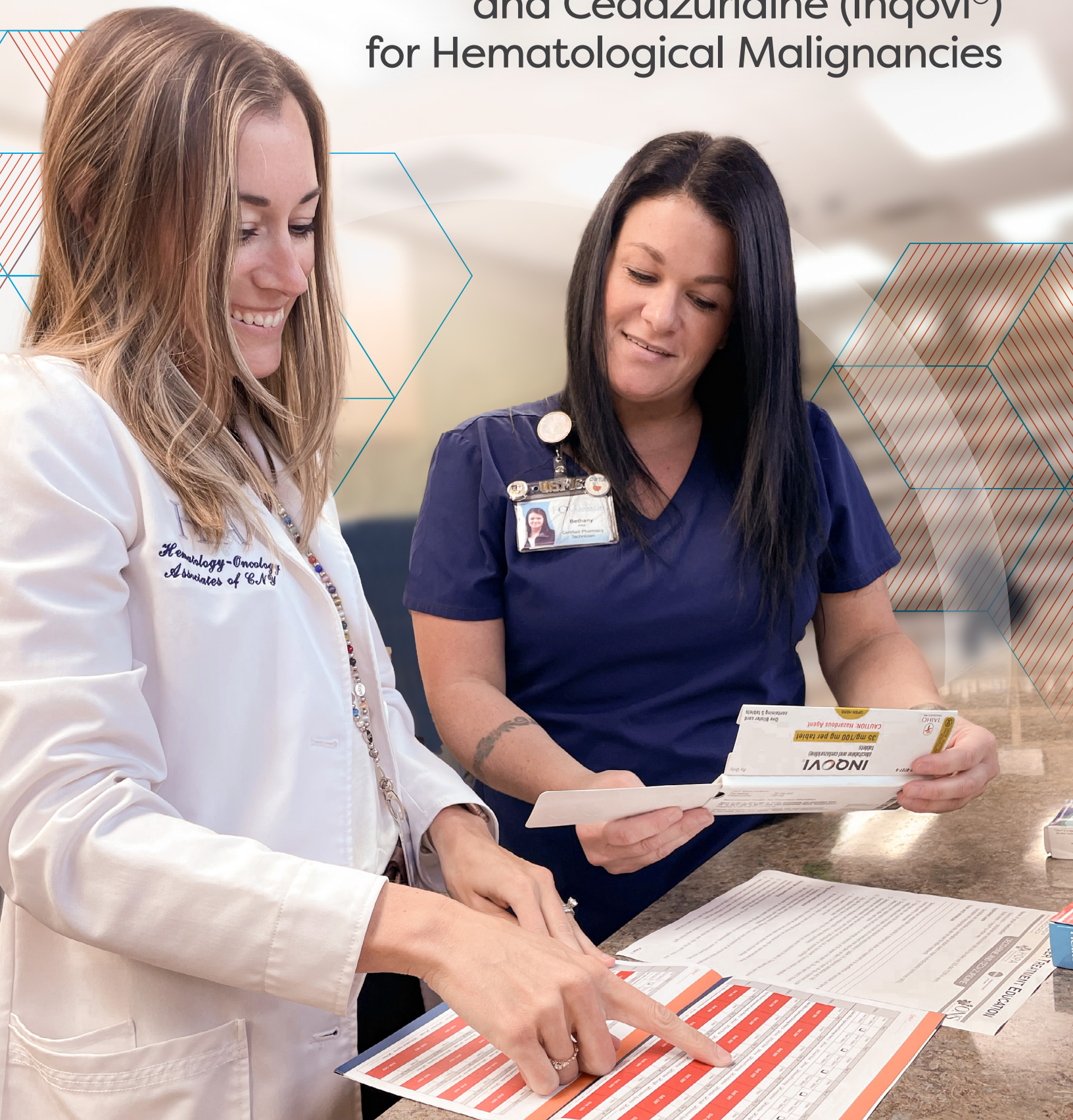
PQI IN ACTION

Positive Quality Intervention

NCODA

Oral Formulation of Decitabine and Cedazuridine (Inqovi®) for Hematological Malignancies



