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Declaration of conflict of interest

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Cancer therapy–induced nausea & vomiting in adults
New clinical practice guidelines

Cheryl Vidall RGN
UKONS Lead Ambassador
UKONS Past President (2010-2012)

WHY DOES CANCER-THERAPY INDUCED NAUSEA AND VOMITING (CINV) MANAGEMENT MATTER?

What do we mean, what do we know and how can we gain control of CINV?

The goal of CINV management

The consequences of uncontrolled CINV

Challenges facing staff in providing optimum CINV management

The contribution made by Oncology Nurses

New EONS Guidelines

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WHAT DO WE MEAN?

Definitions of CINV

Acute (0-24 hr after chemotherapy)

Delayed (24-120 hr after chemotherapy)

- May last up to 6 days
- Incidence without treatment 20%-90%

Anticipatory (prior to chemotherapy)

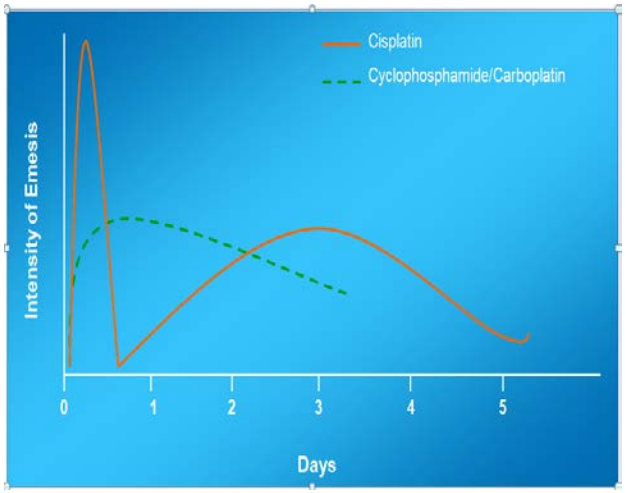
- Experienced by up to 25% of patients by 4th chemotherapy cycle*

Breakthrough (patients experience nausea or vomiting despite optimal prophylaxis)

The goal of CINV management is to prevent nausea and vomiting from cycle 1, rather than treating symptomatic patients

*Aapro MS, et al. *Support Care Cancer*. 2005;13:117-121

Patterns of emesis



Martin M. *Oncology*. 1996;53(suppl 1): 26-31

WHAT DO WE KNOW?

Risk factors: Consider the drug and the person to calculate the risk

Treatment-related risk factors[1]:

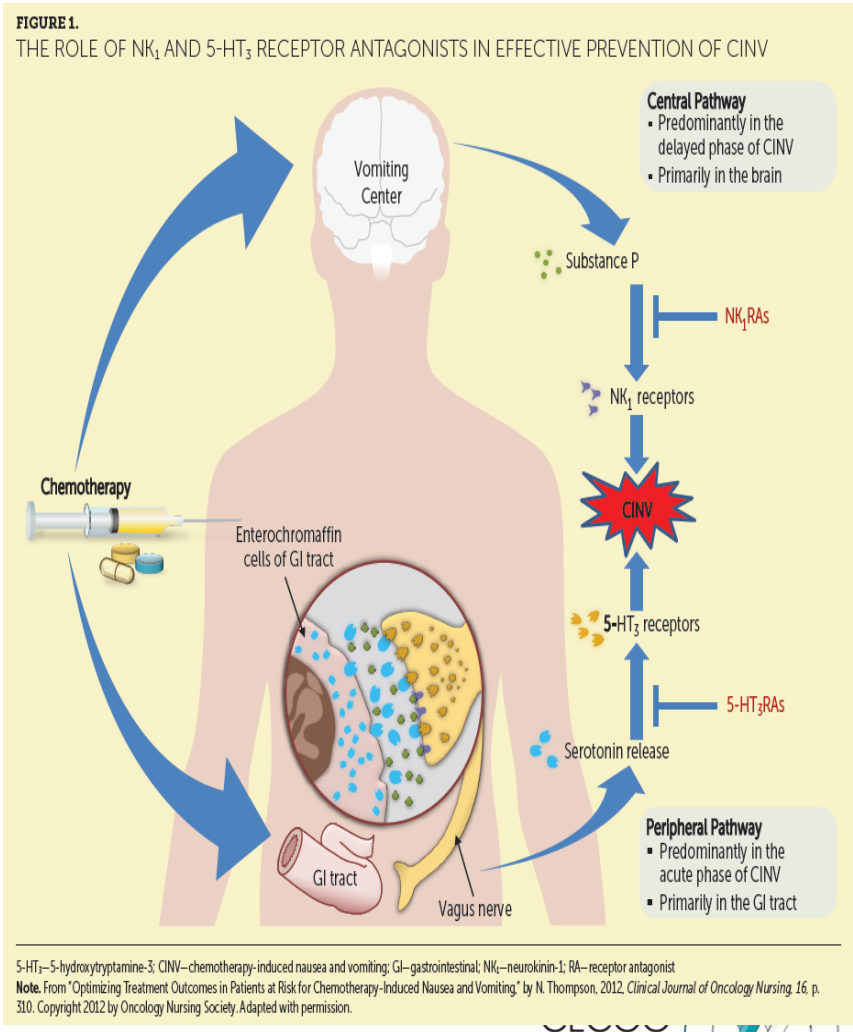
- Emetogenicity of chemotherapy agents or regimens
- Moderate to high drug dose
- Hesketh drug calculator for combination therapies

Patient-related risk factors[2]:

