National Comprehensive Cancer Network®

NCCN Clinical Practice Guidelines in Oncology™

Antiemesis

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NCCN Antiemesis Panel Members

*David S. Ettinger, MD/Chair †
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Debra K. Armstrong, RN #
Vanderbilt-Ingram Cancer Center

Sally Barbour, PharmD, BCOP ∑
Duke Comprehensive Cancer Center

Michael J. Berger, PharmD, BCOP ∑
Arthur G. James & Richard J. Solove Research Institute at The Ohio State University

Philip J. Bierman, MD † ‡
UNMC Eppley Cancer Center at The Nebraska Medical Center

Bob Bradbury, BCPS ∑
H. Lee Moffitt Cancer Center & Research Institute

Georgianna Ellis, MD †
Fred Hutchinson Cancer Research Center/ Seattle Cancer Care Alliance

Steve Kirkegaard, PharmD ∑
Huntsman Cancer Institute at the University of Utah

*Dwight D. Kloth, PharmD, FCCP, BCOP ∑
Fox Chase Cancer Center

*Mark G. Kris, MD †
Memorial Sloan-Kettering Cancer Center

Dean Lim, MD †
City of Hope

Michael Anne Markiewicz, PharmD ∑
University of Alabama at Birmingham Comprehensive Cancer Center

Lida Nabati, MD £ Þ
Dana-Farber/Brigham and Women's Cancer Center | Massachusetts General Hospital Cancer Center

Carli Nesheiwat, PharmD, BCOP ∑
St. Jude Children's Research Hospital/University of Tennessee Cancer Institute

Hope S. Rugo, MD † ‡
UCSF Helen Diller Family Comprehensive Cancer Center

Steven M. Sorscher, MD †
Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine

Lisa Stucky-Marshal, RN, MS #
Robert H. Lurie Cancer Center of Northwestern University

Barbara Todaro, PharmD ∑
Roswell Park Cancer Institute

Susan Urba, MD † £
University of Michigan Comprehensive Cancer Center

‡Hematology/hematology oncology
ÞInternal medicine
†Medical Oncology
#Nurse
∑Pharmacology
£Supportive Care including Palliative, Pain management, Pastoral care and Oncology social work
*Writing Committee member

Disclosure of Conflict of Interest

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Discussion

References

Clinical Trials: The NCCN believes that the best management for any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

To find clinical trials online at NCCN member institutions, click here: nccn.org/clinical_trials/physician.html

NCCN Categories of Evidence and Consensus: All recommendations are Category 2A unless otherwise specified.

See NCCN Categories of Evidence and Consensus

SUMMARY OF GUIDELINES UPDATES

Summary of the major changes in the 1.2009 version of the NCCN Antiemesis Guidelines from the 3.2008 version are:

AE-1

- **Added a new bullet to the Principles of Emesis Control in the Cancer Patient. The bullet states, "For multi-drug regimens, select antiemetic therapy based on drug with the highest emetic risk. See Emetogenic Potential of Antineoplastic Agents (AE-6)."**

AE-2 and AE-3

- **Based on recent FDA approval, added the transdermal patch containing 34.3 mg granisetron to the guidelines for emesis prevention in both high and moderate emetic risk chemotherapy.**
- **Added the oral dose of Palonosetron 0.5 mg PO on day 1 of chemotherapy for emesis prevention in both high and moderate emetic risk chemotherapy.**

AE-2, AE-3, and AE-4

- **Revised footnote b: "Antiemetic regimens should be chosen based on the drug with the highest emetic risk as well as patient specific risk factors."**

AE-3

- **Delete 4 mg PO or IV bid" for dexamethasone for days 2-3.**
- **Revised footnote f: "Aprepitant should be added (to dexamethasone and a 5-HT3 antagonist regimen) for select patients receiving other chemotherapies of moderate emetic risk (for example, carboplatin, cisplatin, doxorubicin, epirubicin, ifosfamide, irinotecan or methotrexate)."**

AE-4

- **Removed dosing for diphenhydramine from the pathway and added it to footnote "h".**

AE-5

- **Modified footnote "j" regarding use of olanzapine. The footnote states "See blackbox warning/label indication regarding type II diabetes, hyperglycemia and death in elderly dementia patients."**

AE-6

- **Added Bendamustine to the list of antineoplastic agents with moderate emetic risk.**

AE-7

- **Added ixabepilone and nilotinib to the list of antineoplastic agents with low emetic risk.**

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PRINCIPLES OF EMESIS CONTROL IN THE CANCER PATIENT

- **Prevention of nausea/vomiting is the goal.**
  - **The risk of nausea/vomiting for persons receiving chemotherapy of high and moderate emetic risk lasts for at least 4 days for high and 3 days for moderate. Patients need to be protected throughout the full period of risk.**
- **Oral and IV antiemetic formulations have equivalent efficacy.**
- **Consider the toxicity of the specific antiemetic(s).**
- **Choice of antiemetic(s) used should be based on the emetic risk of the therapy, prior experience with antiemetics, as well as patient factors.**
- **There are other potential causes of emesis in cancer patients.**
  These may include:
  - **Partial or complete bowel obstruction**
  - **Vestibular dysfunction**
  - **Brain metastases**
  - **Electrolyte imbalance: hypercalcemia, hyperglycemia, hyponatremia**
  - **Uremia**
  - **Concomitant drug treatments including opiates**
  - **Gastroparesis: tumor or chemotherapy (vincristine etc) induced.**
  - **Psychophysiologic:**
    - **Anxiety**
    - **Anticipatory nausea and vomiting**
- **For use of antiemetics for nausea and vomiting that are not related to radiation and/or chemotherapy, See NCCN Palliative Care Guidelines**
- **For multidrug regimens, select antiemetic therapy based on drug with the highest emetic risk. See Emetogenic Potential of Antineoplastic Agents (AE-6)**

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HIGH EMETIC RISK CHEMOTHERAPY - EMESIS PREVENTION[b,c]

High[a] →

- **Start before chemotherapy[b,c]**
  - **Aprepitant 125 mg PO day 1 or fosaprepitant 115 mg IV day 1[d], 80 mg PO daily days 2-3**
  - **and**
  - **Dexamethasone 12 mg PO or IV day 1, 8 mg PO or IV daily days 2-4**
  - **and**
  - **5-HT3 antagonist:[e]**
    Ondansetron 16-24 mg PO or 8-12 mg (maximum 32 mg) IV day 1
    or
    Granisetron 2 mg PO or 1 mg PO bid or 0.01 mg/kg (maximum 1 mg) IV day 1 or transdermal patch containing 34.3 mg granisetron applied 24-48 h prior to first dose of chemotherapy
    or
    Dolasetron 100 mg PO or 1.8 mg/kg IV or 100 mg IV day 1
    or
    Palonosetron 0.5 mg PO or 0.25 mg IV day 1
    and
  - **± Lorazepam 0.5-2 mg PO or IV or sublingual either every 4 or every 6 h prn days 1-4**

(category 1, for combined regimen)

→ **See Breakthrough Treatment (AE-5)**

See Principles of Emesis Control (AE-1)

[a] Data for post-cisplatin (≥ 50 mg/m^2) emesis prevention are category 1, others are category 2A.
[b] Antiemetic regimens should be chosen based on the drug with the highest emetic risk as well as patient specific risk factors.
[c] See Principles for Managing Multi-day Emetogenic Chemotherapy Regimens (AE-A).
[d] Fosaprepitant dimeglumine (115 mg) may be substituted for aprepitant (125 mg) 30 minutes prior to chemotherapy, on Day 1 only of the CINV regimen as an infusion administered over 15 minutes.
[e] Order of listed antiemetics does not reflect preference.

