

HOPA NEWS

Pharmacists Optimizing Cancer Care

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Importance of Cancer Pain Management

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Pharmacists Optimizing Cancer Care®

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Importance of Cancer Pain Management



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Cancer pain is the most feared symptom of both men and women when they receive a cancer diagnosis.¹ Unfortunately, pain affects greater than 50% of the cancer population, including 64% of patients with metastatic disease.² The reported rate of uncontrolled pain varies, but one study found that 41% of patients with cancer had experienced severe pain in the last week.³ This is not ideal since a top priority for the oncology team is to provide the best quality of life for patients with cancer.

There are many multifactorial challenges, including individual and societal beliefs, to navigate when developing pain management plans. There is a further layer of complexity in the dearth of randomized evidence that directly highlights the importance of cancer pain management. Emphasizing the importance of appropriate pain control may be a beneficial approach to achieving patient, family, and care team buy-in. This does not mean to only focus on pain scores and quality of life, as there are other outcomes that may be beneficial. The evidence discussed in this article implies that cancer pain management is vital, not only for quality of life, but also potentially for improved survival. Additionally, there may be significant barriers to achieving desired pain outcomes in this patient population. There is an increasing fear of pain medications, including in the oncology community, and there are multiple barriers to navigate if pain consultation is needed.

This review will focus on the evidence available to advocate for the emphasis on appropriate pain management and provide education points for care team and patient discussion.

Before discussing the reasoning, it is worth noting the challenges that exist in clinical decision making in pain management, which includes the lack of evidence in cancer pain to translate into practice.⁴ Even medications that are commonly used to control cancer pain may not have any evidence that reveals benefit.⁵ The concept of total pain highlights the multifactorial experience that contributes to the perception of appropriate pain control, and these subjective perceptions may explain one piece of the challenge. Total pain acknowledges that pain perception is based on the combination of social, physical, psychological, and spiritual pain.⁶ A common social example is the lack of available evidence in cancer may lead to insurance denial, financial toxicity, and/or abandonment of the pharmacologic or nonpharmacologic analgesic.⁷ This is not limited to opioid medications, but includes all pharmacologic and nonpharmacologic analgesics.⁸ The National Comprehensive Cancer Network (NCCN) guidelines on adult

cancer pain recommend a multidisciplinary approach for pain management.⁹ Randomized controlled trials may fail to account for the multidisciplinary approach that is needed and may not capture the true clinical impact if these approaches are utilized during the study period. This leads to anecdotal evidence and retrospective studies driving decision-making for pain management plans and has shaped the low quality of evidence that is available to inform clinical decision making. More patient-centric evidence, analgesics, and nonpharmacologic modalities are needed to better treat and guide clinical decision making in cancer pain management.

Optimal management of cancer pain may improve outcomes for patients with cancer. As discussed, there are several challenges to obtaining high quality data to prove the importance of supportive care, but there are several concepts and studies that may indicate the magnitude of pain management. The first practical issue that often arises in practice is treatment eligibility. Many clinical trials determine if treatment is appropriate to continue based on the Common Terminology Criteria for Adverse Events (CTCAE). There are many types of pain listed in CTCAE, and they typically are considered a grade 3 symptom if they limit self-care.¹⁰ It is unknown how often inadequate pain management leads to clinical trial ineligibility, treatment holds, and/or the lack of qualifications for subsequent lines of treatment.

Another important outcome that may increase with poor pain control is hospitalizations. The NCCN guidelines on adult cancer pain recommend considering hospitalization or inpatient hospice admission for an acute pain crisis.⁹ A review of chief complaints among hospitalized

oncology patients revealed that almost 80% of patients were admitted for uncontrolled symptoms. The second most common uncontrolled symptom was cancer pain.¹¹ Other practical points to discuss include losing the physical ability to perform basic functions to maintain performance status or present to oncology appointments. Uncontrolled pain may become a grade 3 or higher adverse event and reduce performance status, which may affect treatment eligibility. These points may be easy to understand and appropriate to emphasize to the patient, family, and oncology team.

There is also some evidence that suggests a mortality benefit with good pain control. First, there are multiple studies that indicate that cancer-related pain is associated with shorter survival.^{12,13} Appropriate pain control has not been officially studied in a randomized controlled trial, but there are studies in palliative care and hospice that show extended survival.^{14,15} The most common study referenced was published in the *New England Journal of Medicine* and examined early palliative care consults for metastatic non-small cell lung cancer. Patients (N = 151) were randomized

"More patient-centric evidence, analgesics, and nonpharmacologic modalities are needed to better treat and guide clinical decision making in cancer pain management."

to standard of care or a consult with the palliative care team with monthly follow-ups. The group assigned to early palliative care had better quality of life scores, which included patient-reported pain intensity and functional assessments. Early palliative care was associated with a statistically significant longer survival of 11.6 months compared to 8.9 months with standard of care ($P = 0.02$).¹⁵ The ENABLE trial attempted to explain this survival benefit by conducting two randomized controlled trials in patients with cancer who had comorbid depression. The first trial randomized patients to palliative care versus usual care. The second trial randomized patients to early palliative care or delayed palliative care. The combined data showed lower mortality risk and improved quality of life with earlier palliative care interventions. This benefit was maintained when controlling for confounding variables, including demographics, primary cancer, and illness-related variables.¹⁴ The exact reason for extended survival in these studies is still not known and is controversial, but many researchers believe improved pain control may be a contributing factor. It should be noted that there are many studies that indicate improved quality of life with these consultative services, but survival has not always been explored or proven as a statistically significant benefit.¹⁶ This evidence must be further elucidated to understand the magnitude of benefit of supportive oncology, guide patient selection, and strengthen clinical guideline recommendations. Discussing treatment eligibility and survival outcomes may be beneficial in alleviating any hesitation in addressing uncontrolled cancer pain.

Another barrier to consider when developing pain management follow-up is access and acceptance of pain specialists, palliative care services, and hospice. As oncology professionals, cancer pain control should be a priority with the goal of improving long term patient-centric outcomes. Oncologists typically have on average only 29 minutes (standard deviation of 13.5 minutes) with the patient and may focus on anti-cancer treatment.^{17,18} The limited amount of time available in the oncology appointment may be an appropriate reason to consider outside consultation. However, an additional challenge may be the acceptance of the care team, patient, and family of these consultative services.

There are many studies that have examined barriers to palliative care and hospice. Resource availability and misconceptions tend to be the most prevalent barriers, which may be addressed with

appropriate education.^{19,20} In 2007, it was reported that there was an insufficient number of board certified pain specialists to care for the chronic pain community and that number has been further decreasing in the current climate.²¹ There are many barriers to referral to pain specialists, but being familiar with available resources and addressing misconceptions of palliative care and hospice may result in an improvement in acceptance of these referrals.

Finally, addressing and understanding the fear of pain medications may be an important tool when developing analgesic plans with patients with cancer. Kwekkeboom and colleagues recruited 157 patients with cancer to examine perceived barriers to cancer pain management. The strongest fear identified using the Barriers Questionnaire II (BQ-II) was addiction, but other barriers included concern about side effects, the belief that cancer pain can't be controlled, and not wanting to complain.³ These barriers lead to inadequate pain control. Lower knowledge and lower motivation are other factors, so education and consultation with experts in symptom management may be a way to address these barriers.^{22,23} Oncology professionals are also prescribing less opioid medications.^{24,25} It is worth noting that the exact rate of opioid addiction in patients with cancer is unknown, but it is believed to be less than 10% of patient with cancer who are on opioid therapy. Discussing tools for patient monitoring is one way to alleviate concerns. The primary tools referenced in the Center for Disease Control and Prevention guideline for Chronic Opioid Therapy include urine drug screens, risk assessments, reviewing the Prescription Drug Monitoring Database, and routine history and physical assessments.²⁶ The oncology team must note the barriers to quality pain management and discuss these barriers with the patient when developing analgesic plans.

Cancer pain management is a vital piece of oncology care but may be a challenging topic to navigate today. Pain is a common symptom among our patient population, and uncontrolled pain may affect treatment eligibility. Evidence in cancer pain management may be low quality, but there is some evidence that pain control may be vital for positive patient-centric outcomes. To achieve these, education and addressing barriers may be necessary. It is important to provide education that good pain control may improve more than just symptoms, but survival outcomes, and that pain medications and specialty services may be needed to achieve these outcomes. ●●

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Reflection on Personal Impact and Growth During Unprecedented Times



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HOPA Past President

When I was asked to write a reflection on personal impact and growth, my first thought was: What perfect timing! I am currently wrapping up my sixth year on the HOPA Board of Directors; my first term was as Member at Large and my current term is as Past-President. My second thought was: Where should I begin? I couldn't be prouder of what we have accomplished in recent years.

It has been a period of extraordinary growth for HOPA. We launched new programs like the BCOP Recertification course and the Oral Chemotherapy Collaborative (OCC). Core Competency is getting a makeover so the course experience matches the exceptional content. We switched management companies to EDI, Inc and now have the first oncology pharmacist ever on the HOPA staff as our Director of Strategic Partnerships.

We are emerging from a pandemic stronger than we were going into it and have launched a new 2023-2026 Strategic Plan that will move HOPA into the future, with updated core values to reflect who we are as an organization. Our familiar values of Leadership, Collaboration, Integrity, Responsiveness, and Innovation are now paired with Diversity and Inclusion (Inset 1).

A Unique - and Important - Time for All of Us

Complicated by the pandemic was another public health emergency: Systemic racism which has led to health inequities for marginalized groups. COVID-19 and social and racial injustices put the spotlight on disparities. Along with the Joint Commission of Pharmacy Practitioners and its other members, HOPA issued a call to action for pharmacists to better understand health care disparities and deliver strategies to address them.

This also prompted the HOPA Board of Directors to retain a consultant to help formalize our commitment to diversity, equity and inclusion within our organization. A member survey conducted in late 2020/early 2021 revealed that HOPA leadership does not reflect the diversity of HOPA's membership, and that race, ethnicity, and age play a role in member perceptions of fairness, equity, and trust. Only a little more than half of our members believed that diversity within HOPA was valued.

One of the most difficult things about professional leadership is being willing to take a critical look at ourselves. But, it was clear that there was work to be done to improve transparency, to build opportunities, and to provide more support to our pharmacist members and the patients in their care.

Formation of a Diversity, Equity, and Inclusion Task Force

Efforts were made immediately that would alter the course of HOPA forever. Strategic discussions led to the formation of the Diversity, Equity, and Inclusion (DEI) Task Force under the direction of Maurice Alexander and Britny Brown. I was proud to serve as the Board Liaison for the DEI Task Force because it was a priority for our organization and it was important for me personally and professionally to support and guide the group in paving the way.

The task force reported directly to the HOPA Board of Directors and they were charged with helping HOPA better understand disparities in health care. They set out to develop tools and resources that pharmacists could use to better provide cancer care for patients

and to propose strategies that would help our leadership be a better reflection of a diverse membership in the years to come.

Ultimately, the biggest responsibilities were to develop our DEI statement, which served as our guiding light, and to make recommendations across the four pillars of our strategic plan (Inset 2).

The DEI Task Force developed more than fifty recommendations that would go on to push HOPA to become an organization centered on inclusive excellence. The work led by Maurice and Britny impacts all aspects of the strategic plan and changes the way we think about DEI within our organization. We were compelled to create the HOPA DEI Award, which was awarded to Maurice and Britny in its inaugural year.

Today, the important work continues with a DEI Committee under the leadership of Kamakshi Rao and Eric Chow. This group is currently designing a DEI tool kit and working to diversify committee membership and leadership opportunities within the organization. HOPA is also working on partnerships with other organizations that will help us reach our DEI objectives more quickly.

"At HOPA, we want everyone to feel they belong to our organization regardless of ethnicity, age, gender, sexual orientation, socioeconomic status, race, religion, or ability."


≡ Reflection on Personal Impact and Growth ≡

Ongoing Commitment to DEI

As a part of professional growth, it is so important to listen. We have had many tough conversations, heard stories from members about their engagement within HOPA and the barriers that many of them have faced. Many of our members felt opportunities were out of reach. All of that is changing.

At HOPA, we want everyone to feel they belong to our organization regardless of ethnicity, age, gender, sexual orientation, socioeconomic status, race, religion, or ability. DEI is one of the guiding principles within our new Strategic Plan, which helps ensure we are looking at education, research, advocacy and more through the lens of equity and inclusion.

Inset 1: HOPA's Core Values



HOPA
Hematology/Oncology
Pharmacy Association

Core Values

LEADERSHIP	Lead from within. We are inspired leaders and passionate mentors.
COLLABORATION	Stand together. We maximize our impact through strategic partnerships.
INTEGRITY	Do the right thing. We maintain the highest levels of ethical standards and accountability.
RESPONSIVENESS	Stay accessible. We respond to needs and solve problems thoughtfully and quickly.
INNOVATION	Be creative. We challenge the status quo.
DIVERSITY	Be yourself. We champion diversity within our organization and profession.
INCLUSION	Seek equity. We foster inclusion through equity and justice.

≡ Reflection on Personal Impact and Growth ≡

If you have not had an opportunity to review our DEI statement please do so. As a member of the LGBTQ+ community, the statement speaks to me personally and immediately I feel that I belong at HOPA. I hope all members feel the same.

