

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

Type of change	Previous Recommendation (2002)	Current Recommendation (2008)
Title		
	2002 Update of Recommendations for the Use of Chemotherapy and Radiotherapy Protectants: Clinical Practice Guidelines of the American Society of Clinical Oncology (JCO Vol 20, No 12 (June 15) 2002)	American Society of Clinical Oncology 2008 Clinical Practice Guideline Update: Use of Chemotherapy and Radiation Therapy Protectants
THE USE OF DEXRAZOXANE		
1. Initial Use For Patients With Metastatic Breast Cancer 2. Delayed Use For Patients With Metastatic Breast Cancer Who Have Received More Than 300 mg/m² of Doxorubicin 3. For Patients Receiving Adjuvant Chemotherapy for Breast Cancer 4. For Adult Patients With Other Malignancies 5. For Pediatric Malignancies	<i>2002 Recommendation:</i> It is recommended that dexrazoxane not routinely be used for patients with metastatic breast cancer receiving initial doxorubicin-based chemotherapy.	<i>2008 Recommendation:</i> No change.
	<i>2002 Recommendation:</i> It is suggested that the use of dexrazoxane be considered for patients with metastatic breast cancer who have received more than 300 mg/m ² of doxorubicin in the metastatic setting and who may benefit from continued doxorubicin-containing therapy. Management of patients who received more than 300 mg/m ² in the adjuvant setting and are now initiating doxorubicin-based chemotherapy in the metastatic setting should be individualized, with consideration given to the potential for dexrazoxane to decrease response rates, as well as decreasing the risk of cardiac toxicity. These patients were not included in the clinical trials of dexrazoxane.	<i>2008 Recommendation:</i> No change.
	<i>2002 Recommendation:</i> The use of dexrazoxane in the adjuvant setting is not suggested outside of a clinical trial.	<i>2008 Recommendation:</i> No change.
	<i>2002 Recommendation:</i> The use of dexrazoxane can be considered in adult patients who have received more than 300 mg/m ² of doxorubicin-based therapy. Caution should be exercised in the use of dexrazoxane in settings in which doxorubicin-based therapy has been shown to improve survival.	<i>2008 Recommendation:</i> No change.
	<i>2002 Recommendation:</i> There is insufficient evidence to make a recommendation for the use of dexrazoxane in the treatment of pediatric malignancies.	<i>2008 Recommendation:</i> No change.
Dexrazoxane - Other Anthracycline Doses and Schedules		
6. For Patients Receiving Other Anthracyclines or Other Anthracycline Dose Schedules	<i>2002 Recommendation:</i> On the basis of the available data and extrapolations from the experience with doxorubicin plus dexrazoxane, the use of dexrazoxane may be considered for patients responding to anthracycline-based chemotherapy for advanced breast cancer and for whom continued epirubicin therapy is clinically indicated. Data for using dexrazoxane with epirubicin for treatment of other cancers are limited. Data are insufficient to make a recommendation regarding the use of	<i>2008 Recommendation:</i> No change.

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7. For Patients Receiving High-Dose Anthracycline Therapy	dexrazoxane with other potentially cardiotoxic agents.	
	<i>2002 Recommendation:</i> Since data for superior outcomes with high-dose as compared with standard-dose epirubicin treatment for metastatic breast cancer are lacking, and since there are no new data from randomized trials confirming that efficacy of high-dose epirubicin is preserved when given with dexrazoxane, the panel considered the current data for high-dose epirubicin plus dexrazoxane insufficient to make a recommendation.	<i>2008 Recommendation:</i> There are no new data addressing the use of dexrazoxane, and there are no new data regarding the clinical use of high-dose anthracyclines. Thus, the Panel has elected to delete this particular guideline statement, since its clinical relevance appears limited.
8. For Patients With Cardiac Risk Factors	<i>2002 Recommendation:</i> There is insufficient evidence on which to base a recommendation for the use of dexrazoxane in patients with cardiac risk factors or underlying cardiac disease	<i>2008 Recommendation:</i> No change.
Monitoring Therapy		
9. Termination of Anthracycline Therapy for Patients Receiving Dexrazoxane	<i>2002 Recommendation:</i> Patients receiving dexrazoxane should continue to undergo cardiac monitoring. After cumulative doxorubicin doses of 400 mg/m ² , cardiac monitoring should be frequent. The panel suggests repeating the monitoring study after 500 mg/m ² and subsequently after every 50 mg/m ² of doxorubicin. The panel suggests that the termination of dexrazoxane/doxorubicin therapy be strongly considered in patients who develop a decline in LVEF to below institutional normal limits or who develop clinical congestive heart failure.	<i>2008 Recommendation:</i> No change.
10. Dose of Dexrazoxane	<i>2002 Recommendation:</i> It is suggested that patients who are being treated with dexrazoxane receive dexrazoxane at a ratio of 10:1 with the doxorubicin dose, given by slow IV push or short IV infusion, 15 to 30 minutes before doxorubicin or epirubicin administration. A ratio of 10:1 with the epirubicin dose may be reasonable. However, it should be noted that the optimal dose ratio has not been determined.	<i>2008 Recommendation:</i> No change.
AMIFOSTINE		
Amifostine Use in Chemotherapy-Associated Toxicities		
11. Nephrotoxicity	<i>2002 Recommendation:</i> Amifostine may be considered for the prevention of nephrotoxicity in patients receiving cisplatin-based chemotherapy.	<i>2008 Recommendation:</i> No change.
12. Neutropenia	<i>2002 Recommendation:</i> The panel recommends that	<i>2008 Recommendation:</i> While the use of amifostine

