

PQI IN ACTION



**ZANUBRUTINIB (BRUKINSA®)
PATIENT SELECTION AND MANAGEMENT
IN MANTLE CELL LYMPHOMA**



**NCODA'S POSITIVE QUALITY
INTERVENTION IN ACTION**

INTRODUCTION

In an effort to promote higher quality patient care NCODA created the NCODA Positive Quality Intervention (PQI) as a peer-reviewed clinical guidance document for healthcare providers. By providing Quality Standards and effective practices around a specific aspect of cancer care, PQIs equip the entire multi-disciplinary care team with a sophisticated yet simple-to-use resource for managing patients receiving oral or IV oncolytics. The PQI fosters better care for patients 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. The **Zanubrutinib (BRUKINSA®) Patient Selection and Management in Mantle Cell Lymphoma** PQI achieves all of these standards in an effort to manage Mantle Cell Lymphoma patients at the highest level of care.

The PQI in Action incorporates opinions and experiences from oncology experts within the medically integrated teams at two leading cancer care organizations. These professionals have successfully implemented medically integrated pharmacies (MIP) as well as the use of Positive Quality Interventions throughout their care teams to improve the clinical outcomes of patients. This article will take a look at Arizona Blood and Cancer Specialists and Kootenai Health to see how utilization of consistent clinical information like that contained within NCODA's **Zanubrutinib (BRUKINSA®) Patient Selection and Management in Mantle Cell Lymphoma** PQI standardizes knowledge exchange and improves clinical communication within their organizations. It will also showcase the great work, best practices, and the passion for patients that these two centers of excellence strive for each and every day.

Arizona Blood and Cancer Specialists is built on a foundation of clinical excellence, compassionate support, and a commitment to helping patients through very difficult times in their lives. Since the practice began, they have continued to build on a shared vision of how they can positively impact patients' lives, focusing on their goal to provide community-based, compassionate cancer care close to home. Arizona Blood and Cancer Specialists boasts 10 medical oncologists, 2 radiation oncologists, 2 breast surgeons, and 7 advanced practice practitioners with clinics in Tucson, Oro Valley, and Green Valley. Arizona Blood and Cancer Specialists is also a partner of OneOncology. OneOncology provides access to the latest cancer research and treatment options to provide the best care for patients. The goal of Arizona Blood and Cancer Specialists is to provide a comprehensive and personalized care for each and every cancer patient.

Kootenai Health provides a comprehensive range of medical services to patients in North Idaho, Eastern Washington, Montana, and the Inland Northwest at several facility locations. The main Kootenai Health campus is located in Coeur d'Alene, Idaho and includes a 330-bed community-owned hospital and a wide range of physician clinics including oncology care in Coeur d'Alene, Post Falls, and Sandpoint. Kootenai Health is routinely ranked as a leader in health care by patients, peers and national organizations. This reputation of service excellence, community leadership, and compassionate care has earned Kootenai many awards over the years, all of which demonstrate a commitment to the organization's core values of superior quality and safety, patient focused, healthy culture, stewardship, and visionary leadership. Specifically, their specialty pharmacy is dual accredited through URAC and ACHC, demonstrating a commitment to quality standards and continually striving for excellence.

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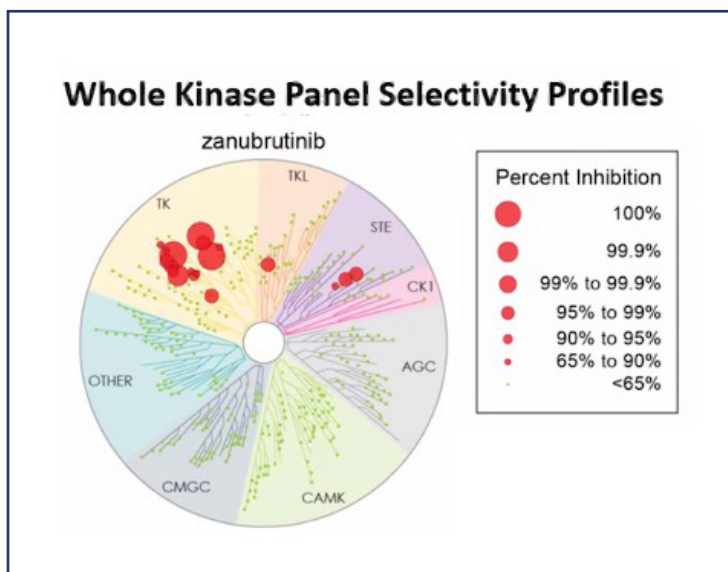


