VOLUME 36 · NUMBER 25 · SEPTEMBER 1, 2018

JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

Integrative Therapies During and After Breast Cancer Treatment: ASCO Endorsement of the SIO Clinical Practice Guideline

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Published at jco.org on June 11, 2018.

G.H.L. and L.C. were Expert Panel co-chairs.

Clinical Practice Guideline Committee Approved: March 8, 2018.

Editor's note: 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 Data Supplement with additional evidence tables, a Methodology Supplement, slide sets, clinical tools and resources, and links to patient information at www.cancer.net, is available at www.asco.org/supportive-care-guidelines.

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0732-183X/18/3625w-2647w/$20.00

ABSTRACT

Purpose

The Society for Integrative Oncology (SIO) produced an evidence-based guideline on use of integrative therapies during and after breast cancer treatment that was determined to be relevant to the American Society of Clinical Oncology (ASCO) membership. ASCO considered the guideline for endorsement.

Methods

The SIO guideline addressed the use of integrative therapies for the management of symptoms and adverse effects, such as anxiety and stress, mood disorders, fatigue, quality of life, chemotherapy-induced nausea and vomiting, lymphedema, chemotherapy-induced peripheral neuropathy, pain, and sleep disturbance. Interventions of interest included mind and body practices, natural products, and lifestyle modifications. SIO systematic reviews focused on randomized controlled trials that were published from 1990 through 2015. The SIO guideline was reviewed by ASCO content experts for clinical accuracy and by ASCO methodologists for developmental rigor. On favorable review, an ASCO Expert Panel was convened to review the guideline contents and recommendations.

Results

The ASCO Expert Panel determined that the recommendations in the SIO guideline—published in 2017—are clear, thorough, and based on the most relevant scientific evidence. ASCO endorsed the guideline with a few added discussion points.

Recommendations

Key recommendations include the following: Music therapy, meditation, stress management, and yoga are recommended for anxiety/stress reduction. Meditation, relaxation, yoga, massage, and music therapy are recommended for depression/mood disorders. Meditation and yoga are recommended to improve quality of life. Acupressure and acupuncture are recommended for reducing chemotherapy-induced nausea and vomiting. Acetyl-L-carnitine is not recommended to prevent chemotherapy-induced peripheral neuropathy because of a possibility of harm. No strong evidence supports the use of ingested dietary supplements to manage breast cancer treatment–related adverse effects. Additional information is available at: www.asco.org/supportive-care-guidelines.

J Clin Oncol 36:2647-2655. © 2018 by American Society of Clinical Oncology

INTRODUCTION

Integrative oncology coordinates the delivery of evidence-based complementary therapies with conventional cancer care.[1] Complementary therapies encompass a broad range of mind and body practices, natural products, and lifestyle modifications, and are commonly used by patients with breast cancer and survivors of breast cancer.[2-4] Although evidence remains limited for many of these therapies, a growing number of well-conducted randomized controlled trials suggests that selected therapies may improve the management of symptoms and adverse effects as a result of breast cancer and its treatment. Of importance, trials have also highlighted therapies that either provide no benefit or pose a risk to patients. To summarize the available evidence for clinicians and to provide evidence-based guidance on the use of integrative therapies during and after breast cancer treatment, the Society for Integrative Oncology (SIO) published an updated clinical practice guideline in 2017.[5] In addition to

ASSOCIATED CONTENT

Appendix
DOI: https://doi.org/10.1200/JCO.2018.79.2721

Data Supplement
DOI: https://doi.org/10.1200/JCO.2018.79.2721

DOI: https://doi.org/10.1200/JCO.2018.79.2721

THE BOTTOM LINE

Integrative Therapies During and After Breast Cancer Treatment: ASCO Endorsement of the SIO Clinical Practice Guideline

ASCO endorses the SIO guideline, Clinical Practice Guidelines on the Evidence-Based Use of Integrative Therapies During and After Breast Cancer Treatment, with some added discussion points.

Guideline Question

What are evidence-based approaches to the use of integrative therapies in the management of symptoms and adverse effects during and after breast cancer treatment?