Another important aspect of professional growth is knowing

that some initiatives require unrelenting commitment. I encourage us all to think about one another, how we can help each other out. I encourage us all to put others before ourselves and to share in opportunity and success. We do this with the understanding that our work may never be completed. ●●

Inset 2: HOPA's Diversity, Equity and Inclusion Statement



At HOPA, we recognize the longstanding systems of racism and inequity that have shaped the experiences of our members and patients, particularly those with diverse backgrounds, beliefs, and lived experiences. Exploited labor, racism, religious persecution, sexism, trans-antagonism, heterosexism, ableism, ageism, and other oppressive violations have had a profound impact on many of our colleagues and the patients whom we serve. We acknowledge the role we have in dismantling these systems of inequity through action and commitment to the ongoing pursuit of equity and justice.

Only through commitment to DEI can we hope to achieve our vision in the areas of innovation, progress, and advancement. Thus, our commitment spans across all our committees, task forces, and working groups. Through diligent attention and focus, HOPA aims to become a model for organizational commitment to diversity, equity, and inclusion.

DIVERSITY, EQUITY AND INCLUSION STATEMENT

HOPA commits now and in the future to creating a more diverse, inclusive, and equitable culture. We aim to align this important work with each of the HOPA Councils:

Professional Practice – we aim to expand the profession of oncology pharmacy to include those from diverse backgrounds, to build systems that encourage and include these pharmacists in active committee work and leadership (mentor/mentee programs, leadership and professional development aimed specifically at marginalized groups), and to pursue a goal of having our membership and our leadership better mirror the populations we serve.

Education – through thoughtful inclusion of educational offerings across multiple venues and platforms, and through resource provision and tools for our membership, we seek to empower our members to provide socially and culturally conscious care, to promote the role of pharmacists in addressing the impacts of social determinants of health, and to pursue more equitable care models.

Research – as an organization that emphasizes the value of scholarship and research, HOPA commits to the support and funding of projects aimed at pursuing more equitable cancer care models, research conducted by members from diverse backgrounds, and oncology research trials that increase representation and diversity.

Advocacy – HOPA intends to align its efforts in advocating for health-care policies that advance the role of pharmacists with advocacy and lobbying in support of initiatives and policies that tackle racism, discrimination, and access inequities for patients with cancer.

Working towards more equitable care and a diverse and inclusive workforce is critical to the success of our organization, our members, and the experiences and outcomes of our patients.



A Roadmap to Navigate Oncology Drug Shortages



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Introduction

Drug shortages are a decades-old problem for the US and international healthcare systems.¹ Despite the persistence of these issues, the necessary changes for improvements in supply chains, production quality, capacity, and information transparency to prevent or minimize shortage impacts have not been implemented.^{2,3} Rather, the number of active shortages was a record high of 295 at the end of 2022 and have already increased in 2023 to the highest level in nearly a decade.^{1,4,5} Pharmacists play a crucial role in shortage mitigation and must have the skills to navigate their patients and practice sites through situations when there are insufficient quantities of critical medications.

Background and Current State of Shortages

Drug shortages present a challenge for patient safety and efficacy of care. To healthcare institutions, they present a major burden on personnel and may lead to significant negative financial impacts. At a global level, shortages create a national security risk and jeopardize public health.^{1,6} Defined as a period when the realized or projected demand for the drug exceeds available supply, drug shortages may occur due to many factors.⁷ Production issues, especially those involving quality of the finished dosage form, are the majority contributor for disruption in supply.⁸ Spare production capacity is minimal in the pharmaceutical industry, limiting the ability for individual companies or alternative manufacturers to quickly react to mitigate shortage issues. This not only limits responsiveness to the main shortage drug, but also may cause a ripple effect of secondary shortages for therapeutic alternatives or additional presentations of the chemical entity. Generic medications are at highest risk of shortages, particularly for those costing less than \$9 USD per dose.⁶ However, modern patent-protected medications are not immune to shortages, as evidenced by recent events for lutetium Lu-177 radiotherapies and semaglutide injection.^{9,10,11} The public health impact of drug shortages has also increased, with medications critical for acute care or life-sustaining treatment impacted with high intensity of shortage.⁶

Anticancer drugs are one such category where drug shortages may have dire consequences for patients. Chemotherapy agents were one of the top therapeutic categories for drug shortages in the first quarter of 2023.⁵ Many common chemotherapy agents are now decades old, reliant on generic manufacturing facilities for global supply. In recent years, shortages of chemotherapy

agents have included vinca alkaloids (vincristine and vinblastine), etoposide, and taxanes (docetaxel and paclitaxel).¹² Newer agents such as Bacillus Calmette-Guerin (BCG) have also been impacted by long-duration shortages, leading institutions to adjust practice.¹² Supportive care agents, concentrated electrolytes, and antidote medications have also been impacted by recent drug shortages, impacting patients undergoing cancer treatment.¹² At the time of writing, national shortages of capecitabine, carboplatin, cisplatin, fludarabine, and methotrexate among others continue to impact therapy decisions for US institutions.⁷

HOPA Drug Shortage Survey

To objectively characterize anticancer drug and supportive care agent shortages, a workgroup of HOPA Public Policy Committee members developed a 36-item survey and electronically distributed to members of the professional organization between December 2019 and July 2020.¹² This survey was inspired by a previous HOPA shortage survey conducted in 2011.¹³ All chemotherapy and supportive care medications were in scope for inclusion. A total of 68

member institutions participated in the survey, 98% of which had onsite infusion services and 84% of sites administering inpatient chemotherapy. Most respondents were high-volume sites, with 52% reporting at least 1000 doses of chemotherapy administered per month for their site.

A majority of survey respondents (64%) reported at least one anticancer drug shortage per month. Over 27 unique pharmaceutical agents were noted to be in

shortage by at least one respondent. Hematologic cancer patients most commonly required treatment delays due to shortages, including acute lymphoblastic leukemia (ALL; 44%), lymphomas (40%), multiple myeloma (16%), and chronic lymphocytic leukemia (14%).¹² Supportive care shortages most commonly impacted antimicrobials, antiemetics, intravenous immune globulin, and immunosuppressants.

From a safety perspective, shortages increase the risk of medication error. Changes to routine practice, especially those that are implemented emergently, introduce the opportunity for mistakes. The recent survey results included a number of member institutions identifying good catches (4%) and errors reaching patients (6%) directly related to shortage impacts.¹² Given the propensity for voluntary medication error reporting to underreport the true medication errors occurring, these findings are of particular concern.¹⁴

A larger portion of respondents noted impacts on clinical trials, usually preventing enrollment of otherwise eligible patients, increasing documentation requirements, or delaying trial launch.¹² Most institutions see increased costs during shortage periods, where scarcity in the market leads to higher acquisition costs.

"Each institution must develop a robust, consistent approach to manage and mitigate drug shortages for their sites and patient populations."

Managing drug shortages consumed a large number of staff hours, especially as 92% reported not receiving additional staff FTE or hours to dedicate for shortage management.¹²

Shortage Mitigation Best Practices

Each institution must develop a robust, consistent approach to manage and mitigate drug shortages for their sites and patient populations. Regardless of whether dedicated personnel are available to assist in managing the institution through a drug shortage, several best practices exist for any drug shortage process:¹⁵

- *Assemble a team:* Pharmacy is the optimal group to lead an effective process, given insight into the supply chain's availability, timelines for expected recovery, and inventory oversight of available drug product on hand. However, multidisciplinary involvement is essential to provide a detailed and comprehensive recommendation for alternatives to the shortage product. This can include ad-hoc representation from different disciplines or incorporation of members into a drug shortage management team. Standing meetings on a regular interval ensure that a shortage team has protected time to focus on new shortages of concern and review ongoing shortages. If available, a dedicated pharmacy leader for drug shortages can coordinate the team activities and meetings.
 - *Prepare for tough decisions:* Especially important for anticancer drug and supportive care shortages, the lack of availability of product may require providers to make difficult decisions around rationing the supply on hand and determining which patients must change to another drug or regimen. When an ethics committee or scarce resource committee is available, these groups should be consulted as critical shortages are identified and maintain a close working relationship with the drug shortage committee, if not represented by the same individuals. In cancer specifically, this may include selection of less-efficacious, more toxic, or more expensive drug regimens for patients. For curative intent regimens, an objective set of criteria for consistent patient selection must be used to ensure equity and equality in the process of allocation of the shortage agent.
 - *Communicate to patients:* Patients and caregivers will need to be made aware of the shortage, even if not directly changing their treatment plan immediately. The unpredictable nature of shortages may require changes to their plan in the future, so upfront discussion is very important. Handouts or standardized statements with patient friendly language can be developed, if time allows.
 - *Develop an expedited P&T process for shortage alternatives:* Invariably, alternative products may require expedited addition to formulary to configure for safe use within an institution's medication use process. Modern pharmacy integration with electronic health records (EHR), smart infusion pumps, and automated dispensing cabinets usually require informatics updates to correspond with use of shortage alternatives, even if temporary. ISMP acknowledged the need to have a fast-track process outside of usual formulary additions, since the latter may take several months to reach a go-live date.¹⁶ An expedited process should be developed if not already available to maintain safety and prevent inadvertent omissions for medication onboarding. Additional suggestions include:¹⁶
 - Conduct an abbreviated safety analysis.
 - Involve all appropriate personnel, including those outside the shortage management process.
 - Maintain a policy, standard operating procedure, or standard work outline for expedited formulary addition process steps.
 - Ensure review and approval by a pharmacist for disposable supplies, devices, and prefilled packaging.
 - Audit post-implementation and enact changes for improvement based on lessons learned.
 - Evaluate non-formulary dispenses routinely.
 - *Be creative:* Utilize all resources at your institution's disposal to implement shortage changes successfully. A combination of communication media can help ensure all staff are aware of the change and required actions. A source of truth in the form of a drug shortage list or database should be developed to organize all ongoing shortages, but targeted communication in the form of emails, physical flyers, and pop-up messaging in technology devices can provide just-in-time reminders.
- Shortages of anticancer and supportive care drugs may be particularly challenging, due to the lack of direct alternatives with the same mechanism or clinical evidence to support use across all disease states. However, the following strategies may prove useful in defining a mitigation strategy for particular agents. Mitigation factors within supply chain purchasing or pharmacy operations prior to dispensing may limit the impacts of the shortage on patients and front-line providers, when feasible.
- *Supply chain opportunities*
 - Determine if direct shipments are available from manufacturers.
 - Utilize group purchasing organization (GPO) safety stock or emergency caches.
 - Check alternative wholesalers for supply but avoid "gray market" supply companies (unofficial vendors hoarding medications and selling to practice sites with inflated markups¹⁷).
 - Increase inventory in moderation for potential first-line alternatives once identified.
 - Consider obtaining alternative dosage forms if clinically acceptable to substitute.
 - Obtain alternative concentrations, package sizes, or packaging types (e.g., syringe vs vial, ampule vs vial) if available.
 - *Pharmacy operations strategies*
 - Review automatic infusion bag replenishment and advanced preparation compounding to determine if inclusion of a shortage medication should be suspended during the shortage.
 - Determine opportunities to batch orders to prevent waste from multidose vials.
 - Consider extemporaneous compounding opportunities.
 - Consider repackaging within pharmacy to reduce waste from large packaging sizes.

PRACTICE MANAGEMENT (continued)

- Make use of virtual or physical kits as required for shortage alternatives.
- *Clinical strategies*
 - Implement clinical restrictions by service, department, or indication.
 - Consider dose reductions, dose delays, or dose density adjustments when no direct alternatives are available.
 - Consider scheduling patients receiving shortage medications on limited days or times within an infusion suite to minimize waste when pharmacy prepares using a multidose container.
 - Prioritize regimens for curative intent.
 - Adopt alternative regimens when feasible.
- Examine clinical trials opportunities for patients who are unable to receive an intended agent in shortage.

Conclusion

Drug shortages are a critical and worsening problem. In patients with cancer, shortages are particularly concerning due to their risk for medication errors, negative impacts on patient outcomes, and financial impact. Healthcare providers, especially pharmacists, are responsible for identifying safe and practical mitigation strategies when products are in shortage. A well-defined process for proactively identifying and responding to shortages is crucial, regardless of practice setting. ●●

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Presenting Quality Efforts to Leadership: Q&A with Pharmacy Quality Experts



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Background

Presenting data on quality initiatives and quality measures to leadership and/or the c-suite (executive-level leaders with “chief” in the title, such as Chief Financial Officer) to request resources or support for oncology pharmacy programs can be daunting. Two pharmacy quality experts, Dr. Hae Mi Choe and Dr. Emily Mackler, provide advice for HOPA members on how to best approach these scenarios.

"Understanding the strategic goals of the leadership or institution and linking your work/outcomes to them is critical."

Quality Expert Q&A

What is your current position and what experiences do you have presenting quality initiatives to the c-suite or receiving quality presentations as part of the c-suite?

Dr. Choe:

It has been a journey! I did not start having conversations with the c-suite overnight, but it started early on. In 1999, I began to develop innovative pharmacy practice in ambulatory care at the University of Michigan. In this practice, I developed the first pharmacy-led clinic in which I established clinical pharmacy services with the intention of improving specified clinic outcomes and tracked results to share with surrounding non-pharmacy departments. Through that work, I became involved with quality improvement committees at the institution level. Fast forward to 10 years later, when the medical group created a Chief Quality Officer position, they appointed me to that role. Then, I took on the role of Associate Chief Clinical Officer for Quality and Care Innovation and now oversee pharmacists, social workers, dieticians, and behavioral health. In this role, I am *at the table* having conversations with the c-suite, instead of going to the c-suite to pitch an idea. We talk

about quality, how this intertwines with our institution priorities, and how we can participate in payer programs to maximize impact.