INTRODUCTION

NCODA developed the peer-reviewed Positive Quality Intervention (PQI) as an easy-to-use and relatable clinical guidance resource for healthcare providers. By consolidating quality standards, real-life effective practices, clinical trial results, package insert information, and other guidance, PQIs equip the entire multidisciplinary care team with a comprehensive yet concise resource for managing patients receiving oral or IV oncolytics.

This PQI in Action is a follow up to the Oral Formulation of Decitabine and Cedazuridine (Inqovi®) for Hematological Malignancies PQI and explores how the medically integrated teams at Hematology-Oncology Associates of Central New York (HOACNY) and the McFarland Clinic collaborate and utilize the information found in the PQI as part of their daily practice. This article will discuss how utilizing the Oral Formulation of Decitabine and Cedazuridine (Inqovi®) for Hematological Malignancies PQI elevates patient care.

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TREATMENT LANDSCAPE FOR MYELODYSPLASTIC SYNDROME

MYELODYSPLASTIC Syndrome (MDS) is one of the most common blood cancers, with 20,000 new cases reported every year in the US.[1] It is characterized by persistent cytopenias due to abnormal cellular maturation.[2] There are several different types of MDS based on how the cells appear under the microscope, cytogenetics, in which cell lines cytopenias are present, and the presence of blasts or ring sideroblasts.[3,4] Severity of disease is categorized based on different scoring systems. Patients are categorized into lower-risk and higher-risk MDS based on the Revised International Prognostic Scoring System (IPSS-R) and reference IPSS-R or NCCN guidelines. These risk categories determine the type and intensity of treatment the patient will receive. MDS primarily affects an older population, making tolerance of treatment difficult.[4] Approximately 30% of people with MDS can progress to a more aggressive acute myeloid leukemia (AML), which results in poor response to treatment, high incidence of relapse, and worse overall survival.[5]

WHAT THE GUIDELINES SAY

The therapeutic options for MDS include supportive care, low-intensity therapy, high-intensity therapy (including allogenic transplant), targeted agents, and clinical trial participation. For those with lower-risk MDS, improvement of cytopenias is the goal. For those with higher-risk MDS, the goal is alteration of the natural history of disease in order to prevent progression to AML.[4]

One of the hallmarks of MDS includes epigenetic dysregulation and DNA hypermethylation. This hypermethylation silences tumor suppressor genes and causes abnormal regulation of other genes that are involved in cell growth and differentiation, leading to development of MDS. Hypomethylating agents (HMAs) like azacitidine and decitabine can reverse these epigenetic modifications and restore normal DNA methylation.[6]

The National Comprehensive Cancer Network (NCCN) guidelines recommend HMAs in both the lower-risk and higher-risk settings. For those with lower-risk MDS, HMAs are indicated in those with clinically relevant thrombocytopenia or neutropenia or upon progression if not used in the first-line setting. For higher-risk MDS, HMAs are indicated in those that are not candidates for intensive therapy like transplant or intensive chemotherapy.[4]

THE CASE FOR ORAL HYPOMETHYLATING AGENTS

There are currently two intravenous (IV) HMAs approved for MDS, azacitidine and decitabine. IV HMAs have been shown to improve response rates and delay progression to AML in patients with MDS. However, real-world outcomes in patients receiving IV HMAs appear less favorable than clinical trials. This data suggests underuse of IV HMAs, including receipt of less than 4 cycles or prolonged gaps of more than 90 days between cycles. Reasons for early discontinuation or cycle interruption could include venous access complications, injection site reactions and pain, and the need for frequent visits to the infusion clinic. Oral HMAs have the potential to reduce the burden of IV therapy, decrease rates of early discontinuation, and improve adherence, quality of life, effectiveness, and survival for patients with MDS.[6]

