COVER STORY
Oncology Pharmacists Are Essential in Therapeutic Interchange
JOSH HOWELL, PHARMD, BCOP

BREAST CANCER
The Impact of COVID-19 on Cervical, Breast Cancer Screenings
BROOKE PETERS, PHARMD, BCOP; AND CHRISTINE PFAFF, RPH

OVARIAN CANCER
Current Standards of Care in Platinum-Resistant Ovarian Cancer
TAE SMITH, PHARMD, BCACP

HEMATOLOGY
Brown Bag Consult®: Chronic Lymphocytic Leukemia
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Assessing the Impact of Patient Assistance Programs on Financial Toxicity in Oral Oncology
MARTHA STUTSKY, PHARMD, BCPS; AND CAROL KIM HUYNH, PHARMD, CSP

SAFE MEDICATION PRACTICES
Developing Standardized Concentrations, Overcoming Barriers
CRAIG KIMBLE, PHARMD, MBA, MS, BCACP
10 cover feature

Oncology Pharmacists Are Essential in Therapeutic Interchange

JOSH HOWELL, PHARMD, BCOP

Biosimilar therapeutic interchange processes can mitigate high costs of cancer drugs.
featured

14 Assessing the Impact of Patient Assistance Programs on Financial Toxicity in Oral Oncology
MARTHA STUTSKY, PHARMD, BCPS; AND CAROL KIM, PHARMD, CSP

16 SAFE MEDICATION PRACTICES
Developing Standardized Concentrations, Overcoming Barriers
CRAIG KIMBLE, PHARMD, MBA, MS, BCACP

BREAST CANCER

19 The Impact of COVID-19 on Cervical, Breast Cancer Screenings
BY BROOKE PETERS, PHARMD, BCOP; AND CHRISTINE PFUFAFF, RPH

OVARIAN CANCER

22 Current Standards of Care in Platinum-Resistant Ovarian Cancer
TAE SMITH, PHARMD, BCACP

HEMATOLOGY

24 Brown Bag Consult®: Chronic Lymphocytic Leukemia
JILL DRURY, PHARMD, BCOP

recaps

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The Role of Pharmacists in Improving Patient Access to Oncology Drugs

IN THE PAST 2 YEARS, great strides have been made toward improving patient access to oncology therapies. The COVID-19 pandemic helped raise awareness about preexisting challenges many patients face when it comes to health care access. However, these challenges have long existed for patients with cancer, who may need to travel extensive distances to access care. Additionally, the specialty pharmacies that provide patients with the medications they need may not always be close by, sometimes requiring extensive travel just to retrieve medication.

These challenges can cause delays in treatment start times, which is a critical period in the treatment journey. Further, barriers to care and treatment can place added strain on the mental health of patients with cancer, as hope in the potential for a positive treatment outcome remains crucial for them to successfully face the difficulties that may lie ahead. When patients learn they may have a multitude of barriers to overcome to access treatments that could save their lives—whether the barriers be financial, travel, or otherwise—it can become far more difficult to maintain the hope they need to persevere and successfully fight the disease.

In this way, maintaining patients’ hope in the potential for positive treatment outcomes is critical. For many, that hope can be made possible with the presence of an oncology drug expert on their team: the pharmacist. Pharmacists can act as a 1-stop shop for everything a patient needs to know and understand about the treatment journey, from co-pay and financial assistance programs to refill coordination and treatment adherence checkups.

In our cover story, on page 10, Josh Howell, PharmD, BCOP, discusses the role of the pharmacist in facilitating biosimilar therapeutic interchange processes, which can help to reduce the cost of care and enable success in value-based delivery models.

On page 19, coauthors Brooke Peters, PharmD, BCOP, and Christine Pfaff, RPh, discuss the importance of using routine screenings for the prevention and early detection of breast and cervical cancer among women, which can help lower the cost of cancer care or eliminate the need entirely.

The efforts of pharmacists remain critical to the success of treatment outcomes, yet their impact can be much greater when they are also included on patient care teams to maximize their role in addressing the access barriers many patients may face during cancer treatment throughout the country.
The Impact of COVID-19 on Cervical, Breast Cancer Screenings
Pharmacists can educate patients on the importance of screenings.

BY BROOKE PETERS, PHARM.D., BCOP; AND CHRISTINE PFAFF, RPH

ROUTINE SCREENING IS AN IMPORTANT TOOL for the prevention and early detection of breast and cervical cancer among women. Breast cancer screening guidelines using mammography vary among guiding bodies, including the American Cancer Society and the American Academy of Family Physicians. For women of age 50 to 74 years with average risk factors, the most liberal guidelines recommend biannual mammography. Through cervical cancer screening, abnormal cells in the cervix may be identified and treated before they progress to cancer.

The US Preventive Services Task Force recommends women at average risk who are between the ages of 21 to 29 receive cervical cytology alone every 3 years and that women of age 30 to 65 years receive primary high-risk human papillomavirus (hrHPV) testing every 5 years, both cervical cytology and hrHPV testing every 5 years, or cervical cytology alone every 3 years. Routine screening for cervical cancer and its precursors has been proven to improve overall cervical cancer outcomes.

Many factors influence adherence with routine cancer screening. Socioeconomic status, access to care, lack of transportation, and lack of insurance are commonly noted barriers. Perceived barriers to mammography were studied between 2006 and 2011 at the Alvin J. Siteman Cancer Center, a National Cancer Institute (NCI)–designated Comprehensive Cancer Center in Missouri. The study was conducted to investigate why women did not get mammograms.

In the study, responses from registrants included fear of cost, mammogram-related pain, and fear of bad news. Compounding these barriers, the COVID-19 pandemic in early 2020 resulted in a sharp reduction in cancer screenings across the United States.

During the first months of the
Recent research has demonstrated that socioeconomic and racial disparities in screening persist.

The COVID-19 pandemic, specifically during the stay-at-home order, several large studies measured a substantial reduction in cervical and breast cancer screenings. The decline in cervical cancer screening was one of the most significant declines in preventive screening rates in the United States. In the years just prior to 2020, there was a slight uptrend in the rates of cervical and breast cancer screenings; however, both declined substantially by spring 2020.

In both breast and cervical cancer screenings, Epic Health Research Network identified a 94% decline compared with averages before the COVID-19 pandemic, as demonstrated in 2.7 million patient records from 39 organizations spanning 23 states. Additionally, another study identified a 68.2% decline in cervical cancer screenings. Furthermore, the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) observed an 87% and 84% decline in NBCCEDP-funded breast and cervical screenings, respectively, during April 2020 compared with the previous 5-year averages for April.

However, multiple studies demonstrated some improvement in breast and cervical cancer screening rates by June 2020. Epic Health Research Network data showed that weekly volumes in June remained 29% and 35% lower than pre–COVID-19 levels for breast and cervical cancer screenings, respectively. The NBCCEDP research showed that in June 2020, screening rates were 39% and 40% below the 5-year average for that month for breast and cervical cancer screenings, respectively.

The impact of this decrease in cervical cancer screenings during the beginning of the pandemic remains unknown. From March to June 2020, Epic Health Research Network estimated that 285,000 breast and 40,000 cervical exams were missed or delayed. Additionally, one modeling study using a 70% decline in cervical and breast cancer screening over a 3-month period projected 38,500 women with a delayed cancer diagnosis.

Although some variation in the United States would be expected, some insight can be gained from a European modeling study that evaluated the impact of 6-month screening delays. This model demonstrated that a 6-month screening delay across the population would result in approximately 4 additional cases of cervical cancer per 100,000 women. On the other hand, women who miss an entire 3- to 5-year screening cycle have a 7-fold higher rate of cervical cancer vs those with a 6-month delay. The impact of screening delays for cervical cancer is expected to be greatest among women of age 40 to 49 years, with vaccination against HPV mitigating the effect of the delay in younger women.

Some reports suggest that screening rates for breast and cervical cancer began to exceed pre-pandemic numbers in late 2020. In one study evaluating patients in the Massachusetts General Brigham system, screening for breast and cervical cancer from September to December 2020 exceeded pre–COVID-19 levels by 14% and 2%, respectively. There was also an increase in positive diagnoses for both breast and cervical cancers during this time.

Despite these improvements in screening rates post pandemic, providers have expressed concerns that we will continue to see an increase in cancers diagnosed at later, less-treatable stages. Additionally, recent research has demonstrated that socioeconomic and racial disparities in screening persist.

Members of the Community Oncology Alliance and Avalere Health looked at the impact of the COVID-19 pandemic on cancer screening rates using a multipayer database that included Medicare, Medicaid, and commercial insurance. Although there was an increase in breast cancer screenings in the months following the stay-at-home order among all groups, the rate of increase was slower for those with a reduced income level and in certain racial and ethnic minority groups. The COVID-19 pandemic highlighted these disparities, giving cancer clinicians a push to focus on improved education and access to care for these groups.

Moving forward, screenings for patients who are overdue must be prioritized. Survey research to
determine why patients are hesitant to pursue timely screening is ongoing.\textsuperscript{13} Not only are some patients anxious to go to a health care facility because of the risk of acquiring COVID-19, but others may have lost employment or child care, making it difficult for them to make time for physician appointments and/or pay for health care. Understanding these barriers will help us improve screening rates and potentially mitigate screening declines in the event of a future pandemic.

Improved access to care and increased patient education require coordinated efforts among providers. For a variety of reasons, many patients do not use primary care providers as their first access point to health care. \textsuperscript{14} Other health care professionals in the community, such as local pharmacists and public health departments, can reinforce the importance of screenings and educate patients.

Furthermore, to reduce issues relating to transportation burdens, coordinating mobile mammography and community outreach projects in underserved areas can bring screenings closer to home. Additionally, grants that provide low-cost or free transportation could also help to remove transportation barriers for patients. Advances in user-friendly, at-home screening tests may also improve cancer screening rates.

Multiple studies have also evaluated the potential impact of at-home HPV tests.\textsuperscript{14,15} Although these at-home tests appear to be accurate and effective, a statistical difference in the detection of precancer lesions has not been demonstrated.

The COVID-19 pandemic impacted cancer care and cancer screenings more than any event in recent history. Although studies show there is movement toward pre-pandemic cervical and breast cancer screening rates, the disparity among patients of different socioeconomic, racial, and ethnic communities continues. To reduce barriers, health care providers must be innovative and work together to serve these patients.

