asco special article

Antiemetics: ASCO Guideline Update

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PURPOSE To update the guideline to include new anticancer agents, antiemetics, and antiemetic regimens and to provide recommendations on the use of dexamethasone as a prophylactic antiemetic in patients receiving checkpoint inhibitors (CPIs).

METHODS ASCO convened an Expert Panel and updated the systematic review to include randomized controlled trials (RCTs) and meta-analyses of RCTs published between June 1, 2016, and January 24, 2020. To address the dexamethasone and CPI question, we conducted a systematic review of RCTs that evaluated the addition of a CPI to chemotherapy.

RESULTS The systematic reviews included 3 publications from the updated search and 10 publications on CPIs. Two phase III trials in adult patients with non–small-cell lung cancers evaluating a platinum-based doublet with or without the programmed death 1 (PD-1) inhibitor pembrolizumab recommended that all patients receive dexamethasone as a component of the prophylactic antiemetic regimen. In both studies, superior outcomes were noted in the PD-1 inhibitor–containing arms. Other important findings address olanzapine in adults and fosaprepitant in pediatric patients.

RECOMMENDATIONS Recommendations for adults are unchanged with the exception of the option of adding olanzapine in the setting of hematopoietic stem cell transplantation. Dosing information now includes the option of a 5-mg dose of olanzapine in adults and intravenous formulations of aprepitant and netupitant-palonosetron. The option of fosaprepitant is added to pediatric recommendations. There is no clinical evidence to warrant omission of dexamethasone from guideline-compliant prophylactic antiemetic regimens when CPIs are administered to adults in combination with chemotherapy. CPIs administered alone or in combination with another CPI do not require the routine use of a prophylactic antiemetic.

Additional information is available at www.asco.org/supportive-care-guidelines.

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ASSOCIATED CONTENT Appendix

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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INTRODUCTION

The goals of this update are to provide oncologists, other health care practitioners, patients, and caregivers recommendations on the use of dexamethasone as a prophylactic antiemetic in patients receiving checkpoint inhibitors and information on new antiemetics, antiemetic regimens, and anticancer agent emetogenicity.

Checkpoint inhibitors (CPIs) represent a significant new therapeutic approach in many cancers. Concerns have been raised about the potential for concurrent corticosteroid use to adversely affect the therapeutic efficacy of CPIs through their immunosuppressive effects. Dexamethasone is a potent corticosteroid that is a critical component of a number of antiemetic guideline—endorsed regimens for use in the prevention of nausea and vomiting caused by chemotherapy.

The first ASCO guideline for antiemetics was published in 1999,¹ with updates in 2006,² 2011,³ 2015,⁴ and 2017.⁵ This update of the 2017 guideline provides guidance on the use of dexamethasone as a prophylactic antiemetic in patients receiving CPIs. This guideline update addresses programmed death-1 (PD-1), programmed death 1–ligand (PD-L1), and cytotoxic T-lymphocyte—associated protein-4 (CTLA-4) CPIs. Other forms of immunotherapies such as chimeric antigen receptor T cells were not addressed. We also used this opportunity to add new anticancer



THE BOTTOM LINE

Antiemetics: ASCO Guideline Update

Guideline Question

Should current guideline-endorsed antiemetic regimens that include dexamethasone be modified when checkpoint inhibitors (CPIs) are incorporated in antineoplastic treatment regimens?

Target Population

Adults and children who receive antineoplastic agents and adults who undergo radiation therapy for cancer.

Target Audience

Medical and radiation oncologists, oncology nurses, nurse practitioners, physician assistants, oncology pharmacists, and patients with cancer.

Methods

An Expert Panel was convened to conduct an update of clinical practice guideline recommendations based on a systematic review of the medical literature.

Recommendations

Note: For adult patients, the addition of a CPI to chemotherapy does not change the guideline recommendation for an antiemetic regimen based on the emetogenicity of the agents administered. CPIs administered alone or in combination with another CPI are minimally emetogenic and do not require the routine use of a prophylactic antiemetic.

Adult Patients

High-emetic-risk antineoplastic agents

- Adults treated with <u>cisplatin and other high-emetic-risk single agents</u> should be offered a 4-drug combination of an NK₁ receptor antagonist, a serotonin (5-HT₃) receptor antagonist, dexamethasone, and olanzapine (day 1). Dexamethasone and olanzapine should be continued on days 2 to 4 (Type: evidence based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).
- Adults treated with an anthracycline combined with cyclophosphamide should be offered a 4-drug combination of an NK₁ receptor antagonist, a 5-HT₃ receptor antagonist, dexamethasone, and olanzapine (day 1). Olanzapine should be continued on days 2 to 4 (Type: evidence based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).

Moderate-emetic-risk antineoplastic agents

- Adults treated with <u>carboplatin area under the curve (AUC) \geq 4 mg/mL/min should be offered a 3-drug combination of an NK₁ receptor antagonist, a 5-HT₃ receptor antagonist, and dexamethasone (day 1) (Type: evidence based; benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).</u>
- Adults treated with moderate-emetic-risk antineoplastic agents (excluding carboplatin AUC ≥ 4 mg/mL/min) should be offered a 2-drug combination of a 5-HT₃ receptor antagonist and dexamethasone (day 1) (Type: evidence based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).
- Adults treated with cyclophosphamide, doxorubicin, oxaliplatin, and other <u>moderate-emetic-risk antineoplastic agents</u> <u>known to cause delayed nausea and vomiting</u> may be offered dexamethasone on days 2 to 3 (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: moderate).

Low-emetic-risk antineoplastic agents

Adults treated with low-emetic-risk antineoplastic agents should be offered a single dose of a 5-HT₃ receptor antagonist
or a single 8-mg dose of dexamethasone before antineoplastic treatment (Type: informal consensus, benefits outweigh
harms; Evidence quality: low; Strength of recommendation: moderate).

Minimal-emetic-risk antineoplastic agents

• Adults treated with minimal-emetic-risk antineoplastic agents should not be offered routine antiemetic prophylaxis (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: moderate).

Antineoplastic combinations

 Adults treated with antineoplastic combinations should be offered antiemetics appropriate for the component antineoplastic agent of greatest emetic risk (Type: informal consensus, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

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THE BOTTOM LINE (CONTINUED)

Adjunctive drugs

• Lorazepam is a useful adjunct to antiemetic drugs but is not recommended as a single-agent antiemetic (Type: informal consensus; benefits outweigh harms; Evidence quality: low; Strength of recommendation: moderate).

Cannabinoids

 Evidence remains insufficient for a recommendation regarding medical marijuana for the prevention of nausea and vomiting in patients with cancer receiving chemotherapy or radiation therapy. Evidence is also insufficient for a recommendation regarding the use of medical marijuana in place of the tested and US Food and Drug Administration-approved cannabinoids dronabinol and nabilone for the treatment of nausea and vomiting caused by chemotherapy or radiation therapy.

Complementary and alternative therapies

• Evidence remains insufficient for a recommendation for or against the use of ginger, acupuncture/acupressure, and other complementary or alternative therapies for the *prevention* of nausea and vomiting in patients with cancer.

High-dose chemotherapy with stem-cell or bone marrow transplantation

- Adults treated with high-dose chemotherapy and stem-cell or bone marrow transplantation should be offered a 3-drug combination of an NK₁ receptor antagonist, a 5-HT₃ receptor antagonist, and dexamethasone (Type: evidence based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).
- (New) A 4-drug combination of an NK₁ receptor antagonist, a 5-HT₃ receptor antagonist, dexamethasone, and olanzapine may be offered to adults treated with high-dose chemotherapy and stem-cell or bone marrow transplantation. (Type: evidence based, benefits outweigh harms; Evidence quality: low; Strength of recommendation: weak).

