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Navigating Drug Costs: Tools to Aid in Determining Comprehensive Drug Value

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COLUMNS

FEATURE

Navigating Drug Costs: Tools to Aid in Determining Comprehensive Drug Value

Jennifer MacDonald, PharmD
PGY-2 Oncology Pharmacy Resident
University of Colorado
Aurora, CO

In an era of both expanding oncologic therapeutic options for patients and escalating drug prices, it is important to consider not only efficacy and safety but also the drug costs for the patient. Although a newer therapy may be indicated, if it comes at extreme cost to the patient, a comprehensive review should be undertaken before the therapy is initiated. In 2016, 21 oncologic agents were approved for the treatment of various malignancies. These approvals consisted mostly of rebranding medications like daratumumab, pembrolizumab, or nivolumab to encompass a broader array of indications.[1] What do these approvals and expanded indications have in common? High cost.

In recent years, the American public has grown increasingly concerned about escalating drug costs and has urged the government to institute price controls.[2] These growing concerns led a number of groups—including the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network (NCCN), and Memorial Sloan Kettering Cancer Center (MSKCC)—to develop tools evaluating the utility of various therapies for a patient.[2] These tools take into account several aspects that are important when one is considering a treatment regimen and attempting to determine a drug's overall value; some factors considered are quality of clinical data, likelihood of serious adverse events, magnitude of treatment effects, cost-effectiveness, product costs, treatment benefits, and effects on the healthcare system.[2] These tools mark an important transition in health care toward a value-based framework. But how do we incorporate these tools to guide clinicians and patients in making value-based treatment decisions?

Before any tool is used, its associated strengths and limitations should be evaluated. Of equal importance is the definition of the value used to develop the tool. In its simplest form, value equals outcomes divided by cost.[3] This vague definition leaves much to interpretation. Outcomes differ for each treatment regimen but also vary significantly from patient to patient. Take, for example, the use of high-dose interleukin-2 (IL-2) for a patient who has metastatic melanoma. The monthly cost is roughly $22,000, based on 2014 drug prices. Only 10% of patients derive a durable response to treatment, and almost 50% of patients experience grade 3–4 adverse events.[4,5] Though outcomes may be acceptable to the 10% of patients who achieve a durable response and the benefits of the regimen may greatly outweigh the associated costs and toxicity experienced, the treatment would likely not have value for a patient who dies during treatment or has no response. In this case, a majority of patients are likely not to associate high-dose IL-2 with an outcome that outweighs the costs.

Faced with the need for a value-based framework tool caused by this drug-cost crisis, a number of organizations have developed scoring tools for providers and patients. The tools developed by NCCN, ASCO, and MSKCC are described in **Table 1**. All these tools offer a means to facilitate dialogue between providers and patients regarding a given regimen's place in therapy that is customized to meet individual patients' goals in accordance with their personal definition of value. Although components of the scoring systems vary, it is clear that cost entails more than just the exchange of money. Cost includes toxicity and loss of quality of life, among other measures. The NCCN Evidence Blocks tool has been incorporated into all previously existing guidelines and is perhaps the simplest scoring tool available but is much less specific to a given patient.[6] ASCO recently adapted its net health benefit (NHB) tool in response to feedback about limitations and suggestions for improvement. The revised tool now emphasizes evidence that includes overall survival benefit and gives more weight to this benefit than, for example, to progression-free survival.[7] The ASCO scoring system is complex, but comparisons of NHB score and drug acquisition cost are made graphically, allowing an easier grasp of the differences. The MSKCC DrugAbacus is probably the most complicated tool and is less personalized.[3]

Each tool for measuring drug value is unique, and providers may find one tool more appealing for their patients in general or for a specific patient. No matter which tool is selected, their incorporation into treatment discussions should become commonplace. In an era of expanding targeted agents and personalized oncologic medicine, and as drug toxicities are minimized and drug costs escalate, value-based discussions will become increasingly important. The place of these agents in practice (i.e., as first- or second-line treatments) and the therapeutic intent behind their use (i.e., for curative vs. palliative care) greatly affect the perceived value of each agent.

The incorporation of these tools into guidelines and clinical practice is growing. Understanding the tools' limitations and applications is fundamental to using them in discussions with patients about treatment options. These tools may allow pharmacists and providers to make a comprehensive comparison of second- or third-line treatment options. In addition, they fulfill a crucial function in facilitating discussions of value-based care that encompass all aspects of treatment, particularly in the palliative setting. As the healthcare system continues to shift toward a value-based framework, adaptation of these tools will continue. More studies are needed regarding the use of these tools in clinical practice and multidisciplinary team recommendations. Perhaps some combination of all the available tools will prove to be the most appropriate course.

With the continuing development of oncologic therapies and understanding of indications, these tools can facilitate shared

decision making about treatment that is personalized to each patient. Value-based decision tools allow therapy choices to be tailored to individual patients' financial circumstances, goals, and preferences. ●●

Table 1. Value-Based Drug Assessment Tools

Organization Tool	Components of Scoring Tool Used to Define Value	Scoring System	Considerations
National Comprehensive Cancer Center (NCCN) Evidence Blocks[6]	5 measures: price, efficacy, safety, quality of clinical data, and consistency of clinical data	Score of 1-5 given for each measure; color blocks used to enable quick comparison of treatment options	Does not take into account specific patient factors; is meant to be a general guide for patients and providers to adapt according to their own formula; can be used to determine value specific to each patient
American Society of Clinical Oncology (ASCO) Value Framework[7]	5-step process: clinical benefit, toxicity, bonus points, net health benefit, and cost	Values calculated and depicted graphically to facilitate discussion between physician and patient	Lacks quality of life and patient-reported outcomes; complicated scoring system requires a hazard ratio and prospective study comparator studies to provide the most appropriate score; flexible scoring allows interpretation by patients and expression of what they personally value
Memorial Sloan Kettering Cancer Center (MSKCC) DrugAbacus[3]	6 modifiable price components: dollars per life-year, toxicity discount, novelty multiplier, cost of development, rarity multiplier, and population burden of disease	Displays an "Abacus" price and compares it to the wholesale acquisition cost pricing	Difficult to use and understand but does allow providers to modify scores based on the user's definition of value

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Reflection on Personal Impact *and* Growth

Caring for Patients in a Different Light: Pharmacists' Experience at Indian Summer Camp for Kids with Cancer

Sarah T. Mitchell, PharmD
PGY-2 Oncology Pharmacy Resident
Norton Children's Hospital
Louisville, KY

Savannah L. Gulley, PharmD
PGY-1 Pharmacy Resident
Norton Children's Hospital
Louisville, KY

For 36 years, Indian Summer Camp has provided children with cancer in Kentucky and southern Indiana a reprieve from fighting cancer and a place where they can just be kids. It began as a summer camp but has now been expanded as part of the Kids Cancer Alliance, an organization that provides more than 50 programs for these children and their families each year. However, the main event remains Indian Summer Camp for Kids with Cancer, a weeklong camp dedicated to serving local children who have battled or are currently battling cancer.

To an outsider, camp may appear to run smoothly, but this amazing experience takes a small army of volunteers to function seamlessly. Volunteers range from students to previous campers and include a full medical staff of physicians, nurses, and pharmacists. Unless a child is hospitalized, none is ever too sick to come to camp, and the medical staff works to accommodate all children regardless of their medical needs. When given the chance to serve as part of the medical staff, our immediate response was "yes." The opportunity to see our patients experience a normal childhood, even for just a week, was something we could not pass up.

The first day of camp is the busiest for all staff members, but especially for the pharmacy staff. We work with campers and families to perform a thorough medication reconciliation, develop medication administration records (MARs) for each camper, and fill individualized medication boxes for the week. Each camper's medications are unit-dosed and divided into four administration times: breakfast, lunch, dinner, and bedtime. Because roughly 60% of our 100-plus campers receive at least one scheduled medication, we have to recruit local pharmacy students as additional volunteers to complete the filling of all campers' medication boxes by dinnertime. After all campers have arrived and their medications are accounted for, the pharmacy team gets to enjoy the waterslides and jump houses and take part in the joy of camp.

Before each meal, we review all campers' MARs and gather medication boxes to ensure that all children receive the appropriate medications at the proper time. As campers enter the dining hall, they stop by the medication table to receive their scheduled doses and then rejoin their cabin mates to hear updates on the Polar Bear Swim and Davy Crockett camp awards. After all campers have received their medications, a final MAR review is conducted to ensure that no child missed a medication administration. This process is repeated four times a day, every day, until the end of camp.

Outside the regular medication administration times, the pharmacy staff also provides around-the-clock pharmacy services. We manage campers' as-needed medications and maintain a small supply of over-the-counter and emergency medications for common concerns that may arise at camp, ranging from bug bites and rashes to headaches and swimmer's ear. We even keep a small supply of intravenous antibiotics in case of unexplained fever. Where the medical management of campers is concerned, there is never a dull moment. This experience helped prepare us to manage a variety of conditions in this patient population, including febrile neutropenia, in the more traditional setting of our residency site.

This experience was a great jump start to our residency year. We had the opportunity to get to know some patients and their families early on and start building relationships with them, which allowed us to better understand our patients' needs and become their advocates early in the residency year. Camp also introduced us to a variety of malignancies, common medications prescribed to these patients, and some effects of treatment, including avascular necrosis, posterior fossa syndrome, and growth factor deficiencies. It allowed us to put faces to different disease states that came up in discussions throughout the year and opened our eyes to the survivorship aspect of these patients' care.

Managing medications for all the campers comes with challenges, but the joy and liveliness of camp are strong enough to outweigh any amount of stress or fatigue. When not administering medications, we spent time with the campers having fun and making memories. Water-gun fights are a constant amusement, and no one is safe within 100 feet of the pool. The campers may say their favorite activities are building with Legos, playing bazooka ball, or preparing for the end-of-camp dance, but for the medical staff the favorite activity is Hug-and-Tuck. Every evening before the campers fall asleep, we tuck each child into bed and wish each one a good night.

