

Overview of the Prevention and Management of CINV

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Despite substantial improvements in cancer treatment and supportive care over the past 4 decades, chemotherapy-induced nausea and vomiting (CINV) remains one of the most distressing and debilitating adverse effects (AEs) of chemotherapy. When left untreated, CINV may affect between 60% and 80% of patients with cancer¹ and be associated with premature discontinuation of treatment, diminished quality of life, complications such as dehydration and electrolyte imbalances,² and ultimately decreased treatment success and increased cost of care.³ Thus, the prevention of CINV is critically important in reducing morbidity and total healthcare costs, as well as increasing the quality of care in patients receiving highly and/or moderately emetogenic chemotherapy.

The pathogenesis of CINV involves multiple organ systems, central and peripheral pathways, and neurotransmitters. It is dependent on several factors, including the emetogenicity of the chemotherapy regimen, the dose and rate of administration of the chemotherapy agent(s), various environmental triggers (ie, smells, sites, or locations that are associated with past experiences of CINV), and patient-related factors.⁴ The process of CINV involves communication between the central nervous system and gastrointestinal (GI) tract; the targetable neurotransmitters and their associated receptors involved in CINV include serotonin (5-hydroxytryptamine [5-HT]) and serotonin receptors, substance P and the neurokinin-1 (NK₁) receptor, and dopamine and dopamine receptors.⁵ There are a number of different 5-HT receptors, with the third type, 5-HT₃ receptor, being the most important in the CINV process. The physiologic process of nausea and/or vomiting in response to chemotherapy administration involves the release of these neurotransmitters and activation of their associated receptor(s) in the chemoreceptor trigger zone, GI tract, and vomiting center located in the medulla.⁶

Five categories are used to classify CINV based on the pathways in which nausea and vomiting (NV) are produced: acute, delayed, anticipatory, breakthrough, and refractory.⁴ Acute CINV occurs within 24 hours of receiving chemotherapy and is triggered primarily by serotonin receptors in the GI tract.⁴ Delayed CINV occurs more than 24 hours after receiving chemotherapy and is mediated primarily by

ABSTRACT

The prevention of chemotherapy-induced nausea and vomiting (CINV) is critically important in reducing morbidity and total healthcare costs in patients receiving emetogenic chemotherapy. The different types of CINV (ie, acute, delayed, anticipatory, breakthrough, and refractory) are controlled through various pathways and neurotransmitters, so the pharmacologic approach to prevention and treatment varies based on the type of CINV. New therapeutic agents and combinations of agents have changed the dynamic of CINV control, and national guidelines have been recently updated based on current evidence. Along with current national guideline recommendations, this educational activity will provide an overview of the pathophysiology of CINV and how the mechanisms of action of various antiemetic agents relate to efficacy and safety in the prevention and treatment of CINV.

Am J Manag Care. 2018;24:S391-S397

For author information and disclosures, see end of text.

substance P.⁴ The actions of substance P are mediated primarily by NK₁ receptors and is a major neurotransmitter in the central, peripheral, and enteric nervous systems that affects sensory and, most notably, nociceptive pathways and inflammation.⁷ The administration of certain chemotherapy agents, such as cisplatin, carboplatin, cyclophosphamide, and/or doxorubicin, is commonly associated with delayed CINV.⁸ Anticipatory CINV is generally considered a conditional response to chemotherapy due to previous poor experiences from chemotherapy.⁴ The incidence of anticipatory CINV ranges from 18% to 57% and is more common in younger patients.⁸ Breakthrough CINV occurs within 5 days of chemotherapy despite appropriate prophylaxis, and refractory CINV occurs in subsequent chemotherapy cycles after the occurrence of breakthrough CINV in prior cycles, excluding anticipatory CINV.^{4,9} Several modifiable and unmodifiable therapy-related and patient-related risk factors have been associated with CINV, as summarized in **Table 1**.^{4,10}