Multiday antineoplastic therapy

- Adults treated with multiday antineoplastic agents should be offered antiemetics before treatment that are appropriate
 for the emetic risk of the antineoplastic agent given on each day of the antineoplastic treatment and for 2 days after
 completion of the antineoplastic regimen (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).
- Adults treated with 4- or 5-day cisplatin regimens should be offered a 3-drug combination of an NK₁ receptor antagonist, a 5-HT₃ receptor antagonist, and dexamethasone (Type: evidence based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).

Breakthrough nausea and vomiting

- For patients with breakthrough nausea or vomiting, clinicians should re-evaluate emetic risk, disease status, concurrent illnesses, and medications; and ascertain that the best regimen is being administered for the emetic risk (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: moderate).
- Adults who experience nausea or vomiting despite optimal prophylaxis and who did not receive olanzapine prophylactically should be offered olanzapine in addition to continuing the standard antiemetic regimen (Type: evidence based; benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).
- Adults who experience nausea or vomiting despite optimal prophylaxis and who have already received olanzapine may
 be offered a drug of a different class (eg, an NK1 receptor antagonist, lorazepam or alprazolam, a dopamine receptor
 antagonist, dronabinol, or nabilone) in addition to continuing the standard antiemetic regimen (Type: informal consensus; benefits outweigh harms; Evidence quality: intermediate for dronabinol and nabilone, low otherwise; Strength of
 recommendation: moderate).

Anticipatory nausea and vomiting

All patients should receive the most active antiemetic regimen appropriate for the antineoplastic agents being administered. Clinicians should use such regimens with initial antineoplastic treatment rather than assessing the patient's emetic response with less-effective antiemetic treatment. If a patient experiences anticipatory emesis, clinicians may offer behavioral therapy with systematic desensitization (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: moderate).

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THE BOTTOM LINE (CONTINUED)

High-emetic-risk radiation therapy

 Adults treated with high-emetic-risk radiation therapy should be offered a 2-drug combination of a 5-HT₃ receptor antagonist and dexamethasone before each fraction and on the day after each fraction, if radiation therapy is not planned for that day (Type: evidence based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: strong).

Moderate-emetic-risk radiation therapy

• Adults treated with moderate-emetic-risk radiation therapy should be offered a 5-HT₃ receptor antagonist before each fraction, with or without dexamethasone, before the first 5 fractions (Type: evidence based, benefits outweigh harms; Evidence quality: high; Strength of recommendation: moderate).

Low-emetic-risk radiation therapy

• Adults treated with radiation therapy to the brain should be offered breakthrough dexamethasone therapy. Patients who are treated with radiation therapy to the head and neck, thorax, or pelvis should be offered breakthrough therapy with a 5-HT₃ receptor antagonist, dexamethasone, or a dopamine-receptor antagonist (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: weak).

Minimal-emetic-risk radiation therapy

 Adults treated with minimal-emetic-risk radiation therapy should be offered breakthrough therapy with a 5-HT₃ receptor antagonist, dexamethasone, or a dopamine-receptor antagonist (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: weak).

Concurrent radiation and antineoplastic agent therapy

Adults treated with concurrent radiation and antineoplastic agents should receive antiemetic therapy appropriate for the
emetic risk level of the antineoplastic agents, unless the risk level of the radiation therapy is higher. During periods when
prophylactic antiemetic therapy for the antineoplastic agents has ended and ongoing radiation therapy would normally
be managed with its own prophylactic therapy, patients should receive prophylactic therapy appropriate for the emetic
risk of the radiation therapy until the next period of antineoplastic therapy, rather than receiving breakthrough therapy for
the antineoplastic agents as needed (Type: informal consensus, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: moderate).

Pediatric Patients

High-emetic-risk antineoplastic agents

- (Updated) Pediatric patients treated with high-emetic-risk antineoplastic agents should be offered a 3-drug combination of a 5-HT₃ receptor antagonist, dexamethasone, and aprepitant or fosaprepitant (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).
- (Updated) Pediatric patients treated with high-emetic-risk antineoplastic agents who are unable to receive aprepitant or fosaprepitant should be offered a 2-drug combination of a 5-HT₃ receptor antagonist and dexamethasone (Type evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).
- (Updated) Pediatric patients treated with high-emetic-risk antineoplastic agents who are unable to receive dexamethasone should be offered a 2-drug combination of palonosetron and aprepitant or fosaprepitant (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).

Moderate-emetic-risk antineoplastic agents

- Pediatric patients treated with moderate-emetic-risk antineoplastic agents should be offered a 2-drug combination of a 5-HT₃ receptor antagonist and dexamethasone (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: strong).
- (Updated) Pediatric patients treated with moderate-emetic-risk antineoplastic agents who are unable to receive dexamethasone should be offered a 2-drug combination of a 5-HT₃ receptor antagonist and aprepitant or fosaprepitant (Type: evidence based, benefits outweigh harms; Evidence quality: intermediate; Strength of recommendation: weak).

Low-emetic-risk antineoplastic agents

 Pediatric patients treated with low-emetic-risk antineoplastic agents should be offered ondansetron or granisetron (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: strong).
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THE BOTTOM LINE (CONTINUED)

Minimal-emetic-risk antineoplastic agents

• Pediatric patients treated with minimal-emetic-risk antineoplastic agents should not be offered routine antiemetic prophylaxis (Type: informal consensus, benefits outweigh harms; Evidence quality: low; Strength of recommendation: strong).

Additional Resources

More information, including a supplement with additional evidence tables, slide sets, and clinical tools and resources, is available at www.asco.org/supportive-care-guidelines. The Methodology Manual (available at www.asco.org/guideline-methodology) provides additional information about the methods used to develop this guideline. Patient information is available at www.cancer.net.

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

agents to the emetic risk tables and to detail new antiemetics and new uses of existing antiemetics in both adult and pediatric populations and the hematopoietic stem cell setting since the 2017 update to the guideline.

GUIDELINE QUESTION

Should current guideline-endorsed antiemetic regimens that include dexamethasone be modified when CPIs are incorporated in antineoplastic treatment regimens?

METHODS

Guideline Update Process

ASCO uses a signals approach to facilitate guideline updating. This approach identifies new, potentially practice-changing data (signals) that might translate into revised practice recommendations. The approach relies on targeted literature searching and the expertise of ASCO guideline panel members to identify signals. For this update, observational studies of CPI efficacy in patients treated with corticosteroids and anecdotal reports of provider concerns about this topic provided the primary signals for an update.

This systematic review-based guideline update was developed by a multidisciplinary Expert Panel, which included a patient representative and an ASCO guidelines staff with health research methodology expertise. The Expert Panel met via teleconference and/or webinar and corresponded through e-mail. Based upon the consideration of the evidence, the authors were asked to contribute to the development of the guideline, provide critical review, and finalize the guideline recommendations. The guideline recommendations were sent for an open comment period of 2 weeks allowing the public to review and comment on the recommendations after submitting a confidentiality agreement. These comments were taken into consideration while finalizing the recommendations. Members of the Expert Panel were responsible for reviewing and approving the penultimate version of guideline, which was then circulated for external review, and submitted to the *Journal* of Clinical Oncology (JCO) for editorial review and consideration for publication. All ASCO guidelines are ultimately reviewed and approved by the Expert Panel (Appendix Table A1, online only) and the ASCO Clinical Practice Guidelines Committee prior to publication. All funding for the administration of the project was provided by ASCO.

