GUIDELINES FOR ANTIEMETIC USE IN ONCOLOGY

SUMMARY

More than half of all cancer patients experience nausea or vomiting during the course of their treatment. If nausea or vomiting becomes severe enough, patients can experience dehydration and other health problems.

In some cases these side effects can cause cancer treatments to be delayed, halted or changed, which may have a detrimental effect on overall treatment outcomes. Importantly, in the past two decades, newer approaches and better antiemetic medications have reduced the incidence of both nausea and vomiting in cancer patients undergoing therapy

The guideline provides information about the risk of vomiting and nausea associated with various anti-cancer agents and radiation therapy, as well as the specific recommended antiemetic regimens for each.

One key recommendation in this update is the reclassification of the risk for vomiting and nausea from the combination of an anthracycline and cyclophosphamide, a commonly used chemotherapy regimen. Each drug alone is classified as having a moderate risk, but based on continued scientific data, the combination now is considered high-risk. This change is significant because of the widespread use of this combination, and the potential to improve the patient's experience during treatment and avoid treatment delays or dose reductions

CLASSIFICATION

1. Optimal treatment to prevent nausea and vomiting from HIGHLY emetogenic antineoplastic agents

The three-drug combination of:

- Neurokinin 1 (NK_1) receptor antagonist (days 1 through 3 for aprepitant (emend); day 1 only for fosaprepitant)
- 5-HT_3 receptor antagonist (day 1 only)
- Dexamethasone (days 1 through 3 or 1 through 4)

The Update Committee also recommended reclassification of the combined anthracycline and cyclophosphamide (AC) regimen as highly emetogenic

2. Optimal treatment to prevent nausea and vomiting from MODERATELY emetogenic antineoplastic agents?

The two-drug combination of:

- Palonosetron (onicit) (day 1 only)
  If Palonosetron is not available, clinicians may substitute a first-generation 5-HT_3 receptor antagonist, preferably Granisetron or Ondansetron.
- Dexamethasone (days 1 through 3)

Limited evidence also supports adding aprepitant to the combination. Should clinicians opt to add aprepitant in patients receiving moderate-risk chemotherapy, any one of the 5-HT_3 antagonists is appropriate.

3. Optimal treatment to prevent nausea and vomiting from LOW emetogenic antineoplastic agents

- A single 8-mg dose of Dexamethasone before chemotherapy is suggested

4. Optimal treatment to prevent nausea and vomiting from MINIMALLY emetogenic antineoplastic agents

- No antiemetic should be administered routinely before or after chemotherapy.

5. Optimal treatment to prevent nausea and vomiting from combination chemotherapy

- Patients should be administered antiemetic appropriate for the component chemotherapeutic (antineoplastic) agent of greatest emetic risk. AC combinations are now classified as highly emetogenic.

SPECIAL POPULATIONS

1. Optimal treatment to prevent nausea and vomiting associated with cancer therapy for PEDIATRIC patients

- The combination of a 5-HT_3 antagonist plus a corticosteroid is suggested before chemotherapy in children receiving chemotherapy of high or moderate emetic risk. Because of the variation of pharmacokinetic parameters in children, higher weight-based doses of 5-HT_3 antagonists than those used in adults may be required for antiemetic protection.

2. Optimal treatment to prevent nausea and vomiting in patients who are undergoing high-dose chemotherapy with STEM CELL or BONE MARROW TRANSPLANTATION

- A 5-HT_3 receptor antagonist combined with dexamethasone is recommended. Aprepitant should be considered, although evidence to support its use is limited.

3. Optimal treatment to prevent nausea and vomiting for patients receiving MULTIDAY CHEMOTHAREPY

- It is suggested that antiemetic appropriate for the emetogenic risk class of the chemotherapy be administered for each day of the chemotherapy and for 2 days after, if appropriate.

4. Optimal antiemetic regimen for patients who experience nausea and vomiting SECONDARY to cancer therapy despite optimal prophylaxis

- Clinicians should re-evaluate emetic risk, disease status, concurrent illnesses, and medications; ascertain that the best regimen is being administered for the emetic risk.

