PQI IN ACTION

Positive Quality Intervention

NCODA

Adagrasib (KRAZATI®)

INTRODUCTION

In an effort to promote higher quality patient care, NCODA created the NCODA Positive Quality Intervention (PQI) as a peer-reviewed clinical guidance resource for healthcare professionals. 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. This PQI in Action is a follow up to the Adagrasib (KRAZATI®) PQI and explores how the medically integrated teams at Johns Hopkins Sidney Kimmel Cancer Center and American Oncology Network incorporate the information found in the PQIs as part of their daily workflow. This article will discuss how utilizing the Adagrasib (KRAZATI®) PQI elevates patient care.

Established in 1973, Johns Hopkins Sidney Kimmel Cancer Center was one of the first programs to earn comprehensive cancer center status and be recognized by the National Cancer Institute as a Center of Excellence. Nine locations in the greater Baltimore and Washington, D.C. region offer patients access to comprehensive, multidisciplinary care and some of the most advanced and innovative therapies in the world. Research scientists and clinicians work together to take new treatments from bench to bedside so that patients are offered the most cutting-edge therapeutic options. Johns Hopkins Sidney Kimmel Cancer Center houses a wide variety of programs including bone marrow transplantation, the Bloomberg-Kimmel Institute of Cancer Immunotherapy, and the Proton Therapy Center.

American Oncology Network (AON) is comprised of a group of physicians and healthcare leaders that serve community oncology practices across the United States. As a member of AON, community oncology practices can provide patients the same access to clinical research and cutting-edge treatment options as academic centers, but in a location closer to home. AON is 100% physician-led, allowing for practice autonomy while still maintaining collaboration and access to necessary resources. As a community oncology practice, being a member of AON enriches the patient experience by supporting the delivery of value-based care through participation in the Principal Care Management Program. The AON network helps community oncology providers increase practice growth and access to new revenue streams by furnishing additional services including clinical lab, pathology, and oral oncolytic pharmacy. AON aims to drive innovative care, with a focus on the future of oncology to continue to ensure accessible and patient-centered care in a location closer to home.

PARTICIPANTS

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Medical Director

Douglas Braun, PharmD, RPh, CSP, CPh
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Scan or click here to access Adagrasib (KRAZATI®) Positive Quality Intervention

MIP, THE PQI, AND ADAGRASIB: AN ORAL OPTION FOR KRAS^{G12C} MUTATIONS

LUNG cancer is the leading cause of cancer deaths for both men and women in the United States.[1] However, death rates have been falling by about 4% each year since 2013.[1] This increase in survival rates has been linked to substantial advancements in lung cancer treatment, particularly with the introduction of new targeted therapies. Targeted therapies are potentially very effective in non-small cell lung cancer (NSCLC). Biomarker testing is critical to guide treatment selection and ensure optimal outcomes.[2]

KRAS mutations are found in up to 30% of patients with NSCLC in Western countries. KRAS is a G-protein that has GTPase activity and is part of the MAP/ERK pathway.[2,3] It cycles between an inactive GDP-bound state and an active GTP-bound state; the active state promotes downstream signaling and cell growth. KRAS mutations are associated with adenocarcinoma histology and smoking history. The most common KRAS mutation is G12C, occurring in up to 14% of patients with lung adenocarcinomas. This mutation prevents deactivation of KRAS.[3] Adagrasib is an irreversible oral KRAS inhibitor that covalently binds to the mutant cysteine in KRAS^{G12C} and locks the mutant KRAS protein in its inactive state. This prevents downstream signaling without affecting the wild-type KRAS protein.[4]

Adagrasib is FDA-approved for the second-line treatment of adult patients with KRAS^{G12C}-mutated locally advanced or metastatic NSCLC.[4] Recently, adagrasib received FDA-approval as a combination treatment with cetuximab for advanced or metastatic colorectal cancer (CRC) for the same patient population.