- Younger age
- Female gender
- No/minimal prior history of alcohol use
- Prior CINV
- Anxiety
- Hyper emesis in pregnancy / travel sickness

1. Hesketh PJ, et al. *J Clin Oncol.* 1997;15:103-109

2. Gregory RE, et al. *Drugs.* 1998;55:173-189.



The Practice Gap

Support Care Cancer
DOI 10.1007/s00520-015-2750-5

ORIGINAL ARTICLE

Impact and management of chemotherapy/radiotherapy-induced nausea and vomiting and the perceptual gap between oncologists/oncology nurses and patients: a cross-sectional multinational survey

Cheryl Vidall[1] · Paz Fernández-Ortega[2] · Diego Cortinovis[3] · Patrick Jahn[4] · Bharat Amlani[5] · Florian Scotté[6]

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Abstract
Purpose Chemotherapy/radiotherapy-induced nausea and vomiting (CINV/RINV) can affect half of oncology patients, significantly impacting daily life. Nausea without vomiting has only recently been thought of as a condition in its own right. As such, the incidence of nausea is often underestimated. This survey investigated the incidence and impact of CINV/RINV in patients compared with estimations of physicians/oncology nurses to determine if there is a perceptual gap between healthcare professionals and patients.
Methods An online research survey of physicians, oncology nurses and patients was conducted across five European countries. Participants had to have experience prescribing/recommending or have received anti-emetic medication for CINV/RINV treatment. Questionnaires assessed the incidence and impact of CINV/RINV, anti-emetic usage and compliance, and attribute importance of anti-emetic medication.
Results A total of 947 (375 physicians, 186 oncology nurses and 386 patients) participated in this survey. The incidence of nausea was greater than vomiting: 60 % of patients reported nausea alone, whereas 18 % reported vomiting. Physicians and oncology nurses overestimated the incidence of CINV/RINV but underestimated its impact on patients' daily lives. Only 38 % of patients reported full compliance with physicians'/oncology nurses' guidelines when self-administering anti-emetic medication. Leading factors for poor compliance included reluctance to add to a pill burden and fear that swallowing itself would induce nausea/vomiting.
Conclusions There is a perceptual gap between healthcare professionals and patients in terms of the incidence and impact of CINV/RINV. This may lead to sub-optimal prescription of anti-emetics and therefore management of CINV/RINV. Minimising the pill burden and eliminating the requirement to swallow medication could improve poor patient compliance with anti-emetic regimens.

Keywords Chemotherapy/radiotherapy-induced nausea and vomiting · Anti-emetic · Incidence · Impact · Perceptual gap

Electronic supplementary material The online version of this article (doi:10.1007/s00520-015-2750-5) contains supplementary material, which is available to authorized users.

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Introduction

Nausea and vomiting induced by treatment are estimated, on any 1 day in routine practice, to affect 35–50 % of patients undergoing chemotherapy and/or radiotherapy [1]. One study found that this had a significant impact on quality of life in approximately 40 % of patients affected [2, 3]. Several studies have reported that the incidence of both nausea and vomiting

Published online: 08 May 2015

Springer

Fixed Combination Antiemetic

A literature review on prevention of chemotherapy-induced nausea and vomiting using netupitant/palonosetron

Rebecca A. Clark-Snow, RN, BSN, OCN®, Cheryl Vidall, RGN, Sussanne Börjeson, RN, PhD, and Patrick Jahn, PhD, MSc

BACKGROUND: Prevention of chemotherapy-induced nausea and vomiting (CINV) can be improved with guideline-consistent use of antiemetics. However, adherence to antiemetic guidelines remains often insufficient. Therefore, new strategies that improve adherence are needed.

OBJECTIVES: To review the latest antiemetic guideline recommendations and provide an update on the use of NEPA, a fixed combination antiemetic composed of the neurokinin-1 receptor antagonist (RA) netupitant and the 5-hydroxytryptamine-3 RA palonosetron (Akynzeo®).

METHODS: Analysis of the literature was performed, including guidelines, published literature, congress data on NEPA, and relevant articles on CINV.

FINDINGS: Increased knowledge about CINV treatment recommendations and new antiemetic agents allow nurses to promote individualized anti-emetic prophylaxis and maximize supportive patient care. Nurses are in a unique position to promote guideline-consistent antiemetic prophylaxis and are central in the education of patients and caregivers.

KEYWORDS
chemotherapy-induced nausea and vomiting; antiemetic guidelines; NEPA

DIGITAL OBJECT IDENTIFIER
10.1188/18.CJON.E52-E63

CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING (CINV) is a common and distressing side effect for patients receiving highly emetogenic chemotherapy (HEC) or moderately emetogenic chemotherapy (MEC) (Hesketh, 2009). Without adequate prophylaxis, greater than 90% of patients receiving HEC and 30%–90% of patients receiving MEC will experience CINV (Aapro et al., 2012). Consequences often include metabolic imbalance, nutrient depletion, and anorexia; impaired daily functioning and reduced quality of life; postponement or dose reduction of chemotherapy; and increased resource use and costs (National Comprehensive Cancer Network [NCCN], 2017; Viale, Grande, & Moore, 2012).

Oncology nurses have observed that clinical challenges, often manifested as obstacles to CINV prophylaxis, may be timely opportunities to provide education to patients, family members, and significant others involved in the ongoing care of patients receiving potentially emetogenic chemotherapy. Patient perceptions may affect the control of CINV. Some patients interpret nausea and vomiting as a positive response to chemotherapy and a sign that it is working. Many patients fear that a dose reduction or discontinuation of treatment will occur if CINV is reported to physicians and nurses, and others expect to suffer during chemotherapy and are concerned that reporting CINV would be interpreted as complaining. These perceptions represent excellent opportunities for nurses to provide comprehensive education regarding planned chemotherapy and all supportive care medications that can be administered (Salsman et al., 2012; Thompson, 2012).

