XVIII CURSO

PARA RESIDENTES

EN CONTROL DE SÍNTOMAS Y TERAPIAS DE SOPORTE

VALENCIA

del 29 de febrero
al 1 de marzo de 2024

HOTEL MELIÁ VALENCIA

@_seom #mirSEOM24

Emesis

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Disclosure Information

- Employment: Servicio Madrileño de Salud (SERMAS)
- Consultant or Advisory Role:Astra Zeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, Gilead, GSK, Janssen, Lilly, Merck Sharp and Dohme, Novartis, Pfizer, Hoffmann- La Roche, Sanofi, Takeda
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- Grant support: Astra Zeneca, Bristol Myers Squibb, Merck Sharp and Dohme, and Hoffmann- La Roche

EMESIS

- Emesis inducida por el tratamiento oncológico
- Clasificación
- Un gran problema oncológico
- Aspectos fisiopatológicos
- Aspectos clínicos
- ¿cómo abordar el tratamiento antiemético?
- Tratamiento antiemético disponible
- Recomendaciones de las guías clínicas
- Adherencia a las guías clínicas
- Abordaje antiemético en los nuevos tratamientos

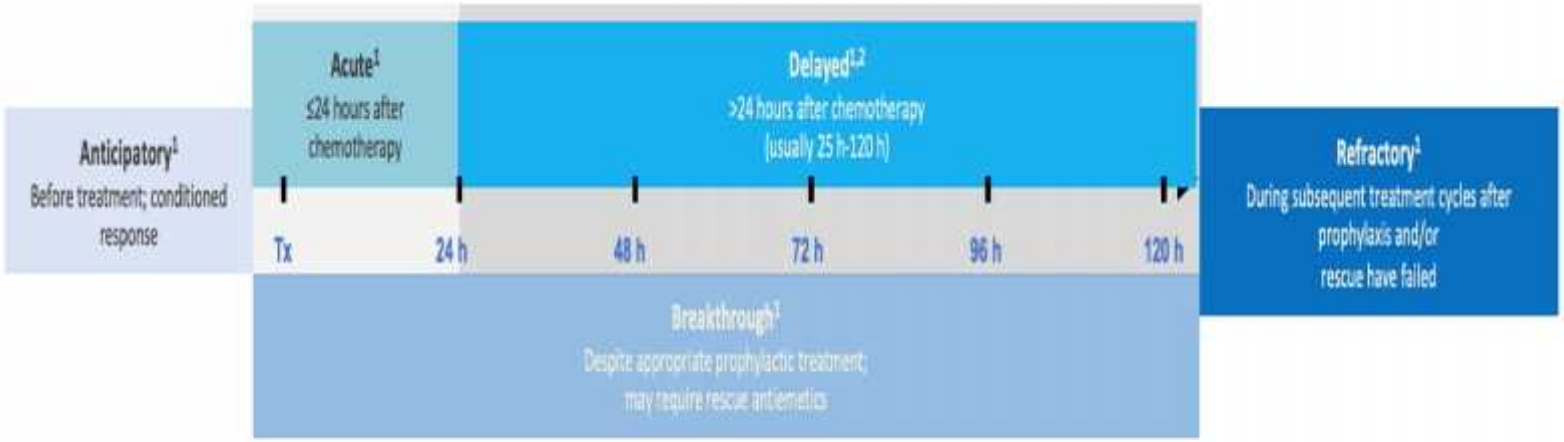
Emesis inducida por el tratamiento oncológico

- **Náuseas y vómitos producidos por**:
  - Quimioterapia
    - **NaVIQ** (náuseas y vómitos inducidos por quimioterapia)
    - **CINV** (chemotherapy induced nausea and vomiting)
  - Otras terapias: TKI,
  - Radioterapia
    - Radiación zona esófago-gástrica y abdominal
  - Cirugías previas (área ORL, abdominal)

- **Pueden asociarse a otros problemas**
  - Anosmia, cambio de sabor de alimentos

- **Precisan de Tratamiento** → **Prevenir** su aparición (riesgo alto de desarrollo)

Clasificación de las NaVIQ

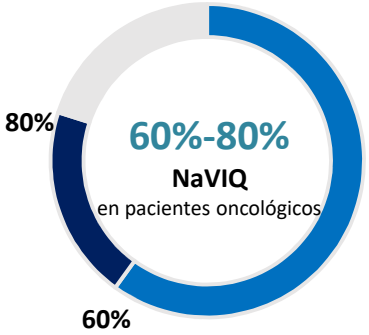


*NCCN Guidelines should be consulted for current recommendations that address each CINV classification.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis V.2.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed August 23, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. 2. Navari RM, Aapro M. N Engl J Med. 2016;374(14):1356-1367.

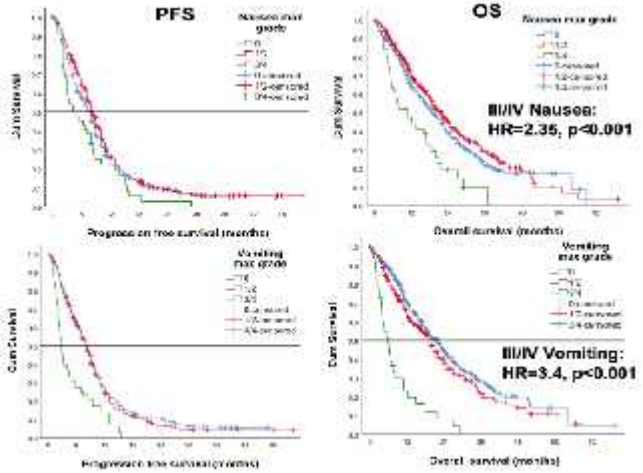
Un gran problema oncológico

La incidencia de NaVIQ es ELEVADA



Se asocial con:

- Interrupción del tratamiento
- ↓ calidad de vida
- Deshidradración
- Desequlibrio electrolítico
- ↓ Reducción de eficacia
- ↑ Costes



1. Natale JI Am J Manag Care. 2018;24:S391-S397
2. Wooden H.et

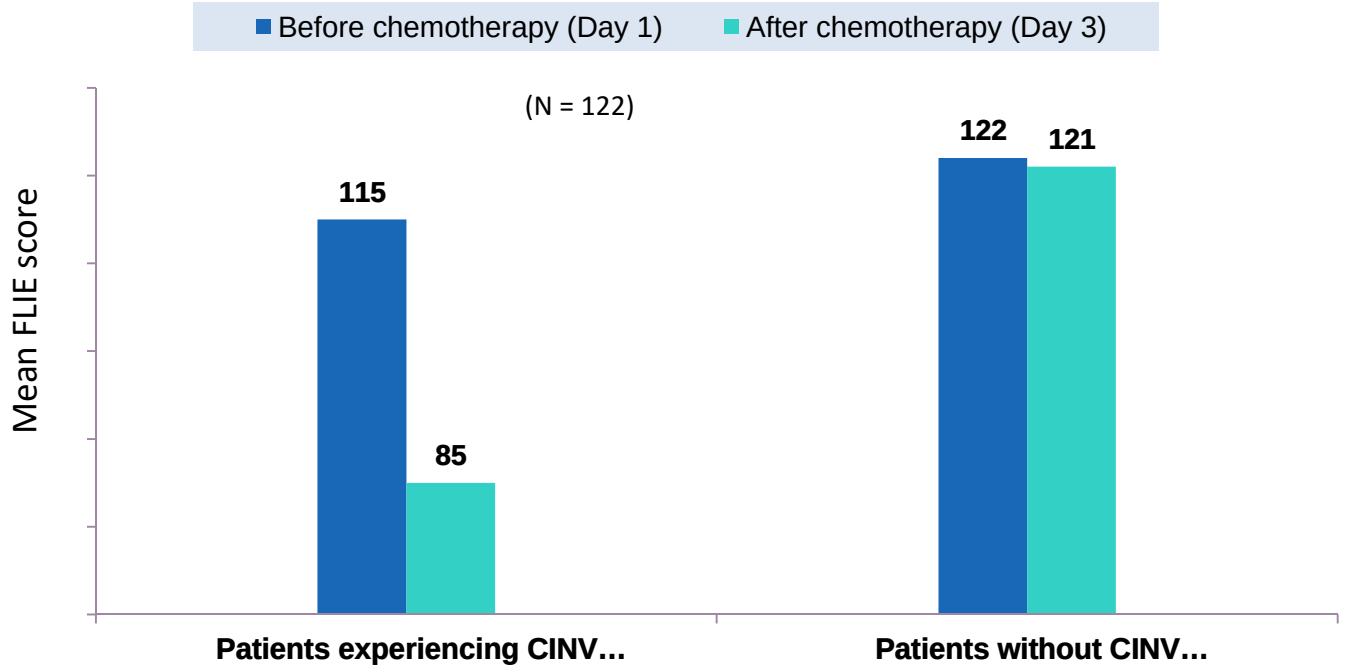
SEOM Sociedad Española de Oncología Médica
Sección SEOM Cuidados Continuos
Fundación SEOM

Potencial emetógeno de la quimioterapia

Frequency of emesis (%)	Antiemesis guidelines
> 90	High (HEC)
30-90	Moderate (MEC)
10-30	Low
< 10	Minimal

1. Roila F, et al. Ann Oncol. 2016;27 Suppl 5:v119-v133. https://www.mascc.org/assets/Guidelines-Tools/mascc_antiemetic_guidelines_english_v.1.5SEPT29.2019.pdf. Accessed July 20202. NCCN Clinical Practice Guidelines in Oncology: Antiemesis Version 1.2024. Available from: www.nccn.org. Accessed January 2024
3. Hesketh PJ, et al. 2020 Aug 20;38(24):2782-2797. Available from: www.asco.org/guidelines/ Accessed September 2020
4. Jordan K, et al. Support Care Cancer. 2016;24:4617-25.
5. J. Herrstedt et al, https://doi.org/10.1016/j.esmoop.2023.102195

