ASCO Guidelines

Antiemetics: American Society of Clinical Oncology Clinical Practice Guideline Update

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Editor's note: This is the complete American Society of Clinical Oncology (ASCO) Clinical Practice Guideline Update and provides the updated recommendations with comprehensive discussions of the relevant literature for each. The executive summary of the guideline and data supplements with evidence tables, other tables, and figures are available at www.asco.org/guidelines/antiemetics.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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A B S T R A C T

Purpose
To update the American Society of Clinical Oncology (ASCO) guideline for antiemetics in oncology.

Methods
A systematic review of the medical literature was completed to inform this update. MEDLINE, the Cochrane Collaboration Library, and meeting materials from ASCO and the Multinational Association for Supportive Care in Cancer were all searched. Primary outcomes of interest were complete response and rates of any vomiting or nausea.

Results
Thirty-seven trials met prespecified inclusion and exclusion criteria for this systematic review. Two systematic reviews from the Cochrane Collaboration were identified; one surveyed the pediatric literature. The other compared the relative efficacy of the 5-hydroxytryptamine-3 (5-HT_3) receptor antagonists.

Recommendations
Combined anthracycline and cyclophosphamide regimens were reclassified as highly emetic. Patients who receive this combination or any highly emetic agents should receive a 5-HT_3 receptor antagonist, dexamethasone, and a neurokinin 1 (NK_1) receptor antagonist. A large trial validated the equivalency of fosaprepitant, a single-day intravenous formulation, with aprepitant; either therapy is appropriate. Preferential use of palonosetron is recommended for moderate emetic risk regimens, combined with dexamethasone. For low-risk agents, patients can be offered dexamethasone before the first dose of chemotherapy. Patients undergoing high emetic risk radiation therapy should receive a 5-HT_3 receptor antagonist before each fraction and for 24 hours after treatment and may receive a 5-day course of dexamethasone during fractions 1 to 5. The Update Committee noted the importance of continued symptom monitoring throughout therapy. Clinicians underestimate the incidence of nausea, which is not as well controlled as emesis.

INTRODUCTION

The first American Society of Clinical Oncology (ASCO) guideline for the use of antiemetics was published in 1999.[1] The first update to the guideline was published in 2006.[2] This document represents the second update, which incorporates new clinical information.

This guideline provides clinicians with recommendations to prevent vomiting and nausea among patients undergoing cancer chemotherapy (chemotherapy-induced nausea and vomiting [CINV]) and/or radiation therapy (radiation-induced nausea and vomiting [RINV]) based on evidence from clinical trials.

A systematic review of the literature found substantial new information related to a variety of clinical questions. Therefore, the guideline was updated in its entirety and all clinical questions were revisited. An executive summary of this update was published in *Journal of Clinical Oncology*.

METHODS

Panel Composition

An Update Committee (Appendix Table A1, online only) was formed to review data published since 2006 and develop updated recommendations.

Consensus Development Based on Evidence

The 2011 Update Committee met once at the ASCO Headquarters Office and once via teleconference to consider available evidence and develop recommendations. Additional work on the guideline was completed electronically. Members of the steering committee and ASCO staff prepared a draft guideline document that was disseminated for review by the entire Update Committee. As per standard ASCO practice, the guideline was submitted to *Journal of Clinical Oncology* for peer review. Feedback from external reviewers with expertise in antiemetics was also

solicited. The Update Committee, the ASCO Clinical Practice Guideline Committee, and the ASCO Board of Directors reviewed and approved the final document.

THE BOTTOM LINE

ASCO GUIDELINE UPDATE

American Society of Clinical Oncology Clinical Practice Guideline Update on Antiemetics

Intervention

- Antiemetics for patients receiving cancer therapy.

Target Audience

- Medical Oncologists, Radiation Oncologists, Oncology Nurses.

Key Recommendations

- Patients who receive highly emetic chemotherapy regimens should receive the three-drug combination of a neurokinin 1 (NK1) antagonist, 5-hydroxytryptamine-3 (5-HT_3) antagonist, and dexamethasone.
- The preferred 5-HT_3 antagonist for patients who receive moderate emetic chemotherapy regimens is palonosetron; antiemetic treatment includes that agent combined with a corticosteroid.
- Antiemetic treatment for patients who receive combination chemotherapy should be determined according to the agent with the greatest degree of emetic risk.
- Both dexamethasone and a 5-HT_3 antagonist are recommended for patients undergoing high-dose chemotherapy.
- Pediatric patients receiving either high or moderate emetic risk chemotherapy should be treated with a 5-HT_3 antagonist and corticosteroids; higher weight-based dosing may be required.
- For those treated with high emetic risk radiation therapy, a 5-HT_3 antagonist before each fraction and a 5-day course of dexamethasone are recommended.
- A 5-HT_3 antagonist before each fraction is also recommended before moderate-risk radiation; a 5-day course of dexamethasone is optional.
- For patients who receive combination chemoradiotherapy, antiemetic therapy is dictated by the emetogenicity of chemotherapy, unless the emetic risk of radiation therapy is higher.

Methods

- A systematic review of the literature published since the last update of the guideline.

Data supplements, including evidence tables and clinical tools and resources, can be found at www.asco.org/guidelines/antiemetics.

Guideline Policy

This practice guideline is not intended to substitute for the independent professional judgment of the treating physician. Practice guidelines do not account for individual variation among patients and may not reflect the most recent evidence. This guideline does not recommend any particular product or course of medical treatment. Use of the practice guideline is voluntary. The executive summary and additional information and practice tools are available at www.asco.org/guidelines/antiemetics.

Update Methodology

The last update of the ASCO antiemetics guideline was published in 2006. The goals of the current update were to review new evidence describing prevention of nausea and vomiting among patients undergoing cancer therapy, including antineoplastic drugs and radiation therapy, and to develop an updated set of recommendations (Table 1). This update reviewed 5-HT_3 receptor antagonist equivalency, considering use of these agents either with or without an NK_1 receptor antagonist. Other key questions included the use of NK_1 receptor antagonists in the moderately emetogenic and high-dose chemotherapy setting, the use of alternative drug formulations, and antiemetic therapy for children; the complete list of questions included in this guideline update is provided in Table 1.