Dr. Mackler:

My current position is Director of POEM (Pharmacists Optimizing Oncology Care Excellence in Michigan). In this role, I work with the Michigan Oncology Quality Consortium (MOQC), the Michigan Institute for Care Management and Transformation (MICMT) and Michigan’s largest commercial payer in a value-based reimbursement model that supports embedding clinical oncology pharmacists in community practices across the state. Michigan’s model of collaborative quality initiatives (CQIs) is unique and has given me the opportunity to learn and leverage quality outcomes in the work we do. In my current role, I present this data to multiple stakeholders including the payer and the practice, both who may have slightly different goals for the “value” we provide.

What have you found to be the most important strategy when presenting quality projects to upper management?

Dr. Choe:

Clinical outcomes data is important, but we also need to tie financial outcomes with that. Patient satisfaction and provider satisfaction are also very important, but when you are asking for resources for pharmacists to complete a clinical activity, it is really the clinical and

financial outcomes that drive the decision making. When discussing with the c-suite about quality, they are not the clinical folks. If they do not practice in the area, they might not have a true appreciation for your clinical outcomes. So, you need to have an understanding of who you’re talking to. The Chief Financial Officer compared to someone in charge of population health or an administrator all have different lenses. Therefore, make sure you are presenting quality in a way they will understand. When you are talking to the Chief Financial Officer or Chief Operating Officer, you have to bring in the financial lens.

Dr. Mackler:

1. Know what data they work with, report on and are responsible. Understanding the strategic goals of the leadership or institution and linking your work/outcomes to them is critical.
2. Try to use benchmarks and/or local or national standards in your presentation as it helps when leadership can see that the outcome you are trying to achieve is validated or supported on a larger scale.
3. Connect the dots if needed. Your outcome/work may lead to the intended goal of your institution, but those you are presenting to may need a connection to understand the impact. For

QUALITY INITIATIVES (continued)

example, if your initiative was focused on providing education to all patients starting oral anticancer agents - you have a couple “selling” points for this.

- Education for chemotherapy is an ASCO QOPI quality measure (and contained in the QOPI Certification Standards).
- Providing education has been shown in clinical studies to enhance patient outcomes (AMBORA trial, Durr, et al., JCO2021).
- Include what you expect to impact with this effort. For example, increased patient confidence in self-management leads to decreased toxicity, which leads to decreased Emergency Department utilization and hospitalizations.

We just heard the importance of knowing your audience and data in your presentation. What specific elements do you consider essential to include when you present to leadership.

Dr. Mackler:

As Dr. Choe mentioned, leadership does not always include individuals with clinical expertise. Because of this, I have found that including examples can be helpful. We have been able to garner some additional understanding of our role and impact by presenting cases that the pharmacists were engaged in and how they really helped the patient. We have also found using patient testimonials is helpful. Ultimately, in all presentations, it’s important to have data. This starts well before your presentation and should include strategy related to your stakeholders, their needs and constraints, and what you know prior to your intervention that you hope to impact.

What general recommendations do you have for others sharing quality improvement efforts with upper management? Best practices? Blunders to avoid?

Dr. Choe:

More is not always better. Less information presented but with the right information is better! Match your audience with what you are presenting. Engage physician champions and physician/nursing/administrative leaders along the way so it’s not a surprise. You want them engaged and providing input along the way.

Dr. Mackler:

1. Use the principles of quality improvement when starting your work, rather than saving it for the presentation. For example, ask a lot of questions up front before starting your intervention. Jumping from problem to solution too quickly leads to missing the root cause of the problem but asking “Why” can help guide you until you reach the true root cause of the problem. Go in

with curiosity so you can see and learn some of the barriers before you even start. Definitely know what you plan to measure before you begin.

2. Engage patients if you can. Partnering with patients in the work I’ve done has made it most effective and also most rewarding. They are the best partners I’ve had.
3. Finally, bring in people with expertise you may not have. It is important to know your limitations and have teammates that excel in the areas you don’t.

What tips do you have for using quality improvement results to impact quality measures to ask for resources or expansion?

Dr. Choe:

Not all c-suite members are the same, so understanding which c-suite member you’re talking to is important. Explain quality in a way they can digest and make sure they understand where you’re coming from.

Dr. Mackler:

I think it is good to start small. It gives you the opportunity to work through barriers, to learn, and to think about what resources are needed for expansion and sustainability. I also think it helps a lot to bring in leadership as you think about that expansion. Were the pilot results compelling enough or a priority where they would support a larger scale effort? What else would they want to know to support it long term? This allows them to come in a bit earlier and for you to learn what their priorities are before you move forward.

Any other information you would like to share with HOPA Members?

Dr. Choe:

As pharmacists, we are very well trained to do quality because we look through the lens of the patient and know how to structure things in a logical, concrete way to be able to track progress and be able to look at the outcome and how to analyze the data and improvise based on that outcome. So, I think pharmacists are very well positioned to do quality work.

Dr. Mackler:

I agree with Dr. Choe’s comment. I cannot overstate the importance of knowing your audience and understanding their priorities. The “sell” is much easier when it is a partnership in achieving similar goals rather than “I need this from you.” I really think good patient care is always a win-win, so it is really ensuring we have the data we need and that we present it clearly. ●●

Challenging the FDA Approval of Sodium Thiosulfate: A Critique of the Evidence from ACCL0431 and SIOPEL 6



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Background

In September 2022, sodium thiosulfate (STS) 12.5% anhydrous formulation was approved by the Food and Drug Administration (FDA) to reduce the risk of ototoxicity associated with cisplatin in pediatric patients one month and older with localized, non-metastatic solid tumors, based on the results of the SIOPEL 6 and Children's Oncology Group (COG) ACCL0431 trials.¹

Cisplatin-based regimens play an important role in the treatment of pediatric malignancies, such as hepatoblastoma (HB), medulloblastoma, neuroblastoma, osteosarcoma, and germ cell tumors. Cumulative doses of > 200-400 mg/m² have been associated with an increased risk of ototoxicity.² Cisplatin influx into the cochlea is driven by transporters such as A1 adenosine receptors.³ The ototoxicity of cisplatin is caused by activation of NADPH oxidase (NOX) 3 and generation of reactive oxygen species (ROS), which disrupt the highly metabolic, intricate antioxidant system in the cochlea, ultimately leading to apoptosis of inner hair cells, spiral ganglion and cochlear cells via Signal Transducer and Activator of Transcription 1 (STAT1) activation.^{3,5}

Various thiol-containing compounds such as amifostine and N-acetyl cysteine have been evaluated as preventative agents for cisplatin-induced ototoxicity.⁶ While amifostine showed some potentially positive data, this was not consistent across malignancies.^{7,8} Due to the poor tolerance of amifostine, which included hypotension, hypocalcemia and severe nausea/vomiting, widespread adoption of this agent into clinical practice has been limited.

STS functions as an antioxidant and protects the antioxidant enzymes in the cochlea, while also reducing ROS, making it a promising candidate for the prevention of cisplatin-induced ototoxicity.² Due to its strong nucleophilic properties, STS readily forms complexes with cisplatin, resulting in the biological inactivation of cisplatin. Initial studies conducted by Otto et al demonstrated the

protective effect of STS against cisplatin-induced hearing loss in guinea pigs.¹⁰ However, STS was administered concurrently with cisplatin, resulting in the formation of cisplatin-ST complexes, which led to reduced levels of cisplatin in circulation and potentially compromised its antitumor activity.^{10,11}

SIOPEL 6

The International Liver Tumors Strategy Group (SIOPEL) 6 was a multicenter, open-label phase 3 prospective study that included 109 patients between the ages of one month and 18 years with previously untreated standard-risk HB.¹² Standard-risk HB was defined as a Pretreatment Extent of Disease (PRETEXT) stage I-III, alpha fetoprotein (AFP) > 100 ng/mL, and no evidence of extrahepatic disease. Patients were randomized 1:1 to cisplatin 80 mg/m² continuous intravenous (IV) infusion over six hours every 14 days with or without STS 20 g/m² IV over 15 minutes, administered six hours after the end of cisplatin infusion.

Therapy was given for a total of six cycles, four preoperative chemotherapy cycles followed by definitive surgery, if possible, and two subsequent cycles of chemotherapy. This treatment schema followed the paradigm outlined by SIOPEL for HB, which recommends deferring definitive surgery until two – three months after chemotherapy. The SIOPEL 1-4 trials utilized this methodology, whereas the North American Study Groups (CCSG, POG, COG) recommend primary surgery as initial treatment when possible.¹³ Currently, there are no controlled comparisons of

these two strategies.

The primary outcome of SIOPEL 6 was the absolute hearing threshold at the end of treatment or at a minimum age of 3.5 years, whichever was later. Pure-tone audiometry was performed prior to and throughout treatment in all children aged 3.5 years and older and graded on the Brock scale, using the hearing level in the child's better ear. The median age of patients in the cisplatin alone and cisplatin + STS groups were 13.4 and 12.8 months, respectively, and the median AFP was 73,760 ng/mL and 154,638 ng/mL. The primary endpoint was evaluated in 101 children. The results among these patients showed that any hearing loss (grade 1-4) occurred in 63% (29/46) vs 33% (18/55) of patients receiving cisplatin and cisplatin + STS, respectively (RR 0.52, P=0.002). At the end of treatment, remission rates among the intention-to-treat (ITT) population were 93% and 100%, with a complete remission in 85% and 91% of patients in the cisplatin alone and cisplatin + STS groups. The median follow-up of patients was 52 months, with survival data not yet mature at the time of publication. The rate of 3-year event-free survival (EFS) was 79% in the cisplatin alone group compared to

"Although STS is one of the few agents shown to reduce cisplatin-associated ototoxicity, caution should be exercised based on the findings from SIOPEL 6 and ACCL0431."

CLINICAL PEARLS (continued)

82% in the cisplatin + STS group, and the 3-year overall survival (OS) was 92% in the cisplatin alone group compared to 98% in the cisplatin + STS group.

ACCL0431

ACCL0431 was a multicenter, randomized, open-label phase 3 trial conducted by the COG that evaluated 125 patients aged 1-18 years old with newly diagnosed HB, medulloblastoma, neuroblastoma, germ cell tumor, osteosarcoma, CNS primitive neuroectodermal tumor, or other cancer types treated with cisplatin.¹⁴ Eligible patients were required to have a planned cumulative cisplatin dose of at least 200 mg/m², administered over a maximum infusion duration of six hours. Patients were randomized 1:1 to receive either STS or observation in addition to a cisplatin-containing chemotherapy regimen. STS was administered as 16 g/m² over 15 minutes, beginning six hours after the completion of each cisplatin dose.

Hearing assessments were completed at baseline, up to eight days prior to each cisplatin course, four weeks after the completion of the final cisplatin course, and one year later. Hearing loss was determined using the American Speech-Language-Hearing Association (ASHA) criteria, which is a dichotomous criteria used for early detection of ototoxicity. The primary endpoint was hearing loss at four weeks after the final cisplatin treatment, according to ASHA criteria.

Patients who were less than five years of age accounted for 34% in the control group and 36% in the STS group. A wide variety of malignancies were included, with germ cell tumor being the most common diagnosis, accounting for 25% and 26% of patients in the control and STS groups, respectively. Median cumulative cisplatin doses were 387 mg/m² and 393 mg/m². The extent of disease was determined retrospectively, with 41% and 34% of patients having disseminated disease.

A total of 104 patients completed the primary endpoint assessment for hearing loss. The results showed that 28.6% (14/49) of patients in the STS group and 56.4% (31/55) of patients in the control group experienced hearing loss, with a statistically significant difference ($P=0.00022$). Patients less than five years of age had lower rates of hearing loss with STS compared to the control group, at 21.4% (3/14) vs 73.3% (11/15), respectively. Among those who received cisplatin as a < two-hour infusion, hearing loss occurred in 40% of control patients (10/25) and 16% of STS patients (4/25).

The median follow-up was 3.5 years for EFS and OS, and neither median EFS nor OS were reached. The 3-year EFS was 64% in the control group and 54% in the STS group, while the 3-year OS was 87% and 70%, respectively. A post-hoc analysis evaluating outcomes based on the extent of disease at enrollment showed significantly lower OS in patients with disseminated disease who received STS compared to the control group, with a 3-year OS of 45% vs 84%.

Discussion

There are significant differences in these trials that should be acknowledged. SIOPEL 6 only evaluated patients with standard-risk HB, whereas ACCL0431 included a heterogeneous population across several different malignancies. Cumulative cisplatin doses of 480 mg/m² were planned in SIOPEL 6, whereas ACCL0431 had median

doses of approximately 390 mg/m² in both groups. The median age of patients in SIOPEL 6 was 13 months, compared to ACCL0431 with most patients being five years or older (~ 65% of all patients). As a result of the vast differences in age, both studies used different hearing assessments to quantify hearing loss.

Obtaining a valid baseline test may be challenging in very young patients, which was the rationale for using the Brock criteria in the SIOPEL trials. In addition, most current literature examining post-cisplatin hearing loss in children utilizes the Brock criteria. However, this criterion does not use comparisons with baseline hearing function to grade ototoxicity, which makes it unclear if there were signs of ototoxicity at baseline that confounded these results. Given that HB can occur in pediatric patients born prematurely or with low birth weight, both of which are risk factors for neonatal hearing loss, it is important to acknowledge that the inability to incorporate baseline evaluations in all patients or make comparisons to baseline audiologic function should be considered as limitations when using the Brock criteria. This is particularly relevant as this patient population may already be predisposed to ototoxicity independent of cisplatin use.^{15,16} Both studies were also limited in that not all the randomized patients were evaluated for the primary endpoints, which means that the results do not reflect the intention to treat population.

