

This material is protected by U.S. copyright law. Unauthorized reproduction is prohibited.
To purchase quantity reprints or request permission to reproduce multiple copies, please e-mail reprints@ons.org.

The Next Generation of Chemotherapy-Induced Nausea and Vomiting Prevention and Control: A New 5-HT₃ Antagonist Arrives

Cynthia N. Rittenberg, RN, MN, AOCN®

Dramatic improvement in the control of chemotherapy-induced nausea and vomiting (CINV) came with the understanding of the role of 5-hydroxytryptamine, sub-type 3 (5-HT₃), or serotonin neurotransmitters. In the 1990s, three first-generation serotonin receptor antagonists became available in oral and IV formulations and revolutionized control of emesis, including improved control of emesis experienced by patients receiving chemotherapy that is highly emetogenic. Antiemetic guidelines published beginning in 1997 emphasize the importance of 5-HT₃ receptor antagonists (in combination with a corticosteroid) as a cornerstone in preventing acute nausea and vomiting and as helpful in preventing emesis occurring after the first 24 hours following initiation of highly and moderately emetogenic chemotherapy (MEC) (“American Society of Health-System Pharmacists,” 1999; Gandara et al., 1998; Gralla et al., 1999; Hesketh, Gralla, du Bois, & Tonato, 1998; Kris, Roila, De Mulder, & Marty, 1998; “National Comprehensive Cancer Network,” 1997).

The next advance in the quest to control CINV occurred in 2003. In March 2003, the U.S. Food and Drug Administration (FDA) approved the use of aprepitant (Emend®, Merck & Co., Inc., Whitehouse Station, NJ) in combination with other antiemetic agents for the prevention of acute and delayed nausea and vomiting associated with initial and repeated courses of highly emetogenic chemotherapy (HEC), including high-dose cisplatin. Aprepitant represents a new class of antiemetic agents. It is a potent, selective,

First-generation serotonin receptor antagonists greatly improved the control of chemotherapy-induced nausea and vomiting (CINV) during the 1990s. A new class of agents, neurokinin-1 receptor antagonists, was introduced in March 2003 and produced even greater control of CINV when used in combination with a serotonin receptor antagonist and a corticosteroid. In July 2003, palonosetron, a new second-generation serotonin receptor antagonist that has greater potency and a longer half-life than first-generation serotonin receptor antagonists, was introduced. This clinical update reviews studies that were conducted to evaluate these new agents.

Key Words: nausea, vomiting, antiemetics

central nervous system penetrant, oral non-peptide antagonist of the neurokinin-1 receptor (Hesketh et al., 2003). A trial conducted by Cocquyt et al. (2001) and de Wit et al.’s (2003) phase III study confirmed better emetic control with the addition of aprepitant to standard “dual” therapy for acute emesis (5-HT₃ + dexamethasone) along with increased efficacy in the delayed phase and over multiple cycles. Aprepitant is an oral agent; a 125 mg dose is taken just prior to chemotherapy, and 80 mg is taken on days 2 and 3 (Merck & Co., Inc., 2003; Rittenberg, 2002).

In July 2003, a new second-generation 5-HT₃ receptor antagonist, palonosetron (Aloxi™, MGI Pharma, Bloomington, MN), was approved by the FDA. Palonosetron has greater potency, displays a higher binding affinity to the 5-HT₃ receptor, and has a much longer plasma elimination half-life than other 5-HT₃ receptor antagonists (i.e., approximately 40 hours compared to four to eight hours for the first-generation 5-HT₃

receptor antagonists, including ondansetron hydrochloride [Zofran®, GlaxoSmithKline, Research Triangle Park, NC], dolasetron mesylate [Anzemet®, Aventis, Parsippany, NJ], and granisetron hydrochloride [Kytrel®, Roche, Nutley, NJ] (Aventis, 2003; GlaxoSmithKline, 2003; MGI Pharma, 2003; Roche, 2003). The strong binding affinity for the 5-HT₃ receptors may contribute to the prolonged effect of palonosetron.

Palonosetron is administered 30 minutes before the start of chemotherapy as a single 0.25 mg IV dose infused over 30 seconds. In clinical trials, side effects included headache (9%) and constipation (5%).

The drug should be administered cautiously to patients with a history of prolonged cardiac conduction intervals, similar to other 5-HT₃ agents (MGI Pharma, 2003).

The phase III clinical evaluation of palonosetron was conducted in multiple centers in North America and Europe. The primary efficacy endpoint in these trials was complete response, defined as no vomiting and no need for rescue medication in the 24 hours after chemotherapy initiation. Secondary endpoints included complete response

Mention of specific products and opinions related to those products do not indicate or imply endorsement by the Clinical Journal of Oncology Nursing or the Oncology Nursing Society. The author is a member of advisory panels for Merck & Co., Inc., and MGI Pharma, the manufacturers of Emend® and Aloxi™, respectively, which are mentioned in this article.

Digital Object Identifier: 10.1188/04.CJON.307-308