Chemotherapy-induced Nausea and Vomiting: The Pharmacist’s Role in Integrating Clinical Guidelines into Patient Care

Presented as a Live Webinar

Wednesday, April 13, 2016
12:00 p.m. – 1:00 p.m. ET

Tuesday, April 26, 2016
3:00 p.m. – 4:00 p.m. ET

Thursday, April 28, 2016
1:00 p.m. – 2:00 p.m. ET

www.ashpadvantage.com/CINV

Planned by ASHP Advantage and supported by educational grants from Eisai and TESARO.
Chemotherapy-induced Nausea and Vomiting: The Pharmacist’s Role in Integrating Clinical Guidelines into Patient Care

Activity Overview

This educational activity will review patient- and drug-specific risk factors for developing chemotherapy-induced nausea and vomiting (CINV). New and revised strategies for the management of CINV will be evaluated taking into account emerging data and updates to national and international guidelines. Data supporting the use of a single antiemetic agent versus combinations of antiemetic therapies will be reviewed. Patient cases will be used to illustrate how CINV can be prevented and managed using a guidelines-based approach to treating patients at risk for developing acute and delayed-onset CINV.

Learning Objectives

At the conclusion of this Application-based educational activity, participants should be able to

• Evaluate new and revised strategies for CINV management based on emerging data and updates to national and international guidelines.
• Review the data supporting the use of individual antiemetic agents and combinations for patients on moderately- and highly-emetogenic regimens, including emerging agents.
• Develop a plan for adequate antiemetic prophylaxis and breakthrough treatment based on antiemetic drug classifications.
• Using patient cases, design optimal guideline-based approaches for the prevention and management of CINV for patients at risk for developing acute and delayed-onset CINV taking into consideration patient- and regimen-specific characteristics.

Continuing Education Accreditation

ASHP is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This activity provides 1.0 hour (0.1 CEU – no partial credit) of continuing pharmacy education credit (ACPE activity #0204-0000-16-449-L01-P).

Participants will process CPE credit online at http://elearning.ashp.org/my-activities. CPE credit will be reported directly to CPE Monitor. Per ACPE, CPE credit must be claimed no later than 60 days from the date of the live activity or completion of a home study activity.

Webinar Information

Visit www.ashpadvantage.com/CINV to find

• Webinar registration link
• Group viewing information and technical requirements
• CPE webinar processing information
Chemotherapy-induced Nausea and Vomiting: The Pharmacist’s Role in Integrating Clinical Guidelines into Patient Care

Faculty

Sally Barbour, Pharm.D., BCOP, CPP
Director of Oncology Pharmacy Programs
Duke University Hospital
Clinical Pharmacist Practitioner
Duke Cancer Center at Duke University Hospital
Durham, North Carolina

Sally Barbour, Pharm.D., BCOP, CPP, is Director of Oncology Pharmacy Programs and Clinical Oncology Pharmacist at the Duke Cancer Institute at Duke University Medical Center in Durham, North Carolina. She is also Program Director for the PGY2 Oncology Residency. In addition to her leadership responsibilities, she maintains a clinical practice in the adult outpatient oncology clinics.

Dr. Barbour earned her Bachelor of Art degree from Duke University and her Doctor of Pharmacy degree from the University of Texas at Austin. She completed a residency in Pharmacy Practice at the University of Illinois at Chicago and in Oncology Pharmacy Practice at the Audie L. Murphy Memorial Veterans Affairs Hospital and University of Texas Health Science Center in San Antonio. She obtained her board certification in oncology pharmacy in 2001 and her Clinical Pharmacist Practitioner certification in 2005.

Dr. Barbour serves as a member of the National Comprehensive Cancer Network (NCCN) Antiemesis Panel, the NCCN Educational Programs Advisory Committee, and the Pharmacy Committee for the Alliance for Clinical Trials in Oncology. She is a member of American Society of Health-System Pharmacists and the Hematology/Oncology Pharmacy Association, where she has served on various committees as both a member and committee leader. She cofounded the North Carolina Oncology Pharmacists Association in 2001 and co-plans their annual meeting. Dr. Barbour has developed numerous supportive care guidelines at Duke and lectured on topics related to chemotherapy-induced nausea and vomiting, myelosuppression, general supportive care, lung cancer, oral chemotherapy, and the role of pharmacy in oncology practice.
Chemotherapy-induced Nausea and Vomiting: The Pharmacist’s Role in Integrating Clinical Guidelines into Patient Care

David Frame, Pharm.D.
Hematology / Oncology / Bone Marrow Transplant Clinical Specialist
University of Michigan Health System
Assistant Professor of Pharmacy
University of Michigan
Ann Arbor, Michigan

David Frame, Pharm.D., is Assistant Professor of Pharmacy at the University of Michigan and Clinical Hematology/Oncology and Bone Marrow Transplant (BMT) Clinical Specialist at the University of Michigan Health System in Ann Arbor, Michigan.