The selection of antiemetic agents for CINV prevention is supported by evidence-based guidelines. The most relevant, up-to-date guidelines include those from the Multinational Association of Supportive Care in Cancer (MASCC)/European Society for Medical Oncology (ESMO) (Roila et al., 2016), American Society of Clinical Oncology (ASCO) (Hesketh et al., 2017), and NCCN (2017). With guideline-consistent use of antiemetics, emesis can be prevented in the majority of patients (Jordan, Jahn, & Aapro, 2015). However, guidelines are not always followed; therefore, CINV remains a challenge for some patients (Aapro et al., 2012; Vidall et al., 2015). Additional antiemetic options are now available, such as netupitant/palonosetron (NEPA) (Akynzeo®) (Helsinn Healthcare

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THE PRACTICE GAP

Impact and management of chemotherapy/radiotherapy-induced nausea and vomiting and the perceptual gap between oncologists/oncology nurses and patients: a cross-sectional multinational survey

A total of 947 participants (375 physicians, 186 oncology nurses and 386 patients).

Group	Findings
Patients	60% nausea alone
	18% vomiting
	38% Fully adherent to antiemetic regimen; reasons for non-compliance were: • sense of no pain, no gain • low symptom severity • a reluctance to increase pill burden • fear that swallowing itself would induce nausea/vomiting
Physicians and Nurses	Overestimated the incidence of CINV/RINV but underestimated its impact on patients' daily lives
	Did not always immediately follow up patients post treatment to assess the effectiveness of the antiemetics administered

•The knowledge gap between health professionals and patients around real experiences of CINV/RINV may lead to sub-optimal prescribing, management and outcomes for CINV/RINV

•Advances in management depend on enhancing health professional-patient communication, and reporting and understanding nausea as a distinct issue

C.Vidall, P. Fernández-Ortega, D. Cortinovis, P. Jahn, B. Amlani & F. Scotté. *Supportive Care Cancer*, May 2015

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THE PRACTICE GAP

Fixed Combination Antiemetic: A literature review on prevention of chemotherapy-induced nausea and vomiting using netupitant/palonosetron (NEPA)

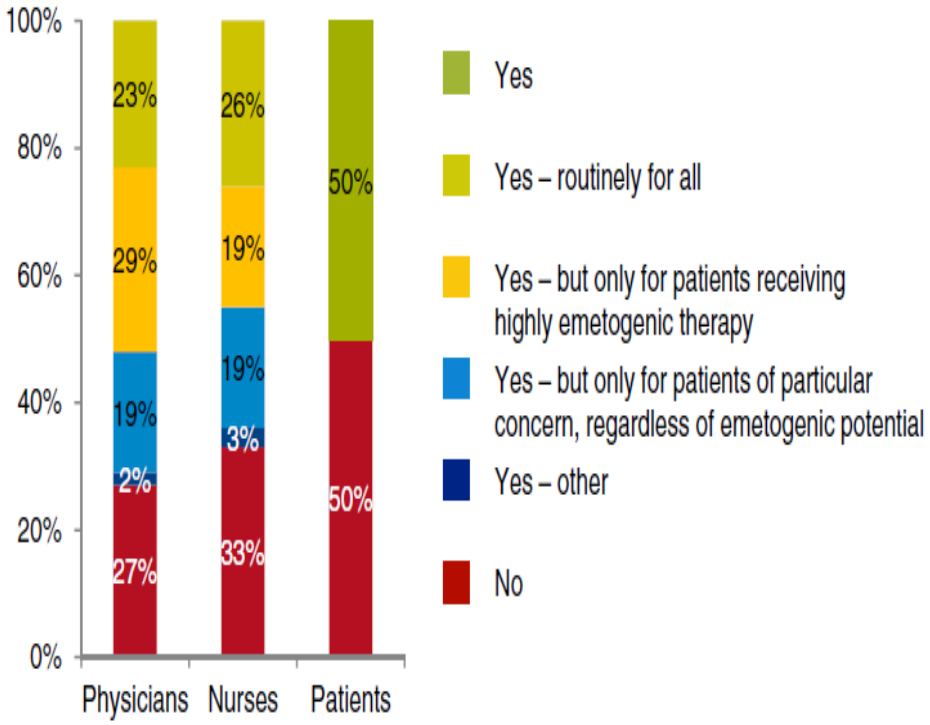
- Oncology nurse responsibilities include:
  - assessing CINV risk
  - educating patients and caregivers
  - administering antiemetic therapy
  - evaluating treatment
  - providing feedback to the medical team when changes in treatment are warranted
- Understanding of CINV and its management can improve patient care and outcomes
- Nurse education relating to CINV treatment recommendations and new antiemetic agents can promote individualized anti-emetic prophylaxis and maximize supportive patient care
- Patient history / risk factor assessment and the emetogenic potential of chemotherapy are essential when addressing individual patient needs
- Prevention of CINV can be improved with guideline-consistent use of antiemetics, however, antiemetic guideline adherence remains insufficient
- New strategies that improve adherence are needed
- Nurses should promote guideline-consistent antiemetic prophylaxis and are central in the education of patients and caregivers
- Nurses have an ideal platform for improving communication regarding patients' concerns and experiences

Rebecca A. Clark-Snow, RN, BSN, OCN®, Cheryl Vidall, RGN, Sussanne Börjeson, RN, PhD, and Patrick Jahn, PhD, MSc
Clinical Journal of Oncology Nursing, April 2018