Target Population

Patients undergoing treatment of breast cancer and survivors of breast cancer

Target Audience

Oncologists, integrative medicine providers, supportive care specialists, nurses, pharmacists, primary care providers, and patients with breast cancer

Methods

An ASCO Expert Panel was convened to consider endorsing the SIO guideline, Clinical Practice Guidelines on the Evidence-Based Use of Integrative Therapies During and After Breast Cancer Treatment. Recommendations in the SIO guideline were based on a systematic review of the medical literature. The ASCO Expert Panel considered the methodology used in the SIO guideline by considering the results from the Appraisal of Guidelines for Research and Evaluation II review instrument. The ASCO Expert Panel also carefully reviewed the SIO guideline content to determine appropriateness for ASCO endorsement.

KEY RECOMMENDATIONS

A description of the recommendation grading system used by the SIO is provided in Table 1. In addition to the following recommendations, the SIO guideline lists several outcomes and therapies for which evidence was insufficient and no recommendation was made. This list is provided in Table 2 of this endorsement, with additional information provided in the SIO guideline. (ASCO Expert Panel's Statements in ***bold italics***.)

Acute Radiation Skin Reaction

- Aloe vera and hyaluronic acid cream should not be recommended for improving acute radiation skin reaction. (Grade D)

Anxiety and Stress Reduction

- Meditation is recommended for reducing anxiety. (Grade A)
- Music therapy is recommended for reducing anxiety. (Grade B)
- Stress management is recommended for reducing anxiety during treatment, but longer group programs are likely better than self-administered home programs or shorter programs. (Grade B)
- Yoga is recommended for reducing anxiety. (Grade B)
- Acupuncture, massage, and relaxation can be considered for reducing anxiety. (Grade C)

Chemotherapy-Induced Nausea and Vomiting

- Acupressure can be considered as an addition to antiemetic drugs to control nausea and vomiting during chemotherapy. (Grade B)
- Electroacupuncture can be considered as an addition to antiemetic drugs to control vomiting during chemotherapy. (Grade B)
- Ginger and relaxation can be considered as additions to antiemetic drugs to control nausea and vomiting during chemotherapy. (Grade C)
- Glutamine should not be recommended for improving nausea and vomiting during chemotherapy. (Grade D)

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THE BOTTOM LINE (CONTINUED)

ASCO Discussion Point: The Grade B recommendations for acupressure and electroacupuncture differ from the 2017 ASCO antiemetic guideline, which states that evidence remains insufficient for a recommendation for or against complementary therapies for chemotherapy-induced nausea and vomiting.[7] The ASCO Expert Panel feels that Grade C would be more appropriate given the limitations of the available evidence.

Depression and Mood Disturbance

- Meditation, particularly mindfulness-based stress reduction, is recommended for treating mood disturbance and depressive symptoms. (Grade A)
- Relaxation is recommended for improving mood disturbance and depressive symptoms. (Grade A)
- Yoga is recommended for improving mood disturbance and depressive symptoms. (Grade B)
- Massage is recommended for improving mood disturbance. (Grade B)
- Music therapy is recommended for improving mood disturbance. (Grade B)
- Acupuncture, healing touch, and stress management can be considered for improving mood disturbance and depressive symptoms. (Grade C)

Fatigue

- Hypnosis and ginseng can be considered for improving fatigue during treatment. (Grade C)
- Acupuncture and yoga can be considered for improving post-treatment fatigue. (Grade C)
- Acetyl-L-carnitine and guarana should not be recommended for improving fatigue during treatment. (Grade D)

ASCO Discussion Point: The safety and efficacy of ginseng may vary by type of ginseng, and patients should seek guidance from a health care professional before using a dietary supplement. Some ginseng preparations may have estrogenic properties. The ginseng studies cited by the SIO guideline used American ginseng (*Panax quinquefolius*) that was tested for quality and potency; the duration of treatment in these studies was short (8 weeks), and the safety and efficacy of ginseng over longer periods remains uncertain.