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MODERATE EMETIC RISK CHEMOTHERAPY - EMESIS PREVENTION[b,c]

Moderate[e] →

Day 1

- **Start before chemotherapy[b,c]**
  - **Aprepitant 125 mg PO or fosaprepitant 115 mg IV day 1[d] in select patients[f]**
  - **and**
  - **Dexamethasone 12 mg PO or IV**
  - **and**
  - **5-HT3 antagonist:[e]**
    Palonosetron 0.5 mg PO or 0.25 mg IV (category 1)
    or
    Ondansetron 16-24 mg PO or 8-12 mg (maximum 32 mg/day) IV (category 1)
    or
    Granisetron 1-2 mg PO or 1 mg PO bid (category 1) or 0.01 mg/kg (maximum 1 mg) IV or transdermal patch containing 34.3 mg granisetron applied 24-48 h prior to first dose of chemotherapy
    or
    Dolasetron 100 mg PO or 1.8 mg/kg or 100 mg IV (category 1)
    and
  - **± Lorazepam 0.5-2 mg PO or IV or sublingual either every 4 or every 6 h prn**

→

Days 2-3

- **Aprepitant 80 mg PO days 2-3 if used on Day 1**
  ± Dexamethasone 8 mg PO or IV daily
  or
- **Dexamethasone 8 mg PO or IV daily**
  or
- **5-HT3 antagonist:[g]**
  Ondansetron 8 mg PO bid or 16 mg PO daily or 8 mg (maximum 32 mg/day) IV
  or
  Granisetron 1-2 mg PO daily or 1 mg PO bid or 0.01 mg/kg (maximum 1 mg) IV
  or
  Dolasetron 100 mg PO daily or 1.8 mg/kg IV or
- **± Lorazepam 0.5-2 mg PO or IV or sublingual either every 4 or every 6 h prn**

→ **See Breakthrough Treatment (AE-5)**

[b] Antiemetic regimens should be chosen based on the drug with the highest emetic risk as well as patient specific risk factors.

[c] See Principles for Managing Multi-day Emetogenic Chemotherapy Regimens (AE-A).

[d] Fosaprepitant dimeglumine (115 mg) may be substituted for aprepitant (125 mg) 30 minutes prior to chemotherapy, on Day 1 only of the CINV regimen as an infusion administered over 15 minutes.

[e] Order of listed antiemetics does not reflect preference.

[f] Aprepitant should be added (to dexamethasone and a 5-HT3 antagonist regimen) for select patients receiving other chemotherapies of moderate emetic risk (for example, carboplatin, cisplatin, doxorubicin, epirubicin, ifosfamide, irinotecan or methotrexate).

[g] Data for post-carboplatin ≥ 300 mg/m^2, cyclophosphamide ≥ 600-1000 mg/m^2, doxorubicin ≥ 50 mg/m^2 emesis prevention are category 1.

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LOW AND MINIMAL EMETIC RISK CHEMOTHERAPY - EMESIS PREVENTION[b,c]

Low →

- **Start before chemotherapy[b,c]**
- **Repeat daily for fractionated doses of chemotherapy**
  - **Dexamethasone 12 mg PO or IV daily**
    or
  - **Prochlorperazine 10 mg PO or IV every 4 or every 6 h[h]**
    or
  - **Metoclopramide 10-40 mg PO or IV either every 4 or every 6 h[h]**
  - **± Lorazepam, 0.5-2 mg PO or IV either every 4 or every 6 h prn**

→ **Breakthrough Treatment For Chemotherapy Induced Nausea/vomiting (AE-5)**

Minimal → **No routine prophylaxis** → **Nausea/emesis (0–24 h)** → **Consider using antiemetics listed under primary prophylaxis as treatment for low emetogenic-potential drugs**

See Principles of Emesis Control (AE-1)

[b]Antiemetic regimens should be chosen based on the drug with the highest emetic risk as well as patient specific risk factors.
[c]See Principles for Managing Multi-day Emetogenic Chemotherapy Regimens (AE-A).
[h]Monitor for dystonic reactions; use diphenhydramine 25-50 mg PO or IV either every 4 or every 6 h for dystonic reactions.

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BREAKTHROUGH TREATMENT FOR CHEMOTHERAPY INDUCED NAUSEA/VOMITING[c,i]

No nausea/emesis → **No change in antiemetic regimen**

Any nausea/emesis →

- **General principle of breakthrough treatment is to give an additional agent from a different drug class prn**
  - **Prochlorperazine 25 mg supp pr every 12 h or 10 mg PO or IV every 4 or every 6 h[h]**
  - **or**
  - **Metoclopramide 10-40 mg PO or IV either every 4 or every 6 h[h]**
  - **or**
  - **Lorazepam 0.5-2 mg PO either every 4 or every 6 h**
  - **or**
  - **Ondansetron 16 mg PO or 8 mg IV daily**
  - **or**
  - **Granisetron 1-2 mg PO daily or 1 mg PO bid or 0.01 mg/kg (maximum 1 mg) IV or transdermal patch containing 34.3 mg granisetron**
  - **or**
  - **Dolasetron 100 mg PO daily or 1.8 mg/kg IV or 100 mg IV**
  - **or**
  - **Haloperidol 1-2 mg PO every 4-6 h prn**
  - **or**
  - **Dronabinol 5-10 mg PO either every 3 or every 6 h**
  - **or**
  - **Nabilone 1-2 mg PO bid**
  - **or**
  - **Dexamethasone 12 mg PO or IV daily**
  - **or**
  - **Olanzapine 2.5-5 mg PO bid (category 2B)[j]**
  - **or**
  - **Promethazine 12.5-25 mg PO or IV every 4 h**

RESPONSE TO BREAKTHROUGH ANTIEMETIC TREATMENT

SUBSEQUENT CYCLES

Nausea and emesis controlled → **Continue breakthrough medications, on a schedule, not prn**

Nausea and/or emesis uncontrolled → **Consider changing antiemetic therapy to higher-level primary treatment**

See Principles of Emesis Control (AE-1)

[c] See Principles for Managing Multi-day Emetogenic Chemotherapy Regimens (AE-A).
[h] Monitor for dystonic reactions; use diphenhydramine 25-50 mg PO or IV either every 4 or every 6 h for dystonic reactions.
[i] See Principles of Managing Breakthrough Treatment (AE-B).
[j] See blackbox warning/label indication regarding type II diabetes, hyperglycemia and death in elderly dementia patients.