Inqovi®: INDICATION & CLINICAL DATA

INQOVI INDICATIONS, MECHANISM OF ACTION, AND CLINICAL TRIAL DATA

Inqovi, the combination of decitabine and cedazuridine (DEC-C), was approved in July 2020 for adult patients with previously treated and untreated de novo and secondary intermediate-1, intermediate-2, and high-risk MDS (previously treated and untreated de novo and secondary) with either refractory anemia, refractory anemia with ringed sideroblasts,

INQOVI®: Indication & Clinical Data - continued

refractory anemia with excess blasts, and chronic myelomonocytic leukemia [CMML])[7] and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups. Inqovi is a fixed-dose combination of the hypomethylating agent, decitabine, and the cytidine deaminase inhibitor, cedazuridine. Cedazuridine prevents the gastrointestinal breakdown of decitabine, allowing for oral administration and improved absorption. The phase 3 ASCERTAIN trial compared the safety and pharmacokinetics of oral DEC-C to IV decitabine and found that the two treatments had equivalent systemic exposure and no significant differences in side effect profiles.[8,9]

NCCN LANDSCAPE

Inqovi is an NCCN category 2A recommendation as a substitution for IV decitabine in patients with IPSS-R risk category of very-low to very-high-risk based on patient specific factors including presence of symptomatic anemia and fitness for hematopoeitic transplant.[4]

MEDICALLY INTEGRATED PHARMACY WITH INQOVI

INQOVI can be dispensed by the Medically Integrated Team, providing patients with more comprehensive care. NCODA defines Medically Integrated Pharmacy (MIP) as a dispensing pharmacy within an oncology center of excellence that promotes a patient-centered, multidisciplinary team approach. The MIP is an outcome-based collaborative and comprehensive model that involves oncology healthcare professionals and other stakeholders who focus on the continuity of coordinated, quality care and therapies for cancer patients.[10] The MIP model can improve management of patients on therapies like Inqovi by improving communication issues, measuring adherence, managing regimen changes, quicker therapy initiation, increased patient satisfaction, securing financial assistance, cost avoidance, and producing less waste.[11]

Iqra Choudary, MD, Medical Oncologist at HOACNY realizes the value of having a pharmacist on-site as part of MIP. She says, "Having a pharmacist on-site, it's vital to our practice. You know there is always something to run by them. I use them often for cross checking home medications versus any supplements versus any treatment I would be starting. I think every site should have a pharmacist."

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>
> Dr. Iqra Choudary, MD, Medical Oncologist

Alexis Skibitski, PA-C, Physician Assistant at HOACNY agrees that a pharmacist has been invaluable to her as a newer practitioner. She says, "It's been important for me just gaining that confidence. Having so many people I can go to for extra support. If the patients have any questions, I can always call the pharmacists to answer."

NCODA offers multiple tools to aid the MIP practice in managing oncolytics. This toolbox contains a Patient Survey that is practice-customizable, a Cost Avoidance and Waste Tracker tool, a Financial Assistance database, Treatment Support Kits, Oral Chemotherapy Education sheets, and of course the Positive Quality Intervention clinical resource documents.

The Postitive Quality Intervention:

A VALUABLE CLINICAL RESOURCE

ANDREA Ketcham, PharmD, clinical oncology pharmacist at McFarland Clinic comments on the value of the PQI as an interdisciplinary resource (Click or Scan QR-Code). She says, "We integrate a lot of different NCODA resources and they are helpful to every person on the team, regardless of what their role is. I think the PQI, along with all the other NCODA resources, is a package deal of what we can use in the office and what we can send home with our patients so that everybody is successful."