TABLE 1. Therapy and Patient Risk Factors for CINV^{4,10}

Therapy-Related Risk Factors	
Agent(s)	Each chemotherapy agent or combination of agents carries its own emetogenic risk.
Dose intensity	More frequent treatments or higher doses of an agent(s) can increase the severity of emesis.
Target site	Treatments targeting the brain and GI tract may cause more nausea and vomiting because the nerve impulses that trigger CINV are in these areas.
Administration	Intravenously administered chemotherapy tends to cause more nausea than orally administered chemotherapy. More rapid IV administration of an agent(s) can increase the risk of CINV.
Patient-Related Risk Factors	
Prior experience	A patient's prior experience of poorly controlled emesis has been shown to impact future responses to chemotherapy (ie, anticipatory CINV).
Gender	Women are more prone to nausea than men.
Hyperemesis	Significant nausea and vomiting during pregnancy are associated with a greater likelihood of CINV when undergoing cancer treatment.
Age	Younger patients tend to experience more nausea than older patients.
Alcohol and drug use	Patients who do not drink alcohol or take prescription drugs may have an increased susceptibility to experiencing CINV.
Motion sickness	Patients with a history of motion sickness are more prone to CINV.
Anxiety	Similar to a poor previous experience, anxiety about therapy can also increase the risk of CINV.

CINV indicates chemotherapy-induced nausea and vomiting; GI, gastrointestinal.

Chemotherapy agents and combinations of agents are categorized as minimal, low, moderate (MEC), or high (HEC) emetogenic chemotherapy, and CINV prevention and treatment strategies are typically dictated by these categories.⁸ The moderate and high emetogenic chemotherapies (MEC and HEC, respectively) are shown in **Table 2**.^{8,11}

Therapy for CINV

The different types of CINV are controlled through various pathways and neurotransmitters working in concert with each other, so the pharmacologic approach to prevention and treatment will need to involve the usage of agents that target each of these pathways and neurotransmitters to maximize outcomes. The agents used in the prevention and treatment of CINV, along with their mechanisms of action, are summarized below.

Dexamethasone

Dexamethasone is a corticosteroid commonly used in 2-, 3-, or 4-drug combinations with other agents.⁶ Per national guidelines, dexamethasone is recommended for first-line use in combination with other agents for the prevention of both acute and delayed CINV in patients receiving HEC and/or MEC.^{8,11} Healthcare providers should be aware of the AE profile that may challenge the benefits of this agent in some patients receiving HEC or MEC.¹² A study by Vardy et al found tolerability issues reported by patients that were attributed to dexamethasone in the week following MEC, including insomnia (45%), indigestion/epigastric discomfort (27%), agitation (27%), increased appetite (19%), weight gain (16%), and acne (15%).¹²

Dexamethasone should not be used with most immunotherapies and cellular therapies concurrently, as it may reduce their efficacy. AEs, such as immunosuppression, that occur with long-term use should be carefully considered for each patient.⁸ Caution should be used in patients with diabetes because dexamethasone may increase serum glucose levels. Dexamethasone may cause dyspepsia, so use of an H₂ antagonist or proton pump inhibitor may be necessary. Additionally, dosing dexamethasone in the morning, when feasible, may minimize insomnia.⁸

5-HT₃ Receptor Antagonists

Because serotonin is the primary mediator of acute CINV, 5-HT₃ receptor antagonists (5-HT₃ RAs) play an integral role in its prevention. 5-HT₃ RAs should be scheduled prior to HEC and/or MEC administration, as opposed to an as-needed basis.⁸ First-generation 5-HT₃ RAs include ondansetron, dolasetron, granisetron, and tropisetron (not available in the United States).¹³ In clinical trials, 5-HT₃ RAs have demonstrated excellent results in preventing acute CINV.⁹ In 2003, a second-generation 5-HT₃ RA, palonosetron, was approved.¹⁴ Compared with first-generation agents, palonosetron has a prolonged plasma half-life (40 vs 3-9 hours), stronger binding affinity to the