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EMETOGENIC POTENTIAL OF ANTINEOPLASTIC AGENTS

LEVEL	AGENT	
High emetic risk (> 90 % frequency of emesis)[k]	• AC combination defined as either doxorubicin or epirubicin with cyclophosphamide • Altretamine • Carmustine > 250 mg/m^2 • Cisplatin ≥ 50 mg/m^2 • Cyclophosphamide > 1,500 mg/m^2	• Dacarbazine • Mechlorethamine • Procarbazine (oral) • Streptozocin
Moderate emetic risk (30- 90 % frequency of emesis[k]	• Aldesleukin > 12-15 million units/m^2 • Amifostine > 300 mg/m^2 • Arsenic trioxide • Azacitidine • Bendamustine • Busulfan > 4 mg/d • Carboplatin • Carmustine ≤ 250 mg/m^2 • Cisplatin < 50 mg/m^2 • Cyclophosphamide ≤ 1,500 mg/m^2 • Cyclophosphamide (oral) • Cytarabine > 1 g/m^2 • Dactinomycin • Daunorubicin • Doxorubicin	• Epirubicin • Etoposide (oral) • Idarubicin • Ifosfamide • Imatinib (oral)[l] • Irinotecan • Lomustine • Melphalan > 50 mg/m^2 • Methotrexate 250 - > 1,000 mg/m^2 • Oxaliplatin > 75 mg/m^2 • Temozolomide (oral) • Vinorelbine (oral)

Low emetic risk, level 2 (See AE-7)

Minimal emetic risk, level 1 (See AE-7)

[k]Proportion of patients who experience emesis in the absence of effective antiemetic prophylaxis
[l]Daily use of antiemetics is not recommended based on clinical experience.

Adapted with permission from:
Hesketh PJ, et al. Proposal for classifying the acute emetogenicity of cancer chemotherapy. J Clin Oncol 1997;15:103-109.
Grunberg SM, Osoba D, Hesketh PJ, et al. Evaluation of new antiemetic agents and definition of antineoplastic agent emetogenicity---an update. Support Care Cancer 2005;13:80-84. Epub 2004 Dec 14.

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EMETOGENIC POTENTIAL OF ANTINEOPLASTIC AGENTS

LEVEL	AGENT	
Low emetic risk (10-30 % frequency of emesis)[k]	• Amifostine ≤ 300 mg • Bexarotene • Capecitabine • Cytarabine (low dose) 100-200 mg/m^2 • Docetaxel • Doxorubicin (liposomal) • Etoposide • Fludarabine (oral) • 5-Fluorouracil • Gemcitabine	• Ixabepilone • Methotrexate > 50 mg/m^2 < 250 mg/m^2 • Mitomycin • Mitoxantrone • Nilotinib • Paclitaxel • Paclitaxel-albumin • Pemetrexed • Topotecan • Vorinostat
Minimal emetic risk (< 10 % frequency of emesis)[k]	• Alemtuzumab • Alpha Interferon • Asparaginase • Bevacizumab • Bleomycin • Bortezomib • Busulfan • Cetuximab • Chlorambucil (oral) • Cladribine (2-chlorodeoxyadenosine) • Decitabine • Denileukin diftitox • Dasatinib • Dexrazoxane • Erlotinib • Fludarabine • Gefitinib • Gemtuzumab ozogamicin • Hydroxyurea (oral)	• Lapatinib • Lenalidomide • Melphalan (oral low-dose) • Methotrexate ≤ 50 mg/m^2 • Nelarabine • Panitumumab • Pentostatin • Rituximab • Sorafenib • Sunitinib • Temsirolimus • Thalidomide • Thioguanine (oral) • Trastuzumab • Valrubicin • Vinblastine • Vincristine • Vinorelbine

[k]Proportion of patients who experience emesis in the absence of effective antiemetic prophylaxis

Adapted with permission from:

Hesketh PJ, et al. Proposal for classifying the acute emetogenicity of cancer chemotherapy. J Clin Oncol,1997; 15: 103-9.

Grunberg SM, Osoba D, Hesketh PJ, et al. Evaluation of new antiemetic agents and definition of antineoplastic agent emetogenicity---an update. Support Care Cancer 2005;13:80-84. Epub 2004 Dec 14.

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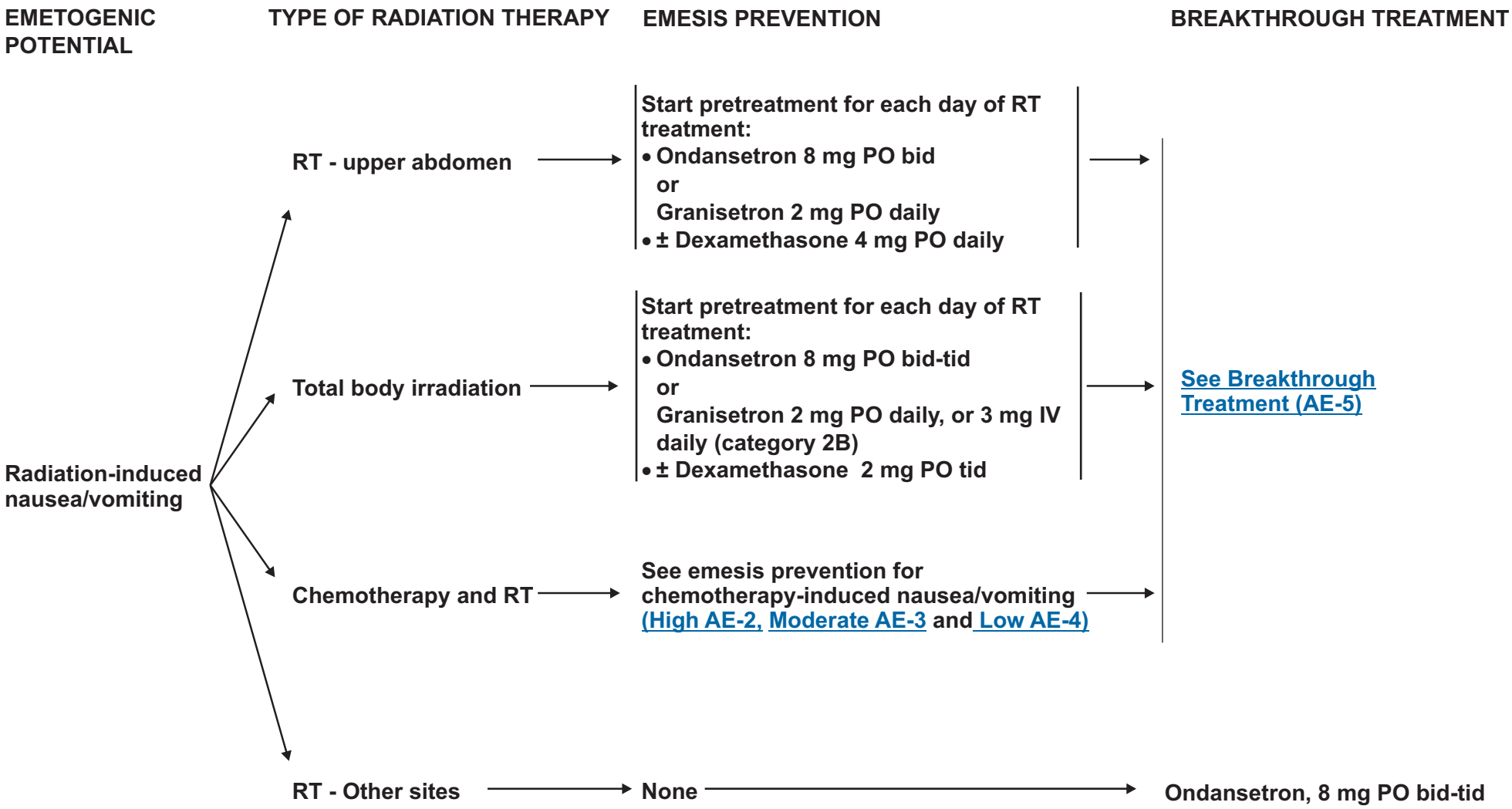
Antiemesis



