Getting a grip on the guidelines: understanding antiemetic usage and barriers to adherence

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  - MSD
  - Pierre Fabre Oncology
  - Roche
  - TESARO
Question 1

Are you familiar with the antiemetic guidelines, and do you use them?

1) Yes, I am familiar with the guidelines and use them

2) Yes, I am familiar with the guidelines, but do not use them

3) No, I am not familiar with the guidelines

4) I do not need the guidelines, I make my own decisions

5) I am not familiar with the guidelines, but am keen to be informed
Patient case: Jeannette

- French woman; age 54 years
- Married; has 2 daughters
- No comorbidities, does smoke
- No morning sickness, sleeps well, no medication use, no anxiety
- NSCLC, stage IIIB (T3N0), resection margin: R0
- Decision for adjuvant therapy:
  - Cisplatin and vinorelbin 4 cycles
- An NK₁ RA + 5-HT₃ RA + steroid regimen is proposed by the multidisciplinary team for supportive cancer care
Question 2

Jeannette will receive a 3-drug regimen:
NK₁ RA + 5-HT₃ RA + steroids

Please select the statement which best applies:

1) I agree, this is consistent with MASCC/ESMO guidelines
2) I agree, this is consistent with ASCO guidelines
3) I agree, this is consistent with our local guidelines
4) I disagree, NK₁ RAs are not necessary for this indication
5) I disagree, I follow other local guidelines
6) I agree with both (1) and (2)

ASCO, American Society of Clinical Oncology;
ESMO, European Society for Medical Oncology;
MASCC, The Multinational Association of Supportive Care in Cancer.
**Patient case: Mauricette**

- Swiss woman; age 68 years
- Married; 1 daughter and 3 granddaughters
- Her symptoms include postpartum blues following pregnancies, nausea, bad mood, insomnia, anxiety with chemotherapy
- Consumes alcohol daily
- Diagnosis: ovarian cancer, peritoneal carcinosis, \textit{BRCA}⁻
- Chemotherapy regimen:
  - Carboplatin and paclitaxel 6 cycles
- A 5-HT₃ RA + steroid association is proposed by the multidisciplinary team for supportive cancer care
Question 3

Mauricette will receive 5-HT₃ RA + steroid

Please select the statement which best applies:

1. I agree, it is consistent with MASCC/ESMO guidelines
2. I agree, it is consistent with our local guidelines
3. I disagree, I follow other local guidelines
4. I disagree, it is not consistent with MASCC/ESMO guidelines
5. I disagree, NK₁ RAs are necessary for this indication
6. Both (4) and (5)
### ACUTE Nausea and Vomiting: SUMMARY

<table>
<thead>
<tr>
<th>Emetic Risk Group</th>
<th>Antiemetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Non-AC</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; + DEX + NK&lt;sub&gt;1&lt;/sub&gt;</td>
</tr>
<tr>
<td>High AC</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; + DEX + NK&lt;sub&gt;1&lt;/sub&gt;</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; + DEX + NK&lt;sub&gt;1&lt;/sub&gt;</td>
</tr>
<tr>
<td>Moderate (other than carboplatin)</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; + DEX</td>
</tr>
<tr>
<td>Low</td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; or DEX or DOP</td>
</tr>
<tr>
<td>Minimal</td>
<td>No routine prophylaxis</td>
</tr>
</tbody>
</table>

5-HT<sub>3</sub> = serotonin<sub>3</sub> receptor antagonist  
DEX = Dexamethasone  
NK<sub>1</sub> = neurokinin<sub>1</sub> receptor antagonist such as Aprepitant or Fosaprepitant or Rolapitant or NEPA (combination of netupitant and palonosetron)  
DOP = dopamine receptor antagonist

Note: If the NK<sub>1</sub> receptor antagonist is not available for AC chemotherapy, palonosetron is the preferred 5-HT<sub>3</sub> receptor antagonist.
### DELAYED Nausea and Vomiting: SUMMARY

<table>
<thead>
<tr>
<th>EMETIC RISK GROUP</th>
<th>ANTIEMETICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Non-AC</td>
<td><strong>DEX</strong> or (if APR 125mg for acute: ( <strong>MCP</strong> + <strong>DEX</strong> ) or ( <strong>APR</strong> + <strong>DEX</strong> ))</td>
</tr>
<tr>
<td>High AC</td>
<td>None or (if APR 125mg for acute: <strong>DEX</strong> or <strong>APR</strong> )</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>None or (if APR 125mg for acute: <strong>APR</strong> )</td>
</tr>
<tr>
<td>Oxaliplatin,</td>
<td><strong>DEX</strong> can be considered</td>
</tr>
<tr>
<td>or anthracycline,</td>
<td></td>
</tr>
<tr>
<td>or cyclophosphamide</td>
<td></td>
</tr>
<tr>
<td>Moderate (other)</td>
<td>No routine prophylaxis</td>
</tr>
<tr>
<td>Low and Minimal</td>
<td>No routine prophylaxis</td>
</tr>
</tbody>
</table>

