Availability and accessibility of antiemetics in the region: Barriers to implement MASCC/ESMO Guidelines

2018
28-30 JUNE
VIENNA, AUSTRIA
SUPPORTIVE CARE MAKES EXCELLENT CANCER CARE POSSIBLE

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Faculty disclosure

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None

Objectives

- MASCC/ESMO Antiemetic Guidelines
- Are Antiemetic Guidelines useful?
- Barriers to the implementation of guidelines
- Limitations in the use of guidelines
- The Eastern European status
- What to do?
- Conclusion

MASCC/ESMO Antiemetic Guidelines

clinical practice guidelines

Annals of Oncology 27 (Supplement 5): v119–v133, 2016
doi:10.1093/annonc/mdw270

2016 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting and of nausea and vomiting in advanced cancer patients

F. Roila[1], A. Molassiotis[2], J. Herrstedt[3], M. Aapro[4], R. J. Gralla[5], E. Bruera[6], R. A. Clark-Snow[7], L. L. Dupuis[8], L. H. Einhorn[9], P. Feyer[10], P. J. Hesketh[11], K. Jordan[12], I. Olver[13], B. L. Rapoport[14], J. Roscoe[15], C. H. Ruhlmann[3], D. Walsh[16], D. Warr[17] & M. van der Wetering[18] on behalf of the participants of the MASCC/ESMO Consensus Conference Copenhagen 2015*

