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Phase II study of neoadjuvant chemotherapy including a metronomic regimen of paclitaxel + cyclophosphamide + capecitabine followed by 5-fluorouracil + epirubicin + cyclophosphamide in patients with operable triple-negative breast cancer (JBCRG-13 study)

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Background: Triple-negative breast cancer (TNBC) is generally associated with a poor prognosis. Combination therapy with anthracyclines and taxanes is widely used as preoperative systemic chemotherapy (PST), but the pathological complete response (pCR) rate in TNBC patients receiving this regimen is ≤50%. We conducted metronomic PST in TNBC patients, which is expected to be more effective than other therapies with regard to exerting anti-angiogenic effects without increasing adverse events. The paclitaxel + cyclophosphamide + capecitabine (PCX) regimen was created to generate a PST with expected synergistic interaction among these three drugs.

Methods: Primary breast cancer patients (T1C-3N0M0 or T1-3N1M0) with low ER expression (<10%) diagnosed with either a triple-negative or HER2-negative invasive tumor. Patients received 4 cycles of a metronomic PCX regimen followed by 4 cycles of 5-fluorouracil (500 mg/m^2, q3w) + epirubicin (100 mg/m^2, q3w) + cyclophosphamide (500 mg/m^2, q3w) (FEC regimen). The metronomic PCX regimen includes weekly administration of paclitaxel (80 mg/m^2; Days 1, 8, 15), cyclophosphamide (50 mg/body; po, days 1-21) and capecitabine (1200 mg/m^2; po, daily), with one cycle set to 21 days. The primary endpoint was pCR rate, and secondary endpoints included overall response rate, safety, breast conservation rate, and overall and disease-free survival.

Results: Between March 2010 and September 2011, 41 patients were enrolled and 40 patients were treated the regimen. Characteristics of the 40 pts (ITT population) were; median age of 52 (range, 33-69), median tumor size of 23.7 mm (range, 3.5-82), 16 pts with N(+) (40%) and 7 estrogen receptor weakly positive (ER;1-9%) pts (17.5%). The median dose intensity was 89.7%, 92.1% and 89.8% with paclitaxel, cyclophosphamide and capecitabine, respectively. Five pts had discontinued the PST during the PCX course and 2 pts during the FEC regimen. Per protocol population was 33 pts because of the discontinuation of PST in 5 and 2 pts during the each PCX and FEC course due to pts' wish mainly according to the adverse events. The pCR (ypT0/Tis ypN0) rate was 54.5%(18/33). 22 pts had achieved CR, and the ORR was 93.9%(95% CI, 79.8-99.3) assessed by MRI or CT. The breast conservation rate was 72.7% (24/33), 5 out of 13 pts had been successful in conversion to partial resection from the pre-planned total mastectomy. The most frequent grade 3-4 adverse events with metronomic PCX followed by FEC were neutropenia (35%), febrile neutronpenia (25%), and Leucopenia (25%), and hand-foot syndrome (7.5%). There was no SAE report, almost all pts had completed the treatment in the outpatients clinic.

Conclusions:

The metronomic PCX followed by FEC provided high pCR rate and was manageable as PST in patients with TNBC in trouble in cure. The findings warrant further studies in larger series of this regimen. (UMIN000003570)