2020 NCODA Fall Summit

Putting Positive Quality Interventions Into Action: Consistent Clinical Standards for Medically Integrated Teams

Ginger Blackmon, PharmD | NCODA (*moderator*)

&

Expert Panel (*listed on next slide*)

#NCODASummit20

Expert Panel

Thomas Butler, MD | *Mitchell Cancer Institute - University of South Alabama*

Chara Reid, PharmD | *Illinois Cancer Specialists*

Ernestine Wigelsworth, PharmD | *Cancer Specialists of North Florida*

Brittney Carden, PharmD | *Mitchell Cancer Institute- University of South Alabama*

Tamara Weinberg RN, BSN, OCN, ONN-CG | *AON Pharmacy, LLC*

Alicia Barnes, CPhT | *Summit Cancer Centers*

NCODA Defines Medically Integrated Dispensing (MID):

A dispensing pharmacy within an oncology center of excellence that promotes a patient-centered, multidisciplinary team approach. The MID is an outcome-based collaborative and comprehensive model that involves oncology health care professionals and other stakeholders who focus on the continuity of coordinated, quality care and therapies for cancer patients.

Medically Integrated Team

- Members of the multidisciplinary team working together to promote positive outcomes and high-quality care for patients.

Please describe your clinic setting and MID/Medically Integrated Team

The Challenges:

- Growing complexity of oral and IV oncology therapies
- Continual changing and evolving of these therapies
- Information overload
- Staff training and communication
- Financial toxicity

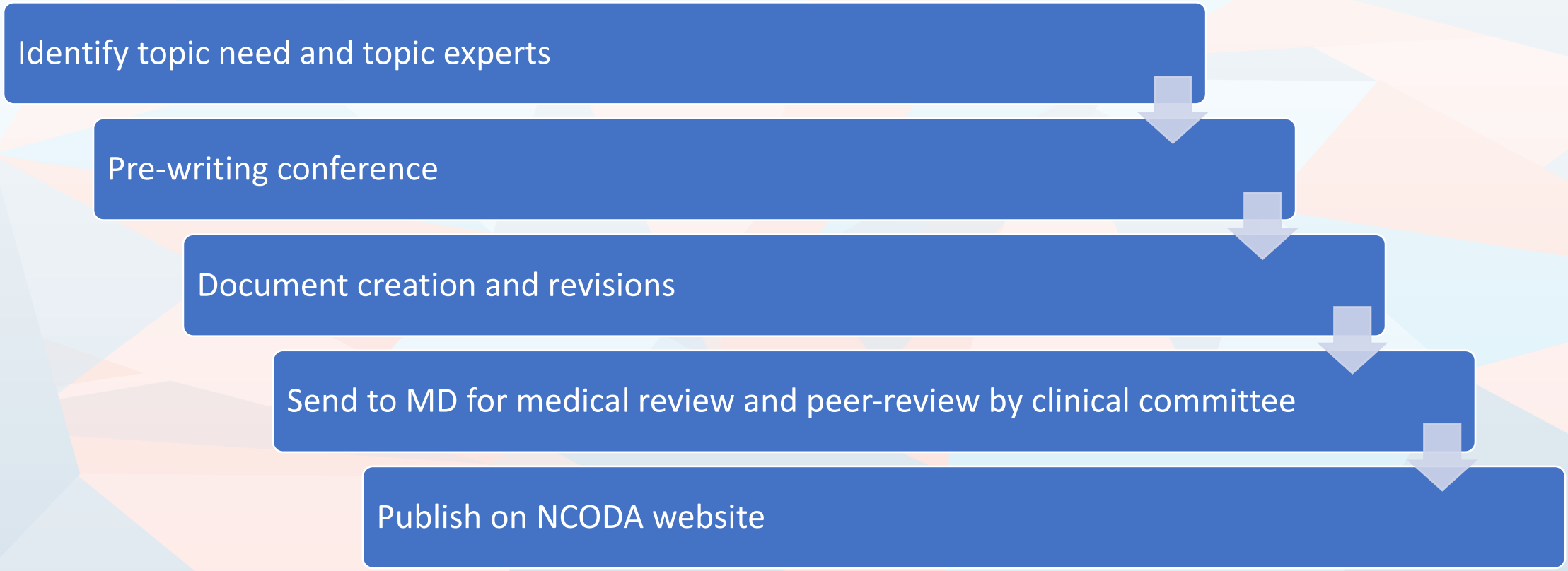
The Positive Quality Intervention (PQI)

By providing Quality Standards and effective practices around a specific aspect of cancer care, PQIs equip the entire multidisciplinary care team with a sophisticated yet concise resource for managing patients receiving oral or IV oncolytics.