5. Options are available for patients who experience ANTICIPATORY nausea and vomiting

RECOMMENDATION

- Use of the most active antiemetic regimens appropriate for the chemotherapy being administered to prevent acute or delayed emesis is suggested. Such regimens should be used with initial chemotherapy, rather than assessing the patient's emetic response with less effective treatment. If anticipatory emesis occurs, behavioral therapy with systematic desensitization is effective and suggested.

6. Optimal prophylaxis for nausea and vomiting caused by HIGH emetic risk RADIATION THERAPY

- 5-HT_3 antagonist before each fraction and for at least 24 hours after completion of radiotherapy.
- Patients should also receive a 5-day course of Dexamethasone during fractions 1 to 5.

7. Optimal prophylaxis for nausea and vomiting caused by MODERATE emetic risk RADIATION THERAPY

- 5-HT_3 antagonist before each fraction for the entire course of radiotherapy.
- Patients may be offered a short course of dexamethasone during fractions 1 to 5.

8. Optimal treatment to manage nausea and vomiting associated with LOW emetic risk RADIATION THERAPY

- 5-HT_3 antagonist alone as either prophylaxis or rescue. For patients who experience RINV while receiving rescue therapy only, prophylactic treatment should continue until radiotherapy is complete

9. Optimal treatment to manage nausea and vomiting associated with MINIMAL emetic risk RADIATION THERAPY

- Patients should receive rescue therapy with either a Dopamine receptor antagonist or
- 5-HT_3 antagonist.
- Prophylactic antiemetic should continue throughout radiation treatment if a patient experiences RINV while receiving rescue therapy.

10. Optimal treatment to manage nausea and vomiting during concurrent radiation and chemotherapy?

Patients should receive antiemetic prophylaxis according to the emetogenicity of chemotherapy, unless the emetic risk with the planned radiotherapy is higher.

The Four Emetic Risk Groups – as in clinical trials

HIGH	Risk in nearly all patients (>90%)
MODERATE	Risk in 30% to 90% of patients
LOW	Risk in 10% to 30% of patients
M INIMAL	Fewer than 10% at risk

Emetic Risk Groups - Single Intra-Venous Agents

HIGH	Cisplatin Mechlorethamine Streptozocin Cyclophosphamide >1500 mg/m2 Carmustine Dactinomycin Dacarbazine
MODERATE	Oxaliplatin Cytarabine> 1 gm/m2 Carboplatin Ifosfamide Cyclophosphamide < 1500 mg/m2 Doxorubicin Daunorubicin Epirubicin Idarubicin Irinotecan

	Alemtuzumab Bendamustine Azacitidine
LOW	Paclitaxel Docetaxel Mitoxantrone Topotecan Etoposide Pemetrexed Methotrexate Doxorubicin HCL liposome injection Mitomycin Gemcitabine Cytarabine<100 mg/m2 5-Fluorouracil Bortezomib Cetuximab Trastuzumab Doxorubicin HCL Liposome injection Etoposide Temsirolimus Panitumumab Ixabepilone Cabazitaxel
Minimal	Bleomycin Busulfan 2-Chlorodeoxyadenosine Fludarabine Vinblastine

	Vincristine Vinorelbine Bevacizumab Cetuximab Rituximab

Emetic Risk Groups - Single Oral Agents

HIGH	Hexamethylmelamine Procarbazine
MODERATE	Cyclophosphamide Etoposide Temozolomide Vinorelbine Imatinib
LOW	CapecitabineTegafururacil
MINIMAL	Chlorambucil Hydroxyurea L-Phenylalanine mustard 6-Thioguanine Methotrexate Gefitinib

Levels of Emetic Risk with Radiation Therapy (Radiation Therapy)