The systematic review consisted of 2 parts:

- 1. An update of the literature search from the 2017 guideline.⁵ PubMed and the Cochrane Library were searched from June 1, 2016, to January 24, 2020, for English-language RCTs and meta-analyses of RCTs. RCTs were required to have at least 25 patients per arm.
- 2. Identification of phase III RCTs that compared chemotherapy alone with chemotherapy plus a CPI. We searched PubMed for trials published through January 24, 2020, with no restriction on start date. We collected information about antiemetic regimens specified by the protocol, exclusion criteria related to steroid use, and the primary safety and efficacy results of the studies. The primary question was whether the addition of a CPI to chemotherapy improved efficacy even when dexamethasone-containing antiemetic regimens were used.

Search terms are provided in the Data Supplement. Articles were excluded from the systematic review if they were (1) meeting abstracts not subsequently published in peer-reviewed journals; (2) editorials, commentaries, letters, news articles, case reports, or narrative reviews; and (3) published in a non-English language.

The Expert Panel also identified new anticancer agents approved by the US Food and Drug Administration (FDA) since the 2017 update and evaluated their emetic potential based on a nonsystematic review of RCTs, information available in the product label, and informal consensus. Due to the specific interest in CPIs and dexamethasone, we not

 TABLE 1. Emetic Risk of Single Intravenous Antineoplastic Agents in
 TABLE 1. Emetic Risk of Single Intravenous Antineoplastic Agents in
 Adults

Risk Level	Agent	
High (> 90%)	Anthracycline/cyclophosphamide combination	
	Carmustine	
	Cisplatin	
	Cyclophosphamide ≥ 1,500 mg/m ²	
	Dacarbazine	
	Mechlorethamine	
	Streptozocin	
Moderate (30%-90%)	Alemtuzumab	
	Arsenic trioxide	
	Azacitidine	
	Bendamustine	
	Busulfan	
	Carboplatin	
	Clofarabine	
	${\it Cyclophosphamide} < 1{,}500~{\it mg/m^2}$	
	Cytarabine > 1,000 mg/m ²	
	Daunorubicin	
	Daunorubicin and cytarabine liposome	
	Doxorubicin	
	Epirubicin	
	Fam-trastuzumab deruxtecan-nxki	
	Idarubicin	
	Ifosfamide	
	Irinotecan	
	Irinotecan liposomal injection	
	Oxaliplatin	
	Romidepsin	
	Temozolomide ^a	
	Thiotepa ^b	
	Trabectedin	
(contin	ued in next column)	

Adults (continued)

Adults (continued) Risk Level	Agent
Low (10%-30%)	Aflibercept
	Axicabtagene ciloleucel
	Belinostat
	Blinatumomab
	Bortezomib
•	Brentuximab
•	Cabazitaxel
•	Carfilzomib
•	Catumaxumab
•	Cetuximab
•	Copanlisib
•	Cytarabine ≤ 1,000 mg/m ²
•	Decitabine
•	Docetaxel
•	Elotuzumab
•	Enfortumab vedotin-ejfv
•	Eribulin
•	Etoposide
•	Fluorouracil
•	Gemcitabine
•	Gemtuzumab ozogamicin
•	Inotuzumab ozogamicin
-	Ixabepilone
•	Methotrexate
•	Mitomycin
•	Mitoxantrone
•	Moxetumomab pasudotox
•	Nab-paclitaxel
•	Necitumumab
•	Nelarabine
•	Paclitaxel
•	Panitumumab
•	Pegylated liposomal doxorubicin
•	Pemetrexed
•	Pertuzumab
	Tagraxofusp-erzs
	Temsirolimus
	Tisagenlecleucel
	Topotecan
	Trastuzumab-emtansine
	Vinflunine
(cor	ntinued on following page)

TABLE 1. Emetic Risk of Single Intravenous Antineoplastic Agents in Adults (continued)

Risk Level	Agent	
Minimal (< 10%)	Atezolizumab	
	Avelumab	
_	Bevacizumab	
	Bleomycin	
	Cemiplimab	
_	2-Chlorodeoxyadenosine	
	Cladribine	
	Daratumumab	
_	Durvalumab	
_	Emapalumab	
	Fludarabine	
	Ipilimumab	
_	Nivolumab	
_	Obinutuzumab	
_	Ofatumumab	
_	Pembrolizumab	
_	Pixantrone	
_	Polatuzumab vedotin	
	Pralatrexate	
	Ramucirumab	
	Rituximab	
<u></u>	Trastuzumab	
<u></u>	Vinblastine	
<u></u>	Vincristine	
	Vinorelbine	

^aNo direct evidence found for intravenous temozolomide; because all sources indicate a similar safety profile to the oral formulation, the classification was based on oral temozolomide.

only added new CPIs to the tables but also reassessed the emetogenicity of CPIs that were addressed in the 2017 guideline. Included CPIs were atezolizumab, avelumab, cemiplimab, durvalumab, ipilimumab, nivolumab, and pembrolizumab. Avelumab, cemiplimab, and durvalumab are new to this version of the guideline. Categories of emetogenicity for intravenous agents were the same as in the prior version of the guideline: high (> 90%), moderate (30%-90%), low (10%-30%), and minimal (<10%).⁵ For oral agents, we used only 2 categories of emetogenicity: minimal to low and moderate to high. This represents a change from the 2017 guideline and is consistent with the emetogenic schema used by the National Comprehensive Cancer Network (NCCN). This change is made given the greater difficulty in classifying the emetogenicity of oral agents given inconsistent reporting of emesis outcomes.

A review of FDA oncology approvals was also conducted to identify any new antiemetic agents or new formulations of antiemetic agents.

The guideline recommendations are crafted, in part, using the Guidelines Into Decision Support (GLIDES) methodology and accompanying BRIDGE-Wiz software. In addition, a guideline implementability review is conducted. Based on the implementability review, revisions were made to the draft to clarify recommended actions for clinical practice. Ratings for the type and strength of recommendation, evidence, and potential bias are provided with each recommendation.

The ASCO Expert Panel and guidelines staff will work with cochairs to keep abreast of any substantive updates to the guideline. Based on formal review of the emerging literature, ASCO will determine the need to update. The ASCO Guidelines Methodology Manual (available at www.asco.org/guideline-methodology) provides additional information about the guideline update process. This is the most recent information as of the publication date.

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^bClassification refers to individual evidence from pediatric trials.