Dr. Frame earned his Bachelor of Science degree in chemistry from St. Louis University in Missouri and his Bachelor of Science degree in pharmacy and Doctor of Pharmacy degree from Wayne State University in Detroit, Michigan. He then completed a fellowship in oncology at the University of Illinois at Chicago.

In addition to his clinical practice, Dr. Frame's experience in hematology and oncology includes authoring supportive care protocols in the areas of nausea and vomiting, anemia, graft versus host disease, and bone health. Dr. Frame has been honored with the American Society of Health-System Pharmacists Drug Research Award. He is a member of the Hematology/Oncology Pharmacy Association Research Committee, the International Society of Oncology Pharmacists’ Publications, Education, and Research Committees, and the American Society of Clinical Oncology.

Dr. Frame has published in several peer-reviewed journals and has presented at many national and international meetings.
Disclosures

In accordance with the Accreditation Council for Continuing Medical Education’s Standards for Commercial Support and the Accreditation Council for Pharmacy Education’s Standards for Commercial Support, ASHP requires that all individuals involved in the development of activity content disclose their relevant financial relationships. A person has a relevant financial relationship if the individual or his or her spouse/partner has a financial relationship (e.g. employee, consultant, research grant recipient, speakers bureau, or stockholder) in any amount occurring in the last 12 months with a commercial interest whose products or services may be discussed in the educational activity content over which the individual has control. The existence of these relationships is provided for the information of participants and should not be assumed to have an adverse impact on the content.

All faculty and planners for ASHP education activities are qualified and selected by ASHP and required to disclose any relevant financial relationships with commercial interests. ASHP identifies and resolves conflicts of interest prior to an individual’s participation in development of content for an educational activity. Anyone who refuses to disclose relevant financial relationships must be disqualified from any involvement with a continuing pharmacy education activity.

- Sally Barbour, Pharm.D., BCOP, CPP, declares that TESARO has previously provided her travel support to present a poster at a meeting.
- All other faculty and planners report no financial relationships relevant to this activity.
Chemotherapy-induced Nausea and Vomiting

The Pharmacist's Role in Integrating Clinical Guidelines into Patient Care

Sally Barbour, Pharm.D., BCOP, CPP
Director of Oncology Pharmacy Programs
Clinical Pharmacist Practitioner
Duke University
Durham, North Carolina

David G. Frame, Pharm.D.
Clinical Assistant Professor of Pharmacy
University of Michigan College of Pharmacy
Clinical Pharmacist
University of Michigan Health System
Ann Arbor, Michigan

Disclosures

- Sally Barbour, Pharm.D., BCOP, CPP, declares that TESARO has previously provided her travel support to present a poster at a meeting.
- All other faculty and planners report no financial relationships relevant to this activity.

Learning Objectives

- Evaluate new and revised strategies for CINV management based on emerging data and updates to national and international guidelines.
- Review the data supporting the use of individual antiemetic agents and combinations for patients on moderately- and highly-emetogenic regimens, including emerging agents.
- Develop a plan for adequate antiemetic prophylaxis and breakthrough treatment based on antiemetic drug classifications.
- Using patient cases, design optimal guideline-based approaches for the prevention and management of CINV for patients at risk for developing acute and delayed-onset CINV taking into consideration patient- and regimen-specific characteristics.