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– Andrea Ketcham, PharmD, Clinical Oncology Pharmacist

Kaitlyn Baumgardner, DNP, ARNP, FNP-C, Nurse Practitioner at McFarland Clinic likes how concise the resource is. When asked about her favorite parts of the PQI, she says, "The dose reduction and dose delay information. That is really helpful, especially for an APP like myself. It's clear, concise, and I'm not digging through and clicking on different links. It's just bam, right there."

This article will explore the benefits of PQI utilization as a core standard of the MIP and how adoption can benefit any practice. HOACNY and McFarland Clinic have each found successful ways to incorporate the PQI clinical resource. These practices position their Medically Integrated Teams in a way to ensure appropriate treatment, increase compliance, and maximize clinical outcomes. We will explore their practice settings, how implementing the **Oral Formulation of Decitabine and Cedazuridine (Inqovi®) for Hematological Malignancies PQI** benefits their staff and patients, and how they advance patient care on a daily basis.

MEDICALLY INTEGRATED PHARMACY: ELEVATING CARE

AS cancer treatment continually grows in complexity containing IV, oral and combination regimens, MIP continues to offer an invaluable option for patient care. The MIP and multidisciplinary staff has unparalleled access to patient information and means of direct communication with other members of the team. The pharmacy members of the team also have direct access to communication with patients and can easily report information back to the providers. This model greatly reduces fragmentation of care.

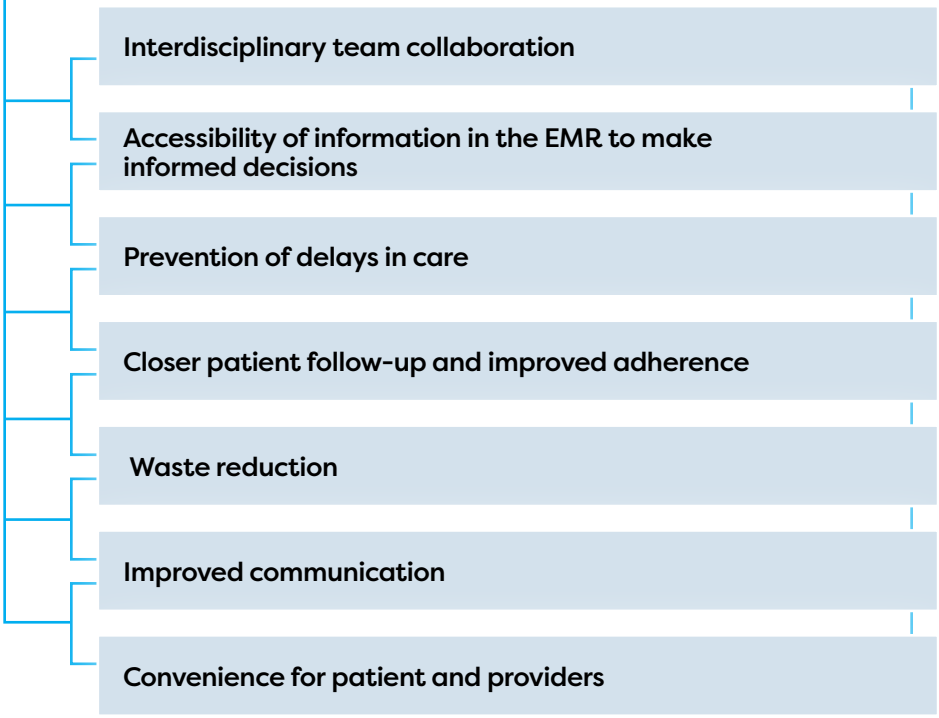
Danielle Maciorowski, PharmD, Pharmacy Manager, comments how integration of an MIP improves engagement between staff members and patients. She says, "Medically-Integrated Pharmacy truly embraces collaboration and allows us to offer comprehensive care. We have all the information right at our fingertips, so I think that is great for patient care. Just overall, better outcomes for the patients."