The NEW ENGLAND JOURNAL of MEDICINE

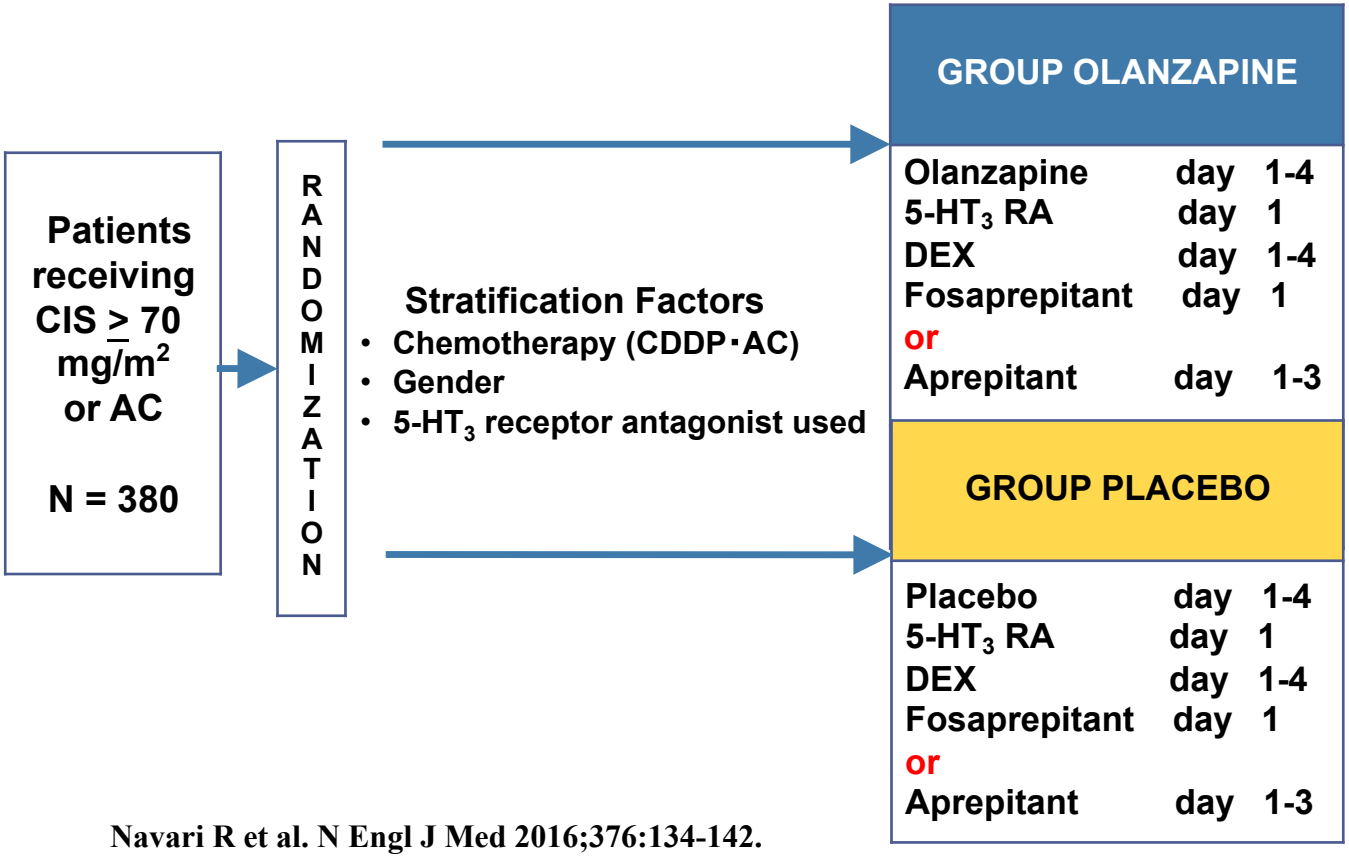
ORIGINAL ARTICLE

Olanzapine for the Prevention of Chemotherapy-Induced Nausea and Vomiting

Rudolph M. Navari, M.D., Rui Qin, Ph.D., Kathryn J. Ruddy, M.D., Heshan Liu, Ph.D., Steven F. Powell, M.D., Madhuri Bajaj, M.D., Leah Dietrich, M.D., David Biggs, M.D., Jacqueline M. Lafky, M.S., and Charles L. Loprinzi, M.D.

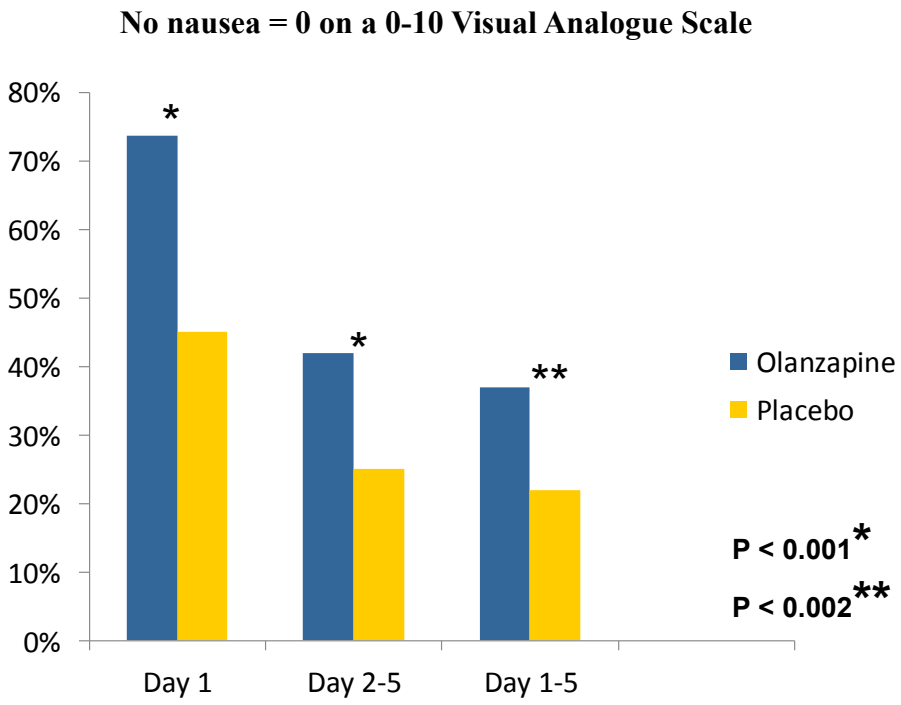
N Engl J Med 2016;375:134-142

STUDY DESIGN



Navari R et al. N Engl J Med 2016;376:134-142.