Patient Perceptions of the Most Severe Side Effects of Cancer Chemotherapy

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Vomiting</td>
<td>Nausea</td>
<td>Nausea</td>
<td>Nausea</td>
<td>Fatigue</td>
</tr>
<tr>
<td>2</td>
<td>Nausea</td>
<td>Constantly tired</td>
<td>Loss of hair</td>
<td>Loss of hair</td>
<td>Nausea</td>
</tr>
<tr>
<td>3</td>
<td>Loss of hair</td>
<td>Loss of hair</td>
<td>Vomiting</td>
<td>Constantly tired</td>
<td>Sleep disturbances</td>
</tr>
<tr>
<td>4</td>
<td>Thought of coming for treatment</td>
<td>Effect on family</td>
<td>Constantly tired</td>
<td>Vomiting</td>
<td>Weight loss</td>
</tr>
<tr>
<td>5</td>
<td>Length of time treatment takes</td>
<td>Vomiting</td>
<td>Having to have an injection</td>
<td>Changes in the way things taste</td>
<td>Hair loss</td>
</tr>
</tbody>
</table>


CINV Remains a Challenge

- National and international guidelines (NCCN, ASCO, and MASCC) exist to guide clinicians in the use of antiemetics for CINV
  - Antiemetic guidelines result in significant improvement in the control of emesis with better resource utilization
  - Many practices have EMRs with chemotherapy regimens prebuilt that include supportive care
  - Multiple classes of drugs available to manage CINV
  - Despite progress in effective antiemetic prophylaxis, many patients still experience emesis from chemotherapy, particularly during the delayed phase

NCCN=National Comprehensive Cancer Network, ASCO=American Society of Clinical Oncology, MASCC=Multinational Association of Supportive Care in Cancer, EMR=electronic medical record, CINV=chemotherapy-induced nausea and vomiting


CINV Remains a Challenge

- Patients are not always prescribed effective guideline-based antiemetic regimens
- Nonadherence to antiemetic regimens, particularly regimens for delayed CINV
- Inability to afford medications
- Guidelines don't address all scenarios
  - Current guidelines based primarily on 2 factors:
    - Emetogenicity of single-dose chemotherapy
    - Pattern of CINV (e.g., acute, delayed)
- Lack of data on:
  - How to incorporate additional patient-specific emetic risk factors
  - Multiday chemotherapy
  - Stem-cell transplantation
  - Oral chemotherapy agents
  - Pediatric patients

Copyright © 2016, American Society of Health-System Pharmacists, Inc. All rights reserved.
CINV Remains a Challenge

- Provider misperceptions lead to undertreatment or overtreatment
- Patient misunderstanding
  - HOPA Patient Survey
    - 400 patients receiving chemotherapy
  - Results
    - Almost one-third thought CINV meant chemotherapy was working
    - Approximately 4 of 5 who had experienced CINV thought that if they weren’t vomiting, CINV was under control
- Lack of communication
  - Don’t want to disclose suffering for fear may alter/stop treatment
  - Don’t report symptoms
  - Lack of follow-up

Patient Case – AH

- AH is a 44-year-old female who is a teacher with no significant PMH.
- Presents with a 4-month history of weakness and fatigue and an associated 8-kg unintentional weight loss.
- She has never smoked and does not drink alcohol.
- She has 3 children and experienced significant morning sickness with all of her pregnancies.
- She is found to have a 10 cm cecal mass and multiple liver lesions. Biopsy of a liver lesion confirms the diagnosis of adenocarcinoma and she is coming in to get her first cycle of FOLFOX.

What are AH’s Risk Factors for CINV?

- Female gender
- Younger age
- Previous history of nausea/vomiting
- Low alcohol intake
- All of the above

Risk Factors For CINV

- Emetogenicity of chemotherapy
- Younger age (<50 years-old)
- Female
- Low alcohol intake history
- History of motion sickness
- History of emesis during pregnancy

What is the emetogenicity of AH’s chemotherapy regimen?

- High
- Moderate
- Low
- Minimal

Emetogenic Potential of Single Antineoplastic Agents

<table>
<thead>
<tr>
<th>Emetogenicity Level</th>
<th>Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>Moderate</td>
<td>30%-90%</td>
</tr>
<tr>
<td>Low</td>
<td>10%-30%</td>
</tr>
<tr>
<td>Minimal</td>
<td>&lt;10% at risk</td>
</tr>
</tbody>
</table>


Copyright © 2016, American Society of Health-System Pharmacists, Inc. All rights reserved.
Emetogenic Potential of IV Antineoplastic Agents

