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ORIGINAL RESEARCH REPORT

Evaluation of weekly paclitaxel plus carboplatin followed by anthracycline chemotherapy on the neoadjuvant treatment of patients with triple-negative breast cancer

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KEYWORDS
Triple negative breast cancer;
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Abstract
Objective: To evaluate the effectiveness and tolerability of neoadjuvant chemotherapy with weekly paclitaxel in combination with weekly carboplatin area under curve 2 followed by anthracycline chemotherapy.
Patients and methods: This is a retrospective review of electronic medical records of patients ($N = 32$) with stage 1c—III triple-negative breast cancer. Patients received neoadjuvant chemotherapy with paclitaxel 80 mg/m^2 once per week for 12 weeks in combination with carboplatin area under curve 2 once per week for 12 weeks (wP + wCb), followed by a standard anthracycline regimen including either doxorubicin 60 mg/m^2 and cyclophosphamide 600 mg/m^2 every 2 or 3 weeks, or epirubicin 90 mg/m^2 and cyclophosphamide 600 mg/m^2 every 3 weeks for four cycles with myeloid growth factor support.
Results: Most patients (91%) received all 12 cycles of wP + wCb, and 88% received all four planned cycles of anthracycline chemotherapy. Of the patients, 84% completed all planned

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therapies. The complete pathologic response rate was 60%. In terms of hematologic toxicity, 96% of the patients experienced grade ≥3 leucopenia, 40% grade ≥3 anemia, and 15% grade ≥3 thrombocytopenia, and neutropenic fever was seen in 22% of the patients.

Conclusion: The combination of neoadjuvant chemotherapy with wP + wCb before anthracycline chemotherapy can be tolerated by patients with triple-negative breast cancer. Complete pathologic response rates were comparable with those historically seen. Careful selection of patients is fundamental as this regimen is associated with a high incidence of hematologic toxicity.

Introduction

Triple-negative breast cancer (TNBC) accounts for approximately 20% of breast cancers diagnosed worldwide, representing almost 200,000 cases each year [1]. The disease affects more commonly women younger than 40 years of age [2]. When compared with the other breast cancer subtypes, patients are also at a higher risk of developing brain or visceral metastasis [3]. In addition, it appears to be more common among black women compared with white women and is associated with the BRCA1 genetic mutation [4]. TNBC is characterized by the absence of expression of the estrogen receptor, progesterone receptor, and lack of amplification of the human epidermal growth factor receptor 2 (*HER2*)/*Neu* gene [5]. Pathologic complete response (pCR) rates to neoadjuvant chemotherapy (NACT) among patients with TNBC range from 27% to 45%, while the pCR rate for patients with HER2-negative/hormone receptor-positive breast cancer is generally around 10—20% [6]. However, while patients with the TNBC who achieve a pCR appear to have good event-free survival, those with TNBC who have more than minimal residual disease at surgery have a much higher risk of early distant disease recurrence [7,8] Results from previous studies indicate that the addition of carboplatin (Cb) to standard neoadjuvant anthracycline—taxane chemotherapy results in an increase in pCR [9,10]. One of the investigational arms of the randomized phase II Cancer and Leukemia Group B (CALGB40603) clinical trial tested paclitaxel 80 mg/m^2 once a week (wP) for 12 weeks with concurrent Cb area under curve (AUC) 6 once every 3 weeks for four cycles, followed by doxorubicin plus cyclophosphamide once every 2 weeks for four cycles. Although effective, this regimen has been difficult to reproduce in daily practice. The purpose of this study was to evaluate the effectiveness and tolerability of weekly paclitaxel in combination with weekly carboplatin (wP + wCb) AUC 2 followed by anthracycline chemotherapy.

Patients and methods

The electronic medical record system was used to identify female patients ≥18 years of age, treated between January 1, 2014 and July 1, 2016, who had operable, biopsy-confirmed, previously untreated breast cancer with a palpable size of >2 cm or a sonographical size of >1 cm in maximum diameter, with estrogen receptor and progesterone receptor expression of 0% and HER2 negativity, defined by immunohistochemical (IHC) staining 0—1+ or fluorescence in situ hybridization ratio <2.0 for IHC 2+ or IHC not performed. Adequate hematologic, renal, and hepatic function, and normal cardiac function by echocardiogram or radionuclide ventriculogram were required. Patients must have received NACT with paclitaxel 80 mg/m^2 once per week for 12 weeks in combination with Cb AUC 2 once per week for 12 weeks, followed by a standard anthracycline regimen including either doxorubicin 60 mg/m^2 and cyclophosphamide 600 mg/m^2 every 2 or 3 weeks, or epirubicin 90 mg/m^2 and cyclophosphamide 600 mg/m^2 every 3 weeks for four cycles with myeloid growth factor support (granulocyte colony stimulating factor [G-CSF]).

The primary outcome was to evaluate the tolerability of fractionating Cb to weekly infusions in combination with weekly paclitaxel. The secondary outcomes included pCR rate, number of cycles received in each chemotherapy regimen, and frequency of hematologic toxicities.

Pathologic evaluation

Pathologic response was determined locally. The pCR was defined as the absence of residual invasive disease in the breast or sampled axillary lymph nodes (ypT0/is ypN0) and an MD Anderson residual cancer burden index score of zero (RCB 0).

Table 1 Stage, BRCA status and KI 67.

	% of patients
KI 67 > 75%	62
KI 67 50—75%	25
KI 67 < 50 %	3
N A	9
Stage I	6
Stage II	53
Stage III	41
BRCA 1/2	12

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