Ixabepilone and cyclophosphamide as neoadjuvant therapy in HER2-negative breast cancer with exploratory Oncotype DX assessments: A Sarah Cannon Research Institute phase II trial.

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Abstract Disclosures

Abstract:

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 were HER2-negative (IHC 0-1+ or FISH negative), node positive or T > 2 cm with inflammatory and 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: 156 women have been enrolled. Baseline characteristics for the first 78 pts are reported (median age 52 years; 86% invasive ductal; 50%/33% T2/T3; 41% triple negative). 50 pts have undergone surgery. 14 pts discontinued treatment early (disease progression – 6; pt/MD request – 5; toxicity – 3). Grade 3/4 toxicity
included: neutropenia (69%), leukopenia (51%), neuropathy (9%), and febrile neutropenia (6%). The pCR rate was 18%. Higher pretreatment recurrence scores (>31) were associated with higher pCR rate (p=0.025) in 38 patients with available data. Non-significant trends were observed for ER and PR by RT-PCR, but not for HER2. None of these measures were predictive of clinical tumor responses after 3 or 6 cycles of therapy, although assessment methods varied across timepoints.

**Conclusions:** Ixabepilone with cyclophosphamide as neoadjuvant therapy is feasible and active. Tumors with higher Oncotype DX recurrence scores at baseline were more likely to achieve pCR.