THE GAP BETWEEN WHAT WE KNOW AND WHAT WE DO

- Knowledge and training (expertise is still rare)
- Keeping up to date with practice changes
- Ability to influence prescribing
- Access – to drugs, guidelines (e.g. ASCO, MASCC, NCCN), support (e.g. EONS, UKONS, ONS)
- Time to do the assessments and review effect
    - 50% patients claim they were not reviewed 5 days post chemo
- Tools to record and report. Validated CINV assessment tools include:

www.mascc.org/mat and http://cinvrisk.org

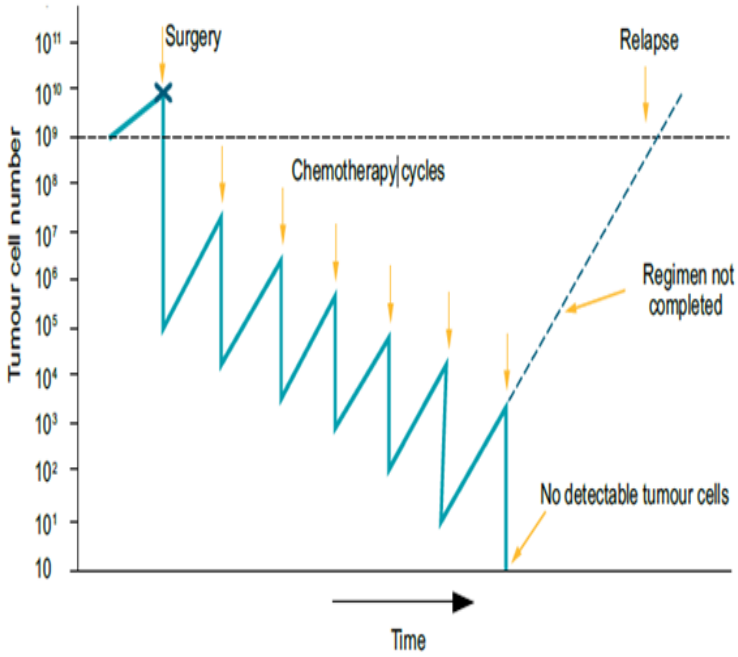


Percentage of patients contacted by their care team in the 5 days immediately following administration of chemotherapy. Vidall et al., Support Cancer Care, May 2015

SO WHAT?

Impact on patients

Rationale for regular cycles of chemotherapy



PDoT. *CNP* 2009

1. Non-adherence to antiemetic guidelines recommendations results in sub-optimal CINV control
2. Only 38% patients follow self-medicating treatment plans
3. Pill burden is a concern for patients and carers
4. Guideline adherence has been found to be suboptimal in oncology practices in Europe and the United States
5. Patients may discontinue chemotherapy due to CINV

1**. Aapro et al**., 2012. The effect of guideline-consistent antiemetic therapy on chemotherapy-induced nausea and vomiting (CINV): The Pan European Emesis Registry (PEER). *Annals of Oncology*

2 &3. **Vidall et al**., 2015. Impact and management of chemotherapy/radiotherapy-induced nausea and vomiting and the perceptual gap between oncologists/oncology nurses and patients: A cross-sectional multinational survey. *Supportive Care in Cancer*

4. **Aapro et al**., 2012; **Gilmore et al**., 2014. Antiemetic guideline consistency and incidence of chemotherapy-induced nausea and vomiting in US community oncology practice: INSPIRE Study. *Journal of Oncology Practice;* **Navari and Aapro**., 2016. Antiemetic prophylaxis for chemotherapy-induced nausea and vomiting. *New England Journal of Medicine*

5. ***Young, Vidall et al. 2009***. Delivery of chemotherapy at planned dose and on time. *Cancer Nursing Practice,* June 2009

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EONS PUBLICATION 'CANCER THERAPY-INDUCED NAUSEA AND VOMITING IN ADULTS'

Clinical Practice Guidance for Nurses

EONS secured funding from Tesaro and Helsinn to produce a practice guide for the management of CINV (cancer-therapy induced nausea and vomiting) and RINV (radiotherapy induced nausea and vomiting)

Developed through multinational collaboration of oncology nursing experts from across Europe (Switzerland, Germany, Sweden, Portugal and UK)

Underpins knowledge and re-iterates physiology, classification of nausea and vomiting, risk factors, risk assessments, emetogenicity of cytotoxic agents, pharmacological and non-pharmacology interventions

Addresses current clinical guidelines and best practice taking a user friendly 'how to' approach to maximize patient outcomes in a range of clinical scenarios