Medically Integrated Pharmacy: Elevating Care - continued

Bethany Joss, Pharmacy Technician at HOACNY notes that MIP improves the speed and accuracy of patient care. She says, "It is the communication, whether decisions on the best treatment option or dose reduction questions. We are able to manage side effects more easily and then able to provide that outcome to the patient faster." She also notes that MIP is so much more convenient for both patients and staff. "It's one stop. A lot of our patients need rideshare or family support to get here. So another stop sometimes isn't doable for them. That in itself is helpful. And just building on that relationship that they're taken care of as a full patient here helps build that trust between staff and patients."

In addition to the points made above, the team members at HOACNY and the McFarland Clinic had many things to say about the benefits of MIP at their institutions. **Figure 1** highlights their collective insights.

Figure 1. Benefits in Using MIP for Inqovi



"Medically Integrated Pharmacy truly embraces collaboration and allows us to offer comprehensive care. We have all the information right at our fingertips, so I think that is great for patient care. Just overall, better outcomes for the patients." – Danielle Maciorowski, PharmD, Clinical Oncology Pharmacist

PUTTING THE ORAL FORMULATION OF DECITABINE & CEDAZURIDINE (INQOVI®) FOR HEMATOLOGICAL MALIGNANCIES PQI INTO ACTION

THE PQI is a peer-reviewed clinical guidance document that provides Quality Standards and effective practices around a specific aspect of cancer care. The Medically Integrated Pharmacy team is in a unique position to ensure appropriate treatment, increase compliance, and maximize clinical outcomes. Positive Quality Interventions (PQIs), an NCODA Quality Standard, are designed to operationalize and standardize those practices to achieve these positive clinical outcomes. The **Oral Formulation of Decitabine and Cedazuridine (Inqovi®) for Hematological Malignancies PQI** is written in sections which review clinical trial data, practical information for treatment initiation, patient counseling pearls, and various references.

Following the description, the background section gives pertinent historical data and information, clinical trial experience, and the main focus of the intervention. Regarding Inqovi, the background discusses the rationale for oral dosing of an HMA, appropriate indications, and clinical trial data from the phase 3 ASCERTAIN trial.

When asked about the benefits of switching from IV to oral HMA therapy, Skibitski says, "Simply quality of life. Our goal is to have these patients in our office as little as possible to make sure they're getting the best of their therapy. As opposed to the IV form, coming into the office 5 days a week. That can be a lot, especially since this patient population is typically the geriatric population." She also discusses the need for transportation for this population, increased risk of infection from frequent clinic visits, and the decreased need to insert an IV.

Dr. Choudary also mentions that oral therapy is beneficial in her practice setting, where people who live in more rural settings often have long commutes to make it to the office. "To me, it's an effort to (1) Have them tolerate treatment, and (2) Minimize visits, rather than giving them an (IV) HMA on days 1 to 5 or 1 to 9."She prefers to give patients the oral formulation and has had success in doing so. She also uses Inqovi for patients who may be younger and healthy but prefer not to receive infusion treatments.

THE PQI PROCESS: A TEAM EFFORT

THE next section of the Oral Formulation of Decitabine and Cedazuridine (Inqovi®) for Hematological Malignancies PQI is the PQI Process. This section lays out the intervention in step-by-step points, contains clinician directed guidance, and critical clinical criteria that can benefit the entire team.

The first step of the Oral Formulation of Decitabine and Cedazuridine (Inqovi®) for Hematological Malignancies PQI includes utilizing appropriate reporting tools within

The PQI Process: A Team Effort- continued

the EMR to identify patients currently receiving IV decitabine for MDS or CMML and discussing the appropriateness of switching to Inqovi with the prescriber. If the patient is currently mid-cycle, wait until the next cycle to initiate Inqovi, as you shouldn't make the switch within a cycle.[9,12]

The next step of the PQI includes appropriate dosing and monitoring of Inqovi. Many team members at both HOACNY and McFarland Clinic emphasized that it's critical to ensure that patients understand how to take Inqovi since it's taken on days 1 to 5 of a 28 day cycle and not a simple daily medication.