Patients with KRAS^{G12C}-mutated NSCLC who had previously received both checkpoint inhibitor therapy and platinum-based chemotherapy were given adagrasib 600 mg twice daily. After a median follow-up of 12.9 months, the objective response rate was 42.9%, with a median duration of response of 8.5 months, median progression-free survival (PFS) of 6.5 months, and median overall survival (OS) of 12.6 months. The most common adverse effects (AEs) were diarrhea, nausea, vomiting, fatigue, increased ALT/AST, and increased serum creatinine. The most common grade 3 or higher AEs were fatigue, nausea, and increased ALT/AST.[5] The phase 3 KRYSTAL-12 trial, evaluating adagrasib as monotherapy in the same patient population as the KRYSTAL-1 trial, recently met its primary endpoint of PFS and key secondary endpoint of overall response rate, but remains ongoing in order to evaluate OS.[6]

Adagrasib is the second KRAS inhibitor to be approved for KRAS^{G12C}-mutated NSCLC in the second-line setting behind sotorasib. Head-to-head comparisons between adagrasib and sotorasib are not available, and selection is largely driven by differences in dosing frequency, adverse effects, patient characteristics, and insurance coverage.[7]

Brian Mulherin, MD, Medical Director at AON offers his perspective on adagrasib. "I have used it on several people. I think it's a pretty tolerable drug. I have several people who are in their eighties, and they are on oxygen. A couple of people have not had side effects, and in some cases they actually tolerated it much better than they did a single agent checkpoint inhibitor."

In the KRYSTAL-1 trial, a cohort of patients with central nervous system metastases and KRAS^{G12C} mutations treated with adagrasib resulted in an intracranial response rate of 42%, disease control rate of 90%, PFS of 5.4 months, and OS of 11.4 months.[8] Douglas Braun, PharmD, RPh, CSP, CPh, Senior Director of Pharmacy at AON says, "You know Krazati itself is good. It is a good drug for this subset of patients. You have to see the CNS penetration, which is really a difference maker for this drug. Knowing that it has that kind of penetration and it could work for those patients is huge. I hope that we continue to see more use of it as long as physicians continue testing for these mutations to ensure they find the right therapy."

Tricia Patel, MS, CRNP, Nurse Practitioner at Johns Hopkins Kimmel Cancer Center mentions that since Krazati's approval, they are still trying to get a good sense of the doses that pa-

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– Douglas Braun, PharmD, RPh, CSP, CP

MIP, the PQI, and Adagrasib: An Oral Option for KRAS^{G12C} Mutations - continued

tients can tolerate. She says, "As far as adagrasib goes, I would say it's quickly becoming our preferred agent. We have a few patients on it right now and we are trying to get a handle on the dose modifications."

Adagrasib can be dispensed by the Medically Integrated Team, and thus offers patients 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.[9] The MIP model can improve management of patients on therapies like adagrasib in several ways including improved communication issues, measuring adherence, managing regimen changes, quicker therapy initiation, increased patient satisfaction, financial assistance, cost avoidance, and producing less waste.[10]

Patel emphasizes the value of having a pharmacist embedded in the MIP team. "I don't even think I can put words to explain it because Stephanie is so well integrated into our practice now. The messages on drug therapy that come to me from our patients go to her as well, and she often responds before me and better than I could. She is great at helping us think through it and come up with plans that are individualized. She is a great resource and really wonderful with the patients. As a whole, she makes the patient experience a lot better."

NCODA offers multiple tools to aid the MIP practice in managing oncolytics. This toolbox contains a Patient Satisfaction 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 POSITIVE QUALITY INTERVENTION: A VALUABLE CLINICAL RESOURCE

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Houseknecht, PharmD, BCOP, Clinical Pharmacy Specialist at Johns Hopkins Sidney Kimmel Cancer Center comments on the value of the PQI. She says, "The PQI documents are a great resource for pharmacists who don't see these medications day in and day out. They may not be a thoracic specialist, but they generally see oncology patients and they want a refresher on, 'How do I apply this prescribing information, but in a practical sense? What are the things that I need to be looking for? What are some tips and tricks that maybe those who have used this drug clinically have learned, whether that be from a supportive care standpoint?' So, I think it takes the information that is available from multiple sources, highlights it in a very streamlined, easy to read document that can be a great resource for dispensing pharmacists or clinical pharmacists that might not be special-

> "We are all coming from different practice settings, some in academia, some in managed care settings, some in more general roles. We are sharing resources. Having resources available to help pharmacists translate good clinical care easily and make it reproducible so that it's a go-to reliable resource is really valuable."
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> – Stefanie Houseknecht, PharmD, BCOP

The Positive Quality Intervention: a Valuable Clinical Resource - continued

ized in a disease state." She goes on to say, "We are all coming from different practice settings, some in academia, some in managed care settings, some in more general roles. We are sharing resources. Having resources available to help pharmacists translate good clinical care easily and make it reproducible so that it's a go-to reliable resource is really valuable."