EONS GUIDANCE

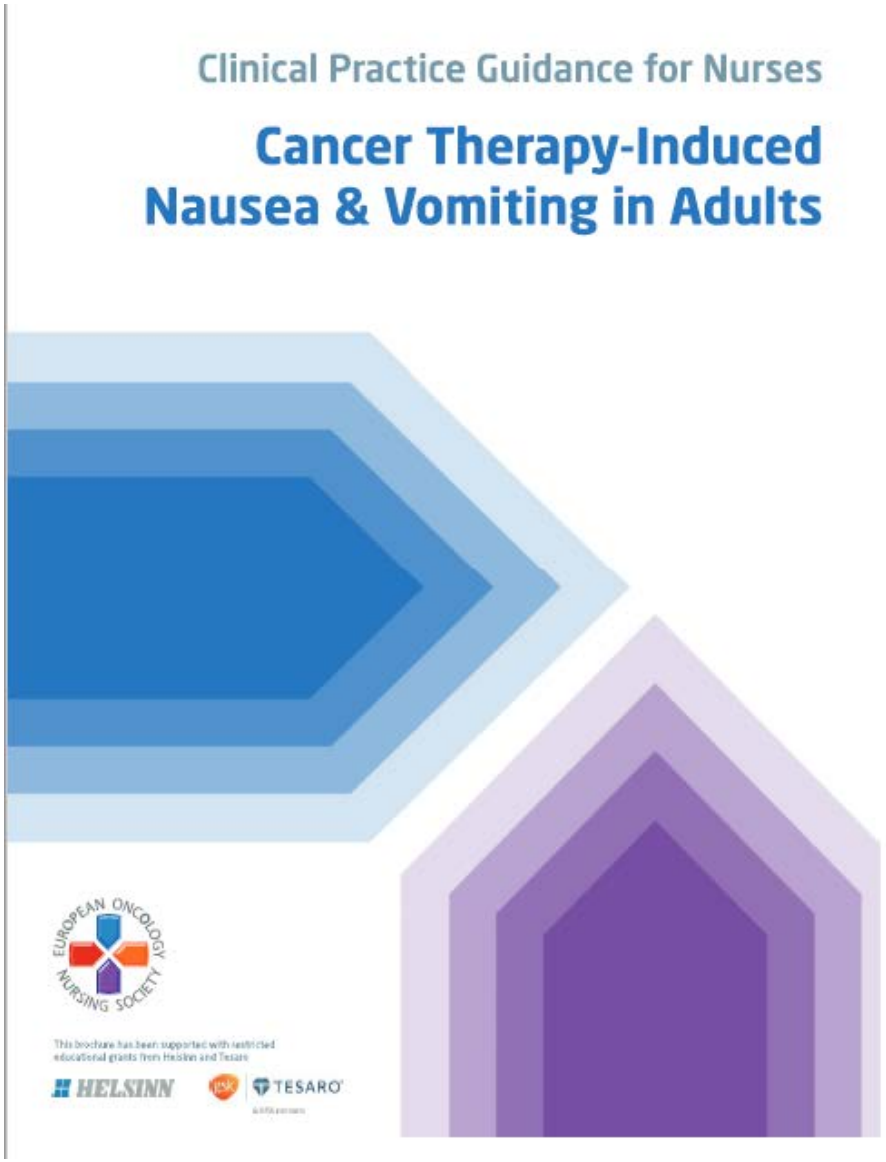
• Evidence based guidance for nurses and other healthcare professionals

• Launched at the ESMO / EONS Congress in Barcelona, September 2019

• Copies available through EONS

• Due to be translated into a range of European languages n coming months to increase access to more Oncology Nurses working in Europe

•User friendly guide to improve patient outcomes and increase nursing knowledge



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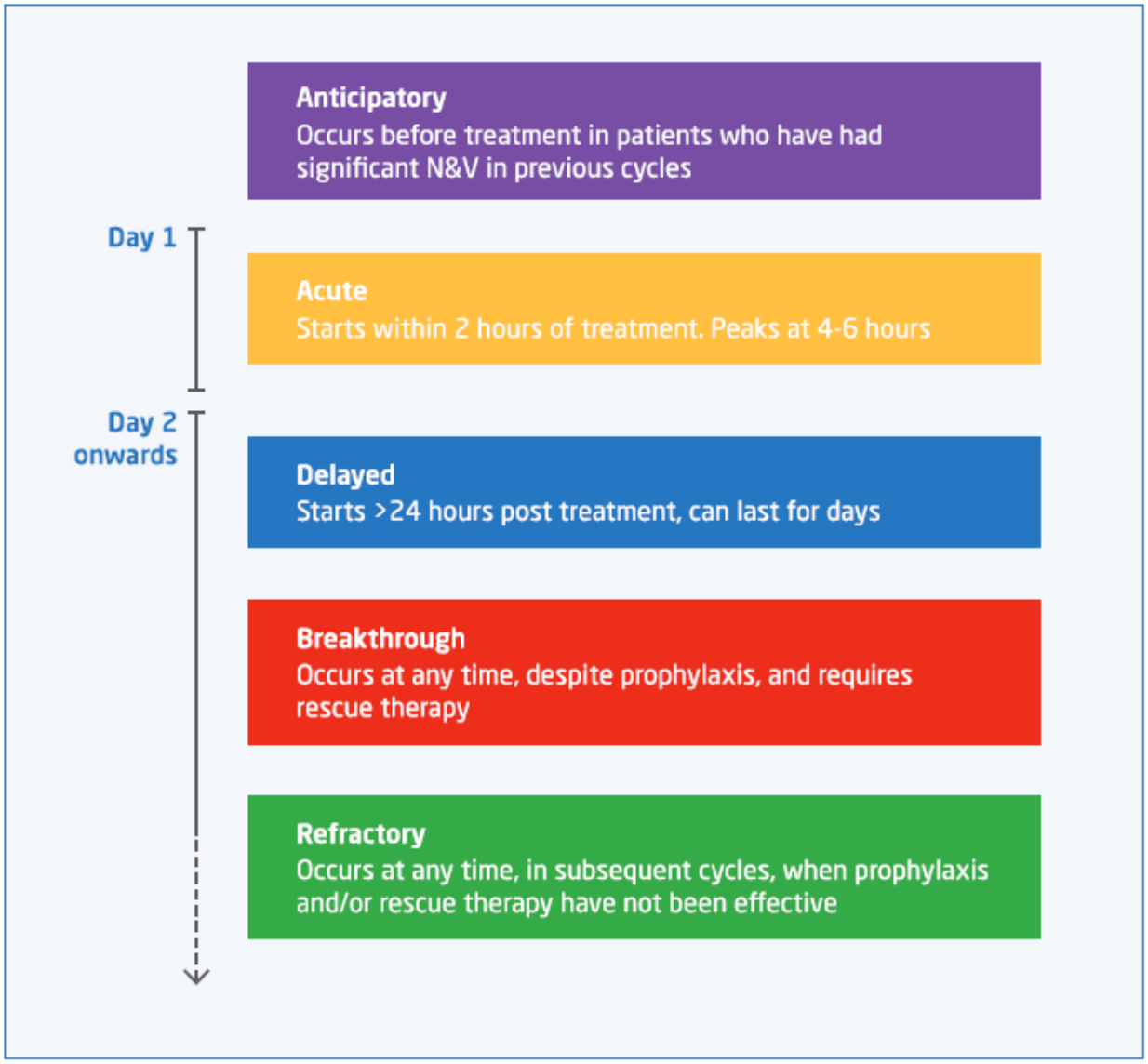
CLASSIFICATION OF THE 5 TYPES OF N&V