NO NAUSEA RATES



Navari R et al. N Engl J Med 2016;376:134-142.

REVIEW

CURRENT OPINION

The latest consensus on antiemetics

Jørn Herrstedt[a,b]

Herrstedt J. Curr Opin Oncol 2018;30:233-239.

Table 2. The latest recommendations for antiemetic prophylaxis

High Emetic Risk (> 90% risk)	Administration	MASCC/ESMO	
All HEC	Day 1	5-HT_3-RA + DEX + NK_1-RA	or
		5-HT_3-RA + DEX + OLA	or
		5-HT_3-RA + DEX + NK_1-RA + OLA	
HEC - Cisplatin	Days 2-4	DEX[1] or DEX + OLA	
HEC - AC	Days 2-3	None[2] or OLA	

1. If aprepitant is used day 1, then aprepitant should be continued days 2-3.
2. If aprepitant is used day 1, aprepitant or dexamethasone should be continued days 2-3.

A, anthracycline; C, cyclophosphamide; DEX, dexamethasone; HEC, high emetic risk; OLA, olanzapine; 5-HT_3-RA, serotonin$_3$-receptor antagonist; NK_1-RA, neurokinin$_1$-receptor antagonist.

Herrstedt J. Curr Opin Oncol 2018;30:233-239.

Table 2. The latest recommendations for antiemetic prophylaxis

Moderate Emetic Risk (30-90% risk)	Administration	MASCC/ESMO
Carboplatin (≥ AUC 4)	Day 1	5-HT_3-RA + DEX + NK_1-RA
Other MEC		5-HT_3-RA + DEX
Carboplatin (≥ AUC 4)	Days 2-3	None[1]
Oxaliplatin or A or C		DEX or none
Other MEC		None

1. If aprepitant is used day 1, then aprepitant should be continued days 2-3.

A, anthracycline; C, cyclophosphamide; DEX, dexamethasone; MEC, moderate emetic risk; OLA, olanzapine; 5-HT_3-RA, serotonin$_3$-receptor antagonist; NK_1-RA, neurokinin$_1$-receptor antagonist.

Herrstedt J. Curr Opin Oncol 2018;30:233-239.

Table 2. The latest recommendations for antiemetic prophylaxis

Emetic Risk	Administration	MASCC/ESMO
Low (10-30%)	Day 1	5-HT_3-RA or DEX or DOP-RA
	Days 2-3	None
Minimal (< 10%)	Days 1-3	No routine prophylaxis

DEX, dexamethasone; 5-HT_3-RA, serotonin$_3$-receptor antagonist; DOP-RA, dopamine-receptor antagonist.

Herrstedt J. Curr Opin Oncol 2018;30:233-239.

Are antiemetic guidelines useful?

N = 991

The effect of guideline-consistent antiemetic therapy on chemotherapy-induced nausea and vomiting (CINV): the Pan European Emesis Registry (PEER)

M. Aapro[1]*, A. Molassiotis[2], M. Dicato[3], I. Peláez[4], Á. Rodríguez-Lescure[5], D. Pastorelli[6], L. Ma[7], T. Burke[7], A. Gu[7], P. Gascon[8] & F. Roila[9]; on behalf of the PEER investigators

Ann Oncol 2012;23:1986-1992.

Guideline-consistent CINV prophylaxis reduces the incidence of CINV after single-day HEC and MEC.

N = 1.295

Antiemetic Guideline Consistency and Incidence of Chemotherapy-Induced Nausea and Vomiting in US Community Oncology Practice: INSPIRE Study

By James W. Gilmore, PharmD, Nancy W. Peacock, MD, Anna Gu, MD, PhD, Stephen Szabo, MD, Melissa Rammage, PharmD, MS, Joyce Sharpe, RN, OCN, Sally T. Haislip, RPh, Toni Perry, RN, Tim L. Boozan, RN, Katherine Meador, RN, Xiting Cao, PhD, and Thomas A. Burke, PharmD, PhD

J Oncol Pract 2014;10:68-74.

