A Randomized, Double Blind, Placebo-Controlled Study Evaluating Efficacy of Combination Olanzapine, Ondansetron and Dexamethasone for Prevention of Chemotherapy-Induced Nausea and Vomiting in Patients Receiving Doxorubicin plus Cyclophosphamide

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Objective: To evaluate efficacy of olanzapine with real-life practice antiemetic drugs; ondansetron and dexamethasone, for CINV prevention from doxorubicin plus cyclophosphamide regimen in early stage breast cancer patients.

Method: In a randomized, double-blind, placebo-controlled trial, we compared olanzapine with placebo in combination with ondansetron and dexamethasone, in early stage breast cancer patients receiving doxorubicin plus cyclophosphamide. The patients received olanzapine 10 mg orally or matching placebo on day 1 through day 4. All patients received ondansetron 8 mg and dexamethasone 20 mg intravenously 30 minutes before chemotherapy administration then dexamethasone 10 mg daily per oral from day 1 though day 4. The primary end point was no nausea rate in the early period. The secondary end points were no nausea rate in the delayed and overall period and a complete response (no vomiting and no use of rescue drug). Outcomes were determined by self-reported daily records of episodes of vomiting or retching, use of rescue therapy and daily levels of nausea according to a visual-analogue scale from the first cycle of chemotherapy.

Results: Total 39 patients were randomized in 1:1 ratio to receive olanzapine (20 patients) and matching placebo (19 patients). There were significantly greater proportions of patients without nausea in the olanzapine group (50%) than the placebo group (10.5%) in both early and overall periods (P=0.008). In the overall period, there were 30.0% and 0% of patients without nausea in the olanzapine and the placebo groups, respectively (P=0.009). In the early period, there was significantly more complete response rate in the olanzapine group (75.0%) than the placebo group (36.8%) (P=0.016). Overall treatment-related adverse events were not different, except somnolence was more common in the olanzapine group.

Conclusions: Olanzapine 10 mg combined with ondansetron and dexamethasone was more effective than placebo for CINV prevention from doxorubicin plus cyclophosphamide in early stage breast cancer patients, especially in the first 24 hours after chemotherapy administration. The short duration of olanzapine was safe and well tolerated.