This is How We’re Going to Do It: Improving Care and Maximizing Value in Chemotherapy-Induced Nausea and Vomiting

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Disclosures

• None
Objectives

• Summarize quality measures for chemotherapy-induced nausea and vomiting (CINV)
• Assess current CINV national guidelines
• Discuss MOQC performance and next steps
Abbreviations

- 5HT3RA – Serotonin Receptor Antagonist
- ABIM – American Board of Internal Medicine
- ASCO – American Society of Clinical Oncology
- CINV – Chemotherapy Induced Nausea and Vomiting
- DEX – Dexamethasone
- ESMO – The European Society of Medical Oncology
- HEC – Highly Emetic Chemotherapy
- MASCC – Multinational Association of Supportive Care in Cancer
- MEC – Moderately Emetic Chemotherapy
- MOQC – Michigan Oncology Quality Consortium
- NK1RA – Neurokinin-1 Receptor Antagonist
- OLZ – Olanzapine
- QOPI – Quality Oncology Practice Initiative
- SMT – Symptom and Toxicity Module (within QOPI)
# CINV – Background

<table>
<thead>
<tr>
<th>Acute</th>
<th>Delayed</th>
<th>Anticipatory</th>
<th>Breakthrough</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Minutes to hours following chemotherapy</td>
<td>• More than 24 hrs after chemotherapy</td>
<td>• Approximately 20% of patients</td>
<td>• Occurs despite prophylaxis</td>
</tr>
<tr>
<td>• Chemotherapy classified by risk</td>
<td>• More common with:</td>
<td>• Often predicated on the development of CINV following prior therapy</td>
<td>• Utilize other agents/mechanisms</td>
</tr>
<tr>
<td>• Patient risk factors</td>
<td>• Carboplatin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Schedule prophylactic</td>
<td>• Cisplatin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>medications</td>
<td>• Cyclophosphamide</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• Doxorubicin</td>
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</tr>
</tbody>
</table>

**Patient-specific risk factors:** Age <50 years, female gender, no/minimal prior history of alcohol use, prior CINV, history of morning sickness during pregnancy, prone to motion sickness, anxiety/high pretreatment expectation of severe nausea

Emetic Risk Classifications

Intravenous Therapy

- High: > 90%
- Moderate: 30-90%
- Low: 10-30%
- Minimal: <10%

Quality Measures – CINV

• ASCO – QOPI
  • SMT28 – NK1 Receptor Antagonist and Olanzapine prescribed or administered with high emetic risk chemotherapy
  • SMT28a – NK1 Receptor Antagonist or Olanzapine administered for low or moderate emetic risk Cycle 1 chemotherapy

• Choosing Wisely (ABIM)
  • Don’t give patients starting on a chemotherapy regimen that has low or moderate risk of causing nausea and vomiting antiemetic drugs intended for use with a regimen that has a high risk of causing nausea and vomiting.

Quality Measures – CINV

History/Recent Changes

• Addition of Olanzapine to both SMT28 and SMT28a
• Emetic classification of carboplatin and anthracycline + cyclophosphamide (AC)-containing regimens
  • AC-containing: Historically MEC
    • NCCN changed to HEC in 2005
    • ASCO & MASCC created a HEC subset for AC in 2006
  • Carboplatin: Historically MEC (60-90% acute emesis)
    • Evidence for improved CR in overall/delayed phases with NK1RA
    • NCCN changed AUC $\geq 4$ to HEC in 2017
    • ASCO & MASCC created a subset for carbo AUC $\geq 4$ and recommend a 3-drug regimen
CINV – Guidelines

• **ASCO**
  • Last updated – April 2017

• **NCCN**
  • www.nccn.org/professionals/physician_gls/pdf/antiemesis
  • Last updated – February 2019

• **MASCC/ESMO**
  • Last updated – March 2016

• **ASCO, NCCN, MASCC/ESMO:** a comparison of antiemetic guidelines for the treatment of chemotherapy-induced nausea and vomiting in adult patients
  • Razvi Y, et al. *Supportive Care in Cancer* 2019;27(1):87-95
HEC – Acute Prophylaxis Day 1