TABLE 2. Anticancer Agents with High or Moderate Emetic Risk^{8,11}

Intravenous Anticancer Agents		
High Emetic Risk (>90% frequency of emesis)		
<ul style="list-style-type: none"> Any regimen that contains an anthracycline and cyclophosphamide Carboplatin AUC ≥4 Carmustine >250 mg/m² 	<ul style="list-style-type: none"> Cisplatin Cyclophosphamide >1500 mg/m² Dacarbazine Doxorubicin ≥60 mg/m² 	<ul style="list-style-type: none"> Epirubicin >90 mg/m² Ifosfamide ≥2 g/m² per dose Mechlorethamine Streptozocin
Moderate Emetic Risk (>30%-90% frequency of emesis) ^a		
<ul style="list-style-type: none"> Aldesleukin >12-15 million IU/m² Amifostine >300 mg/m² Arsenic trioxide Azacitidine Bendamustine Busulfan Carboplatin AUC <4 Carmustine ≤250 mg/m² Clofarabine 	<ul style="list-style-type: none"> Cyclophosphamide ≤1500 mg/m² Cytarabine >200 mg/m² Dactinomycin Daunorubicin Dual-drug liposomal encapsulation of cytarabine and daunorubicin Dinutuximab Doxorubicin <60 mg/m² Epirubicin ≤90 mg/m² 	<ul style="list-style-type: none"> Idarubicin Ifosfamide <2 g/m² per dose Interferon alfa ≥10 million IU/m² Irinotecan Melphalan Methotrexate ≥250 mg/m² Oxaliplatin Temozolomide Trabectedin
Oral Anticancer Agents		
Moderate to High Emetic Risk (≥30% frequency of emesis) ^b		
<ul style="list-style-type: none"> Altretamine Bosutinib Busulfan (>4 mg/day) Cabozantinib Ceritinib Crizotinib Cyclophosphamide (≥100 mg/m²/dose) Enasidenib 	<ul style="list-style-type: none"> Estramustine Etoposide <u>Hexamethylmelamine</u> Lenvatinib Lomustine (single day) Midostaurin Mitotane Niraparib 	<ul style="list-style-type: none"> Olaparib Panobinostat <u>Procarbazine</u> Rucaparib Temozolomide (>75 mg/m²/dose) Trifluridine/tipiracil Vinorelbine (oral vinorelbine not available in United States)

AUC indicates area under the curve.

^aBolded agents may be highly emetogenic in some patients.

^bUnderlined agents considered by other guidelines to be highly emetic (>90% frequency of emesis).

receptor (100 times stronger), and in vitro study results demonstrating specific interactions with receptors that are different from first-generation 5-HT₃ RAs (allosteric binding and positive cooperative vs competitive binding).¹³ In a pooled analysis of phase 3 studies comparing palonosetron to ondansetron, dolasetron, and granisetron, authors found that complete response rates for CINV were significantly higher among patients given palonosetron compared with first-generation 5-HT₃ RAs in the delayed and overall phases (delayed CINV: 57% vs 45%; *P* < .0001; overall CINV: 51% vs 40%; *P* < .0001).¹⁵ Rates of AEs were similar among all 5-HT₃ RAs.¹⁵

Common AEs associated with both first- and second-generation 5-HT₃ RAs are constipation, headache, and increased alanine aminotransferase (ALT).¹⁵ Although 5-HT₃ RAs are recommended in first-line prevention of CINV, there have been concerns raised in the medical literature about cardiovascular AEs.¹⁶ Potential AEs include prolongation of the QT interval, which is associated with serious ventricular arrhythmias, and blockade of voltage-dependent sodium channels and potassium channels.¹⁶

A recent meta-analysis by Tricco et al evaluated the comparative safety and efficacy of 5-HT₃ RAs alone or in combination with

a steroid.¹⁶ The analysis included 299 studies (N = 58,412 patients), and no significant differences between 5-HT₃ RAs were found regarding any reported harms, arrhythmia, and mortality. However, dolasetron with dexamethasone was associated with a greater risk of QT prolongation than ondansetron with dexamethasone.¹⁶ Because dexamethasone is typically used in combination with a 5-HT₃ RA, healthcare providers should maintain awareness of the varying potential for QT prolongation, depending on which 5-HT₃ RA, its dose, and route of administration used.

In efficacy outcomes, Tricco et al found that all agents were superior to placebo regarding prevention of NV and CINV. However, only ondansetron and ramosetron (the latter not commercially available in the United States) were superior to placebo in the treatment of severe vomiting.¹⁶ Overall, the authors found that palonosetron with a steroid to be the safest and most effective agent.¹⁶

NK₁ Receptor Antagonists

The 2003 approval of aprepitant,¹⁷ followed by the 2008 approval of its intravenous (IV) drug, fosaprepitant,¹⁸ brought a new class of antiemetic therapy to market: NK₁ receptor antagonists (NK₁ RAs).¹⁹

