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

Emily Mackler, PharmD, BCOP

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

moqc.org

Disclosures

- None

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Objectives

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

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

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)

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

CINV – Background

Acute	Delayed	Anticipatory	Breakthrough

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

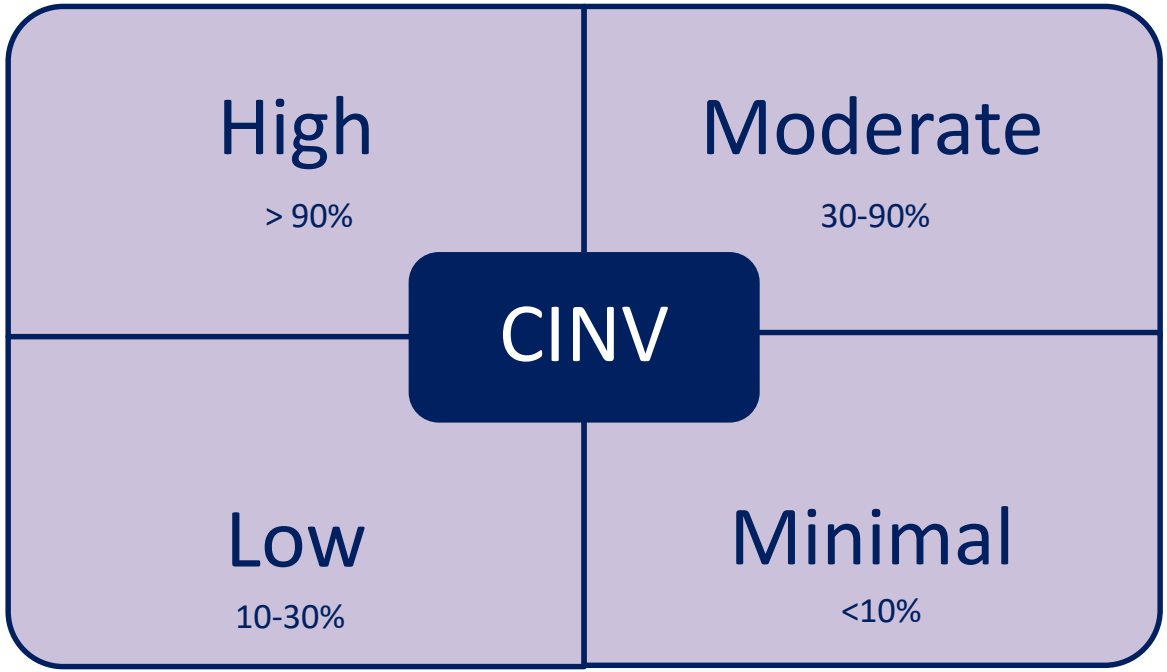
Patient-specific risk factors: Age <50 years, female gender, no/minimal prior history of alcohol use, prior CINV, history of morning sickness during pregnancy, prone to motion sickness, anxiety/high pretreatment expectation of severe nausea

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Gregory RE, et al. Drugs. 1998;55:173-189. National Comprehensive Cancer Network (NCCN) Antiemesis Guidelines V1.2019.

Emetic Risk Classifications

Intravenous Therapy



MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Kris MG, et al. J Clin Oncol. 2006;24(18):2932-47.

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.

VBR measure

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

practice.asco.org/quality-improvement/quality-programs/quality-oncology-practice-initiative/qopi-related-measures; www.choosingwisely.org

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

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

CINV – Guidelines

- ASCO
  - Hesketh P, et al. *J Clin Oncol* 2017;35(28):3240-3261.
  - Last updated – April 2017
- NCCN
  - www.nccn.org/professionals/physician_gls/pdf/antiemesis
  - Last updated – February 2019
- MASCC/ESMO
  - Roila F, et al. *Annals of Oncology* 2016;27(Supp5):v119-v133.
  - 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

	ASCO	NCCN
High (non-carbo/AC)	4 drug regimen: NK1RA + 5HT3RA + Dex + OLZ	3 options (3-4 drug regimen): NK1RA + 5HT3RA + Dex or OLZ + palonosetron + Dex or OLZ + NK1RA + 5HT3RA + Dex
Anthracycline + Cyclophosphamide	4 drug regimen: * NK1RA + 5HT3RA + Dex + OLZ	Same as above
Carboplatin AUC $\geq$ 4	3 drug regimen: NK1RA + 5HT3RA + Dex	Same as above

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Hesketh P, et al. *J Clin Oncol* 2017; Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis V.1.2019.