These kids look forward to Indian Summer Camp all year long. These 6 days help them through their fight with cancer, but the energy provided by camp also has a rejuvenating effect for the staff. When caring for these pediatric patients becomes challenging, we can think back to all our memories of caring for them in a different light over the summer. Indian Summer Camp will forever hold a place in our hearts, and we are already looking forward to this year's camp. ●●

The Selection Process for Oral Chemotherapeutic Agents for a Formulary

Khilna Patel, PharmD BCOP
Clinical Pharmacy Manager, Hematology/Oncology
NewYork-Presbyterian Hospital/Columbia University Medical Center
New York, NY

Sapna Parmar, PharmD BCOP
Clinical Pharmacy Manager, Stem Cell Transplantation
NewYork-Presbyterian Hospital/Columbia University Medical Center
New York, NY

Since its development in the 1950s, the formulary has advanced beyond being a simple list of medications. Today the formulary may be more accurately described as a frequently updated list of medications and related information representing the clinical expertise of a multidisciplinary team. The formulary system, which is intended to guide the safe, appropriate, and cost-effective use of pharmaceuticals in patient care, is an essential tool for institutions.

With the increasing number of cancer diagnoses, an area of particular interest is the accelerating expansion of oral chemotherapeutic agents. In recent years the treatment paradigm has shifted from parenteral to oral cytotoxic or targeted agents for several malignancies. Because of the rising cost of oral antineoplastic agents, healthcare organizations must carefully evaluate the cost-benefit profile of new agents that come on the market. After an oral chemotherapy agent is approved for an institution's formulary, that hospital or system is responsible for obtaining the agent and keeping it in stock. Fulfilling this responsibility is often cost prohibitive and also impractical—depending on the number of patients on each drug.

"The formulary system, which is intended to guide the safe, appropriate, and cost-effective use of pharmaceuticals in patient care, is an essential tool for institutions."

It is ultimately the responsibility of the hospital's Formulary and Therapeutics (F&T) Committee (which may be composed of several subcommittees) to shape the continuously evolving formulary system. Given the complex and multifaceted nature of the decision process, as well as the practical aspects of keeping oral antineoplastic agents on the formulary, a multistep qualitative approach is often required.

At NewYork–Presbyterian Hospital and other institutions, a detailed screening process has been developed to help determine the true need for, or benefit of, adding an agent to the formulary. This process is used for all agents but is particularly important for oral chemotherapy medications.

In our process, a requestor initially completes a questionnaire indicating the purpose of the formulary addition and whether alternatives are available. Methods of use or a treatment protocol must be outlined to determine whether off-label use will occur. Supporting literature should also be included to ensure that safety and efficacy data are evaluated objectively. In addition, the prescriber is encouraged to summarize his or her clinical experience with the requested drug. In order for pharmacoeconomic analyses to be conducted, a projected number of patients anticipated to be treated in a 12-month period and the average duration of therapy should be included. Finally, any conflicts of interest must be noted. The completed form is then submitted to the drug information center to be distributed to the appropriate subcommittee. For example, our institution has a hematology/oncology subcommittee composed of oncologists, clinical pharmacists, and oncology nurses. Typically, the clinical pharmacist is responsible for creating a drug monograph that is presented to the subcommittee. The subcommittee's decision may influence the final verdict of the F&T Committee.

When a request is submitted, a multitude of factors must be considered in the decision-making process. First and foremost, are similar alternative agents available on the formulary? Is there a novel mechanism of action? Would the agent be additive therapy or a replacement therapy for current regimens? Next, the design of the registrational trial must be carefully evaluated; the potential weaknesses of the study design must be assessed, with attention to whether it included an appropriate comparator arm. How do data on the new medication compare with the historical efficacy and safety data of treatment alternatives, if any? The presenter should be aware of any other potential indications the new medication is being studied for.

Given the rising cost of pharmaceuticals, a pharmacoeconomic analysis should also be incorporated into the decision-making process. However, cost-management initiatives must never compromise the pharmacy department's ability to provide the best possible care to patients. In addition, a thorough literature search should be conducted, including expert opinion from national guidelines, issue statements, review articles, and any new abstracts; this information may affect the final decision of the F&T Committee.

After a consensus has been reached and the drug has been added to the formulary, a postdecision course must be considered. We recommend making a checklist of tasks covering the logistical aspects. For example, one task would be to ensure that the medication is available from the manufacturer or wholesaler. Subsequently, paper or electronic order sets must be created and vetted through information technology. Existing guidelines or policies may need to be updated as a result of the formulary addition (e.g., the antiemetic policy, the extravasation and infiltration guideline, the chemotherapy spillage policy, the chemotherapy order-writing or order-processing policies). Depending on the complexity of

the agent, the creation of a new guideline may be necessary to delineate appropriate prescribing, dispensing, and administration. The appropriate managers, staff members, and healthcare personnel must be notified about the new agent so that a supply can be ordered. Finally, ongoing formulary maintenance such as class reviews and routine drug evaluations is a key element in this process. The F&T Committee needs to regularly review its criteria for use of individual drugs in light of changes made to clinical guidelines and newly approved indications.

Although our model will continue to evolve, the aforementioned steps are now our central consideration when selecting oral cytotoxic or targeted medications to be added to the formulary. It is critical to incorporate the perspectives of all concerned parties (pharmacy staff, nursing staff, and prescribers) to ensure effective and efficient delivery of the medications. Our process is intended to rationalize, standardize, and expedite the assessment of new drugs, and institutions should consider adapting this method. ●●

Advice for Interpreting the Literature

Morgan Belling, PharmD
Clinical Hematology/ Oncology Pharmacist
The University of Kansas Health System
Kansas City, KS

One of the essential skills of a hematology/oncology pharmacist is the ability to identify, analyze, and apply available data to patients and use that knowledge to make evidence-based recommendations to the multidisciplinary team, on both a micro level (direct patient care) and a macro level (the institution). And pharmacists are routinely involved with active research themselves, whether as an advisor on a residency research project or as a primary investigator for a trial. How to stay up-to-date on the literature has been discussed in a previous issue of *HOPA News* (Volume 13, Issue 3, "The Resident's Cubicle"). But what about *interpreting* that information? Courses are offered on the subject, of course, but what key points should you think about when reading through those clinical trials, review articles, and guidelines, especially as an up-and-coming or new practitioner?

Evaluating Clinical Studies (Focusing on Randomized Controlled Trials)

Study design: Is the study prospective (ideally) or retrospective? Blinded or open label? Was it conducted at a single center or at multiple institutions? Remember that the strength of study designs is as follows (with the first-listed type providing the strongest evidence): systematic reviews and meta-analysis; randomized controlled trial; cohort study; case-control study; cross-sectional study; case series and case reports; and finally, reviews and expert consensus or opinion. What are potential sources of bias or confounding as a result of the study design? How did the researchers attempt to limit bias and account for confounders? What were the primary and secondary objectives? Typically, when one is evaluating the efficacy of a cancer therapy, overall survival is considered the gold standard, but other end points may be appropriate.

Methods: Were appropriate statistics used, given the type of information analyzed? When one is assessing a randomized controlled trial comparing two treatment groups, it's important to pay attention not only to the intervention arm but also to the comparator arm—is that novel intervention being compared to the current standard of care, or has information been studied and published that perhaps supports a new standard of care? This issue may be especially important if a trial spans several years: the comparator arm may no longer be as relevant as it once was. From a pharmacist's perspective, were there medications that were contraindicated for use with the study drug, or were there drug-drug interactions that warranted a change in the dose of an agent? All these points should be kept in mind.

"What key points should you think about when reading through clinical trials, review articles, and guidelines?"

Patient population: What was the sample size of the patient population? Was it sufficient to meet power? It's important to pay attention to inclusion and exclusion criteria; the latter is just as important as the former. Let's say that an attending physician wants to use blinatumumab (Blincyto) for an adult patient with relapsed Philadelphia chromosome negative B-cell acute lymphoblastic leukemia (ALL) with active malignancy in the central nervous system (CNS). It would be important to know that patients with active CNS involvement were excluded from a key phase 2 study that led to U.S. Food and Drug Administration approval. Essentially, does your patient match the patient population in which the drug was studied? What was the performance status of the patients? How many lines of therapy had they previously received before being included in the current trial? Among the groups studied, were the baseline characteristics similar? If there were differences in baseline characteristics, do those differences matter *clinically*? How might those differences influence your interpretation of the trial results?

Results: By what means were the results analyzed: intention-to-treat versus per-protocol? Was the primary end point one that is appropriate for the disease? Pay close attention to tables and figures of data and interpret them for yourself, looking for trends. Does your interpretation of the data mirror that of the authors? As the saying goes, "Trust, but verify!" Look critically at the available information and ask those questions. In addition to evaluating results of efficacy end points, also consider safety analyses. What were the most common side effects in the intervention arm, and how did that rate compare to the rate seen in the comparator group? What grades of side effects were seen? How many patients required a dose reduction or discontinued treatment in either study group? It's often useful to know the time to onset of efficacy or adverse events—if a patient is starting ruxolitinib for management of steroid-refractory acute graft-versus-host disease, for example, when might a response be expected? If a patient is initiated on nivolumab for metastatic melanoma management, she might ask you how quickly a rash may develop; it would be useful to know this information, referencing the published data on the subject. When you are interpreting results, it's also imperative to take some findings with a grain of salt—for instance, a subgroup analysis deserves your careful appraisal. Remember that a *predefined* subset analysis is more useful than a post-hoc analysis; if a post-hoc analysis is done, it is, by definition, retrospective, and the likelihood of a false positive (identifying a difference between groups when one does not truly exist) increases because typically many

more points or factors are compared versus the number that are assessed in a prespecified subgroup analysis. Also ask: How do the results from this study compare with those from other available literature? Another important question: What does this study contribute to the literature and clinical practice, and what gaps in knowledge remain?