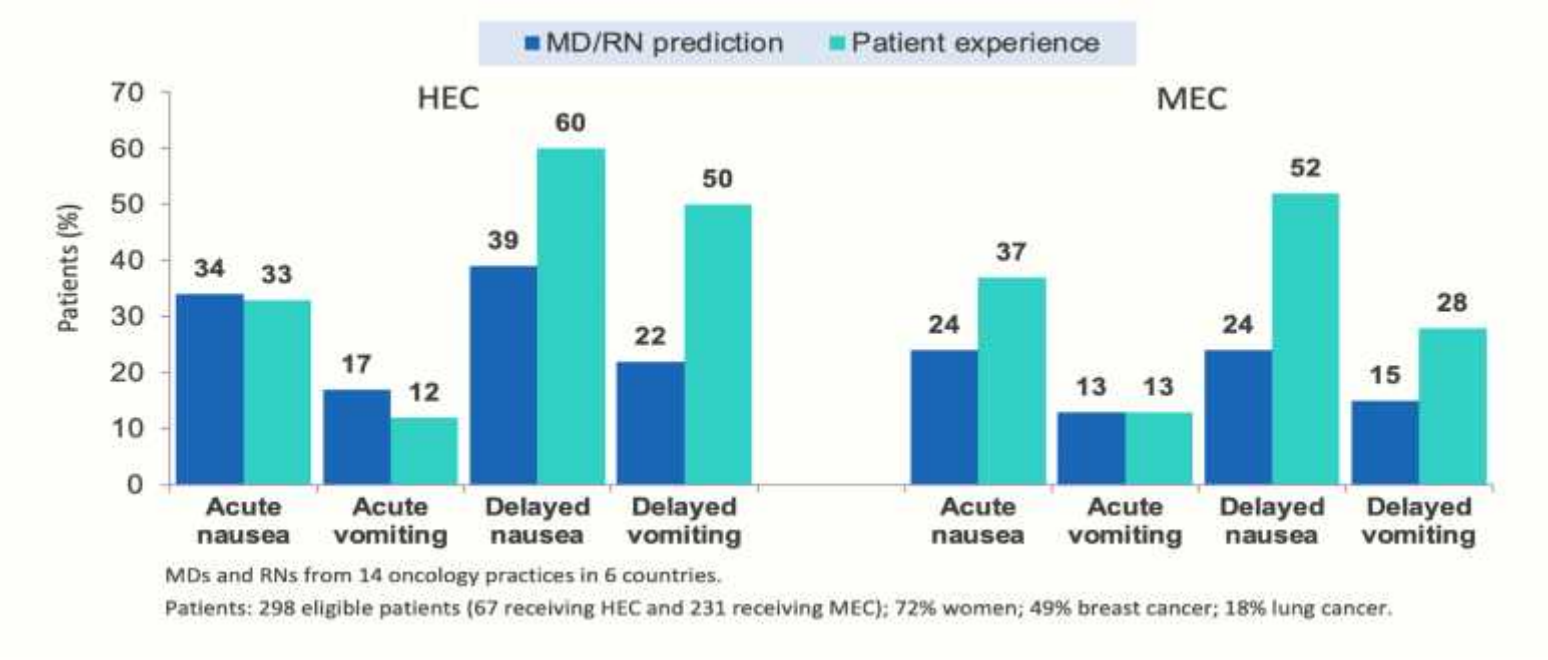
NaVIQ impactan negativamente en la calidad de vida



FLIE, Functional Living Index-Emesis; QoL, quality of life.

- Adapted from: Lindley CM, et al. Qual Life Res. 1992;1:331-40.

Percepción frente a realidad



MDs and RNs from 14 oncology practices in 6 countries.
Patients: 298 eligible patients (67 receiving HEC and 231 receiving MEC); 72% women; 49% breast cancer; 18% lung cancer.

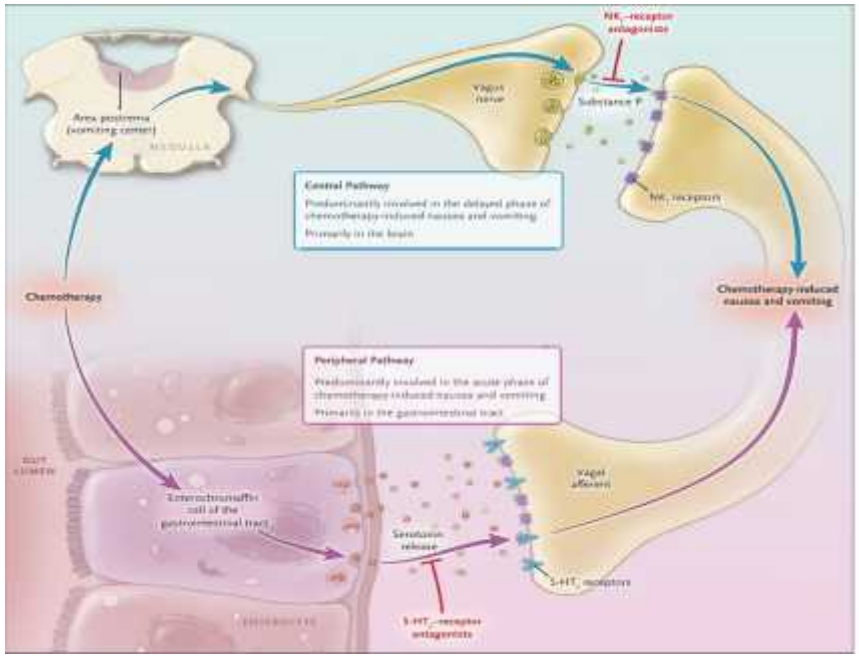
Grunberg SM, et al. Cancer. 2004;100:2261-8

HEC, highly emetogenic chemotherapy; MD, medical doctor; MEC, moderately emetogenic chemotherapy; RN, registered nurse.

¿Cómo debe diseñarse la profiláxis antiemética?

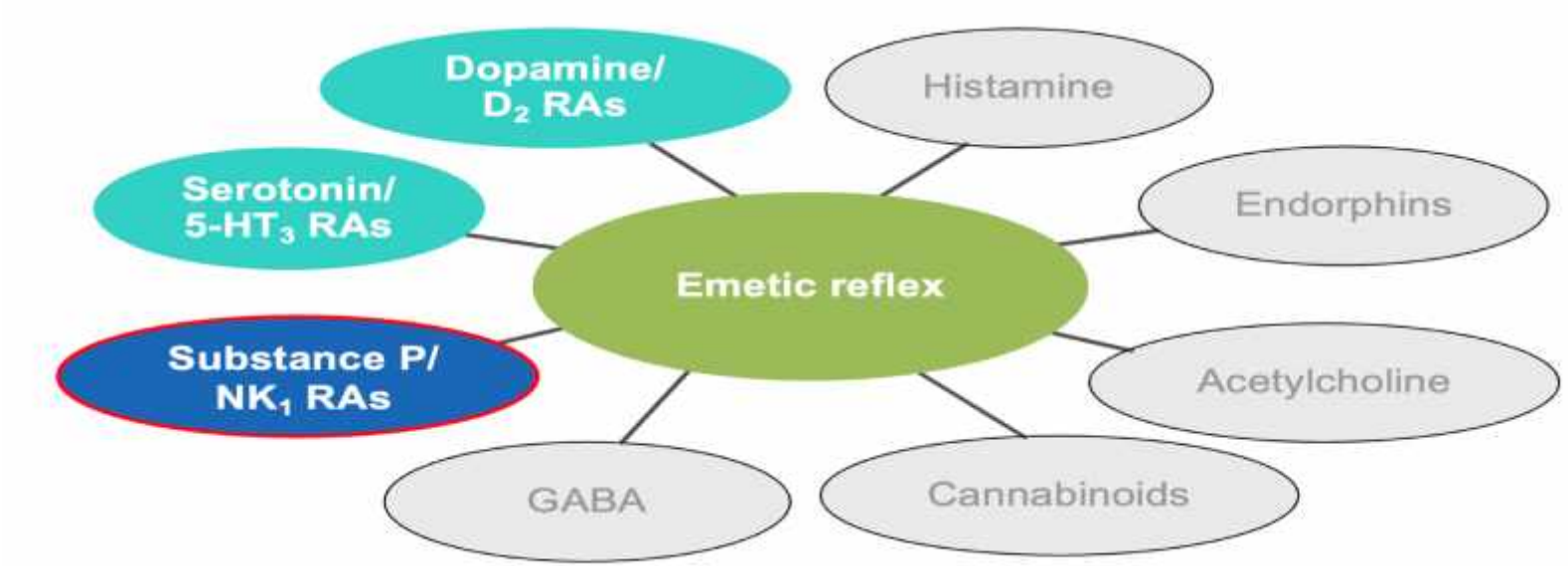
- Conocer la etiopatogenia de la emesis inducida en función de la quimioterapia a administrar
- Conocer las combinaciones de quimioterapia a utiliizar
- Conocer las condiciones individuales del paciente
- Conocer el objetivo del plan de tratamiento (curativo/paliativo)

Aspectos fisiopatológicos de las CINV



Navri R and Aapro M, N Engl J Med. 2016 Apr 7;374(14):1356-67. doi: 10.1056/NEJMra1515442.

Vías de antiemesis y neurotransmisores dianas de control antiemético



- 5-HT_3 RA, 5-hydroxytryptamine type 3 receptor antagonist; D2, dopamine 2; GABA, gamma-aminobutyric acid; NK_1 RA, neurokinin-1 receptor antagonist.

Adapted from: Navari RM. Drugs. 2013;73:249-62.

Frame DG. J Support Oncol. 2010;8(2 Suppl 1):5-9.

Lorusso V, et al. Future Oncol. 2014. https://doi.org/10.2217/fon.14.260.