 TABLE 2. Emetic Risk of Single, Oral Antineoplastic Agents in Adults
 TABLE 2. Emetic Risk of Single, Oral Antineoplastic Agents in Adults
 Risk Level Agent

(continued)

Risk Level	Agent	(continued)
Moderate or high (≥ 30%)	Abemaciclib	Risk Level Agent
	Avapritinib	Fludarabine
	Bosutinib	Gefitinib
	Cabozantinib	Gilteritinib
	Ceritinib	Glasdegib
	Crizotinib	Hydroxyurea
	Cyclophosphamide	Ibrutinib
	Enasidenib	ldelalisib
	Fedratinib	lvosidenib
	Hexamethylmelamine	lxazomib
	Imatinib	Lapatinib
	Lenvatinib	Larotrectinib
_	Lomustine	Lenalidomide
	Midostaurin	Lorlatinib
	Niraparib	Melphalan
	Procarbazine	Methotrexate
_	Ribociclib	Neratinib
_	Rucaparib	Nilotinib
_	Selinexor	Olaparib
_	TAS-102 (trifluridine-tipiracil)	Osimertinib
	Temozolomide	Palbociclib
	Vinorelbine	Panobinostat
Minimal or low (< 30%)	6-Thioguanine	Pazopanib
	Acalabrutinib	Pexidartinib
	Afatinib	Pomalidomide
	Alectinib	Ponatinib
	Alpelisib	Regorafenib
	Axitinib	Ruxolitinib
	Bexarotene	Sonidegib
	Brigatinib	Sorafenib
	Capecitabine	Sunitinib
	Chlorambucil	Talazoparib
	Cobimetinib	Tazemetostat
	Dabrafenib	Tegafur-Uracil
	Dacomitinib	Thalidomide
	Dasatinib	Topotecan
	Duvelisib	Trametinib
	Encorafenib	Vandetanib
	Entrectinib	Vemurafenib
	Erdafitinib	Venetoclax
	Erlotinib	Vismodegib
	Estramustine	Vorinostat
	Etoposide	Zanubrutinib
	Everolimus n next column)	^a Classified emetic potential of oral agents based on a full course therapy and not a single dose.

TABLE 3. Antiemetic Dosing for Adults by Antineoplastic Risk Category

igh: Cisplatin and other agents		
NK1-receptor antagonist		
Aprepitant	125 mg oral or 130 mg IV	80 mg oral on days 2-3 (if ora
Fosaprepitant	150 mg IV	
Netupitant-palonosetron	300 mg netupitant/0.5 mg palonosetron oral in single capsule	
Fosnetupitant-palonosetron	235 mg fosnetupitant/0.25 mg palonosetron IV	
Rolapitant	180 mg oral	
5-HT ₃ receptor antagonist ^a		
Granisetron	2 mg oral or 1 mg or 0.01 mg/kg IV or 1 transdermal patch or 10 mg subcutaneous	
Ondansetron	Single 24-mg dose administered by tablets, successive oral dissolving tablets, or oral dissolving film applications before the start of chemotherapy, or 8 mg or 0.15 mg/kg IV	
Palonosetron	0.50 mg oral or 0.25 mg IV	
Dolasetron	100 mg oral ONLY	
Tropisetron	5 mg oral or 5 mg IV	
Ramosetron	0.3 mg IV	
Dexamethasone		
If aprepitant is used ^b	12 mg oral or IV	8 mg oral or IV once daily of days 2-4
If fosaprepitant is used ^b	12 mg oral or IV	8 mg oral or IV on day 2; 8 m oral or IV twice daily on days 3-4
If netupitant-palonosetron or fosnetupitant- palonosetron is used ^b	12 mg oral or IV	8 mg oral or IV once daily o days 2-4
If rolapitant is used	20 mg oral or IV	8 mg oral or IV twice daily o days 2-4
Olanzapine	10 mg or 5 mg oral	10 mg or 5 mg oral on days 2-
igh: Anthracycline combined with cyclophosphamide ^c		
NK1-receptor antagonist		
Aprepitant	125 mg oral or 130 mg IV	80 mg oral; days 2 and 3 (i oral aprepitant on day 1)
Fosaprepitant	150 mg IV	
Netupitant-palonosetron	300 mg netupitant/0.5 mg palonosetron oral in single capsule	
Fosnetupitant-palonosetron	235 mg fosnetupitant/0.25 mg palonosetron IV	
Rolapitant	180 mg oral	
5-HT ₃ receptor antagonist ^a		
Granisetron	2 mg oral or 1 mg or 0.01 mg/kg IV or 1 transdermal patch or 10 mg subcutaneous	
Ondansetron	Single 24 mg dose administered by tablets, successive oral dissolving tablets, or oral dissolving film applications before the start of chemotherapy, or 8 mg or 0.15 mg/kg IV	
Palonosetron	0.50 mg oral or 0.25 mg IV	
	continued on following page)	

TABLE 3. Antiemetic Dosing for Adults by Antineoplastic Risk Category (continued)

Emetic Risk Category	Dose on Day of Chemotherapy	Dose on Subsequent Days
Dolasetron	100 mg oral ONLY	
Tropisetron	5 mg oral or 5 mg IV	
Ramosetron	0.3 mg IV	
Dexamethasone		
If aprepitant is used ^b	12 mg oral or IV	
If fosaprepitant is used ^b	12 mg oral or IV	
If netupitant-palonosetron or fosnetupitant-palonosetron is used ^b	12 mg oral or IV	
If rolapitant is used	20 mg (oral or IV)	
Olanzapine	10 mg or 5 mg oral	10 mg or 5 mg oral on days 2-4
Moderate ^d		
5-HT ₃ receptor antagonist		
Granisetron	2 mg oral or 1 mg or 0.01 mg/kg IV or 1 transdermal patch or 10 mg subcutaneous	
Ondansetron	8 mg oral twice daily or 8 mg oral dissolving tablet twice daily or 8 mg oral soluble film twice daily or 8 mg or 0.15 mg/kg IV	
Palonosetron	0.50 mg oral or 0.25 mg IV	
Dolasetron	100 mg oral ONLY	
Tropisetron	5 mg oral or 5 mg IV	
Ramosetron	0.3 mg IV	
Dexamethasone	8 mg oral or IV	8 mg oral or IV on days 2-
.ow ^f		
5-HT ₃ receptor antagonist		
Granisetron	2 mg oral or 1 mg or 0.01 mg/kg IV or 1 transdermal patch or 10 mg subcutaneous	
Ondansetron	8 mg oral tablet, oral dissolving tablet, oral soluble film, or IV	
Palonosetron	0.50 mg oral or 0.25 mg IV	
Dolasetron	100 mg oral ONLY	
Tropisetron	5 mg oral or 5 mg IV	
Ramosetron	0.3 mg IV	
Dexamethasone	8 mg oral or IV	

NOTE. For patients who receive 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 or granisetron extended-release injection that delivers therapy over multiple days rather than taking a 5-HT₃ receptor antagonist daily. Abbreviations: 5-HT₃, 5-hydroxytryptamine-3; IV, intravenous; NK1, neurokinin 1.

^alf netupitant-palonosetron or fosnetupitant-palonosetron is used, no additional 5-HT₃ receptor antagonist is needed.

^bThe dexamethasone dose is for patients who are receiving the recommended 4-drug regimen for highly emetic chemotherapy. If patients do not receive an NK1-receptor antagonist, the dexamethasone dose should be adjusted to 20 mg on day 1 and 16 mg on days 2-4.

^cIn nonbreast cancer populations (eg, non-Hodgkin lymphoma) receiving a combination of an anthracycline and cyclophosphamide with treatment regimens incorporating corticosteroids, the addition of palonosetron without the use of an NK1-receptor antagonist and olanzapine is an option.

^dIf the carboplatin area under the curve is \geq 4 mg/mL/min, add an NK1-receptor antagonist to the 5-HT₃ receptor antagonist and dexamethasone. If IV aprepitant is used, 100 mg IV day 1 and then 80 mg oral days 2-3). Dexamethasone dosing is day 1 only: 20 mg with rolapitant; 12 mg with aprepitant, fosaprepitant, or netupitant-palonosetron.

^eFor moderate-emetic-risk agents with a known risk for delayed nausea and vomiting.

Patients treated with low-emetic-risk antineoplastic therapy should be offered a 5-HT₃ receptor antagonist OR dexamethasone.