HEC –Prophylaxis Days 2-4

	ASCO	NCCN
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 $\geq$ 4	Dex days 2,3 + aprepitant 80 mg days 2, 3 (if aprepitant used day 1)	Same as above

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Hesketh P, et al. *J Clin Oncol* 2017; Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis V.1.2019. Accessed 6.17.19 To view most recent and complete version of the guideline go to NCCN.org.

MEC – Acute Prophylaxis Day 1

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

MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Hesketh P, et al. *J Clin Oncol* 2017; Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis V.1.2019.

MEC –Prophylaxis Days 2-3

	ASCO	NCCN
Moderate	Dex days 2, 3	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)

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Hesketh P, et al. *J Clin Oncol* 2017; Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Antiemesis V.1.2019.

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
  - Navari RM, et al. J Support Oncol. 2011;9(5):188-95
- OLZ use following NK1RA failure
  - 74% complete response rate 0-120
  - Mehra N, et al. Med Oncol 2017;35(1):12
- 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/m^2

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)

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

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)

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

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

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

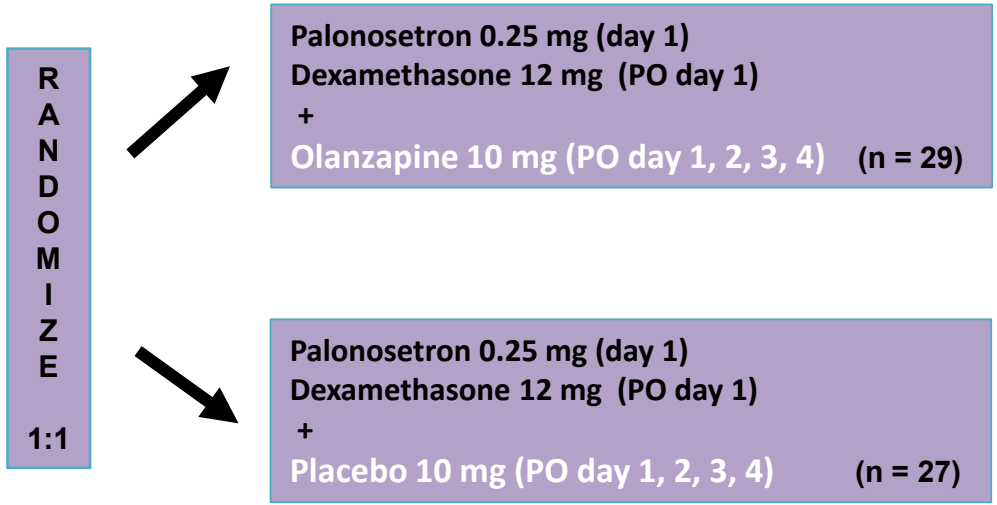
Berger M HOPA 2019 Annual Mtg. Navari RM et al. *N Engl J Med* 2016;375:134-42

Phase III – Olanzapine vs. Placebo in MEC

Patients
- Cycle #1 of MEC: AC or Cisplatin ≥ 70 mg/m^2

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



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)

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Jeon SY, et al. Cancer Res Treat. 2019;51(1):90-97

Olanzapine Controversies

- Side effects
  - Common w short term use: sedation, dry mouth, constipation, orthostasis
  - Rare w 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