Kristin McCauley, CPht
Oncology Pharmacy Technician

MANTLE CELL LYMPHOMA AND THE ROLE OF BRUTON'S TYROSINE KINASE INHIBITORS

Mantle Cell Lymphoma (MCL) is a type of non-Hodgkin's lymphoma (NHL). MCL is a B-cell lymphoma that develops from malignant B-lymphocytes within a region of the lymph node known as the mantle zone, thus being named mantle cell lymphoma.¹ In general MCL is most common among men aged 60 to 70 years of age. According to the National Institute of Health (NIH), MCL is a rare subtype of B-cell NHL with an annual incidence of one case per 200,000 people.² Many people are asymptomatic during the early stages of MCL. When symptomatic, MCL most commonly manifests with painless swelling of lymph nodes of Waldeyer's ring. This is a ring of lymphoid tissue around the base of the tongue, either side of the throat, tonsils and the back of the nasal cavity.^{1,2} Other symptoms may be non-specific, including lack of appetite, nausea, early satiety, abdominal swelling/bloating. Being a B-cell cancer, it comes as no surprise that other symptoms may include what is commonly referred to as "B Symptoms." These include fever, unexplained weight loss, and night sweats. Diagnosis is achieved through a myriad of tests: lymph node and bone marrow biopsy, imaging, FISH, and flow cytometry. Traditionally, first line therapy consists of combination chemotherapy regimens of varying mechanisms. Bruton's tyrosine kinase (BTK) inhibitors are reserved for second-line and subsequent therapy options.

Zanubrutinib is a potent, highly specific, and irreversible BTK inhibitor and is an investigational treatment for B-cell malignancies including chronic lymphocytic leukemia (CLL), mantle cell lymphoma (MCL), Marginal Zone Lymphoma, and Waldenström's macroglobulinemia.³ Zanubrutinib received FDA breakthrough therapy designation for the treatment of adult patients with MCL following at least one prior therapy on November 14, 2019 based on data from a phase I and a phase II trial.^{5,7} After the interviewing of our participants and writing of this article, BRUKINSA® (zanubrutinib) was granted FDA approval for Waldenström's macroglobulinemia. Although not yet FDA approved, zanubrutinib is a preferred regimen (category 2A) for second-line and subsequent therapy in this setting according to the National Comprehensive Cancer Networks (NCCN) guidelines for Marginal Zone Lymphoma and may be considered in patients with an intolerance or contraindication to ibrutinib.⁸ Again, not yet FDA approved, NCCN has listed zanubrutinib as a preferred regimen (category 2A) for CLL/SLL without del(17p)/



TP53 mutations as an added option for patients with an intolerance or contraindication to other BTK inhibitors in the second-line and subsequent setting for frail patients with significant comorbidities and patients under 65 years old without significant comorbidities. For CLL/SLL with del(17p)/TP53 mutations, NCCN lists zanubrutinib as first line with a contraindication to other BTK inhibitors and second-line and subsequent as an added option for patients with intolerance or contraindication to another BTK inhibitor.⁹ In the space of Waldenström's macroglobulinemia, NCCN lists zanubrutinib as a Category 1 recommendation for primary therapy although the FDA has not yet approved this in the labeling information.¹⁰

Zanubrutinib has shown greater selectivity for BTK with fewer off-target receptor interactions compared to the currently approved agents in the class.⁴ Whole kinase panel selectivity profiles give a visual representation of this.¹¹ Potential side effects seen with BTK inhibitors are likely related to off-target interaction with other receptors including epidermal growth factor receptor (EGFR) and interleukin-2-inducible T-cell kinase (ITK).⁵⁻⁷ A phase I/II trial evaluated zanubrutinib 160 mg twice daily or 320 mg once daily in 144 patients with various B-cell malignancies. The pharmacokinetic profile of this once or twice daily dosing is unique as most medications do not have flexible dosing options. The measure of half-maximal inhibitory concentration (IC_{50}) is the most used measure to determine how much medication