Explanation and Purpose of PQIs

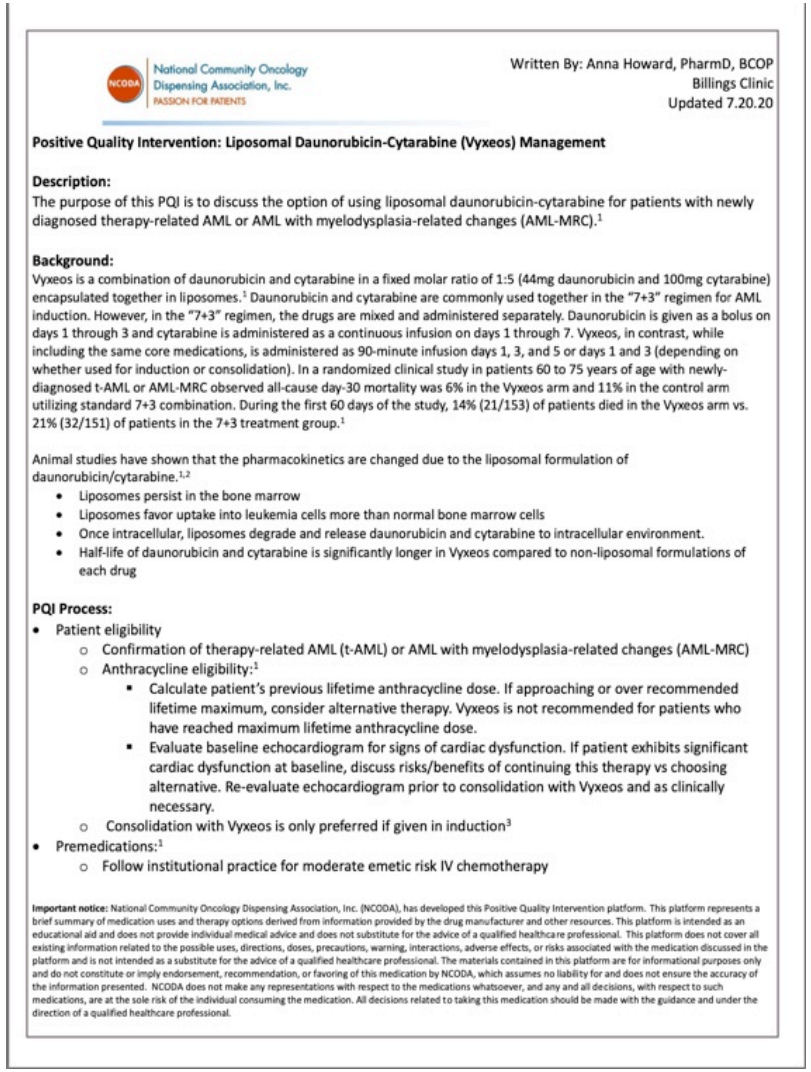
- Peer-reviewed, clinical guidance documents
- Promote higher quality patient care
- Designed to operationalize and standardize best practices to achieve positive clinical outcomes
- Authored by clinical practitioners and based on real-world practice experience and data

PQI Process


Identify topic need and topic experts
Pre-writing conference
Document creation and revisions
Send to MD for medical review and peer-review by clinical committee
Publish on NCODA website

PQI Format

- **Description**: purpose of the PQI
- **Background**: pertinent historical data and information, drug, mechanism of action, clinical trial experience, main focus of intervention