Additionally, the timing of audiologic evaluation should be carefully considered. The utilization of the Brock criteria in patients 3.5 years and older in SIOPEL 6 meant that patients had definitive audiologic assessment at a median of three years after randomization. This raises many issues, namely the potential for unmeasurable confounders, such as genetics and environmental exposures that could contribute to ototoxicity in the time from therapy completion to definitive assessment. Alternatively, ACCL0431 used the ASHA criteria to quantify early ototoxicity. As the ASHA criteria are binary (yes/no), grading of hearing loss cannot be provided to differentiate the severity of ototoxicity, which may lead to higher perceived rates of ototoxicity.

Platinum-DNA adduct levels were collected in 26 patients in ACCL0431, with one-third of those patients receiving cisplatin alone, and two-thirds receiving cisplatin + STS. These levels were plotted against Brock grade, and no correlation was found between levels and ototoxicity. However, these results are difficult to interpret. Due to the heterogeneous nature of the patients included in ACCL0431, both cisplatin dosing and administration times were not standardized among the patients, which could influence the platinum-DNA levels. In addition, no comparison was provided stratifying platinum-DNA levels against the treatment arms, which would have been useful information to assess if levels were decreased among those receiving STS.

The OS difference noted in ACCL0431 among those with disseminated disease raises concern. As described in previous studies, patients who received STS would be expected to have reduced cisplatin activity (due to complexing of STS to cisplatin), and thus it can be speculated that a reduction in efficacy drove this difference. It is unclear why this OS difference was not consistent among all patients or a finding of the SIOPEL 6 trial. Data from other groups,

as seen in the COG AHEP0731 trial, used less chemotherapy and lower cumulative cisplatin doses among patients with lower-risk HB.¹⁵ Perhaps this suggests that patients with low-/standard-risk HB or localized disease have similar outcomes with less cisplatin than studied in the original HB trials, which may explain the similarity in OS as well as the reduction in ototoxicity seen.

The FDA's broad approval of STS in a heterogeneous disease group creates the potential for inappropriate use. As the approval was based on data from ACCL0431, the lack of proper risk stratification among individual disease states adds to this concern. This premature approval puts undue pressure on clinicians who may be asked by primary caregivers of pediatric patients to incorporate STS into practice without fully understanding the potential loss of efficacy. If STS is to be used, the decision should involve a patient-specific risk assessment, as well as sufficient education of families and patients on the knowns and unknowns of the treatment.¹⁶

Conclusion

Although STS is one of the few agents shown to reduce cisplatin-associated ototoxicity, caution should be exercised based on the findings from SIOPEL 6 and ACCL0431. Although some groups have swiftly adopted STS for the treatment of non-metastatic HB, the safety of its use, even among patients with localized disease, needs to be validated with long-term survival data.¹⁷ Notably, an ongoing phase 3 COG trial ACNS2031 is evaluating the use of STS in patients with average-risk medulloblastoma.¹⁸ Additional studies such as these will be needed to evaluate the appropriateness for STS use across various pediatric disease states. It is crucial to continue routine audiologic monitoring throughout chemotherapy to enable early detection of ototoxicity and facilitate appropriate interventions if needed. ●●

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Five Perspectives on Non-Traditional Education and Association Roles in Hematology/Oncology Pharmacy



Morgan Culver, PharmD, BCOP
CE Synergy

Continuing Education Director

Mom, I Swear I'm Still a Pharmacist!

I never envisioned I'd be here – not in the post-pandemic, we finally have enough toilet paper sense, but in the “yes I'm a pharmacist but not that kind of pharmacist” sense. I was going to be a writer, a photojournalist specifically, travelling the world documenting social injustice and capturing one perfectly timed image to portray a story when my verbiage fell short. Viruses mutate and plans change so here we are.

Through a series of unanticipated events, I found myself in pharmacy school orientation believing I needed to choose one of two paths: chain or independent community pharmacist. It took about three days to realize what we all now know to be true – there is so much more out there! It took another 17 years to realize that pharmacists can still be pharmacists without being “pharmacists”.

In my current role as CE Director at CE Synergy, a medical education company with a focus on continuing pharmacy education for oncology specialists, I'm still a pharmacist – board-certified and licensed and everything! My path to get here was mostly traditional from the perspective of any young pharmacy professional that dreams big. I completed two years of residency before working as an assistant professor at a school of pharmacy and later as a full-time clinician at an academic medical center. I served on committees, taught and precepted pharmacy and medical residents and fellows, completed research, wrote manuscripts, created treatment plans, and every now and again saved a few lives. It was good, fulfilling, valued, respected work and I was good at it, fulfilled, valued, and respected. While my role as a clinical oncology pharmacist checked all the boxes of the resident version of my interview checklist, I missed having opportunities that leverage my creativity. My passions for writing, idea generating, and program development weren't fed. Personally, I was beginning to face the challenges of many professionals that fill two full-time FTEs: oncology pharmacist and parent. Amid a pandemic with childcare that hinged on a group of toddlers remaining afebrile, remote work was beginning to fit the ever-changing needs of our family.

Thanks to a dear friend I met through an introvert's worst nightmare – networking – I was given the opportunity to interview for my current position. During my interview, I was drawn to this female-led company that valued professional growth and true mentorship, offered flexibility to allow me to do the work as both a parent and a director, and encouraged independence to determine my daily schedule and tasks. My role is to ensure our company's policies and procedures align with the standards set forth by ACPE and that our CE programs – from staff, planners, speakers, and content – do the same. The variation from day to day is unlike anything I experienced in the academic and clinical environments. The scope of our projects has remained broad, and my daily tasks range from developing independent medical education fundraising grant proposals to coordinating meeting logistics. I manage our CE Administrators, ensuring their programs are on track and in budget, strategize with our CEO to quip our company and staff to grow intentionally and methodically, and perform daily project management for our accredited continuing pharmacy education programs. After years as a clinical oncology pharmacist and academician, I'm now able to use that knowledge and experience to perform at a high level in my current role as an oncology pharmacist who isn't a “pharmacist” but is still a pharmacist, board-certified and licensed and everything!



Julianne Darling, PharmD, BCOP
NCODA

Senior Manager of Education

You'll have to forgive the immediate Taylor Swift reference, but I couldn't help but note the common threads throughout my career “Eras” as I prepared to write this article. Like so many, my career started out traditionally. I graduated pharmacy school and completed two years of post-graduate training. As I look back, I would categorize myself as an average student with an above average interest in people. What drew me to healthcare, and subsequently to oncology, wasn't the science (although it's neat!) but rather the idea that you could build relationships through getting to know people during their care. I loved the idea that I could help them through a difficult time, try to explain tough concepts in common language, and empathize with the difficulties that life may throw our way.

During my PGY2 year, I gravitated toward outpatient pharmacy practice and the challenges posed by new oral oncolytic processes. Through the excellent mentorship I received during my PGY2, I felt I had found my niche. At the time, oncology pharmacy jobs were vastly available, and I was quickly overwhelmed with the possibilities during my job search; however, there was one interview that checked both

of my core requirements: good people and a focus on patient education. I excitedly accepted a position at Indiana University Simon Cancer Center (IUSCC) and promptly went to buy a new winter coat.

My time at IUSCC was invaluable, and I look back on those years with a lot of gratitude. I was able to work with a wonderful team and help develop a process for oral oncolytic education and management. The team at IU, along with mentors from residency, always encouraged (and sometimes volun-told) me to be involved in pharmacy organizations, so I joined HOPA and tried to jump in. If I had to point to one defining moment in my career journey, it was being selected as a member of HOPA's Oral Chemotherapy Education (OCE) Task Force. Worlds collided as my day-to-day responsibilities translated into national impact through the development of patient education handouts as a part of this Task Force. This work is also what introduced me to NCODA for the first time.

To make a long story short, I discovered I loved being involved with pharmacy associations, and I felt incredibly fulfilled by the work being done in those organizations. In addition to trying to build on my clinical role at IU, I found myself being pulled toward additional HOPA and NCODA volunteer roles. Much like any career path, mine eventually led to failure, as I applied for a more formal leadership role at IU Health and was met with rejection. The better candidate got the job, and although I was incredibly disappointed at the time, it forced me to reflect on why I applied in the first place – What was I hoping for? What was I passionate about? Where did I want to go?

Two weeks later, I received a phone call from the founder of NCODA with an idea about a job. I was dumbfounded. The thought of working for a pharmacy association had never crossed my mind. These weren't the types of roles you learn about in pharmacy school, and I had never thought outside of the "clinical box." Initially, I was daunted by the opportunity as it wasn't clear cut, and there certainly wasn't a road map to success in this new role, but deep down I was excited and eager for a change.

After two years with NCODA, I am glad I didn't let fear stop me from taking the job. My love of people and education led me directly to my role as Senior Manager of Education where I focus on national initiatives to improve oncology care. As part of my role, I oversee the OCE and IV Cancer Treatment Education (IVE) initiatives across four organizations, manage NCODA's Continuing Education program, and work with students and trainees to develop educational resources for those interested in pursuing a career in oncology. My job evolves every few months, but I love the variability and never get bored!

It's hard to summarize a decade in a few paragraphs, but I'll close with this:

- Clinical experience is crucial to any role
- Surround yourself with people you admire
- Give it 100% even if it is a volunteer effort – It may lead to a job!
- Failure is inevitable if you're taking enough risks
- Find the Invisible Strings in your career path and follow them wherever they lead



Christan M. Thomas, PharmD, BCOP
Pfizer Oncology Biopharmaceuticals Group

Director, Global Scientific Communications

I've been known to take the long route to my final destinations. My current position—as Director of Global Scientific Communication with Pfizer Oncology—is no exception. In fact, I wasn't even aware that such a position existed back when I was choosing my pharmacy career path, but I'll get to that in a minute.

When I tell people my job title, 99% of them have no idea what I do. I'd call myself a very involved project manager. My coworkers and I are basically responsible for all the publication content—manuscripts; congress presentations; and enhanced content such as plain language summaries or podcasts—for our assigned products. My job entails coordination with the internal medical and development teams for future planning. I manage a team from an external publication agency that provides medical writing support. I also review all our manuscripts/presentations and assist external health care professionals as they navigate the publication process. Part of my job is also attending conferences and keeping up with the latest trends in oncology publications.

This type of position works well for me—particularly because my background is quite varied. I have an undergraduate degree in communications with a focus in print journalism. After undergrad, I spent five years as a full-time writer/editor before deciding to go back to pharmacy school. Even then, I first chose the clinical route—completing a two-year residency post-graduation and working for six years as a hospital pharmacist before making the switch to industry in 2020. My first industry position was as a medical science liaison. Throughout my entire career, however, I worked on publications in some fashion. I've been involved in the Hematology Oncology Pharmacy Association publications committee since 2014 (first as a writer, then member, then vice chair, chair, and now past chair) and I also maintained a freelance writing presence.

Not all of my team have this oddly specific prior career history, though. My coworkers are made up of a group of pharmacists and PhDs. Some worked in other types of pharmacy before switching to industry. Others did a fellowship after pharmacy school and a third cohort worked directly in medical publishing before joining a pharmaceutical company.

THE RESIDENT'S CUBICLE (continued)

Regardless of the path taken to get here, there are definite benefits to this type of position. First, I work remotely (not all my colleagues do, but Pfizer does have a flexible work environment in general). Second, no two days are the same. I may be at a conference one day and helping to review a scientific paper or record a podcast the next. Finally, I really enjoy working on the global team. This allows me not only to connect with colleagues from around the world, but also work with international health care providers.

For me, landing this job was certainly serendipitous. I randomly read a job alert when I wasn't looking for a new job and applied on a whim. Not all pharmaceutical companies have positions exclusively dedicated to publications. Often, this type of work is divided up among members of the medical affairs and medical teams. Had I not seen the job posting and decided to apply, I would have never found such a perfect fit. I love that I get to dedicate my full attention to publications since it perfectly fits my skillset.



Amy H. Seung, PharmD, BCOP, FHOPA, CHCP
Pharmacy Times Continuing Education (PTCE)

Vice President, Scientific Affairs

I have always had a love of education and thinking through innovative ways to teach others and meet them where their learning needs are. In my current role, I oversee oncology content development and strategy for a continuing medical education provider that provides ACPE-accredited education for pharmacists.

Transitioning to an Education-Focused Role

After transitioning out of a health-system role focused on Hematologic Malignancies and Clinical Decision Support along with residency training, I worked remotely for a start-up software company focused on pathways and specialty pharmacy solutions. This role stretched and challenged me daily to think through business development, marketing, and persuasion and enabled me to collaborate closely with individuals that were not healthcare team members including software developers, business development, and executive leaders. While I was able to develop additional skills, I had a critical juncture in deciding what kind of role would be authentic to me as an individual and my strengths. Around the same time, I was asked to serve as faculty for a program on leukemias (my passion!), and I began talking with individuals about how they got into their roles. Fortunately, connections and networking led me to start this new position.

Daily Interactions

My day-to-day work includes varying responsibilities such as interacting closely with a variety of individuals internally from pharmacists within our Scientific Affairs team to program managers, outcomes managers, business development, marketing, and others to externally networking with oncology pharmacist clinicians from around the country. One of the best parts about the CME sector is staying connected with practicing clinicians to learn of breakthroughs, challenges, new ways of problem-solving, and seeing how pharmacists are contributing to improving patient outcomes each day. My team and I work with program faculty to develop and finesse distinct types of education for pharmacists. Some days I spend my time at conferences and others may be in the studio filming actors for counseling scenarios. The role requires constant innovative ideas to reach our learners. Additionally, I work with our business development team members to capture our learners' needs through data analysis of our outcomes from programs matched with what medications and new indications are in the oncology pipeline.