Maciorowski emphasizes this by saying "It is more important to make sure that the patients can express a good understanding of the dosing schedule. So whether we offer them a calendar or we are marking it on the package, making sure that they know when they are starting. And I often have them tell me first, and then I confirm with them, so that I can truly assess if they have a good handle on their dosing."

Ketcham also notes that this is good practice in general, especially in oncology where doses change frequently. She says, "Every therapy is different and we end up having to change these frequently based on patients' blood counts and various other factors with their health status. So I think the biggest thing is to be aware that things are accurate. To be sure that everyone is on the same page is a huge factor in all of it."

The next step in the PQI process includes specific instructions for Inqovi dose adjustments **(Table 1)**.

Cytopenias are one of the most common Inqovi side effects, but are also a product of the disease state itself. Maciorowski says, "A lot of times with these patients, it can be multifactorial. So you want to assess the whole situation and say, Are these from the drug? Or are they from the disease? And then you want to manage that appropriately." Dr. Choudary also lets patients know that more frequent lab monitoring may be needed in the beginning due to the many factors that can affect blood counts. She says, "When I start the medication, I tell them If things do get a little worse before they get better, you will need labs more often than you'd want. But then eventually things will even out."

Even if cytopenias persist, Ketcham likes that you can dose reduce by taking Inqovi on days 1 to 4, without having to hold therapy for a long time. "Patients feel better, knowing they're on therapy." In addition to the strategies listed in the PQI, Skibitski says they will also use growth factor support to help patients who are struggling with neutropenia. They will administer it on the day after the last dose of Inqovi. In one patient, they also added a dose of filgrastim prior to her therapy initiation to ensure her ANC was above 1000/mm^3 prior to treatment. Skibitski says, "That's really worked well for her."

Table 1. Inqovi Dose Adjustments for Toxicity

Toxicity	Parameter	Intervention
Neutropenia	ANC < 1,000/mm^3	Hold (if cytopenias not due to active disease) and if ANC ≥ 1000/mm^3 and platelets ≥ 50,000/mm3 within 2 weeks: Continue same dose
Thrombocytopenia	Platelets < 50,000/mm^3	Hold and if ANC not ≥ 1000/mm^3 or platelets not ≥ 50,000/mm3 within 2 weeks: Hold additional 2 weeks and resume at reduced dose (days 1 to 4). Consider further dose reductions (see below) with persistent myelosuppression.
Hepatotoxicity	Serum bilirubin or AST/ALT ≥ 2x ULN	Hold until serum bilirubin and AST/ALT <2x ULN and resume at same or reduced dose.
Recommended dose reductions:		
	1st dose reduction:	1 tablet PO daily on days 1 to 4
	2nd dose reduction:	1 tablet PO daily on days 1 to 3
	3rd dose reduction:	1 tablet PO daily on days 1, 3, 5

ANC = absolute neutrophil count, ULN = upper limit of normal

PATIENT-CENTERED ACTIVITIES: KEEPING THE FOCUS ON PATIENTS

The Patent-Centered Activities section follows the PQI Process and gives patient-centered guidance for the team. The Oral Formulation of Decitabine and Cedazuridine (Inqovi®) for Hematological Malignancies PQI Patient Centered Activities suggests providing the patient with an Oral Chemotherapy Education (OCE) sheet. OCE sheets are an NCODA-led initiative that provide information about oral chemotherapy and hormone therapy drugs and their side effects to both cancer patients and caregivers.

Janelle Browning, RN, OCN, Nurse at McFarland Clinic likes the OCE because

it groups the possible side effects together instead of listing each individually. In addition, when the patient is receiving a regimen that includes multiple medications, she says, "I think if you're getting a treatment plan, the OCE sheet is easier for the patient because it looks at it as a whole instead of each individual drug." Lastly, she loves that the OCE also includes an Inqovi dosing calendar to keep the patient on track.