Conclusions: On the basis of the study design, are the authors' conclusions indeed supported by the study results? Can the findings from this study be applied to your practice and patient population? Although results may be statistically significant, are they *clinically* significant? Would you change the way you practice on the basis of this study?

Evaluating Guidelines

When reading guidelines, investigate the organization's guideline development process. The American Society of Clinical Oncology and the National Comprehensive Cancer Network, for example, provide detailed descriptions of their processes online. How are categories or levels of evidence defined? Are the guidelines predominantly based on systematic reviews of the literature and randomized controlled trials, or do they also incorporate literature with less robust evidence? How does expert or consensus opinion factor into the guideline development process? And when the guideline makes a recommendation, what is the associated category? Again, the "trust, but verify" mantra applies; go back to the primary literature that is referenced, and read those studies for yourself to become familiar with the reasoning behind those recommendations. It's not realistic to do this for every referenced study, of course, but for the most influential trials, the ones that are prompting the strongest recommendations, that's a good place to focus! What evidence do we have that is definitive, and what clinical questions remain that necessitate further studies but require extrapolation or consensus opinion in the interim? For some clinical questions, a randomized controlled trial to address the issue may never be conducted, for reasons related to ethics, recruitment, or other valid concerns.

Evaluating clinical studies and guidelines is a challenge and a necessary component of our practice as hematology/oncology pharmacists. Like many aspects of your practice, this skill will develop as you gain experience. Participating in the design and implementation of clinical trials will allow insight into the many biases that may be present in various scenarios. The more you read the medical literature and are cognizant of the above questions and actively search for their answers, and the more you practice and face situations in which you have to apply the evidence and also incorporate your clinical judgment, the more your abilities will improve. Your career will become increasingly rewarding as your evidence-based practice contributes to high-quality care for the patients to whom you dedicate your work. These skills will then be passed on to others as you mentor students, residents, and junior practitioners who learn from your methods and insight. ●●

Antifungal Prophylaxis During Induction Therapy for Acute Myeloid Leukemia and High-Risk Myelodysplastic Syndrome

Kathryn Maples, PharmD
PGY-2 Oncology Pharmacy Resident
Virginia Commonwealth University Health System
Richmond, VA

Invasive fungal infections (IFIs) have a significant impact on morbidity and mortality in patients with hematologic malignancies and occur most often in those with acute myeloid leukemia (AML) who are undergoing chemotherapy or hematopoietic cell transplantation.[1] Currently, *Candida* species (spp) and *Aspergillus* are the most common causes of IFIs; however, the incidence of non-*albicans Candida* spp and resistant *Aspergillus* spp is increasing.[2,3] In addition to direct IFI-related mortality, these complications often cause delays in antileukemia treatment, which can affect cure rates for the underlying disease process.[4] Primary prevention of fungal infections has continually been shown to reduce the incidence of IFIs, infection-associated mortality, and overall mortality.[5] Antifungal prophylaxis has therefore become a standard of care for AML and high-risk myelodysplastic syndrome (MDS) patients undergoing traditional chemotherapy induction with cytarabine and an anthracycline.[6] Unfortunately, prophylactic therapy introduces additional risks, including drug toxicities, drug-drug interactions, selection for resistant pathogens, and high costs. Because of the need for balancing the various risks and benefits, the choice of an antifungal prophylaxis agent remains controversial.

Both the National Comprehensive Cancer Network (NCCN) Guidelines and the Infectious Diseases Society of America Clinical Practice Guidelines recommend prophylaxis with posaconazole for AML and MDS patients undergoing intensive chemotherapy until resolution of neutropenia, defined as an absolute neutrophil count greater than 500/microL.[6,7] This recommendation is based upon the landmark randomized multicenter study in which AML/MDS patients undergoing standard induction treatment were randomized in a 1:1 ratio to posaconazole or to either fluconazole or itraconazole.[8] Prophylaxis was administered with each remission-inducing chemotherapy cycle for newly diagnosed AML, first-relapse AML, and MDS requiring induction. Prophylaxis started either 24 hours after the last dose of anthracycline or on day 1 of chemotherapy in patients not receiving an anthracycline. Antifungal prophylaxis was continued until recovery of neutropenia and complete remission, occurrence of IFI, or for up to 12 weeks from randomization, whichever came first. Fifty-seven percent of patients in the posaconazole group received only one chemotherapy cycle, while the remaining 43% were treated with two or more successive cycles of chemotherapy during the study. Similarly, in the control group, 61% received one cycle, and 39% were treated with two or more cycles of chemotherapy. The authors did not report which chemotherapy regimens were used. Patients who received posaconazole 200 mg oral suspension three times daily (n = 304) compared to fluconazole 400 mg oral suspension once daily (n = 240) or itraconazole 200 mg oral solution twice daily (n = 58) were found to have significantly lower proven or probable IFIs (total IFIs: 2% vs. 8%, $p < .001$) and significantly fewer invasive aspergillosis infections (1% vs. 7%, $p < .001$). In addition, the 100-day overall mortality rate was significantly lower in the posaconazole group than in the fluconazole/itraconazole group (14% vs. 21%; $p = .04$). However, serious adverse events possibly or probably related to treatment were significantly higher in the posaconazole group compared with the fluconazole/itraconazole group (6% vs. 2%, $p = .01$). The adverse events more commonly associated with posaconazole were increased hepatic enzymes, hyperbilirubinemia, QTc prolongation, and syncope. The authors concluded that for AML and MDS patients undergoing chemotherapy, posaconazole improved overall survival and was superior to fluconazole or itraconazole in preventing IFIs.[8]

Despite the effectiveness of posaconazole, the oral suspension has several practical limitations, including the need for three daily administrations, variable bioavailability, and the need for administration with a high-fat meal. These restrictions are of utmost concern for AML/MDS patients, who have several factors (e.g., mucositis, nausea, vomiting, and diarrhea) that may affect absorption of posaconazole, and subtherapeutic drug levels have been associated with increased risk of breakthrough IFIs in AML patients.[9] This limitation has been largely overcome by the recent introduction of the delayed-release tablet and intravenous (IV) formulations, which were approved by the U.S. Food and Drug Administration on the basis of pharmacokinetic studies.[10] Unlike the oral suspension, the delayed-release tablet is administered with a loading dose of 300 mg twice daily on day 1, followed by 300 mg once daily without regard to meals, because its absorption is minimally affected by food, mucositis, and gastrointestinal pH.[11] In addition, the therapeutic drug-monitoring recommendation pertains only to use with the oral-suspension formulation. It is important to note that although the clinical success with the suspension formulation was simply extrapolated to the tablet formulation, small studies have confirmed an increase in serum drug levels in AML patients taking the tablet formulation.[10-12]

Further, although current guidelines recommend standard prophylaxis with posaconazole, a potential argument against the use of this agent for primary prophylaxis is the concern of resistance in the setting of breakthrough fungal infections. Posaconazole is one of the broadest antifungal agents available, with activity against resistant *Candida* spp, *Aspergillus*, *Cryptococcus*, *Coccidioides*, *Blastomyces*, *Histoplasma*, and *Zygomycetes*.[4] Prophylaxis with such a highly active and broad-spectrum antifungal agent could favor the emergence and growth of resistant fungal strains. A cohort study of AML patients (N = 250) receiving intensive chemotherapy revealed that 24% of patients experienced a breakthrough IFI (17.6% possible IFI and 6.4% probable or proven). All patients with a breakthrough IFI had

received posaconazole prophylaxis, and 35% of these patients were switched to liposomal amphotericin B for treatment.[13] For the treatment of resistant fungal infections, echinocandins have a limited role outside of resistant *Candida* spp. Amphotericin B is the remaining broad-spectrum antifungal agent with a different mechanism of action that can treat fungal strains resistant to azoles. Liposomal amphotericin B is available only as an IV solution, and administration of this medication requires extensive support, which may not be feasible over a long term. Therefore, some providers may prefer to start with a narrower-spectrum agent and reserve posaconazole for patients who have a breakthrough IFI later in treatment.

Voriconazole is a broad-spectrum, mold-active azole but notably lacks activity against *Zygomycetes*. Although voriconazole has been extensively studied for the treatment of invasive aspergillosis in patients with hematologic malignancies, data on voriconazole for prophylaxis are very limited. In a randomized open-label study (*N* = 127), IV voriconazole was compared with IV itraconazole and found to have no difference in the incidence of IFIs or mortality. However, of note, this study failed to reach its target accrual number.[14] Additional single-center cohort studies have reported rates of proven or probable IFIs between 4% and 7% in AML/MDS patients undergoing induction chemotherapy with voriconazole prophylaxis at 200 mg orally twice daily.[15,16]

Isavuconazole is the newest mold-active triazole, with activity against yeast, molds, and dimorphic fungi. It is currently approved for the treatment of invasive aspergillosis and mucormycosis. Although isavuconazole does not extend posaconazole's spectrum of activity, this agent seems to have more predictable pharmacokinetics in adults and fewer serious adverse effects.[17] Early testing of isavuconazole for antifungal prophylaxis in AML and MDS patients has begun, but additional phase-3 trials are warranted to better determine this novel agent's role.[18]

Fluconazole is a non-mold-active azole with activity against *Candida* spp (except *C. krusei*), *Coccidioides, Histoplasma*, and *Cryptococcus* spp. Despite having no mold coverage, fluconazole remains an attractive antifungal prophylaxis agent because it is available in IV and oral formulations, is well tolerated, has fewer significant drug-drug interactions, and has a significantly lower cost. Fluconazole 400 mg orally once daily has been shown to reduce both the incidence and mortality of IFIs when compared with placebo in adult AML patients receiving induction chemotherapy.[19] Further, when compared with amphotericin B, fluconazole was found to be as efficacious but better tolerated.[20,21] Fluconazole has also been directly compared with itraconazole, which has a wider spectrum of activity that includes *Aspergillus*. Though itraconazole has been shown to significantly reduce IFIs compared with fluconazole, no difference was detected for IFI-associated or all-cause mortality between the two agents, and itraconazole has poor gastrointestinal tolerability.[22,23]