One other aspect of CME is incorporating continuous professional development concepts and standards into our daily work. I am continuously learning, developing, and sharing information to other healthcare professionals that are in education roles. The Alliance for Continuing Education in the Health Professions serves as a home organization for myself and others in my type of role. This organization allows me the opportunity to speak and present to my colleagues on the skills I have developed. My team often presents our work and outcomes within this organization.

Being Authentic

I have been fortunate to find a role that balances my own love for learning new things, continually growing my skill set, and working with talented team members along with interacting daily with strong, smart clinicians. Each day brings new opportunities. Additionally, this position has enabled me to keep myself challenged, but also have time and energy for my family and personal life.



Nicole Watts, PharmD, BCOP
Hematology/Oncology Pharmacy Association

Director of Strategic Partnerships

As The Notorious B.I.G once said, “It was all a dream....” And it was. That is how my non-traditional oncology pharmacy career started: with a dream. After waking up and realizing that I wanted more in my career, the possibilities were endless.

I had been a stem cell transplant clinical pharmacist for ten years empowering myself to become proficient in critical roles including developing treatment plans, monitoring patients for drug interactions and side effects, counseling and educating patients regarding their medications, collaborating in research, publishing, precepting, and volunteering in national organizations. Then, like Notorious B.I.G, I had a dream; it was time to try something new. In my quest for a new path, I discovered the many opportunities available for oncology pharmacists outside of direct-patient care roles. I could move into education and teach other healthcare professionals about cancer treatments, side effects, and drug interactions. Industry provides a wide range of career options from drug development to clinical trials to medical affairs. Consulting remained even another option, providing clinical pharmacy services to healthcare organizations. Then I discovered association management.

I first heard about the Director of Strategic Partnership position at HOPA’s Annual Conference in 2022. At the time, I didn’t think I was qualified. After talking with a colleague already in a non-clinical role with a major oncology organization, I decided to apply. The role attracted me because it permitted collaborating full-time with HOPA, the organization I loved, and had volunteered for several years. I realized such a position empowered teamwork, dreaming, and building a national framework with the colleagues I met and will continue to meet over the years to improve cancer care. Other tangible benefits included leadership training, opportunities to improve communication skills through crucial conversations, and project management competence on a larger scale. Plus, I could travel and connect with other healthcare professionals within oncology and other pharmacy practice settings.

As HOPA’s Director of Strategic Partnerships, I provide oversight and coordination of collaborative opportunities across the organization. I identify potential collaborations and build strong relationships with foundations, non-profit and for-profit organizations, industry, advocacy, and public policy groups to support HOPA’s long-term vision. I coordinate volunteers who represent HOPA on external organizations and attend meetings with or on behalf of the President and/or Executive Director, which typically requires travel. I liaise with HOPA staff to offer guidance and insights into oncology pharmacy while providing insights into advances in the field. Most recently, I developed an integrated collaborations strategy within HOPA’s 2023-2026 Strategic Plan in coordination with senior HOPA leadership.

Although ten months into this role, there is still a lot to learn regarding association management and strategic partnerships. I take online courses to help me grow leadership attributes and continue to be challenged every day. I wouldn’t be writing this piece without the inspiration from other oncology pharmacists, the confidence I received from my husband and friends, and the constant support from the HOPA Staff and Board of Directors.

Through this career change, I learned not to sell myself short and the importance of networking. What started as a dream became a reality. ●●

Clinical Pearls and Predictors of Success with Outpatient CAR-T Cell Therapy



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Introduction

Cellular therapy has become an essential treatment strategy for patients with hematologic malignancies. Products such as chimeric antigen receptor T-cell (CAR-T) therapy have greatly impacted the treatment paradigm of various malignancies including high-grade B-cell lymphoma, acute lymphoblastic leukemia, mantle cell lymphoma, follicular lymphoma, and multiple myeloma.¹⁻³ There are several FDA approved CAR-T products with ongoing indication expansions and numerous products in the pipeline. As CAR-T and other cellular therapy products, such as bispecific antibodies, continue to shift the treatment landscape for hematologic malignancies, it is important to discuss key challenges associated with administration of these products to allow for expanded access to them.

In the six years since the first CAR-T therapy was FDA approved, supportive management of these patients has been continually evolving. While early pivotal trials required inpatient administration due to the risk of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), the data and real-world experience with managing these toxicities has grown, encouraging many centers to transition to outpatient administration. Data supporting safe outpatient CAR-T administration allows hospitals to utilize their resources judiciously and provide outpatient therapy when feasible. Additionally, outpatient administration has shown to improve patient satisfaction and quality of life as well as reduced financial toxicity associated with these therapies.⁴⁻⁵

There are several barriers to administering a product that is associated with urgent toxicities like CRS and ICANS in an outpatient setting that is unable to provide continuous 24-hour medical care. These include, but are not limited to, understanding of the cellular product and associated toxicities warranting prompt intervention, housing with sufficient proximity to the hospital, reliable caregiver support, and ability for efficient admission to an inpatient bed in a semi-emergent situation. While these specific barriers exist with CAR-T therapy, centers have routinely performed outpatient autologous and allogeneic hematopoietic stem cell transplant (HCT) for many years where similar concerns are at play and this has paved the way for successful outpatient administration of other cellular therapies.⁶

Keys to Success

Teamwork

A multidisciplinary healthcare team is the most vital component to an outpatient cellular therapy program and truly serves as its foundation. This group consists of a multitude of professions including specialized physicians, advanced practice providers (APPs), clinical and research nurses, clinical pharmacy specialists, cellular therapy and financial coordinators, apheresis and processing lab personnel, social workers, case managers and procurement personnel.⁷

It is important to create an organized workflow and clear responsibilities for each team member throughout the entire patient care process. The physicians and APPs will first determine if the patient meets outpatient eligibility based on specific criteria. These criteria are highly variable between institutions and may evolve with program experience, but Table 1 serves as an example for initial outpatient eligibility criteria. Physicians and APPs will also be heavily involved

with daily monitoring and management of CAR-T related toxicities. The nurses are responsible for administering the CAR-T product, lymphodepleting chemotherapy and supportive care medications and play a key role in patient and caregiver education as well as patient monitoring. The clinical pharmacist specialists create the lymphodepleting chemotherapy plan and are involved with ensuring adequate tocilizumab stock per Risk Evaluation and Mitigation Strategy (REMS) requirements via communication with procurement personnel.⁸⁻¹³ Additionally, the pharmacist

serves as another key educator to the patients and caregivers and a vital resource to the cellular therapy team regarding supportive care and adverse event management. At our institution, the pharmacists collaborated with the physicians to create a protocol for management of CRS and ICANS to ensure consistent care across providers. We follow the American Society for Transplantation and Cellular Therapy (ASTCT) consensus grading for these toxicities, which was also incorporated into the protocol and is uploaded in each patient's chart for easy accessibility. The cellular therapy coordinators play a role in scheduling and educating on logistics of the treatment process. The financial coordinators help on the front end by developing case rates/agreements and ensuring approval and reimbursement of the therapy. The apheresis and processing lab personnel are involved with collecting, shipping, and storing of the CAR-T product. They also play a crucial role in timely administration of the cell infusion given the short expiration time of most of these cryopreserved products after thawing. Lastly, the case managers and social workers are essential in coordinating temporary housing near the CAR-T center for patients and their dedicated caregivers as well as assisting in other logistics, such as transportation and caregiver support.

"It is important to create an organized workflow and clear responsibilities for each team member throughout the entire patient care process."

Table 1. Eligibility criteria for outpatient CAR-T

- Tumor bulk < 10 cm
- Baseline CRP < 50 mg/L
- Baseline platelets > 20,000
- No primary CNS disease
- Adequate caregiver support

Along with the core members of the cellular therapy team, communication should occur with key alliances such as the emergency department (ED) and intensive care unit (ICU) staff who help with urgent management of these complex patients. It is important for these healthcare professionals to be educated on CAR-T related toxicities and the need for prompt interventions such as tocilizumab or corticosteroids. Education to all core personnel and alliances is paramount to successful outpatient administration.

Similar to outpatient HCT programs, the CAR-T program should document their workflow and processes via policies and standard operating procedures (SOPs). These documents should outline the data supporting CAR-T therapy, patient selection criteria, patient follow-up requirements, toxicity management and supportive care strategies. A dedicated quality team helps update these documents annually to keep up with the rapidly changing landscape of cellular therapy and improve patient care.

Dedicated space

While the team members are the underpinning of the program, it also needs a true foundational space to operate from. A dedicated outpatient cellular therapy center should exist and be equipped to administer lymphodepleting chemotherapy and the CAR-T cell infusion, execute patient and provider visits, and monitor and manage associated toxicities. To effectively perform these tasks, the center should ideally be open seven days a week to provide daily patient visits for at least the first one to two weeks following infusion. During these visits, providers will perform physical exams including neurologic assessments to monitor for CAR-T related toxicities. There is also an opportunity to manage low-grade toxicities, including administration of tocilizumab, in the clinic. Clinical pharmacists can play an important role in CRS management including helping to identify the appropriateness of tocilizumab use and facilitating access to tocilizumab across clinical areas to ensure timely administration and potentially prevent the need for inpatient admission. Telemedicine visits with audio and video are a key component to an outpatient CAR-T program, which allows providers to monitor for toxicities after-hours. If a center does not have the capability to be open on weekends, telemedicine visits can be an alternative option to closely monitor these high acuity patients.

If a patient develops CRS or ICANS requiring inpatient care, many centers have implemented a “scatter” hospital bed to allow for quicker admissions and avoidance of the patient having to progress through the ED. The “scatter” bed should be reserved for cellular therapy patients and should be in a unit that is equipped to rapidly give interventions like tocilizumab and corticosteroids. Not every center is able to have a designated “scatter” bed and therefore ED admissions may still be a feasible mechanism for admission, provided the ED staff is educated and prepared to rapidly evaluate and administer specific interventions. To confer with REMS program requirements,

all ED physicians must be REMS trained and the facility must be able to administer tocilizumab within 2 hours of observed toxicity.⁸⁻¹³

Toxicity management

As mentioned above, telemedicine visits are a useful adjunct to daily clinic visits during a time when more frequent patient care is desired, but 24-hour inpatient monitoring isn't needed. During these telemedicine visits, patients can report their vital signs and providers can perform a review of systems, including a basic neurologic function assessment to identify signs and symptoms of CRS/ICANS.¹⁴

Another strategy some centers have implemented is wearable devices. These devices can be worn for prolonged periods of time (up to 30 days) and provide real time vitals including heart rate, body surface temperature, respiratory rate, and oxygen saturation. These data are relayed to a device the hospital staff are monitoring and can intervene by contacting the patient if concerns for any toxicities arise. Additionally, some pharmaceutical companies provide digital platforms to provide product information and patient support (i.e., Cell Therapy 360®).¹⁵

To prevent inpatient admissions, especially within the first 72 hours following infusion to maintain outpatient reimbursement status, efforts have been made to reduce the incidence and severity of CAR-T toxicities. One strategy has been the implementation of prophylactic steroids in large B-cell lymphoma. In cohort 6 of the ZUMA-1 trial, the use of prophylactic dexamethasone 10 mg orally on days 0, 1 and 2, along with earlier intervention with tocilizumab and/or steroids, resulted in no cases of grade 3 or higher CRS and delayed CRS onset without compromising the CAR-T efficacy.¹⁶

Use of prophylactic and supportive care medications are also essential to mitigating CAR-T toxicities. This includes the use of prophylactic antiepileptic medications, allopurinol and hydration for prevention of tumor lysis syndrome, and prophylactic antimicrobials to reduce the risk of infections.⁷ Growth factor support should also be considered to reduce the incidence of febrile neutropenia.⁷

The choice of lymphodepleting chemotherapy regimen may also impact the incidence of toxicities following CAR-T administration. The combination of fludarabine and cyclophosphamide (FluCy) has been used most commonly; however, this regimen is associated with risks of hematologic toxicities and infections. A recent single-center retrospective review found reduced rates of CRS, ICANS, infections and hospital admissions with bendamustine lymphodepletion compared to FluCy with similar efficacy outcomes.¹⁷ Of note, bendamustine has only been formally studied with tisagenlecleucel but its use with other CAR-T products is under investigation.

Finally, it is worth noting that the currently FDA-approved cellular therapy products differ in the incidence and severity of toxicities.^{7,18} The main driver of these differences is the co-stimulatory domain for the product. CD28 co-stimulatory domains are associated with more rapid in vivo expansion and therefore, tend to have an earlier onset and higher severity of CRS and ICANS.¹⁸ Products with a 4-1BB co-stimulatory domain with slower expansion and typically have a longer time to onset of CRS and ICANS as well as decreased severity.¹⁸ These differences are important to be aware of as they may influence which products a center selects for

FEATURE (continued)

outpatient administration or how patients are monitored. Taking this into consideration along with other patient factors, such as burden of disease, can help guide decision making for offering outpatient or inpatient administration. Generally, outpatient administration should be strongly considered when CRS and ICANS are less common, predictable or later in onset, and anticipated to be mild or moderate. In cases where CRS or ICANS is expected to be frequent, severe, or early or unpredictable in onset then inpatient administration may be more appropriate.¹⁸

Assessing Success

As with outpatient HCT programs, it is important to have regulatory standards in place for CAR-T therapies. The Foundation for the Accreditation of Cellular Therapy (FACT) currently encourages centers to achieve Immune Effector Cell (IEC) accreditation if a program is administering commercial or research CAR-T therapy. However, accreditation is not required per Centers for Medicare & Medicaid Services (CMS) if the program is meeting REMS requirements.¹⁹⁻²⁰ Since there are numerous CAR-T products from various pharmaceutical companies with individualized REMS programs and metrics, it is important for an outpatient program to create their own quality metrics. These could include incidence and grades of CRS/ICANS, usage and efficiency of tocilizumab administration, hospital admission rates, and incidence and type of infections. Obtaining benchmark data helps to identify opportunities for process improvement, patient selection, and patient care management plans. While these metrics help with monitoring the success of an outpatient cellular therapy program, they also help with justifying its expansion, including additional staff and allocation of resources.