Braun uses the PQI as a backbone for provider and patient education. He says, "When a new drug comes out, we like to be able to have those PQIs because they really help guide us to the right way to manage our patients. It's a really good tool as a backbone to what we do as a basis to grow on, to really help educate our patients, and to make sure that they are doing the best they can to stay on therapy." he goes on to say KRAS inhibitors are a newer class of drugs. "People are still trying to build a good knowledge base, a good understanding of this class of medication. And so having the PQI really just kind of guides us to make sure we're doing the proper thing."

This article will explore the benefits of PQI utilization as a core standard of the MIP and how adoption can benefit any practice. Johns Hopkins and AON 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 Adagrasib (Krazati®) 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.

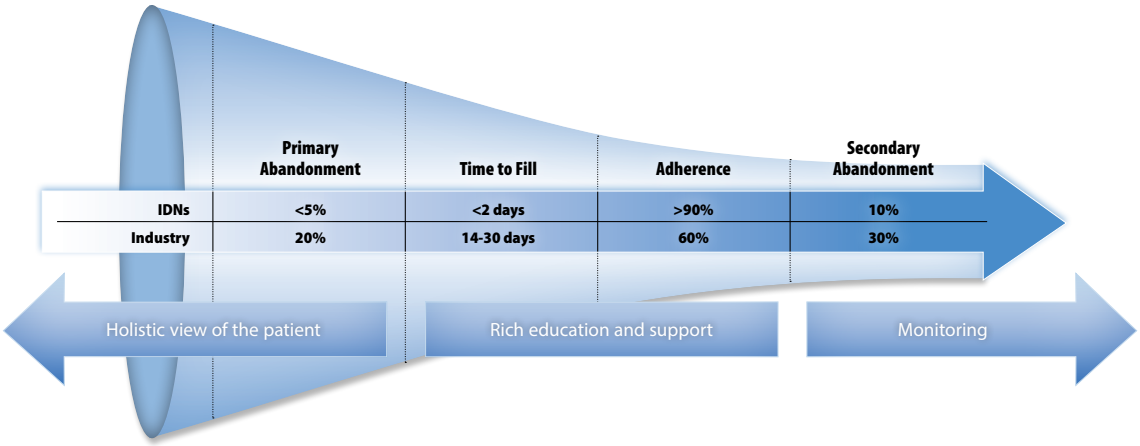
Joseph C. Murray, MD, PhD, Medical Oncologist at Johns Hopkins Kimmel Cancer Center highlights how pharmacist integration has elevated care at their institution. "Having pharmacy as part of a multidisciplinary team is absolutely critical in oncology. I think the specialty pharmacists in oncology really make things happen for our patients. Every pharmacist has a different take on how to approach patient centered care in this way. I feel like pharmacists in oncology, more than many other specialties, take on the role of patient education directly in our infusion centers, and over the phone with patients before starting medications that are delivered to their homes. Stefanie engages with patients in a way that is incredibly meaningful for them and increases their confidence in knowing who to reach out to about any sort of adverse effects. Pharmacists don't just educate with targeted therapies. They educate across immunotherapies and chemotherapy for our patients as well. They integrate their knowledge on different therapeutic modalities, even considerations for local therapies, like surgery or radiation. Their expertise and understanding of those interactions go well beyond just drug-drug interaction lists that I know I can look up as well and adverse event lists, but just thinking about the whole continuity of care. Having that conversation back and forth builds my confidence too as a physician in assuring that we have a team taking care of a patient, much like we don't want patients to feel solitary in their journey. We want them to have providers, family loved ones, caregivers supporting them. I think of it the same way on the care provider side. We need each other on the care provider side to really deliver the best care as well."