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Editor's Note

Today, the positive impact of oncology product approvals has evolved to the point where, in many cases, there are multiple treatment options to choose from when targeting a specific disease state. However, this opportunity for drug selection has opened the door for payers to leverage one drug over another in terms of coverage offerings, creating new challenges for care teams and patients during the treatment process.

Furthermore, the oncology products patients receive may vary from what was ordered by the oncology professional due to not only the broader treatment options available but also the higher costs of treatments and subsequent payer coverage decisions. However, the oncology pharmacy team often has its own reimbursement specialist with the experience, background, and relationships necessary to ensure what was originally ordered remains in the patient’s treatment plan.

Because of this changing dynamic in product selection and access, the role of oncology pharmacists as key patient therapy advocates has strengthened, as oncology pharmacists work on the patient’s care team to ensure patients have access to lifesaving therapies that meet their clinical needs.

The Navigator

Receiving a cancer diagnosis is a life-altering experience for the patient and their family, with therapy selection as just one of many factors to consider on the road ahead. Under the best of circumstances, the healthcare system can be daunting to traverse for patients, but following a cancer diagnosis, it can become significantly more challenging.

However, there are newer and more efficacious therapies available that have evolved and emerged over the past several years. Yet, patients faced with the bewildering task of navigating the healthcare system alone in order to receive these emerging treatments may come up short in terms of reaching the best possible outcome available for the treatment of their disease.

A patient with a new diagnosis will benefit greatly from the support of a care team that includes the medication expertise of oncology pharmacists to help them navigate the complexity of the treatment landscape that lies ahead. With support from an oncology pharmacist, the oncology team can help alleviate a host of anxieties for patients who are starting and then adhering to a complex oncology treatment plan.

When a patient receives a diagnosis, the clinical oncology pharmacist can imme-

Navigating Patient Treatment in Oncology
Pharmacy to Fill Gaps in Care
Oncology pharmacists can help ensure patient access to lifesaving therapies.

BY DAN STEIBER, RPH, PHARMACY TIMES ONCOLOGY EDITION™ EDITOR IN CHIEF

Dan Steiber, RPh
immediately support the care team by helping to develop a treatment plan. Once the drug component is selected, the pharmacy opens their toolkit of solutions for patient access challenges, including setting up prior authorizations and co-pay assistance. Depending on the dosage form, the oncology pharmacy team can also ensure the selected products can be paid for by the patient.

Additionally, the route of administration or dosage form may be infused, subcutaneous, or oral, and in most cases a mixture of all 3. The logistics of ordering the products and ensuring they are all made available to the patient or provider in a timely manner can be coordinated by a clinical oncology pharmacist.

Contemporary Tools
The reimbursement specialist on the oncology pharmacy team also can help minimize the patient’s out-of-pocket costs by ensuring what was ordered remains in the patient’s treatment plan. The reimbursement specialist’s toolkit often includes information technology resources and databases to help handle the required documents in a paperless and expedited manner.

Over the past 3 to 5 years, real-time access to coverage has emerged, and terms, such as electronic benefit verification and electronic prior authorizations, have been refined so the oncology team or specialty pharmacy can identify what is covered; offer alternative therapies, if appropriate; and assess the fiscal impact of each selection, including co-pays. The results of such assessment can help guide decisions around seeking alternative forms of payment, which are often tied to electronic resources such as manufacturer-sponsored patient assistance programs (PAPs).

Alternative Forms of Payment
In the United States, the majority of patients with cancer are often buffered from the extraordinary costs of oncology drugs through employer health insurance, Medicaid, or Medicare. However, payer plans have emerged that create gaps in coverage tied to formulary restrictions that often put a heavy burden on patients, even those with good health insurance coverage. Patients with cancer who don’t have health insurance or adequate prescription drug coverage are often confronted with the challenge of deciding how and whether they can pay for their medications out of pocket, which may total tens of thousands of dollars.

Manufacturers of these higher-cost therapies generally make available reimbursement options for patients in the form of PAPs. These sponsored programs are promoted as a safety net for individuals who may have no health insurance or inadequate financial resources to offset the out-of-pocket costs of these therapies. The objective of these PAPs is to provide financial assistance to help patients access drugs for little to no cost.

There are also options for financial assistance for patients in the form of co-pay assistance, which helps patients with cancer who have insurance pay the co-pays related to their care and treatment. However, such payment assistance can be inadequate for the underinsured, leaving oncology patients’ out-of-pocket costs to have a detrimental impact on their financial well-being, which can potentially eliminate or reduce their access to lifesaving treatments.

To help facilitate patient access to the best therapies available, the oncology team must understand several variables, including the patient’s deductible, out-of-pocket maximum, and percentage paid by the insurance, as well as the amount paid by the insurance over what period of time. Ultimately, the oncology team produces a treatment plan that will include what the patient’s monetary responsibility is before they receive that first therapy, combined with alternative forms of payment.
Oral vs Infused: A Few Facts

Over the past several years, there has been a shift from infusion drugs to oral oncology therapies, which has been a positive trend for the industry. This shift has helped empower patients to maintain a bit more normalcy in their lives during the difficult process of cancer treatment by allowing them to be freed from long and painful infusions.

However, this positive shift has come with trade-offs in relation to reimbursement. In most cases, an oral oncolytic will be covered by the drug benefit of a patient’s insurance, which is most often administered by a pharmacy benefit manager.

Typically, oral therapies have higher cost sharing vs infused products, which are billed by the clinic. This is referred to as buy-and-bill, which means the infused products tend to have better coverage because they are being billed through a patient’s medical benefit. With oral therapies, these higher costs frequently result in significant financial challenges for patients, which is referred to as financial toxicity.

With the challenge that is financial toxicity comes the important role of the oncology pharmacy team in working with payers to obtain prior authorizations and using their knowledge and experience to navigate the reimbursement gauntlet on behalf of the patient. This work can help ensure they are able to break through the bureaucratic requirements necessary for the approvals of the right therapies for the patient’s treatment.

Oral oncology products that have an associated limited distribution policy often have their own specific challenges. This can especially be true if it is mandated that the patient have the product dispensed by a different specialty pharmacy than the one on their care team. When this occurs, not only does the patient receive mixed pharmacy services, but they often experience treatment delays before they can start therapy.

Because of these challenges, oncology pharmacies and oncologist dispensers are working to develop strategies that can help to combat limited distribution drug (LDD) practices by forming networks and advocating with the manufacturer on behalf of patients.

Oncology Specialty Pharmacy

With the growth of oral oncology options, the number of new dispensing specialty pharmacies in hospitals and community oncology clinics has also exponentially increased. This increase is significant because the dispensing specialty pharmacy plays a significant role in facilitating patient access to therapies. The dispensing specialty pharmacy staff are trained to communicate directly with the oncology team, leading the benefits investigation process. Additionally, it is up to the oncology specialty pharmacy to react quickly and communicate with the oncology team on what they learn relative to what is covered and at what cost so any changes to therapy that may be required can happen in a timely manner.

In today’s practice environment, pharmacy systems typically do not interface with the clinic’s overall electronic medical record (EMR) system. Additionally, there is work under way at some institutions to transition oral oncology orders into the overall EMR system. This integration will lead to a faster response time, thereby facilitating better and more cost-effective patient care.

Bringing It All Together

The oncology team and the dispensing specialty pharmacy can work together to help enhance patient adherence to treatment plans and administer supportive care to conquer the potential clinical implications of payer overmanagement of drug benefit and LDDs. Facing this challenge together, they can meet it head-on to navigate the waters of product access for patients, putting their needs above all other concerns.

Despite the challenges of the past 2 years, pharmacists have stronger and better positioned than ever for our future, with the role of oncology pharmacy continuing to grow as oncology pharmacists step up to fill gaps in care.
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WELLBEING CHECKUP

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Deep Dive Into Psychedelic Medicine's Potential
Tiago Reis Marques, MD, PhD, discusses the potential role for ketamine and other psychedelic medicines in the opioid epidemic, both to manage chronic pain and to treat addiction. He also discusses the benefits of in-home infusions for ketamine, which he says are just as safe as in-clinic infusions when administered and overseen by a medical professional.

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Oncology Pharmacists Are Essential in Therapeutic Interchange
Biosimilar therapeutic interchange processes can mitigate high costs of cancer drugs.

By Josh Howell, PharmD, BCOP

Oncology had a pivotal moment with the first FDA approval of a supportive care biosimilar in 2015, bringing to the forefront an alternative therapy to a costly innovator drug. This was followed by the approval of primary therapy biosimilars in 2019. Since then, a multitude of biosimilar oncology treatments have emerged, challenging providers to keep up with the growing body of science that comes with each new development.

Consequently, providers have turned to oncology-trained pharmacists more and more to gain a critical understanding of the emerging new agents on the market. As this increased reliance on pharmacists has come to the fore, the pharmacist has become even more vital as the trusted advisor to medical oncologists and the care team. Because of this shift, pharmacists have supported increased utilization of biosimilars due to their enabling providers to become comfortable using these new agents.

As the cost of cancer drugs continues to escalate, many practices are utilizing biosimilar therapeutic interchange (TI) processes as a way to reduce cost of care, enabling success in value-based delivery models. Given the deep expertise of oncology pharmacists, they are well positioned to play a leading role in developing and managing these rapidly growing TI programs.

Pharmacists Are Integral to TI Success
Traditional distribution activities are still the core function of the work of pharmacists who are specifically trained in oncology, as they oversee the safe acquisition and preparation of specialized oncology drugs prior to patient administration. Additionally, these pharma-
Pharmacists assist the care team in complex drug selection, adverse event monitoring, and treatment of adverse effects. In many organizations, pharmacists are also assuming an even larger role by developing and managing TI programs, making them a vital member of the practice.

TI processes are best driven by pharmacists, as they are highly skilled at navigating the complicated decision-making process of selecting drugs in the same category with similar therapeutic indications. Further, handling biosimilars that have similar nomenclature has introduced the risk of medication-related safety events because of misreading, and pharmacists participating in this workflow can help mitigate these types of errors. Having these clinically trained specialists review and ensure the safe use of biosimilar agents has become a necessary investment every care team should make to improve patient care.

A critical first step in building a TI program is to establish a pharmacy and therapeutics (P&T) committee. Functioning as a governing body of the provider, the P&T committee provides a framework that gives more autonomy to pharmacists to make changes and ensures that physicians agree with the TI processes. Pharmacists tend to support most P&T committees and play a critical role in gathering the clinical and cost data about the drugs to inform decision makers when picking a preferred agent.