Conclusion

As the indications for these CAR-T products continue to expand and more cellular therapies with improved toxicities are introduced, outpatient treatment has the potential to be the mainstay for CAR-T therapy. Outpatient administration helps improve patient satisfaction, reduce financial toxicity, and free up hospital resources. Additionally, transitioning CAR-T to the outpatient setting will greatly aid in the efforts to increase access to these essential therapies. Creating a successful outpatient program requires careful and thoughtful planning to navigate the logistics and challenges of CAR-T therapy. Having a core multidisciplinary healthcare team is the backbone to success. Each member of the team is an invaluable asset to providing optimal patient care. Clear communication and comprehensive education on managing toxicities to staff of all areas where these patients will be treated is paramount to patient safety. Additionally, education to the patients and caregivers during each phase of treatment is a key component to successful and safe outpatient treatment.

A dedicated outpatient infusion center is required to support these patients. Telemedicine visits can be incorporated to allow for enhanced patient monitoring and wearable technology can facilitate tracking of signs and symptoms of CRS or ICANS. To be able to safely administer these therapies outpatient, institutions must have a clear workflow to allow for prompt admissions and rapid tocilizumab and/or corticosteroid administration if toxicities arise. Internal metrics should be collected to dynamically adjust processes and policies to encourage patient safety and program expansion. Cellular therapy continues to rapidly evolve, and it is important that healthcare institutions consistently adapt to the needs of this growing field in order to provide optimal patient care. ●●

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Patient Perspectives on Genetic Testing and Targeted Cancer Therapies



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Introduction

The unveiling of the human genome at the turn of the 21st century marked the beginning of a period of incredible advancement in our understanding and treatment of cancer. The sequencing of the human genome marked a paradigm shift in cancer care from a “one-size-fits-all” methodology to a more tailored approach, which involved utilizing the patient’s genetic information to guide treatment. Advancements in sequencing technology has allowed researchers to timely interrogate the tumor genome with the purpose of identifying and targeting genetic alterations along molecular pathways involved in driving the development and survival of the respective cancer.¹ Tumor genetic testing for acquired genetic alterations have also been used to guide therapy for a variety of cancers, as well as serve a prognostic role in describing the biology of the cancer and its impact on patient outcomes.² Germline genetic testing aids the diagnosis of hereditary cancers and identifies genetic alterations that predict drug pharmacokinetic properties that can influence both efficacy and safety outcomes.³ Despite the undeniable impact of genetic testing on personalized medicine, barriers in its implementation exist, spanning from patient approval of genetic testing stemming from lapses in proper education and distrust in the medical system, to the logistics of implementing genetic testing in daily practice related to cost, timeliness of results, and at times the lack of clear guidance on how to act on the results.⁴ Often used interchangeably, the terms “pharmacogenetics” and “pharmacogenomics” encompass two areas pharmacists can enrich the patient experience through personalized precision medicine. With their expertise in clinical pharmacology, pharmacists are uniquely positioned to assist healthcare teams in selecting regimens based on a

patient’s molecular profile and optimizing medication dosing based on pharmacogenomic test results both for cancer therapies and supportive care regimens.

The terms “precision medicine” or “targeted cancer medicine” are often used in media and by health care providers. Often, it is the physician or the genetic counselor that discusses genetic testing, results, implications for treatment or familial screening, but pharmacists play an important role in decision support and are often the most accessible resource for their patients. As such, it is important to ensure patients understand what targeted therapy represents, how it works, how it differs from traditional antineoplastic therapies, and what to expect from it.

This article illustrates one patient’s experience with genetic testing and use of an associated targeted therapy. Patient PS was diagnosed with stage IV non-small cell lung cancer with an epidermal growth factor receptor (EGFR) exon 19 deletion. PS shared with us his perspective and personal experience with genetic testing, treatment with osimertinib, and the roles of the physician and pharmacist on the team in his cancer care experience to make our interactions with patients both meaningful and relevant.

"Many patients may not have a clear understanding of what a targeted therapy entails: how it works, how it differs from traditional chemotherapy, what to expect from it, and the logistics of acquiring, taking, and monitoring for toxicity. "

The Patient’s Perspective

Each patient’s perspective on genetic testing may be different depending on their personal experiences with genetic testing in healthcare and non-healthcare related settings, their friends and families’ experiences, and information shared in the media. Pharmacogenomic pre-emptive testing to predict responses to medications and streamline therapeutic selection is currently offered in primary care or specialist offices. As such, many patients may have some exposure to certain aspects of genetic testing and may have preconceived notions and concerns related to genetic testing including cost, privacy of genetic information, utility of results, and screening of family members. These are all questions or concerns your patients may have depending on the purpose of the genetic testing.

PS did not have any experience with genetic testing prior to his diagnosis of lung cancer. Upon his diagnosis, PS’s physician discussed the need to screen for genetic alterations that may be driving the cancer with the goal of optimizing treatment selection. When queried if he had any concerns or questions about the test or the test results, PS noted that his main concern was related to his three children carrying the same genetic alteration and developing lung cancer in the future. Fortunately, PS learned early on after his

FOCUS ON PATIENT CARE (continued)

diagnosis that the mutation his cancer carried would not be passed on to his children. Another source of distress noted by the patient was the wait time for the results, which he described as “the most intense 7-10 days I’ve experienced in my life.” While this is beyond the control of pharmacists, being able to address questions about treatment options in the absence of targetable mutations may offer patients peace of mind during an incredibly overwhelming period. Pharmacists’ contributions or involvement with the patient and the healthcare team may differ depending on the clinical setting and on the purpose of genetic testing. In PS’s case, with an increasing number of treatment options targeting the same mutation, the pharmacists’ role is essential in guiding therapy selection for the patient, while considering their comorbid conditions, drug-drug interactions, and financial toxicity.

We use the term “targeted therapy” so often in our daily practices and often do not realize that many of these therapies are relatively new. While they’ve introduced significant changes in the approach to cancer treatment, many patients may not have a clear understanding of what a targeted therapy entails: how it works, how it differs from traditional chemotherapy, what to expect from it, and the logistics of acquiring, taking, and monitoring for toxicity. PS never came across the term targeted therapy nor did he know anyone who was on a targeted agent before. He did however, have a very vivid picture of the side effects of traditional chemotherapy from friends and relatives going through cancer treatment. He remembers being terrified to lose his hair and feeling unwell for days after receiving treatment. This perception of chemotherapy side effects is not uncommon among the general population and while targeted therapies may be associated with less acute reactions compared to cytotoxic chemotherapy, they are not without their own safety concerns and a careful review of the information with the patient is paramount to setting them up for success. Counseling should include a detailed review of administration instructions, handling of missed doses, expected adverse effects

and their expected severity (including home management strategies when appropriate), drug interactions screening with concomitant medications, supplements, or foods, as well as information about medication storage and handling when appropriate. PS recognized that his pharmacist played an essential role throughout his care continuum. Before initiation of osimertinib, PS’s pharmacist completed a comprehensive review of the medication. PS noted that he found it especially helpful learning from his pharmacist what to expect from the medication. He knew that he may develop rash and diarrhea and was well-versed from discussions with his pharmacist on how to utilize non-pharmacologic and pharmacologic measures to manage these side effects at home. He was also aware when to reach out to his pharmacist and physician for further guidance on toxicity management. As PS continued on osimertinib, he had follow up calls with his pharmacist for re-assessments of efficacy and toxicity and had a direct line of communication to consult his pharmacist regarding potential interactions before initiating any new therapies or supplements. While the convenience of taking a pill in the comfort of his own home positively impacted his quality of life, having his clinical pharmacist as a resource when initiating therapy, for toxicity management, and when considering the start of new medications allowed him to feel supported and informed.

Conclusion

Oncology pharmacists have the expertise and are uniquely positioned to provide decision support and contribute to the care of patients on targeted therapies across the patient care continuum. The exact role of the pharmacist may differ depending on the practice setting and the purpose of the genetic testing. In cases such as PS’s case, it is imperative that we listen, address the patients’ concerns, and provide information to empower them in making informed decisions and actively contributing to the design of their own cancer care experience. ●●

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Multicenter Comparison of First Salvage Chemotherapy Versus Novel Therapy Regimens in Adult Relapsed/Refractory Acute Lymphoblastic Leukemia



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Introduction

The optimal therapy for first salvage in patients with relapsed or refractory (R/R) Philadelphia chromosome (Ph-) negative acute lymphoblastic leukemia (ALL) is unknown. Patients who relapse early versus late following remission, those who are primary refractory to induction therapy versus individuals who achieve an initial complete response (CR), and patients requiring first salvage versus second or later salvage have vastly different outcomes with chemotherapy.^{1,2} Thus, patients with R/R ALL are heterogeneous and grouping all patients together does not give a true portrayal of the disease. While blinatumomab and inotuzumab have improved outcomes for some patients with R/R ALL, there are significant flaws to the pivotal phase III TOWER and INO-VATE studies, including suboptimal, underperforming control arms.^{3,4} Additionally, the optimal sequence and which patients derive most benefit, remains unclear. The purpose of this study was to compare outcomes of patients with ALL in first salvage who received chemotherapy versus novel therapies during a time where novel therapies were available to patients upon relapse. Furthermore, we sought to identify factors that predict chemosensitivity in the R/R setting.

Methods

This study was a multicenter, retrospective cohort study at Michigan Medicine (MM), Memorial Sloan Kettering Cancer Center (MSKCC), and University of North Carolina Medical Center (UNC) of patients with first relapse/primary refractory Ph- ALL who received chemotherapy (e.g., HyperCVAD, MOAD, Larson/CALGB-9511) versus novel therapy (blinatumomab or inotuzumab) from January 2012 to 2021. The primary endpoint was overall survival (OS), defined as time from the start of first salvage to death from any cause, censored for last known follow-up. Secondary endpoints included event-free survival (EFS), CR/CRi, 30-day post-salvage all-cause mortality, rate of alloHCT following salvage therapy, duration of neutropenia and thrombocytopenia, and incidence of febrile neutropenia, bacteremia, and ICU admission.

Results

A total of 77 patients with R/R ALL were included, of which 43 patients received chemotherapy and 34 received novel therapy in first

salvage. Overall, 27.3% of patients were primary refractory and 40.3% had an early relapse. Patients were significantly older in the novel therapy arm, with a median age at relapse of 59 years (range 31-74), compared to 38 years (range 18-73) in the chemotherapy arm ($p=0.004$). Numerically, a higher percentage of patients in the chemotherapy arm received BFM-based initial induction (30/43, 69.8%), while more patients in the novel therapy arm received upfront treatment with HyperCVAD (16/34, 47.1%). A similar number of patients in both groups proceeded to alloHCT in first CR (13% overall). Patients in the chemotherapy arm were more likely to have CNS involvement at relapse and had a significantly higher blast percentage at relapse (blasts $\geq 50\%$: 61.5% versus 26.7%, $p=0.007$).

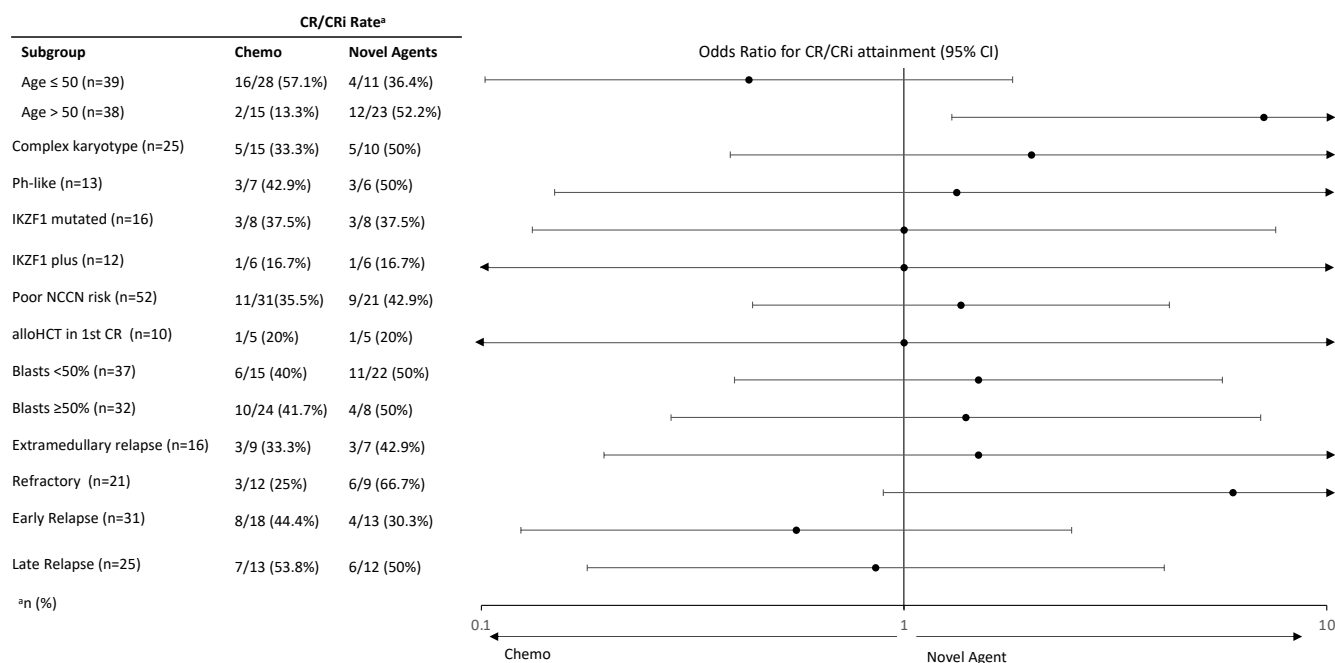
With a median duration of follow up of 10.1 months in the chemotherapy arm and 9.8 months in the novel therapy arm, the primary endpoint, OS, was not significantly different with che-

motherapy compared to novel therapy, with a median OS of 10.6 months (95% CI 3.3–18) and 10.1 months (95% CI 8.1–12.1), respectively. Median EFS was short in both arms, at 1.6 months (95% CI 0.8–2.4) with chemotherapy and 2.4 months (95% CI 1.4–3.4) with novel therapy. Response rates (CR/CRi) were not significantly different between arms, with a CR/CRi in 18 patients (41.9%) treated with salvage chemotherapy versus 16 patients (47.1%) in the novel therapy arm. Subsequent therapy following first salvage was similar between arms, with a median of 2 subsequent lines in the chemotherapy arm and 1 line in the novel therapy arm. Overall, 42.9% proceeded to subsequent

"The purpose of this study was to compare outcomes of patients with ALL in first salvage who received chemotherapy versus novel therapies during a time where novel therapies were available to patients upon relapse."

alloHCT.