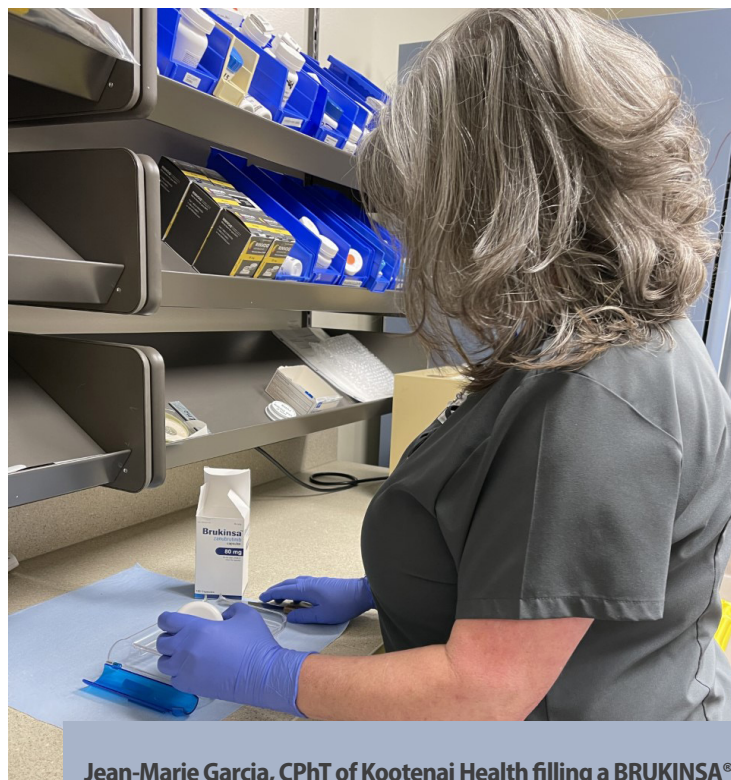
is needed to achieve inhibition of a process by half and thus the potency.¹² Therefore, for the purposes of BRUKINSA® we are looking at the IC₅₀ of BTK. With both the once daily and twice daily dosing options, the free fraction in plasma stayed above the IC₅₀; Showing 100% BTK inhibition in the blood and lymph nodes with the twice daily dosing and 100% inhibition in the blood, with 94% inhibition in the lymph nodes with the once daily dosing.^{13,14} Safety analysis in these patients showed a less than 2% incidence of both atrial fibrillation (Afib) and major hemorrhage, which are potential grade 3 or grade 4 adverse effects seen with other BTK inhibitors.⁷ Clinical trials have shown an increase in neutropenia, but with no increase in febrile neutropenia (MCL studies all Grades 25%, Grade 3/4 5%).¹⁵ This side effect profile makes

zanubrutinib a very viable option in the BTK inhibitor space. Providers from both practices agree that zanubrutinib is of particular interest for BTK inhibitor use in a specific subset of patients. In patients with Afib, Dr. Catherine Azar, MD of Arizona Blood and Cancer Specialists shares, “the solution is something with less side effects and that is more specific, which is zanubrutinib (BRUKINSA®).” At Kootenai Health, Paul White, MD says, “In general I use the second generation BTK inhibitors, like BRUKINSA® (zanubrutinib), for people who have progressed through ibrutinib, have experienced toxicity, or have any kind of history of bleeding or cardiac toxicity.” This subset of patients has traditionally been difficult to manage with BTK inhibitors.