Potencial emetógeno de los antineoplásicos

EMETOGENIC POTENTIAL OF INTRAVENOUS ANTINEOPLASTIC AGENTS[t]

LEVEL	AGENT	
High emetic risk (>90 % frequency of emesis)[q,r]	• AC combination defined as either doxorubicin or epirubicin with cyclophosphamide[q] • Carmustine >250 mg/m^2 • Cisplatin ≥50 mg/m^2 • Cyclophosphamide >1,500 mg/m^2 • Dacarbazine	• Doxorubicin >60 mg/m^2 • Epirubicin >90 mg/m^2 • Ifosfamide ≥10 g/m^2 • Mechlorethamine • Streptozocin
Moderate emetic risk (30% - 90% frequency of emesis)[q,s]	• Aldesleukin > 12-15 million international units/m^2 • Amifostine > 300 mg/m^2 • Arsenic trioxide • Azacitidine • Bendamustine • Busulfan • Carboplatin[s] • Carmustine[s] ≤250 mg/m^2 • Cisplatin[s] <50 mg/m^2 • Clofarabine • Cyclophosphamide ≤1500 mg/m^2 • Cytarabine >200 mg/m^2 • Dactinomycin[s] • Daunorubicin[s] • Doxorubicin[s] ≤60 mg/m^2	• Epirubicin[s] ≤90 mg/m^2 • Idarubicin • Ifosfamide[s] <10 g/m^2 • Interferon alfa ≥10 million international units/m^2 • Irinotecan[s] • Melphalan • Methotrexate[s] ≥ 250 mg/m^2 • Oxaliplatin • Temozolomide

- Combinación de agentes
- Días de tratamiento
- Tratamientos combinados

Categorías de riesgo emetógeno basadas en los antineoplásicos

ALTA	**Riesgo en casi todos los pacientes (>90%)**
MODERADA	**Riesgo en 30-90% de los pacientes**
BAJA	**Riesgo en 10-30% de los pacientes**
MÍNIMA	**Riesgo en menos del 10%**

1. NCCN Clinical Practice Guidelines in Oncology, Antiemesis Version 1.2017. Available at:www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf.
2. MASCC/ESMO Antiemetic Guideline 2016. Available at: www.mascc.org/antiemetic-guidelines.
3. Basch E et al. J Clin Oncol. 2011; 29:4189–4198.
4. Hesketh PJ et al. J Clin Oncol. 2016 Feb 1;34(4):381-6. Available at:http://www.instituteforquality.org/antiemetics-asco-clinical-practice-guideline-update

Factores de riesgo individuales

- Sexo femenino
- Edad joven
- Ausencia de consumo de alcohol

Factores adicionales

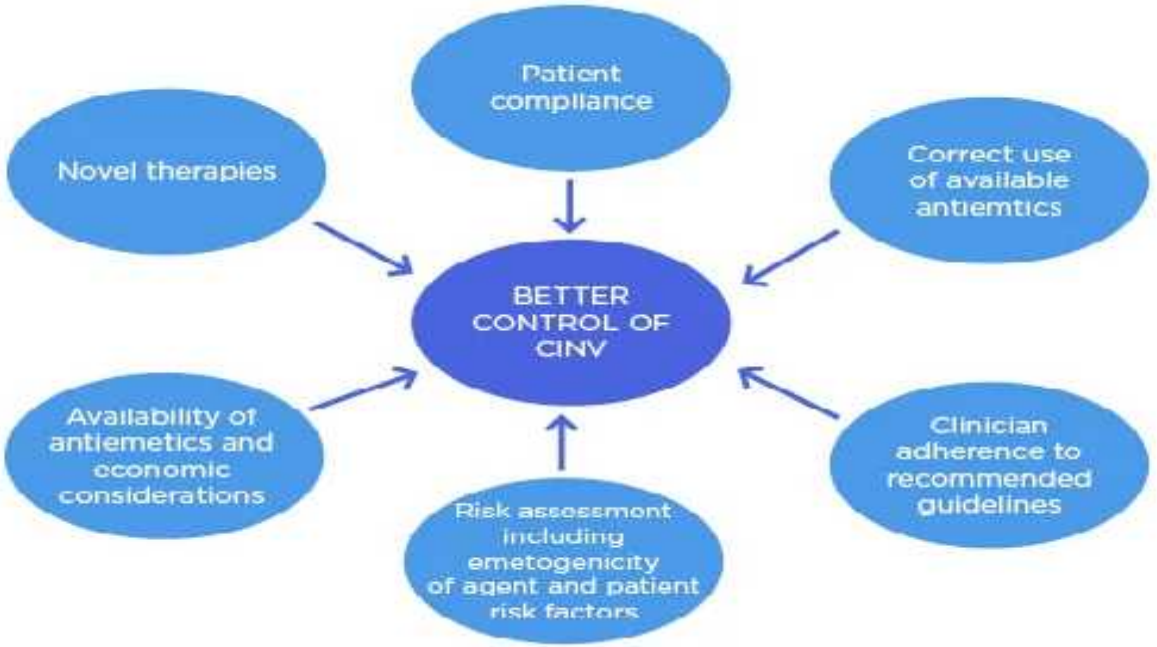
- Ansiedad
- Hiperemesis gravídica
- Historia de cinetosis
- Historia de NaVIQ previa

Deanitsaris et al. 2017 Ann Oncol. 2017
Gregory RE, et al. Drugs. 1998;55:173-89.
Jordan K, et al. Oncologist. 2007;12:1143-50

Factores de riesgo individuales

1. NCCN clinical practice guidelines in oncology, Antiemesis V1.2017.Available at: http://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf.
2. Young A et al. Ecancermedicalscience 2013;7:296.
3. Vidall C et al. Ecancermedicalscience 2011;5:211.
4. Petrella T et al. 2009. J Support Oncol 2009;7:W9.

¿Cómo podemos mejorar el control de las CINV?



M. Aapro, R. Tarricone. EMJ Oncol. 2020;8[Suppl 1]:2-13.

Score de riesgo

ESMO

Annals of Oncology 28: 1,251–1,257, 2017
doi:10.1093/annonc/mdx100
Published online 7 April 2017

ORIGINAL ARTICLE

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]

[1]The Ottawa Hospital Regional Cancer Centre, Ottawa, Canada; [2]Hong Kong Polytechnic University, Hong Kong; [3]UC San Diego Moores Cancer Center, La Jolla; [4]The West Clinic, Memphis, USA; [5]Institut de Cancérologie Gustave Roussy, Villejuif, France; [6]Department of Medicine V, University of Heidelberg, Heidelberg, Germany; [7]Cancer Research Centre, University of Warwick, Coventry, UK; [8]Cancer Center Clinique de Genolier, Genolier, Switzerland

*Correspondence to: Dr George Dranitsaris, The Ottawa Hospital Regional Cancer Centre, 501 Smyth Road, Ottawa, ON, Canada K1H 8L6. Tel: +1-1-6-161-2780; Fax: +1-416-461-4735; E-mail: george.dranitsaris@gmail.com

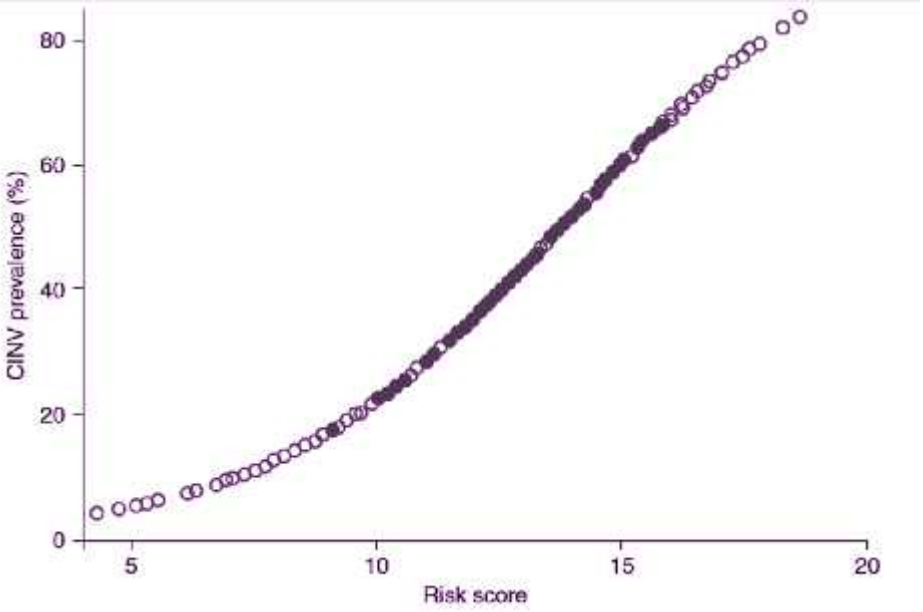
1. Dranitsaris et al Ann Oncol 2017 Jun 1;28(6):1260-1267. doi: 10.1093/annonc/mdx100

Score de riesgo

Table 3. Risk scoring algorithm for ≥grade 2 CINV in cancer patients receiving chemotherapy

Predictive factor	Before a cycle of chemotherapy
Baseline score	10
Impact of patient risk factors	
Patient < age	+*
Patient expects to have CINV	+*
Patient slept <7 h the night before chemotherapy	+*
Patient has a history of morning sickness	+*
Patient is about to receive platinum or anthracycline chemotherapy	+2
Patient on-prescription antiemetics are used at home in the prior cycle	+3
Patient had nausea or vomiting in the prior cycle	+5
About to receive the 2nd cycle	−5
About to receive ≥ 3rd cycle	−6
Total composite risk score[a]	?

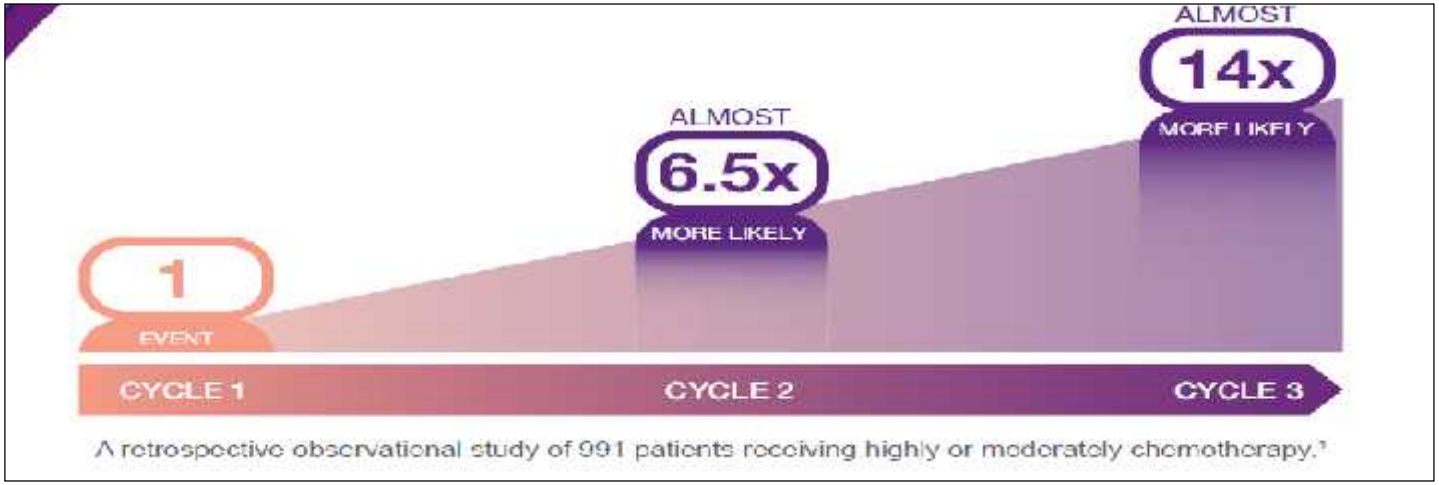
[a]The probability of developing ≥grade 2 CINV during that cycle of therapy can then be estimated from Figure 3.