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SYSTEMIC CANCER TREATMENT RELATED RISK FACTORS

The main treatment related factors are:

- Type and dose of therapy
- Likelihood of causing N&V (emetogenicity)
- The type of prophylaxis used
- Combination of drugs
- Chemotherapy combined with radiotherapy

Type of N&V	Risk factors
Acute	• Emetic potential of cancer treatment • Use of non-prescribed antiemetics at home • Initial cycle/s of chemotherapy • Chemotherapy dose • Route of administration • Anticipatory N&V • N&V in a previous cycle of chemotherapy
Delayed	• Emetic potential of cancer treatment • Guideline-inconsistent prophylaxis • No use of secondary antiemetics • Anticipatory nausea • Acute N&V
Breakthrough	• Inappropriate antiemetic prophylaxis
Anticipatory	• N&V in cycle 1 of chemotherapy

RISK OF ACUTE EMESIS WITH CANCER DRUGS

Degree of emetogenicity	Risk of N&V, %	Parenteral	Oral
High	>90	**Cisplatin** Anthracycline/cyclophosphamide Cyclophosphamide ≥1500 mg/m^2 Dacarbazine	Procarbazine
Moderate	>30–90	Bendamustine Carboplatin Cyclophosphamide <1500 mg/m^2 Doxorubicin Oxaliplatin	Bosutinib Crizotinib Cyclophosphamide Temozolomide Vinorelbine
Low	10–30	Aflibercept Cetuximab Docetaxel 5-fluorouracil Gemcitabine Methotrexate Pemetrexed Topotecan	Afatinib Capecitabine Etoposide Everolimus Lapatinib Regorafenib Tegafur uracil Vandetanib
Minimal	<10	Bleomycin Fludarabine Nivolumab Trastuzumab Vincristine Vinorelbine	Chlorambucil Erlotinib Gefitinib Melphalan Methotrexate Sorafenib

- These are some of the more common examples of emetogenic agents
- Cisplatin is the most emetogenic parenteral agent
- In general, the majority of immunotherapy and monoclonal antibodies have a low to minimal risk of causing N&V
- Most agents associated with delayed emesis have high or moderate emetogenicity
- Some patients may experience N&V, regardless of the drug classification

For more complete lists see:
NCCN 2019
Hesketh et al 2018
Roila et al 2016

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RADIOTHERAPY INDUCED N&V

RINV can occur in 50-80% of patients undergoing treatment. The risk depends not only on the treatment site and volume of tissue irradiated but also on the patient characteristics as previously described

High	Total body irradiation
Moderate	Upper abdomen, craniospinal
Low	Cranium, head and neck, thorax region, pelvis
Minimal	Extremities, breast
Concomitant chemoradiotherapy	Risk is based on the chemotherapy being used, unless the emetogenic risk of radiotherapy is higher

Adapted from Ruhlmann et al, Support Care Cancer 2017;25:309-16

HOW DO WE GAIN CONTROL OF CINV?

Use international best practice guidelines (ASCO 2017)

Risk	%	Definition	Management
High	>90%	Cisplatin therapy	4 agent combination of NK1 & 5-HT3 receptor antagonists day 1 only with Dexamethasone and Olanzapine (days 1-4)
		(AC) Anthracycline & Cyclophosphamide	4 agent combination as above **but** Dexamethasone day 1 only, Olanzapine days 1-4
Moderate	30 - 90%	Carboplatin ≥4mg/ml AUC therapy	3 drug combination of NK1, 5-HT3 receptor antagonists with Dexamethasone day 1 only
		Cyclophosphamide, Oxaliplatin, Doxorubicin and other delayed CINV agents	2 drug combination of 5-HT3 receptor antagonist with Dexamethasone to continue for d 1-3
		All other moderate risk & Carboplatin <4mg AUC	2 drug combination of 5-HT3 and Dexamethasone day 1 only
Low	10 - 30%		5-HT3 and Dexamethasone day 1 only
Minimal	<10%		Routine antiemetic prophylaxis not recommended

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MANAGEMENT GUIDELINES FOR ACUTE N&V