Increased adherence to antiemetic guidelines could significantly reduce the incidence of CINV after HEC and MEC

Barriers to the implementation of guidelines

Barriers to the implementation of guidelines

- Policy, reimbursement and sustainability
- Linguistic problems
- Drugs not available in all countries
- New drugs are expensive
- Physicians and nurses underestimate the incidence of DNV

DNV, delayed nausea and vomiting

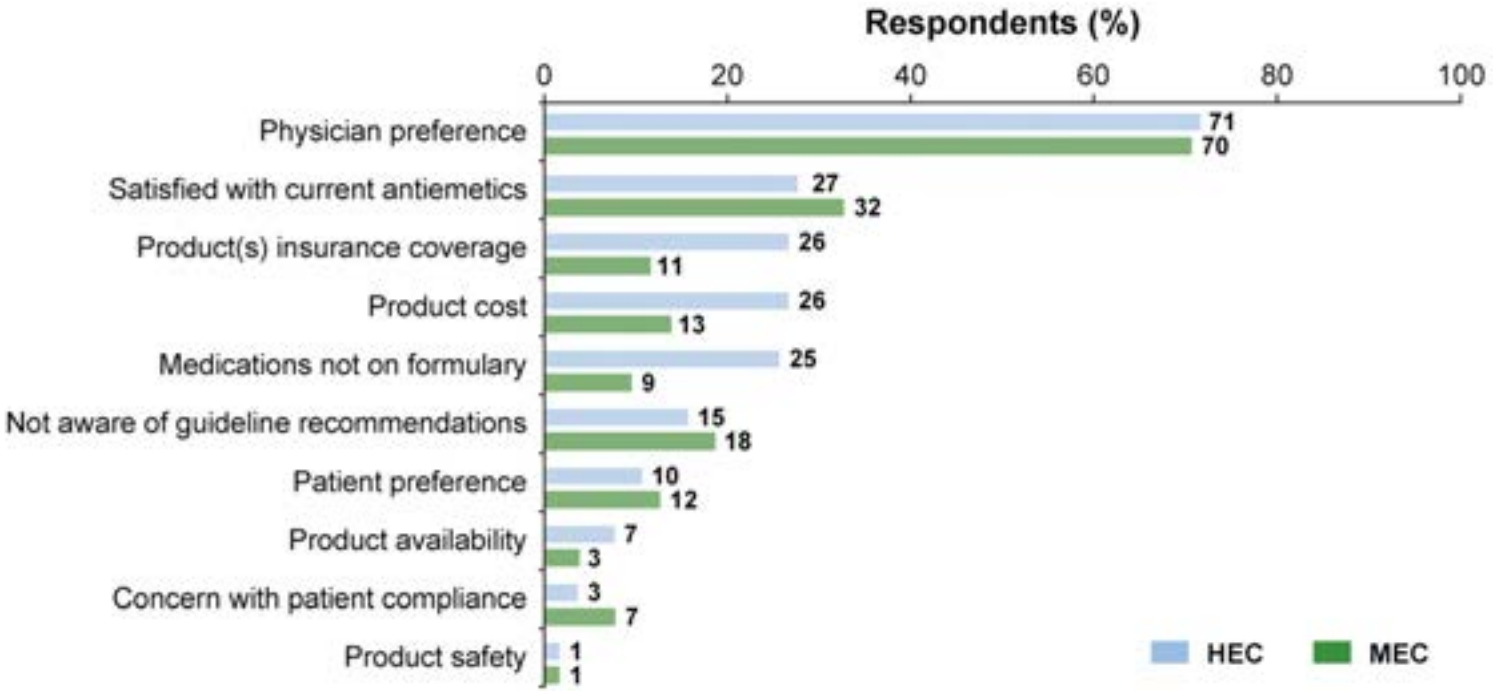
N = 531

Chemotherapy-induced nausea and vomiting (CINV) and adherence to antiemetic guidelines: results of a survey of oncology nurses

Rebecca Clark-Snow[1] · Mary Lou Affronti[2] · Cynthia N. Rittenberg[3]

Support Care Cancer 2018;26:557-564.

