American Society of Clinical Oncology 2008 Clinical Practice Guideline Update Summary: Use of Chemotherapy and Radiation Therapy Protectants

Context

ASCO recently convened an update committee of the expert panel on the use of chemotherapy and radiation therapy protectants to review ASCO's Clinical Practice Guideline on this topic. In 2002, ASCO updated the original 1999 guideline. This 2008 updated guideline addresses the role of currently available chemotherapy and radiation therapy protectants in decreasing the incidence and/or the severity of toxicities associated with the use of chemotherapy and radiation therapy to treat cancer.

The updated guideline includes a new section on the use of palifermin to prevent mucositis associated with stem cell transplantation, and discusses the use of amifostine for the prevention of radiation-associated esophagitis. The US Food and Drug Administration (FDA) approved palifermin, a recombinant keratinocyte growth factor, for prophylaxis against severe mucositis associated with hematopoietic stem-cell transplant (HSCT) in hematologic malignancies. For several recommendations, there was no new evidence and those recommendations remain unchanged. Due to the large number of recommendations in this guideline, this summary describes only those which changed. A complete list of recommendations is available online www.asco.org/guidelines/protectant.

Changes Since 2002 Guideline

Dexrazoxane

Use of Dexrazoxane for Patients Receiving High-Dose Anthracycline Therapy

Because there were no new data on the use of dexrazoxane or on the clinical use of high-dose anthracyclines, the panel felt a recommendation on this topic had limited clinical relevance and deleted its previous recommendation.

Amifostine

Amifostine Use in Chemotherapy-Associated Toxicities: Neutropenia

The panel found that across all studies considered, reports of benefit were inconsistent, specifically whether use of amifostine resulted in lower frequencies of grades 3 to 4 neutropenia. The only large randomized trial published since 2002 showed a significantly lower frequency of grades 3 to 4 neutropenia in the amifostine arm. The panel continues to recommend that amifostine may be considered for reduction of the frequency of grade 3 or 4 of chemotherapy-associated neutropenia, but suggests that clinicians consider alternative strategies to ameliorate neutropenia, such as the use of myeloid growth factors and/or chemotherapy dose reduction.

Amifostine Use in Chemotherapy-Associated Toxicities: Thrombocytopenia

Recent randomized trials showing no benefit to using amifostine for thrombocytopenia led the panel to strengthen its recommendation against the use of amifostine for the prevention of thrombocytopenia associated with alkylating-agent chemotherapy or carboplatin chemotherapy to include any type of chemotherapy. The recommendation against using amifostine for prevention of thrombocytopenia was also extended to include the radiation therapy setting.

Amifostine Use in Chemotherapy-Associated Toxicities: Neurotoxicity or Ototoxicity

Although the trials published since the 2002 update showed some evidence of improvement in certain areas, they have inconsistent results, and the clinical significance is unclear. Because several of these trials used carboplatin, the panel extended the recommendation against using amifostine for prevention of neurotoxicity or ototoxicity to include both carboplatin and cisplatin.

Dose and Administration of Amifostine With Chemotherapy

The guideline recommends that physicians use the FDA-approved dose of amifostine and that they be familiar with the package insert's directions for administration and monitoring for acute toxicities of amifostine.

Amifostine Use in Radiation Therapy–Associated Toxicities: Xerostomia

The panel changed this recommendation slightly to reflect that amifostine is recommended for consideration in the setting of radiation therapy alone, but not in the setting of concurrent platinum-based chemoradiotherapy. The largest and only placebo-controlled new trial involving chemoradiotherapy with or without amifostine showed no benefit to amifostine; consequently, the panel does not recommend it in this setting.

Amifostine Use in Radiation Therapy–Associated Toxicities: Mucositis

This recommendation was changed slightly to specify clearly that data do not support routine use of amifostine for the

prevention of mucositis in the setting of radiation therapy for treatment of head and neck cancer.