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13. Thrombocytopenia	amifostine be considered for the reduction of neutropenia-associated events in patients receiving alkylating-agent chemotherapy. However, in the absence of clinical data supporting maintenance of the chemotherapy dose-intensity, physicians should consider chemotherapy dose reduction as an alternative to the use of amifostine.	may be considered for reduction of the incidence of grade 3 and 4 neutropenia associated with chemotherapy, the clinician may reasonably consider alternative strategies such as the use of myeloid growth factor support or chemotherapy dose reduction to ameliorate neutropenia.
	<i>2002 Recommendation:</i> Present data are insufficient to recommend the use of amifostine for protection against thrombocytopenia in patients receiving alkylating-agent chemotherapy or carboplatin.	<i>2008 Recommendation:</i> The Panel recommends against the use of amifostine for protection against thrombocytopenia in patients receiving chemotherapy or radiotherapy.
14. Neurotoxicity and Ototoxicity	<i>2002 Recommendation:</i> Present data are insufficient to support the routine use of amifostine for the prevention of cisplatin-associated neurotoxicity or ototoxicity.	<i>2008 Recommendation:</i> Present data are insufficient to support the routine use of amifostine for the prevention of platinum-associated neurotoxicity or ototoxicity.
15. Paclitaxel Associated Neurotoxicity	<i>2002 Recommendation:</i> There are no data to support the use of amifostine for prevention of paclitaxel-associated neurotoxicity.	<i>2008 Recommendation:</i> Data are insufficient to support the routine use of amifostine for the prevention of paclitaxel-associated neuropathy.
16. Dose and Administration of Amifostine With Chemotherapy	<i>2002 Recommendation:</i> In adults, the suggested dose of amifostine with chemotherapy is 910 mg/m ² . Amifostine is administered intravenously, over 15 minutes, 30 minutes before chemotherapy. Administration of amifostine requires close patient monitoring, and toxicity is clearly dose related. All patients should be treated with antiemetics before the administration of amifostine, and pretreatment with intravenous fluids should also be considered. Blood pressures are taken every 3 to 5 minutes during the 15-minute infusion. Amifostine is discontinued if blood pressure declines significantly or the patient becomes symptomatic. The hypotension associated with amifostine usually occurs at the end of the infusion and is reversed with discontinuation of the amifostine, administration of saline, and placing the patient in the Trendelenburg position. There are insufficient data to recommend redosing of amifostine after chemotherapy.	<i>2008 Recommendation:</i> The current FDA-approved dose of amifostine is 910 mg/m ² intravenously over 15 minutes, 30 minutes prior to chemotherapy. Familiarity with the package insert and close patient monitoring during the infusion are required. Common toxicities include acute hypotension, nausea, and fatigue.
17. Amifostine Use in Radiation Therapy–Associated Toxicities		
17.A. – Xerostomia	<i>2002 Recommendation:</i> The panel recommends that amifostine may be considered to decrease the incidence of acute and late xerostomia in patients undergoing fractionated radiation therapy in the	<i>2008 Recommendation:</i> The use of amifostine may be considered to decrease the incidence of acute and late xerostomia in patients undergoing fractionated radiotherapy alone for head and neck cancer.