Dr. Mulherin outlines all the ways that MIP helps improve care at AON. "There is instant communication, there is instant awareness of the other medical problems or medical conditions. Our pharmacists can proactively reach out in a way the external mail order pharmacies definitely do not. I think for the physicians, being able to integrate, in-

Medically Integrated pharmacy: Elevating Care - continued

teract directly with someone or a team that you know with questions is invaluable. But really, it is more for the patient. MIP makes it easier for the patient to interact, it is easier for the clinical staff to interact with them. The authorization process is easier. It is also faster if you have to go out to another foundation to get assistance. It's so much faster than if you are having a mail order pharmacy do it."

Houseknecht offers a unique perspective on how MIP may fill a gap in transitions of care. She says, "I also help with transitions of care. Sometimes our patients unfortunately do get admitted to the hospital. And so when they get admitted to the hospital, I get a notification from our electronic medical record. I can add myself to the patient's care team. I know when they get admitted at one of our hospitals and I can check in with the inpatient team to answer 'Why is the patient admitted? Is this potentially related to the oral oncolytic and therefore should we hold the oral oncolytic? Or is this potentially unrelated and would it be safe for them to continue?' Then I can ensure that the patient does have continued access if appropriate in the hospital so that patients have as few delays as is necessary." She also echoes Dr. Mulherin's comments about how increased transparency via access to the integrated electronic medical record (EMR) increases patient safety. She says, "The biggest plus is that it is safer for patients. It also decreases time for problem solving. It provides better communication. We have not personally done a time from prescribing to dispensing study, but I think it shortens that time significantly for patients who are often nervous, anxious, and wanting to get started on treatment very quickly. We can usually turn a prescription around days faster than an outside pharmacy can."



PUTTING THE ADAGRASIB (KRAZATI®) 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 Adagrasib (KRAZATI®) PQI is written in sections, beginning with a Description and ending with Patient-Centered Activities and References.

Following the Description, the Background section gives pertinent historical data and information, clinical trial experience, and the main focus of the intervention. Regarding adagrasib, the background discusses FDA indication, KRAS mutation characteristics, adagra-

Putting the Adagrasib (KRAZATI®) PQI into Action - continued

sib mechanism of action, and clinical trial data that led to adagrasib approval.

Patel likes that all of the information is easy to reference. "It's like a one-stop-shop, in terms of I could pull this up, have the stats, and not have to go to the original article. Having everything in one spot is so useful."

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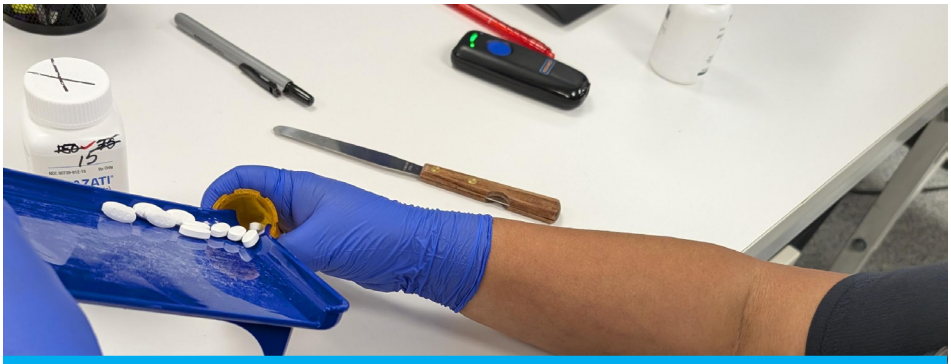
THE PQI PROCESS: A TEAM EFFORT

THE next section of the Adagrasib (KRAZATI®) 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 Adagrasib (KRAZATI®) PQI includes KRAS testing guidance. Specifically, patients with metastatic lung adenocarcinoma, large cell carcinoma, or NSCLC not otherwise specified (NOS) should undergo broad molecular profiling to identify KRAS mutations. Testing can be considered in squamous histology.[11]

In terms of patients with metastatic lung cancer, Dr. Murray says, "I absolutely want the broadest available molecular testing for my patients with a new lung cancer diagnosis. I essentially want broad NGS-based molecular profiling either in tissue or liquid form, but more frequently than not, I am doing both at the time of diagnosis to ascertain what molecular alterations may enable us to better improve patients' outcomes. And so for the metastatic patient, if I am deficient in tissue from a biopsy and only able to get a histology, I am often pursuing additional biopsies unfortunately, to get things like PD-L1 staining levels but, more importantly, to get this broader NGS testing. Fortunately, liquid biopsy has enabled us to do this in the clinic visit when I first meet patients."