A forest plot was created to determine whether the probability of achieving a CR/CRi with chemotherapy versus novel therapy was impacted by any subgroup (**Figure 1**). Notably, age significantly impacted the probability of achieving CR/CRi with novel therapy versus chemotherapy. Among patients 50 years of age and younger, 57.1% versus 36.4% achieved a CR/CRi with chemotherapy and novel therapy salvage, respectively ($p=0.248$). Among those age greater than 50 years, patients who received novel therapy salvage were significantly more likely to achieve a response, with a CR/CRi in 52.2% of patients compared to only 13.3% with chemotherapy ($p=0.024$). Additionally, patients who were refractory to initial induction had a higher response rate to novel therapy salvage compared to chemotherapy, with a CR/CRi of 66.7% versus 25%, respectively ($p=0.065$).

Figure 1: CR/CRi rates in subgroups analyzed by baseline patient characteristics

Discussion and Conclusion

In this real-world, multicenter study, we demonstrated similar efficacy with chemotherapy compared to novel therapy in first salvage. The median OS we observed with chemotherapy exceeds that with chemotherapy in TOWER and INO-VATE. This is likely attributable to thoughtfully selecting a salvage chemotherapy regimen based on a patient's previous therapy and prior response, rather than the limited options in TOWER and INO-VATE, and patients having access to novel agents upon subsequent relapse. While several reports have concluded that novel therapies should be given in first salvage since benefits are more pronounced rather than administering in later lines, without allowing crossover, no conclusions about the optimal timing or sequencing can be drawn.^{5,6} Our findings suggest the sequence may be less important than having access to novel agents as additional lines of therapy.

Patients who are primary refractory represent a subgroup that may benefit from novel therapy in first salvage, based on a numerically higher CR/CRi observed with novel therapy. In addition, age significantly impacted the probability of obtaining a CR/CRi with novel therapy versus chemotherapy. It is not surprising that CR/CRi rates were significantly lower with chemotherapy salvage in patients above 50 years of age as chemotherapy options are limited in this subgroup due to poor tolerability. Conversely, patients' age ≤50 had higher CR/CRi rates with chemotherapy. This aligns with previous studies which have demonstrated chemosensitivity and tolerability for younger patients treated with a pediatric-inspired approach.⁷

Our study has several limitations including retrospective study design, a heterogeneous population despite limiting to first salvage, small sample size, and short duration of follow-up. In addition, there are important differences in baseline characteristics that impact the applicability of our results. While patients in the chemotherapy arm were significantly younger, they were more

likely to have more high-risk disease characteristics, including CNS involvement, higher blast percentage, and MYC translocations, which may offset the more favorable prognosis with younger age. Majority of patients in the novel therapy arm received blinatumomab in first salvage, which limits the ability to apply these results to inotuzumab. Since the time of our publication, we are likely to see increased use of blinatumomab upfront, both for patients with MRD+ based on the BLAST trial (some of our patients were included prior to BLAST trial publication in 2018), and more recently MRD- with preliminary results of ECOG 1910.^{8,9} As only 7 patients (9.1%) previously received blinatumomab for MRD+ prior to frank relapse in our study, this limits the applicability of our results in patients who received upfront blinatumomab.

In conclusion, this multicenter study is hypothesis generating and a prospective, randomized study with adequate chemotherapy comparators and availability of novel agents upon relapse is warranted to determine the optimal sequence of therapy. Despite not detecting a difference in efficacy, novel agents are associated with significant cost increases, with one course of blinatumomab or inotuzumab costing up to \$120,000.^{10,11} Some patients may benefit from novel therapy in first salvage, including older patients who are less likely to tolerate additional chemotherapy and patients with primary refractory disease. However, given the similar efficacy, potential for decreased healthcare resource utilization, and possibility to avoid losing an entire line of therapy, salvage chemotherapy regimens should be considered as an alternative to novel therapy in first salvage, particularly in younger and fit patients, conserving novel therapies for subsequent relapses. ●●

The full manuscript for the research highlighted above can be found at:

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ARPi + PARPi: A One Size Fits All in Metastatic Castration-Resistant Prostate Cancer?



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Introduction

Metastatic castration-resistant prostate cancer (mCRPC) continues to pose significant therapeutic challenges in improving patient outcomes, necessitating the clinical exploration of novel approaches to treatment. In recent years, the utilization of androgen receptor pathway inhibitors (ARPi) in combination with poly (ADP-ribose) polymerase (PARP) inhibitors (PARPi) has emerged as a promising strategy. ARPi include androgen synthesis inhibitors and androgen receptor antagonists. These agents, such as abiraterone and enzalutamide, have previously demonstrated efficacy as standard-of-care treatments for mCRPC patients.^{1,2,3} PARPi, such as olaparib and rucaparib, which exploit synthetic lethality by targeting cancer cells with deficiencies in deoxyribonucleic acid (DNA) repair pathways, have previously shown efficacy in mCRPC patients with DNA repair gene mutations, particularly in those with BRCA 1/2 alterations.^{4,5} The combination of ARPi and PARPi targets both DNA repair mechanisms and androgen receptor signaling pathways, addressing two key drivers of prostate cancer progression. In this article, we will review the available evidence on the use of these combinations in patients with mCRPC, while addressing a controversial question “Is ARPi + PARPi a one size fits all in mCRPC?”

Currently Available Evidence

PROpel, MAGNITUDE, and TALAPRO-2 are the primary studies to consider when evaluating the evidence for the combination of ARPi plus PARPi in patients with mCRPC. A summary of trials is provided below which includes the study design (Table 1), patient baseline characteristics (Table 2), and outcomes (Table 3).

PROpel

The PROpel study was a phase III, randomized, double-blind, placebo-controlled, multicenter study that enrolled patients with mCRPC, independent of homologous recombination repair (HRR) mutation (HRRm) status. In order to be enrolled, patients had to have no prior treatment for mCRPC, no prior abiraterone (prior docetaxel for metastatic hormone-sensitive prostate cancer [mHSPC] was allowed), an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 or 1, and had to maintain ongoing androgen deprivation therapy (ADT). The patients were

randomly assigned (1:1) to receive abiraterone (1000 mg orally once daily) in combination with either olaparib (300 mg orally twice daily) or placebo. All patients received prednisone or prednisolone (5 mg orally twice daily). All patients continued therapy until disease progression, unacceptable toxicity, or withdrawal of consent; crossover was not permitted. The patients were stratified by distant metastasis type and prior docetaxel treatment for mHSPC. The primary endpoint for the study was radiographic progression-free survival (rPFS); secondary endpoints were HRRm prevalence (retrospectively assessed), overall survival (OS), and safety.⁶

The HRRm status for patients was assessed retrospectively using

biopsy and/or blood sampled at baseline using next generation sequencing (NGS). HRRm was defined as ≥ 1 mutation in HRR genes detected by either NGS assay (ATM, BRCA1, BRCA2, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L), non-HRRm was defined as no mutation detected by either NGS assay, and HRRm unknown was defined as no valid results. The HRRm status was established for 97.7% of patients including 535 patients (67.2%) by tumor tissue test, 734 (92.2%) by ctDNA test, and 778 (97.7%) by aggregated tumor tissue and ctDNA test results. The aggregate HRRm population included 226 patients (90 positive by tumor tissue and ctDNA, 28 positive by

tumor tissue, and 108 positive by ctDNA), and the non-HRRm population included 552 patients (328 negative by tumor tissue and ctDNA, 38 negative by tumor tissue, and 186 negative by ctDNA). In the abiraterone and olaparib arm, 27.8% of patients were HRRm, 69.9% of patients were non-HRRm, and 2.3% of patients were HRRm unknown. In the abiraterone and placebo arm, 29.0% of patients were HRRm, 68.8% of patients were non-HRRm, and 2.3% of patients were HRRm unknown.⁶

In the pre-planned primary analysis (data cutoff: July 30, 2021), the median rPFS was significantly longer in the abiraterone and olaparib arm than in the abiraterone and placebo arm (24.8 vs. 16.6 months [m]; hazard ratio [HR], 0.66; 95% confidence interval [CI], 0.54 to 0.81; $P < 0.001$), which was consistent with blinded independent central review (27.6 vs. 16.4 m; HR, 0.61; 95% CI, 0.49 to 0.74). A rPFS benefit was observed across all prespecified subgroups evaluated by investigator assessment, including the aggregate HRRm subgroup (NR vs. 13.9 m; HR, 0.50; 95% CI, 0.34 to 0.73) and the aggregate non-HRRm subgroup (24.1 vs. 19.0 m; HR, 0.76; 95% CI, 0.60 to 0.97); the benefit was maintained with blinded independent central review.⁶

"While the ODAC acknowledged the favorable benefit to risk profile for the treatment of BRCAm mCRPC, most members did not believe this translated to non-BRCAm or HRR undetermined mCRPC."

Table 1: Study designs across ARPi + PARPi combination studies with currently available data*

	MAGNITUDE ⁸	PROpel ^{6,7}	TALAPRO-2 ⁹
Intervention	Abiraterone in combination with either niraparib or placebo	Abiraterone in combination with either olaparib or placebo	Enzalutamide in combination with either talazoparib or placebo
Inclusion criteria	<ul style="list-style-type: none"> • 1L mCRPC • ECOG PS 0 - 1 • BPI-SF worst pain score ≤ 3 • Prior ARPi allowed, if ≤ 4 m (mCRPC) • HRRm only 	<ul style="list-style-type: none"> • 1L mCRPC • ECOG PS 0 - 1 • No prior abiraterone (mCRPC) • Other prior ARPi allowed, if stopped ≥ 12 m prior to randomization • All comers 	<ul style="list-style-type: none"> • 1L mCRPC • ECOG PS 0 - 1 • Prior ARTi and docetaxel allowed (mHSPC) • All comers
Molecular testing	Prospective	Retrospective	Prospective
Gene analysis	ATM, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, HDAC2, PALB2	ATM, BRCA1, BRCA2, BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, RAD51B, RAD51C, RAD51D, RAD54L	ATM, BRCA1, BRCA2, CDK12, CHEK2, FANCA, PALB2, ATR, RAD51C, NBN, MLH1, MRE11A
Stratification	<ul style="list-style-type: none"> • Prior docetaxel (mHSPC) • Prior ARTi (nmCRPC/mHSPC) • Prior ARTi (1L mCRPC) • HRR + cohort: BRCA 1/2 vs. non-BRCA 	<ul style="list-style-type: none"> • Site of metastases • Prior taxane chemotherapy (mHSPC) 	<ul style="list-style-type: none"> • HRR status • Prior ARTi or docetaxel (mHSPC)
Primary endpoint	rPFS in HRRm (central review)	rPFS in all comers (investigator-accessed)	rPFS in all comers (central review)

*The studies cannot be directly compared; currently no head-to-head studies exist.

Table 2: Patient baseline characteristics across ARPi + PARPi combination studies with currently available data*

	MAGNITUDE ⁸		PROpel ^{6,7}		TALAPRO-2 ⁹	
Intervention	Abiraterone + niraparib	Abiraterone + placebo	Abiraterone + olaparib	Abiraterone + placebo	Enzalutamide + talazoparib	Enzalutamide + placebo
Patients, number	212	211	399	397	402	403
HRRm, %	100	100	28	29	21	21
Median age (range), years	69 (45 - 100)	69 (43 - 88)	69 (43 - 91)	70 (46 - 88)	71 (41 - 90)	71 (36 - 91)
ECOG PS, number (%)						
• 0	130 (61)	146 (69)	286 (72)	272 (68)	259 (64)	271 (67)
• 1	82 (39)	65 (31)	112 (28)	124 (31)	143 (36)	132 (33)
Site of metastases, number (%)						
• Bone	183 (86.3)	170 (80.6)	349 (88)	339 (85)	349 (87)	342 (85)
• Visceral	51 (24.1)	39 (18.5)	55 (14)	60 (15)	57 (17)	77 (19)
Prior treatment, number (%)						
• Docetaxel for mHSPC	41 (19.3)	44 (20.9)	90 (23)	89 (22)	86 (21)	93 (23)
• ARPi for nmCRPC/mHSPC	8 (3.8)	5 (2.4)	1 (0.3)	-	21 (5)	25 (6)
• ARPi for first line mCRPC	50 (23.6)	48 (22.7)	-	-	-	-

*The studies cannot be directly compared; currently no head-to-head studies exist.