See Principles of Emesis Control (AE-1)

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ANTICIPATORY EMESIS PREVENTION/TREATMENT

Anticipatory nausea/vomiting →

Prevention:
- Use optimal antiemetic therapy during every cycle of treatment

Behavioral therapy:
- Relaxation/systematic desensitization
- Hypnosis/guided imagery
- Music therapy

Acupuncture/acupressure

Alprazolam 0.5-2 mg PO tid beginning on the night before treatment

Lorazepam 0.5-2 mg PO on the night before and morning of treatment

See primary and breakthrough treatments for chemotherapy-induced nausea/vomiting (Antiemesis TOC)

See Principles of Emesis Control (AE-1)

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PRINCIPLES OF MANAGING MULTI-DAY EMETOGENIC CHEMOTHERAPY REGIMENS

- Patients receiving multi-day chemotherapy are at risk for both acute and delayed nausea and emesis based upon the emetogenic potential of the individual chemotherapy agents and their sequence. It is therefore difficult to recommend a specific antiemetic regimen for each day especially since acute and delayed emesis may overlap after the initial day of chemotherapy until the last day of chemotherapy. The period of risk for delayed emesis after chemotherapy administration has concluded also depends on the specific regimen and the emetogenic potential of the last chemotherapy agent administered in the regimen.

- Examples illustrating the above include BEP (bleomycin 30 units IV weekly, etoposide 100 mg/m^2 IV days 1-5 and cisplatin 20 mg/m^2 IV days 1-5) versus ASHAP (doxorubicin 25 mg/m^2 IV day 1, methylprednisolone 500 mg/day IV days 1-5, cisplatin 25 mg/m^2 IV continuous infusion days 1-4 followed by cytarabine 2000 mg/m^2 on day 5). BEP is moderately emetogenic with risk for emesis on days 1-8) whereas ASHAP is moderately emetogenic on days 1-4 but becomes highly emetogenic on day 5 due to the administration of high-dose cytarabine). Risk for acute and delayed emesis for ASHAP may last up to 10 days.

Accordingly, the panel recommends the following as general principles (category 2B).

- A 5-HT3 receptor antagonist should be administered prior to each days 1st dose of moderately or highly-emetogenic chemotherapy.
- Dexamethasone should be administered once daily either orally or intravenously for every day of moderately or highly emetogenic chemotherapy and for 2-3 days after chemotherapy for regimens that are likely to cause significant delayed-emesis. Dexamethasone should not be added when the chemotherapy regimen already includes a corticosteroid (as in ASHAP illustrated above).
- Intravenous palonosetron may be used prior to the start of a three day chemotherapy regimen instead of multiple daily doses of oral or intravenous 5-HT3 receptor antagonists. Repeat dosing of palonosetron 0.25 mg IV is likely to be safe, based upon the dose ranging Phase II trial where up to 30 times the FDA approved dose (90 mcg/kg) was administered and the 3 Phase III trials that evaluated palonosetron 0.75 mg as a single fixed dose. Compared to the approved dose of palonosetron 0.25 mg, these higher doses were not associated with significantly different grades or durations of adverse events. In terms of efficacy, need for repeat dosing with palonosetron, either daily or less frequently, in the setting of multi-day chemotherapy is not yet known.
- Aprepitant may be used for multi-day chemotherapy regimens likely to be highly-emetogenic and associated with significant risk for delayed nausea and emesis. As per the labeled indication aprepitant should be administered 125 mg orally 1 hour prior to chemotherapy on day one, along with a 5-HT3 receptor antagonist and dexamethasone. Aprepitant 80 mg should be administered daily on days 2 and 3 after the start of chemotherapy along with dexamethasone. Based upon Phase II data, aprepitant 80 mg may be safely administered on days 4 and 5 after chemotherapy. It is not yet known if dosing aprepitant after day 3 improves control of nausea or emesis in this clinical setting.

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PRINCIPLES FOR MANAGING BREAKTHROUGH EMESIS

- Breakthrough emesis presents a difficult situation as correction of refractory ongoing nausea and vomiting is often challenging to reverse. It is generally far easier to prevent nausea and vomiting than to treat it.
- The general principle of breakthrough treatment is to give an additional agent from a different drug class. No one treatment is better than the other for managing breakthrough emesis.
- One should strongly consider routine, around the clock, administration rather than PRN dosing.
- The PO route is not likely to be feasible due to ongoing vomiting, therefore, rectal or IV therapy is often required.
- Multiple concurrent agents, perhaps in alternating schedules or by alternating routes, may be necessary. Dopamine antagonists (eg, metoclopramide), haloperidol, corticosteroids and agents such as lorazepam may be required.
- Ensure adequate hydration or fluid repletion, simultaneously checking and correcting any possible electrolyte abnormalities.
- Prior to administering the next cycle of chemotherapy the patient should be reassessed, with attention to various possible non chemotherapy related reasons for breakthrough emesis with the current cycle:
  - Brain metastases
  - Electrolyte abnormalities
  - Tumor infiltration of the bowel or other gastrointestinal abnormality
  - Other comorbidities
- Prior to the next cycle of chemotherapy, reassess both the Day 1 and post chemo antiemetic regimen which did not protect the patient during the present cycle and consider alternatives: (Suggestions are not in order of preference)
  - Addition of aprepitant
  - Additional other concomitant antiemetics, eg, dopamine antagonists (metoclopramide) or haloperidol
  - Possibly adjusting dose(s), either intensity or frequency, of the 5-HT3 antagonist. Based on the patient's experiences, the chemotherapy regimen in question may actually be more emetogenic than generally classified (eg, Hesketh method)
  - Possibly switching to a different 5-HT3 although not necessarily likely to be effective, anecdotal and limited investigational trial data suggest it may sometimes be efficacious.
  - If the goal of chemotherapy is palliative or adjuvant, consider other appropriate regimens, if any, which might be less emetogenic.
  - Addition of an anxiolytic agent in combination with the antiemetic agents.
- If patient has dyspepsia consider antacid therapy (H2 blocker or proton pump inhibitor).

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Discussion

NCCN Categories of Evidence and Consensus

Category 1: The recommendation is based on high-level evidence (e.g. randomized controlled trials) and there is uniform NCCN consensus.

Category 2A: The recommendation is based on lower-level evidence and there is uniform NCCN consensus.

Category 2B: The recommendation is based on lower-level evidence and there is nonuniform NCCN consensus (but no major disagreement).

Category 3: The recommendation is based on any level of evidence but reflects major disagreement.