1. Dranitsaris et al Ann Oncol 2017 Jun 1;28(6):1260-1267. doi: 10.1093/annonc/mdx100

La importancia del control antiemético en el primer ciclo de Quimioterapia

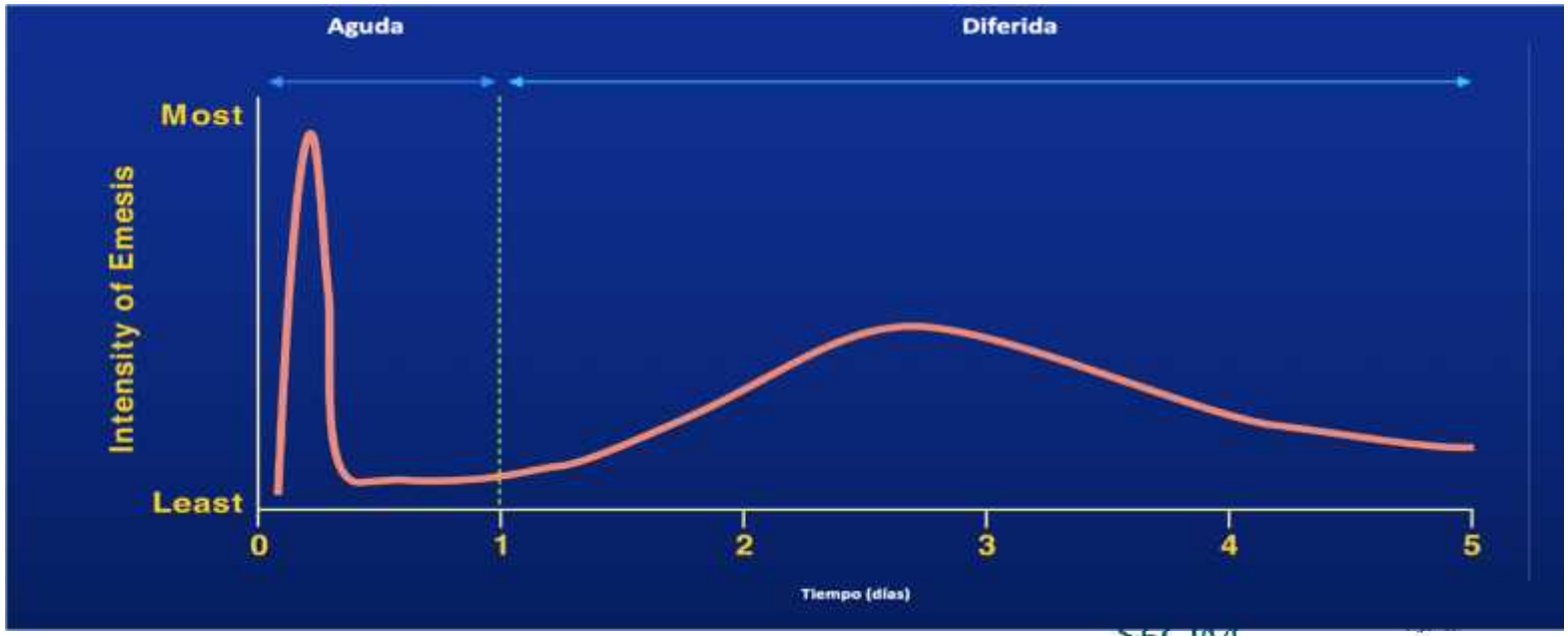
- La existencia de NaVIQ descontroladas en ciclos previos es FUNDAMENTAL



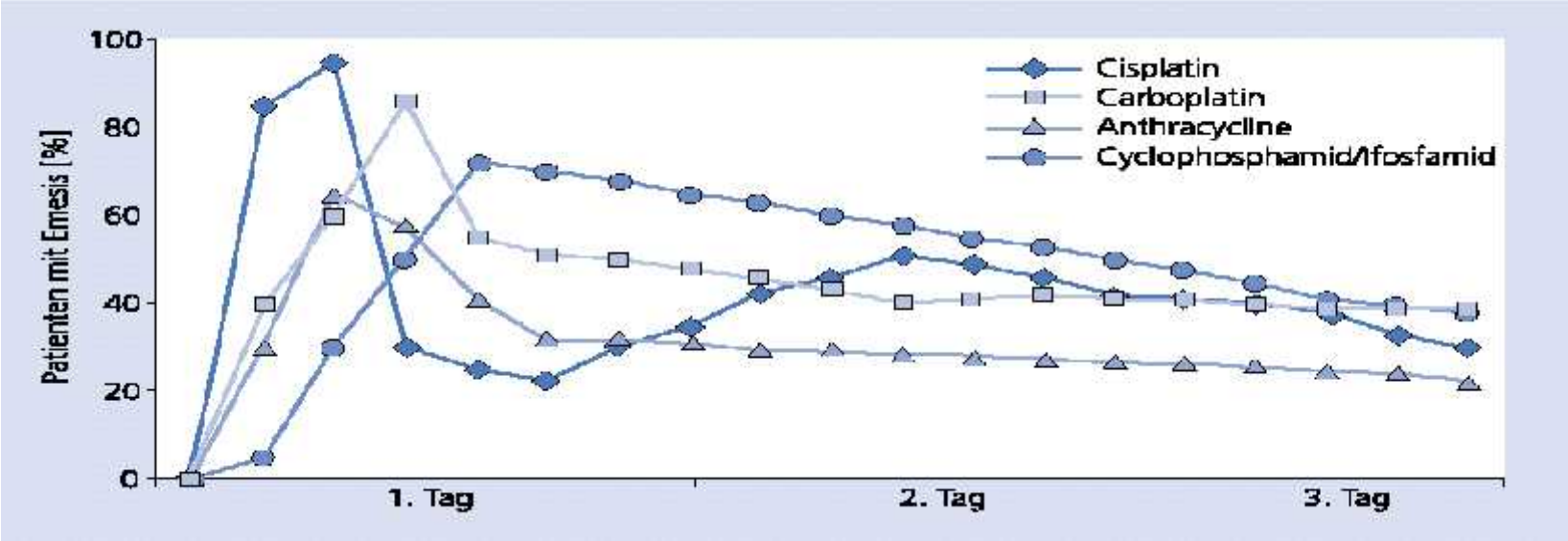
- **Pacientes con alto riesgo debe tratarse desde el principio**

Molassiotis A, et al. J Pain Symptom Manage. 2016;51:987-93.

Patrón bifásico de vómitos inducidos por cisplatino

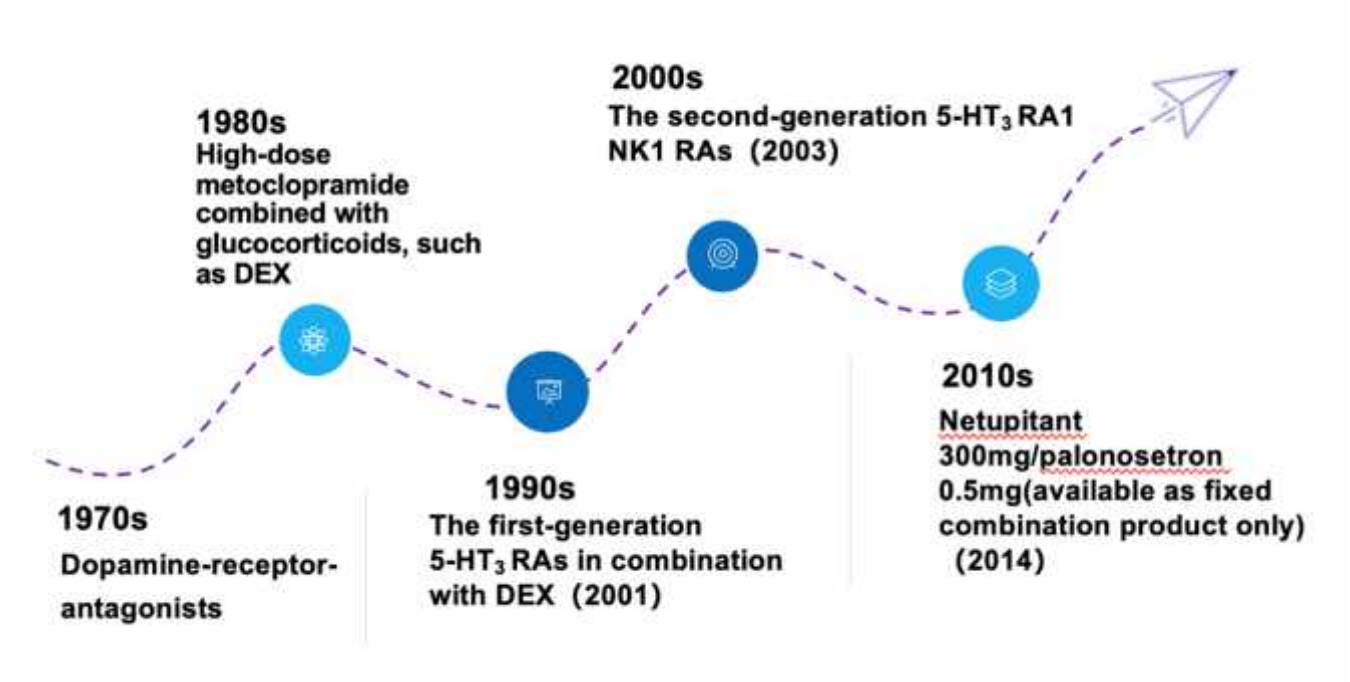


Curvas de emesis por diferentes quimioterápicos




Inhibidores Receptores 5-HT3 de serotonina
Inhibidores Receptores NK-1
Elevación de Serotonina
Elevación de Sustancia P
Día 1
Día 2
Dia 3
Dia 4
Día 5

Desarrollo de los antieméticos



1. Navari RM and Aapro M. N Engl J Med 2016; 374:1356-67.

5-HT$_3$ RA: serotonin 3 receptor antagonist
NK1 RA: neurokinin 1 receptor antagonist
DEX: Dexamethasone

5-HT_3 RAs: vida media y afinidad de unión

5-HT_3 RAs	Binding affinity pK_i (nM)	Half-life (h)
Palonosetron[1]	**10.45**	**40.0**
Granisetron[2]	**8.91**	**9.0**
Ondansetron[1]	**8.39**	**5.5**
Ramosetron[3]	**8.50-9.00**	**4.3-9.0**

[a] pIC_{50}.