With fluconazole, voriconazole, and posaconazole being the three most common azoles currently used for antifungal prophylaxis, cost is an additional factor to be considered. With the average duration of neutropenia being approximately 30 days,[8] the average wholesale price for 30-day prophylaxis with fluconazole, voriconazole, and posaconazole is $859.50, $3,014.70, and $6,777.00, respectively. However, drug cost alone is not the sole contributor to a cost-effective strategy. When medication costs and costs to treat IFIs were analyzed together, Monte Carlo simulations showed that posaconazole is more cost effective when compared with fluconazole/itraconazole or when compared with voriconazole for prophylaxis during induction chemotherapy.[24,25]

The echinocandins (caspofungin, micafungin, and anidulafungin) are exclusively available as IV formulations and have activity against *Candida* and *Aspergillus* spp; however, they have no in vitro activity against *Zygomycetes* and *Fusarium* spp.[4] In an open-label randomized study, patients with AML or MDS undergoing induction chemotherapy were randomized to receive caspofungin (*n* = 106) or itraconazole (*n* = 86) for primary prophylaxis. No differences between the two groups were seen in the incidence of IFIs, IFI-associated and all-cause mortality, or adverse effects.[26] Although no randomized controlled trials have been conducted with micafungin or anidulafungin in the prophylaxis setting, the echinocandins are often thought to be interchangeable, and the institution-specific formulary agent can be used. The NCCN guidelines recommend micafungin as a category-2B alternative to posaconazole for antifungal prophylaxis.[6]

In conclusion, fluconazole has been shown to prevent IFIs in AML patients compared with placebo, but it lacks mold coverage. Epidemiological studies reveal that the characteristics of IFIs in leukemia patients have evolved in the last 2 decades because of the implementation of azole prophylaxis in the early 1990s. *Candida* spp that are fluconazole resistant (C. krusei) or susceptible-dose-dependent (C. glabrata) are estimated to account for more than 80% of candidiasis infections in leukemia patients.[27] In addition, it has been estimated that more than half of proven or probable IFIs in AML patients are caused by molds,[28] and mortality rates from aspergillosis are reported as high as 50% in neutropenic patients.[29] With the high morbidity and mortality associated with an IFI, using an anti-mold agent as primary prevention during induction chemotherapy may outweigh the risks of increases in drug-drug interactions, toxicities, and cost; however, patient-specific characteristics should always be considered. ●●

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Colorectal Cancer in the Millennial Generation

Jordan Hill, PharmD BCOP
Clinical Pharmacy Specialist—Solid Tumor Malignancies
West Virginia University Cancer Institute
Morgantown, WV

Colorectal cancer is the third most common cancer and the second leading cause of cancer death in the United States.[1] With a median age at diagnosis of 68 years, colorectal cancer is commonly considered a malignancy of the elderly, with more than half of colorectal cancer diagnoses occurring in adults 65 years and older.[2] With increased awareness of the risks of smoking and increased utilization of colorectal cancer screenings, the annual percentage of change in incidence for colorectal cancer has steadily declined by 2.28 from 1998 to 2007 and 3.44 from 2007 to 2013.[2] In addition, earlier detection of colorectal cancers and advancements in treatment such as anti-angiogenic drugs, epidermal growth factor receptor blockers, and multikinase inhibitors have led to continued decreased death rates, with rates falling an average of 2.7% each year from 2004 to 2013.[2]

Conversely, in adults aged 54 years and younger, colon cancer incidence has actually risen. From the mid-1980s for people ages 20–39 years and from the mid-1990s for ages 40–54 years, rates increased 2.4% per year in adults ages 20–29 years, 1.0% in ages 30–39, 1.3% in ages 40–49, and 0.5% in ages 50–54. The increases in rectal cancer incidence are even more dramatic, with increases in incidence of 3.2% for adults ages 20–39 since 1980 and 2.3% for adults ages 40–54 years since the 1990s. When examining age-specific trends by birth cohorts from the 1890s, 1950s, and 1980s, the 1980 birth cohort had double the age-specific risk of colon cancer and triple the risk of rectal cancer compared to the 1950 age cohort. This represents similar age-specific relative risks to those in the 1890s age cohort, indicating that rates of colorectal cancer in the millennial generation are as high as for those born in the late 1800s.[3]

The increase in colon cancer rates observed in younger patients is primarily driven by an increase in distal or left-sided tumors.[3] Recently, primary tumor location has been found to have a role in both prognosis and treatment decisions for colon cancer. Most literature supports an association of primary left-sided tumors with an overall improved prognosis, with the exception of those associated with Lynch syndrome, which are predominantly right-sided and still confer a good prognosis.[4-7] Given the increasing trend of mostly distal tumors occurring in younger patients, one could infer an improved prognosis on the basis of primary tumor location alone. Alternatively, some reports show that younger patients are up to 58% more likely to present with distant disease when compared to older patients, most likely due to a delay in a colon cancer workup following recognition of classic signs and symptoms of gastrointestinal malignancy as well as a decreased likelihood of younger adults' being appropriately insured.[8] Taking into account the primary site of the tumor and a generally increased tolerability of cytotoxic chemotherapy, as well as increased rates of more advanced disease at diagnosis, the overall prognosis is likely to be similar for younger adults as compared with older adults. This similar prognosis has been demonstrated in single-center studies as well as in a large population-based retrospective cohort study comparing early-onset colorectal cancer to that in older patients.[8-10] Conversely, inferior survival has also been shown in some single-center studies.[11,12] One argument suggesting a similar overall prognosis is the potential for a higher proportion of early-onset colorectal cancer being attributed to hereditary colorectal cancers and, hence, an overall improved prognosis.

Hereditary colorectal cancers, such as hereditary nonpolyposis colorectal cancer (HNPCC) or Lynch syndrome, account for only 2%–5% of all colorectal cancers; however, they account for up to 20% of young-onset colorectal cancers.[13] In addition to the overall improved prognosis for these cancers compared with that for sporadic colorectal cancer, they are also microsatellite instable. Recent literature indicates that colorectal cancers with high levels of microsatellite instability have high response rates to immunotherapy such as PD-1 blockade; this finding seems to indicate that the prognosis will continue to improve in this small subset of patients.[14]

Even with a higher proportion of young-onset colorectal cancers being attributed to hereditary syndromes compared with colorectal cancers in older patients, the vast majority of these diagnoses are still considered sporadic. This has led to increased discussion supporting alternative contributors to the rise in colorectal cancer rates among young adults. Differences in clinical and molecular features of young-onset colorectal cancer reported in the literature include increased rates of CpG island methylator phenotype, increased frequency of microsatellite and chromosomal stable tumors, and increased LINE-1 hypomethylation. However, for none of these biological mechanisms is substantial data available regarding the significance of their observed differences in age-defined subsets of colorectal cancer.[15-17] Recently, a study evaluating the frequency and spectrum of cancer-susceptibility gene mutations in early-onset colorectal cancer found a 16% rate of gene mutations, with 33% of those not meeting genetic testing criteria, which indicates that a substantial amount remains to be learned about the differences in pathogenesis for early-onset colorectal cancer.[7]

In addition to unique molecular mechanisms found in young-onset colorectal cancer, modifiable risk factors for colorectal cancer are rising at an alarming rate; these include poor dietary habits (e.g., high consumption of processed meat, low consumption of fiber), increased sedentary lifestyles, and higher rates of obesity and diabetes. Over the last 30 years, obesity rates in the United States have doubled among adults and tripled among children. An examination of obesity by birth cohorts has identified an overall increase in cumulative exposure to excess body fat, as more recent birth cohorts are becoming obese in greater numbers and

becoming obese at an earlier age.[18] Therefore, it is not surprising that the trends in early-onset colorectal cancer parallel those of obesity.

With the vast majority of young-onset colorectal cancers occurring in patients without hereditary syndromes, the examination of family history regardless of age, an increased public awareness of the ever increasing risk in young adults, and an increased awareness of the numerous risks of poor dietary habits and obesity are measures that are now more important than ever. Given their accessibility and vital role in the comprehensive care of patients, pharmacists can be essential agents in the effort to increase awareness and ensure that appropriate screenings occur.

After a diagnosis has been made, pharmacists can continue to ensure that patients receive appropriate care by including tumor location, microsatellite instability, and genetic mutational status in treatment considerations. Reversing the current trend in colorectal cancer incidence will ultimately require a significant shift in lifestyle modifications, earlier recognition of signs and symptoms of colorectal cancer by young adults, and a more specialized way to identify appropriate candidates for early screening. It is hoped that an increased awareness of these startling trends will help to reverse the upward trend in modifiable risk factors and that research will continue to aid in the tailored care of those with early-onset colorectal cancer. ●●

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Top Ten Poster Award: HOPA 13th Annual Conference

Sarah K. Kraus, PharmD BCOP BCPS
Hematology/Oncology Clinical Pharmacy Specialist
Pennsylvania Hospital
Philadelphia, PA

HOPA's annual conference provides an opportunity for hematology/oncology practitioners to receive comprehensive education on a variety of topics. Programs at the conference include in-depth analyses of treatment strategies, summaries of the latest drug developments, and reviews of novel practice models. In particular, the poster presentations at the conference highlight the innovative work of our members in the areas of clinical and translational research and practice management.

Each year, more than 100 posters submitted by residents, fellows, and students are presented at the conference. Members of HOPA's Research Abstract Review Work Group use a blind review process to select the Top Ten Posters from all the posters submitted and then with additional volunteers on site select the recipient for the Top Ten Poster Award. The recipients of this award have conducted original, well-designed studies that can influence hematology/oncology pharmacy practice. The 2017 recipient of HOPA's Top Ten Poster Award is Benjamin Andrick, PharmD, PGY-2 hematology/oncology resident at Augusta University Medical Center, Augusta, GA.