**TI Programs Provide Varied Benefits**

TI programs enable practices to efficiently move toward more utilization of biosimilars, providing many benefits to stakeholders, including the following:

- Patients have access to cheaper treatment options without sacrificing clinical efficacy. Specifically, this is facilitated through the growing number of biosimilars increasing competition, decreasing the price to patients who are facing rising deductibles and coinsurance costs.
- Biosimilar utilization that is enabled by TI programs provides a foundation for practices to succeed in value-based care, because biosimilars can provide significant cost savings over innovator products.
- Through TI programs, payer relationships can be enhanced, as biosimilars enable practices to utilize drugs that are still effective but lower priced. This provides tremendous value to payers by helping to control cost of care.

**Challenges to TI**

Obstacles exist that can block or slow TI. In smaller clinics, pharmacies often concentrate on the distribution channel more than other initiatives. However, the emergence of new drugs, such as biosimilars, makes it essential for practices to invest in bringing pharmacists onto care teams. These knowledgeable specialists keep up with changes and new therapies, facilitating adherence to agreed-upon P&T initiatives for preferred drugs.

Additionally, because providers want to remain independent, implementing a TI program can be met with...
resistance because it adds a layer of supervision. To effectively address this resistance, building trust between providers and the pharmacy is critical. Further, pharmacies can implement processes and procedures that can help them overcome any pushback.

The US Oncology Network Offers Remote Clinical Reviewer Services
Evidence continues to demonstrate the value oncology pharmacists bring to a practice. In a recent review of chemotherapy regimen orders within a community oncology practice, investigators found substantial benefits could be gained by using a clinical pharmacist trained in oncology.1

The investigators observed that of the documented reviews over a 10-week period, 49.2% lead to modifications by the pharmacist, resulting in improvements of $106,000 and a $462,000 reduction in total cost of care for medications.2 Based on these results, the investigators concluded that an oncology pharmacist was a cost-effective and valuable member of the care team, improving safety and regimen optimization and demonstrating a significant financial impact for practice, payers, and patients.1

Unfortunately, despite the clear benefits of having pharmacists on the care team, many small community practices either do not have pharmacists or they have a small pharmacy staff with limited time to review regimens, which can make TI less likely to occur. Because of this current deficit in pharmacists at smaller centers, The US Oncology Network developed a clinical pharmacist review program called ClinReview, which provides remote pharmacist services to practices.

Oncology-trained pharmacists electronically review all chemotherapy regimens, identifying opportunities to modify therapies based on clinical components, waste reduction, and responsible stewardship of financial resources. Practice policies determine which modifications may be made by their pharmacy staff, and other recommendations are discussed with the patient’s oncologist. The program provides a strong return on investment by optimizing medication regimens, improving medication utilization and safety, and reducing medication expenses.

Pharmacy’s Role in Step Edits
Many biosimilars that have been around for several years are now highly utilized, with some payers making their own policy decisions for these agents. However, these decisions can often create challenges for practices by requiring step edits. When this occurs, layers of paperwork and scrutiny inhibit care while providers dispute arbitrary drug selection.

Pharmacists can help with these challenges by educating physicians on the payer’s changing landscape of drug selection and showing payers why step edits should not be followed for a particular drug. This ultimately allows the provider to make the best decision in cost-effective drug selection. By demonstrating the continued success of this process, payers may remove the practice from step edit processes.

Every Care Team Needs a Pharmacist
Oncology is getting more complex by the day, not only because of biosimilars and TI programs but also because of the continued evolution of new drugs and oral therapies. These agents are very specific and are targeted to the disease and to specific disease states within a cancer diagnosis.

Because of this growing complexity, a highly knowledgeable specialist should be monitoring all aspects of these treatments—a role ideally suited to oncology pharmacists. These clinically trained professionals should be part of the care team and have clearly defined responsibilities, empowering them to play a vital role in ensuring patients receive safe, high-quality care.

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Assessing the Impact of Patient Assistance Programs on Financial Toxicity in Oral Oncology

PAPs can significantly reduce OOP costs for patients.

BY MARTHA STUTSKY, PHARMD, BCPS, AND CAROLKIM HUYNH, PHARMD, CSP

Specialty pharmacy medications now represent over 50% of pharmacy spending in the United States, with oncology medications accounting for 18.3% of the total expenditure.1 Oral oncology medications are often associated with high out-of-pocket (OOP) costs, and as novel oral anticancer agents are increasingly utilized for treatment, this can lead to financial stress and have a negative impact on the well-being of patients and caregivers.2

Financial toxicity is a relatively new concept that considers the potential health outcomes and other consequences of financial hardship attributed to prescription regimens, such as the impact of skipping doses of medication to delay OOP costs. According to the National Cancer Institute, patients with a cancer diagnosis are more likely than those without cancer to experience financial toxicity, given the combination of OOP drug costs, other medical expenses, and lost work productivity. Even when measures have been taken to address prescription costs, such as the narrowing of the Medicare Part D coverage gap phase, or “donut hole,” the OOP costs of most orally administered anticancer drugs continue to increase at a rate greater than the rate of inflation.3

Patient assistance programs (PAPs) can significantly reduce patient OOP costs for oral oncology therapies. Support through PAPs can be generous,
Financial toxicity is a stark reminder of disparities in health equity, and there is a great deal to be learned about how best to address the financial challenges of cancer treatment. The results from several studies on the impact of financial assistance programs have been reported in the literature, but these reports tend to be observational, without a full assessment of the impact of the programs on clinical outcomes in this population. For example, a retrospective study of prescription anticancer medication costs and PAP coverage from one academic cancer center’s specialty pharmacy demonstrated that a minority of prescriptions received financial assistance from PAPs, and the proportion of financial assistance was small relative to the price billed to insurance.

A retrospective, cross-sectional analysis of outpatient pharmacy, medical, and cancer registry records at The University of Texas MD Anderson Cancer Center in Houston, the largest tertiary cancer center in the United States, demonstrated that fewer than 5% of the patients with cancer who received prescription medications from the outpatient pharmacy were enrolled in a PAP, and the program provided financial support primarily for supportive care medications.

Elsewhere, in a pilot feasibility study, 34 patients with cancer with nonmetastatic solid tumors received a financial education course followed by monthly contact with a financial counselor and case manager for 6 months. Although self-reported financial burden did not change over time, anxiety about treatment costs decreased in 33% of patients enrolled in the financial education program.

In an integrated HSSP model, a patient’s point of contact with a PAP is likely to be a pharmacy liaison or a financial coordinator or navigator. Often embedded in specialty clinics, the liaisons help speed time to start of therapy, assess needs and provide support with every refill, coordinate drug delivery, address any new insurance and/or co-pay challenges, and monitor for adherence. The benefit of an integrated model in addressing financial toxicity—and other social determinants of health, for that matter—is that the risks will be identified as early as possible, often at the time of first fill. Furthermore, all the relevant resources of the health system, including outreach to a PAP, if available, will be targeted toward solving the problem or mitigating it before the clinical outcome is compromised.
SAFE MEDICATION PRACTICES

Developing Standardized Concentrations, Overcoming Barriers

Simplifying processes reduces errors in compounding, IV pump programming, and physician order entry.

BY CRAIG KIMBLE, PHARMD, MBA, MS, BCACP

PAST INITIATIVES IN STANDARDIZING CONCENTRATIONS of intravenous (IV) or liquid oral medications have focused mostly on gaining efficiency in the drug supply chain, improving distribution, and generating cost savings. Improvements in medication safety with standardized concentrations were often a secondary goal of the initiatives and did not address patients moving across different care settings. Even with some standardization, many health systems still have multiple concentrations of the same drug across their own systems.1

Recent data and their promotion by the American Society of Health-System Pharmacists (ASHP), FDA, Institute for Safe Medication Practices (ISMP), and other groups show that IV admixture standardization programs can aid in reducing errors and improving transitions of care.1,2 Using concentrations that vary by location within a health system puts patients at risk of medication errors and is a concern that should be formally addressed by a national standard. Health systems must minimize the number of concentrations they keep to a maximum of 1 to 3 when possible.1 Using commercially available products is a great starting point but does not address all products. Simplifying processes can reduce medication errors in compounding, IV pump programming, and physician order entry.3

Why Standardization Is Important

The ASHP, ISMP, Pediatric Pharmacy Association, and other stakeholders have long argued for a national practice standard for standardized concentrations of IV medications and oral liquid medications. The major driving factor behind these efforts is the prevention of medication errors. Errors occur with these products as patients navigate the health care system through various settings. In addition to improving patient safety, standardizing IV medication concentrations can benefit the drug supply chain with the use of premixed products, improve patient outcomes, reduce overall health care costs, and simplify ordering with fewer choices for prescribers.2,4

What Is Included

Previous attempts to standardize IV concentrations have mostly been health system or product-specific efforts. Any standardization program initiative should aim to address key areas in the compounding, dispensing, and administration processes. These include concentrations and dosing units for continuous pediatric medications and IV continuous medications, concentrations...
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Any standardization program initiatives should aim to address key areas in the compounding, dispensing, and administration processes.

for compounded oral liquid medications, concentrations of epidural and patient-controlled analgesia medications, IV intermittent medications, and doses for oral liquid medications. Sites should evaluate what is commercially available, adopt these products when possible, and use commercially available products as a standard across the system when feasible. Standardizing liquid doses is also key (eg, 250.0 mg vs 225.6 mg). Common drugs that are standardized in concentration include amiodarone, diltiazem, dobutamine, and dopamine.1,4

ASHP Initiative
The ASHP recently received federal funding from the FDA’s Safe Use Initiative to develop and promote a national standardized concentration initiative for IV and oral liquid medications. The Standardize 4 Safety program is a collaboration among nurses, pharmacists, physicians, and other stakeholders. Although previous efforts undertook similar initiatives at the local and state levels, this is the first funded national interdisciplinary effort to promote and standardize medication concentrations. So far, results include the development of standardized concentration lists, with additional lists expected as the program progresses.1,2 This program began looking at evidence-based standardized concentrations for 32 IV medications. The first efforts examined patients with an elevated risk of harm because of dosage errors. The goal is to reduce medication errors that occur during transitions of care.

Conclusion
It is long past time for the pharmacy profession to take the lead in establishing a national standard in IV and oral liquid medication concentrations with a patient safety focus. All pharmacists have a role in promoting such efforts by participating, providing feedback, and educating others. Engaging stakeholders in their organizations with data from the ASHP Standardize 4 Safety initiative will help educate them and remove barriers. Having a national standard helps pharmacies better communicate and coordinate across health care settings to ensure consistency and patient understanding. Interdisciplinary teamwork is essential in this process, and there must be a national effort for adoption to overcome obstacles until the Standardize 4 Safety initiative is complete. To learn more about the effort or to participate, sign up for updates and resources online at https://www.ashp.org/pharmacy-practice/standardize-4-safety-initiative#s4sresources.