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Cost Information

Agent	Dose	Schedule	Price Per Dose (USD)	Total Cost Per Treatment Cycle (USD)
NK_1 receptor antagonists				
Aprepitant oral	125 mg	Prechemotherapy, one dose	284.01	284.01
Aprepitant oral	80 mg	Once daily on days 2, 3	182.14	364.28
Fosaprepitant IV	150 mg	Prechemotherapy, one dose	299.87	299.87
Rolapitant	180 mg	Prechemotherapy, one dose	610.50	610.50
Combination products				
Netupitant/palonsetron)	300 mg/0.5 mg	Prechemotherapy, one dose	632.35	632.35
Antipsychotics				
Olanzapine (generic)	5 mg	Once daily on days 1-3	6.50	6.50
Olanzapine (generic)	10 mg	Once daily on days 1-3	6.50	6.50
Olanzapine (brand)	5 mg	Once daily on days 1-3	15.07	43.22
Olanzapine (brand)	10 mg	Once daily on days 1-3	22.21	64.62

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Hesketh P, et al. *J Clin Oncol* 2017
*2016 pricing

Summary of MOQC CINV Performance

QOPI and Practice Survey Results

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

CINV Quality Measures

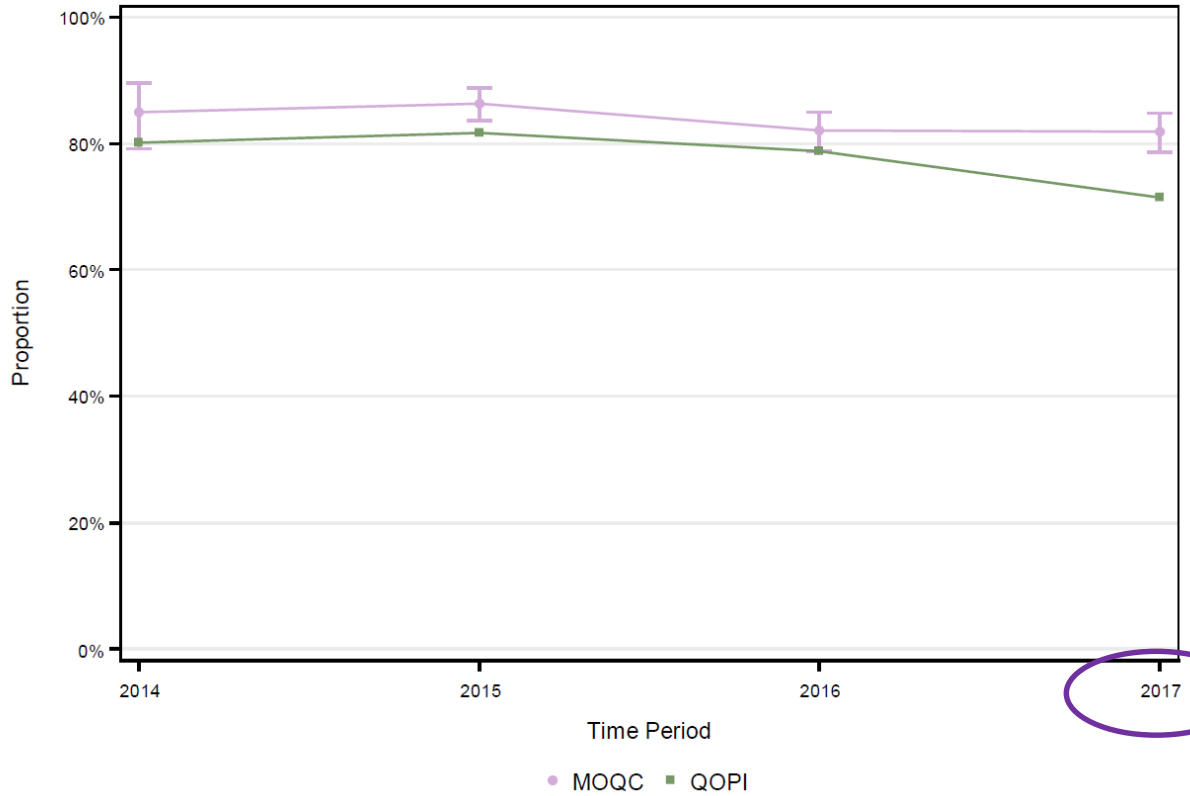
ASCO-QOPI

- 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 $\geq$ 4 from collection
  - Lower is better