Dr. Andrick is recognized for his research titled "Pneumococcal Vaccine Response in Chronic Lymphocytic Leukemia Patients Receiving Ibrutinib." Patients with chronic lymphocytic leukemia (CLL) have impaired immunity resulting from defects in both the humoral and cellular immune pathways. Subsequently, these patients are at a higher risk of infection-related morbidity and mortality. The Centers for Disease Control and Prevention and the Advisory Committee on Immunization Practices recommend that patients with CLL receive the 13-valent pneumococcal conjugate vaccine (PCV13) for protection against pneumococcal infections. However, if these patients have previously received B-cell-depleting anti-CD20 therapies, the recommendation is to wait to administer PCV13 until at least 6 months following the last dose, because patients may not mount an adequate immune response if the vaccine is administered earlier. Ibrutinib, a first-line agent for CLL, works by covalently binding to and inhibiting Bruton's tyrosine kinase (BTK), which is constitutively active in CLL cells. BTK inhibition ultimately leads to impairment in malignant B-cell proliferation, adhesion, and trafficking. Because ibrutinib affects the B-cell signaling pathway, Dr. Andrick and colleagues hypothesized that ibrutinib would attenuate PCV13 vaccination response.

"Prior to this study, the effect of ibrutinib on PCV13 vaccination response was unknown."

The first objective of this study was to determine whether concurrent administration of PCV13 and ibrutinib generates an adequate vaccination response, defined as at least a ≥ twofold titer increase in ≥3 serotype-specific IgG antibodies postvaccination compared to baseline IgG levels. For the second objective, to further evaluate IgG antibody response to the vaccine, SAMSN1 (Src homology domain 3 lymphocyte protein 2, also known as HACS1) and BTK expression was evaluated. SAMSN1 displays an inhibitory role on B-cell proliferation and differentiation processes. Prior to this study, increased SAMSN1 expression had been correlated with impaired pneumococcal vaccine response. The third objective was to determine whether changes in HACS1 correlated with attenuated pneumococcal vaccine response.

This study was an institutional review board–approved prospective pilot cohort study. Adult patients with CLL receiving ibrutinib 420 mg by mouth daily (active arm) or active surveillance (control arm) were included. Patients were excluded if they had received the PCV13 vaccine within the past 2 years, if they had received anti-CD20 monoclonal antibody therapy within the past 6 months, were on immunosuppressive therapies including steroids in the past 14 days (maintenance steroids with ≤20 mg/day prednisone equivalent were allowed), had a recent infection requiring systemic treatment in the past 14 days, or had an Eastern Cooperative Oncology Group performance status of 3 or 4.

At day 0 of study enrollment, both study cohorts received a single dose of PCV13. Peripheral blood samples were collected prevaccination on day 0 and on day 30 postvaccination. Serum pneumococcal antibody assessment was performed on day 0 and day 30 by measuring IgG antibodies specific for 12 pneumococcal serotypes (1, 3, 4, 5, 9, 12F, 14, 19F, 23F, 6B, 7F, and 18C) using microsphere photometry. Mononuclear cells were isolated using Ficoll-Histopaque 1077 density gradient centrifugation, and specific CD19+ cells were isolated using Dynabeads CD19 pan B. Western Blot analysis was performed to evaluate BTK and SAMSN1 expression.

Eight patients with CLL were enrolled in this study, 4 in the ibrutinib arm and 4 in the control arm. All the patients in the control arm (4/4) generated an adequate immune response to PCV13 versus none (0/4) of the ibrutinib-treated patients ($p = .029$). Overall, there was a significant increase in the median change of specific pneumococcal antibody titers in the control group compared to the ibrutinib group ($p < .0001$; confidence interval [CI] 90–124.7). Dr. Andrick noted an interesting secondary finding of significant elevation in SAMSN1 expression prevaccination in the ibrutinib arm ($p < .0115$), which he stated "may mechanistically explain the lack of immune response generated following PCV13 vaccination. Higher baseline SAMSN1 expression could be a parallel mechanism by which CD19+ cells attempt to overcome BTK inhibition, which halts proliferation and differentiation secondary to B-cell receptor signaling. The interaction of an adaptor protein such as SAMSN1 on the phosphorylation of BTK is intriguing."

Prior to this study, the effect of ibrutinib on PCV13 vaccination response was unknown. This pilot study suggests that ibrutinib therapy may attenuate pneumococcal vaccination response. On the basis of these results, Dr. Andrick and colleagues suggest that clinicians consider PCV13 vaccination prior to initiating ibrutinib. However, larger studies should be conducted to provide clear guidance on the clinical implications of vaccinations in patients receiving ibrutinib.

Highlights from HOPA's 2017 Annual Conference in Anaheim, CA (March 29–April 1)

Ashley Glode, PharmD BCOP BCPS
Clinical Oncology Pharmacy Specialist; Assistant Professor
University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences
University of Colorado Anschutz Medical Campus
Aurora, CO

The 13th Annual HOPA Conference, held in the heart of Disneyland at the Disneyland Hotel in Anaheim, CA, went above and beyond expectations. Conference attendance set a record at 1,031, with attendees coming from across the United States and other countries. The annual conference provides an opportunity for hematology/oncology pharmacists, residents, and students to obtain the education and research information they need to deliver the highest-quality care to their patients. This year's conference featured an app that allowed attendees to map out their own schedule for the day, provided alerts, and sent reminders about sessions to attend. The conference also included the option to attend sessions virtually for those unable to attend in person.

The 3½-day conference opened with two optional preconference educational sessions. The first, "The Progression of the Investigational Drug Service: Clinical Practice Pearls and Take-Home Points," was geared toward pharmacists just beginning in investigational pharmacy and also to those with more experience who were looking to expand their practice. The second, "Management Pearls for Oncology Pharmacy Leaders," provided attendees with practical tools and guidance necessary to excel in oncology pharmacy leadership. Eight board certified oncology pharmacist (BCOP) sessions for recertification credit were offered. Some highlights of those sessions included a lecture by Robert Mancini, PharmD BCOP, titled "Cancer Prevention: How to Protect Your Patients"; one by Neelam Patel, PharmD BCOP, "Management of Young Patients with Breast Cancer"; and one by Deborah Ward, PharmD BCOP BCPS, "Dysregulation of Water and Sodium: Implications and Management in Pediatric Cancer Patients." Other high points included a review of significant papers in hematology/oncology and new drugs approved in 2016. Two advocacy-themed sessions covered the provider status initiative and provided an update on HOPA's advocacy efforts. Breakout sessions were held on hematopoietic stem cell transplantation, ambulatory care, practice management, investigational drugs, and practical issues for clinicians.

In her welcome message, President Sarah Scarpace Peters, PharmD MPH BCOP, highlighted the accomplishments of HOPA's board of directors and members over the past year. The organization had a very active year and established several collaborative relationships with other oncology organizations throughout the country.

The second class of HOPA Fellows was inducted at the conference: Sally Yowell Barbour, PharmD BCOP CPP; John G. Kuhn, PharmD FCCP; Susanne E. Liewer, PharmD BCOP; Kerry Parsons, PharmD BCOP; Timothy Tyler, PharmD FCSHP; and Michael Vozniak, PharmD BCOP.

The winners of several 2017 HOPA awards were announced at the conference: the Award of Excellence, Terri G. Davidson, PharmD BCOP FASHP FCCP; the New Practitioner Award, Amber Bradley Clemmons, PharmD BCOP; the Patient Advocacy Award, Kerry Parsons, PharmD BCOP; and the Hematology/Oncology Technician Award, Cheryl Hyk, CPhT.

The first day concluded with special interest group meetings for administration, ambulatory care, bone marrow transplant, investigational drug services, new practitioners, and pediatrics. These meetings allow for discussion of issues or concerns in a small-group setting and also provide a great opportunity for face-to-face networking between hematology/oncology pharmacists with similar interests. An additional networking event gave students attending the conference the opportunity to meet with hematology/oncology pharmacists in a more relaxed setting.

On the second day, the John G. Kuhn Keynote Lecture, titled "Personalized Cancer Therapy: From Discovery to Actionable Genomics," was delivered by James M. Ford, MD, a medical oncologist and geneticist from Stanford University. Dr. Ford discussed the impressive strides that have been made toward a personalized approach to cancer care. On the third day of the conference, incoming president Susannah E. Koontz, PharmD BCOP FHOPA, shared her touching story of the road taken to becoming HOPA president and the impact her mother had on her journey to practicing in oncology.

Poster sessions at the annual HOPA meeting allow pharmacists, residents, and students to present their research. The award winner from the top 10 posters was Benjamin Andrick, PharmD, PGY-2 hematology/oncology resident at Augusta University Medical Center, Augusta, GA, for his poster titled "Pneumococcal Vaccine Response in Chronic Lymphocytic Leukemia Patients Receiving Ibrutinib." You can read more about his research in the Highlights of Member Research column in this issue on page 16. Awards are also given at the conference to authors who have written articles that make a significant contribution to the literature. At this year's conference, Karen Sweiss, PharmD BCOP, received the Oncology Pharmacy Practice Literature Award.

The efforts of HOPA's 2017 Annual Conference Program Committee surpassed our highest expectations again this year, and attendees had a truly wonderful experience. We are looking forward to the 14th Annual HOPA Conference in Denver, CO, to be held March 21–24, 2018, at the Colorado Convention Center. ●●

HOPA'S NEW COMMITTEE STRUCTURE REFLECTS STRATEGIC PLAN INITIATIVES

In 2016, HOPA introduced its ambitious 2016–2020 strategic plan, which will guide volunteer and staff activities toward accomplishing HOPA's goals. As part of that process, HOPA also conducted a thorough review of the current committee structure, reviewed each committee charge, and concluded that the existing committee structure was not optimal for accomplishing all the work in the plan.

For the 2017–2018 HOPA year, a new committee structure is being introduced.

BENEFITS OF THE NEW STRUCTURE

- This new committee structure will allow for a larger volunteer workforce—this means even more opportunities for HOPA members to get involved!
- The changes allow for better communication between the board, committees, and volunteers.
- The structure accommodates newly established programs.
- Volunteers will know how their efforts relate to HOPA's strategic goals.