Lymphedema

- Low-level laser therapy, manual lymphatic drainage, and compression bandaging can be considered for improving lymphedema. (Grade C)

Neuropathy

- Acetyl-L-carnitine is not recommended for the prevention of chemotherapy-induced peripheral neuropathy in patients with breast cancer due to potential harm. (Grade H)

Pain

- Acupuncture, healing touch, hypnosis, and music therapy can be considered for the management of pain. (Grade C)

Quality of Life

- Meditation is recommended for improving quality of life. (Grade A)
- Yoga is recommended for improving quality of life. (Grade B)
- Acupuncture, mistletoe, qigong, reflexology, and stress management can be considered for improving quality of life. (Grade C)

ASCO Discussion Point: The mistletoe trials cited by the SIO guideline evaluated subcutaneous delivery only. Subcutaneous mistletoe is not currently approved by the US Food and Drug Administration. Orally available mistletoe is available in the United States, but ingestion of high doses of mistletoe berry or leaf is known to cause serious adverse reactions.[8]

Sleep Disturbance

- Gentle yoga can be considered for improving sleep. (Grade C)

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THE BOTTOM LINE (CONTINUED)

Vasomotor/Hot Flashes

- Acupuncture can be considered for improving hot flashes. (Grade C)
- Soy is not recommended for hot flashes in patients with breast cancer due to lack of effect. (Grade D)

Additional Resources

More information, including a Data Supplement, a Methodology Supplement, slide sets, and clinical tools and resources, is available at www.asco.org/supportive-care-guidelines. Patient information is available at www.cancer.net.

The SIO guideline is available at http://onlinelibrary.wiley.com/doi/10.3322/caac.21397/epdf.

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.

Recommendations reprinted from Greenlee et al,[5] with permission.

recommendations, the SIO guideline provides training and licensure information for several types of complementary therapy providers (see Table 2 in the SIO guideline).

The purpose of this ASCO guideline endorsement is to critically evaluate the SIO guideline. Upon detailed appraisal of the guideline and supporting evidence, ASCO has decided to endorse the SIO guideline on the use of integrative therapies during and after breast cancer treatment. This endorsement reinforces the recommendations provided in the SIO guideline and acknowledges the effort put forth by SIO to inform practitioners who care for patients with breast cancer. SIO recommendations are listed in the Bottom Line Box, with additional discussion points from the ASCO Expert Panel. The full SIO guideline is available at: http://onlinelibrary.wiley.com/doi/10.3322/caac.21397/epdf.

OVERVIEW OF THE ASCO GUIDELINE ENDORSEMENT PROCESS

The American Society of Clinical Oncology (ASCO) has policies and procedures for endorsing practice guidelines that have been developed by other professional organizations. The goal of guideline endorsement is to increase the number of high-quality, ASCO-vetted guidelines available to the ASCO membership. The ASCO endorsement process includes an assessment by ASCO staff of candidate guidelines for methodologic quality using the Rigor of Development subscale of the Appraisal of Guidelines for Research and Evaluation II instrument (See Methodology Supplement for more detail).

Disclaimer

The clinical practice guidelines and other guidance published herein are provided by the American Society of Clinical Oncology, Inc. ("ASCO") to assist providers in clinical decision making. The information therein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care. With the rapid development of scientific knowledge, new evidence may emerge between the time information is developed and when it is published or read. The information is not continually updated and may not reflect the most recent evidence. The information addresses only the topics specifically identified therein and is not applicable to other interventions, diseases, or stages of diseases. This information does not mandate any particular course of medical care. Further, the information is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. Recommendations reflect high, moderate, or low confidence that the recommendation reflects the net effect of a given course of action. The use of words like "must," "must not," "should," and "should not" indicate that a course of action is recommended or not recommended for either most or many patients, but there is latitude for the treating physician to select other courses of action in individual cases. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. ASCO provides this information on an "as is" basis, and makes no warranty, express or implied, regarding the information. ASCO specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. ASCO 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.