THE AON TEAM DISPENSES KRAZATI FROM THEIR MEDICALLY INTEGRATED PHARMACY.

Dr. Murray also mentions that neoadjuvant chemoimmunotherapy is critical to get pathological, complete responses and improved PFS and OS in patients with earlier stage lung cancers. He goes on to say, "We also have $KRAS^{G12C}$-driven trials in the front line that we're trying to see if using that intervention before resection is relevant for a patient. As you can see, we are pushing this molecular testing into early stage lung cancers to help dictate and guide their care. I'll say that testing specifically for $KRAS^{G12C}$ is always going to be on those panels. Even the smaller panels will include this. Therefore, if we are testing patients for EGFR and ALK before we are giving neoadjuvant chemoimmunotherapy, we are getting this information [KRAS] back as well, and this will only enable us to help guide patients through clinical trials in the future that may change the standard of care with adagrasib or other $KRAS^{G12C}$ inhibitors."

At AON, Dr. Mulherin says they are

The PQI Process: a Team Effort - continued

strongly recommending NGS. "We are not mandating it, and we strongly encourage it. We do not have one central NGS platform that we mandate use on." He says the three platforms they typically use are Caris, Tempus, or FoundationOne. "Those three are going to be far and away the largest, so we encourage them. We want everyone to get checked." When asked which sample types he uses for NGS testing, he says, "I tend to do both at diagnosis. I use tissue and liquid."

The next steps of the PQI include identifying patients who are candidates for adagrasib by confirming the patient has a $KRAS^{G12C}$ mutation and documented progression on prior chemotherapy and/or immunotherapy. Once this is confirmed, patients can obtain adagrasib through a medically integrated pharmacy or dispensary. Adagrasib is part of a limited distribution network.

Joan Martens, CPhT, RPhT, Pharmacy Operations Supervisor at AON shares the importance of allowing dispensing through a MIP. "Many of the commercial plans mandate their own specialty pharmacies. This takes a lot of our patients away from our medically integrated pharmacy. Having manufacturers step up and recognize that medically integrated pharmacies provide a higher level of care and allowing us access to limited distribution medications has helped our patients to get their medications in a timelier manner."

The next step includes reviewing the prescription for any necessary dose adjustments or alternative therapy. Krazati does not require any dose adjustments for renal or hepatic function, but does have some CYP and p-glycoprotein interactions.[4,11]

In terms of drug interactions,

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> – Joseph C. Murray, MD, PhD

Houseknecht says, "The drug interaction screening step for Krazati is more thorough than it is for some of the other drugs because of how sensitive the medication itself, and then also the increased risk of effects on other drugs because it is a more broad CYP inhibitor." She goes on to say, "As a pharmacist the important thing to know is that Krazati has the potential for drug interactions and QT prolongation. I know I need to go consult my resources. I can bring up the PQI and see these are the CYP enzyme systems that I need to look for."

Although the initial starting dose is 600 mg twice a day, clinical judgment is still needed based on the patient's specific situation. Patel shares that dosing is not a one size fits all type situation and that dosing in their center has varied due to patient status when starting the medication as well as how well they tolerate the medication once they begin.

The next step includes ensuring the patient is appropriately educated on rationale for treatment, how to take the medication, side effects, and when to call the healthcare team. At both Johns Hopkins and AON, the pharmacists are key to ensuring the patient is fully educated on how to take adagrasib, side effects to watch out for and how to manage them, and when to call the team for help. At AON, Braun says, "Our clinical pharmacists spend a good deal of time upfront providing proactive counseling so that we can manage patients' expectations and teach them how to handle side effects, and manage those toxicities so that they can stay on therapy. Especially during those first couple of cycles. This is important during those first crucial cycles and then we have a very robust reassessment program. One of the advantages that we have over other external specialty pharmacies is we are integrated with the clinics, we have access to the EMR. Having EMR access really is a game changer for us because we can check every patient's chart. We look at labs, look at pathology, look at office visit notes, check to see when their next appointment is, and it really helps to maximize therapy."