**DEX** = Dexamethasone  
**MCP** = Metoclopramide  
**APR** = Aprepitant
Are we following the guidelines, …and why?
The effect of guideline-consistent antiemetic therapy on chemotherapy-induced nausea and vomiting (CINV): the Pan European Emesis Registry (PEER)

M. Aapro¹*, A. Molassiotis², M. Dicato³, I. Peláez⁴, Á. Rodríguez-Lescure⁵, D. Pastorelli⁶, L. Ma⁷*, T. Burke⁷, A. Gu⁷, P. Gascon⁸ & F. Roila⁹ on behalf of the PEER investigators
Follow-up on the impact of guideline adherence

<table>
<thead>
<tr>
<th>Response rates</th>
<th>GCCP, n (%)</th>
<th>GICP, n (%)</th>
<th>p</th>
<th>Multivariate model</th>
<th>Odds ratio</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 287</td>
<td>n = 704</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complete response</td>
<td>172 (59.9)</td>
<td>357 (50.7)</td>
<td>0.008</td>
<td></td>
<td>1.43 (1.04–1.97)</td>
<td>0.027</td>
</tr>
<tr>
<td>No emesis</td>
<td>182 (63.4)</td>
<td>412 (58.5)</td>
<td>0.154</td>
<td></td>
<td>1.18 (0.86–1.63)</td>
<td>0.301</td>
</tr>
<tr>
<td>No nausea</td>
<td>138 (48.1)</td>
<td>286 (40.6)</td>
<td>0.031</td>
<td></td>
<td>1.37 (0.99–1.90)</td>
<td>0.056</td>
</tr>
<tr>
<td>No CINV</td>
<td>122 (42.5)</td>
<td>242 (34.4)</td>
<td>0.016</td>
<td></td>
<td>1.41 (1.01–1.96)</td>
<td>0.041</td>
</tr>
</tbody>
</table>

Guideline-consistent cohort had higher rates of complete response and no CINV

<table>
<thead>
<tr>
<th>Parameter (over 5 days after chemo initiation)</th>
<th>GCCP, n (%)</th>
<th>GICP, n (%)</th>
<th>Multivariate model</th>
<th>Rate ratio (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 287</td>
<td>n = 704</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GP visit</td>
<td>7 (2.4)</td>
<td>29 (4.1)</td>
<td>0.68 (0.45–1.02)</td>
<td>0.062</td>
<td></td>
</tr>
<tr>
<td>Specialist visit</td>
<td>3 (1.1)</td>
<td>11 (1.6)</td>
<td>0.51 (0.34–0.79)</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>ER visit</td>
<td>4 (1.4)</td>
<td>12 (1.7)</td>
<td>0.57 (0.38–0.84)</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>Hospital days</td>
<td>5 (1.7)</td>
<td>10 (1.4)</td>
<td>1.22 (0.79–1.86)</td>
<td>0.364</td>
<td></td>
</tr>
</tbody>
</table>

Demand on health care resources to manage CINV is lower in GCCP group

CI, confidence interval; CINV, chemotherapy-induced nausea and vomiting; CT, chemotherapy; ER, emergency room; GCCP, guideline-consistent CINV prophylaxis; GP, general practitioner; GICP, guideline-inconsistent CINV prophylaxis.
The perceptual gap: perception vs reality

- Adverse symptom events over time as reported by patients vs clinicians

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**Nausea**

![Nausea Graph]

**Vomiting**

![Vomiting Graph]

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a Patient-reported symptoms (n = 467) across different malignant conditions from a total of 4,034 clinic visits.
b Clinician-reported symptoms were recorded by physicians and nurses treating those patients at the same visits.

Nausea and vomiting with chemotherapy are underestimated

- Healthcare providers’ predictions of incidence rates of nausea and emesis

More than 75% of physicians and nurses underestimate the incidence of delayed CINV in both HEC and MEC

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

Utilization of guideline-recommended antiemetic agents in practice: ONS survey

In HEC, NK_1 RAs are underused on Day 1 and 5-HT_3 RAs are overused on Day 2 and beyond.