National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

Written By: Anna Howard, PharmD, BCOP
Billings Clinic
Updated 7.20.20

Positive Quality Intervention: Liposomal Daunorubicin-Cytarabine (Vyxeos) Management

Description:
The purpose of this PQI is to discuss the option of using liposomal daunorubicin-cytarabine for patients with newly diagnosed therapy-related AML or AML with myelodysplasia-related changes (AML-MRC).[1]

Background:
Vyxeos is a combination of daunorubicin and cytarabine in a fixed molar ratio of 1:5 (44mg daunorubicin and 100mg cytarabine) encapsulated together in liposomes.[1] Daunorubicin and cytarabine are commonly used together in the "7+3" regimen for AML induction. However, in the "7+3" regimen, the drugs are mixed and administered separately. Daunorubicin is given as a bolus on days 1 through 3 and cytarabine is administered as a continuous infusion on days 1 through 7. Vyxeos, in contrast, while including the same core medications, is administered as 90-minute infusion days 1, 3, and 5 or days 1 and 3 (depending on whether used for induction or consolidation). In a randomized clinical study in patients 60 to 75 years of age with newly-diagnosed t-AML or AML-MRC observed all-cause day-30 mortality was 6% in the Vyxeos arm and 11% in the control arm utilizing standard 7+3 combination. During the first 60 days of the study, 14% (21/153) of patients died in the Vyxeos arm vs. 21% (32/151) of patients in the 7+3 treatment group.[1]

Animal studies have shown that the pharmacokinetics are changed due to the liposomal formulation of daunorubicin/cytarabine.[1,2]

- Liposomes persist in the bone marrow
- Liposomes favor uptake into leukemia cells more than normal bone marrow cells
- Once intracellular, liposomes degrade and release daunorubicin and cytarabine to intracellular environment.
- Half-life of daunorubicin and cytarabine is significantly longer in Vyxeos compared to non-liposomal formulations of each drug

PQI Process:

- Patient eligibility
  - Confirmation of therapy-related AML (t-AML) or AML with myelodysplasia-related changes (AML-MRC)
  - Anthracycline eligibility:[1]
    - Calculate patient's previous lifetime anthracycline dose. If approaching or over recommended lifetime maximum, consider alternative therapy. Vyxeos is not recommended for patients who have reached maximum lifetime anthracycline dose.
    - Evaluate baseline echocardiogram for signs of cardiac dysfunction. If patient exhibits significant cardiac dysfunction at baseline, discuss risks/benefits of continuing this therapy vs choosing alternative. Re-evaluate echocardiogram prior to consolidation with Vyxeos and as clinically necessary.
  - Consolidation with Vyxeos is only preferred if given in induction[3]
- Premedications:[1]
  - Follow institutional practice for moderate emetic risk IV chemotherapy

Important notice: National Community Oncology Dispensing Association, Inc. (NCODA), has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.

PQI Format

- **The PQI Process:** intervention in step by step points, clinician directed guidance, critical clinical criteria that may be missed/overlooked, IV preparation, dose modifications
- **Patient Centered Activities:** patient-directed guidance, key counseling points, administration, drug-drug interactions

PQI Format

- **Supplemental Information:** additional tables, graphs, background, billing information, or other drug information not critical to the intervention
- **References:** AMA format

Supplemental Information (if applicable)

Example 28-Day Dosing Calendar (Ixazomib, lenalidomide, dexamethasone)								
	Week 1		Week 2		Week 3		Week 4	
	Day 1	Days 2-7	Day 8	Days 9-14	Day 15	Days 16-21	Day 22	Days 23-28
Ixazomib	✓		✓		✓			
Lenalidomide	Take every day on days 1-21							
Dexamethasone	✓		✓		✓		✓	

References:

1. Ninlaro (ixazomib) [prescribing information]. Cambridge, MA: Takeda Pharmaceutical Company Limited; February 2020.
2. SEER Stat Fact Sheets: Myeloma. Available at http://seer.cancer.gov/statfacts/html/mulmy.html. (accessed 04/16/2019)