REFERENCES
Current Standards of Care in Platinum-Resistant Ovarian Cancer

Folate receptor α may be an important treatment target for ovarian tumors.

BY TAE SMITH, PHARMD, BCACP

The standard of care for epithelial ovarian cancer (EOC) and fallopian tube and primary peritoneal cancers at any stage has long been platinum agents. When disease recurs, sensitivity or resistance to platinum agents determines the next choice of therapy.

Based on criteria from the Fourth Ovarian Cancer Consensus Conference, patients are considered platinum refractory if the interval between the last dose of a platinum agent and the date of relapse is less than 1 month, resistant if the relapse is between 1 and 6 months, and sensitive if the platinum-free interval is 6 months or more. Standard guidelines recommend carboplatin or cisplatin doublet therapy with or without bevacizumab (Avastin; Genentech) as first-line agents for a recurrence in platinum-sensitive disease. PARP inhibitors are also recommended for patients that meet certain criteria. However, once the cancer becomes resistant or refractory to platinum agents, there are limited, less-effective options available.

Preferred regimens include the sequential use of single-agent nonplatinum cytotoxic therapy, including liposomal doxorubicin, paclitaxel, gemcitabine (Gemzar; Eli Lilly and Company), and intravenous (IV) topotecan (Hycamtin; GlaxoSmithKline). The overall response rates (ORRs) and progression-free survival (PFS) intervals between these agents are similar at 10% to 15%, with PFS between 3 to 4 months and overall survival (OS) approximately 12 months.

Single-agent bevacizumab has an ORR between 16% and 21%. Adding bevacizumab to chemotherapy improved PFS to 6.7 months in the AURELIA trial (NCT00976911) but did not change OS. Single-agent immunotherapy given without regard to PD-L1 status in EOC has been disappointing, as evidenced by data from the phase 2 KEYNOTE-100 trial (NCT02674061). For pembrolizumab (Keytruda; Merck & Co), the ORR was approximately 9%.

However, patients with ovarian cancer included in KEYNOTE-158 (NCT02628067) who had DNA mismatch repair–deficient disease or microsatellite instability had a much better ORR of 33%. A study that combined all modalities, including oral cyclophosphamide, bevacizumab, and pembrolizumab, reported the ORR at 47.5% in a single-arm phase 2 trial (NCT02853318).

The PARP inhibitors have improved ORR vs traditional cytotoxic chemotherapy in later lines of therapy, but for this indication, they require BRCA mutation positivity or homologous recombination deficiency, depending on the agent. These genomic mutations or instability are found in a minority of patients.

Currently approved agents in EOC are rucaparib (Rubraca; Clovis Oncology, Inc), niraparib (Zejula; GlaxoSmithKline), and Olaparib (Lynparza; AstraZeneca). For rucaparib, the...
recently reported subgroup analysis in the ARIEL4 trial (NCT02855944) showed an ORR of 47% in the platinum-resistant population. In ARIEL4, olaparib has a reported ORR of 31.1%. Further, in the QUADRA trial (NCT02354586), which was evaluating niraparib, investigators reported ORRs of 29% in patients who were platinum resistant and 19% in those who were platinum refractory.

The trials for the later lines of therapy all excluded patients who had received PARP inhibitors in prior lines of therapy. As this class of agents becomes the standard of care in earlier maintenance lines of therapy, further data will be needed to assess whether they retain their activity if patients have already been exposed to PARP inhibitors.

**Folate Receptor α**

There is still a need to improve the ORR in trials assessing agents for ovarian cancer that give further options to patients without a targetable mutation with currently approved agents. One target for investigation in this area is folate receptor α (FRα), the most widely expressed of several folate receptors. Folate receptors transport folate into cells via a receptor-mediated endocytosis, which then uses the folate in the synthesis of DNA and RNA.

FRα is an exciting target, as it is expressed in over 80% of ovarian tumors, and its distribution in normal cells is limited. The luminal cells it is expressed in (eg, choroid plexus, kidney, lung, and placenta) are generally inaccessible to circulation, except for the tubules of the kidney, limiting the off-target effect of IV-administered drugs. As FRα-targeted agents are generally bound to macromolecules that are excluded from glomerular filtration, renal toxicities are expected to be limited, and initial safety data support that.

Initial research targeting FRα looked at small molecule–folate conjugates (vintafolide) and FRα-directed monoclonal antibodies, such as farletuzumab (MORAb-003). Although they had promising phase 2 trials, both approaches failed in phase 3 trials. However, antibody-drug conjugates (ADCs) have shown more promise. Currently, mirvetuximab soravtansine (IMGN853), an ADC, is on fast-track approval with the FDA for ovarian cancers after a recent readout from the phase 3 SORAYA trial (NCT04296890).

Mirvetuximab soravtansine works by the antibody attaching to FRα. Via endocytosis, the molecule enters the cell and the antibody is cleaved from its ADC maytansinoid DM4 (DM4), which exerts potent antimitotic activity via the inhibition of tubulin, resulting in cell death. One advantage of DM4 is that its active metabolites may also diffuse into neighboring cells and induce further cell death, which is called bystander killing, so cells that do not have the FRα receptor are also vulnerable.

The SORAYA trial met its primary end point of improved ORR at 32.4% in comparison with the 12% standard of single-agent nonplatinum chemotherapy. The duration of response was 5.9 months, which is an improvement vs the expected 3 to 4 months with chemotherapy. Adverse events (AEs) were similar to those in previous studies of mirvetuximab soravtansine, with no new safety concerns reported.

Treatment-related AEs (TRAEs) led to dose reductions in 19% of patients, dose delays in 32% of patients, and discontinuations in 7% of patients. The most common TRAEs included blurred vision (41% all grades; 6% grade 3+), keratopathy (35% all grades; 9% grade 3+), and nausea (29% all grades; 0% grade 3+). If approved, mirvetuximab soravtansine would be the first available agent targeting the FRα receptors.

Patient selection is critical for the FRα-targeted agents. The FORWARD I trial (NCT02631876) of mirvetuximab soravtansine, which included medium (50%-74% of cells) and high expression (≥75%) of FRα on targeted tumors, failed its primary end point of PFS improvement vs chemotherapy, but, the high-expression subgroup did show improvement. Based on this improvement, the SORAYA trial recruited only high-expression patients, and it is likely that this will be reflected in its indication if the drug is approved.

Because FRα is expressed on other solid tumors, these results could be applicable to other disease states. Farletuzumab, which failed as a monotherapy, has been conjugated with eribulin, and this ADC (MORAb-202; farletuzumab-ecteribulin) reported phase 1 data that include not only ovarian cancer, but also other solid tumors with FRα overexpression, such as triple-negative breast cancer and non–small cell lung cancer. The phase 2 trial is ongoing.
Brown Bag Consult®: Chronic Lymphocytic Leukemia
A patient with CLL relies on his pharmacy team for support.

BY JILL DRURY, PHARMD, BCOP

Patients who receive a diagnosis of chronic lymphocytic leukemia (CLL) should not be overlooked in any pharmacy setting. Many of these patients are in dire need of support, encouragement, and care coordination. They will endure a grueling process of coping with diagnosis, treatment, and, in cases of recovery, the fear of recurrence. All these stages will impact the patient emotionally and physically.

As the most accessible member of the health care team, the pharmacist can provide the information and support patients with cancer need to get through what might be the most challenging period of their lives. Pharmacists’ willingness to help at this crucial time demonstrates a caring and concern that patients will likely never forget.

The Patient
Originally, EM came into the pharmacy complaining of extreme fatigue. At the time, the pharmacist on duty told EM to follow-up with his primary care provider for an evaluation because the fatigue was out of the ordinary and not due to any lifestyle change.

Case
EM is a 68-year-old man who has CLL and frequents your health care system. CLL has been a burden in addition to his multiple comorbidities. EM continuously struggles to understand CLL treatment options and is concerned about what this cancer means for his overall quality of life.

None of EM’s family members have had cancer or blood disorders, so receiving a CLL diagnosis threw an unexpected curve ball into his life. A retired salesman, EM has a limited support system because he is divorced and his adult children live out of state. To manage this disease, EM relies on his pharmacy team and other members of the hematology clinic.
During their conversation, the pharmacist also noticed EM seemed to have lost a lot of weight, yet his abdomen looked enlarged compared with the rest of his body. Upon evaluation with his primary care provider, EM had laboratory work done, with the results showing EM had an enlarged spleen; this led to him receiving a diagnosis of active CLL.

During the evaluation, EM admitted to having awful night sweats and fevers. He was tested repeatedly for COVID-19, thinking he may have been infected. When his tests came back negative, he resorted to trying to ignore his symptoms before ultimately receiving the CLL diagnosis.

**Brown Bag Consult®**

Today, EM returns for follow-up after completing chemotherapy, and he is asking you to refill some of his monthly medications. As the 2 of you talk, he complains of worsening back pain to the point where he cannot stand up straight or walk well. He also mentions he feels short of breath and is still very fatigued.

When looking at the laboratory values on the paperwork EM has handed you, you see he has normal liver and renal function but his platelets and white blood cell counts are off. You explain to him that the immune system of individuals with CLL may not work efficiently because it may be making abnormal antibodies against its own red blood cells and/or platelets. These antibodies may then destroy the red blood cells, causing anemia or low numbers of platelets.

Antibodies that attack the body’s own red blood cells are called autoantibodies, and individuals with CLL can develop these autoantibodies at any time. However, the development of these autoantibodies is not necessarily related to the severity of the CLL. You stress to EM not to panic over the numbers and offer to help him arrange a follow-up with his hematologist to get further clarity over their meaning.

EM explains to you that he often wonders why he is not feeling better, is stressed over needing more tests and treatments, and doesn’t understand the different type of leukemias. He also explains that he often feels anxious about his future and has a hard time going to sleep and getting up in the morning.

After listening to EM, you encourage him to share these thoughts and feelings with his immediate care team so they can better support his needs holistically.

Based on what he has explained, it seems possible EM is clinically depressed.

In this situation, as the pharmacist, you are not a primary decision maker on the care team. However, you can see many nonpharmacological ways that you can help EM, and you can make recommendations to his health care providers based on your observations.