Reported barriers/reasons interfering with using guideline-recommended antiemetics



Clarck-Snow R et al. Support Care Cancer 2018;26:557-564.

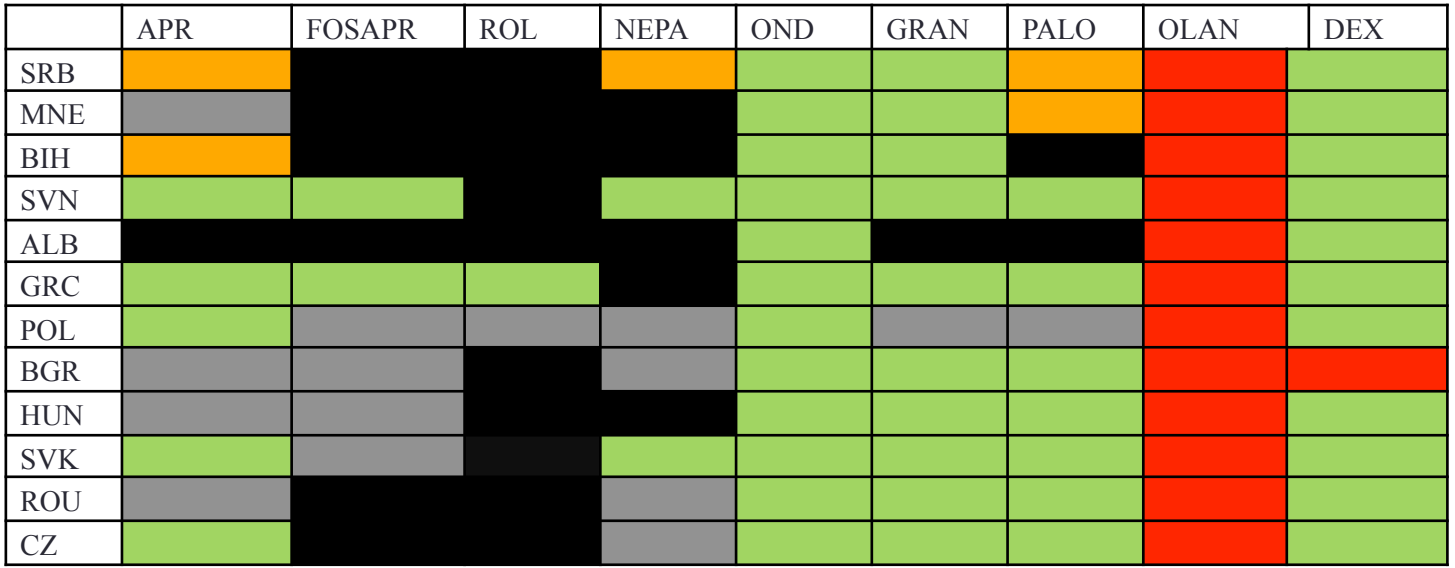
Limitations in the use of guidelines

Limitations in the use of guidelines

- Studies do not always reflect true clinical situations
- Not all clinical situations have been studied
- Only updated guidelines are useful

The Eastern European status

Availability of antiemetics in Eastern Europe



SRB=Serbia, **MNE**=Montenegro, **BIH**=Bosnia, **SVN**=Slovenia, **ALB**=Albania, **GRC**=Greece, **HRV**=Croatia, **POL**=Poland, **BGR**=Bulgaria, **TUR**=Turkey, **AUT**=Austria, **HUN**=Hungary, **SVK**=Slovakia, **ROU**=Romania

APR=aprepitant, **FOSAPR**= fosaprepitant, **ROL**=rolapitant, **NEPA**=netupitant, **OND**=ondansetron, **GRAN**=granisetron, **PALO**=palonosetron, **OLAN**=olanzapine, DEX=dexamethasone

Courtesy of Dr Ana Zilic

What to do?