Literature Review and Analysis

Literature search strategy. The initial search for this systematic review identified relevant articles from an Agency for Healthcare Research and Quality–funded Evidence-Based Practice Center report completed at Oregon Health and Science University (OHSU).[3] The dates of the OHSU literature search of MEDLINE were 1966 through October 2008. That evidence review was limited to trials including the newer antiemetics: aprepitant (NK_1 receptor antagonist) and 5-HT_3 receptor antagonists. Initially, two literature searches of MEDLINE were completed by ASCO staff. The first included all relevant search terms (Data Supplement, available online only at www.asco.org/guidelines/antiemetics), overlapping minimally with the OHSU search, from September 2008 through December 2009. A second search, excluding the OHSU intervention search terms, overlapped briefly with the search for the 2006 ASCO update, ranging from February 2004 to February 2010. This second search was designed to identify new adjunctive therapy. The Cochrane Collaboration Library electronic database was also searched, using the terms emesis, vomiting, and nausea. Data presented at the ASCO and the Multinational Association of Supportive Care in Cancer (MASCC) annual meetings available since the 2006 update[2] were also searched systematically using the terms vomiting, emesis, and nausea, but only presentations or posters were included. Data presented only in abstract form were excluded. Yield from hand searches of bibliographies from relevant articles and materials provided by Update Committee members was also assessed for inclusion. Another search of MEDLINE was completed, including all intervention terms, after preparation of the preliminary draft to determine if any new trials had been published. Meeting materials were not searched again.

Inclusion and exclusion criteria. Trial reports of randomized studies or other systematic reviews from scholarly articles or meetings eligible for inclusion met the following criteria: (1) intervention was for the treatment of nausea or vomiting secondary to cancer therapy, (2) nausea and/or vomiting outcomes were reported, (3) patients were observed for a minimum of 5 days (120 hours) after initial chemotherapy administration, and (4) each trial arm included a minimum of 25 randomly assigned patients.

Data extraction. Eligible reports were identified in a first round of review by an ASCO staff member; these were later discussed with the Co-Chairs to reach a final decision. Full text copies were obtained for assessment of inclusion/exclusion criteria. Articles that provisionally met inclusion criteria underwent data extraction by ASCO staff for patient characteristics, study design and quality, interventions, outcomes, and adverse events. Evidence summary tables (Data Supplement) were reviewed for accuracy and completeness by an ASCO staff member who was not involved in their original preparation.

Study quality and limitations of the literature. Trial characteristics extracted to rate quality included study design, definition of terms, and outcomes. One limitation of the trials was that a number of studies included

Table 1. Summary of Recommendations

Clinical Situation	2006 Recommendation	2011 Reccomendation
Chemotherapy-induced nausea and vomiting		
Highly emetogenic agents	The three-drug combination of a 5-HT_3 receptor antagonist, dexamethasone, and aprepitant is recommended before chemotherapy. In all patients receiving cisplatin and all other agents of high emetic risk, the two-drug combination of dexamethasone and aprepitant is recommended. The Update Committee no longer recommends the combination of a 5-HT_3 serotonin receptor antagonist and dexamethasone on days 2 and 3.	The three-drug combination of an NK_1 receptor antagonist (days 1-3 for aprepitant; day 1 only for fosaprepitant), a 5-HT_3 receptor antagonist (day 1 only), and dexamethasone (days 1-3 or 1-4) is recommended for patients receiving highly emetogenic chemotherapy. This recommendation is unchanged since the 2006 update, but reworded for clarification. The Update Committee also recommended reclassification of the combined AC regimen as highly emetogenic.
Moderately emetogenic agents	The three-drug combination of a 5-HT_3 receptor antagonist, dexamethasone, and aprepitant is recommended for patients receiving AC. For patients receiving chemotherapy of moderate emetic risk other than AC, we recommend the two-drug combination of a 5-HT_3 receptor antagonist and dexamethasone. In patients receiving AC, aprepitant as a single agent is recommended on days 2 and 3. For all other chemotherapies of moderate emetic risk, single-agent dexamethasone or a 5-HT_3 receptor antagonist is suggested for the prevention of emesis on days 2 and 3.	The two-drug combination of palonosetron (day 1 only) and dexamethasone (days 1-3) is recommended for patients receiving moderately emetogenic chemotherapy. If palonosetron is not available, clinicians may substitute a first-generation 5-HT_3 receptor antagonist, preferably granisetron or ondansetron. Limited evidence also supports adding aprepitant to the combination. Should clinicians opt to add aprepitant in patients receiving moderate-risk chemotherapy, any one of the 5-HT_3 antagonists is appropriate.
Low emetogenic agents	Dexamethasone 8 mg is suggested. No routine preventive use of antiemetics for delayed emesis is suggested.	A single 8-mg dose of dexamethasone before chemotherapy is suggested. No change since 2006.
Minimally emetogenic agents	No change from the original guideline. No antiemetic should be administered routinely before or after chemotherapy.	No antiemetic should be administered routinely before or after chemotherapy. No change from the original guideline.
Combination chemotherapy	No change from the original guideline. Patients should be administered antiemetics appropriate for the chemotherapeutic agent of greatest emetic risk.	Patients should be administered antiemetics appropriate for the component chemotherapeutic (antineoplastic) agent of greatest emetic risk. No change from the original guideline. AC combinations are now classified as highly emetogenic.
Adjunctive drugs	Lorazepam and diphenhydramine are useful adjuncts to antiemetic drugs but are not recommended as single agents.	Lorazepam or diphenhydramine are useful adjuncts to antiemetic drugs but are not recommended as single-agent antiemetics. No change since 2006.
Complementary therapy	New question for 2011 update.	No published randomized controlled trial data that met inclusion criteria are currently available to support a recommendation about such therapies.
Pediatric patients	The combination of a 5-HT_3 antagonist plus a corticosteroid is suggested before chemotherapy in children receiving chemotherapy of high or moderate emetic risk. Because of variation of pharmacokinetic parameters in children, higher weight-based doses of 5-HT_3 antagonists than those used in adults may be required for antiemetic protection.	The combination of a 5-HT_3 antagonist plus a corticosteroid is suggested before chemotherapy in children receiving chemotherapy of high or moderate emetic risk. Because of variation of pharmacokinetic parameters in children, higher weight-based doses of 5-HT_3 antagonists than those used in adults may be required for antiemetic protection. No change since 2006.
High-dose chemotherapy with stem-cell or bone marrow transplantation	No change from original guideline. A 5-HT_3 receptor antagonist antiemetic combined with dexamethasone is suggested. Aprepitant should be considered, although evidence to support its use specifically in these patients is lacking.	A 5-HT_3 receptor antagonist combined with dexamethasone is suggested. Aprepitant should be considered, although evidence to support its use is limited.
Multiday chemotherapy	No change from the original guideline. It is suggested that antiemetics appropriate for the risk class of the chemotherapy, as outlined earlier, be administered for each day of the chemotherapy and for 2 days after, if appropriate.	It is suggested that antiemetics appropriate for the emetogenic risk class of the chemotherapy be administered for each day of the chemotherapy and for 2 days after, if appropriate. No change from the original guideline. The Update Committee suggests, based on limited data, that patients receiving 5-day cisplatin regimens be treated with a 5-HT_3 antagonist in combination with dexamethasone and aprepitant.
Emesis or nausea despite optimal prophylaxis	No change from original guideline. The Update Committee suggests that clinicians conduct a careful re-evaluation of emetic risk, disease status, concurrent illnesses, and medications; ascertain that the best regimen is being administered for the emetic risk; consider adding lorazepam or alprazolam to the regimen; and consider substituting a high-dose intravenous metoclopramide for the 5-HT_3 antagonist or adding a dopamine antagonist to the regimen.	Clinicians should re-evaluate emetic risk, disease status, concurrent illnesses, and medications; ascertain that the best regimen is being administered for the emetic risk; consider adding lorazepam or alprazolam to the regimen; and consider adding olanzapine to the regimen or substituting high-dose intravenous metoclopramide for the 5-HT_3 antagonist or adding a dopamine antagonist to the regimen.
Anticipatory nausea and vomiting	No change since the original guideline. Use of the most active antiemetic regimens appropriate for the chemotherapy being administered to prevent acute or delayed emesis is suggested. Such regimens may be used with the initial chemotherapy, rather than assessing the patient's emetic response with less effective treatment. If anticipatory emesis occurs, behavioral therapy with systematic desensitization is effective and suggested.	Use of the most active antiemetic regimens appropriate for the chemotherapy being administered to prevent acute or delayed emesis is suggested. Such regimens should be used with initial chemotherapy, rather than assessing the patient's emetic response with less effective treatment. If anticipatory emesis occurs, behavioral therapy with systematic desensitization is effective and suggested. No change since the original guideline.