It is also important to remember you are EM’s most accessible resource. For this reason, you set aside some time to talk to EM and explain the different types of CLL treatments available. After finding out that he’s not up-to-date on his immunizations, you encourage him to get those updated and you review with him the benefits of stopping smoking. EM tells you he appreciates your patience and how you talk things through with him in ways he can understand.

You also review EM’s “as needed” medications and realize he is overusing his prescribed anxiety, sleep, and pain medications. Upon noticing this, you offer to follow-up with EM’s care team, address the issues, and get him on a plan that can help have more lasting effects.

EM also explains he is not drinking water, which means he has been frequently dehydrated. In addition, he is not eating a balanced diet or getting any exercise.

After hearing this, you observe that, despite his weight loss due to the CLL, his most recent lipid panel is out of range, so you take his blood pressure and notice it is significantly elevated. EM does have documented dyslipidemia and hypertension, and he admits he no longer takes the medications for the chronic conditions. You express concern for his cardiac health and suggest he follow-up with his care team and get back on his prescribed medications after evaluation.

Regarding exercise, you talk about a support group that EM’s son recommended he seek out in his community because the group has a walking club. This type of regular activity may be beneficial, so you tell EM that once his pain is more managed, it may be easier for him to move around and perform his daily activities. This ease in movement could also help with his fatigue and mood.

Lastly, you note how important EM’s bone health and deep vein thrombosis prevention are and encourage him to join the walking club. These small efforts may seem minimal, but you mention that they all help aid his fight against the disease and support improvements in his quality of life.
FOLLICULAR AND MARGINAL ZONE LYMPHOMAS (MZLs) are incurable malignancies requiring multiple lines of treatment over time. The treatment landscape for relapsed/refractory MZL and follicular lymphoma (FL) is shifting from intravenous chemotherapy and monoclonal antibodies to oral oncolytic therapy or CD19-directed chimeric antigen receptor (CAR) T-cell therapy. A trio of experts updated pharmacists on “Emerging Treatments for Indolent Lymphomas: The Role of the Oncology Pharmacist in Treatment and Toxicity Management” at the 2022 Hematology/Oncology Pharmacy Association Annual Meeting.

Jordan Miller, PharmD, BCPS, BCOP, CPP, reviewed first-line therapy of FL and MZL, which consists of chemotherapy combined with an anti-CD20 monoclonal antibody. He explained that management of relapsed or refractory MZL and FL has largely shifted to oral oncolytic therapies which have diverse mechanisms of action. He presented data supporting FDA approval and inclusion in the National Comprehensive Cancer Network guidelines for oral oncolytic and CAR T-cell therapies. The immunomodulator lenalidomide in combination with rituximab is an option in both first-line and relapsed/refractory FL and MZL. The PI3K inhibitors idelalisib, copanlisib, duvelisib, and umbralisib are preferred options in third-line and subsequent therapy in FL and MZL. The Bruton tyrosine kinase (BTK) inhibitors ibrutinib and zanubrutinib are preferred treatment options in second-line therapy of MZL, Tazemetostat, an EZH2 inhibitor, is appropriate for third-line therapy of FL. Axicabtagene ciloleucel is a CD19-directed CAR T-cell therapy recently approved for third-line and subsequent therapy of FL. Dr Miller touched on bispecific antibodies under investigation in FL including mosunetuzumab, epcoritamab, and glofitamab and PI3K inhibitors under investigation in MZL, such as parsaclibisib and zandelisib.

Dr Miller highlighted that the unique mechanisms of action for all of the novel therapies in FL and MZL correspond to unique adverse effect profiles. He noted class effects associated with BTK inhibitors include bleeding, atrial fibrillation, and pneumonia. Diarrhea, hyperglycemia, neutropenia, hepatotoxicity, and infection are observed in patients receiving PI3K inhibitors. Tazemetostat is associated with myelosuppression. Significant grade 3 or 4 adverse effects, including myelosuppression, infection, cytokine release syndrome, and neurotoxicity, are observed in patients receiving CAR T-cell therapies. Dr Miller explained that the transition from intravenous to oral therapy in lymphoma poses new challenges including facilitating medication adherence, mitigating drug–drug interactions, and monitoring and managing adverse effects. He reminded pharmacists that with the exception of lenalidomide, oral oncolytic therapies used to manage FL and MZL are subject to drug–drug interactions mediated by the CYP450 pathway.

Karen Fancher, PharmD, BCOP; Kelly Valla, PharmD, BCOP; and Dr Miller then applied the data to personalize treatment for patients with FL and MZL in a case-based panel discussion. They provided strategies to mitigate adverse effects and optimize care for patients receiving treatment with oral oncolytics, CD19-directed CAR T-cell therapy, and bispecific antibodies.

“Understanding the pharmacology and toxicity profile of the various treatment options guides appropriate treatment selection and management of treatment-related adverse effects when they arise.”

—Jordan Miller, PharmD, BCPS, BCOP, CPP

Multiple Options Mean More Time for Patients With Indolent Lymphoma

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/INDOLENT-LYMPHOMAS

IN A VIRTUAL PANEL DISCUSSION at the 2022 Hematology/Oncology Pharmacy Association Annual Meeting, expert oncology pharmacists engaged the audience in “Optimizing Care for Patients With Endometrial Cancer: A Focus on Pharmacist Interventions and Mitigation of Health Equity Issues.”

Sarah Hayward, PharmD, BCOP, began by defining biomarkers used to guide therapy in endometrial cancer, including microsatellite instability-high (MSI-H)/mismatch repair deficient (dMMR); tumor mutational burden-high (TMB-H); and human epidermal growth factor receptor 2 (HER2). Dr Hayward explained that carboplatin and paclitaxel remain preferred initial therapy in patients with recurrent or metastatic disease, and trastuzumab may be added for patients with stage III/IV HER2-positive serous carcinoma for initial therapy or recurrent disease. She highlighted pembrolizumab as the preferred biomarker-directed therapy in the second-line setting for TMB-H or MSI-H/dMMR tumors. Dr Hayward reviewed other recommended therapies for second-line therapy of dMMR/MSI-H tumors, including avelumab, dostarlimab, and nivolumab. Lastly, she noted lenvatinib plus pembrolizumab is a preferred regimen for second-line therapy in patients with non-MSI-H/non-dMMR tumors.

Following a review of the efficacy of biomarker-directed therapies, Dr Hayward shifted the focus to management of adverse effects. She explained that immune checkpoint inhibitors (ICIs) have a very different adverse effect profile compared with cytotoxic chemotherapy, termed immune-related adverse events (irAEs). She highlighted that irAEs can affect any organ or tissue in the body, but pharmacists should be able to recognize common irAEs, including colitis, hepatitis, nephritis, pneumonitis, endocrinopathies, and skin rash/pruritus. Dr Hayward emphasized that often irAEs can be managed if treated early, and stopping ICIs is not always necessary. She explained that grade 1 irAEs are usually managed symptomatically without treatment interruption. Whereas grade 3-4 irAEs also receive symptomatic treatment, she contrasted that management generally involves treatment delay or discontinuation, initiation of corticosteroids, hospitalization, and specialist referral. She noted that management of grade 2 irAEs falls somewhere in between; in addition to symptom management, topical and/or systemic corticosteroids and holding treatment may be necessary.

Dr Hayward illustrated some key areas of pharmacist involvement in supporting patients with irAEs, including dose selection and tapering of corticosteroids. She emphasized patients should receive appropriate supportive therapies including high-dose steroids, a proton pump inhibitor, Pneumocystis jirovecii pneumonia prophylaxis, fungal infection prophylaxis in patients receiving high-dose prednisone for more than 6 weeks, and calcium and vitamin D supplementation to prevent osteoporosis.

Lastly, she reviewed health equity concerns in patients with endometrial cancer. She highlighted ways for pharmacists to support patients, such as patient education, medication adherence strategies, facilitating medication access, and ensuring care is provided with cultural awareness, especially because pharmacists are often easier to contact than other health care professionals.

Rachel Justus, PharmD, BCPS, BCOP, and Jennifer MacDonald, PharmD, BCOP, joined Dr Hayward in a case discussion to illustrate similarities and differences in various biomarker-directed therapies for endometrial cancer along with management of adverse effects.

“...providing good patient and caregiver education on irAEs to facilitate prompt recognition and therapy to limit progression.”

—Sarah Hayward, PharmD, BCOP
Despite significant improvement in overall survival in the past 2 decades, multiple myeloma (MM) remains incurable. Patients who become refractory to proteasome inhibitors (PIs), immunomodulatory agents (IMiDs), and anti-CD38 monoclonal antibodies have poor outcomes. Targeting B-cell maturation antigen (BCMA) is a novel strategy with proven efficacy for patients with relapsed/refractory (RR) MM. In a panel discussion at the 2022 Hematology/Oncology Pharmacy Association Annual Meeting, experts helped pharmacists understand how to manage BCMA-targeted therapies in a presentation titled “Optimizing Care in Relapsed/Refractory Multiple Myeloma Through Pharmacist Interventions: A Focus on BCMA-Directed Therapies.”

Joseph A. Kalis, PharmD, BCOP, began with a primer on the role of BCMA in development of MM. There are currently 3 types of FDA-approved or in-development therapies targeting BCMA: antibody-drug conjugate (ADC) (eg, belantamab mafodotin-blmf); chimeric antigen receptor (CAR) T cell (eg, idecabtagene vicleucel [ide-cel], ciltacabtagene autoleucel [cilta-cel]); and bispecific antibodies (eg, teclistamab, elranatamab). BCMA-targeted therapies currently approved by the FDA include belantamab mafodotin-blmf, cilta-cel, and ide-cel. These therapies are approved for patients who have received at least 4 prior therapies including PI, IMiD, and an anti-CD38 monoclonal antibody. In heavily pretreated patients with RRMM, both agents reported a median overall survival of more than 1 year. Belantamab mafodotin-blmf is an off-the-shelf infusion administered every 3 weeks until progression. In contrast, CAR T-cell therapies are developed from each patient’s own T cells and administered as a single infusion. Bispecific antibodies under investigation are formulated for subcutaneous administration or infusion but require repeated dosing.

While all of these agents target BCMA, the adverse effect profiles have distinct differences. Belantamab mafodotin-blmf is associated with development of ocular toxicities thought to be related to the cytotoxin, monomethyl auristatin F (MMAF). Ocular toxicities reported with belantamab mafodotin-blmf include microcyst-like epithelial changes, blurred vision, dry eye, and changes in visual acuity. Ocular toxicity is typically managed with regular eye exams, corticosteroid eye drops, and preservative-free lubricants.