What to do?

- Focus on the recommendations with the highest level of confidence
- Focus on patients with the highest risk of nausea and vomiting
- What can be done using the available antiemetics?

Level of confidence and level of consensus

HIGH EMETIC RISK CHEMOTHERAPY

Anthracycline-cyclophosphamide (AC)

Aprepitant Warr DG et al. J Clin Oncol 2005;23:2822-2830.

Aprepitant Rapoport B et al. Support Care Cancer 2010;18:423-31.

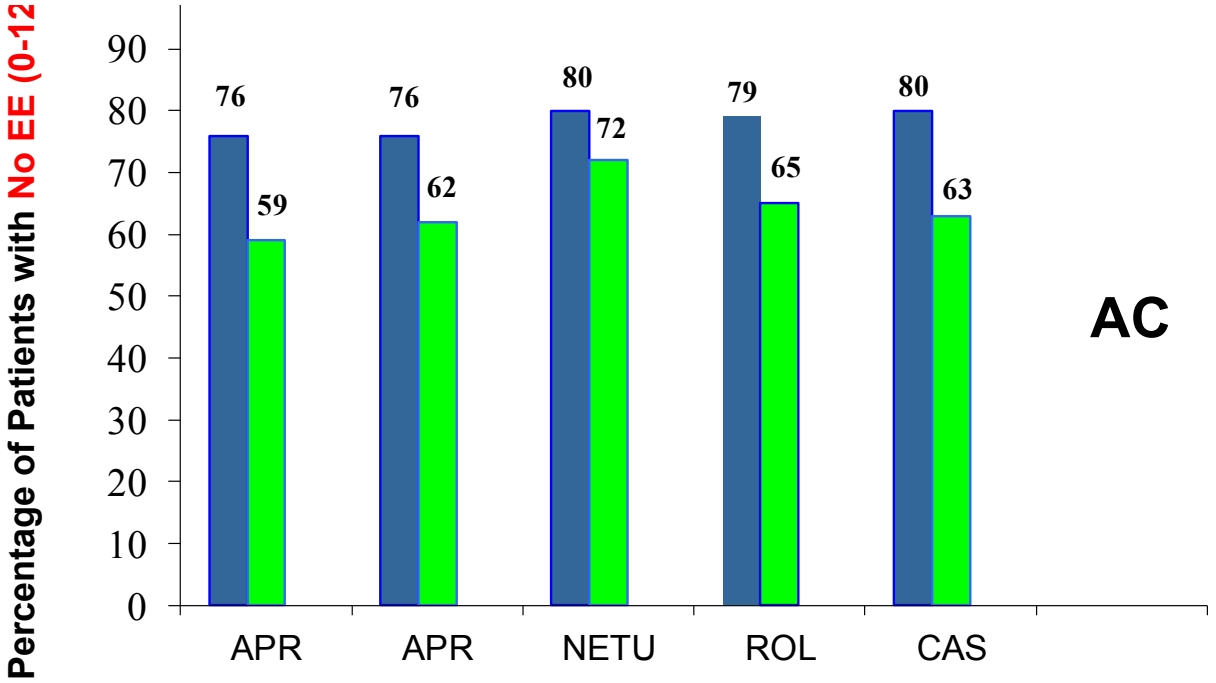
Netupitant Aapro MS et al. Ann Oncol 2014;25:1328-33.

Rolapitant Schwartzberg L et al. Lancet Oncol 2015;16:1071-78.

Casopitant Herrstedt J et al. J Clin Oncol 2009; 27:5363-5369.

5-HT_3-receptor antagonist + dexamethasone + placebo or a NK_1-receptor antagonist

Number of patients 848-1917



COMMITTEE II (3/6):

Prevention of Acute Nausea and Vomiting Following Anthracycline-Cyclophosphamide-Based Chemotherapy of High Emetic Risk

In women with breast cancer, a three-drug regimen including single doses of a 5-HT_3 receptor antagonist, dexamethasone, and an NK_1 receptor antagonist (aprepitant, fosaprepitant, netupitant* or rolapitant), given before chemotherapy is recommended.