(continued on following page)

Table 1. Summary of Recommendations (continued)

Clinical Situation	2006 Recommendation	2011 Reccomendation
Radiation-induced nausea and vomiting		
High risk	No change from original guideline. The Update Committee suggests administration a 5-HT_3 antagonist with or without a corticosteroid before each fraction and for at least 24 hours after. There is no change from the original guideline.	On the basis of extrapolation from indirect evidence, the Update Committee recommends that all patients should receive a 5-HT_3 antagonist before each fraction and for at least 24 hours after completion of radiotherapy. Patients should also receive a 5-day course of dexamethasone during fractions 1-5.
Moderate risk	The Update Committee recommends a 5-HT_3 antagonist before each fraction.	The Update Committee recommends that patients receive a 5-HT_3 antagonist before each fraction for the entire course of radiotherapy. Patients may be offered a short course of dexamethasone during fractions 1-5.
Low risk	No change from original guideline. The Update Committee recommends a 5-HT_3 antagonist before each fraction.	The Update Committee recommends a 5-HT_3 antagonist alone as either prophylaxis or rescue. For patients who experience radiation-induced nausea and vomiting while receiving rescue therapy only, prophylactic treatment should continue until radiotherapy is complete.
Minimal risk	No change from original guideline. The Update Committee suggests that treatment be administered on an as-needed basis only. Dopamine or serotonin receptor antagonists are advised. Antiemetics should be continued prophylactically for each remaining radiation treatment day.	Patients should receive rescue therapy with either a dopamine receptor antagonist or a 5-HT_3 antagonist. Prophylactic antiemetics should continue throughout radiation treatment if a patient experiences radiation-induced nausea and vomiting while receiving rescue therapy.
Combined chemotherapy and radiation therapy	Patients should receive antiemetic prophylaxis according to the emetogenicity of chemotherapy, unless the emetic risk with the planned radiotherapy is higher. No change from the original guideline.	Patients should receive antiemetic prophylaxis according to the emetogenicity of chemotherapy, unless the emetic risk with the planned radiotherapy is higher. No change from the original guideline.

Abbreviations: 5-HT_3, 5-hydroxytryptamine-3; AC, anthracycline and cyclophosphamide; NK_1, neurokinin 1.

patients who received either moderately or highly emetogenic chemotherapy without reporting subset analyses for patient groups according to emetic risk. Findings from such combined trials are challenging to interpret in the context of an evidence-based recommendation for a specific risk class.

Guideline and Conflict of Interest

The Update Committee was assembled in accordance with the ASCO Conflict of Interest Management Procedures for Clinical Practice Guidelines ("Procedures," summarized at http://www.asco.org/guidelinescoi). Members of the Update Committee completed the ASCO disclosure form, which requires disclosure of financial and other interests that are relevant to the subject matter of the guideline, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as the result of promulgation of the guideline. Categories for disclosure include employment relationships, consulting arrangements, stock ownership, honoraria, research funding, and expert testimony. In accordance with the Procedures, the majority of the members of the Update Committee did not disclose any such relationships.

Revision Dates

At intervals, the Steering Committee will determine the need for updates to the guideline based on examinations of current literature. If necessary, the Update Committee will be reconvened to discuss potential changes. When appropriate, the Update Committee will recommend updating the guideline to the Clinical Practice Guideline Committee and the ASCO Board for review and approval.

RESULTS

The literature search yielded a total of 271 unique citations from MEDLINE and 48 from the MASCC and ASCO meetings; the QUOROM diagram is included in the Data Supplement. Additional materials evaluated were from the personal libraries of Update Committee members. Thirty-six reports met the inclusion criteria (previously described) and were selected for full-text review. Eleven (30.6%) of those included were either posters or presentations from meetings.

Eight studies evaluated antiemetic regimens according to emetic risk, five of which applied to highly emetic chemotherapy[4-8] and the remainder to moderately emetic therapy.[9-11] Five trials evaluated the comparative efficacy of 5-HT_3 receptor antagonists, including a systematic review from the Cochrane Collaboration.[12-16] Five described findings from dosing studies specifically for palonosetron.[17-21] Two trials described new delivery methods of two previously approved therapies.[22,23] A number of studies assessed special populations. Three trials detailed results in patients undergoing myeloablative therapy before transplantation,[24-26] two described efforts in patients receiving multiday chemotherapy regimens,[27,28] and three evaluated antiemetic therapies in pediatric patients undergoing cancer therapy.[29-31]

Three studies examined complementary therapies in patients receiving cancer treatment.[32-35] Two studies that specifically considered therapy for delayed nausea and vomiting were identified.[36,37] Among the studies reviewed, only one trial evaluating therapy for patients undergoing radiation was identified.[38]

GUIDELINE RECOMMENDATIONS

CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING

Highly and moderately emetogenic antineoplastic agents have the potential to induce both acute ($\leq$ 24 hours) and delayed ($>$ 24 hours) nausea and vomiting after chemotherapy. The guideline recommendations include prophylaxis for both types of nausea and vomiting where appropriate.