THE PQI – THE VALUE OF POSITIVE QUALITY INTERVENTIONS

Positive Quality Interventions (PQIs), are designed to operationalize and standardize practices to achieve positive clinical outcomes. These one to two page clinical reference documents help to boil down the vast and sometimes overwhelming amount of information around a product into a concise, easy to digest format. The treatment and management of oncology patients on oral drug therapy is continually changing and evolving. The growing complexity creates a need for healthcare professionals to have a quick resource to turn to for drug therapy management information. The medically integrated pharmacy team is in a unique position to ensure appropriate treatment, increase compliance, and maximize outcomes. Jamie Bankey, RPh of Kootenai Health shared that bringing in Medically Integrated Dispensing helped their process by, “streamlining clinic calls, helping take the load off providers, nurses, and MAs, and allowing us to do our due diligence on the medication side of things. The feedback we receive from the physicians has been overwhelmingly positive.” Loan Lam, PharmD also of Kootenai Health shares that, “previously pharmacists were dedicated to just the IV side or just the orals. Now we are all very integrated. We have begun cross training and bridging the gap between the traditionally segregated roles. This allows for growth and change which is extremely helpful with these complex, multi-drug regimens.” The Medically Integrated Teams at both Kootenai Health and Arizona Blood and Cancer Specialists both utilize PQIs in different manners, but both agree that



Jean-Marie Garcia, CPhT of Kootenai Health filling a BRUKINSA® prescription for a Mantle Cell Lymphoma patient.

they have gained great benefit from this resource. Dr. Paul White of Kootenai Health states, “the PQI is really nice and concise. It gives a summary of indications, a background of

the product, and things to look out for.” Dr. White goes on to share, “in my own practice, any time I am prescribing a medication I need to ensure that it is appropriate and that I am not putting my patient at any undue risk and the PQI helps to ensure this.” Although not currently integrated into the electronic systems, Stacey Silvain, RN of Arizona Blood and Cancer Specialists feels, “every nurse should have links to the PQI as well as hard copies. Everyone learns differently.” She went on to share that this is something that she aims to integrate into their electronic systems for ease of use and to allow all members of the Medically Integrated Team access. Speaking on the value of the PQI initiative, Stacy Silvain, RN states, “the PQI is a natural extension and complement to what we do.” Carol Hemersbach, CPhT, BSHCA shares her thoughts as well regarding the value of the PQI stating, “the PQI allows us to provide better care for the patient. It allows us to identify side effects faster or helps to prevent the patient from experiencing them. It also just increases our confidence in our abilities to be able to provide the patient the best care.”

The first step in the **Zanubrutinib (BRUKINSA®) Patient Selection and Management in Mantle Cell Lymphoma** PQI is to ensure that the patient is an appropriate candidate for zanubrutinib based on the indication. According to the FDA labeling and NCCN guidelines, zanubrutinib is indicated as second line or subsequent therapy in mantle cell lymphoma patients. As mentioned earlier, NCCN guidelines do recommend zanubrutinib in other off label indications as well. After the interviewing of our participants and the writing of this article, BRUKINSA® (zanubrutinib) was granted FDA approval for Waldenström’s macroglobulinemia. With so many BTK inhibitors to choose from, both practices find it important to know when to use each in the most appropriate scenario. Next, the PQI dives into specific dosing and dose

"THE PQI IS A NATURAL EXTENSION
AND COMPLEMENT TO WHAT WE DO. "

Stacey Silvain, RN

adjustments based on interactions. Carol Hemersbach, CPhT, BSHCA of Arizona Blood and Cancer Specialists shares that the PQI is particularly useful in helping to identify possible medication interactions and the suggested dosing based on the particular situation. She is able to communicate this information to the provider who ultimately makes the dosing decisions. At Kootenai Health, the oncology pharmacy technicians and pharmacists screen for these important interactions and also communicate with their oncologists to determine the best course of action as well as the appropriate dose reduction.

Another important point in the PQI Process is the consideration of prophylaxis for herpes simplex virus, Pneumocystis jirovecii pneumonia (PJP), and other infections according to standard of care in patients at increased risk for infections. Grade 3 or higher infections occurred in 23% of patients on zanubrutinib, with pneumonia being the most common infection.¹⁵ With the complexity of MCL, it is often easy to forget things like PJP or infection prophylaxis. Carol Hemersbach, CPhT, BSHCA states, “one of the things I love about Arizona Blood and Cancer Specialists is the communication and openness.” This ultimately prevents things from falling through the cracks and allows patients access to superior care.

| DESCRIPTION | DOSING |
|------------------------------------|-----------------------------|
| Starting Twice Daily Dosing | 160 mg by mouth twice daily |
| Starting Once Daily Dosing | 320 mg by mouth once daily |
| With Strong CYP3A Inhibitor | 80 mg by mouth once daily |
| With Moderate CYP3A Inhibitor | 80 mg by mouth twice daily |
| With Moderate/Strong CYP3A Inducer | Avoid Concomitant Use |
| Severe Hepatic Impairment | 80 mg by mouth twice daily |

PATIENT EDUCATION – PUTTING PATIENTS AT THE CENTER OF CARE

The patient-centered activities section of the PQI is an integral part of every PQI, because being patient centered is the goal of every NCODA member as well as one of NCODA's guiding values. In this particular PQI, counseling the patient is the first step of the patient-centered activities.