WHAT'S NEW?

- **Committees:** The composition and charges for some committees have changed, allowing for better coordination of work with a similar focus.
- **Subcommittees:** *Subcommittees* (replacing the *workgroups*) better reflect the reporting structure and work areas.
- **Councils:** Committees and subcommittees are grouped into four categories (each aligning with a goal area of HOPA's strategic plan) and report to one of four newly established Councils.

You can view a 30-minute webinar at hoparx.org/misc-membership/hopa-committee-restructure-orientation-webinar that provides details on the new structure. Current volunteers will also receive updates from their committee leaders.

Potential Innovative Breakthroughs for BRAF V600E Mutated Metastatic Colorectal Cancer: What Does the Future Hold?

Jane E. Rogers, PharmD BCOP
Pharmacy Clinical Service
University of Texas MD Anderson Cancer Center
Houston, TX

Overview of Metastatic Colorectal Cancer

Substantial improvements in localized and systemic treatment modalities have increased the overall survival (OS) of metastatic colorectal cancer (mCRC) to approximately 30 months.[1-2] Despite these improvements, mCRC clearly remains a heterogeneous disease with a 5-year OS of only 13%.[3] Publications continue to reveal additional heterogeneity to decipher outcome differences and recognize unmet needs. Recent distinctions in antineoplastic predictive outcomes and prognostic differences in age, mutational analysis, and primary tumor location are surfacing (**Table 1**).[2,4,5]

Critical Intracellular Pathway: MAPK Pathway

The epidermal growth factor receptor (EGFR)–mediated mitogen-activated protein kinase (MAPK) signaling pathway plays a significant role in mCRC.[6] The MAPK signaling pathway is activated by extracellular signals that initiate a downstream cascade of phosphorylation from one protein to the next, leading to transcription and cell proliferation.[6,7] The downstream cascade consists of rat sarcoma (RAS)/rapid accelerated fibrosarcoma (RAF)/mitogen-activated protein (MEK)/extracellular signal-regulated kinase (ERK). Mutations present in these kinases, such as a BRAF V600E mutation, lead to constitutive activation that causes upregulated cell proliferation.

BRAF V600E Mutated mCRC: Current Practice and Knowledge

BRAF V600E mutations are a rare entity in mCRC, seen in 8%–12% of patients, compared to RAS mutations, which account for about 50%–60% of the mCRC population.[2,6] Although the mutations are infrequent, patients who harbor BRAF V600E mCRC have shown dramatic differences in biology and prognosis compared to wild-type BRAF mCRC. BRAF V600E mutated CRC is a strong negative prognostic marker, correlating with high-risk clinicopathological characteristics such as advanced age, poorly differentiated histology, right-sided tumors, T4 tumors, mucinous histology, microsatellite instability, early relapse of oligometastic liver resection, peritoneal disease, and distant lymph node metastases.[2, 8-11]

With standard antineoplastic therapy, the median OS of BRAF V600E mutated mCRC is reported at approximately 12 months, with a lower probability reported of these patients receiving second-line therapy following front-line progression.[1,6] 5-Fluorouracil, oxaliplatin, and irinotecan (FOLFOXIRI) with bevacizumab in phase-2 and phase-3 trials reveal promising outcomes for the BRAF mutated subset, with a median OS range of 19–24 months.[6] Considering the historically low probability of second-line therapy and the improvement seen with this regimen in this challenging aggressive tumor population, bevacizumab plus FOLFOXIRI should be considered a front-line regimen for BRAF V600E mutated mCRC patients who have a suitable performance status.[2]

The predictive role of BRAF mutated mCRC for EGFR monoclonal antibodies (mAb) remains an area of uncertainty, given the rarity of BRAF and the retrospective nature of these evaluations. A BRAF mutation is understood to be constitutively active, and therefore the cell proliferation mechanism would bypass the inhibition target of these mAbs. Current guidelines recognize the issues surrounding this determination.[2,4] The National Comprehensive Cancer Network[4] has added wording to its guidelines indicating that a BRAF V600E mutation makes response to EGFR mAb therapy (as monotherapy or in combination with cytotoxic chemotherapy) highly unlikely, and the European Society of Medical Oncology[2] lists RAS wild-type and BRAF wild-type for EGFR mAb options.

Heterogeneity Among BRAF mCRC Mutations

Current retrospective reviews evaluating non-V600 mutated mCRC have recently been presented. Jones and colleagues reviewed mCRC patients at the Mayo Clinic between 2013 and 2015 and found that 18.9% of BRAF mutations identified were non-V600 mutations.[12] The authors found a more favorable profile (lower-grade tumors, left-sided tumors, and longer OS) than the comparator V600 mutated patients. Cremolini and colleagues retrospectively examined mCRC patients at three Italian institutions from 2006 to 2014.[13] BRAF mutated codons 594 and 596 (n = 10) were compared to V600E mutations (n = 77). Results showed a more favorable clinicopathological profile (left-sided tumors, nonmucinous subtype, an absence of peritoneal disease, and markedly longer OS) with the non-V600E mutated group. The evidence of the heterogeneity within this class of mutations is compelling, despite the rarity of non-V600 mutation occurrence (<1%).[13]

New Treatment Strategies for BRAF Mutated mCRC

BRAF inhibitors (vemurafenib or dabrafenib) given as monotherapy in mCRC BRAF mutated patients exposed disconcerting results of minimal activity (response rates [RRs] = 5%–11%), in dramatic contrast to BRAF mutated melanoma (RRs = approximately 50%–60%).[14,15] A combination BRAF mCRC trial, following a similar pathway of blockade seen with melanoma, looked at dabrafenib in combination with trametinib, an MEK inhibitor.[16] This combination showed a 12% RR, again exposing a distinction in BRAF mutated melanoma compared to mCRC. A breakthrough in the complex understanding of this population was the resistance-mechanism discovery of rapid feedback reactivation of EGFR when in the presence of BRAF blockade, allowing for continued cell proliferation.[17,18]

Dual blockade with EGFR and BRAF inhibition represented the next investigative step.[19,20] Dual blockade revealed promising results, with slightly increased RRs and progression-free survival

Table 1. BRAF Mutated Metastatic Colorectal Cancer (mCRC)

BRAF V600E mutated mCRC represents an unmet need with a poor prognosis.
FOLFOXIRI plus bevacizumab should be considered front-line therapy.
Prognostic differences exist among specific BRAF mutations.
Single-agent BRAF inhibitors revealed minimal activity.
Dual blockade with EGFR and BRAF inhibition represents the new backbone for trial design.
Triplet combination results are eagerly awaited.

Note. FOLFOXIRI = 5-Fluorouracil, leucovorin, oxaliplatin, irinotecan; EGFR = epidermal growth factor receptor.

(PFS) than those seen with BRAF inhibitor monotherapy, while at the same time these trials revealed that continued improvement is necessary. Currently, the BRAF mutated mCRC trial design involves dual EGFR and BRAF blockade with the addition of a third agent (traditional cytotoxic, MEK inhibitor, or PI3K inhibitor).[21-24] Recently presented, Kopetz and colleagues reported on a randomized trial of irinotecan + cetuximab +/- vemurabenib in BRAF mutated mCRC showing a statistically significant difference in median PFS, RR, and disease control rate in the triplet arm.[23] The recent steps in treatment discovery in this poor prognostic population hold a promising outlook. Combination study results with EGFR and BRAF inhibition plus additional agents are eagerly awaited. ●●

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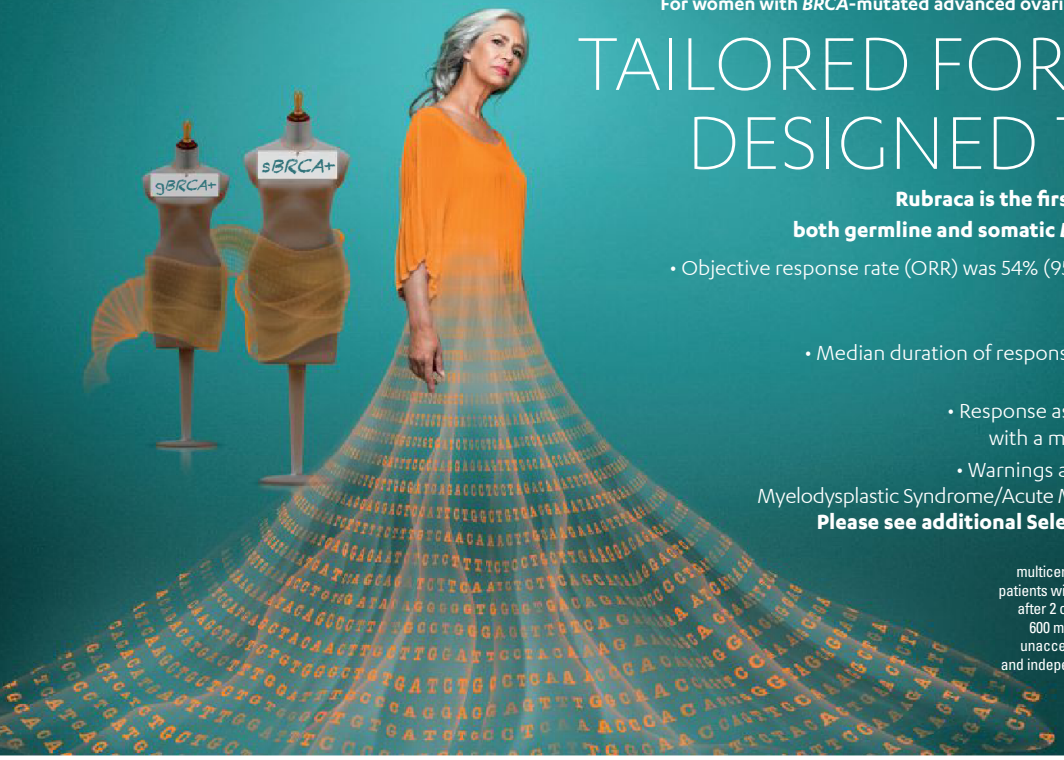

For women with *BRCA*-mutated advanced ovarian cancer after two or more chemotherapies,

TAILORED FOR RESPONSE, DESIGNED TO ENDURE

Rubraca is the first FDA-approved PARP inhibitor to treat both germline and somatic *BRCA*-mutated advanced ovarian cancer

- Objective response rate (ORR) was 54% (95% CI [44, 64]) per investigator assessment
  - Complete response rate was 9%
  - Partial response rate was 45%
- Median duration of response (DOR) was 9.2 months (95% CI [6.6, 11.6]) per investigator assessment
- Response assessment by IRR was 42% (95% CI [32, 52]), with a median DOR of 6.7 months (95% CI [5.5, 11.1])
- Warnings and precautions: Rubraca is associated with Myelodysplastic Syndrome/Acute Myeloid Leukemia and Embryo-Fetal Toxicity

Please see additional Select Important Safety Information below.