This guideline update includes the most recent recommendations (Table 1) developed by the Update Committee. A table with

intravenous agents organized by emetic risk (Table 2) is included. The intravenous risk stratification schema was originally published in 1997[39] and was updated at the MASCC/European Society for Medical Oncology 2009 consensus conference.[40] The modified stratification from MASCC was adopted by ASCO for this guideline update.[41] Dosing schedules are also detailed herein (Table 3).

Table 2. Emetic Risk of Intravenous Antineoplastic Agents

Emetic Risk	Agent
High	Carmustine
	Cisplatin
	Cyclophosphamide ≥ 1,500 mg/m^2
	Dacarbazine
	Dactinomycin
	Mechlorethamine
	Streptozotocin
Moderate	Azacitidine
	Alemtuzumab
	Bendamustine
	Carboplatin
	Clofarabine
	Cyclophosphamide < 1,500 mg/m^2
	Cytarabine > 1,000 mg/m^2
	Daunorubicin*
	Doxorubicin*
	Epirubicin*
	Idarubicin*
	Ifosfamide
	Irinotecan
	Oxaliplatin
Low	Fluorouracil
	Bortezomib
	Cabazitaxel
	Catumaxomab
	Cytarabine ≤ 1,000 mg/m^2
	Docetaxel
	Doxorubicin HCL liposome injection
	Etoposide
	Gemcitabine
	Ixabepilone
	Methotrexate
	Mitomycin
	Mitoxantrone
	Paclitaxel
	Panitumumab
	Pemetrexed
	Temsirolimus
	Topotecan
	Trastuzumab
Minimal	2-Chlorodeoxyadenosine
	Bevacizumab
	Bleomycin
	Busulfan
	Cetuximab
	Fludarabine
	Pralatrexate
	Rituximab
	Vinblastine
	Vincristine
	Vinorelbine

NOTE. This list of agents is not exhaustive.
*These anthracyclines, when combined with cyclophosphamide, are now designated as high emetic risk.

Clinical Question 1

What is the optimal treatment to prevent nausea and vomiting from highly emetogenic antineoplastic agents?

Recommendation 1. The three-drug combination of an NK_1 receptor antagonist (days 1 through 3 for aprepitant; day 1 only for fosaprepitant), a 5-HT_3 receptor antagonist (day 1 only), and dexamethasone (days 1 through 3 or 1 to 4) is recommended for patients receiving highly emetogenic chemotherapy. This recommendation remains unchanged since the 2006 update but has been reworded for clarification. The Update Committee also recommended reclassification of the combined anthracycline and cyclophosphamide (AC) regimen as highly emetogenic.

Literature update and analysis 1. Five new trials were identified.[4-8] The study by Hoshi et al,[6] presented at the 2007 MASCC meeting, provided additional data (Data Supplement) to support the 2006

Table 3. Antiemetic Dosing by Chemotherapy Risk Category

Risk Category	Dosing on Day of Chemotherapy	Dosing on Subsequent Days
High emetic risk*		
NK_1 antagonist		
Aprepitant	125 mg oral	80 mg oral; days 2 and 3
Fosaprepitant	150 mg IV	
5-HT_3 antagonist		
Granisetron	2 mg oral; 1 mg or 0.01 mg/kg IV	
Ondansetron	8 mg oral twice daily; 8 mg or 0.15 mg/kg IV	
Palonosetron	0.50 mg oral; 0.25 mg IV	
Dolasetron	100 mg oral ONLY	
Tropisetron	5 mg oral; 5 mg IV	
Ramosetron	0.3 mg IV	
Corticosteroid†		
Dexamethasone	12 mg oral or IV	8 mg oral or IV; days 2-3 or days 2-4
Moderate emetic risk‡		
5-HT_3 antagonist		
Palonosetron	0.50 mg oral; 0.25 mg IV	
Corticosteroid		
Dexamethasone	8 mg oral or IV	8 mg; days 2 and 3
Low emetic risk		
Corticosteroid		
Dexamethasone	8 mg oral or IV	

NOTE. For patients receiving multiday chemotherapy, clinicians must first determine the emetic risk of the agent(s) included in the regimen. Patients should receive the agent of the highest therapeutic index daily during chemotherapy and for 2 days thereafter. Patients can also be offered the granisetron transdermal patch that delivers therapy over multiple days rather than taking a serotonin antagonist daily.
Abbreviations: 5-HT_3, 5-hydroxytryptamine-3; IV, intravenous; NK_1, neurokinin 1.
*Includes combination of an anthracycline and cyclophosphamide.
†The dexamethasone dose is for patients who are receiving the recommended three-drug regimen for highly emetic chemotherapy. If patients do not receive aprepitant, the dexamethasone dose should be adjusted to 20 mg on day 1 and 16 mg on days 2 to 4.
‡Clinicians who choose to use an NK_1 antagonist should follow high emetic risk chemotherapy dosing. Importantly, corticosteroid is only given on day 1; dexamethasone dose is 12 mg.

recommendation to include aprepitant for patients undergoing high-risk chemotherapy. In the Yeo et al[8] trial, rates of both total control and complete protection were marginally higher among patients who received ondansetron and dexamethasone compared with those who also received aprepitant (Data Supplement). The inconsistency of the main outcome measures in the Yeo et al trial compared with data that support use of aprepitant[5,6] is likely related to the small sample size.

An equivalency study including more than 2,200 patients compared fosaprepitant, an intravenous formulation of aprepitant, with oral aprepitant.[4,42] Findings demonstrate equivalence between the two agents for complete response and both emesis and nausea control. Fosaprepitant is dosed intravenously only once before chemotherapy and is endorsed by the Committee as an acceptable NK_1 receptor antagonist.

The pilot study by Herrington et al[5] compared one oral dose (125 mg) with the standard 3 days of oral aprepitant. No differences in rates of complete response and emetic episodes for the overall study period were reported. Additional studies to validate the noninferiority of single-day oral aprepitant dosing are necessary to establish the equivalence of the two oral dosing regimens.

A pilot study, presented at the 2010 MASCC meeting, compared olanzapine with aprepitant, both in combination with palonosetron and dexamethasone.[7] Patients randomly assigned to olanzapine experienced complete response rates similar to those of patients who received aprepitant (Data Supplement). The olanzapine arm was superior for nausea control during the overall study period ($P < .01$). Additional trials are necessary to define the role of olanzapine in this setting.