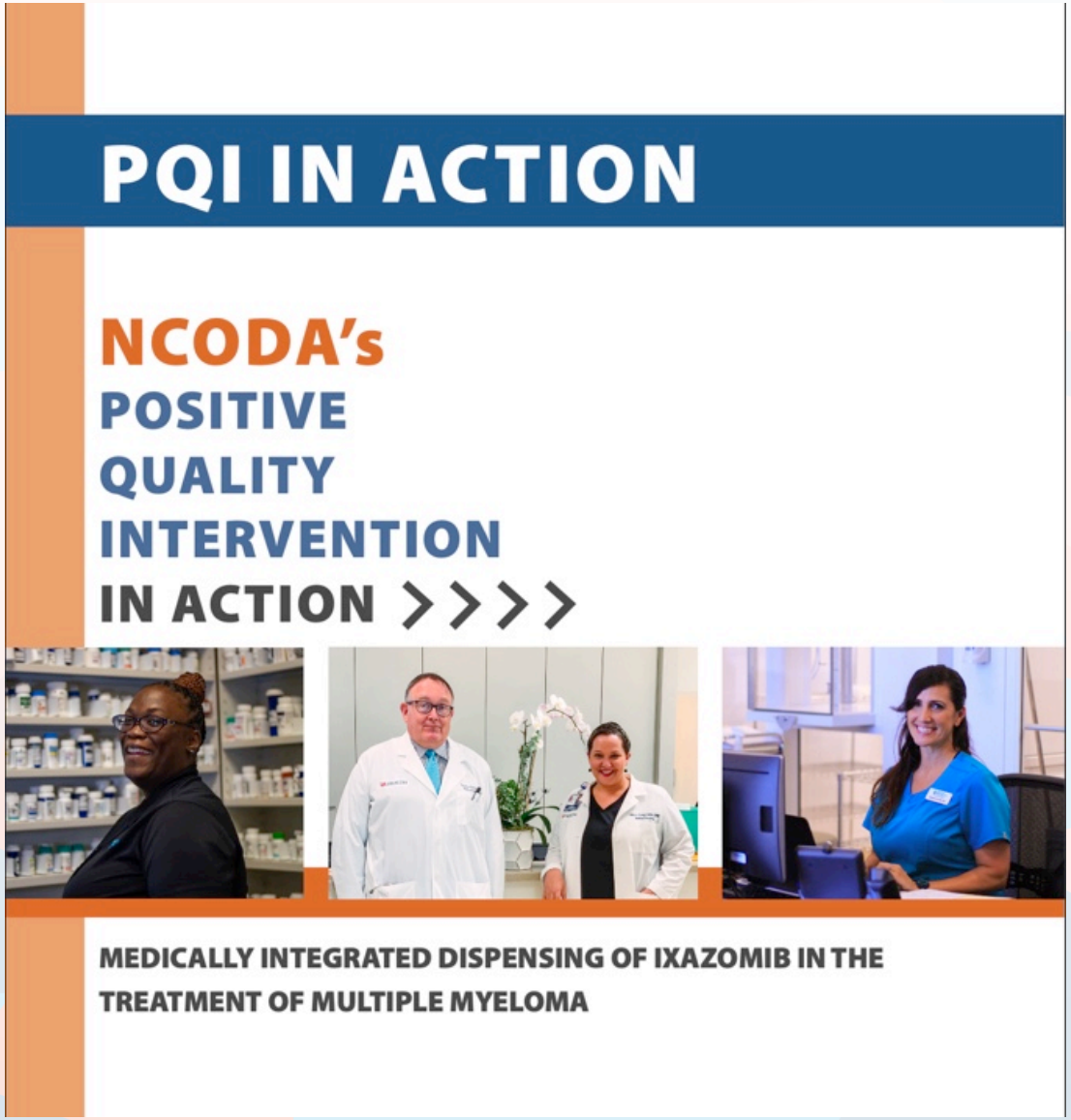
PQI to Date

- Over 55 Positive Quality Intervention Resources
- Multiple oncology experts from across the country involved in PQI process and committee
- PQIs utilized in practices across the world

PQI in Action

- Incorporates opinions and experiences from oncology experts within the medically integrated teams at leading cancer care organizations.
- Practices have successfully implemented the use of Positive Quality Interventions throughout their care teams to improve the clinical outcomes of patients.