Amifostine Use in Radiation Therapy–Associated Toxicities: Esophagitis

There is a growing body of evidence on amifostine use in the prevention of esophagitis. Data, however, are insufficient to recommend the routine use of amifostine in the setting of chemoradiotherapy in non–small-cell lung cancer for the prevention of esophagitis.

Palifermin

Palifermin is new to the guideline. Mucositis is a common adverse effect of autologous and allogeneic HSCT and can be severe. Palifermin acts on epithelial tissue to protect it from chemotherapy and radiation-induced mucosal injury.

There are no data to support using palifermin in the nonstem-cell transplantation setting or in the treatment of solid tumors.

Palifermin Use in Autologous HSCT

Palifermin is recommended for patients receiving autologous HSCT (autoHSCT) for a hematologic cancer that involves total-body irradiation (TBI) to decrease the frequency of severe mucositis. Evidence from a multicenter double-blind, placebo-controlled, randomized study supports this recommendation.

Because the incidence of severe mucositis is also high with autoHSCT conditioning regimens that include involved-field radiotherapy to the oral cavity, oropharynx, and/or esophagus, palifermin may be considered. The panel cautions, however, that data are lacking from randomized controlled trials to support this extrapolation for palifermin use to non-TBI conditioning regimens.

Given insufficient data, palifermin is not recommended for routine use for patients undergoing autologous HSCT for a hematologic malignancy with a chemotherapy-only conditioning regimen.

Palifermin Use in Allogeneic HSCT

Palifermin may be considered for myeloablative allogeneic HSCT (alloHSCT) with TBI conditioning regimens to decrease the incidence of severe mucositis. It is not recommended for chemotherapy-only conditioning regimens. Since the severity of regimen-induced oral mucositis is dependent on the conditioning regimen and not the source of hematopoietic stem cells, the ability of palifermin to reduce the incidence of severe regimen-induced oral mucositis in patients undergoing alloHSCT is not expected to be different than in patients undergoing autologous HSCT, although a randomized trial has not directly evaluated this.

Dose and Administration of Palifermin With HSCT

Administration of palifermin should follow the protocol used in the randomized controlled trial and in the FDA-approved label. Palifermin is not to be given within 24 hours of the conditioning regimen. Common toxicities of palifermin include rash and/or erythema (55% to 95% of patients), pruritus, edema, sensation of increased tongue thickness, and alteration of taste. The severity of the rash or skin reaction, though it has varied somewhat across trials, has generally been mild to moderate.

Mesna

There were no changes to recommendations regarding Mesna.

Cost-Effectiveness Analysis

Finally, although the update committee did not conduct a cost-effectiveness analysis on chemotherapy and radiation therapy protectants, they did include information on these agents' costs in the full-text guideline.

Discussion With People With Cancer

Clinicians should apprise patients of the risks and benefits of these chemotherapy and radiation therapy protectant agents and that the goal of the use of these agents is ameliorating the toxicities of treatment. Clinicians and patients should understand that these agents have not been shown to increase disease-free or overall survival, nor have they been shown to allow greater doses to be delivered or to prevent treatment delays. The short-term adverse effects of the chemo- and radiation therapy protectant agents have generally been well-characterized (eg, hypotension and nausea with amifostine; rash/erythema with palifermin), and in some studies have led to high rates of discontinuation of use of the proctectant agent.

Methodology

The update committee of the expert panel on the Use of Chemotherapy and Radiation Therapy Protectants reviewed searches of MEDLINE, preMEDLINE, and the Cochrane Collaboration Library and conducted a systematic review of the literature published between 2002 and June 2007 for previously covered agents. The searches for palifermin had no date limit. The panel noted that the quality of the published literature overall was limited.

Additional Resources

Journal of Clinical Oncology published a full-text version of this guideline online ahead of print on November 17, 2008. The full-text is available at www.asco.org/guidelines/protectant,

along with a slide set and several summary tables. A patient guide is available at www.cancer.net.

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