All recommendations are category 2A unless otherwise noted.

Overview

Chemotherapy-induced vomiting (emesis) and nausea can significantly affect a patient's quality of life, leading to poor compliance with further chemotherapy treatment. In addition, nausea and vomiting can result in metabolic imbalances, degeneration of self-care and functional ability, nutrient depletion, anorexia, decline of the patient's performance status and mental status, wound dehiscence, esophageal tears, and withdrawal from potentially useful or curative anticancer treatment.[1-4]

The incidence and severity of nausea and/or vomiting in patients receiving chemotherapy are affected by numerous factors, including: (1) the specific chemotherapeutic agents used; (2) dosage of the agents; (3) schedule and route of administration of the agents; and (4) individual patient variability (for example, age, sex, prior chemotherapy, history of alcohol use). Approximately 70% to 80% of all cancer patients receiving chemotherapy experience nausea and/or vomiting,[5,6] whereas 10% to 44% experience anticipatory nausea and/or vomiting.[7-10] Patients often experience more nausea than vomiting.[11]

Pathophysiology of Emesis

Vomiting results from stimulation of a multistep reflex pathway controlled by the brain. Vomiting is triggered by afferent impulses to the vomiting center (located in the medulla) from the chemoreceptor trigger zone, pharynx and gastrointestinal (GI) tract (via vagal afferent fibers), and cerebral cortex. Vomiting occurs when efferent impulses are sent from the vomiting center to the salivation center, abdominal muscles, respiratory center, and cranial nerves.[12]

The chemoreceptor trigger zone, vomiting center, and GI tract have many neurotransmitter receptors. Activation of these receptors by chemotherapeutic agents or their metabolites may be responsible for chemotherapy-induced emesis. The principal neuroreceptors involved in the emetic response are the serotonin (5-hydroxytryptamine [5-HT3]) and dopamine receptors.[13,14] Other neuroreceptors involved in emesis include acetylcholine, corticosteroid, histamine, cannabinoid, opiate, and neurokinin-1 (NK-1) receptors, which are located in the vomiting and vestibular centers of the brain.[15]

Antiemetic agents can block different neuronal pathways, exert their effects at different points during the course of emesis, or behave synergistically with other antiemetic agents to potentiate an antiemetic effect. When used at a certain concentration, each antiemetic agent predominantly blocks one receptor type. A final common pathway for emesis has yet to be identified. Therefore, no single agent can be expected to provide complete protection from the various emetic phases of chemotherapy.

Types of Nausea and/or Vomiting

Chemotherapy-Induced Nausea and/or Vomiting

Nausea and/or vomiting induced by chemotherapy is commonly classified as acute, delayed, anticipatory, breakthrough, or refractory. *Acute-onset* nausea and/or vomiting usually occurs within a few minutes to several hours after drug administration and commonly resolves within the first 24 hours. The intensity of acute-onset emesis generally peaks after 5 to 6 hours. The occurrence of acute emesis is influenced by the patient's age and gender (females and younger patients [age < 50 years] are more prone to emesis), environment in which chemotherapy is administered, whether the patient has a history of chronic alcoholism (which decreases the incidence of emesis) or motion sickness, previous episodes of nausea and vomiting, dosage of the emetogenic agent, and efficacy of the antiemetic regimen.[16,17]

Delayed-onset nausea and/or vomiting develops in patients more than 24 hours after chemotherapy administration.[16,17] It occurs commonly with the administration of cisplatin, carboplatin, cyclophosphamide, and/or doxorubicin. For cisplatin, emesis reaches its maximal intensity 48 to 72 hours after chemotherapy and can last 6 to 7 days.

Anticipatory nausea and/or vomiting occurs before patients receive their next chemotherapy treatment. Because it is a conditioned response, anticipatory emesis can occur only after a negative past experience with chemotherapy. The incidence of anticipatory nausea and/or vomiting ranges from 18% to 57%, and nausea is more common than vomiting.[18,19] Younger patients may be more susceptible to anticipatory nausea and vomiting, because they generally receive more aggressive chemotherapy and, overall, have poorer emesis control than older patients.[20] *Breakthrough* emesis refers to vomiting that occurs despite prophylactic treatment and/or requires “rescue” with antiemetic agents. *Refractory* emesis refers to emesis that occurs during subsequent treatment cycles when antiemetic prophylaxis and/or rescue have failed in earlier cycles.

Radiation-Induced Nausea and/or Vomiting

Patients receiving whole body or upper abdominal radiation therapy have the greatest likelihood of developing nausea and/or vomiting.[21,22] The GI tract (specifically, the small intestine) contains rapidly dividing cells that are particularly sensitive to radiation. In addition, the potential for nausea and vomiting increases with larger daily fractional doses of radiotherapy, larger total doses, and larger amounts of irradiated tissue. Total body irradiation, when given before bone marrow transplantation, also commonly induces nausea and/or vomiting.[22,23]

Emetogenicity of Chemotherapy

The frequency of chemotherapy-induced emesis depends primarily on the emetogenic potential of the specific chemotherapeutic agents used. Several classifications have been developed to define the emetogenicity of chemotherapy; however, none has been universally accepted.[12,24-27]

Hesketh and colleagues developed a classification of the acute emetogenicity of anticancer chemotherapeutic agents and developed an algorithm to define the emetogenicity of combination chemotherapeutic regimens.[28] The classification was updated by Grunberg and colleagues and divides chemotherapeutic agents into 4 levels according to the percentage of patients not receiving antiemetic prophylaxis who experience acute emesis.[29] This classification, which has been updated with recently introduced drugs, is used in these NCCN practice guidelines. Panel members from all of the published antiemetic treatment guidelines met to prepare a single consensus document. Although this process is ongoing, the consensus guidelines have been published.[30] NCCN guidelines currently outline treatment

using 4 categories of emetogenic potential (see AE-6 and AE-7), which correspond to the Grunberg classification as follows:

- High emetic risk—90% or more of patients experience acute emesis
- Moderate emetic risk—30% to 90% of patients experience acute emesis
- Low emetic risk—10% to 30% of patients experience acute emesis
- Minimal emetic risk—fewer than 10% of patients experience acute emesis.

In addition, the NCCN guidelines attempt to define antiemetic regimens for particular chemotherapy drugs that cover the entire duration of time a patient is at risk for nausea and vomiting. Panel members were concerned that some patients may not receive adequate prophylaxis for delayed emesis; therefore, the algorithms were revised for high and moderate emetogenic potential agents to incorporate a dosing schedule that covers both acute and delayed emesis into a single algorithm.

Types of Antiemetic Therapies

In general, to provide maximal protection against chemotherapy-induced emesis, antiemetic therapy should be initiated before chemotherapy. The antiemetic therapy should also be continued for the same length of time as the duration of the emetic activity of the chemotherapeutic agent being used. However, daily use of antiemetics is not recommended for some therapeutic agents that are taken long term (for example, imatinib) (see AE-6). Antiemetic agents can be administered by the oral, rectal, intravenous (IV), intramuscular, or transdermal route. When compared with other routes of administration, oral formulations of antiemetic agents are equally effective, safe, more convenient, and less costly. For patients unable to swallow or digest tablets because of emesis, IV antiemetics are required. In selected patients who are unable to swallow, transdermal antiemetics may be of value. Although studies may show drugs to be equally effective on a population basis, individual patients may respond differently. Therefore, some drug options may be based on a patient's individual experience.