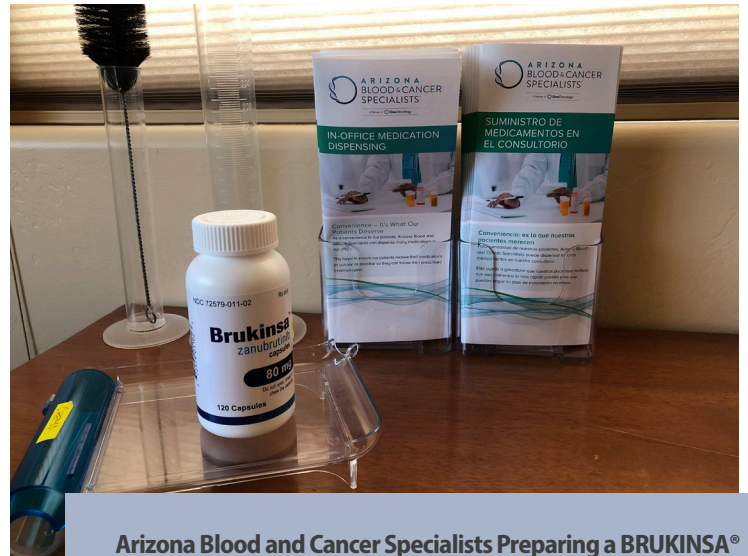
In 2019 the Patient-Centered Standards for Medically Integrated Dispensing: ASCO/NCODA Standards were published to provide standards for medically integrated dispensing of oral anticancer drugs and supportive care medications.¹⁶ Standard 1.2 of the ASCO/NCODA Standards reads:

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's 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.¹⁶

Both practices utilize Oral Chemotherapy Education (OCE) Sheets for educating on oral medications to meet the ASCO/NCODA Standards mentioned above. Much of the important educational information on zanubrutinib can be found in the NCODA-led Oral Chemotherapy Education sheets. In collaboration with HOPA, ONS, and ACCC, these education sheets are a resource to provide information about oral chemotherapy drugs and their side effects to both cancer patients and caregivers. We know having cancer or caring for someone with it can be overwhelming, but finding reliable

information about the medicines should not. We aim to help caregivers by providing them a tool to pass on to their patients with cancer that will answer drug related questions and help empower patients to become a more active participant in their cancer treatment. OCE sheets are written with the needs of cancer patients in

mind. We have strived to use appropriate language and to present pertinent content in an easy-to-understand format to improve patients' understanding of how to take medications correctly. A medication schedule and an outline of potential side effects, as well as information about how to manage



Arizona Blood and Cancer Specialists Preparing a BRUKINSA® Prescription.

those side effects, are key components of the OCE Sheets. The BRUKINSA® OCE sheet is a perfect supplement to pair with the this PQI. At Arizona Blood and Cancer Specialists, Dr. Azar shares that they hit education from many different points. She says, “I will counsel the patient, then one of the nurses may counsel, and then at the time of dispensing the patient will get educated.”

With many OCE sheets printed out and ready for use, Kootenai Health shared their best practice regarding patient education. Dr. White shares that the provider will educate the patient on the medication as well as general cancer precautions prior to sending the prescription to the Kootenai Health Pharmacy. Lauren Wagner, PharmD, BCPS explains the process further, stating, “because we know that they are bombarded with all this new information on day one of treatment, we call the patient and actually do the counseling over the phone beforehand to give them a preview of what to expect. Then when they come to pick up the medication and have additional questions, we are here. We also will counsel the patient at the time of medication pick up. On the future pickups/refills, we are reviewing the notes and seeing if they noted some side effects going on and we get an opportunity to review their labs and can always pop over to address any issues that we may see.” In an ideal setting, being able to counsel patients more than once is definitely of benefit, providing patients the same information multiple times.