The last step includes important monitoring parameters for adagrasib including liver function tests, creatinine, complete blood count, ECG/electrolytes for QT interval prolongation, and interstitial lung disease/pneumonitis. The PQI also includes a helpful table for dose adjustments based on toxicity and drug interactions. Dosing considerations for

The PQI Process: a Team Effort - continued

adagrasib in the table below:

Dr. Murray notes that dose reductions

Dosage form	200 mg tablets
Usual starting dose	600 mg (3 tablets) twice daily orally +/- food
Dose adjustments (renal/hepatic)	None reported
Dose reductions for toxicity	400 mg twice daily –-> 600 mg daily –-> discontinue

are not uncommon with adagrasib. He says, "Dose reductions are the real deal for a lot of the KRAS^{G12C} Inhibitors. One of the things that is hard to counsel patients on is dosing of medications. Patients are more worried about, 'If I'm taking too low of a dose is it affecting my ability to have a response?' I always counsel patients that, especially in the metastatic setting, our goal is to maintain their quality of life, not at the expense of just quantity of life, so counseling patients through what dose reductions mean. Some patients totally ignore it and say, 'Okay, great. You're the doctor. Just tell me what dose I need to take.' Others get very nervous. It is about reminding patients that we have data to show that the trials are conducted in this manner too, and that our goal is to maintain quality of life. I think that is critical to explain when that comes up. It doesn't come up for every patient, but when it does, having a way to balance that risk and benefit for patients."

Braun mentions that adagrasib's availability as a 200 mg tablet actually allows for easier dose adjustments. The standard dose is 600 mg (or three tablets) twice a day.[4,11] "We like the dosing structure. It is a pill burden issue with the multiple amounts of pills taken, but it's very easy to dose adjust. So if the doctor needs to drop a pill due to tolerability, we are not looking at having to get a whole new prescription and require another prior authorization or another copay that the patient is going to have to pay out of pocket."

Houseknecht also offers some helpful pointers in managing drug interactions related to QT prolongation. "Krazati can prolong the QTc interval. We also know that some of the supportive care medications that we need to prescribe to help tolerate Krazati also prolong the QT interval. We have the patient medication profile and we have patients' inherent baseline QT. So we usually start off by looking at baseline QT with the medications they are already on. How much wiggle room do we have with Krazati causing a mean change in QT of about 18 msec? If I have someone who is 470 msec and I'm a little worried, we are going to be closely monitoring that patient's QT interval by bringing them back to clinic and getting an EKG maybe a week or two weeks after they start Krazati. We know the risk for torsades increases with electrolyte abnormalities. So if a patient is having really bad diarrhea that's not well controlled, I'm a little more nervous."

PATIENT-CENTERED ACTIVITIES

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

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.[12] Standard 1.2 of the ASCO/NCODA Standards reads:

Patient-Centered Activities - continued

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.[12]

Both Johns Hopkins and AON use the OCE sheets in their patient counseling sessions. Braun says, "We use them just about every opportunity we can. They're terrific. They're so well written, they're so easily laid out. Every time there is one available we always put it in with our new starts because it's just such great, relevant information. It's not full of fluff. It's not full of technical jargon. It has exactly what the patient needs and can understand. I think it's very well written for most patients to be able to understand very clearly."

At Johns Hopkins, Houseknecht says she loves the OCE sheets because "They identify the side effects. I like that they give the patient some self-care strategies. That is probably my favorite aspect of the OCE sheets because I think it is so important to educate patients to empower them to take control of their care. You know, like I said, we are busy clinics and I have over 250 patients. I cannot check in on a patient every single week and so I am hoping that my education initially is going to help empower my patient to self-manage some minor side effects at home and then know what is that threshold where I want them to call the clinic."

The next section of the Patient-Centered Activities mentions that adagrasib is associated with a moderate to high emetic potential and that antiemetics may be needed to prevent nausea and vomiting. The final section mentions counseling pearls like how to take the medication, how to minimize gastrointestinal (GI)-related side effects, and to remind the patient to notify the care team about any new prescription or over-the-counter medications as well as any herbal supplements due to potential for interactions. The last bullet also mentions the potential for infertility and to talk with the patient about fertility preservation if they are of child-bearing age.