RISK LEVEL	AREA OF TREATMENT
HIGH	TBI Total nodal irradiation
MODERATE	Upper Abdomen Upper body irradiation Half body irradiation
LOW	Lower thorax region, Pelvis, Cranium (radiosurgery), Craniospinal Head and neck
MINIMAL	Extremities Breast

RECOMMENDED DOSES – CHEMOTHERAPY RISK GROUP

AGENT	ROUTE	DOSE
HIGH EMETIC RISK		
Ondansetron	IV	8mg or 0.15 mg/kg
	Oral	8mg twice daily
Granisetron	IV	1 mg or 0.1 mg/kg
	Oral	2 mg (or 1 mg**)
Dolasetron	Oral	100 mg
Tropisetron	IV	5mg
	Oral	5 mg

Palonosetron	Oral	0,5 mg
	IV	0.25 mg
Aprepitant	Oral	125mg on chemo day 80mg subsequent days (day 2&3)
Fosaprepitant	IV	150mg
Dexamethasone (if aprepitant is used)	IV/Oral	12mg and 8md day 2 & 3
Dexamethasone (if fosaprepitant is used)	IV/Oral	12mg and 8mg twice a day on day 3&4
MODERATE EMETIC RISK		
5-HT antagonist Palonosetron	IV/Oral	0.25mg iv or 0.50mg oral
Dexamethasone	IV/Oral	8mg , days 2 & 3
LOW EMETIC RISK		
Dexamethasone	IV/Oral	8mg iv or oral

DEXAMETHASONE		**Dose and Schedule**
High Risk	Acute Emesis	20 mg once
	Delayed Emesis	8 mg bid for 3-4 days
Moderate	Acute Emesis	8 mg once
	Delayed Emesis	8 mg daily for 2-3 days (can be given as 4 mg bid)

Low Risk	Acute Emesis	4-8 mg once

RECOMMENDED DOSES – RADIOTHERAPY RISK GROUP

AGENT	ROUTE	DOSE
HIGH EMETIC RISK		
5HT antagonist		Before each # throughout XRT continue for at least 24 hrs before completion of xrt
Ondansetron	IV	8mg or 0.15 mg/kg
	Oral	8mg twice daily
Granisetron	IV	1 mg or 0.1 mg/kg
	Oral	2 mg (or 1 mg**)
Dolasetron	Oral	100 mg
Tropisetron	IV	5mg
	Oral	5 mg
Dexamethasone	IV/Oral	4mg during # 1 - 5
MODERATE EMETIC RISK		
5-HT antagonist (Any of the above are acceptable)	IV/Oral	5 HT before each #
Dexamethasone	IV/Oral	During # 1-5
MINIMAL EMETIC RISK		
5-HT antagonist (Any of the above are acceptable)	IV/Oral	Patient should be offered either class or rescue therapy.

		If rescue therapy is used, then prophylactic therapy should be given until the end of XRT
Dopamine receptor antagonist • Metoclopramide • Prochlorperazine	• Oral • IV/Oral	• 20mg • 10mg

DRUG KEY

GENERIC NAMES	REGISTERED TRADE NAMES
Ondansetron	Zofran Inj 4mg 2 ml Zofran Inj 8mg 4 ml
Granisetron	Kytril IV Inj 1mg/ml 1 ml Kytril IV Inj 3mg 3 ml Kytril Tab 1mg Kytril Tab 2mg
Dolasetron	Zamanon Tab 50mg Zamanon Tab 200mg Zamanon Amp Inj 100mg 5 ml Zamanon Amp Inj 12.5mg/0.625ml
Tropisetron	Navoban Cap 5mg Navoban Inj 1mg/ml 5 ml
Palonosetron	Onicit
Aprepitant	Emend Cap 80mg Emend Cap 125mg Emend Combi Pack Cap
Dexamethasone	Decadron Tab 0.5mg

	Decasone Inj 4mg 1 ml Micro Dexamethasone Inj 4mg/1m Oradexon Inj 5mg/ml 1 ml

SOURCES:

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Date Reviewed: 15/02/2016

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Next review date: 15/02/2019