[CLICK HERE
TO VIEW
THIS OCE SHEET](#)

PUTTING THE PQI INTO ACTION

Communication is the key to best practice. Both Kootenai Health and Arizona Blood and Cancer Specialists share their best practices around communication along with Medically Integrated Dispensing. For providers with experience in a medically integrated setting, it is apparent that Medically Integrated Dispensing elevates patient care. Dr. Azar shares, “I absolutely think that is great for somebody in house to hand the patient the prescription vial face to face, make sure they understand the directions, make sure they know the side effects, and make sure they know when to call us.” These sentiments were echoed across all participants. Regarding Medically Integrated Dispensing, Dr. White states, “we are lucky that we have an in house specialty pharmacy. This is a really useful tool for us and a great resource for a lot of reasons.”

Sometimes patients are required to fill their specialty oncology medications through a mail order pharmacy. Jamie Bankey, RPh shares, “we are often able to provide the first fill of a medication. We educate the patients thoroughly and set them up for success. Most patients are very upset when they find out they then have to fill through a mail order after working with us. We are constantly trying to gain contracts and are always pushing for different accreditations to give us a little more leverage in gaining the trust of these insurance companies. Showing insurance companies that we are a specialty and to see that we provide better care, better outcomes.” Lauren Wagner, PharmD, BCPS shares, “I feel like we are a great resource for the patients, we can ease their worries a little bit. Patients really depend on us, even our mail order patients, they all somehow find their way back to us. That is something that I am really proud of.” Both practices follow not only the patients to whom they dispense, but also follow mail order patients ensuring that their care is not interrupted or lost in the shuffle. Stacey Silvain, RN strongly states, “I think there is no debate that medically integrated dispensing is a very personalized experience, compared to the mail order experience. Having Medically Integrated Dispensing shows that as a practice we have an inherent investment in our patients, their outcomes, and their experience.” Her colleague, Carol Hemersbach, CPhT, BSHCA elaborates, saying, “patients like the personal relationship as opposed to having to call a phone tree and be transferred and have so many different people involved in processing of one prescription.” Jamie Bankey, RPh of Kootenai expands on his practice experiences following



Kootenai Health Pharmacist Ana Livingston, PharmD verifying a BRUKINSA® prescription prior to dispensing.

up with outside pharmacies, stating, “this is a service that we are not getting paid for, but we make sure things are taken care of for the patient. We are a godsend to some of these patients.” Kootenai Health leverages technology to help with managing this vast number of patients. Through their electronic health record, they are able to flag patients that fill in house or through a mail order for follow up and keep them in the queue as long as needed. The system will also flag patients for monthly and/or yearly follow ups as well. Loan Lam, PharmD of Kootenai Health says, “the system is set up to provide a lot of extra care.”

**"THERE IS NO DEBATE THAT
MEDICALLY INTEGRATED
DISPENSING IS A VERY
PERSONALIZED EXPERIENCE."**

Stacey Silvain, RN

One of the unique aspects of Arizona Blood and Cancer Specialists is their Oral Chemotherapy Adherence and Toxicity Assessment Forms. Stacey Silvain, RN shares more about their best practice stating, “this involves working with the regimen building team, MID team, and the clinical providers through utilization of our Oral Chemotherapy Adherence and Toxicity Assessment Forms. The goal here is to engage the patient at the start of therapy in identifying financial, transportation needs, or unexpected side effects that may interfere with their treatment compliance. I feel this Oral Chemotherapy Adherence and Toxicity Assessment form is extremely impactful as it organizes important talking points/questions and engages the patient more proactively before their actual office visits with their provider. Tracking this form, communication can be especially critical, as it is a kind of a bridging point.” This practice developed form is integrated into their medical record allowing for a streamlined workflow and increasing communication across the Medically Integrated Team.