Guideline-recommended agents

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2 and beyond</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NK_1 RA</td>
<td>95</td>
<td>81</td>
</tr>
<tr>
<td>DEX</td>
<td>93</td>
<td>30</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Phenothiazine</td>
<td>16</td>
<td>0.4</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>30</td>
<td>4</td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>81</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2 and beyond</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NK_1 RA</td>
<td>95</td>
<td>89</td>
</tr>
<tr>
<td>DEX</td>
<td>23</td>
<td>13</td>
</tr>
<tr>
<td>Other</td>
<td>13</td>
<td>4</td>
</tr>
<tr>
<td>Phenothiazine</td>
<td>17</td>
<td>0.4</td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>61</td>
<td>11</td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>47</td>
<td>30</td>
</tr>
</tbody>
</table>

*An oral NK_1 RA (APR) would be considered guideline-recommended on Day 2 and beyond if it had been administered on Day 1. ONS, Oncology Nursing Society.*

Awareness and use of antiemetic guidelines: survey among European oncology nurses

**Familiarity with antiemetic guidelines**

- ASCO: 46%
- Individual: 41%
- MASCC: 40%
- NCCN: 34%
- Other: 10%
- None: 10%

**Antiemetic guidelines utilized**

- Individual: 47%
- ASCO: 27%
- MASCC: 25%
- NCCN: 16%
- Other: 8%
- None: 7%

**Perceived barriers interfering with implementation of guideline-recommended prophylaxis**

- Physician preference: 39%
- Medications not on formulary: 27%
- Product cost: 25%
- None: 22%
- Patients do not report CINV: 19%
- Satisfied with current antiemetics: 16%
- Not aware of guideline recommendations: 15%
- Complexity of antiemetic regimens: 9%
- Product insurance coverage: 3%

Dielenseger P, et al. Poster presented at ESMO. 2017; abstract 1552P.
NERO study: evaluation of antiemetic usage across Eastern Europe

• NERO (Nausea/Emesis Registry in Oncology)
  – Multicentre, non-interventional prospective study

• Registry objectives
  – Assess antiemetic guidelines adherence in CINV prophylaxis
  – Evaluate effect of CINV on QoL in patients receiving HEC or MEC

• Outcomes
  – Primary outcome
    • Estimate the impact of adherence to antiemetic guidelines in patients receiving repeated cycles of either HEC or MEC
    • Complete response (overall period, 0–120 h)
  – Secondary outcome
    • Effect of CINV on QoL

h, hours. QoL, quality of life.

European countries/centres involved in NERO

- Austria
- Bulgaria
- Czech Republic
- Hungary
- Poland
- Romania
- Slovakia

Number of patients currently enrolled: 708
Number of clinical sites: > 80

What about patient-related characteristics?
Why do patients not report nausea and/or vomiting?

- Accept that nausea and/or vomiting is a normal side effect of chemotherapy/radiotherapy that has to be tolerated
- Do not feel it is severe enough to warrant reporting
- Reluctant to bother the doctor/nurse
- The notion that feeling sick demonstrates that the chemotherapy/radiotherapy is working
- Can be difficult to contact a member of the care team
- Other

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

G. Dranitsaris¹*, A. Molassiotis², M. Clemons¹, E. Roeland³, L. Schwartzberg⁴, P. Dielenseger⁵, K. Jordan⁶, A. Young⁷ & M. Aapro⁸
## Risk scoring algorithm for ≥ grade 2 CINV in cancer patients receiving chemotherapy

<table>
<thead>
<tr>
<th>Predictive factor</th>
<th>Before a cycle of chemotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline score</strong></td>
<td>10</td>
</tr>
<tr>
<td><strong>Impact of patient risk factors</strong></td>
<td></td>
</tr>
<tr>
<td>Patient &lt; age</td>
<td>+1</td>
</tr>
<tr>
<td>Patient expects to have CINV</td>
<td>+1</td>
</tr>
<tr>
<td>Patient slept &lt; 7 hours the night before chemotherapy</td>
<td>+1</td>
</tr>
<tr>
<td>Patient has a history of morning sickness</td>
<td>+1</td>
</tr>
<tr>
<td>Patient is about to receive platinum or AC chemotherapy</td>
<td>+2</td>
</tr>
<tr>
<td>Patient on-prescription antiemetics are used at home in the prior cycle</td>
<td>+3</td>
</tr>
<tr>
<td>Patient had nausea or vomiting in the prior cycle</td>
<td>+5</td>
</tr>
<tr>
<td>About to receive the 2nd cycle</td>
<td>-5</td>
</tr>
<tr>
<td>About to receive ≥ 3rd cycle</td>
<td>-6</td>
</tr>
<tr>
<td><strong>Total composite risk score</strong></td>
<td>?</td>
</tr>
</tbody>
</table>

*a* Estimation of probability of developing ≥ grade 2 CINV during that cycle of therapy.