CAR T-cell therapies and bispecific antibodies cause cytokine release syndrome (CRS) and immune effector cell-associated encephalopathy (ICANS). CAR T-cell therapies must be administered in specialized centers equipped to manage these unique toxicities. Management of CRS includes best supportive care with intravenous fluids, vasopressors, and ventilatory support in addition to tocilizumab and/or dexamethasone. The mainstay of therapy for ICANS is corticosteroids along with best supportive care; tocilizumab is reserved for patients with concurrent CRS. Preliminary data on bispecific antibodies suggest a lower risk of CRS and neurologic toxicity. It is unclear if it will be feasible to administer these agents in a community setting if BCMA-targeted bispecific antibodies are able to attain FDA approval. All 3 types of BCMA-directed therapies cause myelosuppression.

During the latter half of the presentation, Dr Kalis engaged in a case-based discussion with KIrollos Hanna, PharmD, BCPS, BCOP, and Rebecca Miller, PharmD, BCOP.
HER2-Directed Therapies: Not Just for Breast Cancer

**Human Epidermal Growth-Factor Receptor 2** (HER2)-directed therapies are approved for HER2+ breast cancer and gastric/gastric esophageal junction (GEJ) adenocarcinoma and are under investigation in colon and lung HER2-positive cancers. Multiple therapy options exist for patients with HER2 overexpression; thus patient, disease, and therapy characteristics drive optimal therapy selection. At the 2022 Hematology/Oncology Pharmacy Association Annual Meeting, an expert panel of oncology pharmacists provided “Clinical Updates in ERBB2 and HER2-Targeted Therapies: The Impact on Oncology Pharmacy Practice.”

In the first portion of the presentation, Allison Schepers, PharmD, provided an update on the role of the HER2 biomarker in a variety of malignancies. She explained that HER2 gene amplification and receptor overexpression lead to tumor growth and metastasis in a variety of solid tumors. Dr Schepers underscored assessment of HER2 overexpression is indicated in all patients with breast cancer, locally advanced, recurrent, or metastatic gastric/GEJ adenocarcinoma, and metastatic colon adenocarcinoma—primary or recurrent. Overexpression of HER2 can be determined by immunohistochemistry or in situ hybridization, explained Dr Schepers. Several classes of medication target HER2: monoclonal antibodies (trastuzumab, pertuzumab, margetuximab); tyrosine kinase inhibitors (lapatinib, neratinib, tucatinib); and antibody-drug conjugates (trastuzumab emtansine, trastuzumab deruxtecan). Zanidatamab, zenocutuzumab, poziotinib, and pyrotinib are investigational HER2-directed therapies.

Trastuzumab combined with chemotherapy, with or without pertuzumab, is indicated in patients with localized breast cancer and the combination is appropriate for first-line treatment of metastatic disease. Adjuvant trastuzumab deruxtecan improves invasive disease-free survival in patients with localized breast cancer not achieving a pathologic complete response; neratinib may be considered for maintenance therapy. Trastuzumab emtansine and trastuzumab deruxtecan are recommended for second-line treatment of metastatic HER2+ breast cancer. In combination with chemotherapy, margetuximab, trastuzumab, tucatinib, neratinib, and lapatinib are all appropriate for metastatic HER2+ breast cancer in the third-line setting and beyond; trastuzumab plus lapatinib is a chemotherapy-free option. Trastuzumab is combined with platinum doublet chemotherapy in first-line treatment of HER2+ metastatic gastric/GEJ adenocarcinoma and trastuzumab deruxtecan is an option for second-line or subsequent therapy. Trastuzumab emtansine or trastuzumab deruxtecan have demonstrated efficacy in patients with metastatic HER2+ non–small cell lung cancer. Trastuzumab deruxtecan, and trastuzumab combined with lapatinib or pertuzumab, are recommended as front-line or subsequent treatment in HER2+ and RAS/BRAF wildtype metastatic colorectal cancer for patients who are not candidates for intensive therapy.

HER2-directed therapies have improved outcomes for patients with malignancies that overexpress HER2, but they also carry unique toxicities. Toxicities of HER2-directed therapies include cardiotoxicity, neutropenia, diarrhea, nausea/vomiting, and interstitial lung disease. The pharmacology, route of administration, dosing, and schedule influence the toxicity profile of individual agents. In the latter portion of the presentation, Allison R. Butts, PharmD; Amber Draper, PharmD; and Dr Schepers reviewed several clinical scenarios to help pharmacists ascertain the nuances of HER2-directed therapy. The cases illustrated several decision points including selecting treatment, sequencing, adverse effect recognition, and management.

“As HER2-directed treatments become more complex, pharmacists play a key role in patient selection, therapy determination, monitoring, and toxicity management.”

—Allison Schepers, PharmD

**TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT** www.pharmacytimes.org/her2-therapy

**THE ACTIVITY IS AVAILABLE THROUGH APRIL 15, 2023.**
Biomarkers Drive Therapy in Non–Small Cell Lung Cancer

Lung cancer remains the leading cause of cancer-related deaths in both men and women in the United States. The rate of new cases and deaths has declined in the past 3 years driven by screening, minimally invasive surgical techniques, novel treatment strategies, and declines in smoking rates. A panel of experts at the 2022 Hematology/Oncology Pharmacy Association Annual Meeting provided “Updates for the Oncology Pharmacist in the Management of Non–Small Cell Lung Cancer With KRAS, MET, and RET Mutations.”

Jason Bergsbaken, PharmD, MBA, BCOP, engaged the audience in the didactic portion of the presentation starting with the basics on predictive and prognostic biomarkers in non–small cell lung cancer (NSCLC), noting that molecular testing is now standard of care for all advanced patients. He highlighted that at a minimum, patients with metastatic NSCLC (adenocarcinoma, large cell, or not otherwise specified) should have screening for EGFR, ALK, KRAS, ROS1, BRAF, METex14, RET, and NTRK gene mutations. He provided practical reasons the National Comprehensive Cancer Network strongly advises broader next-generation sequencing in patients with advanced disease.

After touching on EGFR and ALK mutations, Dr Bergsbaken drilled down into the evidence linking RET, METex14, and KRAS G12C genetic mutations with targeted therapies in advanced NSCLC. He noted pralsetinib and selpercatinib are appropriate for first-line therapy in patients with RET mutations. Capmatinib and tepotinib are FDA approved as first-line therapy in patients with METex14 mutations. Lastly, he highlighted the FDA approval of sotorasib for patients with at least one prior therapy for advanced NSCLC in those with KRAS G12C mutations. Dr Bergsbaken reviewed adverse effects associated with targeted agents, including hepatotoxicity and interstitial lung disease. He noted a commonality among the agents is the potential for drug–drug interactions mediated by CYP3A4. He differentiated some of the agents are subject to p-glycoprotein and/or acid suppressing medications, thus a careful medication history and drug–interaction review is essential.

Following a deep dive into the clinical trial data, Dr Bergsbaken highlighted the pharmacist’s role in management of patients with advanced NSCLC. He emphasized pharmacists should provide comprehensive management of oral oncolytics using the key points below:

<table>
<thead>
<tr>
<th>Molecular profile review</th>
<th>Patient education</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review molecular testing results</td>
<td>Medication dosing and administration</td>
</tr>
<tr>
<td>Participate in molecular tumor board</td>
<td>Missed dose instructions</td>
</tr>
<tr>
<td>Recommend appropriate target-based therapy to optimize outcomes</td>
<td>Drug–drug and drug–food interactions</td>
</tr>
<tr>
<td>Potential adverse effects and management</td>
<td>Adherence strategies</td>
</tr>
<tr>
<td>Facilitate medication access (prior authorization, dispensing pharmacy, financial support)</td>
<td>Medication safe handling, storage, and disposal</td>
</tr>
<tr>
<td>Patient monitoring and follow-up plan</td>
<td></td>
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</tbody>
</table>

Eve Segal, PharmD, BCOP; Josiah D. Land, PharmD, BCOP; and Dr Bergsbaken discussed patient cases to demonstrate the role of the pharmacist along the continuum from interpreting molecular testing results to helping patients manage their medications and optimize outcomes from oral oncolytics.

“Of all the members on the health care team, pharmacists are best positioned to help patients optimize their outcomes from targeted NSCLC therapies given we touch multiple areas along the continuum of care.”

—Jason Bergsbaken, PharmD, MBA, BCOP

To view the on-demand CE session, please visit www.pharmacytimes.org/nsclc-therapy. The activity is available through April 15, 2023.
IN THE PAST DECADE, management of chronic lymphocytic leukemia (CLL) has shifted from chemotherapy combined with anti-CD20 monoclonal antibodies to targeted oral therapies with or without anti-CD20 monoclonal antibodies. These new options require prolonged therapy and management of adverse effects to enable patients to remain on therapy. Three expert pharmacists engaged the audience in a panel discussion, “Exploring Combination Strategies for the Treatment of Chronic Lymphocytic Leukemia: Oncology Pharmacy Pearls for Optimizing Patient Care”, at the 2022 Hematology/Oncology Pharmacy Association Annual Meeting.

Emily Dotson, PharmD, BCOP, began by illustrating the preferred regimens in the National Comprehensive Cancer Network (NCCN) guidelines for front-line and relapsed/refractory treatment of CLL, including Bruton tyrosine kinase (BTK) inhibitors, BCL2 inhibitors, and anti-CD20 monoclonal antibodies in patients with and without del(17p)/TP53 mutations. Preferred regimens include acalabrutinib with or without obinutuzumab; venetoclax plus obinutuzumab; ibrutinib; and zanubrutinib. She explained the shift in practice from traditional chemotherapy is based on improvement in progression-free survival (PFS) and response rates. Dr Dotson then reviewed ongoing clinical trials evaluating doublet and triplet therapies with different BTK inhibitors. She explained that resistance to BTK inhibitors occurs with long-term use in patients with CLL and the combination of venetoclax with a BTK inhibitor may prevent this resistance. She also highlighted trials using achievement of undetectable minimal residual disease as a guide to predict durable PFS and the ability to discontinue therapy after a fixed duration without a negative impact on outcomes.