The efficacy of Rubraca was investigated in 106 patients in two multicenter, single-arm, open-label clinical trials, Study 1 and Study 2, in patients with advanced *BRCA*-mutant ovarian cancer who had progressed after 2 or more prior chemotherapies. All 106 patients received Rubraca 600 mg orally twice daily as monotherapy until disease progression or unacceptable toxicity. ORR and DOR were assessed by the investigator and independent radiology review (IRR) according to Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1.

g*BRCA*, germline *BRCA*; IRR, independent radiology review; s*BRCA*, somatic *BRCA*.

Rubraca is indicated as monotherapy for the treatment of patients with deleterious *BRCA* mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with two or more chemotherapies. Select patients for therapy based on an FDA-approved companion diagnostic for Rubraca.

This indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

Select Important Safety Information

Myelodysplastic Syndrome (MDS)/Acute Myeloid Leukemia (AML) was reported in 2 of 377 (0.5%) patients with ovarian cancer treated with Rubraca. The duration of Rubraca treatment prior to the diagnosis of MDS/AML was 57 days and 539 days. Both patients received prior treatment with platinum and other DNA damaging agents.

AML was reported in 2 (<1%) patients with ovarian cancer enrolled in a blinded, randomized trial evaluating Rubraca versus placebo. One case of AML was fatal. The duration of treatment prior to the diagnosis of AML was 107 days and 427 days. Both patients had received prior treatment with platinum and other DNA damaging agents.

Do not start Rubraca until patients have recovered from hematological toxicity caused by previous chemotherapy (≤ Grade 1).

Monitor complete blood count testing at baseline and monthly thereafter. For prolonged hematological toxicities, interrupt Rubraca and monitor blood counts weekly until recovery. If the levels have not recovered to Grade 1 or less after 4 weeks, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics. If MDS/AML is confirmed, discontinue Rubraca.

Based on its mechanism of action and findings from animal studies, Rubraca can cause fetal harm when administered to a pregnant woman. Apprise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 6 months following the last dose of Rubraca.

Most common adverse reactions (≥ 20%; Grade 1-4) were nausea (77%), asthenia/fatigue (77%), vomiting (46%), anemia (44%), constipation (40%), dysgeusia (39%), decreased appetite (39%), diarrhea (34%), abdominal pain (32%), dyspnea (21%), and thrombocytopenia (21%).

Most common laboratory abnormalities (≥ 35%; Grade 1-4) were increase in creatinine (92%), increase in alanine aminotransferase (ALT) (74%), increase in aspartate aminotransferase (AST) (73%), decrease in hemoglobin (67%), decrease in lymphocytes (45%), increase in cholesterol (40%), decrease in platelets (39%), and decrease in absolute neutrophil count (35%).

Because of the potential for serious adverse reactions in breast-fed infants from Rubraca, advise lactating women not to breastfeed during treatment with Rubraca and for 2 weeks after the final dose.

You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Clovis Oncology, Inc. at 1-844-258-7662.

Please see Brief Summary of full Prescribing Information on adjacent pages for additional Select Important Safety Information.

Reference: Rubraca [prescribing information]. Boulder, CO: Clovis Oncology; 2016.

CLOVIS ONCOLOGY

Rubraca® (rucaparib) tablets

PP-RUCA-US-0245 05/2017

RUBRACA™ (rucaparib) tablets, for oral use

BRIEF SUMMARY: Please see package insert for full prescribing information.

INDICATIONS AND USAGE

Rubraca™ is indicated as monotherapy for the treatment of patients with deleterious *BRCA* mutation (germline and/or somatic) associated advanced ovarian cancer who have been treated with two or more chemotherapies. Select patients for therapy based on an FDA-approved companion diagnostic for Rubraca *[see Dosage and Administration (2.1) in the full prescribing information]*.

This indication is approved under accelerated approval based on objective response rate and duration of response *[see Clinical Studies (14) in the full prescribing information]*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia

Myelodysplastic syndrome (MDS)/Acute Myeloid Leukemia (AML) was reported in 2 of 377 (0.5%) patients with ovarian cancer treated with Rubraca. The duration of Rubraca treatment prior to the diagnosis of MDS/AML was 57 days and 539 days. Both patients received prior treatment with platinum and other DNA damaging agents.

In addition, AML was reported in 2 (< 1%) patients with ovarian cancer enrolled in a blinded, randomized trial evaluating Rubraca versus placebo. One case of AML was fatal. The duration of treatment prior to the diagnosis of AML was 107 days and 427 days. Both patients had received prior treatment with platinum and other DNA damaging agents.

Monitor complete blood count testing at baseline and monthly thereafter. Do not start Rubraca until patients have recovered from hematological toxicity caused by previous chemotherapy (≤ Grade 1). For prolonged hematological toxicities, interrupt Rubraca and monitor blood counts weekly until recovery. If the levels have not recovered to Grade 1 or less after 4 weeks, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics. If MDS/AML is confirmed, discontinue Rubraca.

Embryo-Fetal Toxicity

Rubraca can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings from animal studies. In an animal reproduction study, administration of rucaparib to pregnant rats during organogenesis resulted in embryo-fetal death at maternal exposure that were 0.04 times the AUC in patients receiving the recommended dose of 600 mg twice daily. Apprise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 6 months following the last dose of Rubraca *[see Use in Specific Populations (8.1, 8.3) and Clinical Pharmacology (12.1) in the full prescribing information]*.

ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in the labeling:

- Myelodysplastic Syndrome/Acute Myeloid Leukemia *[see Warnings and Precautions]*.

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Rubraca 600 mg twice daily as monotherapy, has been studied in 377 patients with ovarian cancer treated in two open-label, single arm trials. In these patients, the median age was 62 years (range 31 to 86), 100% had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, 38% had *BRCA*-mutated ovarian cancer, 45% had received 3 or more prior lines of chemotherapy, and the median time since ovarian cancer diagnosis was 43 months (range 6 to 197).

Adverse reactions led to dose reduction or interruption in 62% of patients, most frequently from anemia (27%), and fatigue/asthenia (22%). Adverse reactions led to dose discontinuation in 10% of patients, most frequently from fatigue/asthenia (2%). The median duration of treatment was 5.5 months (range 0.1 to 28.0).

Table 2 and Table 3 summarize the common adverse reactions and abnormal laboratory findings, respectively, observed in patients treated with Rubraca.

Table 2. Adverse Reactions Reported in ≥ 20% of Patients with Ovarian Cancer Treated with Rubraca 600 mg Twice Daily

	All Ovarian Cancer Patients (N = 377) %	
Adverse Reaction	**Grades[a] 1-4**	**Grades 3-4**
Gastrointestinal Disorders		
Nausea	77	5
Vomiting	46	4
Constipation	40	2
Diarrhea	34	2
Abdominal Pain	32	3
General Disorders		
Asthenia/Fatigue	77	11
Blood and Lymphatic System Disorders		
Anemia	44	25
Thrombocytopenia	21	5
Nervous System Disorders		
Dysgeusia	39	0.3
Metabolism and Nutrition Disorders		
Decreased appetite	39	3
Respiratory, Thoracic, and Mediastinal Disorders		
Dyspnea	21	0.5

[a] National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE version 4.03)

The following adverse reactions have been identified in < 20% of the 377 patients treated with Rubraca 600 mg twice daily: dizziness (17%), neutropenia (15%), rash (includes rash, rash erythematous, rash maculopapular and dermatitis) (13%), pyrexia (11%), photosensitivity reaction (10%), pruritus (includes pruritus and pruritus generalized) (9%), Palmar-plantar erythrodysaesthesia syndrome (2%), and febrile neutropenia (1%).

Table 3. Laboratory Abnormalities Reported in ≥ 35% of Patients with Ovarian Cancer Treated with Rubraca 600 mg Twice Daily

	All Patients with Ovarian Cancer (N = 377) %	
Laboratory Parameter	**Grade 1-4 [a]**	**Grade 3-4**
Clinical Chemistry		
Increase in creatinine	92	1
Increase in ALT[b]	74	13
Increase in AST[b]	73	5
Increase in cholesterol	40	2
Hematologic		
Decrease in hemoglobin	67	23
Decrease in lymphocytes	45	7
Decrease in platelets	39	6
Decrease in absolute neutrophil count	35	10

[a] At least one worsening shift in CTCAE grade and by maximum shift from baseline.

[b] Increase in ALT/AST led to treatment discontinuation in 0.3% of patients (1/377).

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Based on findings from animal studies and its mechanism of action, Rubraca can cause fetal harm when administered to pregnant women. There are no available data in pregnant women to inform the drug-associated risk. In an animal reproduction study, administration of rucaparib to pregnant rats during organogenesis resulted in embryo-fetal death at maternal exposure that were 0.04 times the $AUC_{0\text{-}24h}$ in patients receiving the recommended dose of 600 mg twice daily *[see Data]*. Apprise pregnant women of the potential risk to a fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

In a dose range-finding embryo-fetal development study, pregnant rats received oral doses of 50, 150, 500, or 1000 mg/kg/day of rucaparib during the period of organogenesis. Post-implantation loss (100% early resorptions) was observed in all animals at doses greater than or equal to 50 mg/kg/day (with maternal systemic exposures approximately 0.04 times the human exposure at the recommended dose based on $AUC_{0\text{-}24h}$).