<table>
<thead>
<tr>
<th>ASCO</th>
<th>NCCN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High (non-carbo/AC)</strong>&lt;br&gt;4 drug regimen:&lt;br&gt;NK1RA + 5HT3RA + Dex + OLZ</td>
<td><strong>3 options (3-4 drug regimen):</strong>&lt;br&gt;NK1RA + 5HT3RA + Dex&lt;br&gt;or&lt;br&gt;OLZ + palonosetron + Dex&lt;br&gt;or&lt;br&gt;OLZ + NK1RA + 5HT3RA + Dex</td>
</tr>
<tr>
<td><strong>Anthracycline + Cyclophosphamide</strong>&lt;br&gt;4 drug regimen:&lt;br&gt;NK1RA + 5HT3RA + Dex + OLZ</td>
<td>Same as above</td>
</tr>
<tr>
<td><strong>Carboplatin AUC ≥ 4</strong>&lt;br&gt;3 drug regimen:&lt;br&gt;NK1RA + 5HT3RA + Dex</td>
<td>Same as above</td>
</tr>
</tbody>
</table>

# HEC – Prophylaxis Days 2-4

<table>
<thead>
<tr>
<th>ASCO</th>
<th>NCCN</th>
</tr>
</thead>
</table>
| **High (non-carbo/AC)** | Dex + OLZ days 2, 3, 4 + aprepitant 80 mg days 2, 3 (if aprepitant used day 1) | 3 options:  
Dex days 2, 3, 4 + aprepitant 80 mg days 2,3 (if aprepitant on day 1)  
or  
OLZ days 2, 3, 4  
or  
OLZ + Dex days 2, 3, 4 + aprepitant 80 mg days 2,3 (if aprepitant on day 1) |
| **Anthracycline + Cyclophosphamide** | OLZ days 2, 3, 4 + aprepitant 80 mg days 2, 3 (if aprepitant used day 1) | Same as above |
| **Carboplatin AUC > 4** | Dex days 2,3 + aprepitant 80 mg days 2, 3 (if aprepitant used day 1) | Same as above |
MEC – Acute Prophylaxis Day 1

<table>
<thead>
<tr>
<th>ASCO</th>
<th>NCCN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>2 drug regimen: 5HT3RA + Dex</td>
</tr>
<tr>
<td></td>
<td>3 options (2-3 drug regimen): 5HT3RA + Dex</td>
</tr>
<tr>
<td></td>
<td>or OLZ + palonosetron + Dex</td>
</tr>
<tr>
<td></td>
<td>or NK1RA + 5HT3RA + Dex (only for select patients w additional risk factors or previous tx failure with 5HT3RA/Dex alone)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>ASCO</th>
<th>NCCN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>Dex days 2, 3</td>
<td>3 options: 5HT3RA or Dex days 2, 3 (monotherapy) or OLZ days 2, 3 or Dex days 2, 3 + aprepitant 80 mg days 2, 3 (if aprepitant on day 1)</td>
</tr>
</tbody>
</table>

Olanzapine Data

• Prophylaxis in MEC and HEC added to standard therapy (following slides)
• HEC – 3 drug OLZ vs 3 drug aprepitant (non-inferiority)
  • CR 0-120: 77% OLZ vs 73% aprepitant, p = NS
  • No nausea 0-120: 69% OLZ vs 38% aprepitant, p<0.05
• OLZ use following NK1RA failure
  • 74% complete response rate 0-120
• Phase III Alliance trial – ongoing (NCT03578081)
  • OLZ + NK1RA vs OLZ (both with 5HT3RA/Dex) in HEC
Phase III – Olanzapine vs. Placebo in HEC

Patients
- Cycle #1 of HEC: AC or Cisplatin ≥ 70 mg/m²

Co-primary endpoints
- No nausea time 0-120 hrs
- No nausea time 0-24 hrs
- No nausea time 25-120 hrs

Randomize 1:1

Fosaprepitant or Aprepitant (day 1)
Palonosetron, Granisetron or Ondansetron (day 1)
Dexamethasone 12 mg (PO day 1)
+ 
Olanzapine 10 mg (PO day 1, 2, 3, 4) (n = 192)