After reviewing efficacy of therapies for CLL, Dr Dotson shifted the focus to challenges encountered in the management of CLL. She highlighted myelosuppression, diarrhea, headache, arthralgia, edema, atrial fibrillation, and bleeding/bruising as adverse effects that vary among BTK inhibitors. She emphasized the role of pharmacists in managing adverse effects of CLL therapies, and highlighted that 15% to 36% of patients in clinical trials discontinue treatment with BTK inhibitors due to treatment-related adverse effects. Dr Dotson underscored medication adherence can be especially challenging for patients with CLL due to duration of therapy until disease progression and potential for financial toxicity associated with therapy. Dr Dotson also highlighted drug–drug interactions to consider with oral agents to manage CLL involving the CYP3A4 enzyme, P-glycoprotein, and acid-reducing pharmacotherapies.

Peter Campbell, PharmD, BCOP, and Arpita Gandhi, PharmD, BCOP, joined Dr Dotson in applying the science to optimize patient care for patients with CLL in a case-based panel discussion. The panel helped to differentiate BTK inhibitors based on key adverse effects, including atrial fibrillation, hypertension, and hemorrhage. In addition, the trio provided insight into common scenarios in CLL, including how to manage patients receiving anticoagulation and those with drug–drug interactions withazole antifungal therapy.

“Facilitating medication adherence is a crucial service provided by pharmacists for patients with CLL because data show adherence rates above 80% with BTK inhibitors are associated with improved PFS.”

—Emily Dotson, PharmD, BCOP

HE TREATMENT LANDSCAPE OF RELAPSED/REFRACTORY (R/R) diffuse large B-cell lymphoma (DLBCL) has rapidly evolved in the past 6 years with few patients now receiving chemotherapy. A multidisciplinary panel discussed recent changes in DLBCL in a satellite symposium at the 2022 Hematology/Oncology Pharmacy Association Annual Meeting in a presentation titled “Differentiating Novel Treatment Modalities in Relapsed/Refractory Diffuse Large B-Cell Lymphoma: A Focus on Antibody-Drug Conjugates and CAR T-Cell Therapies.”

Kelly Valla, PharmD, BCOP, kicked off the session with a review of the pharmacology of antibody-drug conjugates (ADCs). She described the phase 2, randomized trial of polatuzumab vedotin-piiq in combination with bendamustine and rituximab that led to approval of polatuzumab vedotin-piiq in R/R DLBCL. Amy Goodrich, CRNP, joined in to highlight the data leading to FDA approval of loncastuximab tesirine-lpyl in patients with at least 2 prior therapies for DLBCL. Nilanjan Ghosh, MD, PhD, discussed the data supporting tafasitamab-cxix in combination with lenalidomide for patients with at least one prior therapy. The trio then discussed treatment selection and sequencing of these therapies in R/R DLBCL, noting controversy around the potential for tafasitamab-cxix or loncastuximab tesirine-lpyl or any other CD19-directed therapy to impart a negative effect on the efficacy of subsequent anti-CD19 chimeric antigen receptor (CAR) T-cell therapy.

Dr Ghosh then turned to approved CD19-directed CAR T cells for DLBCL: axicabtagene ciloleucel, which is approved for patients with R/R large B-cell lymphoma (LBCL) after one line of therapy; as well as tisagenlecleucel (tisa-cel) and lisocabtagene maraleucel (liso-cel), which are approved after 2 prior therapies. The panelists described the differences in the 3 products and the clinical results in the third-line setting. Dr Ghosh reviewed initial results for recent clinical trials randomizing patients either with early relapses within 12 months, or those with refractory DLBCL. Patients either received CAR T-cell therapy or standard of care with platinum-based salvage chemotherapy, followed by autologous stem cell transplant for those patients achieving a response. He noted that the trials for axi-cel and liso-cel found an improvement in event-free survival.

Considering these data, the faculty shared thoughts on therapy selection, given the lack of comparative trials among the different options. Amy Goodrich, CRNP, underscored that the adverse effect (AE) profile may drive treatment decisions. She noted all options reviewed cause myelosuppression to varying degrees; however, the different products cause unique AEs. Loncastuximab tesirine-lpyl may cause edema/effusions, polatuzumab vedotin-piiq may cause peripheral neuropathy, and tafasitamab-cxix plus lenalidomide requires a Risk Evaluation and Mitigation Strategy (REMS) program due to the risk for teratogenicity with lenalidomide. Dr Valla noted the CAR T-cell therapies are also associated with several life-threatening AEs, including cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome, and all have a REMS program as well. The panelists wrapped up by reviewing cost, cost-effectiveness, indirect costs, and logistics associated with management of patients with R/R DLBCL.

“All the emerging data really drive home how rapidly this treatment paradigm could expand in the coming years.”

—Kelly Valla, PharmD, BCOP

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/DLBCL-TREATMENT

LIKE MANY OTHER MALIGNANCIES, improvement in the understanding of disease biology has led to novel therapeutic strategies and improvement in outcomes for patients with Waldenström macroglobulinemia (WM). A virtual panel discussion led by Karen M. Fancher, PharmD, BCOP, at the 2022 Hematology/Oncology Pharmacy Association Annual Meeting updated pharmacists on the current and emerging treatment paradigm in a presentation titled “Clinical Updates in the Treatment and Care of Patients With Waldenström Macroglobulinemia.”

In an A to Z narrative of WM, Dr Fancher explained that WM is denoted by lymphoplasmacytic cells that produce monoclonal immunoglobulin M (IgM). Patients may present with symptoms of lymphoma in addition to cryoglobulinemia, hyperviscosity, cold agglutinin, peripheral neuropathy, and paraprotein deposition in organs secondary to accumulation of IgM. Dr Fancher pointed out the presence and severity of symptoms drive the choice in therapy, whereas the Revised International Prognostic Scoring System for Waldenström Macroglobulinemia (IPSSWM) speaks more to prognosis of patients. Dr Fancher highlighted that mutations in MYD88 are present in more than 90% of patients and patients with this mutation are sensitive to inhibition of Bruton tyrosine kinase (BTK). In contrast, patients with CXCR4 mutations have lower and slower responses to BTK inhibitors and testing is only recommended for patients with neurologic symptoms.

Dr Fancher explained that asymptomatic patients with WM can be observed rather than starting therapy, and those with mild symptoms receive rituximab monotherapy. Patients with hyperviscosity and significant symptoms initiate plasmapheresis before proceeding with first-line treatment. First-line options endorsed by the National Comprehensive Cancer Network (NCCN) Guidelines as category 1 recommendations include ibrutinib and zanubrutinib with or without rituximab.

Dr Fancher emphasized that rituximab administration may lead to a transient rise in IgM and this may cause symptomatic hyperviscosity, worsening of IgM-related neuropathy, or other IgM-related complications. Dr Fancher noted significant differences in efficacy were not observed in a randomized study comparing zanubrutinib to ibrutinib for first-line therapy of WM; however, the agents can be differentiated based on adverse effects. Chemotherapy may also be used for first-line treatment in patients with significant symptoms. No trials have compared BTK inhibitors to chemotherapy plus rituximab in WM. A key difference noted by Dr Fancher is that chemotherapy is prescribed for a fixed number of cycles, whereas BTK inhibitors are administered until disease progression. BTK inhibitors are preferred for patients with central nervous system disease. The same regimens recommended for first-line treatment of WM are recommended for relapsed or refractory WM. Acalabrutinib and venetoclax are also included in the NCCN Guidelines as other recommended regimens for relapsed or refractory WM. Dr Fancher wrapped up the didactic portion of the presentation by reviewing management of adverse effects, highlighting those that may overlap with symptoms of WM.

During the latter half of the presentation, Dr Fancher discussed clinical pearls of management of WM with other experts Jordan Miller, PharmD, BCPS, BCOP, CPP, and Joslyn Rudoni, PharmD, BCOP.

“Choice of treatment for WM should consider the patient’s clinical presentation, comorbidities, genomic profile, and preferences.”

—Karen M. Fancher, PharmD, BCOP

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/WM
MULTI-AGENT REGIMENS to manage cancer are evolving. Historically, combination chemotherapy referred to multiple cytotoxic chemotherapies to manage a type of cancer. In 2022, many combination approaches across different diseases consist of targeted tyrosine kinase inhibitors (TKIs) or intravenous monoclonal antibodies combined with immune checkpoint inhibitors (ICIs). The growth of this approach across multiple different malignancies is challenging for pharmacists to manage because of the potential for overlapping toxicities.

Jessica Davis, PharmD, BCOP, CPP, helped pharmacists in a virtual symposium, affiliated with the 2022 Hematology/Oncology Pharmacy Association Annual Meeting, gain confidence in managing patients receiving combination therapy in a presentation titled, “The Growing Use of Immune Checkpoint Inhibitor-Targeted Therapy Combinations and Challenges in Managing Associated Toxicities.”

Dr Davis began explaining how combination therapy with ICIs with targeted therapies may overcome therapeutic or innate resistance and lead to improved outcomes. Vascular endothelial growth factor, multikinase, BRAF, and MEK inhibitors are FDA approved in combination with ICIs in a variety of tumors, including renal cell and hepatocellular carcinomas, melanoma, lung, cervical, and endometrial cancers. Dr Davis highlighted research is ongoing to determine the efficacy of PARP, signal transducer and activator of transcription 3, and CXCR4 inhibitors in combination with ICIs.

Dr Davis explained that immune-related adverse events (irAEs) occur when patients receiving ICIs develop a heightened autoimmunity against healthy tissues and organs. She noted that irAEs can occur at any time throughout treatment or after discontinuation; however, the median onset is 2 to 16 weeks after treatment initiation. Using the body to illustrate, Dr Davis emphasized the diverse manifestations of irAEs. Encephalitis, thyroiditis, pneumonitis, hepatitis, nephritis, myositis, hypophysitis, myocarditis, colitis, dermatitis, and arthritis are all possible irAEs associated with ICI therapy. She explained that symptoms of irAE overlap with AEs associated with TKIs, including diarrhea, hepatitis, skin rash, arthralgias, and fatigue. Dr Davis underscored differing patient populations and doses of TKIs also affect the incidence of AEs, adding another layer of complexity managing patients receiving combination therapies.

Dr Davis provided practical tips for managing AEs so patients can remain on therapy. Her initial approach is to determine which therapy is the most likely cause of the symptoms based on time to onset, frequency of the AE with a given therapy, and co-presenting symptoms. Next, she determines if a dose modification, interruption, or change in therapy is the most appropriate course of action. Dr Davis noted grades 2 to 4 irAEs are managed by holding the ICI and initiating corticosteroids, and a secondary immunosuppressive agent if needed; dose modifications are not used to manage irAEs. In contrast, TKIs are typically held initially and then resumed at a lower dose; supportive care is used to manage symptoms without immunosuppressive therapy. Dr Davis reviewed specific management of different irAEs before using cases to illustrate how to manage toxicities of patients receiving combinations of ICIs and TKIs.