Table 1. Recommendation Grading System Used in the SIO Guideline[5]

Grade	Definition
A	Recommends the modality (there is high certainty that the net benefit is substantial—offer/provide this modality).
B	Recommends the modality (there is high certainty that the net benefit is moderate, or there is moderate certainty that the net benefit is moderate to substantial—offer/provide this modality).
C	Recommends selectively offering or providing this service to individual patients based on professional judgment and patient preferences (there is at least moderate certainty that the net benefit is small—offer/provide this modality for selected patients, depending on individual circumstances).
D	Recommends against the service (there is moderate or high certainty that the modality has no net benefit—discourage the use of this modality).
H	Recommends against the service (there is moderate or high certainty that the harms outweigh the benefits—discourage the use of this modality).
I	Insufficient evidence

NOTE. Grading was performed with a modified version of the US Preventive Services Task Force grading system.[6]

CLINICAL QUESTION AND TARGET POPULATION

The SIO guideline addressed the use of integrative therapies to manage symptoms and adverse effects during or after breast cancer treatment. Integrative medicine was defined as "the coordinated use of evidence-based complementary practices and conventional care."[5(p196)] The guideline excluded several lifestyle and psychological interventions, including those that are already well summarized elsewhere (eg, diet and exercise in survivors of cancer), those with a strong evidence base that tend to be viewed as mainstream (eg, cognitive–behavioral therapy and support groups), those still in an early or pilot phase of research (eg, attention-restoration therapy), or those that were not viewed as an integrative oncology therapy for the purposes of the SIO guideline (eg, prayer or spirituality). Although not consistently discussed within an oncology setting, assessment of diet, exercise, and psychological status, and appropriate counseling are important components of comprehensive cancer care to improve symptom control and clinical outcomes.

Symptoms and adverse effects addressed in the SIO guideline include anxiety and stress, depression and mood disorders, fatigue, quality of life and physical functioning, chemotherapy-induced nausea and vomiting, lymphedema, chemotherapy-induced peripheral neuropathy, pain, and sleep disturbance.

SUMMARY OF THE SIO GUIDELINE DEVELOPMENT METHODOLOGY

The 2017 SIO guideline[5] updates the original 2014 SIO guideline[9] on this topic. The 2014 guideline was based on a systematic review of the literature from January 1, 1990, through December 31, 2013. The systematic review for the 2017 guideline updated the search through December 31, 2015. Searches focused on randomized controlled trials (RCTs) that were published in English and included at least 50% patients with breast cancer, or that reported results separately for breast cancer. Details of search strategies and study inclusion criteria and outcomes of interest are available at: http://onlinelibrary.wiley.com/doi/10.3322/caac.21397/epdf.

Grades of evidence were assigned to each therapy as applied to a specific clinical outcome using a modified version of the US Preventive Services Task Force grading system.[6] Grades A and B recommend a therapy for a particular indication, grade C indicates more equivocal evidence or a small net benefit, grades D and H recommend against a therapy for a particular indication, and grade I indicates that the evidence is inconclusive (Table 1).

Recommendations were drafted by an SIO Guideline Working Group, then distributed to a multidisciplinary group of internal and external reviewers.

RESULTS OF THE ASCO METHODOLOGY REVIEW

The methodology review of the SIO guideline was completed independently by two ASCO guideline staff members using the Rigour of Development subscale from the Appraisal of Guidelines for Research and Evaluation II review instrument. The two reviewers rated the guideline highly on rigor of development, with an overall score of 90% (Methodology Supplement). The preliminary ASCO content reviewers of the SIO guideline, as well as the ASCO Expert Panel, found the recommendations to be well supported in the original guideline. Each section was clear and well referenced from the systematic review. The SIO guideline provides definitions of each integrative therapy for which recommendations were made, and also includes a section on the challenges of implementing integrative therapies in breast oncology.

For updates, the most recent information, and to submit new evidence, please visit www.asco.org/supportive-care-guidelines.

METHODS AND RESULTS OF THE ASCO UPDATED LITERATURE REVIEW

This systematic review-based guideline product was developed by a multidisciplinary expert panel, which included a patient representative and an ASCO guidelines staff member with health research methodology expertise (Appendix Table A1, online only). PubMed was searched from January 1, 2016, to December 15, 2017. The search was designed to update the SIO literature search and was restricted to articles published in English and to RCTs. The updated search was guided by the signals[10] approach that is designed to identify only new, potentially practice-changing data—signals—that might translate into revised practice recommendations. The approach relies on targeted routine literature searching and the expertise of ASCO Expert Panel members to help identify potential signals. All funding for the administration of the project was provided by ASCO. The Methodology Supplement—available at www.asco.org/supportive-care-guidelines—provides additional information about the signals approach.