TABLE 3. Guideline Recommendations for the Management of CINV^{8,11}

Emetic Risk and Administration	Antiemetic Therapy			
	ASCO 2017 Guidelines		NCCN 2018 Guidelines	
	Acute Phase	Delayed Phase	Acute Phase	Delayed Phase
High, intravenous	Cisplatin/HEC single agents 4-Drug combo: NK ₁ RA + 5-HT ₃ RA + dexamethasone + olanzapine	Dexamethasone + olanzapine	3-Drug combo: NK ₁ RA + 5-HT ₃ RA + dexamethasone <i>...Or...</i>	Dexamethasone +/- aprepitant (if aprepitant used on day 1)
	Anthracycline + cyclophosphamide HEC 4-Drug combo: NK ₁ RA + 5-HT ₃ RA + dexamethasone + olanzapine	Olanzapine	3-Drug combo: Olanzapine + palonosetron + dexamethasone <i>...Or...</i>	Olanzapine
			4-Drug combo: Olanzapine + NK ₁ RA + 5-HT ₃ RA + dexamethasone	Olanzapine + aprepitant (if aprepitant used on day 1) + dexamethasone
Moderate, intravenous	Carboplatin AUC ≥4 mg/mL/min 3-Drug combo: NK ₁ RA + 5-HT ₃ RA + dexamethasone		2-Drug combo: 5-HT ₃ RA + dexamethasone <i>...Or...</i>	Dexamethasone... <i>Or...</i> 5-HT ₃ monotherapy
	All other MEC agents 2-Drug combo: 5-HT ₃ + dexamethasone	If treated with cyclophosphamide, doxorubicin, oxaliplatin, or other MEC known to cause delayed CINV Dexamethasone	3-Drug combo: Olanzapine + palonosetron + dexamethasone <i>...Or...</i>	Olanzapine
			3-Drug combo: NK ₁ RA + 5-HT ₃ RA + dexamethasone	Aprepitant (if aprepitant used on day 1) ± dexamethasone
Low, intravenous		1 Drug: Dexamethasone... <i>Or...</i> 5-HT ₃ RA	1 Drug: Dexamethasone... <i>Or...</i> Metoclopramide... <i>Or...</i> Prochlorperazine... <i>Or...</i> 5-HT ₃ RA	
Minimal, intravenous	No routine prophylaxis		No routine prophylaxis	
High-moderate, oral	ASCO guideline recommendations do not distinguish between intravenous and oral agents. All recommendations above apply to both.		1 Drug: 5-HT ₃ RA	
Low-minimal, oral			As needed (recommended): Metoclopramide... <i>Or...</i> Prochlorperazine... <i>Or...</i> 5-HT ₃ RA	

5-HT₃ RA indicates 5-hydroxytryptamine receptor antagonist; ASCO, American Society of Clinical Oncology; CINV, chemotherapy-induced nausea and vomiting; HEC, high emetogenic chemotherapy; MEC, moderate emetogenic chemotherapy; NCCN, National Comprehensive Cancer Network; NK₁ RA, neurokinin-1 receptor antagonist.

These agents reduce the activity of substance P through blockage of NK₁ receptors, which works primarily against delayed CINV, but also has been shown to help with acute CINV.²⁰ The addition of an NK₁ RA to 5-HT₃ RA/dexamethasone has been shown to be more effective in preventing acute and delayed CINV in patients receiving HEC than 5-HT₃ RA/dexamethasone alone.⁹ These agents are recommended alongside dexamethasone and 5-HT₃ RAs as first-line therapy in the prevention of CINV for HEC and MEC, with additional risk factors, previous prevention/treatment failures, or therapies associated with

greater emetogenic risk (ie, irinotecan or oxaliplatin).⁸ In recent years, 3 additional NK₁ RAs have received approval for use in CINV: netupitant and fosnetupitant, both in a fixed combination with palonosetron (NEPA) (ie, the fixed combination of fosnetupitant/palonosetron IV and netupitant/palonosetron capsule), and rolapitant.^{17,21,22}

Rolapitant demonstrated superior efficacy in the prevention of delayed CINV (>24-120 hours after MEC or HEC) over placebo in combination with a 5-HT₃ RA and dexamethasone during phase 3 trials.^{23,24} In a phase 3 trial evaluating rolapitant in patients receiving

MEC, AEs were similar between the treatment and control groups, with the most common being fatigue, constipation, and headache.²⁴ AEs were also similar between groups in 2 phase 3 trials evaluating rolapitant in patients receiving HEC, and these events included neutropenia, anemia, and leukopenia.²³

In a phase 3 trial comparing NEPA to oral palonosetron, both in addition to dexamethasone, a significantly greater proportion of patients who received NEPA achieved a complete response compared with those who received palonosetron alone over multiple cycles of HEC (for each cycle, cycles 1-4: $P \leq .001$; cumulative over all 4 cycles, $P < .0001$).²⁵ AEs were similar between groups, with the most common being neutropenia, alopecia, leukopenia, asthenia, headache, and fatigue.²⁵ A recently published trial by Zhang et al showed that NEPA administered just on day 1 only was noninferior to a 3-day course of aprepitant and granisetron, both in addition to dexamethasone, with a similar safety and tolerability profile between groups.²⁶