The combination of an anthracycline and cyclophosphamide was reclassified based on the high emetic potential of the agents when used together. Data from placebo-controlled studies indicate that this combination causes vomiting in 85% of patients not receiving antiemetic prophylaxis.[39] This borders on the 90% cutoff originally defined for highly emetogenic agents in the 1997 article published by Hesketh et al.[39] The most recent antiemetic guideline from MASCC recommends treating patients who receive this chemotherapy regimen with the same agents used for highly emetogenic antineoplastic therapies.[41] The 2011 ASCO Update Committee concurs.

Clinical Question 2

What is the optimal treatment to prevent nausea and vomiting from moderately emetogenic antineoplastic agents?

Recommendation 2. The two-drug combination of palonosetron (day 1 only) and dexamethasone (days 1 through 3) is recommended for patients receiving moderately emetogenic chemotherapy. If palonosetron is not available, clinicians may substitute a first generation $5\text{-}HT_3$ receptor antagonist, preferably granisetron or ondansetron.

Limited evidence also supports adding aprepitant to the combination. Should clinicians opt to add aprepitant for patients receiving moderate-risk chemotherapy, any one of the $5\text{-}HT_3$ receptor antagonists is appropriate.

Literature update and analysis 2a: $5\text{-}HT_3$ receptor antagonist equivalency. The Update Committee evaluated the therapeutic equivalence of the $5\text{-}HT_3$ receptor antagonists (ondansetron, granisetron, dolasetron, tropisetron, and palonosetron). Of particular interest was palonosetron, a second-generation $5\text{-}HT_3$ receptor antagonist with a longer half-life.

A review of $5\text{-}HT_3$ receptor antagonists used to prevent chemotherapy-induced nausea and vomiting from the Cochrane Collaboration was identified.[15] Most trials (16 trials; 7,808 patients) compared ondansetron and granisetron. Few involving dolasetron and tropisetron were identified, and only one study with palonosetron was included,[13] which is also described in this section. Findings from the Cochrane systematic review suggest equivalency between ondansetron and granisetron. This is supported by a meta-analysis of nine trials completed by the review authors (Data Supplement). Results indicate similar efficacy with respect to both nausea and vomiting outcomes during acute and delayed treatment phases as well as a combined nausea and vomiting end point. The adverse event profiles of these two first-generation $5\text{-}HT_3$ receptor antagonists were generally similar.

Another meta-analysis from Jordan et al[43] assessed only first-generation $5\text{-}HT_3$ receptor antagonists. This analysis supported equivalency of granisetron and ondansetron, considering data from 27 published trials. Additional evaluation from the report by Jordan et al indicates that granisetron is superior to tropisetron.

Three studies compared palonosetron, with ondansetron[12] and granisetron.[13,14] Findings from the two larger studies[12,13] suggest that palonosetron provides superior protection against both nausea and vomiting, particularly during the period from 24 to 120 hours after chemotherapy (Data Supplement). Complete response rates were 48% and 57% (both with 0.75 mg of palonosetron), compared with 39% and 45%, from Aapro et al[12] and Saito et al[13] studies, respectively. However, findings from the third study yielded a nonsignificant difference in complete response during the first 24 hours after chemotherapy.[14] Complete response rates during the delayed phase were 83% versus 72% ($P < .07$), comparing palonosetron with granisetron. Each arm included 104 patients in this noninferiority trial not designed to assess between-group differences.

These studies were conducted in a combined emetic risk population, but not in a non-AC moderately emetogenic population, comparing palonosetron with a first-generation $5\text{-}HT_3$ receptor antagonist, in which dexamethasone was also included. The preference for palonosetron is an extrapolation from the Saito et al[13] data; when an NK_1 receptor antagonist was not employed in the setting of cisplatin and AC chemotherapy, the combination of palonosetron and dexamethasone was superior to that of granisetron and dexamethasone. By inference, with non-AC moderately emetogenic chemotherapy, the combination of palonosetron and dexamethasone is also likely to be superior to that of a first-generation $5\text{-}HT_3$ receptor antagonist and dexamethasone.

A study in *Japanese Journal of Oncology* compared ramosetron and granisetron, both combined with dexamethasone, in patients receiving either moderate or highly emetic chemotherapy.[16] Findings indicate similar rates of complete response during the first 24 hours after chemotherapy, meeting the prespecified noninferiority margin of 15%. Importantly, the efficacy of ramosetron during the 7 days after chemotherapy has yet to be published.

Literature update and analysis 2b: NK_1 receptor antagonist for moderately emetogenic chemotherapy. One trial evaluated the benefits of adding aprepitant to antiemetic regimens for patients undergoing moderately emetogenic chemotherapy.[11] Subgroup analyses were completed according to type of chemotherapy received: AC or non-AC regimen (Data Supplement). Improved CINV protection with aprepitant was noted.

An advantage of using aprepitant with moderate-risk agents is the shorter duration of dexamethasone treatment required. Patients receive only one dose of dexamethasone on day 1,[44] compared with 3 days without aprepitant.

Literature update and analysis 2c: Dexamethasone dosing. The literature search identified two trials,[9,45] both of which evaluated 1-day dexamethasone dosing versus 3-day dosing in combination with intravenous palonosetron. Findings from both trials suggest similar outcomes between patients who received 1 versus 3 days of dexamethasone. Importantly, both trials accrued patients who received combined anthracycline and cyclophosphamide and patients receiving moderately emetogenic chemotherapy regimens. Additional trials validating these findings may warrant a change to the current recommendation.

Clinical Question 3

What is the optimal treatment to prevent nausea and vomiting from low emetogenic antineoplastic agents?

Recommendation 3. A single 8-mg dose of dexamethasone before chemotherapy is suggested. No change from 2006.

Literature update and analysis 3. No new evidence was identified.

Clinical Question 4

What is the optimal treatment to prevent nausea and vomiting from minimally emetogenic antineoplastic agents?

Recommendation 4. No antiemetic should be administered routinely before or after chemotherapy. No change from the original guideline.

Literature update and analysis 4. No new evidence was identified.

Clinical Question 5

What is the optimal treatment to prevent nausea and vomiting from combination chemotherapy?

Recommendation 5. Patients should be administered antiemetics appropriate for the component chemotherapeutic (antineoplastic) agent of greatest emetic risk. No change from the original guideline. Anthracycline-cyclophosphamide combinations are now classified as highly emetogenic.