5-HT_3 RA, 5-hydroxytryptamine type 3 receptor antagonist; h, hour; IC_{50}, half-maximal inhibitory concentration.

1. Wong EHF, et al. Br J Pharmacol. 1995;114:851-9. 2. Eisenburg P, et al. Ann Oncol. 2004;15:330-7. 3. Muchatuta NA, Paech MJ. Ther Clin Risk Manag. 2009;5:21-34

NK_1 RAs y NK_1 receptores cerebrales en humanos

NK_1 RA	Dose (mg)	n (subjects)	Time (h)	Occupancy (striatum), %
Netupitant[1]	300	2	120	75
Aprepitant[2]	165	3	120	37-76
Fosaprepitant[3]	150	3	120	41-75
Rolapitant[4,5]	180	?	120	73

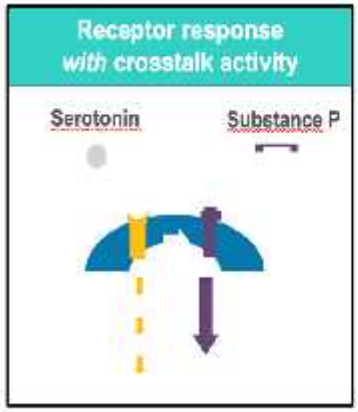
Rolapitant PO has been approved in US and EU but it is no longer authorized in EU

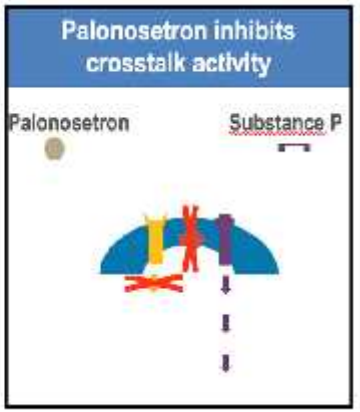
1. Bernareggi A, Spinelli T. Support Care Cancer. 2015;23 Suppl 1:abstract 11-30-P 2. Van Laere K, et al. Clin Pharmacol Ther. 2012;92:243-50. 3. Ivemend ® SPC. Available from: www.ema.europa.eu.

h, hour; IV, intravenous; NK1 RA, neurokinin 1 receptor antagonist

Crosstalk entre receptores 5-HT_3 y NK_1

Receptor crosstalk is defined as activation of one receptor by its ligand affecting cellular responses to another receptor system(s)



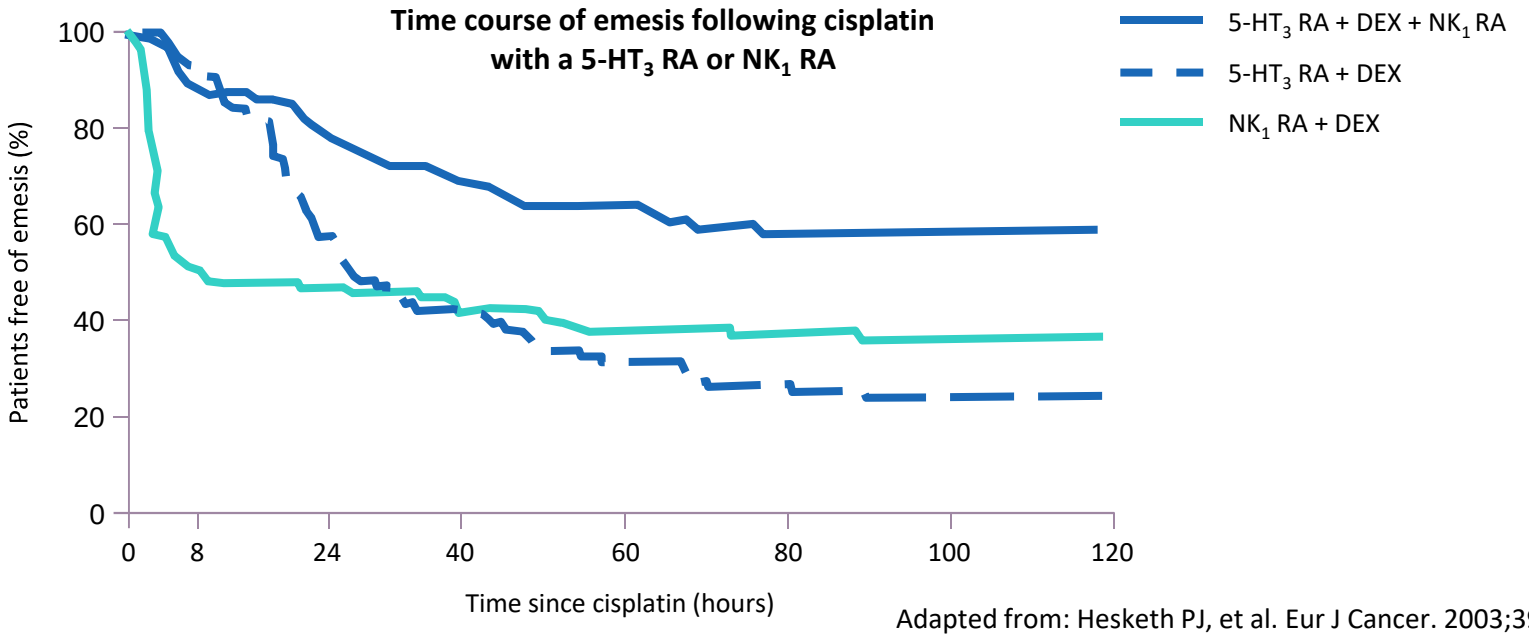


- Crosstalk between NK_1 and 5-HT_3 receptors has been demonstrated even though the mechanism is not completely understood

- 5-HT_3, 5-hydroxytryptamine type 3; NK_1, neurokinin-1.

Adapted from: Rojas C, et al. J Pharmacol Exp Ther. 2010;335:362-8.

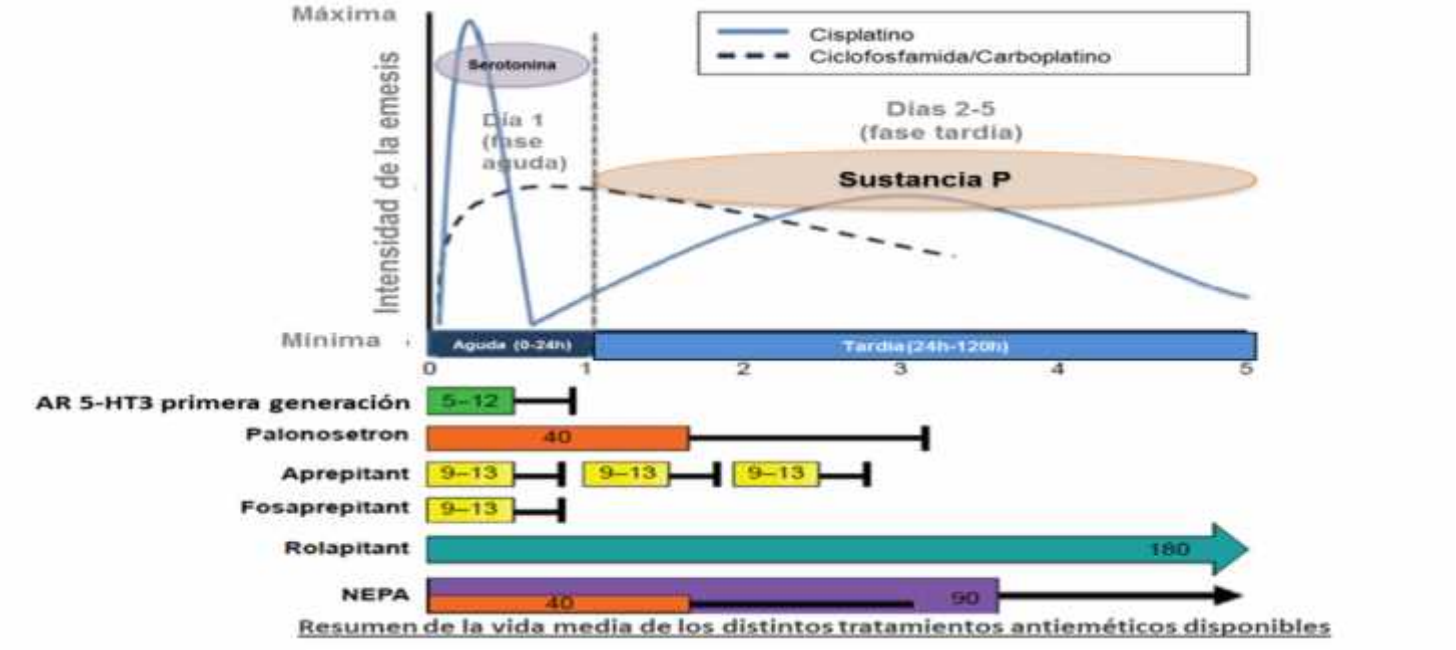
Combo anti NK_1 y anti 5-HT_3 controla las NaVIQ



Adapted from: Hesketh PJ, et al. Eur J Cancer. 2003;39:1074-80

5-HT_3 RA, 5-hydroxytryptamine type 3; CINV, chemotherapy-induced nausea and vomiting; DEX, dexamethasone; NK_1 RA, neurokinin-1 receptor antagonist.

Secuencia temporal de la emesis y duración de efectos de los fármacos



Resumen de la vida media de los distintos tratamientos antieméticos disponibles

Adaptado de Lorusso V, Karthaus M, Aapro M. Review of oral fixed-dose combination netupitant and palonosetron (NEPA) for the treatment of chemotherapy-induced nausea and vomiting. Future Oncol. 2015;11(4):565–577.

