

ESMO Minimum Clinical Recommendations for prophylaxis of chemotherapy-induced nausea and vomiting (NV)

Definitions

- Acute nausea and vomiting: Initial 24 hours after chemotherapy.
- Delayed nausea and vomiting: Later than 24 hours after chemotherapy.
- Anticipatory nausea and vomiting: Days to hours before chemotherapy.

Low (emetic risk between 10–30%):

Oral agents:

Cyclophosphamide
Etoposide
Temozolomide
Vinorelbine
Imatinib

Intravenous agents:

Topotecan
Gemcitabine
Liposomal doxorubicin
Mitoxantrone
Docetaxel
Paclitaxel
Etoposide
Teniposide
Pemetrexed
Methotrexate
Mitomycin
Fluorouracil
Cytarabine < 100 mg/m²
Bortezomib
Cetuximab
Trastuzumab

Other causes of nausea and vomiting to be considered

- Radiotherapy, radiosensitizers, infection, metabolic disorders, electrolyte disturbances, constipation, gastrointestinal obstruction, cachexia syndrome, metastases (brain, liver, bone), paraneoplasia, other emetogenic medication (e.g. opioids, antibiotics, antifungals, amifostine) and psychological. The relative emetogenic potentials of chemotherapy are listed in Table 1.

Table 1. Relative emetogenic potential of chemotherapy (if no anti-emetic prophylaxis is used)

High (emetic risk 90% or more):	Intravenous agents:	Minimal (emetic risk less than 10%):	Oral agents:
	Cisplatin		Capecitabine
	Mechlorethamine		Fludarabine
	Streptozocin		Intravenous agents:
	Carmustine		Bleomycin
	Cyclophosphamide >1500 mg/m ²		Busulfan (not for high-dose therapy)
	Dacarbazine		2-Chlorodeoxyadenosine
	Oral agents:		Fludarabine
	Hexamethylmelamine		Vincristine
	Procarbazine		Vinblastine
	Intravenous agents:		Vinorelbine
	Oxaliplatin		Bevacizumab
	Cytarabine >1 gm/m ²		Oral agents:
	Carboplatin		Chlorambucil
	Ifosfamide		Hydroxyurea
	Cyclophosphamide <1500 mg/m ²		L-Phenylalanine mustard
	Doxorubicin		6-Thioguanine
	Epirubicin		Methotrexate
	Daunorubicin		Gefitinib
	Idarubicin		
	Irinotecan		

Anti-emetics

- 5-hydroxytryptamine type 3 receptor (5HT₃) (serotonin) antagonists, corticosteroids and aprepitant are usually given

once daily. However, for delayed emesis corticosteroids are given b.i.d. Dopamine antagonists are given 3–4 times daily. For routine use oral doses are recommended [I, A]. Palonosetron is only available as an i.v. formulation.

Table 2.

Anti-emetic drug and schedule	Oral dose (mg)
Serotonin antagonists (once daily):	
Ondansetron ^a	16–24
Granisetron ^b	2
Tropisetron	5
Dolasetron	100
Palonosetron	0.25 mg i.v. (no oral formulation available)
Dopamine antagonists (3–4 times daily):	
Metoclopramide	20–30
Prochlorperazine	10–20
Domperidone ^c	20
Metopimazine ^d	15–30
Corticosteroids (once daily):	
Dexamethasone ^e	20
Prednisolone	100–150
Methylprednisolone ^f	100
Neurokinin antagonists (once daily):	
Aprepitant ^g	125 mg day 1 followed by 80 mg days 2 and 3 after chemotherapy
Others (1–4 times daily):	
Lorazepam	1–2

^aIntravenous dose of ondansetron is 8 mg.

^bIntravenous dose of granisetron is 1 mg.

^cNot for intravenous use.

^dIntravenous administration only as continuous infusion.

^eDose is evidence-based for intravenous dexamethasone only. For cisplatin-induced emesis a single i.v. 20 mg dose and for cyclophosphamide/anthracycline-based chemotherapy a single i.v. 8 mg dose is recommended day 1 after chemotherapy. Corticosteroids b.i.d. for delayed emesis.

^fFor intravenous use only.

^gAprepitant is metabolized via CYP3A4 and various drugs could be influenced. When cortico-steroids are combined with aprepitant, the dose of the corticosteroids should be reduced to 50%.

Table 3. Acute nausea and vomiting

Emetogenic potential	Anti-emetics
High	Serotonin antagonist + corticosteroid + aprepitant [I, A]
Moderate ^a	Serotonin antagonist + corticosteroid [I, A]
Low	A single agent such as a corticosteroid [III, IV, D]
Minimal	No routine prophylaxis [V, D]

Substances of the same class are of comparable efficacy [I, A]. Anti-emetic drugs, their schedules and oral doses are listed in Table 2.

Treatment

- Anti-emetics are given prophylactically 30–60 min before the start of chemotherapy. If a patient has nausea and vomiting, treatment should be given intravenously. Recommendations concern chemotherapy-naïve patients. In patients, who have experienced nausea and vomiting during previous chemotherapy, anti-emetic therapy should be individualized. Table 3 lists levels of emetogenic potential and the required anti-emetic treatments for acute nausea and vomiting, Table 4 for delayed nausea and vomiting and Table 5 describes specific problems.

Note

Levels of Evidence [I–V] and Grades of Recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the expert authors and the ESMO faculty.

Table 4. Delayed nausea and vomiting

Emetogenic potential	Anti-emetics
High	Corticosteroid + aprepitant [II, A]
Moderate ^b	Corticosteroid [II, A] or serotonin antagonist [II, B]
Low	No routine prophylaxis
Minimal	No routine prophylaxis

Table 5. Specific problems recommendations

Multiple day chemotherapy	As acute NV on chemotherapy days As delayed NV 1–2 days after chemotherapy Aprepitant and palonosetron have not been investigated in this setting [II, A]
Refractory nausea and vomiting	Add dopamine antagonists to serotonin antagonists and corticosteroids [V, D]
Anticipatory nausea and vomiting	Lorazepam or similar drugs Behavioural techniques [V, D]
High-dose chemotherapy	Corticosteroids, serotonin and dopamine antagonists in full doses intravenously [III, C]

^aThe oral agents are those with the lowest emetic risk. A single anti-emetic is often sufficient as prophylaxis. In patients receiving daily imatinib, anti-emetics given on demand only is a reasonable approach.

^bThe oral agents rarely induce delayed nausea and vomiting. No routine prophylaxis after day one is recommended.

Literature

1. Anti-emetic Subcommittee of the Multinational Association of Supportive Care in Cancer: Results of the Perugia Consensus Conference. *Ann Oncol* 1998; 9: 811–819.
2. Gralla RJ, Osoba D, Kris MG et al. Recommendations for guidelines for the use of anti-emetics: Evidence-based clinical practice guidelines. *J Clin Oncol* 1999; 17: 2971–2994.
3. Anti-emetic Resource Center at <http://www.mascc.org> (date last accessed 28 February 2005).
4. Navari RM. Role of neurokinin-1 receptor antagonists in chemotherapy-induced emesis: summary of clinical trials. *Cancer Invest* 2004; 22: 569–576.

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