Literature update and analysis 5. No new evidence was identified.

Clinical Question 6

What is the role of adjunctive drugs for nausea and vomiting induced by cancer treatments?

Recommendation 6. Lorazepam and diphenhydramine are useful adjuncts to antiemetic drugs but are not recommended as single-agent antiemetics. No change from 2006.

Literature update and analysis 6. No new evidence was identified. The search completed for this guideline update identified one study[33] that evaluated adjunctive therapies for patients undergoing chemotherapy. This trial evaluated the utility of incorporating olanzapine into antiemetic regimens.

Tan et al[33] evaluated the role of olanzapine in combination with azasetron and dexamethasone. Benefits of olanzapine were most noted during the delayed period (Data Supplement). Health-related quality of life data also suggested benefits of olanzapine, particularly with respect to nausea and vomiting control as well as appetite loss.

Clinical Question 7

What is the role of complementary and alternative medicine therapies to prevent or control nausea and vomiting induced by chemotherapy?

Recommendation 7. No published randomized controlled trial data meeting the inclusion criteria are currently available to support a recommendation about such therapies.

Literature update and analysis 7. At the 2009 ASCO Annual Meeting, a phase III trial of ginger was presented.[32] No significant differences in the prevalence of vomiting and nausea between patients who received ginger and those who received placebo were reported (Data Supplement).

The Cochrane Collaboration published a systematic review in early 2010 that evaluated the benefits of acupuncture-point stimulation for chemotherapy-induced nausea and vomiting.[35] This effort did not meet prespecified inclusion and exclusion criteria for this systematic review. A number of different modalities were considered, including stimulation with needles, electroacupuncture, manual acupuncture, acupressure, and noninvasive electrostimulation.

Perhaps the most relevant finding from this trial[35] is the seemingly protective effect of self-administered acupressure with respect to nausea. This benefit, according to data reviewed in the report, is only apparent on the day of chemotherapy administration and offers no protective effects against emesis. This approach may offer benefits when combined with the appropriate pharmacologic intervention. It may also be a beneficial approach for patients with anticipatory or uncontrolled nausea and vomiting.

SPECIAL POPULATIONS

Clinical Question 8

What is the optimal treatment to prevent nausea and vomiting associated with cancer therapy for pediatric patients?

Recommendation 8. The combination of a 5-HT_3 receptor antagonist plus a corticosteroid is suggested before chemotherapy in children receiving chemotherapy of high or moderate emetic risk. Because of the variation of pharmacokinetic parameters in children, weight-based doses of 5-HT_3 receptor antagonists higher than those used in adults may be required for antiemetic protection. No change from 2006.

Literature update and analysis 8. The Cochrane Collaboration published a systematic review of available therapies to treat and prevent CINV in children.[46] A total of 28 trials were identified, but few trials had similarities in intervention characteristics, so the review was primarily qualitative. The authors reported that the addition of dexamethasone to the newer 5-HT_3 receptor antagonists provides benefits in the highly emetic setting, based on the one pooled analysis completed. Qualitative assessment suggests that the newer 5-HT_3 receptor antagonists are superior to the early agents in this class.

Two trials were also identified during the literature search. One trial assessed the use of aprepitant in this population,[29] and the second evaluated the efficacy and safety of palonosetron in pediatric patients.[30]

Clinical Question 9

What is the optimal treatment to prevent nausea and vomiting in patients who are undergoing high-dose chemotherapy with stem-cell or bone marrow transplantation?

Recommendation 9. A 5-HT_3 receptor antagonist combined with dexamethasone is recommended. Aprepitant should be considered, although evidence to support its use is limited.

Literature update and analysis 9. Two new studies were identified; one was presented at the annual meeting of the American Society of Hematology and the other at the ASCO meeting.[24,25] Giralt et al[24] detailed superior emetic control with palonosetron (Data Supplement); data suggest that 2 days of palonosetron therapy will decrease the likelihood of CINV compared with 1 day or, alternatively, 3 days of palonosetron. The study[25] presented at the American Society of Hematology meeting compared treatment with aprepitant versus placebo, both dosed on each day of the chemotherapy conditioning regimen. All patients also received ondansetron and dexamethasone daily. Patients in the aprepitant arm experienced markedly improved vomiting control (Data Supplement). The Update Committee believes this trial provides evidence of benefit with an NK_1 antagonist in patients undergoing high-dose chemotherapy before transplantation.

Clinical Question 10

What is the optimal treatment to prevent nausea and vomiting for patients receiving multiday chemotherapy?

Recommendation 10. It is suggested that antiemetics appropriate for the emetogenic risk class of the chemotherapy be administered for each day of the chemotherapy and for 2 days after, if appropriate. No change from the original guideline. The Update Committee suggests, on the basis of limited data, that patients receiving 5-day cisplatin regimens be treated with a 5-HT_3 receptor antagonist in combination with dexamethasone and aprepitant.

Literature update and analysis 10. The literature search identified one trial of patients receiving 5-day cisplatin for germ cell tumors.[28] The study evaluated the utility of incorporating metopimazine with tropisetron. The small trial findings suggest improved nausea and vomiting control with this adjunctive agent (Data Supplement).

A noninferiority, placebo-controlled trial was conducted with the newly approved granisetron transdermal system.[23] This alternative delivery method was evaluated in patients receiving either moderately or highly emetogenic chemotherapy for multiple, consecutive days (Data Supplement). The trial found treatment with the granisetron patch to be noninferior to oral daily dosing of the same 5-HT_3 receptor antagonist.

Clinical Question 11

What is the optimal antiemetic regimen for patients who experience nausea and vomiting secondary to cancer therapy despite optimal prophylaxis?

Recommendation 11. Language from the 2006 guideline was reformatted for clarity. Clinicians should (1) re-evaluate emetic risk, disease status, concurrent illnesses, and medications; (2) ascertain that the best regimen is being administered for the emetic risk; (3) consider adding lorazepam or alprazolam to the regimen; and (4) consider adding olanzapine to the regimen or substituting high-dose intravenous metoclopramide for the 5-HT_3 receptor antagonist or adding a dopamine antagonist to the regimen.

Literature update and analysis 11. No new evidence was identified.

Table 4. Emetic Risk by Site of Radiation Therapy

Emetic Risk	Site of Radiation Therapy
High	Total-body irradiation
	Total nodal irradiation
Moderate	Upper abdomen
	Upper body irradiation
	Half-body irradiation
Low	Cranium
	Craniospinal
	Head and neck
	Lower thorax region
	Pelvis
Minimal	Extremities
	Breast

NOTE. Data adapted.[41]

Clinical Question 12

What treatment options are available for patients who experience anticipatory nausea and vomiting?