In 2019 the Patient-Centered Standards for Medically Integrated Dispensing: ASCO/NCODA Standards were published to provide standards for medically integrated dispensing of oral anticancer drugs and supportive care medications.[13]

Standard 1.2 of the ASCO/NCODA Standards reads:

Prior to initiation of an oral anticancer drug, a formalized patient education session should occur with an experienced clinical educator such as a nurse, physician, pharmacist, nurse practitioner, or physician assistant. The discussion should include drug name (generic and brand), drug dose, schedule, potential adverse effects and how to properly manage them, fertility (where applicable), treatment goal, duration of therapy, and financial and affordability considerations.[13]

In addition to providing an OCE, the patient-centered activities mention that the patient should be educated on the administration schedule, how to take Inqovi, which side effects to look out for, and how to manage them.

Skibitski notes that it is important to counsel on side effects related to cytopenias since those are the most common. She says, "We have a lot of patient education regarding neutropenic precautions, what to look for, when they should call our office. I think that's often a big struggle for patients, they almost feel like they're being a nuisance if they call us. We need to recognize that it can be hard for them to call us and reinforce that they should."

Baumgardner says that patient education is one of the aspects of her job that she loves the most. She says the OCEs really help her with actionable side effect management.

FINANCIAL ASSISTANCE: A BENEFIT OF MIP AND THE MULTIDISCIPLINARY TEAM

IN addition to close follow up and detailed education, MIP allows the practice to provide excellent customer service, unmatched patient care, and help with finding funding so the patient can afford to take the medication.

Joss says that having an in-house pharmacy speeds up the dispensing process for both staff and patients. Regarding affordability of the medication, she shares that around 95% of their patients require some sort of copay assistance and that their goal is always a $0 copay. The pharmacy staff utilizes coupon cards, free drug and foundation assistance. The financial assistance process is automatic at HOACNY so patients don't need to go through the arduous process of finding assistance themselves. Joss says, "A lot of times they will show up, and they'll be like 'Oh, $0 Copay! I was expecting it to be a certain price.' And we're like no, we just go ahead and take care of that beforehand, so you don't have to."

CONCLUSION:
NCODA, THE MIP & PQI: OPTIMIZING PATIENT OUTCOMES

ALL team members agree that the MIP model and the PQI Clinical Resource are valuable to the team and to patients. Every day the MIP team can make a difference in the life of patients.

The team can continually learn something new or can begin a process that optimizes care. The PQI fosters this through appropriate patient identification, increased speed to therapy, reduced cost, and by improving adherence techniques for the patient and their Medically Integrated Teams.

Browning notes that MIP can be implemented in a practice setting of any size. "They come to one place. They park their car and they have minimal walking when they get in the building. Everything they need is there." She goes on to say, "With the size of our facility and the number of staff we have, our patients are very much individuals to us. They are not just another patient. We are able to know our patients well and have that close connection with them."

Resources like the PQI, OCE sheet, and PQI in Action benefit both patients and practitioners. Maciorowski says, "Having all of the resources that NCODA offers really sets not only us as pharmacists up for success, but ultimately it sets our patients up for success. We have access to resources so we can really provide them the highest level of care."

The PQI provides the MIP program with an easy to use, compact clinical resource guide when discovering the right patient and dispensing Inqovi. It helps the team ensure they are providing patients with the tools and education to improve clinical outcomes. Pairing Medically Integrated Pharmacy with the Oral Formulation of Decitabine and Cedazuridine (Inqovi®) for Hematological Malignancies PQI meets NCODA's Guiding Values of being Patient-Centered and Always Collaborative.