Lactation

Risk Summary

There is no information regarding the presence of rucaparib in human milk, or on its effects on milk production or the breast-fed infant. Because of the potential for serious adverse reactions in breast-fed infants from Rubraca, advise lactating women not to breastfeed during treatment with Rubraca and for 2 weeks after the final dose.

Females and Males of Reproductive Potential

Pregnancy Testing

Pregnancy testing is recommended for females of reproductive potential prior to initiating Rubraca.

Contraception

Females

Rubraca can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations]*. Advise females of reproductive potential to use effective contraception during treatment and for 6 months following the final dose of Rubraca.

Pediatric Use

The safety and effectiveness of Rubraca in pediatric patients have not been established.

Geriatric Use

One hundred and sixty (42%) of the 377 ovarian cancer patients in clinical trials of Rubraca were 65 years of age or older. No overall differences in safety were observed between these patients and younger patients, but greater sensitivity of some older individuals cannot be ruled out. The effectiveness of Rubraca in patients with *BRCA*-mutant ovarian cancer who were 65 years of age or older could not be assessed due to the small number of patients (N=38).

Hepatic Impairment

No starting dose adjustment is recommended for patients with mild hepatic impairment (total bilirubin less than or equal to upper limit of normal [ULN] and AST greater than ULN, or total bilirubin between 1.0 to 1.5 times ULN and any AST). No recommendation of starting dose adjustment is available for patients with moderate to severe hepatic impairment (total bilirubin greater than 1.5 times ULN) due to a lack of data *[See Clinical Pharmacology (12.3) in the full prescribing information]*.

Renal Impairment

No starting dose adjustment is recommended for patients with mild to moderate renal impairment (creatinine clearance [CLcr] between 30 and 89 mL/min, as estimated by the Cockcroft-Gault method). There is no recommended starting dose for patients with CLcr less than 30 mL/min or patients on dialysis due to a lack of data *[See Clinical Pharmacology (12.3) in the full prescribing information]*.

OVERDOSAGE

There is no specific treatment in the event of Rubraca overdose, and symptoms of overdose are not established. In the event of suspected overdose, physicians should follow general supportive measures and should treat symptomatically.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

MDS/AML: Advise patients to contact their healthcare provider if they experience weakness, feeling tired, fever, weight loss, frequent infections, bruising, bleeding easily, breathlessness, blood in urine or stool, and/or laboratory findings of low blood cell counts, or a need for blood transfusions. These may be signs of hematological toxicity or a more serious uncommon bone marrow problem called 'myelodysplastic syndrome' (MDS) or 'acute myeloid leukemia' (AML) which have been reported in patients treated with Rubraca *[see Warnings and Precautions]*.

Embryo-Fetal Toxicity: Advise females to inform their healthcare provider if they are pregnant or become pregnant. Inform female patients of the risk to a fetus and potential loss of the pregnancy *[see Use in Specific Populations]*. Advise females of reproductive potential to use effective contraception during treatment and for 6 months after receiving the last dose of Rubraca *[see Warnings and Precautions and Use in Specific Populations]*.

Photosensitivity: Advise patients to use appropriate sun protection due to the increased susceptibility to sunburn while taking Rubraca *[see Adverse Drug Reactions]*.

Lactation: Advise females not to breastfeed during treatment and for 2 weeks after the last dose of Rubraca *[see Use in Specific Populations]*.

Dosing Instructions: Instruct patients to take Rubraca orally twice daily with or without food. Doses should be taken approximately 12 hours apart. Advise patients that if a dose of Rubraca is missed or if the patient vomits after taking a dose of Rubraca, patients should not take an extra dose, but take the next dose at the regular time *[see Dosage and Administration (2.1) in the full prescribing information]*.

Distributed by:
Clovis Oncology, Inc.
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1-844-258-7662

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Board Update

Momentum

Sarah Scarpace Peters, PharmD MPH BCOP, HOPA President (2016–2017)
Associate Professor of Pharmacy Practice
Albany College of Pharmacy and Health Sciences
Albany, NY

I am writing this last installment of the 2016–2017 Board of Directors update just hours before boarding my flight to attend HOPA's 13th Annual Conference. It has been a busy year—as evidenced by the voluminous board agendas (more than 1,500 pages!), the number of external collaborations, the inaugural offering of HOPA's Board Certified Oncology Pharmacist Recertification Program, the approval of the framework for a new committee structure, a bylaws review and update, and the incredible progress that our committees and several task forces have made to keep our strategic plan moving forward. The 1,000 words allotted to this update can never fully capture the extent of HOPA's activities and progress.

The new committee structure will be implemented for the 2017–2018 HOPA year, and if you encounter references to the "final" structure (with quotation marks), it's because we know that, as with any major structural change, some fine tuning will likely be needed along the way as the new committees and councils gain momentum. For an overview of the new structure and the opportunity to preview all of HOPA's new volunteer opportunities, please visit the Volunteer Activity Center at hoparx.org, where we've recorded a 30-minute webinar to explain in some detail how the new structure is intended to work.

At our February meeting, the board approved the budget for the Leadership Development Committee's Women in Leadership Summit, an invitation-only meeting to be held in conjunction with HOPA's Practice Management Program in September 2017. The Summit will call together female leaders in the profession to describe the progress and gaps in leadership opportunities for women that are unique to oncology practice, and, even more important, to create an action plan so that HOPA's Leadership Development Committee (which in the new structure is a subcommittee of the Governance Committee) can design programs to help strengthen members' skills for meeting the specific challenges identified at the Summit.

Expanding the Resource Library has been and will continue to be an important strategy to support the Professional Resources and Tools goal in our strategic plan. To that end, the board also approved the charges and members' skill-set requirements for an Oral Chemotherapy Educational Pamphlet Task Force; watch for these tools to be posted in the Resource Library in late summer 2017.

March marked the release of the "Time to Talk CINV" toolkit, an 18-month collaboration between HOPA, Eisai, and Helsinn. A study of patients and pharmacists undertaken in October 2015 to identify (mis)perceptions about chemotherapy-induced nausea and vomiting from both patients and oncology pharmacists led to the collaborative development of the toolkit. Please visit the Resource Library to download these tools for your practice; you can also watch a 30-minute webinar that provides more details about the tools.

The Standards Committee's newest resource—*Dose Rounding of Biologic and Cytotoxic Anticancer Agents: A Position Statement of the Hematology/Oncology Pharmacy Association*—was approved by the board and is posted on the HOPA website. The committee has also finalized three guidance documents for groups of authors assigned to create HOPA standards, guidelines, and position papers. The documents will be instrumental in standardizing the appearance of each type of paper and will more clearly define timelines, deliverables, and expectations of all involved—authors, Standards Committee members, and board and staff liaisons—to ensure timely completion of these important tools for our members.

"We have accomplished so much in 2016–2017, . . . and I have no doubt that all our future leaders will keep this momentum going."

Several other tools are also near completion. A draft of the *ASHP/HOPA Guidelines on the Role and Responsibilities of the Pharmacy Technician in Ambulatory Oncology Pharmacy* will be released for comments by members of both the American Society of Health-System Pharmacists and HOPA in late spring 2017, with ultimate publication in the *American Journal of Health-System Pharmacy* planned for late 2017 after comments have been addressed and each organization's board of directors has given approval. The Hematology/Oncology Pharmacist-Patient Task Force has also completed its charge to create patient-appropriate documents to help facilitate communication between patients and their oncology pharmacists; these documents are currently undergoing a revision to make them accessible to a wider range of patients and should be available in the Resource Library in late spring 2017 as well. The Scope of Hematology/Oncology Pharmacy Practice (Part 2) Task Force has also made significant progress on granular details related to job descriptions, roles, and responsibilities that members frequently seek from one another; the task force met at HOPA headquarters in May to spend uninterrupted time writing. The Entry-Level Competencies in Hematology/Oncology Pharmacy Practice Task Force has made excellent progress in meeting another frequent request from members: to better define expectations of pharmacy students or PGY-1 residents on oncology rotations. Notably, the group identified an opportunity to comment on the American College of Clinical Pharmacy's Pharmacotherapy Didactic Curriculum Toolkit that was published in *Pharmacotherapy* in late 2016 and wrote a response regarding the recommendations for oncology teaching. The task force's response letter was approved by the board and was published in the March 1, 2017, issue of *Pharmacotherapy*.

Our advocacy momentum continues to be strong. The board approved HOPA's participation in the Pediatric Pharmacy Advocacy Group's Pharmacy Vaccine Coalition through December 31, 2017, to lend our support in addressing the resurgence of the antivaccination movement, given the critical role that vaccines play in protecting cancer patients, and, in the case of the human papillomavirus vaccines, in cancer prevention. Some very important work has been completed by the Value of the Hematology/Oncology Pharmacist Task Force, which will lay the foundation for the new Research-Practice Outcomes and Professional Benchmarking Committee to help strengthen the evidence base as we advocate for inclusion in payment-reform models. A group of HOPA members participated in the 1-hour *Voice of America* radio program led by the Cancer Support Community on March 7, 2017, to advocate that patients use us more—you can listen to this at https://www.voiceamerica.com/episode/97736/an-inside-look-at-the-pharmacists-role-in-cancer-care. Finally, look for a proceedings document to follow HOPA's first policy summit focused on drug waste, held in Washington, DC, on May 8, 2017.

We have accomplished so much in 2016–2017; by the time you read this, HOPA's 2017–2018 Board of Directors and our new committees will be in place—and I have no doubt that all our future leaders will keep this momentum going. It has been my pleasure to be on this journey with you during the past year. ●●

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8735 W. Higgins Road, Suite 300
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