PQI in Action



Three New PQIs in Action!

- **Ixazomib (Ninlaro) in the Treatment of Multiple Myeloma**
- **Zanubrutinib Patient Selection and Management in Mantle Cell Lymphoma**
- **Liposomal Daunorubicin-Cytarabine (Vyxeos) Management - Our first IV PQI in Action!**

How have PQIs been implemented at your practice?

- What value does MID bring to your staff and patients?
- What value does the pharmacy as part of the Medically Integrated Team bring to your staff and patients?

Background

Background:

Vyxeos is a combination of daunorubicin and cytarabine in a fixed molar ratio of 1:5 (44mg daunorubicin and 100mg cytarabine) encapsulated together in liposomes.[1] Daunorubicin and cytarabine are commonly used together in the "7+3" regimen for AML induction. However, in the "7+3" regimen, the drugs are mixed and administered separately. Daunorubicin is given as a bolus on days 1 through 3 and cytarabine is administered as a continuous infusion on days 1 through 7. Vyxeos, in contrast, while including the same core medications, is administered as 90-minute infusion days 1, 3, and 5 or days 1 and 3 (depending on whether used for induction or consolidation). In a randomized clinical study in patients 60 to 75 years of age with newly-diagnosed t-AML or AML-MRC observed all-cause day-30 mortality was 6% in the Vyxeos arm and 11% in the control arm utilizing standard 7+3 combination. During the first 60 days of the study, 14% (21/153) of patients died in the Vyxeos arm vs. 21% (32/151) of patients in the 7+3 treatment group.[1]

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PQI Process

PQI Process:

Upon receipt of an order for zanubrutinib:

- Ensure patient is appropriate candidate for zanubrutinib based on indication
  - Patient comorbidities may make zanubrutinib a safer option (i.e., history of Afib, recent hemorrhage, hypertension, concomitant PPI or H2R antagonists)
- Dose of zanubrutinib is either 160 mg twice daily or 320 mg once daily based on patient preference/ability to adhere to twice daily medication
- Reduce zanubrutinib dose accordingly if co-administered with:
  - Strong CYP3A inhibitor – 80 mg once daily
  - Moderate CYP3A inhibitor – 80 mg twice daily
  - Moderate or strong CPY3A inducer – avoid concomitant use
- Reduce zanubrutinib dose to 80 mg twice daily in patients with severe hepatic impairment (Child-Pugh Class C)
- Consider prophylaxis for herpes simplex virus, *Pneumocystis jirovecii* pneumonia, and other infections according to standard of care in patients at increase risk for infections. Grade 3 or higher infections occurred overall in 23% of patients on zanubrutinib with pneumonia being the most common infection.

PQI Process

PQI Process continued:

- Verify monitoring parameters:
  - CBC with differential, hepatic function
  - Signs/symptoms of Afib/flutter, bleeding, or infections including opportunistic infections

PQI Process: IV Specifics

PQI Process Continued:

- Preparation:[1]
  - Calculate the volume of reconstituted VYXEOS required based on daunorubicin dose: **[volume required (mL) = daunorubicin dose (mg/m^2) X BSA (m^2) ÷ 2.2 (mg/mL)]**
  - Review Vyxeos PI for complete admixture details which must be followed to increase homogeneity of final product
  - Vyxeos is compatible with NS or D5W
  - Resulting product will be a deep purple, opaque, homogeneous dispersion with no visible particulates
- Dosing:[1]
  - Dose adjustments:
    - Renal: not required. Not studied in severe renal impairment or end-stage renal disease
    - Hepatic: not required. Not studied in patients with bilirubin >3 mg/dL
  - Induction:
    - 44mg/m^2 daunorubicin + 100mg/m^2 cytarabine IV infusion over 90 minutes on Days 1, 3, and 5
  - Second induction (administered 2 to 5 weeks after first induction, if remission is not achieved with first induction cycle):
    - 44mg/m^2 daunorubicin + 100mg/m^2 cytarabine IV infusion over 90 minutes on Days 1 and 3
  - First consolidation cycle (administered 5 to 8 weeks after start of last induction cycle) and second consolidation cycle (administered 5 to 8 weeks after start of first consolidation cycle):
    - 29 mg/m^2 daunorubicin + 65mg/m^2 cytarabine IV infusion over 90 minutes on Days 1 and 3
    - Do not administer consolidation until neutrophils and platelets have recovered to >0.5 Gi/L and >50 Gi/L respectively.[1]
- Administration:
  - May be administered as outpatient in an infusion center if patient is clinically stable[4,5]
  - Due to risk for tissue necrosis from extravasation, only administer through central line[1]
  - Review the PI regarding specifics surrounding infusion filtration[1]