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

SMT28 Trend

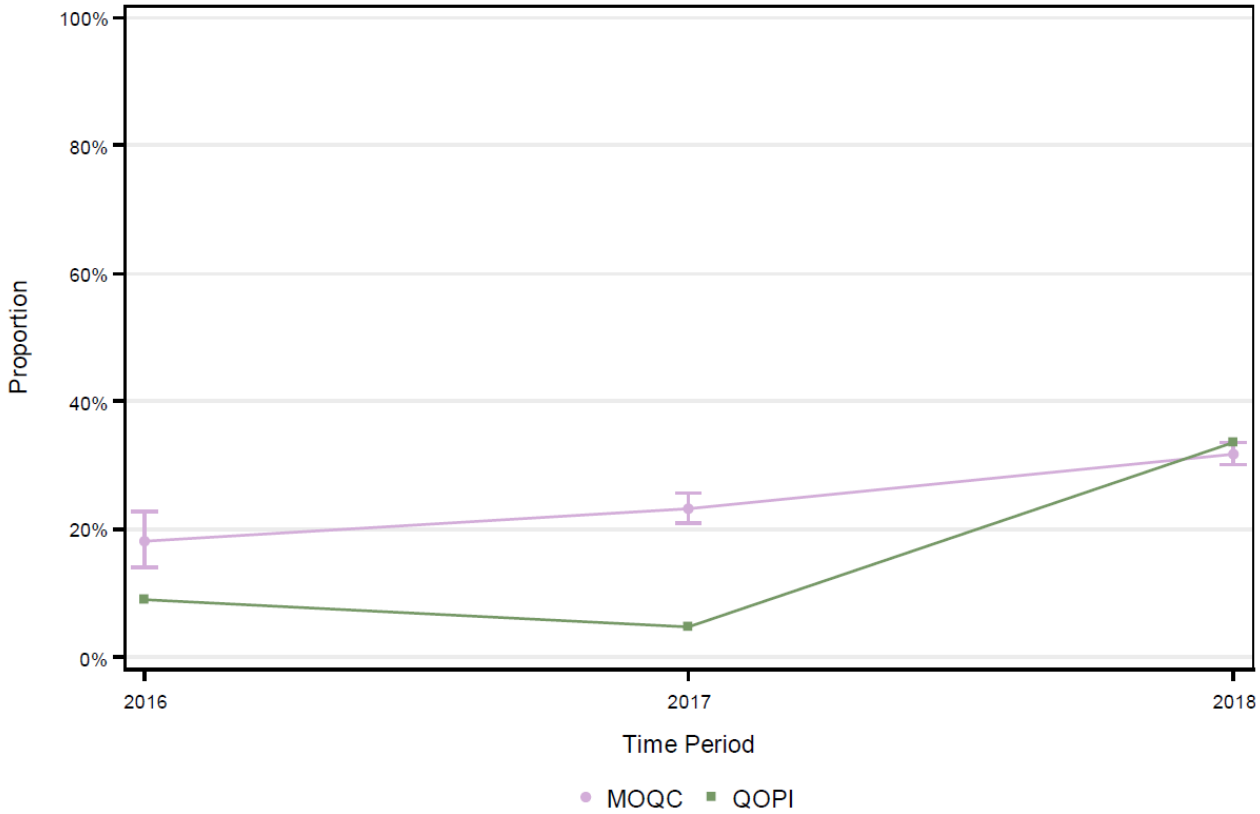
NK1RA ~~and Olanzapine~~ for HEC



MICHIGAN
QUALITY CC

SMT28a Trend

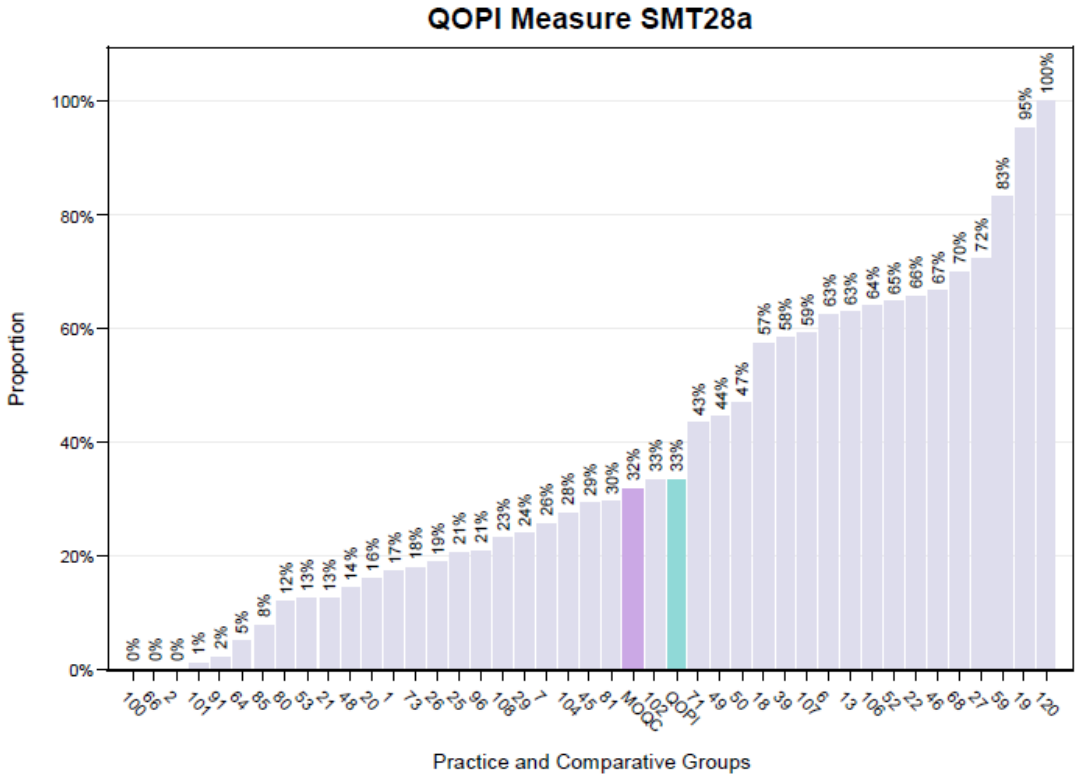
NK1RA or Olanzapine for MEC or low risk – lower is better



MICHIGA
QUALITY

Spring/Fall 2018 – SMT28a

Lower is better



VBR measure 2020 target – 30%

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

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 $\geq$ 4 regimens
- 7 MEC regimens

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

HEC Regimens

- Lung
  - Gemcitabine/Cisplatin
  - Cisplatin/Etoposide
- Head and Neck
  - Cisplatin (100 mg/m2)
  - Cisplatin (30-40 mg/m2) + XRT
- Bladder
  - Dose Dense MVAC

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

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

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

MEC Regimens

- Breast
  - TC
- Colorectal
  - FOLFOX
  - FOLFIRI
  - CapeOx
- Head and Neck
  - Carbo (AUC 1.5) + RT
- NHL
  - R-Bendamustine
- Pancreatic
  - FOLFIRINOX

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Survey Results – HEC Regimens

	NK1RA	OLZ	NK1RA + OLZ	NK1RA OR OLZ	5HT3RA	DEX
HEC	87%	22%	19%	68%	99%	99%
AC-Regimens	72%	21%	19%	53%	100%	94%
Carbo AUC ≥ 4	46%	17%	12%	38%	99%	99%
TOTAL	69%	20%	18%	54%	99%	98%

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Survey Results – MEC Regimens

	NK1RA	OLZ	NK1RA AND/OR OLZ	5HT3RA	DEX
MEC	18%	8%	23%	100%	98%

Range = 7 – 45%

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

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

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
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

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 $\geq$ 4 and to parse out NK1RA from olanzapine
- Resources available to practices and on the MOQC website

MOQC
MICHIGAN ONCOLOGY QUALITY CONSORTIUM

Patient Perspective

MOQC
MICHIGAN ONCOLOGY
QUALITY CONSORTIUM

Questions

MOQC
MICHIGAN ONCOLOGY
QUALITY CONSORTIUM