<table>
<thead>
<tr>
<th>Level</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Cisplatin, Cyclophosphamide, Paclitaxel, Fludarabine, Olanzapine</td>
</tr>
<tr>
<td></td>
<td>Epirubicin (&gt;40 mg/m²)</td>
</tr>
<tr>
<td></td>
<td>Doxorubicin (&gt;0.1 mg/kg)</td>
</tr>
<tr>
<td>Moderate</td>
<td>Albendazole (&lt;0.3 mg/kg)</td>
</tr>
<tr>
<td></td>
<td>Mitomycin (&lt;0.1 mg/kg)</td>
</tr>
<tr>
<td></td>
<td>Vinorelbine (&lt;0.3 mg/kg)</td>
</tr>
<tr>
<td></td>
<td>Idarubicin (&lt;0.2 mg/kg)</td>
</tr>
<tr>
<td></td>
<td>Mitoxantrone (&lt;0.1 mg/kg)</td>
</tr>
<tr>
<td>Minimal</td>
<td>Aut × 2 (1× 3 mg/m²)</td>
</tr>
</tbody>
</table>

**Guidelines suggest the appropriate antiemetic regimen for AH would be:**

- **a.** 5-HT₃ receptor antagonist (RA) + dexamethasone
- **b.** 5-HT₃ RA + dexamethasone + NK₁ RA
- **c.** 5-HT₃ RA + dexamethasone + olanzapine
- **d.** Any of the above
- **e.** A or C

**Neurotransmitters and Antiemetic Pathways**

- **Dopamine/DA, RAs**
- **Serpotonin/NK, RAs**
- **Substance P/IP, RAs**
- **Histamine**
- **Endorphins**
- **GABA**
- **Cannabinoids**

**Emetogenic Potential of Oral Antineoplastic Agents**

<table>
<thead>
<tr>
<th>Level</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>Alkeran, Carmustine, Cyclophosphamide (≤0.1 mg/kg/day)</td>
</tr>
<tr>
<td>High</td>
<td>Etoposide, Epoetin, Lomustine (single IV), Mitomycin, Mitoxantrone</td>
</tr>
<tr>
<td></td>
<td>Fludarabine, Gemcitabine, Idarubicin, Mitoxantrone, Paclitaxel</td>
</tr>
<tr>
<td>Minimal</td>
<td>Adriamycin, Bleomycin, Etoposide, Ifosfamide, Vinorelbine, Vinblastine</td>
</tr>
<tr>
<td>Low</td>
<td>Adriamycin, Bleomycin, Etoposide, Ifosfamide, Vinorelbine, Vinblastine</td>
</tr>
</tbody>
</table>

**ASCO, NCCN, and MASCC/ESMO Guidelines for Acute CINV**

<table>
<thead>
<tr>
<th>Emeticency</th>
<th>NCCN</th>
<th>ASCO</th>
<th>MASCC/ESMO</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>5-HT₃ RA + dexamethasone + NK₁ RA OR Olanzapine + palonosetron + dexamethasone OR Olanzapine + palonosetron + dexamethasone</td>
<td>Any 5-HT₃ RA + dexamethasone + NK₁ RA OR Olanzapine + palonosetron + dexamethasone</td>
<td>Any 5-HT₃ RA + dexamethasone + NK₁ RA OR Olanzapine + palonosetron + dexamethasone</td>
</tr>
<tr>
<td>Moderate</td>
<td>5-HT₃ RA (palonosetron preferred) + dexamethasone</td>
<td>Any 5-HT₃ RA (palonosetron preferred) + dexamethasone</td>
<td>Any 5-HT₃ RA (palonosetron preferred) + dexamethasone</td>
</tr>
<tr>
<td>Low</td>
<td>Dexamethasone</td>
<td>Any 5-HT₃ RA + palonosetron + dexamethasone</td>
<td>Any 5-HT₃ RA + palonosetron + dexamethasone</td>
</tr>
</tbody>
</table>

*HEC = highly emetogenic chemotherapy*
ASC0, NCCN, and MASCC/ESMO Guidelines for Delayed CINV

### Emetogenicity

<table>
<thead>
<tr>
<th>Emetogenicity</th>
<th>AGID</th>
<th>ASC0</th>
<th>NCCN</th>
<th>MASCC/ESMO</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Moderate</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Low</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

*unless a granisetron regimen

**unless a granisetron regimen and only if aprepitant used

***if NK, RA used on day 1

---

Netupitant/Palonosetron – A New NK₁ RA and 5-HT₃ RA Combination Therapy

- Oral, NK₁-selective, competitive RA (300 mg) in combination with a long acting 5-HT₃ receptor antagonist (0.5 mg)
- FDA approval: For the prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy
- One capsule administered approximately 1 hour prior to the start of chemotherapy
- Can be taken with or without food
- Causes inhibition of CYP3A4 which can last for multiple days
  - Dexamethasone doses should be reduced. A two-fold increase in the systemic exposure of dexamethasone was observed 4 days after single dose of netupitant.

