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# The Oncologist\*

Symptom Management and Supportive Care

Guidelines for Antiemetic Treatment of Chemotherapy-Induced Nausea and Vomiting: Past, Present, and Future Recommendations

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**Key Words:** Antiemetic therapy • ASCO antiemetic guidelines • MASCC antiemetic guidelines

NCCN practice antiemesis guidelines • 5-HT<sub>3</sub> serotonin-receptor antagonists • Neurokinin-1 receptor antagonists

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## LEARNING OBJECTIVES

After completing this course, the reader will be able to:

1. Explain the optimal antiemetic prophylaxis for patients receiving chemotherapy in regard to the emetogenic potential of the therapy.
2. Describe the difference between acute and delayed emesis.
3. Discuss the properties and optimal use of the different antiemetic drugs.

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**ABSTRACT**  
Clinicians should be aware that chemotherapy-induced nausea and vomiting (CINV) is still one of the most feared side effects of chemotherapy. With the correct use of antiemetics, CINV can be prevented in almost 70% up to 80% of patients. Treatment guidelines are used to assist the physician to integrate the latest clinical research into clinical practice. The large number of rapidly evolving clinical data has been summarized and incorporated into treatment recommendations by well-known and reliable institutions, including the Multi-

tational Association of Symptom Care in Cancer, the American Society of Clinical Oncology, and the National Comprehensive Cancer Network. Despite the availability of such guidelines, however, there is evidence that adherence to and implementation of evidence-based guidelines are less than optimal. This review focuses, in particular, on the similarities and differences of these three guidelines. Furthermore, open questions and trends in the field of antiemesis are discussed as well. *The Oncologist* 2007;12:1143–1150

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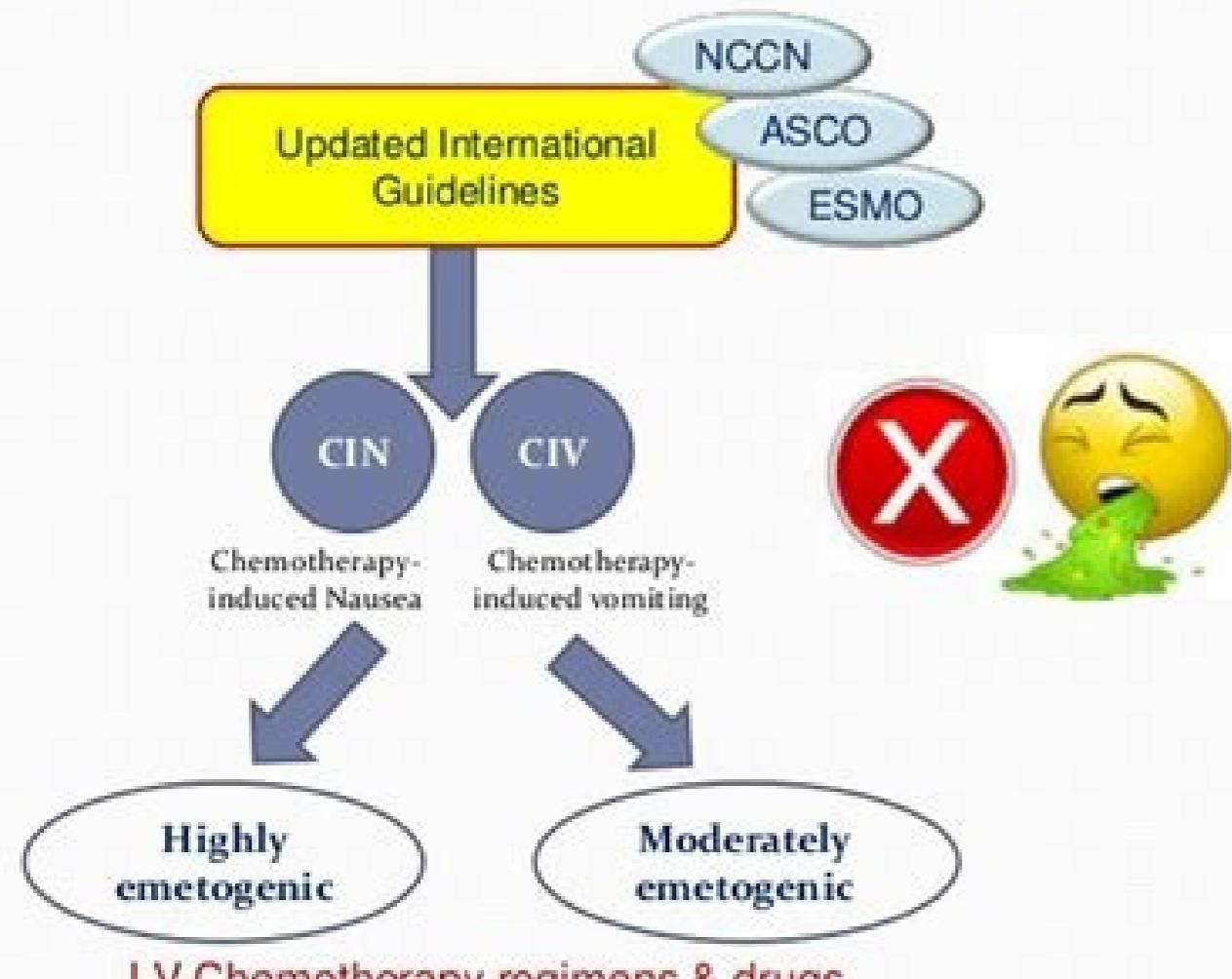
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First Author	Country	No. of Patients	Chemotherapy Schedule	Nausea (%)	Vomiting (%)
Chan <sup>13</sup>	Malaysia	99	PC: 36.7% of patients GEM: 16.7% of patients DOX: 13.3% of patients	83.3	78.9
Williams <sup>15</sup>	Philippines	63	ALK, ANT, WIN, other*	73.0	52.4
Chan <sup>12</sup>	Singapore	235	IV CIS on day 1 of a 7-day (40 mg/m <sup>2</sup> ) or 21-day (100 mg/m <sup>2</sup> ) cycle	73.7	24.7
			IV CIS 20 mg/m <sup>2</sup> /d and IV FU 1,000 mg/m <sup>2</sup> /d on days 1, 2, 3, and 4 of a 28-day cycle	48.9	28.9
Shih <sup>14</sup>	Singapore	91	IV DOX 60 mg/m <sup>2</sup> + CYC 600 mg/m <sup>2</sup> every 14 or 21 days for up to five cycles	25.3†	68.1†
Yap <sup>16</sup>	Singapore	710	IV DOX 60 mg/m <sup>2</sup> /d + CYC 600 mg/m <sup>2</sup> /d, or IV DOX 50 mg/m <sup>2</sup> /d + CYC 500 mg/m <sup>2</sup> /d + FU 500 mg/m <sup>2</sup> /d, or IV EPI 75–100 mg/m <sup>2</sup> /d + CYC 500 mg/m <sup>2</sup> /d + FU 500 mg/m <sup>2</sup> /d, or IV OXA 130 mg/m <sup>2</sup> /d + oral CAP 2,000 mg/m <sup>2</sup> /d, or IV CIS 20–100 mg/m <sup>2</sup> /d ± FU 1,000 mg/m <sup>2</sup> /d	55.0‡	15.0‡
Chan <sup>17</sup>	Singapore	156	CAP days 1–14 (median, 1,775 mg/m <sup>2</sup> /d) + OXA day 1 (median, 104 mg/m <sup>2</sup> ) every 21 days	35.3‡	6.4‡
				46.8‡	14.7‡