The updated search yielded 163 records, 26 of which were potentially eligible for inclusion based on title and abstract review. Four

Table 2. Clinical Outcomes and Integrative Therapies With Insufficient Evidence to Form a Clinical Recommendation[5]

Outcome	Integrative Therapy
Adherence	Acupressure, multimodal
Anemia	LCS101 combination botanical, RG-CMH combination botanical, shenqi fuzheng injection
Anxiety/stress reduction	Art therapy, comprehensive coping strategy, electrical nerve stimulation, healing touch, hypnosis, myofascial release, multimodal, reflexology, reiki, Tai Chi
Cardiomyopathy	N-Acetylcysteine
Chemotherapy-induced nausea and vomiting	Aromatherapy, *Agaricus sylvaticus*, Cocculine (complex homeopathic Rx), comprehensive coping strategy, massage, nevasic audio program, yoga
Cognition	Natural environment, ginkgo biloba, meditation, yoga
Constipation	Self-management program
Depression/mood	Art therapy, biofield healing, comprehensive coping strategy, CoQ10, electrical nerve stimulation, *Ganoderma lucidum*, guarana, hypnosis, multimodal, myofascial release, qigong, reflexology, Tai Chi
Fatigue	Acupressure, biofield healing, comprehensive coping strategy, CoQ10, *Ganoderma lucidum*, light treatment, massage, meditation, mind-body cognitive therapy, movement, multimodal, multivitamin, polarity therapy, stress management, qigong, reflexology, relaxation, stress management, yoga
Lymphedema	CYCLO 3 FORT, electrotherapy, ginkgo forte, pentoxifyline and vitamin E, yoga
Neuropathy	Omega 3 fatty acids, vitamin E, acupuncture
Neutropenia/leukopenia	Cat's claw, LCS101 combination botanical, RG-CMH combination botanical, mistletoe, shenqi fuzheng injection
Pain	Comprehensive coping strategy, stress management, vitamin D2, electrical nerve stimulation, cognitive and behavioral therapy, massage, myofascial release, reflexology
Quality of life	Acupressure, biofield healing, calendula cream, cannabis, chlorella extract, CoQ10, curcuminoids, electrical nerve stimulation, electrotherapy, flaxseed, *Ganoderma lucidum*, gingko forte, guided imagery, healing touch, homeopathy, hypnosis, laser therapy, manual lymphatic draining, massage, meditation, movement, music therapy, multimodal, multivitamin, polarity therapy, relaxation, shenqi fuzheng, shark cartilage, soy, supportive-expressive group therapy, Tai Chi
Physical functioning	Mind-body cognitive therapy, music therapy, multimodal, myofascial release, reflexology, stress management, Tai Chi, yoga
Radiation therapy–induced toxicity outcomes	Adlay bran extract, alpha ointment with henna, aquaphor-biafine-radiacare, boswellia cream, calendula cream, chamomile, curcumin, glutamine, homeopathic pills, honey, hydration, massage, oil-in-water emulsion, glutathione and anthocyanin gel, wheat grass extract, pentoxifylline and vitamin E
Sleep disturbance	Acupuncture, calendula cream, meditation, qigong, stress-management techniques
Vasomotor outcomes	Black cohosh, flaxseed, homeopathy, hypnosis, magnetic therapy, meditation, peppermint, vitamin E, yoga

Abbreviations: CoQ10, coenzyme Q10; CYCLO 3 FORT, fluid extract of *Ruscus aculeatus*, hesperidin methyl chalcone, and vitamin C; LCS101, a botanical compound mixture; RG-CMH, a Chinese medicinal herb complex. Reprinted with permission.[5]

additional publications were identified by panel members. Potentially eligible publications were reviewed by one of the SIO guideline panel members (H.G.), and nine were shared with the ASCO Expert Panel for further discussion. Based on the opinion of the ASCO Expert Panel, these publications do not lead to substantive modifications of the SIO recommendations at this time. In general, these articles support, and in some cases may strengthen, current recommendations. Symptoms and adverse effects addressed by the nine publications are the following:

Acute radiation skin reaction: A double-blind RCT compared oral curcumin—four 500 mg capsules, three times daily—with placebo in 686 women with breast cancer. Curcumin did not significantly reduce the severity of radiation dermatitis.[11]

Fatigue: Two types of daily, self-administered acupressure—stimulating or relaxing—were compared with usual care in an RCT among 288 survivors of breast cancer who experienced cancer-related fatigue.[12] At 6 weeks, the frequency of normal fatigue levels (Brief Fatigue Inventory score < 4) was significantly higher in both acupressure arms than in the usual care arm. Relaxing acupressure also produced improvements in sleep quality and quality of life.

Lymphedema: Physical activity alone was compared with physical activity plus self-manual lymphatic draining in an RCT that enrolled 1,000 patients with breast cancer who had undergone modified radical mastectomy. Addition of manual lymphatic drainage improved scar contracture, shoulder abduction, and upper limb circumference.[13]

Neuropathy: In a small pilot trial among 62 survivors of cancer with chemotherapy-induced peripheral neuropathy, those who were assigned to 20 sessions of EEG neurofeedback had greater improvement in the Brief Pain Inventory worst-pain item than control patients assigned to a waitlist. Changes in EEG activity were predictive of symptom reduction.[14] Although preliminary, these findings are of interest given the few effective treatments for chemotherapy-induced peripheral neuropathy.

Pain, aromatase inhibitor–induced arthralgias: At the 2017 San Antonio Breast Cancer Symposium, Hershman et al[15] presented results from a three-arm trial of acupuncture for aromatase inhibitor–related joint symptoms in 226 postmenopausal women with early-stage breast cancer. Study participants were randomized to true acupuncture, sham acupuncture, or a waitlist control group. After 6 weeks, patients in the true acupuncture arm reported lower Brief Pain Inventory worst-pain scores than patients in either of the comparison arms.

Pain, other: In an RCT among 129 women treated for breast cancer and who experienced late post-treatment pain, those assigned to 8 weeks of mindfulness-based cognitive therapy reported lower pain intensity than women assigned to a waitlist control arm.[16]

Quality of life: Caregiver-delivered reflexology during treatment of advanced breast cancer was compared with attention control in an RCT among 256 patient–caregiver dyads. Patients in the reflexology arm experienced reductions in average symptom severity and interference over 11 weeks. There were no significant differences between study arms in functioning, social support, quality of relationship, or satisfaction with life at weeks 5 and 11.[17]

Sleep disturbance: In a randomized, partially blinded, noninferiority trial among 90 survivors of breast cancer, 3 months of Tai Chi Chih was compared with 3 months of cognitive behavioral therapy for insomnia for the treatment of insomnia. Based on insomnia treatment response as measured by the Pittsburgh Sleep Quality Index, Tai Chi Chih was noninferior to cognitive behavioral therapy for insomnia, with both treatments improving sleep outcomes at 3, 6, and 15 months of follow-up.[18]

Vasomotor symptoms/hot flashes: The addition of acupuncture to enhanced self-care was evaluated in a multicenter RCT among 190 patients with breast cancer. Compared with enhanced self-care alone, the addition of 10 acupuncture treatment sessions resulted in lower hot flash scores at the end of treatment and at the 3- and 6-month post-treatment follow-up visits.[19]

DISCUSSION

The ASCO Expert Panel reviewed the SIO guideline and concurs that the recommendations are clear, thorough, based on the most relevant scientific evidence in this content area, and present options that will be acceptable to patients. Overall, the ASCO Expert Panel agrees with the recommendations as stated in the guideline, with the following discussion points.