Alozreo (netupitant and palonosetron) prescribing information. Eisai Inc. 2015 Apr.

---

Phase III Study by Aapro et al.

- Randomized phase III study evaluating the efficacy and safety of a fixed-dose combination of netupitant and palonosetron, for prevention of CINV following moderately emetogenic chemotherapy (MEC)

**Randomized 1:1**

- Oral netupitant 300 mg/palonosetron 0.50 mg + oral dexamethasone 12 mg
- Oral palonosetron 0.50 mg + oral dexamethasone 20 mg


---

Primary Endpoint: Complete Response in Delayed Phase

CR: no emesis, no rescue medication

Based on full analysis set of 1449 patients


---

Secondary Endpoints: Complete Response Overall and in Acute Phase

CR: no emesis, no rescue medication

Based on full analysis set of 1449 patients

Patient Case – AH (Continued)

AH received ondansetron/aprepitant/dexamethasone and experienced 2 episodes of acute emesis in the first 24 hours with severe nausea. What would you give for breakthrough CINV?

- Ondansetron
- Metoclopramide
- Prochlorperazine
- Lorazepam

Breakthrough CINV

- Give additional agent from a different class
- Consider around-the-clock rather than as PRN administration
- If the patient is vomiting, IV or rectal administration may be required
- Before next cycle of chemotherapy, reassess response to antiemetics in both acute and delayed setting
  - Consider an alternative regimen if needed
  - Add NK₁ RA if not previously included


Patient Case – AH (Continued)

AH received prochlorperazine around the clock with ondansetron and dexamethasone again the following day. No more emesis experienced but she still had significant nausea over the following 2 days. Which regimen would you use when she comes in for her next cycle?

- Ondansetron/aprepitant/dexamethasone
- Palonosetron/dexamethasone/olanzapine
- Palonosetron/rolapitant/dexamethasone/olanzapine

Rolapitant – a New NK₁ RA: Background and Results

- Oral, NK₁ selective, competitive receptor antagonist
- FDA approval: in combination with other antiemetic agents in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy
- The metabolic route is an important differentiating factor from other available NK₁ RAs
  - Moderate inhibitor of CYP3A4, breast cancer resistance protein (BCRP) and P-glycoprotein (Pgp)
  - Does NOT inhibit or induce CYP3A4
  - Low potential for significant drug interactions
  - No adjustment to dexamethasone required
  - Half life of 180 hours


Phase III Study by Schwartzberg et al.

- Randomized, double-blind, placebo-controlled phase III study evaluating the efficacy and safety of rolapitant for prevention of CINV after MEC

Rolapitant 180 mg + granisetron 2 mg PO + dexamethasone 20 mg PO (n=684)

Placebo + granisetron 2 mg PO + dexamethasone 20 mg PO (n=685)


Phase III Study by Schwartzberg et al.

- Primary endpoint – proportion of patients achieving a complete response (defined as no emesis or use of rescue medication) in the delayed phase (>24-120 hr after initiation of chemotherapy) in cycle 1
- Secondary endpoints:
  - Proportions of patients with complete response in the acute (0-24 hr after chemotherapy) and overall (0-120 hr) phases
  - No emesis in acute, delayed, and overall phases
  - No clinically significant nausea (maximum nausea on a visual analogue scale <25 mm) in the overall phase
  - Time-to-first emesis or use of rescue medication
- All patients received granisetron 2 mg PO days 2-3

Primary Endpoint: Complete Response in Delayed Phase

<table>
<thead>
<tr>
<th>mITT population</th>
<th>Complete Response Rate (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delayed Phase (72-120 hr)</td>
<td>61.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Acute Phase (0-24 hr)</td>
<td>80.1%</td>
<td>0.043</td>
</tr>
<tr>
<td>Overall Phase (0-120 hr)</td>
<td>57.8%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Secondary Endpoints: Complete Response Overall and in Acute Phase