Braun notes that overall side effects are manageable in patients on adagrasib. He says, "They are staying on therapy and toxicity-wise, it is manageable. Diarrhea and nausea are the most common, which is not surprising, but easy to manage. We spend a lot of time talking to patients about anti-diarrheal use and anti-nausea use. Everyone is getting loperamide when they start therapy and they are instructed on how to use it. We are always making sure they have antiemetics on hand. We don't want them starting the medicine without that antiemetic prescription because we do not want a patient who is nauseous in the middle of the night that has to wait until the next day to call the doctor and get a prescription, and then go to the drugstore when they're already feeling sick."

When counseling patients, Dr. Murray provides some unique perspective on some of the gastrointestinal (GI) side effects that patients can experience. "I talk a lot about GI side effects of KRAS^{G12C} inhibitors. In particular I have had patients have the range of GI side effects from dysgeusia, or changes in taste, pretty profoundly in a couple of patients that required dose adjustment, as well as dyspepsia, nausea, and vomiting in some patients. I describe it to patients as a range of symptoms that can be from vomiting to what I call food aversion. Some patients may not feel the nausea, but the nausea is presenting as being just averse to food." He goes on to say, "I do also speak broadly with patients about how some symptoms are common, the most common side effects being GI and also fatigue. That's always surprising for patients to hear, sometimes they think that pill-based medicines may not cause the same symptoms [as chemotherapy]."

Scan or click here to access adagrasib OralChemotherapy Education Sheet

FINANCIAL ASSISTANCE: A BENEFIT OF MIP AND THE MULTIDISCIPLINARY TEAM

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

Martens says, "Obviously having access to the EMR is a huge benefit for us. We're able to gather the clinical information we need to get the prior authorizations submitted. Chart notes, labs, test results, and office visits. We can obtain signatures much quicker. We can make interventions that outside pharmacies cannot. The turn-around for benefits approval, financial assistance, final approval, and just getting medication out the door is so much quicker than an outside pharmacy. We have what we need. It just gives us a huge advantage."

Houseknecht mentions that even though adagrasib is covered by most Medicare Part D plans, out of pocket costs are still cost prohibitive. This is where adagrasib's financial assistance program comes into play. Houseknecht says, "It has been very easy to navigate. The program seems very patient friendly, the form is patient friendly." She also mentions that the income thresholds to qualify for the program are very generous. "Their income thresholds are on par with where we need to be for oncology medications. When you are talking about a patient on a fixed income who has other medical expenses and also has other financial needs associated with the diagnosis, that higher [income cutoff] level of $150,000 for a household of two is really on par with today's economy and the financial toxicity of a stage 4 cancer diagnosis."

"Obviously having access to the EMR is a huge benefit for us. We're able to gather the clinical information we need to get the prior authorizations submitted. Chart notes, labs, test results, and office visits. We can obtain signatures much quicker. We can make interventions that outside pharmacies cannot."

– Joan Martens, CPhT, RPhT

When deciding between KRAS^{G12C} inhibitors, sometimes the decision comes down to medication access. Houseknecht says, "If both are clinically appropriate and I have a patient with some financial toxicity who needs to apply for assistance, I'm going to as them to estimate their household income and then I may choose which direction we go based off what I've learned about access. "

For commercially insured patients, there is a copay card available that helps to bring the cost down for qualifying patients. Lastly, Houseknecht mentions that lung cancer doesn't get a lot of funding for grants and what little funds are available are gone by mid-January. She says, "That reliance on pharmaceutical assistance programs is high in our patient population."

CONCLUSION: NCODA, THE MIP AND 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, selection, increased speed to therapy, reduced cost, and hospitalization and by improving adherence techniques for the patient and their Medically Integrated Teams.

Dr. Mulherin has this to say about the future of KRAS mutations and inhibitors: "The main thing is the importance

Conclusion: NCODA, the MIP and PQI: Optimizing Patient Outcomes - continued

of doing NGS testing and looking for KRAS^{G12C} mutations. I think there is still undertesting in the general, even in the NSCLC-member institutions. If you don't look, you will never find it. So this is not the end of the story."

The PQI provides the MIP program with an easy to use, compact clinical resource guide when discovering the right patient and dispensing adagrasib. It helps the team ensure they are providing patients with the tools and education to improve clinical outcomes.