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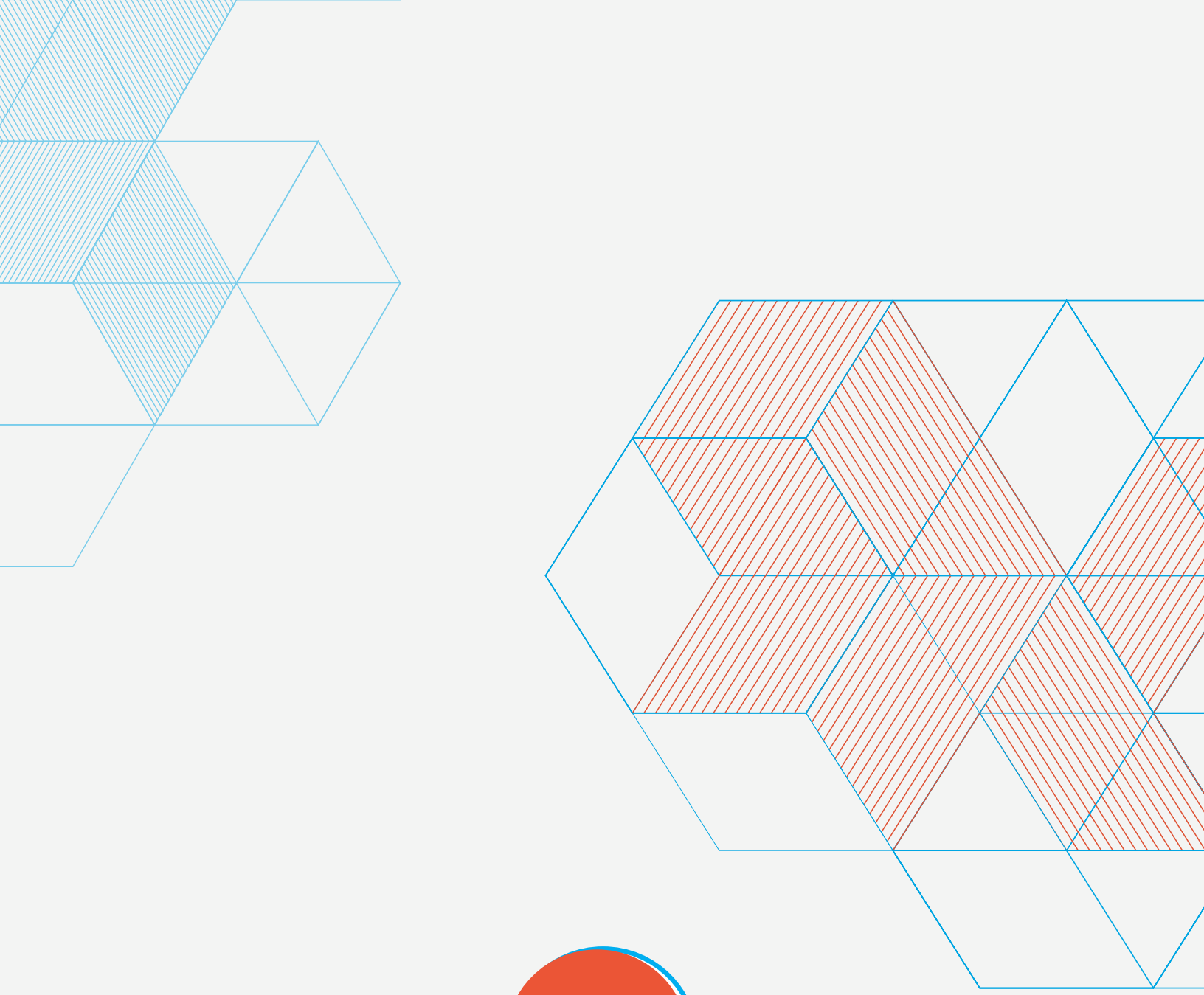

Practice panelist's comments reflect their experiences and opinions and should not be used as a substitute for medical judgment.