<table>
<thead>
<tr>
<th>mITT population</th>
<th>Complete Response Rate (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delayed Phase (72-120 hr)</td>
<td>61.6%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Acute Phase (0-24 hr)</td>
<td>80.1%</td>
<td>0.143</td>
</tr>
<tr>
<td>Overall Phase (0-120 hr)</td>
<td>57.8%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Potential Advantages/Challenges with Oral NK₁ RA

**Challenges**
- Patients unable to tolerate PO
- Cost, procurement, and reimbursement
- Administration challenges
  - Drug availability
  - Timing of dosing
  - Anticipatory N/V

**Potential advantages**
- Administration as an all-oral combination agent
- No injection site reactions
- A single-dose schedule given on the day of chemotherapy only (netupitant/palonosetron)
- A dexamethasone-sparing regimen
  - No steroids given on days 2-4 in any of the netupitant/palonosetron trials

Phase III Trial of Olanzapine combined with NK₁ RA, 5-HT₃ RA, and Dexamethasone

- Randomized, double-blind, phase III trial in chemotherapy-naïve patients receiving cisplatin (>70 mg/m²) or cyclophosphamide-anthracycline-based chemotherapy

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Olanzapine 10 mg PO + aprepitant* 125 mg PO + SHT, RA PO + dexamethasone 12 mg PO (n=202)</th>
<th>Placebo + aprepitant* 125 mg PO + SHT, RA PO + dexamethasone 12 mg PO (n=199)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/ vomiting</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Phase III Trial of Olanzapine combined with NK₁ RA, 5-HT₃ RA, and Dexamethasone

<table>
<thead>
<tr>
<th>End point</th>
<th>3 Drugs + olanzapine (n = 202)</th>
<th>3 Drugs + placebo (n = 199)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Nausea: Acute</td>
<td>74%</td>
<td>45%</td>
<td>&lt;0.0006</td>
</tr>
<tr>
<td>No Nausea: Delayed</td>
<td>42%</td>
<td>24%</td>
<td>&lt;0.0006</td>
</tr>
<tr>
<td>No Nausea: Overall</td>
<td>39%</td>
<td>22%</td>
<td>&lt;0.0006</td>
</tr>
<tr>
<td>Complete Response: Acute</td>
<td>83%</td>
<td>65%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Complete Response: Delayed</td>
<td>67%</td>
<td>52%</td>
<td>&lt;0.0078</td>
</tr>
<tr>
<td>Complete Response: Overall</td>
<td>64%</td>
<td>41%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sedation scores &gt;5 on day 2</td>
<td>20%</td>
<td>7%</td>
<td>Not reported</td>
</tr>
</tbody>
</table>

Patient Case – AH (Continued)

After surgical resection there was an area of tumor that could not be removed so it is decided to add radiation therapy. Which antiemetic regimen would you give AH?

a. Palonosetron/dexamethasone
b. Palonosetron/dexamethasone/fosaprepitant
c. Palonosetron/dexamethasone/olanzapine
d. Olanzapine
Olanzapine versus Fosaprepitant for the Prevention of Nausea and Vomiting in Patients Receiving Concurrent Chemoradiation Treatment

- Randomized, double-blind, phase III trial in chemotherapy and radiation therapy naïve patients receiving concurrent local radiation and cisplatin, >70 mg/m², based chemotherapy

<table>
<thead>
<tr>
<th>Olanzapine (n=51)</th>
<th>Fosaprepitant (n=49)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete response: Acute</td>
<td>88%</td>
<td>84%</td>
</tr>
<tr>
<td>Complete response: Delayed</td>
<td>76%</td>
<td>73%</td>
</tr>
<tr>
<td>Complete response: Overall</td>
<td>76%</td>
<td>73%</td>
</tr>
<tr>
<td>No Nausea: Acute</td>
<td>86%</td>
<td>77%</td>
</tr>
<tr>
<td>No Nausea: Delayed</td>
<td>71%</td>
<td>41%</td>
</tr>
<tr>
<td>No Nausea: Overall</td>
<td>71%</td>
<td>41%</td>
</tr>
</tbody>
</table>

- No grade 3 or 4 toxicities
- CR and control of nausea in subsequent chemotherapy cycles were equal to or greater than cycle one for both regimens
- CR: no emesis, no rescue

Navari R et al. / Clin Oncol 33, 2015 (suppl; abstr 9502).