Adapting the antiemetic regimen to patient characteristics

<table>
<thead>
<tr>
<th>ESMO-MASC Guidelines</th>
<th>High emetogenic chemotherapy</th>
<th>Moderate emetogenic chemotherapy carboplatin</th>
<th>Moderate emetogenic chemotherapy non carboplatin</th>
<th>Low emetogenic chemotherapy</th>
<th>No emesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triple (NK1 inhibitor+ setron + corticosteroids)</td>
<td>Triple (NK1 inhibitor+ setron + corticosteroids)</td>
<td>Double (setron + corticosteroids)</td>
<td>Setron or corticosteroid</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

Dranitsaris score

- Very high risk: Quadruple (Olanzapine + NK1 inhibitor+ setron + corticosteroids)
- High risk: Triple (NK1 inhibitor+ setron + corticosteroids)
- Moderate risk carbo: Triple (NK1 inhibitor+ setron + corticosteroids)
- Moderate risk non carbo: Double (setron + corticosteroids)
- Low risk: Setron or corticosteroid
- No risk: None
CINV Risk Assessment

CINV
Chemotherapy Induced Nausea and Vomiting

CINV can be prevented with the correct antiemetic drug combination.
Use this tool to estimate your patient’s risk.

This educational tool is derived from a number of published references and is based on MASCC emetogenicity classification (Jordan, et al. 2017). The tool was developed from 1196 patients who received 4197 cycles of chemotherapy. It has undergone internal validation and it has to be prospectively validated in a new sample of patients. The health information contained herein is provided for educational purposes only and is not meant to be a substitute for the advice of other healthcare professionals. All decisions regarding patient care must be made with a healthcare professional considering the unique characteristics of the patient.


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I declare that I am a HealthCare professional. Get Started
Patient case: Jeannette

- French woman; age 54 years
- Married; has 2 daughters
- No comorbidities, does smoke
- No morning sickness, sleeps well, no medication use, no anxiety
- NSCLC, stage IIB (T3N0), resection margin: R0
- Decision for adjuvant therapy:
  - Cisplatin and vinorelbine 4 cycles
- An NK1 RA + 5-HT3 RA + steroid regimen is proposed by the multidisciplinary team for supportive cancer care

Courtesy of Dr Scotté.
RECOMMENDATION: Based on MASCC/ESMO emetogenicity level & CINV risk assessment tool, your patient should receive:

NK1 RA + 5-HT3 RA + Corticosteroid + No Additional Antiemetic

Chemotherapy Emetogenicity Level*

>90%: High Emetogenic

Chemotherapy: Cisplatin

Based on MASCC/ESMO emetogenicity level, your patient should receive:

NK1 RA + 5-HT3 RA + Corticosteroid
Patient case: Mauricette

- Swiss woman; age 68 years
- Married; 1 daughter and 3 granddaughters
- Her symptoms include postpartum blues following pregnancies, nausea, bad mood, insomnia, anxiety with chemotherapy
- Consumes alcohol daily
- Diagnosis: ovarian cancer, peritoneal carcinosis, BRCA-
- Chemotherapy regimen:
  - Carboplatin and paclitaxel 6 cycles
- A 5-HT$_3$ RA + steroid association is proposed by the multidisciplinary team for supportive cancer care

Courtesy of Dr Scotté.
RECOMMENDATION: Based on MASCC/ESMO emetogenicity level & CINV risk assessment tool, your patient should receive:

NK1 RA + 5-HT3 RA + Corticosteroid + Additional Antiemetic (e.g. Olanzapine, ...)

Chemotherapy Emetogenicity Level*

30 - 90%: Moderate Emetogenic
Chemotherapy: Paclitaxel, Carboplatin

Patient Emetogenicity Risk Profile

57.4% High Risk

- Expecting to develop CINV
- Morning sickness history
- <7 hours sleep before chemotherapy
- Anthracycline-based, Platinum-based or Anthracycline and Platinum-based

Based on this CINV risk assessment tool, your patient should receive:

Additional Antiemetic

* "%" indicates the risk of emesis in absence of antiemetic prophylaxis. Please visit MASCC/ESMO, NCCN and ASCO for complete CINV recommendations.

The health information contained herein is provided for educational purposes only and is not meant to be a substitute for the advice of a physician or other HealthCare professional. All decisions regarding patient care must be made with a HealthCare professional, considering the unique characteristics of the patient.
“Supportive care makes excellent cancer care possible”