XVIII CURSO SEOM PARA RESIDENTES
EN CONTROL DE SÍNTOMAS Y TERAPIAS DE SOPORTE

Antiemesis guidelines

MASCC
Multinational Association of Supportive Care in Cancer
WWW.MASCC.ORG

NCCN National Comprehensive Cancer Network®

ASCO
American Society of Clinical Oncology

ESMO
GOOD SCIENCE
BETTER MEDICINE
BEST PRACTICE
European Society for Medical Oncology

SEOM Sociedad Española de Oncología Médica

Organiza SEOM Cuidados Continuos

Fundación SEOM

Potencial emetógeno de la quimioterapia

Frequency of emesis (%)	Antiemesis guidelines
> 90	High (HEC)
30-90	Moderate (MEC)
10-30	Low
< 10	Minimal

- The moderate class includes a broad range of emetogenic agents
- AC has been classified as HEC in ASCO, NCCN, and MASCC/ESMO guidelines[1-3]
- Carboplatin is considered as "high MEC" by ASCO (only when AUC ≥ 4) and MASCC/ESMO[5] (AUC>5), and reclassified as HEC (when AUC ≥ 4) by NCCN: the use of NK_1 RAs is recommended in all cases.[1-3] Studies had shown the benefit of the NK_1 RA-containing regimens in patients receiving carboplatin[4]
- NCCN recommends the inclusion of NK_1 RAs in MEC for selected patients with additional risk factors or previous treatment failure with a steroid plus 5-HT_3 RA alone[2]

- 5-HT_3 RA, 5-hydroxytryptamine type 3 receptor antagonist; AC, anthracycline, cyclophosphamide;
ASCO, American Society of Clinical Oncology; AUC, area under the curve; ESMO, European Society for Medical Oncology; HEC, highly emetogenic chemotherapy; MASCC, Multinational Association of Supportive Care in Cancer; MEC, moderately emetogenic chemotherapy; NCCN, National Comprehensive Cancer Network; NK_1 RA, neurokinin-1 receptor antagonist.

1. Roila F, et al. Ann Oncol. 2016;27 Suppl 5:v119-v133. https://www.mascc.org/assets/Guidelines-Tools/mascc_antiemetic_guidelines_english_v.1.5SEPT29.2019.pdf. Accessed July 2020
2. NCCN Clinical Practice Guidelines in Oncology (Antiemesis) Version 1.2024. Available from: www.nccn.org. Accessed January 2024
3. Hesketh PJ, et al. 2020 Aug 20;38(24):2782-2797. Available from: www.asco.org/guidelines/ Accessed September 2020
4. Jordan K, et al. Support Care Cancer. 2016;24:4617-25
5. J. Herrstedt et al, https://doi.org/10.1016/j.esmoop.2023.102195

Náuseas y Vómitos agudos

NK_1 RA recommendations for acute nausea and vomiting

	ASCO	MASCC/ESMO	NCCN
HEC including Cispatin	√	√	√
AC/EC	√	√	√
Carboplatin[a]	√	√	√
ADC (such as Trastuzumab Deruxtecan and Sacituzumab Govitecan)[b]		√	√
Oxaliplatin		√	√
MEC			√[c]

- NK_1 RA is a recommended option by ASCO, MASCC/ESMO, and NCCN for HEC and AC-based regimens[1–3]
- NK_1 RA is a recommended option by ASCO, MASCC/ESMO, and NCCN for carboplatin-based chemotherapy[1–3]
- NK_1 RA is a suggested option by MASCC/ESMO and NCCN for Trastuzumab Deruxtecan and Sacituzumab Govitecan treated patients
- NK_1 RA is a recommended option by NCCN in MEC for selected patients with additional risk factors or previous treatment failure with a steroid plus 5-HT_3 RA alone[2]

* Carboplatin is considered as "high MEC" by ASCO (only when AUC ≥ 4 mg/mL per minute) and MASCC/ESMO, and reclassified as HEC (when AUC >5) by NCCN; an NK1 RA should be added in all cases c Selected patients with additional risk factors or previous treatment failure with a steroid plus 5-HT3 RA alone
b: The emetic potential of sacituzumab-govitecan and trastuzumab-deruxtecan appears to be at the high end of the moderate category, most closely resembling that of carboplatin. While prospective studies are needed it is suggested to prevent emesis as for carboplatin.

1J. Herrstedt et al, https://doi.org/10.2016/j.esmoop.2023.102195
2. NCCN Clinical Practice Guidelines in Oncology; Version 1.2024. Available from: www.nccn.org.
3. Hesketh P. J. et al. J Clin Oncol. 2020 J Clin Oncol 38:2782-2797. Available from: www.asco.org/guidelines/.

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Control de náuseas y vómitos agudos

EMETIC RISK GROUP	ANTIEMETICS						
High Non-AC	5-HT_3	+	DEX	+	NK_1	+	OLZ
High AC	5-HT_3	+	DEX	+	NK_1	+	OLZ
Moderate Carboplatin ≥ AUC 5 Oxaliplatin women ≤ 50 years	5-HT_3	+	DEX	+	NK_1		
Moderate (other than above)*	5-HT_3	+	DEX				
Low	5-HT_3	OR	DEX	OR	DOP		
Minimal	No routine prophylaxis						

*The emetic potential of sacituzumab-govitecan and trastuzumab-deruxtecan appears to be at the high end of the moderate category, most closely resembling that of carboplatin. While prospective studies are needed it is suggested to prevent emesis as for carboplatin.

5-HT_3 = serotonin$_3$ receptor antagonist	DEX = DEXAMETHASONE	NK_1 = neurokinin$_1$ receptor antagonist such as APREPITANT or FOSAPREPITANT or ROLAPITANT or oral or i.v. NEPA (combination of netupitant and palonosetron)	OLZ = OLANZAPINE	DOP = dopamine receptor antagonist

Presented at ESMO 2023
J. Herrstedt et al, https://doi.org/10.1016/j.esmoop.2023.102195

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Control de náuseas y vómitos tardíos

EMETIC RISK GROUP	ANTIEMETICS		
High Non-AC*	OLZ	+	DEX
High AC*	OLZ		
Moderate Carboplatin ≥ AUC 5* Oxaliplatin women ≤ 50 years*	No additional routine prophylaxis		
Moderate (other than above)	No additional routine prophylaxis		
Low and Minimal	No additional routine prophylaxis		

*If aprepitant 125 mg is used on day 1, then aprepitant 80 mg x 1 should be administered days 2-3.

DEX = DEXAMETHASONE

OLZ = OLANZAPINE

Presented at ESMO 2023
J. Herrstedt et al, https://doi.org/10.1016/j.esmoop.2023.102195

SEOM: Profilaxis antiemética

Recomendaciones para el control de NaVIQ	Pauta altamente emetógena: Consenso general		
Grupo de riesgo emetógeno	Opción	Prevención en la fase aguda DÍA 1	**Prevención en la fase tardía DÍAS 2,3 y 4**
Elevado y combinaciones con AC >90%	A	AR 5-HT_3*+ AR NK_1 + DEX	**(AR NK_1**) + DEX**
	B	NEPA + DEX	**DEX**
	C	Olanzapina + palonosetrón + DEX	**Olanzapina**

*Se recomienda palonosetrón debido a su superioridad en el control de la emesis tardía.
**Cuando se administra aprepitant el día 1. Administrar aprepitant días 2 y 3.

QAE: quimioterapia altamente emetógena; NEPA: netupitant + palonosetrón.

SEOM Clinical Guideline update for the prevention of chemotherapy-induced nausea and vomiting (2016). Clin Transl Oncol. 2016 Dec;18(12):1237-1242.

SEOM: Profilaxis antiemética

Recomendaciones para el control de NaVIQ		Pauta moderadamente emetógena: Consenso general	
Grupo de riesgo emetógeno	Opción	Prevención en la fase aguda DÍA 1	Prevención en la fase tardía DÍAS 2 y 3
Moderado: Carboplatino	A	AR 5-HT_3*+ DEX ± AR NK_1[+]	Si no AR NK_1: DEX Si APR125mg día 1: APR 80 mg D2 y D3 Si no APR: Nada
	B	NEPA + DEX[+]	Nada
Resto moderado 30-90%	A	AR 5-HT_3*+ DEX ± AR NK_1	DEX[#] Alternativa: AR 5-HT_3 + OLA[#]
	B	NEPA + DEX	DEX[#] Alternativa: AR 5-HT_3 + OLA[#]
	C	Olanzapina + palonosetrón + DEX	OLA

*Se recomienda palonosetrón debido a su superioridad.
[+] Para carboplatino, algunas guías recomiendan utilizar triple terapia.
[#] Administrar dexametasona o AR 5-HT_3 + OLA para esquemas con potencial de emesis retardada; no como tratamiento de rutina.

QME: quimioterapia moderadamente emetóena; NEPA: netupitant + palonosetrón

SEOM Clinical Guideline update for the prevention of chemotherapy-induced nausea and vomiting (2016). Clin Transl Oncol. 2016 Dec;18(12):1237-1242.