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	head and neck region.	Current data do not support the routine use of amifostine with concurrent platinum-based chemoradiotherapy for head and neck cancer.
17.B. – Mucositis	<i>2002 Recommendation:</i> Present data are insufficient to recommend amifostine to prevent mucositis associated with radiation therapy.	<i>2008 Recommendation:</i> Data are insufficient to recommend amifostine to prevent mucositis associated with radiation therapy for head and neck cancer.
17.C. –Esophagitis Note: New to Guideline	-	<i>2008 Recommendation:</i> Data are insufficient to recommend the routine use of amifostine to prevent esophagitis in patients receiving concurrent chemoradiotherapy for non-small cell lung cancer.
18. Dose and Administration of Amifostine With Radiation Therapy	<i>2002 Recommendation:</i> When given with radiation therapy, the recommended amifostine dose is 200 mg/ m ² /d, given as a slow IV push over 3 minutes, 15 to 30 minutes before each fraction of radiation therapy. Administration of amifostine requires close patient monitoring, but side effects are fewer at this lower dose. Many patients require antiemetics. Blood pressure should be measured just before and immediately after the 3-minute amifostine infusion. The hypotension associated with amifostine at this dose is less frequent but still requires close monitoring.	<i>2008 Recommendation:</i> No change.
PALIFERMIN – NEW TO GUIDELINE		
19. Autologous Hematopoietic Stem Cell Transplantation	<i>2008 Recommendation:</i> Palifermin is recommended for use in patients undergoing autologous stem cell transplantation for a hematologic malignancy with a total body irradiation (TBI) conditioning regimen to decrease the incidence of severe mucositis. There are insufficient data to recommend the routine use of palifermin for patients undergoing autologous stem cell transplantation for a hematologic malignancy where the conditioning regimen is chemotherapy-only.	
20. Allogeneic Hematopoietic Stem Cell Transplantation	<i>2008 Recommendation:</i> Palifermin is recommended for use in patients undergoing myeloablative allogeneic hematopoietic stem cell transplant with a TBI-based conditioning regimen. There are insufficient data to recommend its use in myeloablative conditioning regimens consisting of chemotherapy alone in this setting.	
22. Dose and Administration of Palifermin With Hematopoietic Stem Cell Transplantation	<i>2008 Recommendation:</i> Palifermin should be administered intravenously at 60 µg/kg daily for 3 days preceding the start of the conditioning regimen and 60 µg/kg daily for 3 days beginning on the day of stem cell infusion. It should not be administered within 24 hours of the initiation of the conditioning regimen.	
21. Non-Stem Cell Transplantation and Solid Tumors	<i>2008 Recommendation:</i> There are insufficient data to recommend the use of palifermin in the non-stem cell transplant setting, or for use in the treatment of solid tumors.	
MESNA – NO CHANGES TO 2002 RECOMMENDATION		
22. Use With Ifosfamide	<i>2002 Recommendation:</i> The use of mesna is recommended to decrease the incidence of ifosfamide-	

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23. Dosing With Standard-Dose Ifosfamide	associated urothelial toxicity. <i>2002 Recommendation:</i> It is suggested that the daily dose of mesna be calculated to equal 60% of the total daily dose of ifosfamide, administered as three bolus doses given 15 minutes before and 4 and 8 hours after administration of each dose of ifosfamide, when the ifosfamide dose is less than 2.5 g/m ² /d administered as a short infusion. For use with continuous-infusion ifosfamide, mesna may be administered as a bolus dose equal to 20% of the total ifosfamide dose followed by a continuous infusion of mesna equal to 40% of the ifosfamide dose, continuing for 12 to 24 hours after completion of the ifosfamide infusion.
24. Mesna Dosing With High-Dose Ifosfamide	<i>2002 Recommendation:</i> There is insufficient evidence on which to base a recommendation for the use of mesna with ifosfamide doses in excess of 2.5 g/m ² /d. The efficacy of mesna for urothelial protection with very high-dose ifosfamide has not been established. Given the longer half-life of ifosfamide in these dosages, more frequent and prolonged mesna dosage regimens may be necessary for maximum protection from urotoxicity.
25. Mesna Administration by the Oral Route With Ifosfamide	<i>2002 Recommendation:</i> Mesna tablets have been approved by the United States Food and Drug Administration (FDA) to prevent hemorrhagic cystitis in patients receiving ifosfamide chemotherapy. The recommended dose and schedule is to administer mesna as an IV bolus injection in a dosage equal to 20% of the ifosfamide dosage (weight/ weight) at the time of ifosfamide administration. Mesna tablets are given orally in a dosage equal to 40% of the ifosfamide dose at 2 and 6 hours after each dose of ifosfamide. The total daily dose of mesna is 100% of the ifosfamide dose. Patients who vomit within 2 hours of taking oral mesna should repeat the dose or receive IV mesna. The dosing schedule should be repeated on each day that ifosfamide is administered.
26. Use With Cyclophosphamide	<i>2002 Recommendation:</i> Mesna plus saline diuresis or forced saline diuresis is recommended to decrease the incidence of urothelial toxicity associated with high-dose cyclophosphamide in the setting of stem-cell transplantation.
27. Surveillance of Patients Receiving Ifosfamide and/or Cyclophosphamide and Mesna	<i>2002 Recommendation:</i> There are insufficient data to make a recommendation regarding specific monitoring for hemorrhagic cystitis in patients receiving mesna to ameliorate ifosfamide or high-dose cyclophosphamide-associated urothelial toxicity. Recommendations for monitoring reflect the design of clinical trials involving mesna use and the opinion of the panel.

This table is derived from recommendations in the American Society of Clinical Oncology 2008 Clinical Practice Guideline Update: Use of Chemotherapy and Radiation Therapy Protectants. This table is a practice tool based on ASCO® practice guidelines and is not intended to substitute for the independent professional judgment of the treating physician. Practice guidelines do not account for individual variation among patients. This tool does not purport to suggest any particular course of medical treatment. Use of the practice guidelines and this resource are voluntary. The practice guidelines and additional information are available at <http://www.asco.org/guidelines/protectants>. Copyright © 2008 by the American Society of Clinical Oncology. All rights reserved.