TABLE 4. Emetic Risk in Adults by Site of Radiation Therapy
Risk Level Site

High (> 90%)	Total body irradiation	
Moderate (30%-90%)	Upper abdomen, craniospinal irradiation	
Low (10%-30%)	Brain, head and neck, thorax, pelvis	
Minimal (< 10%)	Extremities, breast	

assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information, or for any errors or omissions.

Guideline and Conflicts of Interest

The Expert Panel was assembled in accordance with ASCO's Conflict of Interest Policy Implementation for Clinical Practice Guidelines ("Policy," found at http:// www.asco.org/rwc). All members of the Expert Panel completed ASCO's disclosure form, which requires disclosure of financial and other interests, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as a result of promulgation of the guideline. Categories for disclosure include employment; leadership; stock or other ownership; honoraria, consulting or advisory role; speaker's bureau; research funding; patents, royalties, other intellectual property; expert testimony; travel, accommodations, expenses; and other relationships. In accordance with the Policy, the majority of the members of the Expert Panel did not disclose any relationships constituting a conflict under the Policy.

RESULTS

Antiemetic Interventions

A total of 77 publications were potentially eligible based on abstract review (a list of publications is provided in the Data Supplement). Of these, 3 trials were selected for further review by the Expert Panel: a 2019 trial of the NK1-receptor antagonist fosaprepitant in pediatric patients, ¹⁰ a 2019 trial of a 5-mg dose of olanzapine in adult patients treated with cisplatin-based chemotherapy, ¹¹ and a 2018 trial of olanzapine in patients with hematologic malignancies who received highly emetogenic chemotherapy and stem cell transplantation. ¹²

The phase III <u>fosaprepitant</u> trial evaluated the addition of fosaprepitant to ondansetron plus dexamethasone in 163 <u>children</u> ages 1-12 years who were receiving highly or moderately emetogenic chemotherapy. ¹⁰ Children who received the 3-drug antiemetic regimen experienced lower rates of vomiting than children who received only ondansetron plus dexamethasone. The primary outcome of delayed-phase complete response occurred in 79% of children in the intervention arm and 51% of children in the intervention arm (P < .001).

The phase III olanzapine trial evaluated the addition of 5 mg of olanzapine to the combination of a 5HT-3 antagonist,

dexamethasone, and an NK1-receptor antagonist. The trial enrolled 710 adults who were scheduled to receive cisplatin-based chemotherapy. Patients in the olanzapine arm demonstrated significant improvements in nausea and vomiting prevention. The primary outcome of delayed-phase complete response occurred in 79% of patients in the intervention arm and 66% of patients in the comparison arm (P<.0001). The 5-mg and 10-mg doses of olanzapine have not been compared directly in this setting.

The addition of 10 mg of olanzapine to a 3-drug antiemetic regimen (fosaprepitant, ondansetron, and dexamethasone) was evaluated in a phase III trial among 101 patients with hematologic malignancies who received highly emetogenic chemotherapy and hematopoietic cell transplant (HCT) regimens. Thirty-three of the patients received chemotherapy alone and 68 received conditioning chemotherapy for HCT. Overall, the addition of olanzapine to the 3-drug antiemetic regimen improved complete response compared with the 3-drug regimen alone (55% v 26%; P = .003). A benefit of olanzapine was observed in the delayed but not in the acute phase. In subgroup analysis, a benefit was observed among patients receiving HCT (autologous only) but not among the smaller group of patients treated with chemotherapy alone.

Addition of CPIs to Chemotherapy

Two trials of chemotherapy plus phased ipilimumab either discouraged ¹⁸ or prohibited ¹⁴ the use of steroids for antiemetic purposes. The first trial evaluated etoposide and a platinum with or without ipilimumab in patients with extensive-stage SCLC, ¹⁸ and the second trial evaluated paclitaxel and carboplatin with or without ipilimumab in patients with advanced squamous NCLC. ¹⁴ Ipilimumab did not improve OS in either trial. In an earlier trial, in which the addition of ipilimumab to dacarbazine improved OS among patients with untreated metastatic melanoma, the recommended antiemetic agents listed in the protocol did not include dexamethasone. ¹⁹

Four trials of chemotherapy plus atezolizumab noted that nausea and vomiting "should" or "may" be controlled with adequate antiemetics, but researchers also cautioned that systematic corticosteroids may attenuate the benefit of atezolizumab. The addition of atezolizumab to chemotherapy improved PFS but not OS in patients with triplenegative breast cancer, and improved both PFS and OS in patients with metastatic nonsquamous NSCLC, attensive-stage SCLC, and patients with stage IV nonsquamous NSCLC with no ALK or EGFR mutations.

TABLE 5. Antiemetic Administration in Adults by Radiation Therapy Risk Category

Risk Category	Dose	Schedule
High: Total-body irradiation		
5-HT ₃ receptor antagonist ^a		
Ondansetron	8 mg oral or 8 mg oral dissolving tablet, or 8 mg oral soluble film, or 8 mg or 0.15 mg/kg IV	Use as prophylactic therapy. Once daily to twice daily on days of radiation therapy, with first dose given before radiation therapy. Once daily to twice daily on day after each day of radiation therapy, if radiation therapy is not planned for that day
Granisetron	2 mg oral or 1 mg or 0.01 mg/kg IV	Use as prophylactic therapy. Once daily on days of radiation therapy, before radiation therapy Once daily on day after each day of radiatior therapy, if radiation therapy is not planned for that day
Corticosteroid		
Dexamethasone	4 mg oral or IV	Use as prophylactic therapy. Once daily on days of radiation therapy, before radiation therapy. Once daily on day following each day of radiation therapy, if radiation therapy is not planned for that day
Moderate: Upper abdomen, b craniospinal irradiation		
5-HT ₃ receptor antagonist ^c		
Ondansetron	8 mg oral or 8 mg oral dissolving tablet, or 8 mg oral soluble film, or 8 mg or 0.15 mg/kg IV	Use as prophylactic therapy. Once daily to twice daily on days of radiation therapy, with first dose given before radiation therapy ^d
Granisetron	2 mg oral or 1 mg or 0.01 mg/kg IV	Use as prophylactic therapy. Once daily on days of radiation therapy, before radiation therapy
Tropisetron	5 mg oral or IV	Use as prophylactic therapy. Once daily on days of radiation therapy, before radiation therapy
Corticosteroid		
Dexamethasone	4 mg oral or IV	Use as prophylactic therapy. Once daily on days of first 5 radiation therapy fractions, before radiation therapy
Low: Brain, head and neck, thorax, pelvise		
5-HT ₃ receptor antagonist ^f		
Ondansetron	8 mg oral or 8 mg oral dissolving tablet, or 8 mg oral soluble film, or 8 mg or 0.15 mg/kg IV	Use as breakthrough therapy. ^g
Granisetron	2 mg oral or 1 mg or 0.01 mg/kg IV	Use as breakthrough therapy.g
Corticosteroid		
Dexamethasone	For brain, if not already taking corticosteroid, 4 mg oral or IV; for other anatomic regions, 4 mg oral or IV	Use as breakthrough therapy. Titrate up as needed to maximum of 16 mg oral or IV daily. ^g
Dopamine receptor antagonisth		
Prochlorperazine	5-10 mg oral or IV.	Use as breakthrough therapy. Titrate up as needed to maximum of 3-4 administrations daily. ^g
Metoclopramide	5-20 mg oral or IV.	Use as breakthrough therapy. Titrate up as needed to maximum of 3-4 administrations daily. ^g
Minimal: Extremities, breast		
5-HT ₃ receptor antagonist ⁱ		
3 111/11 1		

TABLE 5. Antiemetic Administration in Adults by Radiation Therapy Risk Category (continued)

Risk Category	Dose	Schedule
Ondansetron	8 mg oral, 8 mg oral dissolving tablet, or 8 mg oral soluble film, or 8 mg or 0.15 mg/kg IV	Use as breakthrough therapy. ^j
Granisetron	2 mg oral or 1 mg or 0.01 mg/kg IV	Use as breakthrough therapy. ^j
Corticosteroid		
Dexamethasone	4 mg oral or IV	Use as breakthrough therapy. ^j
Dopamine receptor antagonisth		
Prochlorperazine	5-10 mg oral or IV.	Use as breakthrough therapy. ^j
Metoclopramide	5-20 mg oral or IV.	Use as breakthrough therapy. ^j

^aEither 5-HT₃ receptor antagonist is appropriate.

