Abstract

An interim analysis of double-blind placebo control trial study comparing standard 3-drugs; ondansetron, dexamethasone and olanzapine to netupitant-containing regimen for preventing high-dose cisplatin induced nausea and vomiting

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Background: Prevention of chemotherapy-induced nausea and vomiting (CINV) is an important in cancer treatment. Here, we compared the efficacy of netupitant-containing regimen; composed of NEPA (netupitant, palonosetron), dexamethasone and olanzapine (NEPAs) which is recommended for prevention CINV from high-emetogenic chemotherapy (HEC) to in-house standard 3-drugs combination regimen; ondansetron, dexamethasone, olanzapine for preventing CINV from high-dose cisplatin (>75 mg/m2).

Methods: The randomized, double-blind, placebo-control trial, we randomly assigned chemotherapy-naive patients who receiving high-dose cisplatin in 1:1 ratio to receive either NEPAs or in-house standard 3-drugs combination regimen. The stratification factors including concurrent with radiation and sex. The primary endpoint was complete response (CR) rate defined as no vomiting and no use of rescue drugs. The protocol allowed crossover to NEPAs for whom received in-house standard 3 drugs and do not reach CR in the first cycle. This trial was registered with clinicaltrials.in.th, number TCTR20190508001.

Results: Between January 2019, and December 15, 2019, 48 eligible patients were randomly assigned to NEPAs (n = 24) and in-house standard 3-drugs (n = 25) treatment groups. Demographic characteristics were well-balance in both arm; female 25% vs. 29%, concurrent with radiation 79% vs. 79% in NEPAs and standard 3-drug respectively. On first treatment cycle, CR rate was 75% in NEPAs and 91% in standard 3-drugs (Chi-square p-value 0.058). According to emesis phase, CR in acute (0- 24 hrs.) and delay phase (24-120 hrs.) were 91% vs. 100% (Chi-square p-value 0.091) and 75% vs. 91% (Chi-square p-value 0.114) in NEPAs and standard 3-drugs respectively. Subgroup analysis for patients who received CCRT with high-dose cisplatin shown similar efficacy as ITT population, overall CR were 75% vs. 89% (Chi-square p-value 0.370). Nausea and sleepiness VAS were similar between groups. There were 3 patients who had grade 3/4 acute renal injuries after first-cycle of chemotherapy, 3 patients in NEPAs and 1 patient in in-house standard arm. The mean QT interval change did not different between two groups (+6.80 ms vs +9.40 ms, p-value=0.628).

Conclusions: Preliminary analysis shown NEPA containing regimen didn't shown superiority than in-house standard 3 drugs in term of efficacy for high-dose cisplatin CINV prevention.