MASCC Level of Confidence: High
MASCC Level of Consensus: High

* Netupitant administered with palonosetron as part of the fixed-dose oral combination agent NEPA

NOTE: If a NK1 receptor antagonist is not available for AC chemotherapy, palonosetron is the preferred 5-HT3 receptor antagonist.

NK_1 RA Regimen in Patients Receiving Carboplatin

Overall (0-120 h) No Emesis Rate	APR + 5-HT_3 RA + DEX	5-HT_3 RA + DEX	Absolute Difference	
Gralla (N = 192)*	84%	70%	14%	S
Overall (0-120 h) Complete Response	**APR + 5-HT_3 RA + DEX**	**5-HT_3 RA + DEX**	**Absolute Difference**	
Tanioka (N = 91)†	62%	52%	10%	NS
Ito (N = 134)	80%	67%	13%	NS
Yahata (N = 324)††	62%	47%	15%	S
Hesketh (N = 401)	80%	65%	15%	S
Weinstein (N = 513)	78%	63%	15%	S

*Posthoc analysis of the Rapoport study in a subgroup of patients
†98% of patients received carboplatin-based chemotherapy
††All patients received carboplatin and paclitaxel
APR = aprepitant, DEX = dexamethasone

Gralla R, J Clin Oncol 2010; 28: A9057.
Tanioka M, et al. Br J Cancer. 2013;109(4):859-865.
Ito Y, et al. Lung Cancer. 2014;84(3):259-264.
Yahata H, et al. Int J Clin Oncol 2015;Epub ahead of print December 10..
Hesketh PJ, et al. Cancer 2016;122:2418-25.
Weinstein C. ESMO 2016 (abstract 14350).

COMMITTEE III (3a/3):

Prevention of Acute Nausea and Vomiting in Patients Receiving Carboplatin-Based Chemotherapy

A combination of an NK_1 receptor antagonist, $5\text{-}HT_3$ receptor antagonist, and dexamethasone is recommended for the prophylaxis of nausea and vomiting induced by carboplatin-based chemotherapy.

MASCC Level of Confidence: Moderate

MASCC Level of Consensus: Moderate

The development of a prediction tool to identify cancer patients at high risk for chemotherapy-induced nausea and vomiting

G. Dranitsaris[1*], A. Molassiotis[2], M. Clemons[1], E. Roeland[3], L. Schwartzberg[4], P. Dielenseger[5], K. Jordan[6], A. Young[7] & M. Aapro[8]

Ann Oncol 2017;28:1260-1267.

Table 2. Predictive factors for nausea and vomiting from days 0 to 5

Predictive factor[a]	Odds ratio[b]	(95% CI)	Impact on risk
Age <60 years	1.41	(1.12–1.77)	↑ by 41%
Anticipatory nausea and vomiting	1.41	(1.13–1.77)	↑ by 41%
Sleep <7 h	1.34	(1.10–1.48)	↑ by 34%
History of morning sickness	1.30	(1.04–1.64)	↑ by 30%
Use of non-prescribed antiemetics at home	2.70	(1.45–2.60)	↑ 2.7 times
Platinum- or anthracycline-based chemotherapy	1.94	(1.45–2.60)	↑ by 94%
Nausea or vomiting in the prior cycle	5.17	(3.72–7.18)	↑ 5.17 times
Cycle number (vs. cycle 1)			
Cycle 2	0.17	(0.12–0.24)	↓ by 83%
≥Cycle 3	0.15	(0.10–0.24)	↓ by 85%

Dranitsaris G et al. Ann Oncol 2017;28:1260-1267.

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Conclusion

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- Always use guideline recommended antiemetic prophylaxis
- If not all antiemetics are available focus
  - **on the antineoplastic agents with the highest emetic risk**
  - **on the patients with the highest emetic risk**
  - **on the recommendations with the highest level of evidence**
- Follow-up and modify if necessary