The addition of durvalumab to a platinum and etoposide was evaluated among patients with extensive-stage SCLC.¹⁶ Premedication with steroids for chemotherapy was permitted. In a planned interim analysis, the addition of durvalumab to chemotherapy improved OS.

Emetogenicity

All CPIs were classified as minimally emetogenic (Table 1). In the case of atezolizumab and ipilimumab, this represents a change from the 2017 guideline,⁵ in which each was classified as having low emetic risk. In trials published since the 2017 guideline, the difference in risk of vomiting with ipilimumab versus placebo was < 10%.^{23,24} Similarly, the addition of atezolizumab to chemotherapy produced only small increases in vomiting compared with chemotherapy alone.^{15,20-22} No RCTs were available for cemiplimab, and emetogenicity was classified as minimal based on the informal consensus of the Expert Panel. Emetic risk information was also added for 47 other new antineoplastic agents (Tables 1 and 2).

New Formulations of Antiemetic Agents

No new antiemetic agents were identified. An intravenous formulation of aprepitant that does not contain polysorbate 80 (a solubilizing agent associated with hypersensitivity reactions) was approved by the FDA for the treatment of chemotherapy-induced emesis in 2018. An intravenous formulation of netupitant-palonosetron was also approved by the FDA in 2018.

RECOMMENDATIONS

There is no evidence from clinical trials in adults to warrant omitting dexamethasone from guideline-compliant prophylactic antiemetic regimens when CPIs are administered in combination with chemotherapy. CPIs administered alone or in combination with another CPI are minimally emetogenic in adults and do not require routine use of a prophylactic antiemetic.

The full list of recommendations is provided in the Bottom Line Box. Recommendations for adults are unchanged with the exception of the option of adding olanzapine in the setting of hematopoietic stem cell transplantation. This change was prompted by the trial by Clemmons et al. 12 Evidence for the remaining recommendations is discussed in the 2017 guideline, 5 with no signals for change in the updated literature search. Updated information regarding the emetic risk of intravenous and oral antineoplastic agents in adults is provided in Tables 1 and 2. Table which lists antiemetic dosing information for adults antineoplastic risk category, has been revised to include 15-mg dose of olanzapine 11 as an option and to include 1 intravenous formulations of aprepitant and netupitant-palanosetron. Tables 4 and 5, which list emetic risk and

Recommendations for children have been updated to add fosaprepitant as an NK1-receptor antagonist option for children who receive highly or moderately emetogenic

antiemetic dosing for adult patients treated with radiation

therapy, remain the same as in the 2017 guideline.

bRadiation therapy involving (at least in part) the anatomic region from the superior border of the 11th thoracic vertebra to the inferior border of the third lumbar vertebra.

^cOndansetron or granisetron preferred because of the larger body of evidence for these agents.

^dMonitor patients during radiation therapy schedules spanning multiple weeks to detect symptoms experienced during interspersed days when radiation therapy and prophylaxis are not administered (eg, weekends) and to balance benefits and toxicities of prolonged 5-HT₃ receptor antagonist therapy.

^eCorticosteroid is the preferred first agent for the brain. Any antiemetic class is appropriate for head and neck, thorax, and pelvis.

^fEither 5-HT₃ receptor antagonist is appropriate.

^gDepending on the severity of symptoms and the remaining duration of radiation therapy, patients can receive subsequent breakthrough therapy as needed or begin receiving prophylactic therapy for the remainder of radiation therapy.

^hEither dopamine-receptor antagonist is appropriate. Metoclopramide is a dual dopamine/5-HT₃ receptor antagonist.

Either 5-HT₃ receptor antagonist is appropriate.

ⁱPatients can receive breakthrough therapy as needed. Alternative explanations for symptoms should be investigated to avoid the need for prophylactic therapy for the remainder of radiation therapy.

chemotherapy. This is based on the trial by Radhakrishnan et al¹⁰ and the addition of pediatric patients to US prescribing information for fosaprepitant.²⁵ Other recommendations for pediatric patients remain unchanged. The evidence for these recommendations is discussed in the 2017 guideline,⁵ with no signals for change in the updated literature search. Pediatric patients were not included in the statement regarding dexamethasone and CPIs due to a lack of direct evidence in this population.

DISCUSSION

Chemotherapy-induced nausea and vomiting (CINV) have been consistently demonstrated to be among the most feared adverse effects of cancer treatment. Significant progress has been made in limiting CINV through the introduction of several classes of antiemetics and their evidence-based incorporation into antiemetic regimens. Corticosteroids—almost exclusively dexamethasone—have been shown to be effective and safe agents for use either as single agents with low emetogenic chemotherapy or as essential components of multiagent, combination antiemetic regimens with moderate and highly emetogenic chemotherapy.

CPIs have recently become an integral component of antineoplastic treatment in a variety of settings.30-32 Some theoretical concerns have been expressed that concurrent corticosteroid use might potentially compromise the antineoplastic efficacy of CPIs.33,34 No definitive data are currently available to prove or disprove this hypothesis. Small retrospective series have suggested inferior survival outcomes in patients receiving concurrent corticosteroid (≥ 10 mg of prednisone equivalent daily) used as largely palliative therapy for various conditions (eg, chronic obstructive pulmonary disease, anorexia—not as antiemetics) and CPIs administered as monotherapy. 7,8,35 These 3 series are small and have inadequate information on corticosteroid dose, duration, and indication for use. In 1 series, patients receiving corticosteroids for nonpalliative indications had comparable survival as patients not receiving corticosteroids.8 A systematic review of the literature was reported in 2017 assessing clinical outcomes of patients with cancer treated with CPIs and concomitant corticosteroids.³⁶ No clear evidence of a poorer clinical outcome was noted in the reviewed populations.

The 2017 ASCO Antiemetic Guideline update⁵ listed both atezolizumab and ipilimumab in the low-emetic-risk category. Based upon available updated data, the guideline panel recommends that these agents and all other approved anti–PD-1, anti–PD-L1, and the anti–CTLA-4 agent ipilimumab now be listed as minimally emetogenic. The current NCCN guidelines also categorize all available CPIs as minimally emetogenic.³⁷ Therefore, no routine antiemetic prophylaxis is indicated when these agents are used

as monotherapy or combined with another CPI in the absence of chemotherapy.