Fosaprepitant or Aprepitant (day 1)
Palonosetron, Granisetron or Ondansetron (day 1)
Dexamethasone 12 mg (PO day 1)
+ 
Placebo 10 mg (PO day 1, 2, 3, 4) (n = 188)

All patients – DEX 8 mg PO once - days 2, 3, 4

No nausea 0-120: 37% (OLZ) vs. 22% (placebo), $p = 0.002$

NK-1 RA regimen + OLZ is superior to NK-1 RA regimen

Phase III – Olanzapine vs. Placebo in MEC

Patients
• Cycle #1 of MEC: AC or Cisplatin ≥ 70 mg/m²

Primary endpoint
• CR 0-24 hrs

Secondary endpoints
• CR 24-120 hrs
• Overall CR 0-120 hrs
• Proportion of significant nausea (VAS)
• Rescue med use
• QOL

Palonosetron 0.25 mg (day 1)
Dexamethasone 12 mg (PO day 1)
+ Olanzapine 10 mg (PO day 1, 2, 3, 4) (n = 29)

Palonosetron 0.25 mg (day 1)
Dexamethasone 12 mg (PO day 1)
+ Placebo 10 mg (PO day 1, 2, 3, 4) (n = 27)

No stat difference in CR between groups for acute, delayed, or overall
Significant nausea lower with OLZ – 17% vs 44% (p = 0.032)
Freq of rescue med lower with OLZ – 0.03+0.10 vs 1.88±2.88 (p=0.002)
Functional Living Index (QOL) better with OLZ (p=0.009)

Olanzapine Controversies

- Side effects
  - Common with short term use: sedation, dry mouth, constipation, orthostasis
  - Rare with short term use: hyperglycemia, hypercholesterolemia, EPS, increased appetite, weight gain
  - No warning for QTc prolongation in FDA label
- 5 mg vs 10 mg dose
- Drug interactions – use of rescue agent
- Fear of prescribing
## Cost Information

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dose</th>
<th>Schedule</th>
<th>Price Per Dose (USD)</th>
<th>Total Cost Per Treatment Cycle (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NK₁ receptor antagonists</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aprepitant oral</td>
<td>125 mg</td>
<td>Prechemotherapy, one dose</td>
<td>284.01</td>
<td>284.01</td>
</tr>
<tr>
<td>Aprepitant oral</td>
<td>80 mg</td>
<td>Once daily on days 2, 3</td>
<td>182.14</td>
<td>364.28</td>
</tr>
<tr>
<td>Fosaprepitant IV</td>
<td>150 mg</td>
<td>Prechemotherapy, one dose</td>
<td>299.87</td>
<td>299.87</td>
</tr>
<tr>
<td>Rolapitant</td>
<td>180 mg</td>
<td>Prechemotherapy, one dose</td>
<td>610.50</td>
<td>610.50</td>
</tr>
<tr>
<td><strong>Combination products</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Netupitant/palonsetron</td>
<td>300 mg</td>
<td>Prechemotherapy, one dose</td>
<td>632.35</td>
<td>632.35</td>
</tr>
<tr>
<td><strong>Antipsychotics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olanzapine (generic)</td>
<td>5 mg</td>
<td>Once daily on days 1-3</td>
<td>6.50</td>
<td>6.50</td>
</tr>
<tr>
<td>Olanzapine (generic)</td>
<td>10 mg</td>
<td>Once daily on days 1-3</td>
<td>6.50</td>
<td>6.50</td>
</tr>
<tr>
<td>Olanzapine (brand)</td>
<td>5 mg</td>
<td>Once daily on days 1-3</td>
<td>15.07</td>
<td>43.22</td>
</tr>
<tr>
<td>Olanzapine (brand)</td>
<td>10 mg</td>
<td>Once daily on days 1-3</td>
<td>22.21</td>
<td>64.62</td>
</tr>
</tbody>
</table>


*2016 pricing*
Summary of MOQC CINV Performance

QOPI and Practice Survey Results
CINV Quality Measures

ASCO-QOPI

- SMT28 – NK1 Receptor Antagonist and Olanzapine prescribed or administered with high emetic risk chemotherapy
  - HEC → 4-drug regimen
  - Higher is better
- SMT28a – NK1 Receptor Antagonist or Olanzapine administered for low or moderate emetic risk Cycle 1 chemotherapy
  - MEC → 2-drug regimen
  - Remove Carbo AUC > 4 from collection
  - Lower is better
SMT28 Trend