Serotonin (5-HT3) Receptor Antagonists

The development of the 5-HT3–receptor antagonists (such as ondansetron, granisetron, dolasetron mesylate, palonosetron) represents a significant advance in antiemetic therapy.[31-33] All of these agents have been shown to be effective in controlling the acute nausea and/or vomiting associated with cancer chemotherapy.[33-47]

Palonosetron is a 5-HT3 antagonist with an approximately 100-fold higher binding affinity for the 5-HT3 receptor compared to the other serotonin antagonists (that is, ondansetron, granisetron, and dolasetron). It has a half-life of approximately 40 hours, which is significantly longer than other commercially available 5-HT3 antagonists.[33] Initial studies in patients receiving moderately emetogenic chemotherapy showed that a single IV dose of palonosetron was comparable to a single IV dose of dolasetron for the prevention of acute chemotherapy-induced nausea and emesis; however, IV palonosetron was superior to dolasetron in preventing delayed emesis.[48] The safety and side-effect profiles of palonosetron were indistinguishable from the control 5-HT3 antagonists (ondansetron and dolasetron) using data submitted to the Food and Drug Administration (FDA). Palonosetron is administered intravenously or orally. Intravenous palonosetron is FDA approved as a single dose on day 1; it is recommended (category 1) for acute and delayed emesis prevention when using moderate emetic risk chemotherapy.[48] Oral palonosetron is now available (http://www.fda.gov/cder/foi/label/2008/022233LBL.pdf), and it is comparable to IV palonosetron for acute emesis prevention when using moderate emetic risk chemotherapy.[49]

Intravenous palonosetron is superior to other 5-HT3 antagonists for preventing delayed nausea.[50] However, repeat dosing of palonosetron in the days after chemotherapy (that is, days 2 or 3) is not supported by the scientific literature. Repeat dosing of palonosetron in the setting of multiday chemotherapy regimens has not been studied.

All of the 5-HT3 antagonists can be delivered orally or intravenously. In addition, the FDA recently approved the use of a granisetron transdermal system for chemotherapy-induced nausea and vomiting (http://www.fda.gov/cder/foi/label/2008/022198lbl.pdf). The patch containing 34.3 mg of granisetron is applied 24 to 48 hours before the first dose of chemotherapy. A phase III randomized study compared the patch to oral granisetron in patients receiving either highly emetogenic or moderately emetogenic chemotherapy. The patch proved noninferior to repeat dosing of the oral antiemetic granisetron over 3 to 5 days.[51]

Many clinical trials directly comparing ondansetron, granisetron, dolasetron mesylate, and palonosetron have been conducted. These trials have used various doses, routes, and schedules of administration.[48,52-71] Studies have demonstrated that the 5-HT3 antagonists are equally effective and have mild, infrequent side effects. A recent meta-analysis found no difference in efficacy.[72] The addition of dexamethasone improves the efficacy of the antiemetic regimen containing 5-HT3 antagonists.

Ondansetron, granisetron, and dolasetron are effective in preventing acute emesis but appear to be less effective for delayed emesis. However, IV palonosetron is effective for preventing both delayed and acute emesis. A meta-analysis of randomized controlled trials found that adding a 5-HT3 antagonist to dexamethasone did not improve the antiemetic effect of dexamethasone for preventing delayed emesis.[73] Another study found that 5-HT3 antagonists (except palonosetron, which was not studied) were not more effective than prochlorperazine for preventing delayed emesis.[11]

NK-1–Receptor Antagonist

Aprepitant selectively blocks the binding of substance P at the NK-1 receptor in the central nervous system. Thus, aprepitant provides a different and complementary mechanism of action to all other commercially available antiemetics. Aprepitant has been shown to augment the antiemetic activity of the 5-HT3–receptor antagonists and the corticosteroid dexamethasone to inhibit both acute and delayed cisplatin-induced emesis. The FDA has approved the use of aprepitant for preventing emesis in patients receiving moderately emetogenic chemotherapy. An IV version of aprepitant (fosaprepitant dimeglumine), which can be given on day 1 only, has recently been approved by the FDA (http://www.fda.gov/cder/foi/label/2008/022023lbl.pdf).

When combined with 5-HT3 antagonists and dexamethasone on day 1 before cisplatin-based highly emetogenic chemotherapy and continued orally along with dexamethasone on days 2 and 3 after chemotherapy, aprepitant significantly improved control of acute and delayed chemotherapy-induced nausea and emesis.[74,75] The oral doses of aprepitant are 125 mg on day 1 (before chemotherapy) and then 80 mg on days 2 and 3 (after chemotherapy).[76] There are no studies showing efficacy or safety of chronic dosing with aprepitant. It is possible that the drug-drug interaction profile may change with chronic dosing.

A randomized phase III study (866 patients) showed that an aprepitant regimen is better than a standard regimen for preventing vomiting in patients receiving moderately emetogenic chemotherapy (non-cisplatin based) during 120 hours after initiation of chemotherapy (complete response, 50.8% versus 42.5%, *P*=.015); however, 40% of patients (receiving either regimen) still had significant nausea.[77,78] The aprepitant regimen included aprepitant, ondansetron, and dexamethasone; the standard regimen included ondansetron and dexamethasone. An analysis of 2 phase III randomized trials found that

an aprepitant regimen is useful for patients receiving moderately emetogenic chemotherapy plus high-dose cisplatin.[79]

A meta-analysis (7 randomized controlled trials) in patients receiving highly emetogenic chemotherapy found that NK-1 receptor antagonists used alone or with standard therapy for acute emesis were not better than the control; however, for delayed emesis, NK-1 receptor antagonists were better than the control.[80] A phase II study (58 patients) found that combining palonosetron, aprepitant, and dexamethasone was useful for various chemotherapeutic regimens (moderate to moderate-highly emetogenic); 78% of patients had a complete response (no emetic episodes and no rescue medication).[81]

Drug Interactions

Aprepitant is simultaneously a substrate, moderate inducer, and moderate inhibitor of cytochrome P450 enzyme 3A4 (CYP3A4); aprepitant also induces CYP2C9.[82] Thus, aprepitant can alter the metabolism of certain drugs and change their plasma concentrations (that is, AUCs [area under the curve]). These interactions are more significant with orally administered forms of these drugs than with IV forms because of first-pass metabolism. Patients should not take aprepitant with pimozide, terfenadine, astemizole, or cisapride; these combinations are contraindicated, because they may cause "serious or life-threatening reactions" (see the aprepitant package insert http://www.fda.gov/cder/foi/label/2007/021549s012lbl.pdf).

Chemotherapeutic agents known to be metabolized by CYP3A4 include docetaxel, paclitaxel, etoposide, irinotecan, ifosfamide, imatinib, vinorelbine, vinblastine, and vincristine. In clinical trials, aprepitant was used concurrently with etoposide, vinorelbine, or paclitaxel; although chemotherapy doses were not adjusted for potential drug interactions in phase III trials, caution is urged when using any chemotherapeutic agent that is metabolized by CYP3A4.