A number of phase III trials in NSCLC, 13,14,17 SCLC, 15,16 and breast cancer²⁰ have demonstrated superior PFS, OS, or both when a CPI is combined with chemotherapy compared with chemotherapy alone. A variety of different prophylactic antiemetic regimens were used in these studies. With regard to corticosteroid use as a component of antiemetic prophylaxis, some trials either prohibited14 or actively discouraged¹⁸ corticosteroid use. Other trials^{15,16,20} allowed but did not specifically recommend corticosteroid use. Two trials in NSCLC, however, specified a guideline-compliant antiemetic regimen that included a corticosteroid. 13,17 KEYNOTE 189 and KEYNOTE 407 evaluated the role of platinum-based chemotherapy used alone or in combination with the anti-PD1 agent pembrolizumab in patients with metastatic nonsquamous and squamous NSCLC, respectively. The combination of a 5-hydroxytryptamine type 3 receptor antagonist, dexamethasone (or equivalent), and the NK1receptor antagonist aprepitant were recommended as the antiemetic regimen to use prior to chemotherapy administration. PFS and OS in these 2 trials were significantly superior in the arms containing pembrolizumab. Thus, the panel has concluded there is no clinical evidence to warrant deleting dexamethasone from guideline-compliant prophylactic antiemetic regimens when CPIs are administered in combination with chemotherapy.

No new antiemetic agents have been introduced since the 2017 antiemetic update. Intravenous formulations of aprepitant and netupitant-palonosetron were approved by the FDA for the treatment of chemotherapy-induced emesis in 2018, and a 5-mg dose of olanzapine has been shown to be safe and effective when used in combination with a 5-HT₃ receptor antagonist, dexamethasone, and an NK1-receptor antagonist with highly emetogenic chemotherapy. Olanzapine also showed promising efficacy in the setting of high-dose chemotherapy and stem cell transplantation, ¹² and is an option to be added to the combination of a 5-HT₃ receptor antagonist, an NK1 receptor antagonist, and dexamethasone. Finally, this update has categorized the emetogenic potential of the new antineoplastic agents FDA approved since the 2017 update.

EXTERNAL REVIEW AND OPEN COMMENT

The draft recommendations were released to the public for open comment from February 28, 2020, through March 13, 2020. Response categories were "Agree as written," "Agree with suggested modifications," and "Disagree. See comments" were captured for every proposed recommendation with 10 written comments received. The level of agreement with each recommendation (either agree as written or agree with slight modifications) ranged from 90% to 100%. The full guideline was also reviewed by 2 external reviewers with content expertise.

GUIDELINE IMPLEMENTATION

ASCO guidelines are developed for implementation across health settings. Each ASCO guideline includes a member from ASCO's Practice Guideline Implementation Network (PGIN) on the panel. The additional role of this PGIN representative on the guideline panel is to assess the suitability of the recommendations to implementation in the community setting and also to identify any other barrier to implementation a reader should be aware of. Barriers to implementation include the need to increase awareness of the guideline recommendations among front-line practitioners and survivors of cancer and caregivers, and also to provide adequate services in the face of limited resources. The guideline Bottom Line Box was designed to facilitate implementation of recommendations. This guideline will be distributed widely through the ASCO PGIN. ASCO guidelines are posted on the ASCO web site and most often published in the Journal of Clinical Oncology and the JCO Oncology Practice.

ASCO believes that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

ADDITIONAL RESOURCES

More information, including a supplement with additional evidence tables, slide sets, and clinical tools and resources, is available at www.asco.org/supportive-care-guideliness. Patient information is available at www.cancer.net.

RELATED ASCO GUIDELINES

- Integration of Palliative Care into Standard Oncology Practice³⁸ (http://ascopubs.org/doi/ 10.1200/JC0.2016.70.1474)
- Patient-Clinician Communication³⁹ (http://ascopubs.org/doi/10.1200/JC0.2017.75.2311)

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EDITOR'S NOTES

This American Society of Clinical Oncology (ASCO) Clinical Practice Guideline provides recommendations, with comprehensive review and analyses of the relevant literature for each recommendation. Additional information, including a supplement with additional evidence tables, slide sets, clinical tools and resources, and links to patient information at www.cancer.net, is available at www.asco.org/supportive-careguidelines.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

Disclosures provided by the authors and data availability statement (if applicable) are available with this article at DOI https://doi.org/10.1200/JCO.20.01296.

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REFERENCES

- 1. Gralla RJ, Osoba D, Kris MG, et al: Recommendations for the use of antiemetics: Evidence-based, clinical practice guidelines. J Clin Oncol 17:2971-2994, 1999
- 2. Kris MG, Hesketh PJ, Somerfield MR, et al: American Society of Clinical Oncology guideline for antiemetics in oncology: Update 2006. J Clin Oncol 24:
- 3. Basch E, Prestrud AA, Hesketh PJ, et al: Antiemetics: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 29:4189-4198, 2011 [Erratum: J Clin Oncol 36:1459, 2018]

