Prevention and Management of Chemotherapy-Induced Peripheral Neuropathy in Survivors of Adult Cancers: ASCO Guideline Update

Loprinzi et al.
Introduction

- Chemotherapy-induced neuropathy is a serious clinical problem and common treatment-related adverse effect caused by a substantial number of cytotoxic drugs.

- Chemotherapy-induced peripheral neuropathy (CIPN) can markedly affect the quality of life of patients. Additionally, it may be detrimental to their cancer outcomes, as it may limit the amount of chemotherapy that clinicians can give.

- ASCO first published a guideline on the prevention and management of CIPN in survivors of adult cancers in 2014.

- The purpose of this guideline update is to systematically review new evidence reported in the literature since the original guideline was published, compare outcomes among trials, and provide updated guidance on the effectiveness of prevention and treatment options for CIPN in adults with a history of cancer.
ASCO Guideline Development Methodology

The ASCO Clinical Practice Guidelines Committee guideline process includes:

• a systematic literature review by ASCO guidelines staff
• an expert panel provides critical review and evidence interpretation to inform guideline recommendations
• final guideline approval by ASCO CPGC

The full ASCO Guideline methodology manual can be found at:
www.asco.org/guideline-methodology
Clinical Questions

This clinical practice guideline update addresses two overarching clinical questions:

1. What are the recommended **prevention** approaches in the management of chemotherapy-induced neuropathies in adult cancer survivors?
2. What are the recommended **treatment** approaches in the management of chemotherapy-induced neuropathies in adult cancer survivors?
Target Population
Adult cancer survivors with, or at risk of developing, chemotherapy-induced neuropathies.

Target Audience
Health care practitioners who provide care to cancer survivors, patients and their caregivers.
Summary of Recommendations

Prevention of Chemotherapy-induced Peripheral Neuropathy

Recommendation 1.1.
Clinicians should assess the risks and benefits of agents known to cause CIPN among patients with underlying neuropathy and with conditions that predispose to neuropathy such as diabetes and/or a family or personal history of hereditary neuropathy. (Type: Informal consensus; benefits outweigh harms; Evidence quality: Low; Strength of recommendation: Moderate).

Recommendation 1.2
Clinicians should not offer, and should discourage use of, acetyl-L-carnitine for the prevention of CIPN in cancer patients. (Type: Evidence based; harms outweigh benefits; Evidence quality: High; Strength of recommendation: Strong)
Summary of Recommendations

**Recommendation 1.3**

Outside the context of a clinical trial, no recommendations can be made on the use of the following interventions for the prevention of CIPN:

- Acupuncture
- Cryotherapy
- Compression therapy
- Exercise therapy
- Ganglioside-monosialic acid (GM-1)

(Type: No recommendation; Evidence quality: Low; Strength of recommendation: Not applicable)
Summary of Recommendations

**Recommendation 1.4**

Clinicians should not offer the following agents for the prevention of CIPN to cancer patients undergoing treatment with neurotoxic agents:

- All-trans retinoic acid
- Amifostine
- Amitriptyline
- Calcium magnesium
- Calmangafodipir
- Cannabinoids
- Carbamazepine
- L-carnosine
- Diethyldithio-carbamate (DDTC)
- Gabapentin/pregabalin
- Glutamate
- Glutathione (GSH) for patients receiving paclitaxel/carboplatin chemotherapy
- Goshajinkigan (GJG)
- Metformin
- Minocycline
- N-acetylcysteine
- Nimodipine
- Omega-3 fatty acids
- Org 2766
- Oxcarbazepine
- rhuLIF
- Venlafaxine
- Vitamin B
- Vitamin E

(Type: Evidence based; no benefits; Evidence quality: Intermediate; Strength of recommendation: Moderate)
Summary of Recommendations

Treatment of chemotherapy-induced peripheral neuropathy that develops while patients are receiving neurotoxic chemotherapy

Recommendation 2.1.

Clinicians should assess, and discuss with patients, the appropriateness of dose delaying, dose reduction or stopping chemotherapy (or substituting with agents that do not cause CIPN) in patients who develop intolerable neuropathy and/or functional nerve impairment. (Type: Informal consensus; benefits outweigh harms; Evidence quality: Low; Strength of recommendation: Moderate).
Summary of Recommendations

Treatment of chemotherapy-induced peripheral neuropathy for patients who have completed neurotoxic chemotherapy

Recommendation 3.1.
For cancer patients experiencing painful CIPN, clinicians may offer duloxetine. (Type: Evidence based; benefits equal harms; Evidence quality: Intermediate; Strength of recommendation: Moderate)

Recommendation 3.2.
Outside the context of a clinical trial, no recommendations can be made on the use of the following interventions for the treatment of CIPN:

- Exercise therapy
- Acupuncture
- Scrambler therapy
- Gabapentin/pregabalin
- Topical gel treatment containing baclofen, amitriptyline HCL, plus/minus ketamine
- Tricyclic antidepressants
- Oral cannabinoids

(Type: No recommendation; Evidence quality: Low; Strength of recommendation: Not applicable).
Discussion

- The current review found no additional studies supporting the use of any preventative approach for neuropathy.

- For treatment of established painful neuropathy, duloxetine remains the sole recommended treatment.

- While recent preliminary evidence suggests a potential for benefit from exercise, acupuncture, and scrambler therapy, larger sample sized definitive studies are needed to confirm efficacy and clarify risks.

- While the current guideline is primarily focused on means of preventing CIPN and/or treating established CIPN, CIPN can involve physical dysfunction; patients with CIPN have balance troubles and a higher chance of falling.\(^1,2\) Therefore, it is reasonable to consider physical therapy and/or occupational therapy approaches for patients with such CIPN-related disabilities.
Limitation of the Research and Future Research

- Inconsistent subjective and objective outcome measures, choice of control group, and duration of exposure have resulted in challenges in interpreting some of the prior studies. NCI sponsored studies are ongoing to better define the phenotype of CIPN, to ensure consistency in outcome measures going forward.

- Better interventions are needed to prevent CIPN. Ongoing and planned trials will better clarify the role of exercise, compression therapy, cryotherapy, and other targeted interventions. Several planned and/or ongoing pre-clinical studies are evaluating the role of neuronal transport, neuroprotection, neuro-inflammation, serotonin-norepinephrine reuptake, and nociceptor sodium channel inhibition, mitochondrial enzymes and oxidative stress.

- Better agents are also needed to treat established CIPN. Ongoing and planned clinical trials should better clarify the role of exercise, acupuncture, Scrambler therapy, and other targeted interventions. Topical therapies, such as capsaicin might also be further explored.
Additional Resources

More information, including a Data Supplement, slide sets, and clinical tools and resources, is available at

www.asco.org/survivorship-guidelines

Patient information is available at www.cancer.net
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