BRCA1 and EGFR as prognostic biomarkers in triple negative metastatic breast cancer patients treated with cisplatin plus docetaxel

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Abstract

Background: The triple negative (TN) metastatic breast cancer (MBC) patients are known to have worse prognosis, shorter progressive free survival (PFS), and overall survival (OS), that mandates using aggressive chemotherapy regimens.

Aim: This phase II study aimed at investigating the efficacy and safety of using Cisplatin and Docetaxel in patients with triple negative metastatic breast cancer, and the possibility of using breast cancer susceptibility gene1 (BRCA1) expression as a predictive marker of chemotherapy response, and epidermal growth factor receptor (EGFR) as prognostic marker.

Patients and Method: Between January 2006 and March 2009, 40 eligible patients with TN MBC were included in the study; we examined BRCA1 expression and EGFR protein in their specimens using immunohistochemistry. The patients were treated with cisplatin 75 mg/m2 and docetaxel 75 mg/m2 every 3 weeks, TN measurable MBC patients previously treated with anthracycline in their adjuvant or neo adjuvant settings were included in the study.

Results: The median age of the treated patients was 43.5 years. Nearly half of the patients had an ECOG performance status of 0 or 1, and about third of them had one metastatic site. These metastatic sites were predominantly visceral in 80% of the patients. Fifty five percent of TNMBC stained positive for BRCA1 and sixty five percent for EGFR. Positivity for both markers was significantly associated with grade III tumors *(p=0 .004)*, OS, and PFS *(p= 0.001 and 0.009)* respectively. Overall, the regimen was well tolerated as GIII vomiting and neurological side effects were observed in 20% of the patients. Other toxicities were generally mild and medically manageable; with no treatment mortality was recorded. The overall disease control rate (ODCR) was 60 %; the median PFS was 8 months, with a median overall OS of 17.5 months; while the median OS among responders was 23 months (95% CI 21.35 to 25.32). The patients with negative EGFR had a significantly better OR, PFS, and OS than EGFR positive cases. There was no significant difference concerning OR, PFS, and OS, between positive and negative BRCA1 cases, which could be attributed to the better efficacy of cisplatin in the positive BRCA1 cases.

Conclusion: This chemotherapy regimen is effective with tolerable toxicity profile, our results point out the importance of BRCA1 expression as predictive marker of chemotherapy response, and EGFR as prognostic marker, which could identify a certain group of patients with more aggressive disease who might benefit from using anti EGFR targeted therapy plus cisplatin.