XVIII CURSO SEOM PARA RESIDENTES
EN CONTROL DE SÍNTOMAS Y TERAPIAS DE SOPORTE

Clinical and Translational Oncology
https://doi.org/10.1007/s12094-022-02802-1

CLINICAL GUIDES IN ONCOLOGY

SEOM clinical guideline emesis (2021)

Margarita Majem[1] · Ramon de las Peñas[2] · Juan Antonio Virizuela[3] · Luís Cabezón-Gutiérrez[4] · Patricia Cruz[5] · Rafael Lopez-Castro[6] · Miriam Méndez[7] · Rebeca Mondéjar[8] · María del Mar Muñoz[9] · Yolanda Escobar[10]

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SEOM: Profilaxis antiemética

Table 3 Emesis prevention recommendations for high, moderate, low and minimal emetic risk IV anticancer drugs

	ASCO guidelines	NCCN guidelines	MASCC/ESMO guidelines
Emesis prevention for high emetic risk IV anticancer drugs			
ACUTE Day 1 (start before anticancer treatment)	*Single dose of NK1-RA (choose one):* Aprepitant 125 mg oral or 130 IV Fosaprepitant 150 mg IV Netupitant-palonosetron 300 mg netupitant/0.5 mg palonosetron oral in single capsule *Single dose of 5-HT3-RA (choose one):* Granisetron 2 mg PO / 1 mg IV once Ondansetron 8 mg PO or IV once Palonosetron 0.25 mg IV *Dexamethasone* 12 mg PO/IV *Olanzapine* 5-10 mg PO	OPTION A (PREFERRED) *Olanzapine* 5–10 mg PO once *Single dose of NK1-RA (choose one):* Aprepitant 125 mg oral Fosaprepitant 150 mg IV Netupitant-palonosetron 300 mg netupitant/0.5 mg palonosetron oral in single capsule *Single dose of 5-HT3-RA (choose one):* Granisetron 2 mg PO / 1 mg IV once Ondansetron 8–16 mg PO or 16–24 IV once Palonosetron 0.25 mg IV *Dexamethasone* 12 PO/IV OPTION B *Palonosetron* 0.25 mg IV once *Dexamethasone* 12 mg PO/IV *Olanzapine* 5-10 mg PO once OPTION C *Single dose of NK1-RA (choose one):* Aprepitant 125 mg oral Fosaprepitant 150 mg IV Netupitant-palonosetron 300 mg netupitant/0.5 mg palonosetron oral in single capsule *Single dose of 5-HT3-RA (choose one):* Granisetron 2 mg PO / 1 mg IV once Ondansetron 8–16 mg PO or 16–24 IV once Palonosetron 0.25 mg IV *Dexamethasone* 12 mg PO/IV once	*Single dose of NK1-RA (choose one) :* Aprepitant 125 mg oral Fosaprepitant 150 mg IV Netupitant-palonosetron 300 mg netupitant/0.5 mg palonosetron oral in single capsule *Single dose of 5-HT3-RA (choose one):* Granisetron 2 mg PO / 1 mg IV once Ondansetron 8 mg PO or IV once Palonosetron 0.25 mg iIV *Dexamethasone* 12 mg once *Olanzapine* 5–10 mg PO when nausea is an issue
DELAYED Days 2–4	*Aprepitant* 80 mg PO on days 2–3 (if aprepitant PO on day 1) *Dexamethasone* 8 mg oral or IV once daily on days 2–4 (*) *Olanzapine* 5–10 mg oral on days 2–4	OPTION A *Olanzapine* 5-10 mg PO daily on days 2-4 *Aprepitant* 80 mg PO daily on days 2,3 (if aprepitant PO on day 1) *Dexamethasone* 8 mg PO/IV once daily OPTION B *Olanzapine* 5-10 mg PO daily on days 2-4 OPTION C *Aprepitant* 80 mg PO daily on days 2,3 (if aprepitant PO on day 1) *Dexamethasone* 8 mg PO/IV daily on days 2-4	*Aprepitant* 80 mg PO on days 2-3 (if aprepitant PO on day 1) *Dexamethasone* 8 mg once daily (*) *Olanzapine* 5–10 mg PO when nausea is an issue

Guideline-consistent Antiemetic Therapy in CINV: Pan European Emesis Registry (PEER)

Is non-adherence of antiemetic guidelines a risk factor for CINV?

Study Objective:

To evaluate the effect of Guideline-Consistent CINV Prophylaxis (GCCP*) on patients' outcomes by comparing the proportion of patients with Complete Response during the first 120 hours post-chemotherapy among patients who received GCCP with those who received Guideline-Inconsistent CINV Prophylaxis (GICP) during Cycle 1

Study Design:

- Prospective, observational, multicenter study that enrolled chemotherapy-naïve adults initiating single-day HEC or MEC for cancer. Study conducted in Austria, Belgium, France, Italy, Spain, Sweden, the Netherlands, and United Kingdom
- Patients completed a 6-day daily diary for 3 cycles of chemotherapy

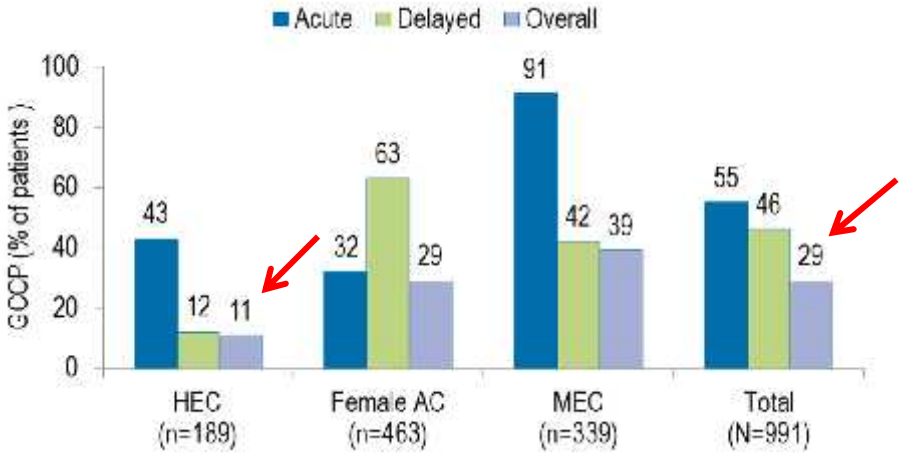
Chemotherapy	Acute phase (day 1) GCCP*	Delayed phase (days 2–4) GCCP*
HEC	DEX + NK_1 RA + 5-HT_3 RA†	DEX days 2–4 + NK_1 RA days 2–3
Female AC	DEX + NK_1 RA + 5-HT_3 RA†	DEX +/or NK_1 RA days 2–3§
MEC	DEX + 5-HT_3 RA†,‡	DEX +/or 5-HT_3 RA days 2–3§

*GCCP definition was based on the MASCC 2006 antiemesis guidelines.

HEC: highly emetogenic chemotherapy; MEC: moderately emetogenic chemotherapy; GCCP: guideline-consistent CINV prophylaxis; GICP: guideline-inconsistent CINV prophylaxis

Guideline-consistent Antiemetic Therapy in CINV: Pan European Emesis Registry (PEER)

Is non-adherence of antiemetic guidelines a risk factor for CINV?



- Use of GCCP* varied between acute and delayed phases among the 3 categories of emetogenicity
  - Higher in MEC than HEC
  - Higher in acute than delayed phase (in both HEC and MEC)

- Use of GCCP* was relatively low overall (29%), and lowest for patients in the highest emetic risk category (11%)

*GCCP definition was based on the MASCC 2006 antiemesis guidelines.

HEC: highly emetogenic chemotherapy; MEC: moderately emetogenic chemotherapy; GCCP: guideline-consistent CINV prophylaxis; GICP: guideline-inconsistent CINV prophylaxis

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https://doi.org/10.1007/s12094-021-02623-8

RESEARCH ARTICLE

Prevention of chemotherapy-induced nausea and vomiting in the real-world setting in Spain

Y. Escobar Álvarez[1] · J. De Castro Carpeño[2] · D. Bell[3] · A. Drago[3] · A. Franceschetti

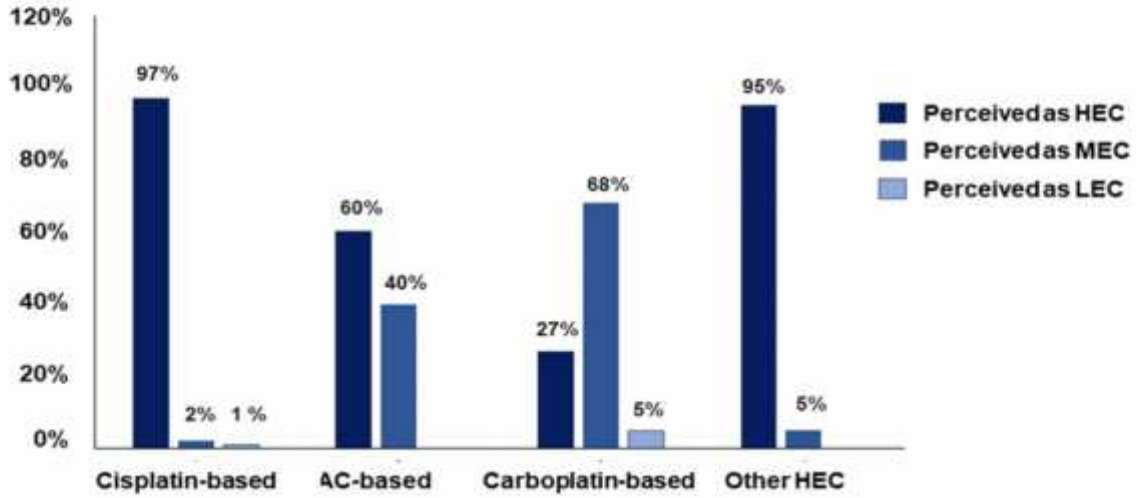
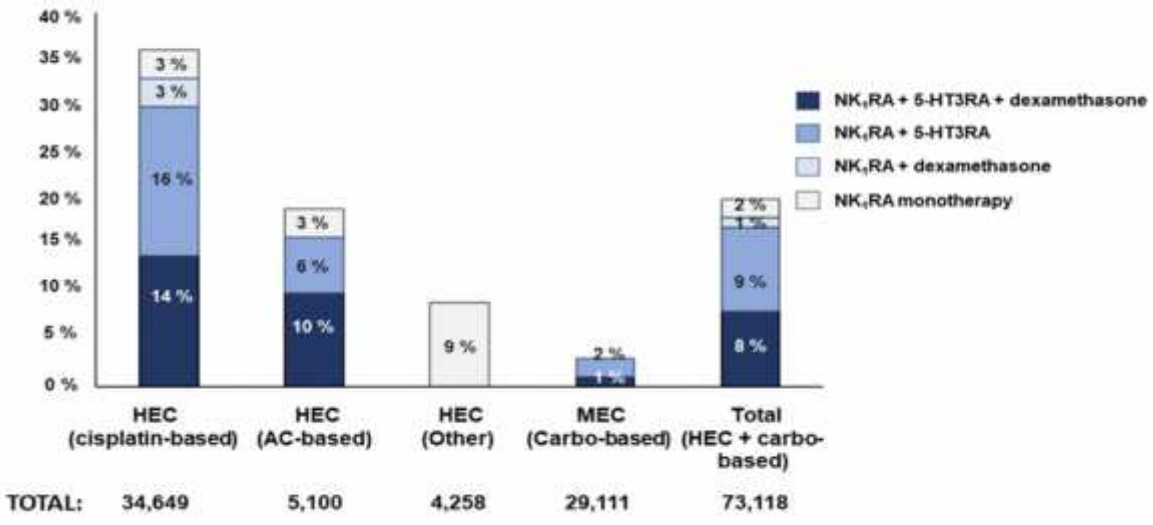