Olanzapine Summary

- Improvement in nausea control
- Provides 4-drug option for CINV
- Option for a regimen without NK₁ RA
- Major side effect is sedation

Impact of CINV on Quality of Life

- HOPA patient survey
  - 400 patients receiving chemotherapy
- Results
  - Nearly 3 of 4 patients who had experienced CINV said it made them want to avoid future chemo, and the majority said it had caused them to alter their lives
    - 56% cancelled personal plans
    - 46% changed eating habits
    - 43% avoided exercise or physical activity
    - 38% called in sick to work
    - 30% had more negative outlook on prognosis

www.hoparx.org/resources/default/talkcinv.htm

The Pharmacist’s Role in Managing CINV

- Participate in development or implementation of institution-specific guidelines
  - Tailor guidelines to patient population
- Ensure adherence to guidelines
  - Build into EMR order sets
  - Part of chemotherapy order verification process
- Participate in planning patient therapy
  - Assess for additional CINV risk factors
- Educate oncology team, including physicians, nurses, physician assistants, and pharmacists
- Provide patient education
  - Address insurance obstacles
  - Improve adherence with greater involvement in patient education
- Assess initial and ongoing patient risk factors
- Create medication management protocols

ANGLOR Study: CINV Decreases Quality of Life

- Functional Living Index - Emesis
- Nausea has a greater negative impact on quality of life than vomiting, P = .0097
- HEC has a greater negative impact on quality of life than MEC, P = .0049

ANCOHR=Anti-nausea Chemotherapy Registry

Developing Local Guidelines Using a Consensus of National/International Guidelines Will Help to...

- Optimize patient care!
- Standardize the ordering, preparation, and administration of antiemetic therapies
- Serve as an educational tool for new staff
- Provide a systematic method of assessment and adjustment of treatment in challenging patients
- Aid in containing the cost of medications
- Avoid unnecessary healthcare resource utilization

Pharmacist-driven Management Can Improve Adherence to Institutional Protocol and Guidelines

- Single-center chart review study at major academic medical center
- 106 patients receiving inpatient chemotherapy
  - 55 managed according to pharmacist-driven protocol; 51 by physician-driven protocol
- In physician-managed group, 20% of patients received excessive CINV prophylaxis vs. 2% in pharmacist-managed group
- Number of breakthrough doses (primary end point) did not differ between groups
  - Excessive prophylaxis could have contributed to excess cost without improved results

<table>
<thead>
<tr>
<th>Adherence to guidelines</th>
<th>Pharmacist-managed group (n = 55)</th>
<th>Physician-managed group (n = 51)</th>
<th>All patients (n = 106)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes, number (%)</td>
<td>47 (85)*</td>
<td>17 (33)</td>
<td>64 (60)</td>
</tr>
<tr>
<td>No, number (%)</td>
<td>8 (15)</td>
<td>34 (67)</td>
<td>42 (40)</td>
</tr>
</tbody>
</table>

* P < 0.001 vs. physician-managed group

Key Takeaways

- **Key Takeaway #1**
  - CINV is still a significant problem for many patients, especially delayed CINV
- **Key Takeaway #2**
  - A therapeutic approach of combining antiemetics with different mechanisms gives best results in preventing CINV
- **Key Takeaway #3**
  - Pharmacists should play key roles in helping to assess and manage CINV

Consequences of Overtreatment and Undertreatment

- Financial costs
  - Copays
- Side effects
  - Constipation, headaches
  - Blood sugars, insomnia
- Excess pill burden
- Patient confusion
- Nonadherence

- Uncontrolled CINV
- Anticipatory CINV
- Poorly controlled CINV may result in
  - Increased utilization of healthcare resources
  - Clinic visits for fluids and/or additional antiemetics
  - Hospitalization
  - Dehydration and electrolyte imbalance
  - Impaired health-related quality of life
  - Negative impact on activities of daily living
  - Hesitancy to continue with potentially curative treatment

Copyright © 2016, American Society of Health-System Pharmacists, Inc. All rights reserved.
Self-assessment Questions

1. What are AH’s risk factors for chemotherapy-induced nausea and vomiting (CINV)?
   a. Female gender
   b. Younger Age
   c. Previous History of N/V
   d. Low Alcohol Intake
   e. All of the above

2. What is the emetogenicity of AH’s chemotherapy regimen?
   a. High
   b. Moderate
   c. Low
   d. Minimal

3. The combination drug netupitant/palonosetron can be taken with or without food.
   a. True
   b. False

Answers

1. e
2. b
3. a