Aprepitant has been shown to interact with several nonchemotherapeutic drugs (including warfarin, dexamethasone, methylprednisolone, oral contraceptives). These interactions are more significant with orally administered forms of these drugs than with IV forms because of first-pass metabolism.

Induction of warfarin metabolism by aprepitant may lead to clinically significant reductions in INR (international normalized ratio) values, particularly for patients on therapeutic (as compared to prophylactic) warfarin regimens. These changes, although brief in duration, may require increased patient monitoring (http://www.fda.gov/cder/foi/label/2007/021549s012lbl.pdf).

When given with aprepitant, the AUC of dexamethasone is increased; thus, the NCCN guidelines include reduced dose recommendations for dexamethasone in this setting. The AUC of methylprednisolone is also increased when given with aprepitant; thus, the methylprednisolone dose should also be decreased in this setting. However, if dexamethasone (or prednisone or any corticosteroid) is being administered as part of anticancer therapy (for example, CHOP regimen), the corticosteroid dose should not be reduced.[23]

Aprepitant decreases the AUC for patients taking oral contraceptives; the package insert should be consulted in this setting.

Certain drugs can affect the AUCs of aprepitant. Concomitant administration with CYP3A4 inhibitors (for example, ketoconazole, itraconazole, erythromycin) may lead to increased aprepitant AUCs, whereas concomitant administration with CYP3A4 inducers (for example, carbamazepine, rifampin, phenytoin) may lead to decreased levels of aprepitant.

Other Non–5-HT3–Receptor Antagonist Antiemetics

Before the advent of the 5-HT3–receptor antagonists, the available antiemetic agents included phenothiazines,[83] substituted benzamides,[84,85] antihistamines,[86] butyrophenones,[87] corticosteroids,[88-90] benzodiazepines,[91,92] and cannabinoids.[93,94] Most drugs used to prevent chemotherapy-induced emesis are classified as dopamine antagonists, serotonin antagonists, and other antagonists. Combination antiemetic therapy is more effective than single-agent therapy. Olanzapine (thiobenzodiazepine) was found to be effective for acute and delayed emesis in a phase II trial in patients (n = 30) who received cyclophosphamide, doxorubicin, and/or cisplatin;[95,96] other studies have also showed the value of olanzapine for delayed and refractory emesis and nausea.[97-100] However, olanzapine should be used with caution in elderly patients (see boxed warning/label indication regarding death, type II diabetes, and hyperglycemia (http://www.fda.gov/cder/foi/label/2007/020592s042s043,021086s022s023,021253s026lbl.pdf).[101]

Treatment Issues

Selected issues that arose in the panel's deliberations on the guidelines are discussed in the following sections. As new data about the use of antiemetics in patients receiving chemotherapy become available, clinicians should consider these data when caring for such patients, even if the information has not been included in the guidelines. In contrast to other NCCN guidelines in which most of the recommendations are category 2A, many of the recommendations for antiemetic management are classified as category 1, reflecting the large number of randomized controlled trials that have focused on antiemetic management.

Principles of Emesis Control

These principles are discussed in the algorithm (see AE-1).

- The goal is to prevent nausea and/or vomiting.
- The risk of emesis and nausea for persons receiving chemotherapy of high and moderate emetogenic potential lasts at least 4 days for high and 3 days for moderate. Patients need to be protected throughout the full period of risk.
- Oral and IV antiemetic formulations have equivalent efficacy.
- The toxicity of the specific antiemetic(s) should be considered.
- Antiemetic regimens should be chosen based on the drug with the highest emetic risk in the chemotherapy regimen, previous experience with antiemetics, and patient-specific risk factors.

In addition to emesis induced by chemotherapy, emesis in cancer patients can also potentially be caused by:

- Partial or complete bowel obstruction
- Vestibular dysfunction
- Brain metastases
- Electrolyte imbalance: hypercalcemia, hyperglycemia, hyponatremia
- Uremia
- Concomitant drug treatments, including opiates
- Gastroparesis induced by a tumor or chemotherapy (such as vincristine).
- Psychophysiologic factors, including anxiety and anticipatory nausea and vomiting.
- For use of antiemetics for nausea and vomiting that is not related to radiation and/or chemotherapy, see the NCCN Palliative Care Guidelines.
- For multidrug regimens, select antiemetic therapy based on drug with the highest emetic risk (see AE-6).[28,29]

Prevention of Acute Emesis

To prevent acute emesis, antiemetic therapy should start before the administration of chemotherapy and then should cover the first 24

hours. For highly emetogenic drugs, the regimens are described on AE-2. For moderately emetogenic drugs, the regimens are described on AE-3. For low and minimally emetogenic drugs, the regimens are described on AE-4. This section discusses prechemotherapy and postchemotherapy emesis prevention rather than primary treatment.

Prechemotherapy Emesis Prevention

The guidelines specify different prophylactic antiemetic regimens for cancer patients receiving chemotherapy of different emetogenic potential (that is, high, moderate, low, minimal). Prophylactic antiemetics should be administered before chemotherapy. The recommendations for prophylactic antiemetic treatment include drug dosages. The guidelines reflect accumulating experience with the 5-HT3–serotonin antagonists, demonstrating their effectiveness in a range of doses. Unless indicated, the order of listed antiemetics in the algorithm does not reflect preference.

Highly emetogenic drugs include altretamine, carmustine > 250 mg/m^2, cisplatin at 50 mg/m^2 or more, cyclophosphamide > 1500 mg/m^2, dacarbazine, mechlorethamine, procarbazine (oral), streptozocin, or anthracycline and cyclophosphamide (AC) combinations (doxorubicin or epirubicin with cyclophosphamide). The antiemetic regimen for these highly emetogenic drugs on day 1 includes aprepitant (or fosaprepitant), dexamethasone, and a 5-HT3 antagonist with or without lorazepam (category 1 for the combined regimen [see AE-2]);[22,23,74] note that the regimen and doses are often modified on days 2 to 4 after chemotherapy.

A Canadian meta-analysis suggests that it is not cost-effective to use 5-HT3 antagonists (that is, ondansetron) on days 2 to 4 to prevent delayed emesis; however, ondansetron (when used alone) did protect against delayed emesis in this meta-analysis.[102] Palonosetron was not assessed in these studies. The NCCN panel recommends the use of 5-HT3 antagonists as one of several options to prevent delayed emesis for moderately emetogenic agents (see AE-3).

The antiemetic regimen for moderately emetogenic drugs (see AE-6) on day 1 includes dexamethasone and a 5-HT3 antagonist with or without lorazepam (see AE-3).[78] Aprepitant should be added (to dexamethasone and a 5-HT3 antagonist) for select patients receiving other chemotherapies of moderate emetic risk (for example, carboplatin, cisplatin, doxorubicin, epirubicin, ifosfamide, irinotecan, or methotrexate) (see AE-3), because these agents are more emetogenic than the other moderately emetogenic agents.[23,28] Any one of the 5-HT3 antagonists can be used, because they are all category 1. Note that the regimens differ on days 2 to 3. There are 3 possible regimens on days 2-3 (lorazepam can be added to each of these regimens) including: 1) aprepitant with or without dexamethasone; 2) dexamethasone; or 3) 5-HT3 antagonist, such as ondansetron, granisetron, or dolasetron. Note that palonosetron is not given on days 2-3.

