High Pathologic Complete Response (pCR) in Her2-positive Breast cancer to Novel Non-anthracycline Neoadjuvant Chemotherapy

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Abstract

Background: The addition of trastuzumab to preoperative chemotherapy for Her2-positive breast cancers has been shown to increase pCR rates. The purpose of this study was to evaluate the efficacy of trastuzumab in combination with dose-dense nab-paclitaxel followed by weekly vinorelbine.

Methods: Patients with Stage I (>1.0 cm), II, or IIA Her2-positive (defined as either immunohistochemical 3+ or fluorescence in situ hybridization-positive) breast cancer received nab-paclitaxel 260 mg/m² iv every 2 weeks for 4 cycles in combination followed by vinorelbine 25 mg/m² iv weekly with simultaneous trastuzumab (4 mg/kg loading dose then 2 mg/kg weekly) for 20 weeks. Tissue was collected at baseline, at optional midway biopsy, and post-therapy. Primary endpoint was pCR rate; secondary endpoints included response rate and toxicity. Cardiac evaluation was performed at baseline, after 4 cycles of nab-paclitaxel, after 12 weeks of vinorelbine and every 3 months thereafter.

Results: To date, 21 of 50 planned patients have been accrued (3/2008 to 12/2009). 11 patients are evaluable for primary endpoint. Median age was 50.5 years (38-64). Median tumor size was 3.7 cm (1.5-7.0). 4 of 11 (36.4%) were clinically node-positive at study entry. Patients were accrued from a university center (45.5%), community hospital (18.2%), and community sites (27.3%). 4 patients were African American (36.4%), 7 were Caucasian (63.6%). The regimen was well-tolerated. 2 patients experienced grade 3 neuropathy, 1 patient grade 3 neutropenia, 1 patient had trastuzumab held for asymptomatic decrease in left ventricular ejection fraction. Median complete response rate was 72%. Partial response rate was 27.3%. Of 11 patients (80%) had pCR.

Conclusion: The combination of preoperative trastuzumab with dose-dense nab-paclitaxel followed by vinorelbine was well-tolerated and resulted in a high rate of pCR in Her2-positive breast cancer.

Methods

Primary Objective
- Pathologic complete response rate (pCR) in the breast and axilla at the time of surgery

Secondary Objectives
- Clinical response rate
- Safety profile
- Correlative studies (ER, PR, HER2/neu, EGFR)

Eligibility Criteria
- Histologically confirmed invasive breast cancer
- HER2/neu 3+ by IHC or positive by FISH
- T1c-T3, N0-2 (Stage I-IIIA)
- ECOG performance status of 0 to 1
- Measurable disease by either breast imaging or physical exam
- No prior chemotherapy, radiation therapy, or hormonal therapy for breast cancer for breast cancer is not allowed
- Age >18 years
- Adequate renal, hepatic, and hematologic function
- Left ventricular ejection fraction greater than 50% as measured by MUGA or echocardiogram
- Peripheral neuropathy above grade 1 is not allowed

Treatment Plan
- Patients received nab-paclitaxel 260 mg/m² iv over 30 minutes every 14 days for 4 cycles followed by vinorelbine 25 mg/m² iv weekly with simultaneous trastuzumab (4 mg/kg loading dose then 2 mg/kg weekly) for 20 weeks
- Tissue was collected at baseline, optional midway biopsy, and at the time of surgery

Response (n=21)
- Complete Response 16 (72.7%)
- Partial Response 5 (27.3%)
- Stable Disease 0 (0%)
- pCR 11 (52.4%)

Conclusions
- The combination of trastuzumab with dose-dense nab-paclitaxel is well tolerated. Main toxicities observed were fatigue and neuropathy. Two patients had trastuzumab held for asymptomatic drop in ejection fraction.
- pCR rate of 52.4% is higher than previously reported with non-anthracycline based chemotherapy in combination with trastuzumab.
- Additional evaluation of residual cancer burden planned.

References


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