Cancer Cachexia: ASCO Guideline Rapid Recommendation Update

Eric J. Roeland, MD[1]; Kari Bohlke, ScD[2]; Vickie E. Baracos, PhD[3]; Thomas J. Smith, MD[4]; and Charles L. Loprinzi, MD[5]; for the Cancer Cachexia Expert Panel

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ASCO Rapid Recommendations Updates highlight revisions to select ASCO guideline recommendations as a response to the emergence of new and practice-changing data. The rapid updates are supported by an evidence review and follow the guideline development processes outlined in the ASCO Guideline Methodology Manual. The goal of these articles is to disseminate updated recommendations, in a timely manner, to better inform health practitioners and the public on the best available cancer care options. See the Appendix for disclaimers and other important information (Appendix 1 and Appendix 2, online only).

ACCOMPANYING CONTENT

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Appendix

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BACKGROUND

In 2020, ASCO published a guideline on the management of cancer cachexia in adults with advanced cancer.[1] Evidence was insufficient to strongly endorse any pharmacologic agent, but recommendations supported clinicians in offering a short-term trial of a progesterone analog or corticosteroid to patients experiencing loss of weight and/or appetite. The Expert Panel discussed a potential role for olanzapine but concluded that the evidence was insufficient for a recommendation. The publication of a 2023 randomized controlled trial (RCT) of olanzapine prompted the Expert Panel to revisit this topic.[2]

METHODS

An updated literature search identified RCTs published from October 1, 2019, to April 19, 2023. Five addressed pharmacologic interventions.[2-6] The Expert Panel reviewed the evidence and approved the revised recommendations. The quality of evidence and strength of recommendation were classified using the methods of the 2020 guideline.[1]

EVIDENCE REVIEW

Investigators evaluated olanzapine's impact on chemotherapy-related anorexia in a double-blind, placebo-controlled RCT that enrolled 124 adults (median age 55 years) with locally advanced or metastatic gastric, hepatopancreaticobiliary, or lung cancer. Starting with chemotherapy initiation, patients received olanzapine (2.5 mg once a day) or placebo for 12 weeks. During the 4 days after chemotherapy, all patients received olanzapine 5 mg once a day and dexamethasone as antiemetics.[2] Weight gain > 5% occurred in 60% of patients in the olanzapine arm versus 9% in the placebo arm ($P < .001$). Patients receiving olanzapine also experienced improved appetite. Grade ≥3 chemotherapy toxicity was less common with olanzapine (12%, *v* 37% with placebo, $P = .002$). Grade ≥3 toxicity attributed to the trial drug occurred in one patient in the olanzapine arm and two patients in the placebo arm.

Additional data from a 2010 trial of 80 patients with advanced GI or lung cancers showed that adding olanzapine to megestrol acetate resulted in significantly more weight gain than megestrol acetate alone. The effect on appetite was even more pronounced.[7] Finally, a pilot RCT supported olanzapine's impact on appetite over 1 week in patients with advanced cancer and nausea unrelated to chemotherapy (appetite numeric rating score was 2/10 with placebo *v* 7/10 with olanzapine 5 mg once daily).[6] This trial included 30 patients with breast, head and neck, gynecologic, genitourinary, GI, or lung cancer. Patients in these latter two trials did not receive

concurrent chemotherapy. Currently, it is unclear whether olanzapine improves strength or body composition in patients with cancer-associated anorexia.

In the opinion of the Expert Panel, the other identified trials[3-5] did not change prior pharmacologic intervention guideline recommendations. Notably, mirtazapine 15 mg once nightly was no better than placebo for cancer-related anorexia and cachexia,[4] which aligns with the 2020 guideline recommendations.

UPDATED RECOMMENDATIONS

Note: There are currently no FDA-approved medications to treat cancer cachexia.

Recommendation 2.1

For adults with advanced cancer, clinicians may offer low-dose olanzapine once daily to improve weight gain and appetite (Type: Evidence based; Evidence quality: Intermediate; Strength of recommendation: Moderate).

Qualifying statement: The majority of evidence for Recommendation 2.1 involves patients with lung or GI cancer, and the largest study enrolled patients receiving cytotoxic chemotherapy.

Recommendation 2.2

For patients who cannot tolerate low-dose olanzapine, clinicians may offer a short-term trial of a progesterone analog or a corticosteroid to those experiencing loss of weight and/or appetite (Type: Evidence based; Evidence quality: Intermediate; Strength of recommendation: Moderate).

A table of all guideline recommendations is available at www.asco.org/supportive-care-guidelines.

AFFILIATIONS

[1]Oregon Health and Science University, Knight Cancer Institute, Portland, OR
[2]American Society of Clinical Oncology, Alexandria, VA
[3]University of Alberta, Edmonton, Alberta, Canada
[4]Johns Hopkins Medicine, Baltimore, MD
[5]Mayo Clinic, Rochester, MN

CORRESPONDING AUTHOR

American Society of Clinical Oncology, 2318 Mill Rd, Suite 800, Alexandria, VA 22314; e-mail: guidelines@asco.org.

EDITOR'S NOTE

This ASCO Clinical Practice Guideline Recommendation Update provides a recommendation update, with a review and analysis of the relevant literature for the recommendation. Additional information, including links to patient information at www.cancer.net, is available at www.asco.org/supportive-care-guidelines

EQUAL CONTRIBUTION

E.J.R. and C.L.L. were Expert Panel cochairs.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

Conception and design: All authors
Collection and assembly of data: Kari Bohlke, Thomas J. Smith, Charles L. Loprinzi
Data analysis and interpretation: All authors
Manuscript writing: All authors
Final approval of manuscript: All authors
Accountable for all aspects of the work: All authors

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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Eric J. Roeland
Consulting or Advisory Role: Napo Pharmaceuticals, Helsinn Therapeutics, Byomass, Veloxis, PRA Health, Actimed Therapeutics, Takeda, Meter Health
Travel, Accommodations, Expenses: Pfizer

Vickie E. Baracos
Honoraria: Pfizer, Nestle health science
Consulting or Advisory Role: Nestle Health Science, Pfizer
Research Funding: Baxter

Thomas J. Smith
Employment: UpToDate
Honoraria: Athenex, Association of Community Cancer Centers
Patents, Royalties, Other Intellectual Property: Royalties from Oxford Textbook of Cancer Communication, co-editor
Open Payments Link: https://openpaymentsdata.cms.gov/physician/202382

Charles L. Loprinzi
Consulting or Advisory Role: Metys Pharmaceuticals, Disarm Therapeutics, OnQuality Pharmaceuticals, NKMax, Mitsubishi Tanabe Pharma, Veloxis, Metys Pharmaceuticals, Hengrui Pharmaceutical, Osmol Therapeutics, Grunenthal, Neuropathix, Denali Therapeutics, Bexion, Veloxis, Vevro, Galendia, Hengrui Pharmaceutical, Neuropathix, Neuropathix, Denali Therapeutics, Bexion, Bexion, Bexion, Genentech
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APPENDIX 3. CANCER CACHEXIA GUIDELINE PANEL

The following are members of the Cancer Cachexia Guideline Panel: Eric J. Roeland, MD; Vickie E. Baracos, PhD; Eduardo Bruera, MD; Egidio del Fabbro, MD; Suzanne Dixon, MPH, MS, RD; Marie Fallon, MD; Jørn Herrstedt, MD, DMSci; Harold Lau, MD; Mary Platek, PhD, MS, RD; Hope S. Rugo, MD; Thomas J. Smith, MD; Winston Tan, MD; Charles L. Loprinzi, MD.