Fig. 4 Emetogenic risk of chemotherapy as perceived by physicians who prescribe NK_1RAs. *HEC* highly emetogenic chemotherapy, *MEC* moderately emetogenic chemotherapy, *LEC* low emetogenic chemotherapy, *AC* anthracycline-cyclophosphamide

Prevention of chemotherapy-induced nausea and vomiting in the real-world setting in Spain

Fig. 2 Distribution of NK_1RA-based regimens according to the different HEC regimens



Escobar Y et al, Clin Transl Oncol. 2021; 23: 2155

ADCs-deruxtecan
Potencial emetógeno

- A similar pattern of increased gastro-toxicity was observed in the recent trials, in relation with the other ADCs with deruxtecan payload, despite of antiemetic prophylaxis treatment
- Nausea pattern emerging on ADCs show that this can be present for days beyond the delayed phase.[1]

Patritumab deruxtecan (HER3-DXd)[2]	Datopotamab-deruxtecan (Dato-DXd)	Raludotatug deruxtecan (R-DXd)	Ifinatamab deruxtecan (I-DXd)
•HERTHENA-Lung01: nausea G1/2: 63%, G3: 3%	•TROPION-Lung01, nausea any grade: 34%, G3: 2%[3] •TROPION-Lung05, nausea G1/2: 58%, G3 :2%[4] •TROPION-Breast01, nausea G1/2: 51%, G3: 1%[5] •Begonia trial, nausea any grade: 65%[6]	•FIH trial: nausea any grade: 58.3%, G3: 1.7%[7]	•Advanced solid tumors trial: nausea any grade: 60.3%, G3: 3.4%[8]

1. Rugo et al. - Optimizing treatment management of trastuzumab deruxtecan in clinical practice of breast cancer; https://doi.org/10.1016/j.esmoop.2022.100553
2. Helena A. Yu et al. - HERTHENA-Lung01; https://doi.org/10.1200/JCO.23.01476
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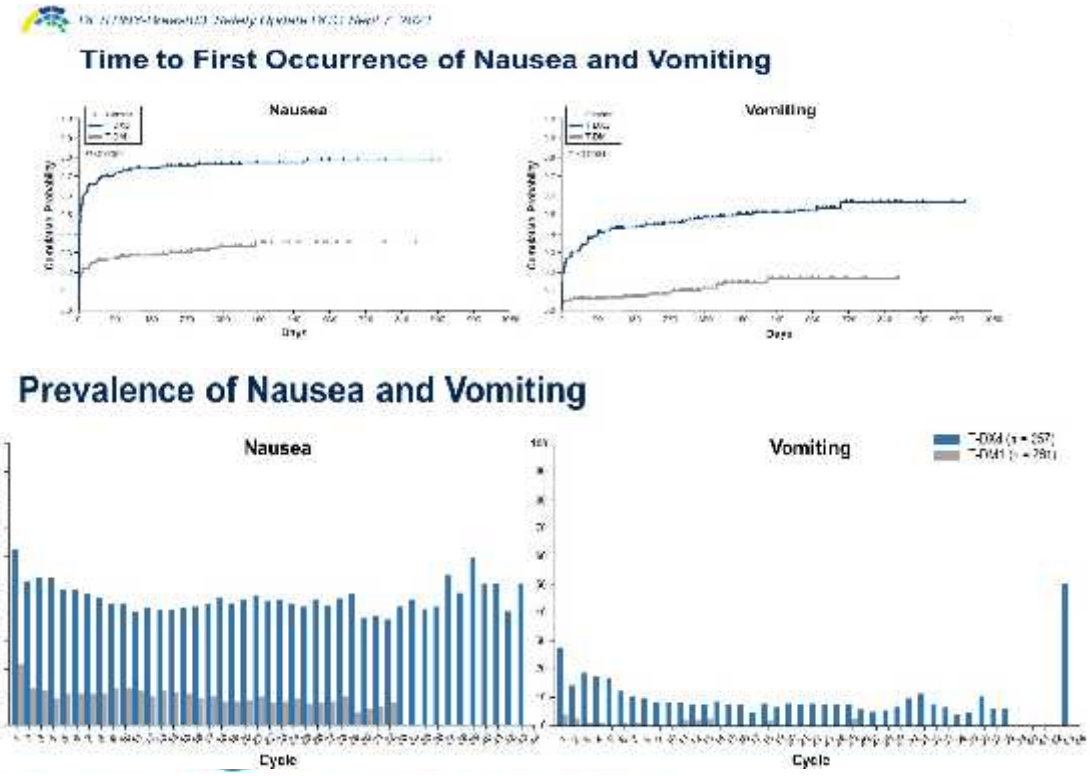
4. Paz-Ares et al. - TROPION-Lung05Annals of Oncology (2023) 34 (suppl_2): S755-S851. 10.1016/annonc/annonc1331
5. Bardia A, et al. - ESMO Congress 2023, Abstract LBA11
6. P. Schmid - ESMO Congress 2023, Abstract 379MO
7. K.N. Moore - ESMO Congress 2023 , Abstract 745MO
8. Manish R. Patel - ESMO Congress 2023 , Abstract - 690P

T-DXd-related nausea and vomiting: an early and persistent problem



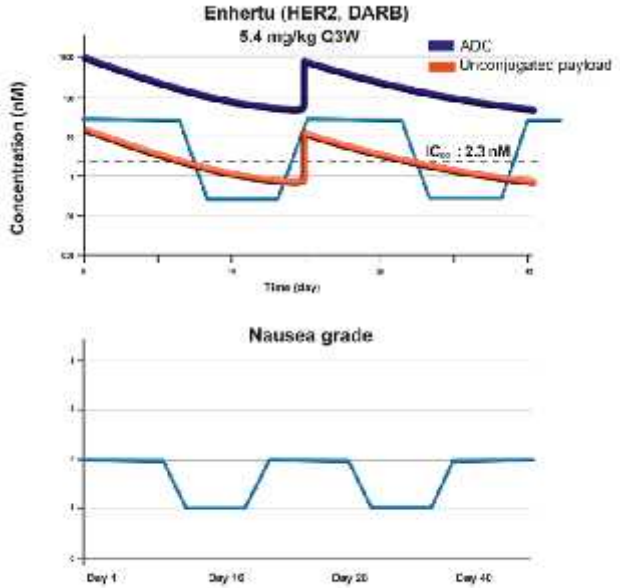
"The impressive therapeutic success of new ADCs is well represented by the long median treatment duration observed in clinical trials , which requires raising the bar of emesis control from desirable to optimal to fulfill the promise of these compounds in terms of compliance and efficacy"

Bianchini Cancers 2022, 14, 1022.https://doi.org/10.3390/cancers14041022

Hamilton et al. ASCO 2022

ADC Peculiar PK Profile: Explanation for Persistent Nausea

T-DXd pharmacokinetics requires antiemetic strategies
that should be effective for an extended period



- The pattern of nausea and vomiting may vary, presenting as early as Day 1 and as late as 1 week or later in the cycle.[2]
- Nausea pattern (blue line)[3]:
  - Correlates well with the PK pattern of free deruxtecan
  - Grades 1-2 tend to persist over time and in subsequent cycles[4].

1. Tarcsa E. et al. Drug Discovery Today 2020; 37:13-22.
2. Rugo et al. ESMO Open 2022;7(4):100553.
3. Expert Personal Communication.
4. Bianchini et al. Cancer 2022; 14:1022.

Long delayed CINV is now recognized by the medical community

Prevalence and predictors of long-delayed (> 120 h) chemotherapy-induced nausea and vomiting (CINV)—a systematic review and individual patient data meta-analysis

Ronald Chow[1] · Leyi Bellinda Yin[1] · Wafa Baqri[1] · Ryan Huang[1] · Gabriel Boldt[2] · Jawaid Younus[2] · Michael Lock[2] · Elizabeth Prsic[3] · Camilla Zimmermann[1] · Jørn Herrstedt[4]

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Nausea %	acute	delayed	Long delayed
HEC	24	49	31
MEC	7	38	24

Vomiting %	acute	delayed	Long delayed
HEC	8	14	6
MEC	2	14	6

Nausea and vomiting data emerging on some of the targeted therapies such as antibody drug conjugates (eg, trastuzumab deruxtecan) show that nausea can be present for days beyond the delayed phase.[3,4]
Nausea in the long-delayed phase was as severe as in the delayed phase
Patients experiencing nausea and vomiting on days 4 and 5 were at significant risk of experiencing long-delayed CINV

1. Rugo H, et al. ESMO Breast 2023; Oral Presentation #1850.
2. Rugo et al. ESMO Open 2022;7(4):100553

Principales dificultades:

- Control de las náuseas
- Emesis tardía
- Pediatría
- Tratamientos en múltiples días
- Mejorar la adhesión a las recomendaciones basadas en la evidencia

1. El seguimiento de las recomendaciones clínicas mejora de forma significativa el control de la emesis y propicia un mejor uso de los recursos[1,2].
2. Es necesario mejorar la práctica clínica siguiendo lo establecido en las recomendaciones y facilitar la adhesión al tratamiento[3].
3. Una pauta oral efectiva, basada en una dosis única administrada inmediatamente antes de la quimioterapia podría constituir un tratamiento muy práctico con una efectividad mejorada[2].

1. Hesketh PJ. et al. Biomed Res Int. 2015;2015:651879.
2. Aapro M, et al. Ann Oncol. 2012;23(8):1986-1992
3. Navari RM and Aapro M. N Engl J Med 2016;374:1356-67.

- Es fundamental conocer el potencial emetógeno de la QT
- La profilaxis antiemética con anti-5-HT3, anti-NK-1 y dexametasona es el tto de elección de la QT altamente emetógena
- El uso inadecuado de antieméticos puede reducir eficacia y aumentar efectos secundarios
- Un control adecuado del tratamiento antiemético permite cumplir correctamente el tto QT
- Un mal control antiemético puede comprometer la supervivencia del paciente oncológico

Muchas gracias por vuestra atención

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