Patient Centered Activities

Patient Centered Activities:

- Provide Oral Chemotherapy Education (OCE) sheet and therapy calendar to all patients
- Ensure patients understand the dosing schedule. Ixazomib is administered on days 1, 8 and 15 every 28 days. IMiDs and steroids will have a different schedule.
- Advise patients that a missed dose should not be taken with 3 days of the next scheduled dose. If vomiting occurs, do not repeat dose.
    - Steroid component of regimen may be taken prior to ixazomib to help with nausea control but steroids should be taken with food. Ixazomib should be taken on an empty stomach (at least 1 hour before or 2 hours after a meal or snack.
- Financial resources are available through Takeda Oncology: (https://www.ninlaro.com/cost)

Supplemental Information

Supplemental Information:

myBeiGene Patient Support Program

Patient Assistance Program Co-pay/Co-insurance Assistance:

- Co-pay as low as $0/prescription for commercially insured patients
- Bridge supply for insurance coverage delays
- Free product for uninsured and underinsured patients

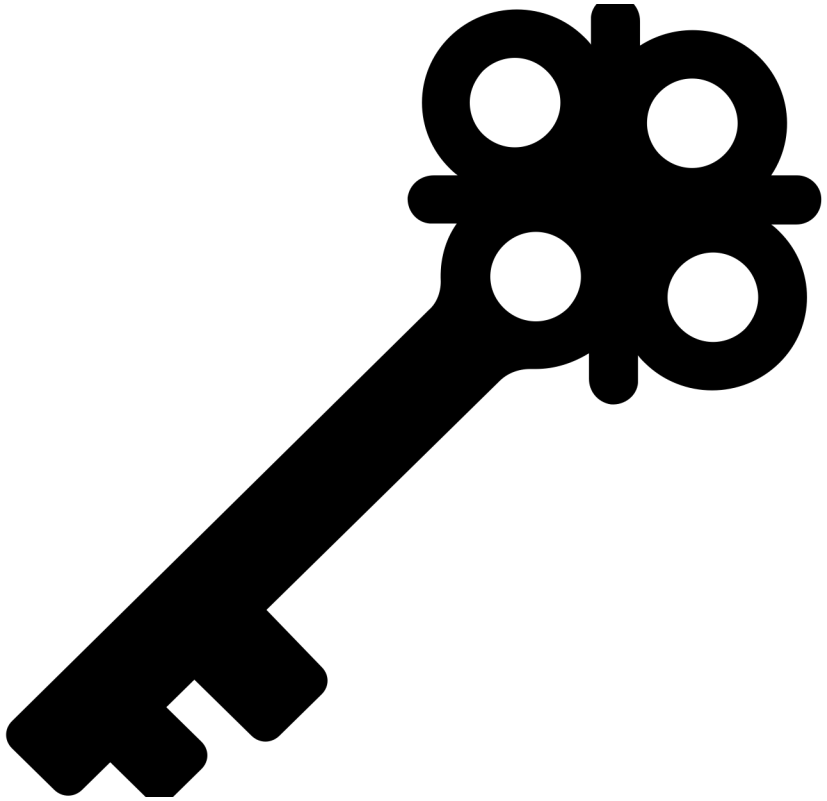
Patient Education

- Dedicated Oncology Nurse Advocates for practices, patients and caregivers
- Patient and caregiver follow-up support
- Connecting patients and caregivers with advocacy groups and local/national free resources

Enroll online or by calling myBeiGene at 1-833-234-4363

Education is Key!