Recommendation 12. Use of the most active antiemetic regimens appropriate for the chemotherapy being administered to prevent acute or delayed emesis is suggested. Such regimens should be used with initial chemotherapy, rather than assessing the patient's emetic response with less effective treatment. If anticipatory emesis occurs, behavioral therapy with systematic desensitization is effective and suggested. No change from the original guideline.

Literature update and analysis 12. No new evidence was identified.

RADIATION-INDUCED NAUSEA AND VOMITING

This guideline update includes an updated risk stratification table according to site of radiation treatment. MASCC updated the radiation therapy emetic risk table at the MASCC/European Society for Medical Oncology 2009 consensus conference (Table 4); this was adopted by ASCO for this guideline update.[41] Dosing schedules, according to risk level, are detailed in Table 5.

Clinical Question 13

What is the optimal prophylaxis for nausea and vomiting caused by high emetic risk radiation therapy?

Recommendation 13. On the basis of extrapolation from indirect evidence, the Update Committee recommends that all patients receive a 5-HT_3 receptor antagonist before each fraction and for at least 24 hours after completion of radiotherapy. Patients should also receive a 5-day course of dexamethasone during fractions 1 to 5.

Literature update and analysis 13. No new evidence was identified. The updated recommendation was modified to suggest dexamethasone for all patients, based on evidence relevant to the moderate-risk category.[38] The Update Committee speculates that patients undergoing more highly emetogenic therapy would also experience a benefit.

Clinical Question 14

What is the optimal prophylaxis for nausea and vomiting caused by moderate emetic risk radiation therapy?

Recommendation 14. The Update Committee recommends that patients receive a 5-HT_3 receptor antagonist before each fraction for

Table 5. Antiemetic Dosing by Radiation Risk Category

Risk Category	Dose	Schedule
High emetic risk		
5-HT_3 antagonist		5-HT_3 antagonist before each fraction throughout XRT; continue for at least 24 hours after completion of XRT
Granisetron*	2 mg oral; 1 mg or 0.01 mg/kg IV	
Ondansetron*	8 mg oral twice daily; 8 mg or 0.15 mg/kg IV	
Palonosetron†	0.50 mg oral; 0.25 mg IV	
Dolasetron	100 mg oral only	
Tropisetron	5 mg oral or IV	
Corticosteroid		
Dexamethasone	4 mg oral or IV	During fractions 1-5
Moderate emetic risk		
5-HT_3 antagonist	Any of the above listed agents are acceptable; note preferred options†	5-HT_3 antagonist before each fraction throughout XRT
Corticosteroid		
Dexamethasone	4 mg IV or oral	During fractions 1-5
Low emetic risk		
5-HT_3 antagonist	Any of the above listed agents are acceptable; note preferred options	5-HT_3 either as rescue or prophylaxis; if rescue is used, then prophylactic therapy should be given until the end of XRT
Minimal emetic risk		
5-HT_3 antagonist	Any of the above listed agents are acceptable; note preferred options	Patients should be offered either class as rescue therapy; if rescue is used, then prophylactic therapy should be given until the end of XRT
Dopamine receptor antagonist		
Metoclopramide	20 mg oral	
Prochlorperazine	10 oral or IV	

Abbreviations: 5-HT_3, 5-hydroxytryptamine-3; IV, intravenous; XRT, radiation therapy.
*Preferred agents.
†No data are currently available on the appropriate dosing frequency with palonosetron in this setting. The Update Committee suggests that dosing every second or third day may be appropriate for this agent.

the entire course of radiotherapy. Patients may be offered a short course of dexamethasone during fractions 1 to 5.

Literature update and analysis 14. Only one new trial was identified.[38] This compared the addition of a 5-day course of dexamethasone during the first five fractions of radiation with placebo among patients undergoing radiation to the upper abdomen. Only two comparisons were statistically significant; both were secondary end points and considered the whole study period (fractions 1 to 15). The addition of dexamethasone proved superior for complete emetic protection (23% *v* 12%; $P = .02$) and lower average nausea score (0.28 *v* 0.39; $P = .03$). Complete nausea control showed a trend favoring dexamethasone treatment (50% *v* 38%; $P = .06$) during the first five fractions. Patients were also less likely to use rescue medications (71% *v* 82%; $P = .09$) throughout the entire study period.

Clinical Question 15

What is the optimal treatment to manage nausea and vomiting associated with low emetic risk radiation therapy?

Recommendation 15. The Update Committee recommends a 5-HT_3 receptor antagonist alone as either prophylaxis or rescue. For patients who experience RINV while receiving rescue therapy only, prophylactic treatment should continue until radiotherapy is complete.

Literature update and analysis 15. The recommendation was modified to include rescue therapy. Previously published studies suggest that prophylactic treatment does not offer benefits over rescue therapy.

Clinical Question 16

What is the optimal treatment to manage nausea and vomiting associated with minimal emetic risk radiation therapy?

Recommendation 16. Patients should receive rescue therapy with either a dopamine receptor antagonist or a 5-HT_3 receptor antagonist. Prophylactic antiemetics should continue throughout radiation treatment if a patient experiences RINV while receiving rescue therapy.

Literature update and analysis 16. No new evidence was identified.

Clinical Question 17

What is the optimal treatment to manage nausea and vomiting during concurrent radiation and chemotherapy?

Recommendation 17. Patients should receive antiemetic prophylaxis according to the emetogenicity of chemotherapy, unless the emetic risk with the planned radiotherapy is higher. No change from the original guideline.

Literature update and analysis 17. No new evidence was identified.

DRUG FORMULATIONS AND AGENT DOSING

A study published in 2007 compared an orally disintegrating tablet of ondansetron with a standard tablet[22] (Data Supplement). No differences were reported in emesis or nausea control between the two agents. Notably, it is not clear whether this study was designed as a nonequivalence trial a priori. The orally disintegrating tablet formulation is an acceptable alternative to the standard ondansetron tablet.

Two antiemetic agents have received regulatory approval in alternative formulations since the 2006 update. Granisetron is also available as a transdermal patch that delivers therapy over 7 days. As described earlier, this is an option for patients receiving multiday chemotherapy regimens.[47] The Update Committee also suggests that the granisetron patch may be useful for patients undergoing high- or moderate-risk radiation.

Oral palonosetron was approved by the US Food and Drug Administration in 2008.[48] Data detailing antiemetic similarity of the oral and intravenous formulations and agent safety were presented at the 2007 European Cancer Organisation meeting.[18] This trial also supported the 0.50-mg dose.