Risk group	ESMO	ASCO	NCCN (parenteral cancer treatment)		
High, non-AC High, AC	5HT$_3$ RA + NK$_1$ RA + Dexamethasone	5HT$_3$ RA + NK$_1$ RA + Dexamethasone + Olanzapine	5HT$_3$ RA + NK$_1$ RA + Dexamethasone	5HT$_3$ RA + Dexamethasone + Palonosetron	5HT$_3$ RA + NK$_1$ RA + Dexamethasone + Olanzapine
Moderate, carboplatin	5HT$_3$ RA + NK$_1$ RA + Dexamethasone	5HT$_3$ RA + NK$_1$ RA + Dexamethasone	5HT$_3$ RA + Dexamethasone	5HT$_3$ RA + Dexamethasone + Palonosetron	5HT$_3$ RA + NK$_1$ RA + Dexamethasone
Moderate, non-carboplatin	5HT$_3$ RA + Dexamethasone	5HT$_3$ RA + Dexamethasone			
Low	Dexamethasone or 5HT$_3$ RA or Dopamine RA	5HT$_3$ RA or Dexamethasone	Dexamethasone or Dopamine RA or 5HT$_3$ RA or prochlorperazine		
Breakthrough	Addition of an agent with a mechanism different to that used prophylactically				
Anticipatory	The best approach is the optimal control of acute and delayed N&V				
	± Benzodiazepines ± Behavioural therapy	± Behavioural therapy	± Benzodiazepines ± Behavioural therapy		

Key

- 5HT$_3$ RA
- NK$_1$ RA
- Dexamethasone
- Olanzapine
- Dopamine RA
- Benzodiazepines
- Behavioural therapy

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OTHER AGENTS USED TO CONTROL N&V

Class of agent	Name	Recommended dosing*	Adverse events/comments
Corticosteroids	Dexamethasone Methylprednisolone	IV, oral	• Widely used, generally in combination with other agents
Dopamine RAs	Metoclopramide	Oral: 10 mg (up to three-times a day)	• Be aware of higher doses of metoclopramide according to the recommendations from EMA. Increased neuropathy has been reported as a severe side effect
Benzodiazepines and derivatives	Lorazepam	Oral: 1 mg	• May be a useful adjunctive agent (not for single-agent use)
Other	Olanzapine	Oral: 5-10 mg	• Sedation is a problem with the 10 mg/day dose, particularly in older patients

EMA = European Medicines Agency

PATIENT' PERCEPTION AND FEARS ABOUT USING N&V ANTIEMETIC MEDICATION

I knew I would have to put up with sickness when I had chemotherapy

I don't want doctors and nurses to think I'm complaining

I don't want doctors and nurses to stop my anticancer treatment

I'm worried about the effect on my body of yet more medication

I'll wait until I feel sick before I take the medication

I'm scared to take the antisickness pills in case they make me vomit

Nausea and vomiting must mean that the anticancer treatment is working

The treatment is so complicated - I can't remember which drugs to take on which days

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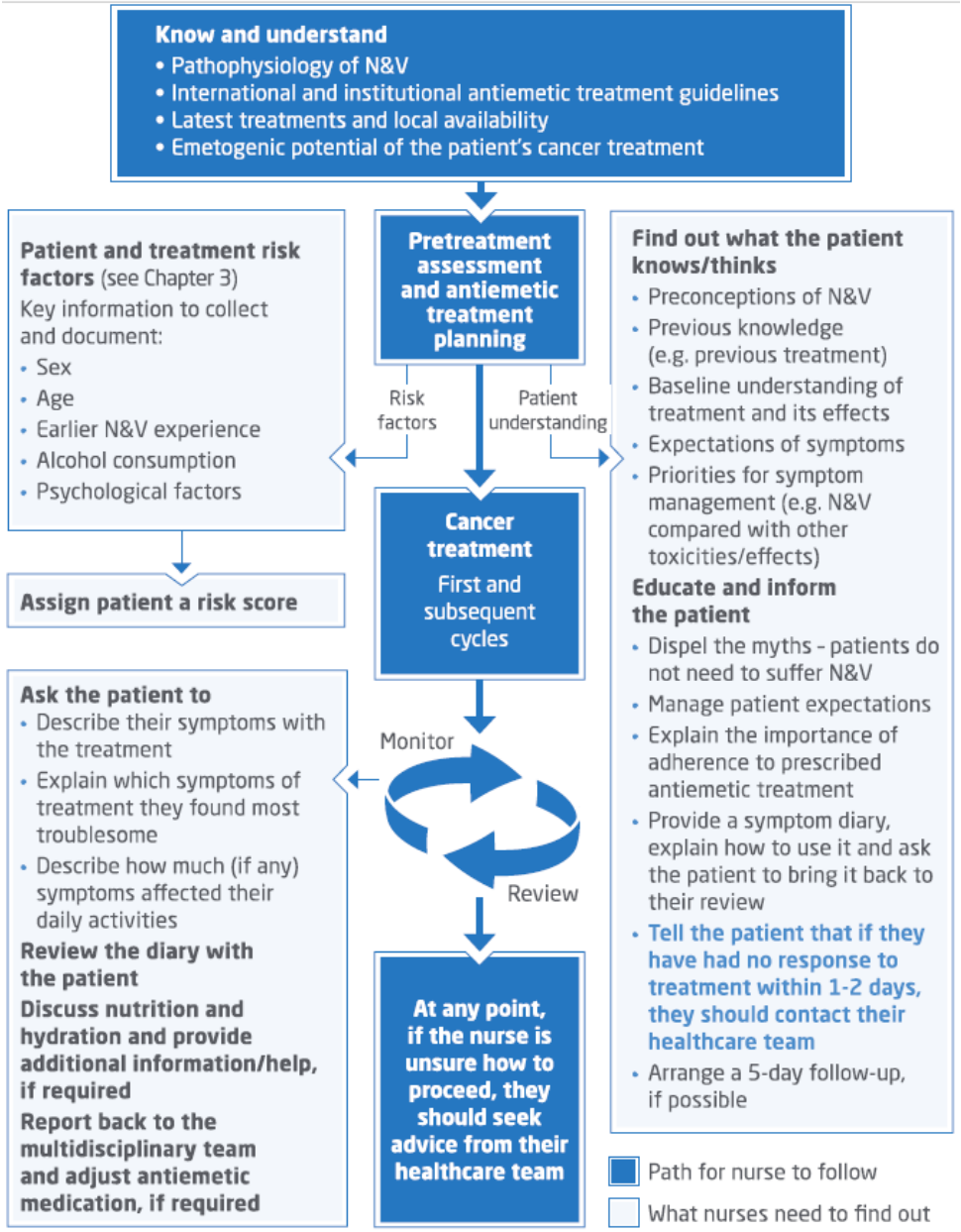
NURSE'S ROLE