The antiemetic regimen for low emetogenic drugs (see AE-7) includes non–5-HT3 antagonists, such as dexamethasone, prochlorperazine, or metoclopramide, with or without lorazepam (see AE-4). When using prochlorperazine or metoclopramide, patients should be monitored for dystonic reactions; diphenhydramine (25-50 mg PO or IV either every 4 or every 6 hours) can be used for dystonic reaction.

For regimens with high emetogenic potential, aprepitant is used at a oral dosage of 125 mg on day 1 and then 80 mg on days 2 and 3 (see AE-2). When given with aprepitant, dexamethasone is used at a dosage of 12 mg on day 1 and then 8 mg on days 2 to 4; the dose can be oral or IV. Because aprepitant increases dexamethasone levels, it is necessary to reduce the dose of dexamethasone when using it as an antiemetic with aprepitant.[74,103] However, if dexamethasone (or any corticosteroid) is being administered as part of anticancer therapy, the

corticosteroid dose should not be reduced.[23] All four 5-HT3–receptor antagonists (that is, ondansetron, granisetron, dolasetron, palonosetron) are considered to have similar effectiveness for control of acute emesis. If appropriate, lorazepam (0.5-2 mg either every 4 or every 6 hours on days 1-4; either oral, IV, or sublingual) may be used with each of these regimens (that is, high, moderate, or low).

Postchemotherapy/Delayed Emesis Prevention

The best management for delayed emesis is prevention. For chemotherapy involving agents with high emetogenic potential, the prophylactic treatment is continued through the period when delayed emesis may occur. Using this strategy, prophylaxis continues for 2 to 3 days after completion of a chemotherapy cycle.

For drugs with moderate emetogenic potential, postchemotherapy prevention depends on what antiemetics were used before chemotherapy. For example, palonosetron (category 1) is only administered on day 1 (see AE-3).[52] If aprepitant was used on day 1, then it is continued on days 2 and 3 and is given with or without dexamethasone or lorazepam. Alternatively, either dexamethasone or a 5-HT3 antagonist can be used; lorazepam may be used with either agent.

Breakthrough Treatment

Breakthrough emesis presents a difficult situation, because refractory ongoing nausea and/or vomiting is often challenging to reverse (see AE-B). Generally, it is much easier to prevent nausea and/or vomiting than to treat it. Thus, routine around-the-clock administration of antiemetics should be strongly considered to prevent emesis, rather than PRN (as required) dosing. The general principle of breakthrough treatment is to give an additional agent as needed from a different drug class. However, no one treatment is better than another for managing breakthrough emesis.[104] The oral route is not likely to be feasible because of ongoing vomiting; therefore, rectal or IV therapy is often required. Multiple concurrent agents, perhaps in alternating schedules or by alternating routes, may be necessary. Dopamine antagonists (for example, metoclopramide), haloperidol, corticosteroids, and agents such as lorazepam may be required. Nabilone (which is a cannabinoid) is approved by the FDA for nausea and vomiting in patients who have not responded to conventional antiemetic agents. Adequate hydration or fluid repletion should be ensured, and any possible electrolyte abnormalities should be assessed and corrected. Before administering the next cycle of chemotherapy, the patient should be reassessed with attention to various possible nonchemotherapy-related reasons for breakthrough emesis with the current cycle, such as brain metastases, electrolyte abnormalities, tumor infiltration of the bowel or other GI abnormality, and other comorbidities (see AE-B). In addition, before the next cycle of chemotherapy, the antiemetic regimen (both the day 1 and postchemotherapeutic) that did not protect the patient during the present cycle should be assessed and alternatives should be considered (see AE-B). Consider using antacid therapy (for example, proton pump inhibitors, H2 blockers) if patients have dyspepsia, because patients sometimes have difficulty discriminating heartburn from nausea.

Radiation-Induced Nausea and/or Vomiting

Prophylaxis for radiation-induced nausea and/or vomiting is based on the site of radiation and whether it is combined with chemotherapy (see AE-8). When radiation is combined with chemotherapy, prophylaxis is dictated by the emetogenic potential of the chemotherapy regimen.

Radiation to the upper abdomen may be treated with oral ondansetron (8 mg 2 to 3 times daily), with or without oral dexamethasone, based on the results of a randomized study comparing oral ondansetron with placebo in patients receiving daily fractionated radiotherapy including the abdomen. In this study, 67% of patients given ondansetron had

complete control of emesis compared with 45% of patients who received placebo.[105] A study showed that the addition of oral dexamethasone (4 mg daily) to the ondansetron regimen decreases emesis and nausea, although the effect is modest.[106] Another option is oral granisetron (2 mg every day) with or without oral dexamethasone.

Total body irradiation may be treated with either ondansetron (8 mg 2 to 3 times daily) or granisetron; either agent can be given with or without oral dexamethasone (2 mg 3 times daily).[106] The dose of granisetron is either 2 mg oral every day or 3 mg IV every day[107,108] (category 2B recommendation, because this dose of granisetron is higher than the dose typically used). No prophylaxis is recommended for patients receiving irradiation to other sites.

Treatment of breakthrough radiation-induced emesis is similar to chemotherapy-induced emesis. Patients who do not receive primary prophylaxis and experience breakthrough nausea and/or vomiting may be treated with ondansetron, similar to primary prophylaxis.

Anticipatory Nausea and/or Vomiting

The most effective way to treat anticipatory nausea and/or vomiting is to prevent it by using optimal antiemetic therapy during every cycle of treatment (see AE-9). Behavioral therapy has been used in patients with anticipatory nausea and/or vomiting.[109-111] Systematic desensitization may also be helpful.[110] Hypnosis with guided imagery is another behavioral technique that has shown some success in treating this condition.[111] The antianxiety agents lorazepam and alprazolam have been combined with antiemetics for anticipatory nausea and/or vomiting with mixed results.[112] The usual starting dose of alprazolam is 0.25 to 0.5 mg orally 3 times daily, beginning on the night before treatment. In elderly patients, patients with debilitating disease, and patients with advanced liver disease, the usual starting dose of alprazolam is 0.25 mg orally 2 or 3 times daily for treatment of anxiety (http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=5816#nlm34068-7). This dose may be gradually increased if needed. Note that the elderly are especially sensitive to the effects of benzodiazepines. The dose should be gradually reduced when decreasing or discontinuing alprazolam therapy.

Managing Multiday Emetogenic Chemotherapy Regimens

Patients receiving multiday chemotherapy are at risk for both acute and delayed nausea and vomiting based on the emetogenic potential of the individual chemotherapy agents and their sequence.[75,113-116] It is difficult to recommend a specific antiemetic regimen for each day, especially because acute and delayed emesis may overlap after the initial day of chemotherapy until the last day of chemotherapy. The period of risk for delayed emesis after chemotherapy administration has concluded also depends on the specific regimen and the emetogenic potential of the last chemotherapy agent administered in the regimen. General principles for managing multiday emetogenic chemotherapy regimens recommended (category 2B) by the panel are described in the algorithm (see AE-A).

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