Granisetron transdermal delivery system is effective in the control of chemotherapy-induced nausea and vomiting in patients receiving moderately emetogenic chemotherapy (MEC) or highly emetogenic chemotherapy (HEC) in China

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Chemotherapy-induced nausea and vomiting (CINV) remains the major adverse effect of cancer treatment which impairs patients' quality of life and affects their compliance with further treatment (1,2). The pivotal role of 5-hydroxytryptamine 3 (5-HT3) in the process of emesis has been well established (3). The development of 5-hydroxytryptamine 3 receptor antagonists (5-HT3RAs) is a significant advance in the CINV control over the past 3 decades (4). However, the application of 5-HT3RAs to the management of CINV associated with multiday chemotherapy presents challenges (5,6). Repeated administration of 5-HT3RAs over several days will result in unstable blood drug concentration. Furthermore, such inconvenient dosing regimen may have negative impact on patients' compliance with treatment. Therefore, granisetron transdermal delivery system (GTDS; Sancuso®, ProStrakan, Inc., USA) which containing 34.3 mg of granisetron and can continuously release granisetron through the skin over 7 days may be valuable for patients receiving multi-day chemotherapy (7). As such, Liu-Qing Yang and colleagues conducted a randomized, double-blind, phase III study to compare the efficacy and tolerability of the GTDS with those of oral granisetron in Chinese patients receiving moderately emetogenic chemotherapy (MEC) or highly emetogenic chemotherapy (HEC).

The primary endpoint was percentage of complete control (CC; no vomiting, no more than mild nausea, and no need for rescue medication) from the first administration until 24 hours after the last administration of chemotherapy. The study found that the CC rate was comparable between the GTDS group and the oral granisetron group in the per protocol population (47.52% *vs.* 59.29%, P=0.0559). The toxicity profile of GTDS was favorable, with all the adverse events categorized as mild to moderate. The most common study drug-related adverse event in both groups was constipation, which was more frequent in oral granisetron group (7.64% *vs.* 9.62%). Thus, GTDS was effective and well-tolerated for the management of CINV in Chinese patients. Two previous large randomized studies also evaluated the efficacy of GTDS in the prevention of CINV. The Boccia study, in which 641 patients receiving moderately or highly emetogenic multi-day chemotherapy were randomized to oral granisetron or GTDS, found that GTDS was non-inferior to oral granisetron: CC rate was 60% in the GTDS group and 65% in the oral granisetron group (8). Another study conducted in Korea also showed that GTDS had non-inferior efficacy to intravenous and oral granisetron in CINV control (9). In summary, there was enough evidence

to support the application of GTDS to the management of CINV associated with multiday chemotherapy.

Notably, according to the subgroup analysis of the present study, the effectiveness of GTDS was unsatisfactory in female patients or patients receiving cisplatin-containing chemotherapy. Currently, the standard regimen for prevention of emesis induced by highly emetogenic chemotherapy is the combination of 5-HT3RAs, neurokinin-1 (NK-1) receptor antagonists and dexamethasone. For patients with risk factors for substantial CINV (female sex, younger age, propensity for motion sickness, abstinence from alcohol, prior adverse experience with chemotherapy), the addition of Olanzapine to the standard antiemetic regimen is suggested by some experts. Therefore, GTDS should be used in combination with other proper antiemetic agents according to the emetogenicity of the chemotherapy regimens as well as the risk factors of the patients.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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