## Aim:



### I.V Chemotherapy regimens & drugs

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Full text of estimated impact for NHS. This is a phase 3 Comparing Netupitant / Palonosetron with Palonosetron in 1455 adults (for most women with breast cancer) subjected to anthracycline-based chemotherapy mon cyclophosphamide (AApro et al. in AApro et al. The study program also included a phase 2 study 2 At variable dose that compared 3 different doses of Netupitant / Palonosetron with Palonosetron in subjects subjected to highly emetogenic cisplatin-based chemotherapy (Hesketh et al. The primary outcome was the complete answer (defined as the absence of emesis and rescue therapy ) During the delayed phase of the cycle 1 (25a-120 hours after chemotherapy). Overall, the EPAR concluded that Netupitant / Palonosetron is well tolerated, with many adverse reactions probably associated with the basic pathology or cytotoxic treatments Associati. Full text of product overview. The recommended dose in the summary of product features is a Netupitant / Pa capsule LONOSETRON 300Á, mg / 500Á, micrograms to take about 1Á, now before the beginning of each chemotherapy cycle. Palonosetron is already available in oral and injectable formulations. Akenzeo Capsule contains 300 mg of Netupitant (a neurokinin receptor antagonist) and 500 micrograms of Palonosetron (a 5-HT3 receptor antagonist). Serious adverse events and deaths similarly reflect the patient's population and current treatment. (2014), a greater number of people reached the primary outcome of complete response during the overall phase (from 0 to 120 hours after chemotherapy) of the cycle 1 with Netupitant / Palonosetron 300Á, mg / 500Á, micrograms compared to Palonosetron 500Á, micrograms (89.6% [121/135] 36); p = 0.004). People can also vary in their predisposition to *>nausea and vomiting induced by drugs; most often affected people include women, age less than 50 years old, anxious people and adiug adiug and rep ICN inoizamrofini ellen ozillituiR eredev ,itunetnoz itseuq ittu o inucla errudorip arisedis eS .isotenit ad etteffa Copyright and permissions. The costs for the other 5 Á~ receptor antagonist treatment regimens range from approximately ÁE48 to ÁE103 per cycle of chemotherapy. There are limited data comparing NetUPitant / Palonosetron with other neurokinin receptor antagonists (ad Aprepitant) and 5 Á~ HT3 receptor antagonists (such as Ondansetron or Granisetron) provided in combination. Regulatory status: NetUPitant / Palonosetron Capsules (Akynzeo received a marketing authorisation from the United Kingdom in May 2015 and were launched in the United Kingdom in September 2015. Two neurokinin 1 receptor antagonists are available in the UK: aprepitant capsules and fosaprepitant intravenously (a proÁ~ drug of aprepitant) [see summaries of product characteristics]. NetUPITANT/Palonosetron (Akynzeo) is licensed in adults for the prevention of neurokinin 1 receptor antagonists. Acute and delayed nausea and vomiting associated with chemotherapy with highly emetogenic cisplatin-based cancer chemotherapy or moderately emetogenic cancer chemotherapy. Ad AApro et al. NetUPitan/Palonosetron capsules are provided as a single dose before each chemotherapy cycle, which may simplify the treatment regimen and be preferable to some people. NetUPitan / Palonosetron costs ÁE69.00 per cycle of chemotherapy. Full text of introduction and current guide. In line with other 5 Á~ HT3 receptor antagonists, the PSC also includes warnings and precautions on the risk of serotonin syndrome and QT prolongation. NetUPitan / Palonosetron capsules are provided as a single dose prior to each chemotherapy cycle. (2014), participants were randomised to receive Netupitant / Palonosetron 300 mg / microgram of 300 mg / 500 or Palonosetron 500 micrograms. (both given in len len ostamrevo emoC .)47.0, = P .99.78 la ottepsir %3.78 otalutisr otseuq rep ippurG 2 i art avitacifincs ethemacitats aznereffid anula are c' non atuca esaf al rep aivatutl .aiapretoimehc id olcic ompr led onroig li otad jenosatemed no cases of severe constipation and complications due to constipation were seen during the clinical trial programme and information on this has been included in the SPC. Full text of context. Full text of evidence review. In both AApro et al. Chemotherapy regimens vary in the extent to which they cause nausea and vomiting, usually classed as having a minimal, low, moderate or high degree of emetogenicity. In Hesketh et al. (2014) and Gralla et al. The EPAR for netupitant/palonosetron capsules states that a total of 1538A Apeole received netupitant/palonosetron at the licensed dose during the clinical study programme, with 1169A Apeole with cancer having at least 1A Adose while participating in a phase 2 or 3 study and 317A Apeole having 6 or more cycles of treatment. In the case of permitted digital reproduction, please credit the National Cancer Institute as the source and limit to the original NCI product using the original product's title; e.g., cAAA Nausea and Vomiting Related to Cancer Treatment (PDQ®) A cAAA Health Professional Version was originally published by the National Cancer Institute. cAAA Netupitant/palonosetron shows statistically significant benefit compared with palonosetron alone (both in combination with dexamethasone) in people receiving emetogenic chemotherapy, mainly in the prevention of delayed nausea and vomiting. This evidence summary discusses the best available evidence on the safety and efficacy of netupitant/palonosetron. Two other 5cÁAAHT3 receptor antagonists are also available in the UK: ondansetron (available in oral, injectable and rectal formulations) and granisetron (available in oral, injectable and transdermal formulations). (2014) netupitant/palonosetron was compared with palonosetron. More participants in the netupitant/palonosetron group had no significant nausea (defined as a score of less than 25Á Ámm on a visual analogue scale from 0Á Ámm [no nausea] to 100Á Ámm [nausea as bad as it].la te htsekseH dna )4102( smeniger yparehtomehc desab edimahpsohpolcyc sulp enlycicartha ro cingetome ylhgh gniviecer elpoep ni gntimov dna aseuan fo noitneverp eft ro tsinogatna rotpecer 3THAAcE5 a htob gnidulcn smeniger dneumocer seniledig citemetna JOMSE(ygolochN lacideM fo yteicS naeporuE eht dna )CCSAM(recaC ni erac evitropuS rof noitaicossA lanotanitluM eht gnidulcn senilediG .la te allarG (yparehtomehc cinegoteme ylhgh ro yletredom gnivah elpoep 803 ni nortesonolap/tnatipten fo ytefas eht dessessa tcr C 3 esaph a dna )4102 .)4102=p ,%3.17 htw derapmoc %9.67 puor nortesonolap eht htw derapmoc 1 elcyt fo esaph deyed eht gnirud )'eb*

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