Three studies assessed dosing of intravenous palonosetron. A meta-analysis of eight studies suggested similar outcomes (Data Supplement) with respect to complete response among patients treated with either 0.25-mg or 0.75-mg doses.[20] The other two trials reported that a dose of 0.075 mg is clearly inferior to both 0.25-mg and 0.75-mg doses.[19,21]

PATIENT AND CLINICIAN COMMUNICATION

The purpose of this section is to address aspects of patient-provider communication that play a role in decision making about antiemetic therapy and the selection of agents. The Update Committee encourages clinicians to provide patients with a prescription for a rescue antiemetic therapy before the patient leaves the treatment facility on the first day of treatment. Data suggest that physicians frequently underestimate rates of nausea and vomiting secondary to radiation therapy and chemotherapy.[49]

To ensure optimal symptom management, clinicians should assess symptoms throughout the course of therapy. Clinicians and clinical researchers should consider collecting direct reports of symptom presence and severity by patients with a checklist. Patient response to treatment may change over time, thus requiring ongoing assessments and modification to antiemetic strategies. For example, the National Cancer Institute is developing a Patient-Reported Outcomes version of its Common Terminology Criteria for Adverse Events, which includes two items to assess nausea.[50] These items are as follows: (1) "In the last 7 days, how OFTEN did you have NAUSEA?" (Never/Rarely/Occasionally/Frequently/Almost constantly) and (2) "In the last 7 days, what was the SEVERITY of your NAUSEA at its WORST?" (None/Mild/Moderate/Severe/Very severe).

Clinicians and patients are also encouraged to discuss cost of treatment (Table 6). This should occur particularly to assess if cost is prohibitive, is a hardship to patients, or may affect treatment compliance.

Table 6. Antiemetic Estimated Cost Table

Agent	Price per Dose (USD)	Total Cost per Treatment Cycle (USD)*
NK_1 antagonists		
Aprepitant, 125 mg oral	150.45	343.03
Aprepitant, 80 mg oral	96.29	
Fosaprepitant, 150 mg IV	262.65	262.65
$5\text{-}HT_3$ antagonists		
Granisetron, 2 mg oral	0.68	0.68
Granisetron, 1 mg IV	17.92	17.92
Ondansetron, 8 mg oral	1.04	2.08
Ondansetron, 8 mg IV	1.19	2.38
Palonosetron, 0.25 mg IV†	188.70	188.70
Dolasetron, 100 mg oral	65.21	65.21
Ramosetron	Pricing not available	Pricing not available

NOTE. Drug prices were estimated from a third-party payer perspective, based on reimbursement rates from the Centers for Medicare and Medicaid Services as of the first quarter of 2011, computed at the manufacturer's average sales price plus 6%. Other treatment-related direct and indirect costs or discounts were not considered. Actual treatment costs and reimbursement vary considerably across regions, payers, institutions, and practices, as well as over time, and the reader should consult current local cost information specific to his or her specific context.

Abbreviations: $5\text{-}HT_3$, 5-hydroxytryptamine-3; IV, intravenous; NK_1, neurokinin 1; USD, US dollars.

*Treatment cycle assumed for single-day agents.

†Not available as a generic. Price based on Aloxi (Eisai, Woodcliff Lake, NJ; Helsinn, Lugano, Switzerland).

HEALTH DISPARITIES

Although ASCO clinical practice guidelines represent evidence-based expert recommendations on the best practices in disease management to provide the highest level of cancer care, it is important to note that many patients have limited access to medical care. Racial and ethnic disparities in health care contribute significantly to this problem in the United States. Patients of racial/ethnic minorities with cancer suffer disproportionately from comorbidities; they experience more substantial obstacles to receiving care, are more likely to be uninsured or underinsured, and are at greater risk of receiving poor-quality care than other Americans.[51-54] Other patients lack access to care because of geography and, specifically, distance from appropriate treatment facilities. Other factors associated with disparities in either health or health care include advanced age, low educational attainment, and low socioeconomic status. Awareness of these disparities in access to care should be considered in the context of this clinical practice guideline, and health care providers should strive to deliver the highest level of cancer care to these vulnerable populations.

FUTURE DIRECTIONS

For most patients, antiemetic regimens prevent emesis and lessen nausea during cancer therapy. However, patients continue to report nausea.[55] Identification of new approaches to improve nausea control is required. There has been limited research conducted in special populations of patients who may experience nausea and vomiting secondary to cancer treatment, particularly pediatric patients. Research to control symptoms in these patients is also necessary.

Similarly, few randomized controlled trials have investigated the role of antiemetics in patients undergoing radiation therapy. As such, limited evidence is available to support current recommendations. This lack of evidence is compounded by an underestimation of RINV among clinicians treating these patients.

Although most trials reported vomiting outcomes, nausea was less completely reported. Moreover, various measures to assess the incidence of nausea were utilized, and in some cases, methods to assess nausea were not specified by the authors. Some trials reported complete protection, which is defined as no nausea or vomiting and no use

of rescue therapy. The Update Committee recommends that studies including nausea as an outcome include patient-reported measures of nausea and other symptoms, consistent with the recommendations of the US Food and Drug Administration guidance in this area.[56] Standardized approaches to the assessment of nausea that can be employed across trials will allow for improved ability to compare regimens.

ADDITIONAL RESOURCES

Data Supplements, including evidence tables and clinical tools and resources, can be found at www.asco.org/guidelines/antiemetics. Patient information is available there as well as at www.cancer.net.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Appendix

Table A1. Update Committee Members, 2011

Member	Affiliation
Ethan Basch, MD, Co-Chair	Memorial Sloan-Kettering Cancer Center
Gary H. Lyman, MD, Co-Chair	Duke University
Paul J. Hesketh, MD, Steering Committee	Lahey Clinic Medical Center
Mark G. Kris, MD, Steering Committee	Memorial Sloan-Kettering Cancer Center
Maurice Chesney	Patient Representative
Rebecca Anne Clark-Snow, RN	Lawrence Memorial Hospital Oncology Center
Petra C. Feyer, MD	Vivantes Clinic of Radiooncology and Nuclear Medicine
Anne Marie Flaherty, RN	Memorial-Sloan Kettering Cancer Center
Barbara Freundlich, BA	Patient Representative
Gary Morrow, PhD	University of Rochester Cancer Center
Kamakshi V. Rao, PharmD	University of North Carolina Hospital
Rowena N. Schwartz, PharmD, BCOP, CPP	The Johns Hopkins Hospital