Acupressure and Electroacupuncture for Chemotherapy-Induced Nausea and Vomiting

These treatment modalities received a grade B recommendation in the SIO guideline, which supports the addition of either one to a standard antiemetic regimen to improve chemotherapy-induced nausea and vomiting. This varies from the 2017 ASCO antiemetic guideline, which concluded that the evidence for complementary therapies, including acupressure and acupuncture, remains insufficient for a recommendation.[7] The ASCO Expert Panel noted that the two guidelines address different patient populations—the ASCO antiemetic guideline applies to all cancer types, whereas the SIO guideline focuses only on patients with breast cancer—and also discussed the low risk of adverse events from acupressure and electroacupuncture. Nevertheless, the ASCO Expert Panel favored a grade C recommendation for these therapies. As noted in the SIO guideline, several of the cited trials were conducted before current pharmacologic antiemetic regimens became available. Furthermore, trials to date have tended to be small; two of the three cited acupressure trials[20-22] and one of the two cited electroacupuncture trials[23,24] enrolled fewer than 40 patients.

Ginseng for Fatigue

This was a not a strong recommendation in the SIO guideline (grade C), but the ASCO Expert Panel wanted to highlight that the efficacy and safety of ginseng may vary by type of ginseng and extraction method. The studies cited by the SIO guideline tested 8 weeks of treatment with a single form of ginseng, the pure ground root of American ginseng (*Panax quinquefolius*), which was tested for quality and potency.[25,26] There is concern that some ginseng preparations, especially those derived from ethanol extracts, may have estrogenic properties[27-29]; therefore, caution should be used in patients with estrogen receptor–positive breast cancer. However, this has not been extensively studied, and the estrogen receptor affinity of ginseng—whether it preferentially binds alpha or beta estrogen receptors—has not been thoroughly investigated. This is an important consideration as phytoestrogens that bind estrogen receptor-β may lead to decreased cell proliferation and better outcomes versus endogenous estrogens that bind estrogen receptor-α and stimulate cell growth.[30-34] Furthermore, over-the-counter dietary supplements can vary in their content and quality, and patients with cancer should not use dietary supplements without the guidance of a health care professional.

Mistletoe and Quality of Life

The studies cited by the SIO used subcutaneous mistletoe, which is not approved by the US Food and Drug Administration. Where subcutaneous mistletoe is available and provided and administered by a health care professional, it may be considered for improving quality of life in selected patients, as indicated by the SIO's grade C recommendation. Orally available mistletoe is available in the United States, but ingestion of high doses of mistletoe berry or leaf is known to cause serious adverse reactions.[8]

ADDITIONAL RESOURCES

More information, including a Data Supplement, a Methodology Supplement, slide sets, and clinical tools and resources, is available at www.asco.org/supportive-care-guidelines. Patient information is available at www.cancer.net.

Related ASCO Guidelines

- Antiemetics[7] (http://ascopubs.org/doi/10.1200/JCO.2017.74.4789)
- Integration of Palliative Care into Standard Oncology Practice[35] (http://ascopubs.org/doi/10.1200/JCO.2016.70.1474)
- Patient-Clinician Communication[36] (http://ascopubs.org/doi/10.1200/JCO.2017.75.2311)
- Breast Cancer Survivorship Care[37] (http://ascopubs.org/doi/10.1200/JCO.2015.64.3809)
- Management of Chronic Pain in Survivors of Adult Cancers[38] (http://ascopubs.org/doi/10.1200/JCO.2016.68.5206)
- Prevention and Management of Chemotherapy-Induced Peripheral Neuropathy in Survivors of Adult Cancers[39] (http://ascopubs.org/doi/10.1200/jco.2013.54.0914)

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

Disclosures provided by the authors are available with this article at jco.org.

AUTHOR CONTRIBUTIONS

Provision of study materials or patients: Heather Greenlee
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

Integrative Therapies During and After Breast Cancer Treatment: ASCO Endorsement of the SIO Clinical Practice Guideline

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/site/ifc.

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Consulting or Advisory Role: Halozyme, G1 Therapeutics, Coherus Biosciences
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Research Funding: Pfizer (Inst), Genentech (Inst), Incyte (Inst), Veridex (Inst), Calithera Biosciences (Inst)
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Acknowledgment

The Expert Panel wishes to thank Mariana Chavez-MacGregor, MD, MSc, and Vered Stearns, MD, and the Clinical Practice Guidelines Committee for their thoughtful reviews and insightful comments on this guideline endorsement.

Appendix

Table A1. Expert Panel Membership

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Abbreviation: PGIN, Practice Guideline Implementation Network.