Currently, NK₁ RAs are only approved in the prevention of CINV, not treatment.⁸ Additionally, most NK₁ RAs, except rolapitant, inhibit the metabolism of dexamethasone and therefore require a lower dose of dexamethasone when administered concurrently. This is not the only drug interaction known with most NK₁ RAs. Other significant interactions include, but are not limited to, various other nonchemotherapy agents (eg, warfarin and oral contraceptives) as well as various chemotherapy agents (eg, vinca alkaloids, taxanes, and etoposide). These interactions vary in terms of significance and dose modification or monitoring recommendations. Additionally, rolapitant has an extended half-life and it should not be administered more frequently than every 2 weeks.⁸

Olanzapine

Olanzapine is an antipsychotic agent initially approved for schizophrenia, bipolar disorder, and depression; however, olanzapine inhibits 5-HT₂, 5-HT₁, and dopamine receptors, thereby providing antiemetic effects.² In a phase 3 trial, olanzapine plus palonosetron and dexamethasone (OPD) demonstrated efficacy in controlling acute and delayed CINV in patients receiving HEC, with complete response (CR) (no emesis, no rescue) rates of 97%, 77%, and 77% for the acute, delayed, and overall phases, respectively.²⁷ When compared with the OPD regimen, aprepitant plus palonosetron and dexamethasone (APD) demonstrated a similar CR (87%, 73%, 73% for the acute, delayed, and overall phases, respectively), but the differences in nausea control (patients with no nausea) favored the OPD group (OPD: 87% acute, 69% delayed, and 69% overall; APD: 87% acute, 38% delayed, and 38% overall).²⁷ AEs associated with olanzapine antiemetic regimens include fatigue, drowsiness, disturbed sleep, and dry mouth.²

Miscellaneous Agents

In addition to the agents most commonly seen in first-line therapy for CINV, healthcare providers should be aware of alternative agents

with antiemetic effects, including dopamine antagonists, cannabinoids, and complementary and alternative medicines. Dopamine antagonists, which include phenothiazines (eg, metoclopramide, prochlorperazine) and butyrophenones (eg, droperidol, haloperidol), were historically the foundation of antiemetic therapy; however, a high level of blockade at dopamine receptors leads to extrapyramidal reactions, disorientation, and sedation. With the advent of newer therapies with fewer dose-limiting AEs, dopamine antagonists are typically reserved for CINV refractory to other treatments or chemotherapy with low emetic risk.^{6,8,9}

The main active ingredient in marijuana, delta-9-tetrahydrocannabinol (THC), binds to cannabinoid receptors types 1 and 2 (CB₁, CB₂). These receptors are located throughout the body, and activation of CB₁ in the brain has been shown to decrease the incidence of NV.²⁸ Patients unresponsive to other forms of antiemetic therapy may respond to medical marijuana, which is available in approximately half of the states in the United States, albeit controversially, or synthetic pharmaceutical-grade THC, such as dronabinol capsules, nabilone capsules, and dronabinol oral solution.²⁸ Dronabinol is FDA approved for CINV in adults whose conventional therapies have failed and recommended by clinical guidelines for refractory CINV and as a rescue antiemetic.^{11,29}

A meta-analysis by Smith et al found that cannabinoids are better than placebo and similar to other antiemetics in terms of absence of NV.³⁰ Additionally, patients prefer cannabinoid therapy over other antiemetic regimens (risk ratio [RR], 2.8; 95% CI, 1.9-4.0; RR >1 favors cannabinoids); however, patients more frequently withdraw from cannabinoid therapy for any reason (RR, 3.5; 95% CI, 1.4-9.0; RR <1 favors cannabinoids) and due to AEs (RR, 3.2; 95% CI, 1.3-8.0; RR <1 favors cannabinoids) compared with other antiemetic regimens.³⁰ AEs that were reported with higher frequency in patients taking cannabinoids compared with other antiemetic therapies included dizziness, dysphoria, euphoria, "feeling high," and sedation.³⁰ Additionally, cannabinoids have a significant drug interaction profile so this must be taken into consideration when they are used in combination with other agents.