- Education for staff
- Education for patients



NCODA Educational Resources

Patient Education:

- Better health related QOL
- Less anxiety
- OCE sheets

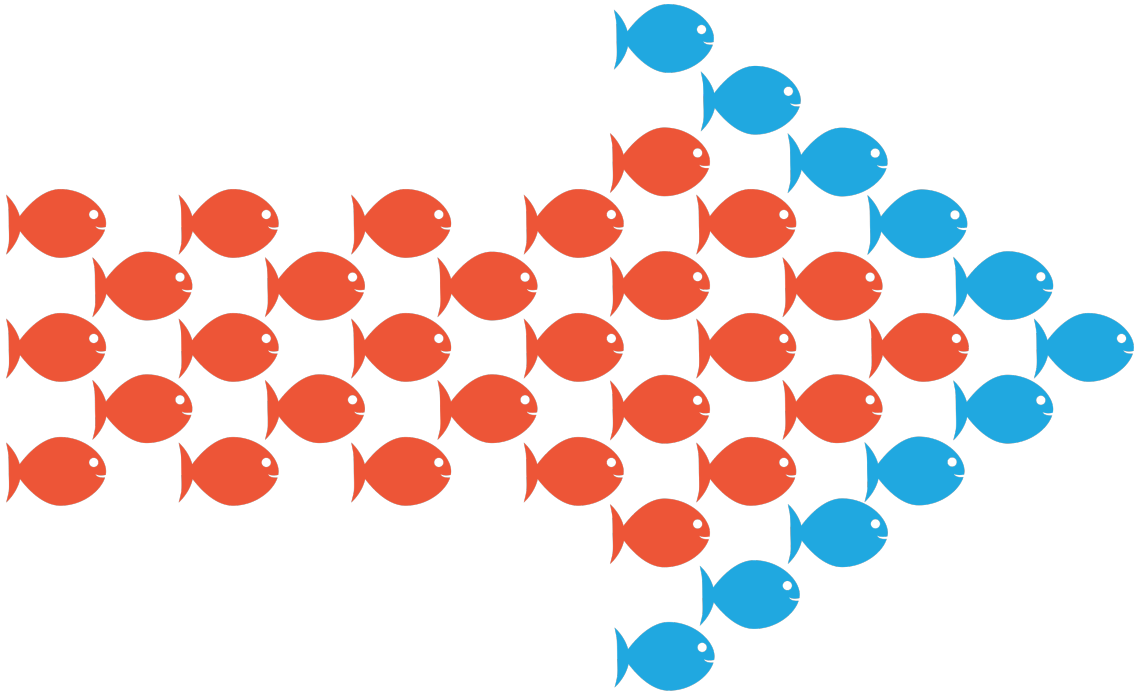
Staff Education:

- Employee retention
- Practice efficiency
- Patient satisfaction
- PQI and PQI in Action
- Webinars

Get Involved!

- We are always looking for more amazing practitioners and practices to be involved
- Share your knowledge and what works for your practice with others!
- PQI:Joshua.Nubla@ncoda.org
- PQIiA: Ginger.Blackmon@ncoda.org

Thank you!



Working Together, We Become Stronger

References:

1. NCODA. NCODA Announces the defining of the Medically Integrated Dispensing Pharmacy. https://www.ncoda.org/medically-integrated-dispensing-pharmacy/. Accessed September 2020.
2. Husson O, Mols F, van de Poll-Franse LV. “The relation between information provision and health-related quality of life, anxiety and depression among cancer survivors; a systematic review. “ *Ann Onc.* 2011; 22:761-772
3. Lambourne T, Minard LV, Deal H, et al. “Optimizing Patient Education of Oncology Medications: A Patient Perspective.” *J Canc Educ.* 2019; 34:1024-1030.
4. Gesme D, Towle E, Wiseman M. “Essentials of Staff Development and Why You Should Care.” *J Oncol Prac.* 2010;6(2):104-106