- 4. Hesketh PJ, Bohlke K, Lyman GH, et al: Antiemetics: American Society of Clinical Oncology focused guideline update. J Clin Oncol 34:381-386, 2016
- 5. Hesketh PJ, Kris MG, Basch E, et al: Antiemetics: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 35:3240-3261, 2017
- 6. Shojania KG, Sampson M, Ansari MT, et al: How quickly do systematic reviews go out of date? A survival analysis. Ann Intern Med 147:224-233, 2007
- Arbour KC, Mezquita L, Long N, et al: Impact of baseline steroids on efficacy of programmed cell death-1 and programmed death-ligand 1 blockade in patients with non-small-cell lung cancer. J Clin Oncol 36:2872-2878, 2018
- 8. Ricciuti B, Dahlberg SE, Adeni A, et al: Immune checkpoint inhibitor outcomes for patients with non-small-cell lung cancer receiving baseline corticosteroids for palliative versus nonpalliative indications. J Clin Oncol 37:1927-1934, 2019
- Shiffman RN, Michel G, Rosenfeld RM, et al: Building better guidelines with BRIDGE-Wiz: Development and evaluation of a software assistant to promote clarity, transparency, and implementability. J Am Med Inform Assoc 19:94-101, 2012
- Radhakrishnan V, Joshi A, Ramamoorthy J, et al: Intravenous fosaprepitant for the prevention of chemotherapy-induced vomiting in children: A double-blind, placebo-controlled, phase III randomized trial. Pediatr Blood Cancer 66:e27551, 2019
- 11. Hashimoto H, Abe M, Tokuyama O, et al: Olanzapine 5 mg plus standard antiemetic therapy for the prevention of chemotherapy-induced nausea and vomiting (J-FORCE): A multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol 21:242-249, 2020
- 12. Clemmons AB, Orr J, Andrick B, et al: Randomized, placebo-controlled, phase III trial of Fosaprepitant, Ondansetron, Dexamethasone (FOND) versus FOND Plus Olanzapine (FOND-O) for the prevention of chemotherapy-induced nausea and vomiting in patients with hematologic malignancies receiving highly emetogenic chemotherapy and hematopoietic cell transplantation regimens: The FOND-O Trial. Biol Blood Marrow Transplant 24:2065-2071, 2018
- Gandhi L, Rodríguez-Abreu D, Gadgeel S, et al: Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer. N Engl J Med 378:2078-2092, 2018
- Govindan R, Szczesna A, Ahn MJ, et al: Phase III trial of ipilimumab combined with paclitaxel and carboplatin in advanced squamous non-small-cell lung cancer. J Clin Oncol 35:3449-3457, 2017
- Horn L, Mansfield AS, Szczęsna A, et al: First-line atezolizumab plus chemotherapy in extensive-stage small-cell lung cancer. N Engl J Med 379:2220-2229, 2018
- Paz-Ares L, Dvorkin M, Chen Y, et al: Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): A randomised, controlled, open-label, phase 3 trial. Lancet 394:1929-1939, 2019
- 17. Paz-Ares L, Luft A, Vicente D, et al: Pembrolizumab plus chemotherapy for squamous non-small-cell lung cancer. N Engl J Med 379:2040-2051, 2018
- 18. Reck M, Luft A, Szczesna A, et al: Phase III randomized trial of ipilimumab plus etoposide and platinum versus placebo plus etoposide and platinum in extensive-stage small-cell lung cancer. J Clin Oncol 34:3740-3748, 2016
- 19. Robert C, Thomas L, Bondarenko I, et al: Ipilimumab plus dacarbazine for previously untreated metastatic melanoma. N Engl J Med 364:2517-2526, 2011
- 20. Schmid P, Adams S, Rugo HS, et al: Atezolizumab and nab-paclitaxel in advanced triple-negative breast cancer. N Engl J Med 379:2108-2121, 2018
- 21. Socinski MA, Jotte RM, Cappuzzo F, et al: Atezolizumab for first-line treatment of metastatic nonsquamous NSCLC. N Engl J Med 378:2288-2301, 2018
- 22. West H, McCleod M, Hussein M, et al: Atezolizumab in combination with carboplatin plus nab-paclitaxel chemotherapy compared with chemotherapy alone as first-line treatment for metastatic non-squamous non-small-cell lung cancer (IMpower130): A multicentre, randomised, open-label, phase 3 trial. Lancet Oncol 20:924-937, 2019
- 23. Beer TM, Kwon ED, Drake CG, et al: Randomized, double-blind, phase III trial of ipilimumab versus placebo in asymptomatic or minimally symptomatic patients with metastatic chemotherapy-naive castration-resistant prostate cancer. J Clin Oncol 35:40-47, 2017
- 24. Eggermont AM, Chiarion-Sileni V, Grob JJ, et al: Prolonged survival in stage III melanoma with ipilimumab adjuvant therapy. N Engl J Med 375:1845-1855, 2016
- US Food and Drug Administration: Prescribing information, EMEND (fosaprepitant) for injection, for intravenous use. 2019. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/022023s019lbl.pdf
- 26. de Boer-Dennert M, de Wit R, Schmitz PI, et al: Patient perceptions of the side-effects of chemotherapy: The influence of 5HT3 antagonists. Br J Cancer 76: 1055-1061, 1997
- Lorusso D, Bria E, Costantini A, et al: Patients' perception of chemotherapy side effects: Expectations, doctor-patient communication and impact on quality of life - An Italian survey. Eur J Cancer Care (Engl) 26:26, 2017
- 28. Aapro M, Molassiotis A, Dicato M, et al: The effect of guideline-consistent antiemetic therapy on chemotherapy-induced nausea and vomiting (CINV): The Pan European Emesis Registry (PEER). Ann Oncol 23:1986-1992, 2012
- loannidis JP, Hesketh PJ, Lau J: Contribution of dexamethasone to control of chemotherapy-induced nausea and vomiting: A meta-analysis of randomized evidence. J Clin Oncol 18:3409-3422, 2000
- 30. Wieder T, Eigentler T, Brenner E, et al: Immune checkpoint blockade therapy. J Allergy Clin Immunol 142:1403-1414, 2018
- 31. Lievense LA, Sterman DH, Cornelissen R, et al: Checkpoint blockade in lung cancer and mesothelioma. Am J Respir Crit Care Med 196:274-282, 2017
- 32. Schadendorf D, van Akkooi ACJ, Berking C, et al: Melanoma. Lancet 392:971-984, 2018
- 33. Cook AM, McDonnell AM, Lake RA, et al: Dexamethasone co-medication in cancer patients undergoing chemotherapy causes substantial immunomodulatory effects with implications for chemo-immunotherapy strategies. OncoImmunology 5:e1066062, 2015
- 34. Giles AJ, Hutchinson MND, Sonnemann HM, et al: Dexamethasone-induced immunosuppression: Mechanisms and implications for immunotherapy. J Immunother Cancer 6:51, 2018
- 35. Fucà G, Galli G, Poggi M, et al: Modulation of peripheral blood immune cells by early use of steroids and its association with clinical outcomes in patients with metastatic non-small cell lung cancer treated with immune checkpoint inhibitors. ESMO Open 4:e000457, 2019
- 36. Garant A, Guilbault C, Ekmekjian T, et al: Concomitant use of corticosteroids and immune checkpoint inhibitors in patients with hematologic or solid neoplasms: A systematic review. Crit Rev Oncol Hematol 120:86-92, 2017
- 37. National Comprehensive Cancer Network: NCCN Clinical Practice Guidelines in Oncology: Antiemesis. Plymouth Meeting, PA, National Comprehensive Cancer Network, 2019
- 38. Ferrell BR, Temel JS, Temin S, et al: Integration of palliative care into standard oncology care: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 35:96-112, 2017
- 39. Gilligan T, Coyle N, Frankel RM, et al: Patient-clinician communication: American Society of Clinical Oncology Consensus Guideline. J Clin Oncol 35: 3618-3632, 2017

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Antiemetics: ASCO Guideline Update

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Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

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APPENDIX

TABLE A1. Antiemetics Expert Panel Membership

Name	Affiliation/Institution	Role/Area of Expertise
Paul J. Hesketh, MD (co-chair)	Lahey Hospital and Medical Center, Burlington, MA	Medical oncology, thoracic oncology, supportive care, investigational therapeutics
Mark G. Kris, MD (co-chair)	Memorial Sloan Kettering Cancer Center, New York, NY	Medical oncology, thoracic oncology, supportive care, investigational therapeutics
Ethan Basch, MD, MSc	University of North Carolina at Chapel Hill, Chapel Hill, NC	Medical oncology, health services research, patient-reported outcomes, comparative effectiveness research
Gary H. Lyman, MD, MPH	Fred Hutchinson Cancer Research Center and University of Washington, Seattle, WA	Hematology and oncology, health economics, epidemiology and biostatistics
Sally Y. Barbour, PharmD, BCOP, CPP	Duke University Medical Center, Durham, NC	Oncology pharmacy
Rebecca Anne Clark-Snow, RN, BSN, OCN	Overland Park, KS	Oncology nursing, supportive care
Michael A. Danso, MD (PGIN representative)	Virginia Oncology Associates, Norfolk and Virginia Beach, VA	Medical oncology, community oncology, clinical trials
Kristopher Dennis, MD, PhD	The Ottawa Hospital and the University of Ottawa, Ottawa, Ontario, Canada	Radiation oncology, supportive care
L. Lee Dupuis, RPh, ACPR, MScPhm, PhD	The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada	Supportive care of children with cancer
Stacie B. Dusetzina, PhD	Vanderbilt University School of Medicine and Vanderbilt-Ingram Cancer Center, Nashville, TN	Health economics, pharmaceutical outcomes and policy
Cathy Eng, MD	Vanderbilt-Ingram Cancer Center, Nashville, TN	Gastrointestinal medical oncology
Petra C. Feyer, MD, PhD	Vivantes Clinics Neukoelln, Berlin, Germany	Radiation oncology, supportive care
Karin Jordan, MD	University of Heidelberg, Heidelberg, Germany	Medical oncology, supportive care
Kimberly Noonan, MS, RN, ANP, AOCN	Dana-Farber Cancer Institute, Boston, MA	Oncology nursing
Dee Sparacio, MS	Hightstown, NJ	Patient representative
Kari Bohlke, ScD	American Society of Clinical Oncology (ASCO), Alexandria, VA	ASCO Practice Guideline Staff (Health Research Methods)