Additional alternative agents to conventional therapies include ginger, which failed to demonstrate a benefit controlling CINV in 3 of 6 clinical trials³¹⁻³⁶; acupuncture, which is limited in evidence due to a high risk of bias and a lack of standardization of treatment; and nonpharmacologic therapies, which have limited support and include cognitive distraction (eg, video games during treatment), systematic desensitization, exercise, hypnosis, and transcutaneous electrical nerve stimulation.³⁷

Current Guideline Recommendations for Management of CINV

Various national guidelines provide recommendations for the prevention and management of CINV.^{8,11} Two of the most recognizable

and followed guidelines are the National Comprehensive Cancer Network (NCCN) guidelines, which were updated in June 2018, and the American Society of Clinical Oncology (ASCO) guidelines, which were last updated in October 2017.^{8,11} The most current versions of these guidelines are summarized in **Table 3**.^{8,11} Antiemetics should be started before chemotherapy for prevention of acute CINV as well as for 2 to 4 days afterward, depending on the level of emetogenicity present.^{8,11}

Notably, both guidelines now recommend a 4-drug combination of an NK₁ RA, 5-HT₃ RA, dexamethasone, and olanzapine for prevention of CINV in HEC.^{8,11} Of note, NCCN guidelines give the option of a 3- or 4-drug combination for HEC. Additionally, NEPA was added as a first-line agent in HEC and MEC regimens in the NCCN guidelines and HEC regimens in the ASCO guidelines.^{8,11}

Breakthrough CINV

For breakthrough CINV, the general principle of therapy is to add an agent with a different mechanism of action than the antiemetic agents the patient is already taking.⁸ Effective options for breakthrough CINV include olanzapine, 5-HT₃ RAs, dexamethasone, phenothiazines (eg, prochlorperazine or promethazine), cannabinoids, and/or the benzodiazepine, lorazepam.⁸ Although the NCCN guidelines do not recommend a specific agent, the ASCO guidelines recommend olanzapine for breakthrough CINV if not already a part of the patient's antiemetic regimen.¹¹ Other agents are recommended with equal weight by the ASCO guidelines if olanzapine is already being given to the patient.¹¹ Importantly, usage of shorter-acting 5-HT₃ RAs after receiving palonosetron, the granisetron patch, or granisetron extended-release injection is limited during the delayed phase, so breakthrough therapy following these agents should focus on different mechanisms of action.⁸ Granisetron extended-release injection is for subcutaneous administration only and is not recommended to be given more frequently than once per week.

If breakthrough CINV then becomes controlled, the additional antiemetic(s) should be maintained on a scheduled basis; if not controlled, reevaluate and consider dose adjustments or add another agent from a different class.⁸ Regardless of controlled status, patients experiencing breakthrough CINV should be considered for a higher level of prophylaxis during subsequent cycles of chemotherapy.⁸

Anticipatory CINV

The most important risk factor for the development of anticipatory CINV is the control of both acute and delayed CINV in previous cycles of chemotherapy. This should be one of the primary motivators in ensuring patients receive, with the first cycle of chemotherapy, the most effective prophylactic antiemetic regimen for the emetogenicity level of that chemotherapy regimen. Prevention of CINV is key.^{8,11} If anticipatory CINV occurs, the NCCN and ASCO guidelines suggest the use of behavioral therapy, which may include

systematic desensitization (ASCO, NCCN), hypnosis (NCCN), relaxation exercises (NCCN), cognitive distraction (NCCN), yoga (NCCN), or acupuncture/acupressure (NCCN).^{8,11} Additionally, the NCCN guidelines recommend the use of anxiolytic therapy, such as lorazepam, beginning on the night before chemotherapy and repeating 1 to 2 hours before chemotherapy is administered the next day.⁸

Conclusions

Although therapy has evolved considerably over the past 4 decades, 60% to 80% of patients still experience CINV alongside chemotherapy. New agents, such as rolapitant and NEPA, along with 4-drug combination regimens, have improved control of acute and delayed CINV, and better prevention also improves the rates of anticipatory, refractory, and breakthrough CINV. Healthcare providers must be aware of the new guideline recommendations, along with the safety and efficacy data on antiemetic agents. Successfully incorporating these evidence-based strategies and effective therapies into clinical practice is critical to improving morbidity and quality-of-life outcomes among patients undergoing HEC and/or MEC. ■

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Funding source: This activity is supported by an independent educational grant from Helsinn Therapeutics (U.S.), Inc.

Author disclosure: Dr Natale reports receiving consultancies/honoraria from Tesaro's advisory board and Merck's speakers bureau.

Authorship information: Concept and design, drafting of the manuscript, and critical revision of the manuscript for important intellectual content.

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Dr Natale gratefully acknowledges Rachel Brown, PharmD, MPH, for her contributions to the development of this article.

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