Kristin McCauley, CPhT of Kootenai Health shares her most valued piece of the PQI document as a pharmacy technician, stating, “I like the patient support program. This section of the PQI is the most valuable to me. Just being able to have the resources to be able to let the patient know there is more support if needed.” She continued by sharing that the role of the technician at her practice has expanded, “we as technicians have started getting more involved with the different manufacturer programs and patient support. It's really great to have a resource to be able to make sure that we are checking all the right boxes and getting the appropriate information for the patient to get the medication approved faster.” The cost of cancer care can be crippling, making the support of charitable foundations and manufacturer support a necessity in the daily workings of those in Medically Integrated Dispensing. Loan Lam,

PharmD shared that the technicians at Kootenai Health perform many essential roles from funding, to follow up, and providing additional support to the patient and pharmacists as needed. The myBeiGene Patient Support Program can provide additional support to patients in the way of a dedicated Oncology Nurse Advocate of practices, patients, and caregivers. They can provide patient and caregiver follow-up support and connect patients and caregivers with advocacy groups and local/national free resources. Copay support, a bridge program during insurance delays, and free product are available in certain situations. Kristin McCauley, CPhT shares that her favorite part of her job is taking care of patients. She says, “the best part about where I work is the fact that we are going to get them their medication and they are not going to be put out financially by having to spend thousands and thousands of dollars. Making them choose whether they are going to take their medication or not because they cannot afford living expenses. I think it's great that we can offer assistance to them.”

"MEDICALLY INTEGRATED DISPENSING PROVIDES FASTER ACCESS TO MEDICATIONS, LESS WASTE, LESS RISK FOR MEDICATION ERRORS, AND MORE PROVIDER INVOLVEMENT IN THE PATIENT'S CARE."

Carol Hemersbach, CPhT, BSHCA

CONCLUSION- MAKING A DIFFERENCE EVERY DAY

Every day the Medically Integrated Team has the opportunity to make a difference in the lives of patients. Every day the team can learn something new or can begin a process that optimizes care. Dr. White shares, “I like helping people navigate through difficult situations and helping them make tou-

gh decisions, hopefully with good outcomes, and getting that continuity with them in which you do not necessarily get with other specialties.” The PQI fosters this through the identification of the appropriate patient, accurate selection, increased speed to therapy, reduced cost, and by improving adherence techniques for the patient.

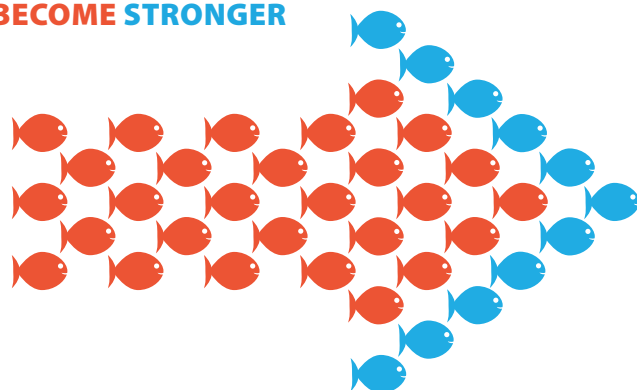
Carol Hemersbach, CPhT, BSHCA states it perfectly by saying, “Medically Integrated Dispensing provides faster access to medications, less waste, less risk for medication errors, and more provider involvement in the patient's care.” The PQI gives the Medically Integrated Team an easy to use, succinct clinical resource guide for identification of the right patient and best practices. It helps the team ensure they are providing patients with the tools and education to improve their own clinical outco-

mes. Pairing Medically Integrated Dispensing with the **Zanubrutinib (BRUKINSA®) Patient Selection and Management in Mantle Cell Lymphoma PQI** meets NCODA’s Guiding Values of being Patient-Centered and Always Collaborative. Loan Lam, PharmD, sums up the sentiments of all participants stating, “our passion is helping patients.”

