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Olanzapine, an alternative to dexamethasone for preventing nausea and vomiting induced by cisplatin-based doublet highly emetogenic chemotherapy: A non-inferiority, prospective, multi-centered, randomized, controlled, phase III clinical trial

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Background

Chemotherapy induced nausea and vomitting (CINV) is associated with significant deterioration in quality of life. The standard antiemetic therapy for highly emetogenic chemotherapy are combination therapies, and dexamethasone is a necessary component. However, dexamethasone has diverse side effects and it may not be an appropriate antiemetic for use in immunotherapy. Guidelines recommend using olanzapine (10mg) in preventing CINV, but excessive sedation was reported. A trail reported that lower dose olanzapine (5mg) was effective in control of CINV and had less serious sedation events. We initiated this trial to validate whether olanzapine (5mg) could be a non-inferiority alternative of dexamethasone in the triplet antiemetic combination therapy.

Methods

The predicted sample size in this trial (NCT04437017) is 548 (power=80%, α=0.05, non-inferiority margin=10%). Eligible patients are randomized in a 1: 1 ratio into two groups to receive olanzapine or dexamethasone plus a 5-HT3 receptor antagonist (5-HT3 RA) and a NK-1 receptor antagonist (NK-1 RA). The primary endpoint is 0–120 h complete response (CR) rate, and the secondary endpoints are 25–120 h CR rate and 0–120 h no nausea rate. The endpoints and side effects will be recorded after the initiation of chemotherapy for 5 days.

Results

Patients in the olanzapine group achieved a 0–120 h CR rate (83.6% v.s. 84.9%, difference [one-sided 95% CI]: 1.2% [-∞, 6.4%], $P_{noninferiority}$ = 0.003), 25–120 h CR rate (85.5% v.s. 85.6%, difference [one-sided 95% CI]: 0.1% [-∞, 5.1%], $P_{noninferiority}$ = 0.024) and 0–120 h no nausea rate (38.7% v.s. 39.9%, difference [one-sided 95% CI]: 1.2% [-∞, 8.1%], $P_{noninferiority}$ = 0.001) non-inferior to that in patients in the olanzapine group. Moreover, side effects such as constipation (P = 0.045), hiccups (P < 0.001) as well as insomnia (P < 0.001) were more frequent in patients receiving dexamethasone than in those receiving olanzapine.

Conclusions

Olanzapine (5mg) could be a non-inferiority alternative of dexamethasone in the triplet combination anti-emetic therapy and has less side effects than dexamethasone.

Legal entity responsible for the study

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Disclosure

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