- Nurses have a key role in assessing risk factors, planning treatment and monitoring the effectiveness of the intervention
- We can have a significant impact on reducing the chances of the patient developing N&V
- We should listen to, support and educate patients and caregivers on the management of symptoms
- We should apply our knowledge of international guidelines to help plan antiemetic programmes, prescribe and / or administer the appropriate treatment
- We are integral in assessing the risk and monitoring and reviewing the effectiveness of the antiemetic treatment



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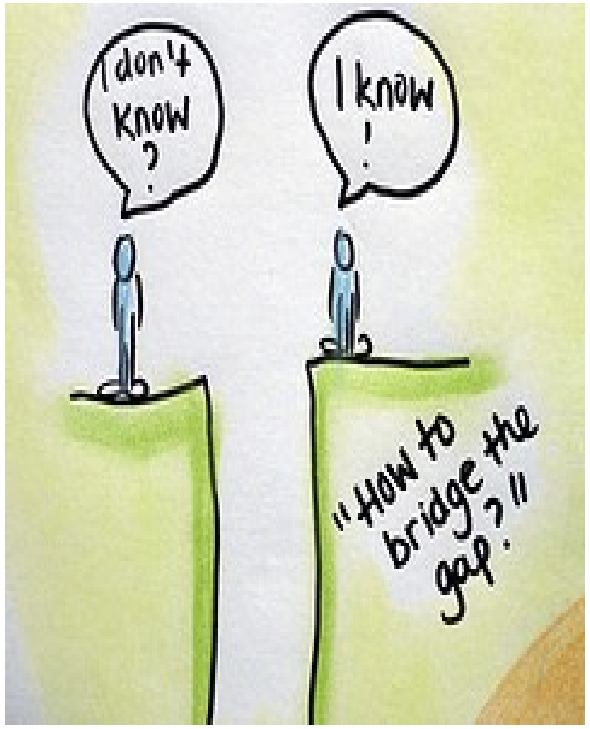
NOW WHAT?

Bridge the gap

- Use the guidelines to improve chemotherapy-induced nausea and vomiting (CINV) control
- Reduce pill burden wherever possible
- Share best practice to increase knowledge regarding the appropriate use of most recently approved agents for optimal CINV management for patients with cancer
- Stay up to date, help others update and share what you know to improve patient outcomes
- Influence decision making as part of a multi-disciplinary team
- Review the patient in a timely manner to assess the effectiveness of the intervention
- Encourage nurses to speak up!



SUMMARY: KEY TO SUCCESS

- Prevention is better than cure – manage risks from the 1st cycle
- Identify the drug emetogenicity potential
- Identify the individual patient risk factors
- Apply best practice guidelines (and local guidelines) when prescribing antiemetics to optimise care
- Check (and re-check) effectiveness of intervention
- Listen to the patient and their caregivers, as they often have 'out of hospital' experiences of CINV which we need to better understand
- Encourage patients to take control of their symptom management and engage them in key decision making processes
- Get a copy of the EONS guidance for nurses

With up-to-date knowledge about therapy strategies and considerations of patient and caregiver needs, nurses can have a very positive impact on the outcomes of CINV

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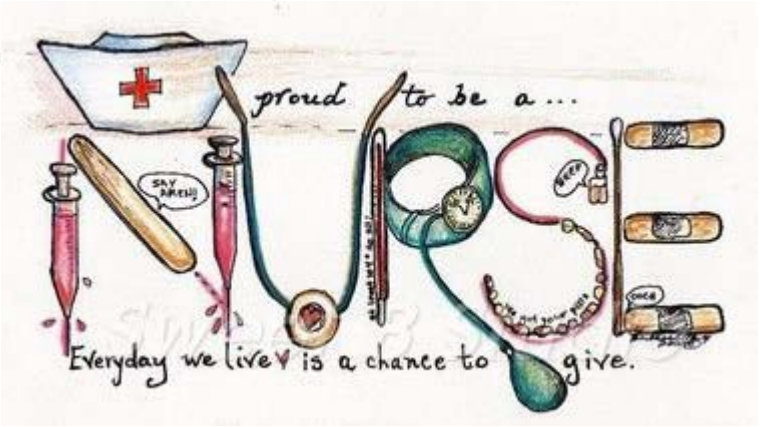
Thank you



"Nursing is an art,
and if it is to be made an art, it requires as exclusive a devotion,
as hard a preparation, as any painter's or sculptor's work;
for what is the having to do with dead canvas or cold marble,
compared with having to do with the living body-
the temple of God's spirit?
It is one of the Fine Arts;
I had almost said, the finest of the Fine Arts."
-Florence Nightingale
-1893