**"OUR PASSION IS
HELPING PATIENTS."**

Loan Lam, PharmD

**WORKING TOGETHER,
WE BECOME STRONGER**



Helpful Online Resources

- [NCODA Website](#)
- [Oral Chemotherapy Education Sheets](#)
- [Are you interested in authoring a PQI?](#)
- [Positive Quality Interventions](#)
- [Brukina PQI](#)
- [Are you interested in taking part in a PQI In Action?](#)

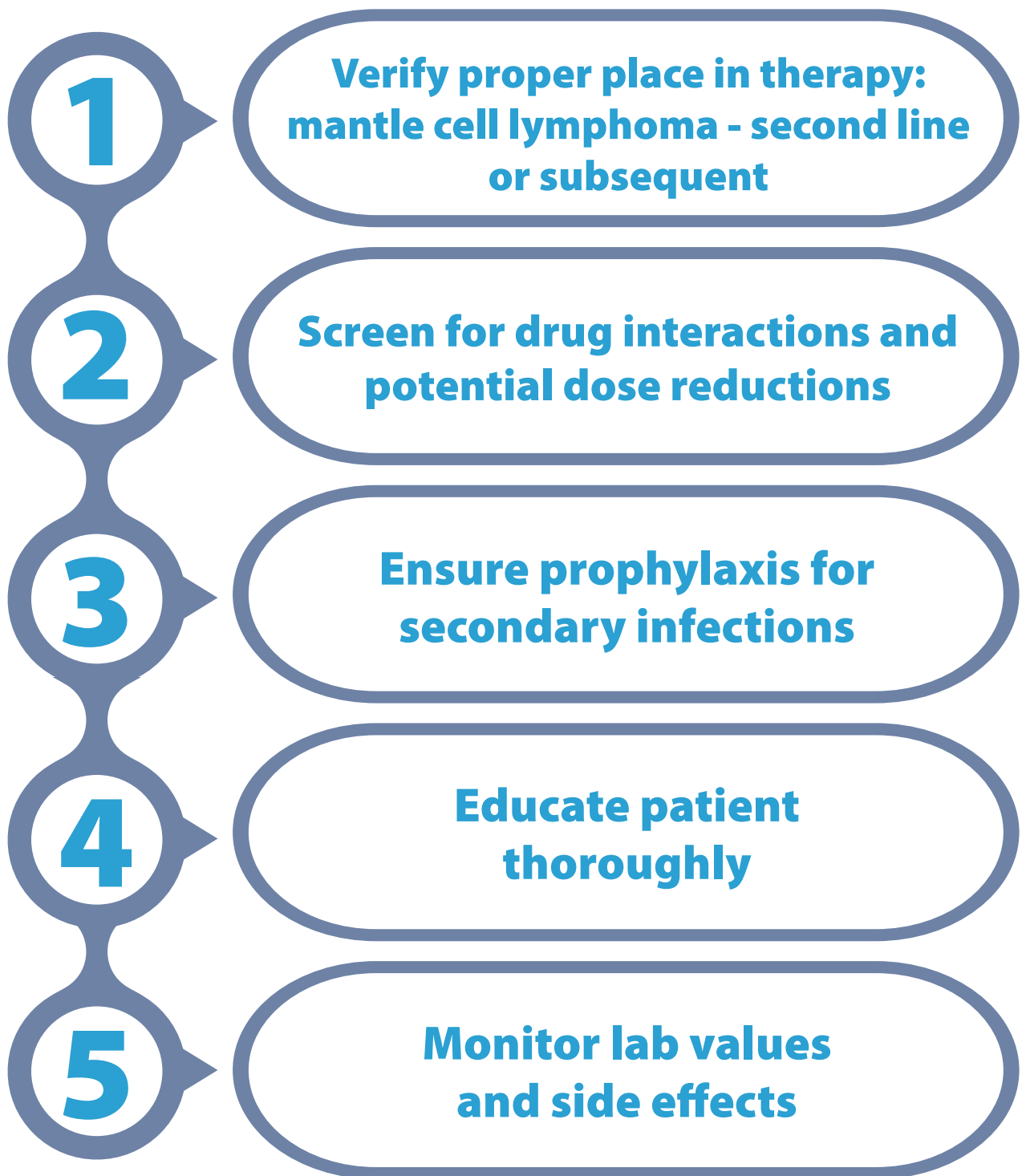
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ON THE COVER:

- Kootenai Health pharmacist Loan Lam, PharmD counseling a Brukinsa patient.

PQI PRINCIPLES:



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

Important notice: NCODA has developed this Positive Quality Intervention in Action 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.



NCODA'S POSITIVE QUALITY INTERVENTION IN ACTION