“Pharmacists play a key role in effectively managing AEs of combination therapies so patients can successfully remain on therapy.”

—Jessica Davis, PharmD, BCOP, CPP

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/ICI-THERAPY
New Options for Older Patients With Acute Myeloid Leukemia

“The treatment of elderly patients with AML has a bright outlook with expanding treatment options; however, care remains complex and requires a multimodal approach to ensure safety, improve outcomes, and prolong survival.”

—Charlene Kabel, PharmD, BCOP

S EVEN MEDICATIONS TO manage acute myeloid leukemia (AML) have been approved by the FDA in the past 6 years. Many of these medications have been evaluated specifically in elderly populations to improve both survival and tolerability. Three expert pharmacists, Charlene Kabel, PharmD, BCOP; Anthony Perissinotti, PharmD, BCOP; and Alison Duffy, PharmD, BCOP; provided a panel discussion on AML in a virtual symposium affiliated with the 2022 Hematology/Oncology Pharmacy Association Annual Meeting, titled “Updates in Induction and Maintenance Regimens for Older Patients With AML.”

Dr Kabel began by highlighting genetic mutations associated with AML that drive pharmacotherapy selection. Recent oral FDA approvals in AML include midostaurin and gilteritinib for patients with FLT3 mutations, enasidenib for patients with IDH2 mutations, and ivosidenib for patients with IDH1 mutations as well as venetoclax, a B-cell lymphoma 2 inhibitor. Dr Kabel emphasized that elderly patients are often ineligible for intensive chemotherapy, so the focus is on improving survival and tolerability rather than curative therapy. She noted options for elderly patients without actionable mutations include venetoclax with azacitidine or low-dose cytarabine, and glasdegib with low-dose cytarabine. She illustrated data supporting benefit in combination with azacitidine for ivosidenib in patients with an IDH1 mutation, enasidenib in patients with an IDH2 mutation, and gilteritinib in patients with a FLT3 mutation; however, an improvement in survival has not been demonstrated. Lastly, Dr Kabel noted that maintenance therapy with a hypomethylating agent may improve overall survival and replace chemotherapy consolidation in select patients. Oral azacitidine is the only agent currently approved for this indication.

Dr Kabel linked the shift in therapy to more targeted therapies and a transient increase in white blood cell count. Unique AEs reported with glasdegib include dysgeusia and muscle spasms. While oral targeted therapies in other cancers may not cause myelosuppression and febrile neutropenia, Dr Kabel underscored this is still observed with targeted therapies for AML. The addition of venetoclax to azacitidine or low-dose cytarabine is associated with an increased incidence of myelosuppression, febrile neutropenia, and gastrointestinal toxicities. Dr Kabel emphasized that patients with AML receiving less intensive regimens still require intensive monitoring for myelosuppression and may need transfusions, prevention, and treatment for febrile neutropenia and infections.

After exploring the clinical trial data in older patients with AML, Dr Kabel described some of the challenges in treating older adults that are encountered by clinicians and patients. Dr Perissinotti, Dr Duffy, and Dr Kabel then engaged audience members in several patient case discussions. The panelists illustrated several nuances of the management of elderly patients with AML including the use of venetoclax and azacitidine for induction therapy and challenges in the selection of patients for and use of maintenance therapy. They shared perspectives based on their experiences and offered pearls for successful management.

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/AML
Currently, there are limited T-cell bispecific antibodies (BsAbs [blinatumomab and tebentafusp-tebn]) that are FDA approved; however, encouraging data support potential for widespread use of BsAb-based technology in cancer therapy. Sarah E. Stump, PharmD, BCPS, BCOP, brought audience members up-to-date on the pharmacology, clinical data, and management of BsAbs in a presentation titled, “T-Cell Engaging Bispecific Antibodies: Preparing Oncology Pharmacists to Optimize Patient Care” in a virtual symposium, affiliated with the 2022 Hematology/Oncology Pharmacy Association Annual Meeting.

Dr Stump began with basic pharmacology, explaining that BsAbs are genetically engineered, recombinant antibodies with 2 distinct antigen-binding sites to allow for dual specificity. She focused on BsAbs that bring together a T cell and a tumor cell. Simultaneous binding forms a cytolytic synapse between cells, then the activated T cell releases perforin and granzymes through exocytosis to induce cell lysis. Dr Stump explained that BsAbs are divided into 2 main categories: those with a fragment crystallizable (Fc) region (full-length immunoglobulin G based) or without an Fc region (single-chain variable fragment based). The Fc region increases solubility and stability, facilitates purification, and induces Fc-mediated effector functions such as antibody-dependent cellular cytotoxicity, complement-dependent cytotoxicity, and antibody-dependent cellular phagocytosis. Antibody fragments (ie, bispecific T-cell engager) are smaller molecules often with a short serum half-life, necessitating continuous infusion or more frequent dosing. Attributes that may affect pharmacology of BsAbs highlighted by Dr Stump include antigen specificity, affinity, on- and off-rates, avidity, potency, stability, half-life, and product-related impurities.

Dr Stump highlighted several BsAbs under investigation in multiple hematologic malignancies (see Table below), including one agent under review by the FDA at the time of her presentation (teclistamab).

Dr Stump explained that cytokine release syndrome (CRS) and neurotoxicity are known adverse effects (AEs) of blinatumomab and are anticipated with future BsAbs based on their mechanism of action. She indicated the hope is that rates of CRS and neurotoxicity will be manageable with BsAbs, which may allow for outpatient administration in the clinic rather than requiring hospital admission. Dr Stump noted that prompt AE recognition and aggressive management will be key to successful outcomes with BsAbs. Pharmacotherapy management for CRS and neurotoxicity may include vasopressors, corticosteroids, and tocilizumab. Administration and scheduling of BsAbs in development differ, with some products formulated for intravenous and others for subcutaneous administration. Similarly, some products have loading doses and others do not and schedules range from weekly to monthly. Dr Stump concluded by noting the time is right to start planning for BsAb administration because T-cell engaging BsAbs represent a promising therapeutic strategy within the immunotherapy landscape, owing to relatively easy production coupled with diverse targets for tumor specificity.

<table>
<thead>
<tr>
<th>Investigational agent</th>
<th>Antibody targets</th>
<th>Therapeutic area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glofitamab Epocrizamab Mosunetuzumab</td>
<td>CD20 – CD3</td>
<td>Lymphoma/chronic lymphocytic leukemia</td>
</tr>
<tr>
<td>REGN5458 Tocistamab</td>
<td>BCMA – CD3</td>
<td>Multiple myeloma</td>
</tr>
<tr>
<td>Cezostamab</td>
<td>FcRHS – CD3</td>
<td>Multiple myeloma</td>
</tr>
<tr>
<td>APVO436 MGD024</td>
<td>CD123 – CD3</td>
<td>Acute myeloid leukemia</td>
</tr>
</tbody>
</table>

“Pharmacists play a critical role in toxicity recognition and management as well as maneuvering through operational and practical challenges associated with T-cell engaging BsAbs.”

—Sarah E. Stump, PharmD, BCPS, BCOP
EGAN MAY, PHARMD, BCOP, provided updates in multiple myeloma (MM) across the spectrum in a virtual symposium, affiliated with the 2022 Hematology/Oncology Pharmacy Association Annual Meeting, in a presentation titled, “Providing Well-Rounded Care to Patients With Multiple Myeloma: Updates in Proteasome Inhibitor Use, Bone Health, and Digital Monitoring Strategies.”

Dr May began with an overview of treatment considerations for MM, explaining disease-related and treatment-related factors are weighed alongside patient preferences for therapy. She noted that MM remains incurable, thus appropriate sequencing of therapy is critical to optimize outcomes and subsequent treatment selection. Proteasome inhibitors (bortezomib, carfilzomib, and ixazomib) are key components in first-line, maintenance, and subsequent therapies in both transplant-eligible and ineligible patients. Dr May updated pharmacists on recent phase 3, randomized controlled trials including the IKEMA trial that resulted in improvement in progression-free survival (PFS) in patients with relapsed/refractory MM with the addition of isatuximab to carfilzomib and dexamethasone. She also highlighted the ENDURANCE trial findings that carfilzomib, lenalidomide, and dexamethasone (KRd) did not improve PFS compared with bortezomib, lenalidomide, and dexamethasone (VRd) in patients with newly diagnosed (ND) MM; KRd was associated with increased toxicity, thus VRd remains the standard of care for induction therapy for patients with standard- and intermediate-risk NDMM. She also presented updated results for the CASSIOPEIA and GRIFFIN trials that found the addition of daratumumab to induction triplet therapy in transplant-eligible patients improves depth of response and PFS, with acceptable safety. Dr May pointed out all 3 proteasome inhibitors may cause peripheral neuropathy and myelosuppression; however, the risk for cardiopulmonary toxicities is increased with carfilzomib.

Through video clips, a patient shared his experiences of being diagnosed with MM and of receiving therapies with different proteasome inhibitors and supportive care medications.

Dr May shifted the focus to management of skeletal-related events (SREs), underscoring all patients should initiate pharmacotherapy targeting SRE at the same time as the antimyeloma regimen, even when there is no evidence of osteolytic lesions. She noted the Bone Working Group of the International Myeloma Working Group issued new recommendations in 2021, with recommendations for denosumab in lieu of bisphosphonates for patients with renal insufficiency. Denosumab was shown to be noninferior to zoledronic acid for time to SRE to zoledronic acid in patients with NDMM, with at least one documented lytic bone lesion; however, denosumab discontinuation can result in rebound osteoclastogenesis within 6 to 12 months, thus patients may need to continue denosumab administration every 6 months or receive a dose of a bisphosphonate. Dr May described other treatment strategies for SRE highlighted in the guidelines including cement augmentation for vertebral compression fractures, radiotherapy for pain relating to spinal cord compression or other pathologic features, and surgery for some patients.

In the final portion of the presentation, Dr May described recent studies evaluating digital tools to capture patient-reported outcomes. Studies engaging patients with MM via electronic reporting and smart watches have demonstrated that patients are willing to document symptoms and adherence via these tools and use improves overall satisfaction with care.

“Digital health products and solutions will increasingly be integrated into the care that pharmacists provide.”

—Megan May, PharmD, BCOP

TO VIEW THE ON-DEMAND CE SESSION, PLEASE VISIT WWW.PHARMACYTIMES.ORG/MM-CARE