negative (IHC 0-1+ or FISH negative), and node positive or T > 2 cm. Patients with inflammatory breast cancer or T1N0 tumors excluded. Patients (pts) received Ixa 40mg/m² with Cyc 600 mg/m² day 1 of each 21-day cycle. Following 6 cycles, pts went to surgery. Postoperative radiation and hormonal treatments were at discretion of the treating MD. Core biopsies (pretreatment and at surgery) were analyzed using the Oncotype DX RT-PCR assay; the associations between recurrence scores and clinical responses were investigated in an interim analysis.

Results: 168 women have been enrolled. Baseline characteristics for the first 118 pts are reported (median age 52 years; 90% invasive ductal; 52%/31% T2/T3; 42% triple negative). 81 pts have undergone surgery. 25 pts discontinued treatment early (toxicity – 12; disease progression – 8; pt/MD request – 3; patient non-compliance - 2). Grade 3/4 toxicity included: neutropenia (65%), leukopenia (47%), neuropathy (10%), and febrile neutropenia (7%). Toxicity results with this neoadjuvant treatment have been previously reported (Peacock et al, ASCO 2011 Abstract #81825). The pCR rate was 19%. Oncotype DX evaluations were conducted on 38 patients with paired biopsy specimens; a logistic regression of recurrence score on pCR

demonstrated a significant correlation ($p = 0.025$). There was no evidence that recurrence scores predicted clinical response.

Conclusions: Neoadjuvant therapy with Ixa and cyclophosphamide produces a pCR rate of 19%, similar to results with other 2-drug combination chemotherapy regimens. The interim results of the Oncotype DX assessments indicate that recurrence scores may predict pCR with this regimen. Updated results, including the final results of the Oncotype DX recurrence scores, will be presented.