Pairing Medically Integrated Dispensing with the Adagrasib (KRAZATI®) PQI meets NCODA's Guiding Values of being Patient-Centered and Always Collaborative.

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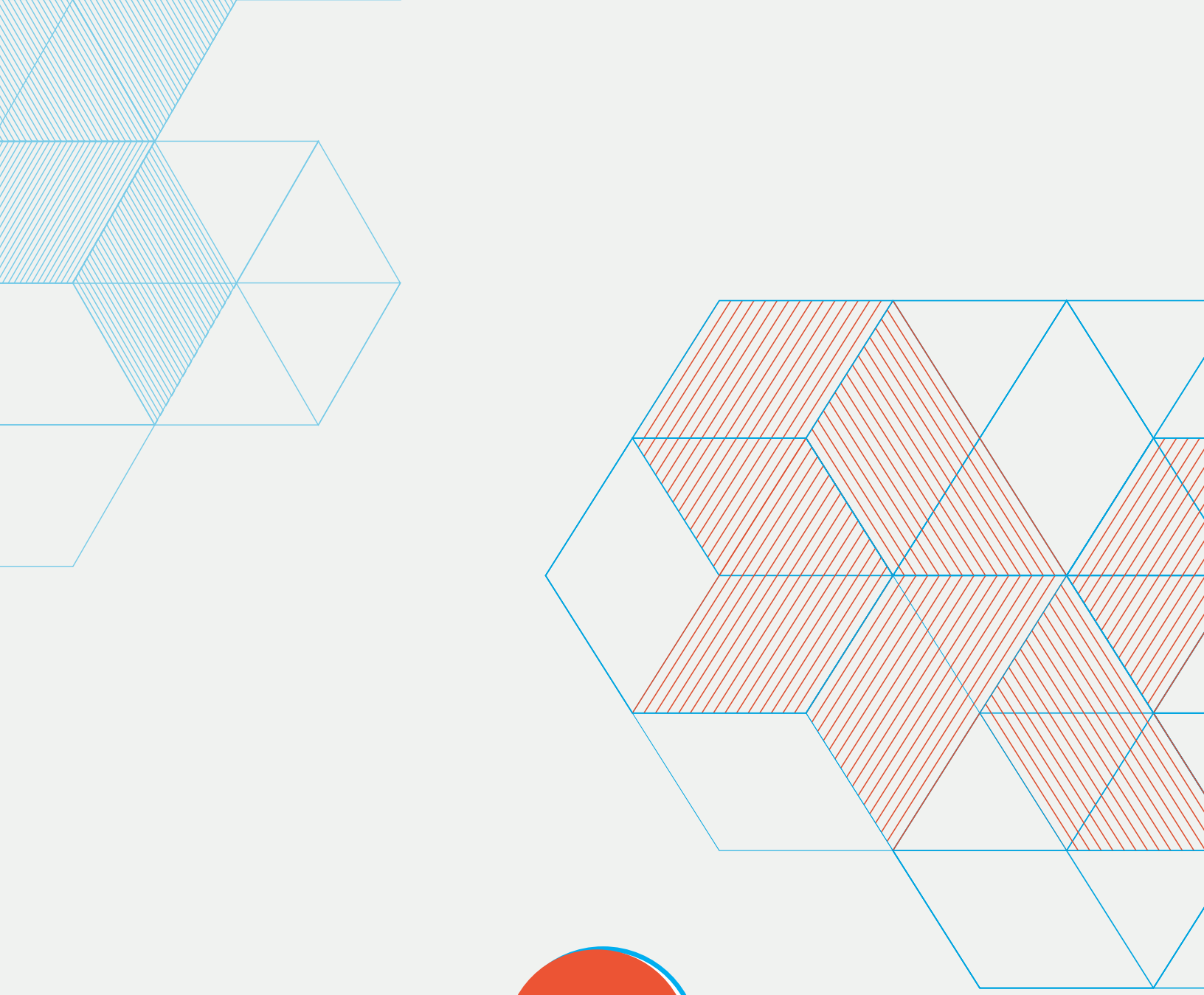

Practice panelist's comments reflect their experiences and opinions and should not be used as a substitute for medical judgment.