NK1RA and Olanzapine for HEC

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Proportion

Time Period

2014 2015 2016 2017

MOQC QOPI
SMT28a Trend

NK1RA or Olanzapine for MEC or low risk – lower is better
Spring/Fall 2018 – SMT28a

Lower is better

VBR measure 2020 target – 30%
MOQC Practice Survey

Antiemetic Standards for select HEC/MEC regimens

• 32/43 (74%) practices responded
• 29/32 (91%) have orders pre-populated within an EMR
• 5 HEC regimens
• 2 AC-based regimens
• 4 Carbo AUC ≥ 4 regimens
• 7 MEC regimens
HEC Regimens

• Lung
  • Gemcitabine/Cisplatin
  • Cisplatin/Etoposide

• Head and Neck
  • Cisplatin (100 mg/m2)
  • Cisplatin (30-40 mg/m2) + XRT

• Bladder
  • Dose Dense MVAC
AC and Carbo Regimens

AC – Containing Regimens
• Breast
  • Dose Dense AC
• NHL
  • R-CHOP

Carboplatin AUC > 4 Regimens
• Breast
  • TCH +/- Pertuzumab
• Lung
  • Carbo/Paclitaxel
  • Carbo/Etoposide
• Ovarian
  • Carboplatin
MEC Regimens

- Breast
  - TC
- Colorectal
  - FOLFOX
  - FOLFIRI
  - CapeOx

- Head and Neck
  - Carbo (AUC 1.5) + RT
- NHL
  - R-Bendamustine
- Pancreatic
  - FOLFIRINOX
# Survey Results – HEC Regimens

<table>
<thead>
<tr>
<th></th>
<th>NK1RA</th>
<th>OLZ</th>
<th>NK1RA + OLZ</th>
<th>NK1RA OR OLZ</th>
<th>5HT3RA</th>
<th>DEX</th>
</tr>
</thead>
<tbody>
<tr>
<td>HEC</td>
<td>87%</td>
<td>22%</td>
<td>19%</td>
<td>68%</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td>AC-Regimens</td>
<td>72%</td>
<td>21%</td>
<td>19%</td>
<td>53%</td>
<td>100%</td>
<td>94%</td>
</tr>
<tr>
<td>Carbo AUC &gt; 4</td>
<td>46%</td>
<td>17%</td>
<td>12%</td>
<td>38%</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>69%</td>
<td>20%</td>
<td>18%</td>
<td>54%</td>
<td>99%</td>
<td>98%</td>
</tr>
</tbody>
</table>
## Survey Results – MEC Regimens

<table>
<thead>
<tr>
<th></th>
<th>NK1RA</th>
<th>OLZ</th>
<th>NK1RA AND/OR OLZ</th>
<th>5HT3RA</th>
<th>DEX</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MEC</strong></td>
<td>18%</td>
<td>8%</td>
<td>23%</td>
<td>100%</td>
<td>98%</td>
</tr>
</tbody>
</table>

Range = 7 – 45%

- **NK1RA and/or OLZ**
  - FOLFIRINOX: 47%
  - TC: 28%
  - FOLFOX: 22%
  - FOLFIRI: 22%
  - Carbo + XRT: 16%
  - R-Bendamustine: 13%
  - CapeOx: 13%
Summary

• National Guidelines for CINV are not consistent nor are they easy to follow
• HEC Regimens
  • 3 drug vs 3 drug: OLZ non-inferior to NK1RA
  • 3 drug vs 4 drug: NK1RA + OLZ > NK1RA alone
  • Pending: OLZ + NK1RA compared to OLZ alone
• NK1RA are not recommended up front in MEC
• Ideal dosing of OLZ is under evaluation (5 mg vs 10 mg)
MOQC Next Steps

• Work to address pre-printed/pre-populated orders to be consistent with national guidelines and clinical data
• Standardize QOPI collection to account for carboplatin AUC > 4 and to parse out NK1RA from olanzapine
• Resources available to practices and on the MOQC website
Patient Perspective
Questions