Table 3: rPFS benefit across ARPi + PARPi combination studies with currently available data*

	MAGNITUDE ⁸	PROpel ^{6,7}	TALAPRO-2 ⁹
All comers	-	24.8 m vs. 16.6 m HR 0.66 (95% CI 0.54 - 0.81) P<0.001	NR vs. 21.9 m HR 0.63 (95% CI 0.5 - 0.78) P<0.001
BRCA 1/2	16.6 m vs. 10.9 m HR 0.66 (95% CI 0.36 - 0.79) P=0.0014	NR vs. 8.4 m HR 0.23 (95% CI 0.12 - 0.43)	-
HRRm	16.5 m vs. 13.7 m HR 0.73 (95% CI 0.56 - 0.96) P=0.0217	NR vs. 13.9 m HR 0.50 (95% CI 0.34 - 0.73) P=0.0014	27.9 vs. 16.4 m HR 0.46 (95% CI 0.3 - 0.7) P<0.001
non-HRRm/unknown	-	24.1 m vs. 19 m HR 0.76 (95% CI 0.60 - 0.97)	NR vs. 22.5 m HR 0.70 (95% CI 0.54 - 0.89) P<0.001

*The studies cannot be directly compared; currently no head-to-head studies exist.

CLINICAL CONTROVERSIES (continued)

The median OS data were immature at the pre-planned primary analysis (28.6% maturity; HR, 0.86; 95% CI, 0.66 to 1.12; $P=0.29$).⁶ However, in the pre-planned final analysis (data cutoff: October 12, 2022), the median OS in the intention-to-treat (ITT) population was longer in the abiraterone and olaparib arm than in the abiraterone and placebo arm but did not meet statistical significance (maturity 47.9%, 42.1 vs. 34.7 m; HR, 0.81; 95% CI, 0.67 to 1.00, $P=0.0544$). The OS trend appears to be driven by patients with a BRCA mutation (BRCAm): median OS for BRCAm (NR vs. 23.0 m; HR, 0.29; 95% CI, 0.14 to 0.56), HRRm (NR vs. 28.5 m; HR, 0.66; 95% CI, 0.45 to 0.95), non-HRRm (42.1 vs. 38.9 m; HR, 0.89; 95% CI, 0.70 to 1.14), and non-BRCAm (39.6 vs. 38.0 m; HR, 0.91; 95% CI, 0.73 to 1.13). The median OS of > 42 m is the longest median reported to date in a phase III trial in first line mCRPC.⁷

The most common adverse events (AEs) in the abiraterone and olaparib arm were anemia, fatigue, and nausea. Anemia was the most common grade 3 or higher AE, occurring in 60 patients (15.1%) in the abiraterone and olaparib arm and 13 patients (3.3%) in the abiraterone and placebo arm. Fifty-five patients (13.8%) discontinued olaparib and 31 patients (7.8%) discontinued placebo because of an AE. Abiraterone discontinuation, as a result of AEs, occurred in 34 patients (8.5%) in the abiraterone and olaparib arm and 35 patients (8.8%) in the abiraterone and placebo arm. The rate of cardiovascular events (i.e., myocardial infarction, congestive heart failure, and ischemic stroke) was similar between the treatment arms. Twenty-six cases of pulmonary embolism occurred (6.5% of patients) in the abiraterone and olaparib arm and seven (1.8% of patients) in the abiraterone and placebo arm; one event in the abiraterone and olaparib arm was fatal.⁶

MAGNITUDE

The MAGNITUDE study was a phase III, randomized, double-blind, placebo-controlled, multicenter study that enrolled patients with mCRPC, pre-screened for HRR biomarker status (i.e., HRR- cohort or HRR+ cohort). In order to be enrolled, patients had to have no prior treatment for mCRPC (prior abiraterone for mCRPC was allowed if ≤ 4 m prior to randomization while completing HRR testing), no prior PARPi, an ECOG PS of 0 or 1, and had to maintain ongoing ADT. The patients in the HRR+ and HRR- cohorts were randomly assigned (1:1) to receive abiraterone (1000 mg orally once daily) in combination with either niraparib (200 mg orally once daily) or placebo. All patients received prednisone or prednisolone (5 mg orally twice daily) and continued therapy until disease progression, unacceptable toxicity, or death. The patients were stratified by prior docetaxel treatment for mHSPC, prior ARTi treatment for non-metastatic castration-resistant prostate cancer (nmCRPC) or mHSPC, and prior ARTi for first line (1L) mCRPC. Additionally, patients in the HRR+ cohort were stratified by BRCA 1/2 versus non-BRCA. The primary endpoint for the study was rPFS; secondary endpoints were OS and safety.⁸

The HRR status was determined using a required assay on tissue and/or blood samples. All patients must have been tested by both tissue and plasma to be randomly assigned in the HRR- cohort; patients had to have a gene alteration detected by ≥ 1 assay

to be eligible for the HRR+ cohort. The HRR+ cohort consisted of patients with either monoallelic or biallelic pathogenic gene alterations in ≥ 1 of the following: ATM, BRCA1, BRCA2, BRIP1, CDK12, CHEK2, FANCA, HDAC2, or PALB2. The HRR- cohort included patients who had no detectable alterations in any of these genes. A fertility analysis for the HRR- cohort was pre-planned when approximately 200 patients had been enrolled and approximately 125 composite end point events (i.e., the first of either PSA progression, radiographic progression, or death) had been observed.⁸

In the pre-planned primary analysis (data cutoff: October 8, 2021) within the HRR+ cohort, the median rPFS was significantly longer in the abiraterone and niraparib arm than in the abiraterone and placebo arm (16.5 vs. 13.7 m; HR, 0.73; 95% CI, 0.56 to 0.96; $P=0.022$). In the BRCA 1/2 subgroup, median rPFS was significantly longer in the abiraterone and niraparib arm than in the abiraterone and placebo arm (16.6 vs. 10.9 m; HR, 0.53; 95% CI, 0.36 to 0.79; $P=0.001$). Notably, an HR of 0.99 (95% CI, 0.68 to 1.44) was observed for rPFS in the subgroup of patients with HRR alterations other than BRCA 1/2. The median OS data were immature at the pre-planned primary analysis (46.3% maturity; HR, 0.94; 95% CI, 0.65 to 1.36; $P=0.73$).⁸

In the pre-planned fertility analysis within the HRR- cohort, 233 patients (abiraterone and niraparib, $n = 117$; abiraterone and placebo, $n = 116$) were evaluated for the composite end point of time to PSA progression and/or rPFS (HR, 1.09; 95% CI, 0.75 to 1.57; $P=0.66$). On the basis of the prespecified criteria, fertility was declared for the HRR- cohort in August 2020, which was closed to further enrollment. All patients in the HRR- cohort were unblinded, and patients randomly assigned to the abiraterone and niraparib arm were allowed to continue abiraterone and niraparib or abiraterone alone per the investigator's discretion; additional efficacy assessments were not performed once patients entered a safety data collection phase.⁸

The most common AEs in the abiraterone and niraparib arm were anemia, hypertension, and constipation. Anemia was the most common grade 3 or higher AE in the abiraterone and niraparib arm, occurring in 60 patients (28.3%). Hypertension was the most common grade 3 or higher AE in the abiraterone and placebo arm, occurring in 26 patients (12.3%). Twenty-three patients (10.8%) discontinued niraparib and 10 patients (4.7%) discontinued placebo because of an AE. Abiraterone discontinuation, as a result of AEs, occurred in 19 patients (9.0%) in the abiraterone and niraparib arm and 12 patients (5.7%) in the abiraterone and placebo arm. The rate of cardiovascular events (i.e., myocardial infarction, congestive heart failure, and ischemic stroke) was similar between the treatment arms. Thirty-eight patients died during study treatment: 19 in each arm. In patients who died due to AEs, infections (i.e., COVID-19, pneumonia) were the leading cause of death in the abiraterone and niraparib arm; cardiac disorders were the leading cause of death in the abiraterone and placebo arm.⁸

TALAPRO-2

The TALAPRO-2 study was a phase III, randomized, double-blind, placebo-controlled, multicenter study that enrolled patients with

mCRPC who were pre-screened for HRR biomarker status. The study included two cohorts: cohort 1 (all comers, including HRR nondeficient or unknown and HRRm) and cohort 2 (HRRm only). In order to be enrolled, patients had to have no prior treatment for mCRPC, an ECOG PS of 0 or 1, and had to maintain ongoing ADT. The patients in the two cohorts were randomly assigned (1:1) to receive enzalutamide (160 mg orally once daily) in combination with either talazoparib (0.5 mg orally once daily) or placebo. All patients continued therapy until disease progression, unacceptable toxicity, or death. The patients were also stratified by prior ARTi or docetaxel for mHSPC and HRR alteration status. The primary endpoint for the study was rPFS; secondary endpoints were OS and safety.⁹

The HRR status was determined using a required assay on tissue and/or blood samples; HRR status was prospectively informed by tumor tissue in 99.9% of patients. HRRm was demonstrated by either monoallelic or biallelic pathogenic gene alterations in ≥ 1 of the following: ATM, BRCA1, BRCA2, CDK12, CHEK2, FANCA, PALB2, ATR, RAD51C, NBN, MLH1, MRE11A; the non-HRRm cohort included patients who had no detectable alterations in any of these genes.⁹

In the pre-planned primary analysis of cohort 1 (all comers, including HRR nondeficient or unknown and HRRm), the median rPFS was significantly longer in the enzalutamide and talazoparib arm than in the enzalutamide and placebo arm (NR vs. 21.9 m; HR, 0.63; 95% CI, 0.51 to 0.78; $P < 0.001$), which was consistent with investigator-assessed rPFS (HR, 0.64; 95% CI, 0.50 to 0.81; $P < 0.001$). A rPFS benefit was observed across all prespecified subgroups evaluated by blinded independent central review, including the HRRm subgroup (27.9 vs. 16.4 m; HR, 0.46; 95% CI, 0.30 to 0.70; $P < 0.001$) and the aggregate HRR nondeficient or unknown subgroup (NR vs. 22.5 m; HR, 0.70; 95% CI, 0.54 to 0.89; $P = 0.004$). The benefit was maintained in the HRR nondeficient cohort by prospective tumor tissue testing (NR vs. 22.1 m; HR, 0.66; 95% CI, 0.49 to 0.91; $P = 0.009$). The median OS data were immature at the pre-planned primary analysis (31% maturity; 36.4 vs. NR m; HR, 0.89; 95% CI, 0.69 to 1.14; $P = 0.35$).⁹

The most common AEs in the enzalutamide and talazoparib arm were anemia, neutropenia, and fatigue. Anemia was the most common grade 3 or higher AE, occurring in 185 patients (46.5%) in the enzalutamide and talazoparib arm and 17 patients (4.2%) in the enzalutamide and placebo arm. Seventy-six patients (19.1%) discontinued talazoparib and 49 patients (12.2%) discontinued placebo because of an AE. Ten cases of pulmonary embolism occurred (2.5% of patients) in the enzalutamide and talazoparib

arm and three (0.7% of patients) in the enzalutamide and placebo arm. Myelodysplastic syndrome was reported in 1 patient and acute myeloid leukemia was reported in 1 patient, both in the enzalutamide and talazoparib arm.⁹

Recent Regulatory Discussions

The US Food and Drug Administration (FDA) Oncologic Drugs Advisory Committee (ODAC) recently met to discuss the olaparib supplemental new drug application for the treatment of adult patients with mCRPC in combination with abiraterone and prednisone or prednisolone. While the ODAC acknowledged the favorable benefit to risk profile for the treatment of BRCAm mCRPC, most members did not believe this translated to non-BRCAm or HRR undetermined mCRPC. The committee raised concerns for overtreatment in the non-BRCAm subgroup, potentially exposing this population to significant toxicity without evidence of efficacy. In the briefing document to the committee, the FDA stated that olaparib may represent a “toxic placebo” in non-BRCAm patients. Ultimately, the committee voted 11 to 1, with 1 abstention, that the indication should be limited to patients with BRCAm disease.¹⁰ The decision of the committee is likely to have a significant influence on forthcoming studies, underscoring the importance of genetic testing and personalized medicine in identifying patients who are most likely to benefit from PARPi combinations, while further highlighting the need for ongoing research in patients with non-HRRm disease.

Conclusion

The combination of ARPi and PARPi has demonstrated substantial clinical benefit in mCRPC patients with specific genetic alterations, especially BRCA 1/2 alterations, as evidenced by the PROpel, MAGNITUDE, and TALAPRO-2 studies.⁶⁻⁹ The combination has shown improvement in rPFS along with a manageable safety profile consistent with the known side effects of the individual agents. However, controversy remains regarding the use of the combination in patients without known mutations. The currently available evidence suggests potential efficacy of the combination,^{6-7,9} with ongoing research aiming to elucidate the potential benefit of PARPis through the investigation with alternative combination therapies.¹¹ However, the recent recommendation from the ODAC suggests well designed trials and adequate subgroup analyses are essential for ARTi plus PARPi combination trials.¹⁰ As the field of precision medicine continues to evolve, the design and execution of prospective trials comparing different PARPi combination regimens, utilizing patient-reported outcomes, are needed to better define the patient population that would benefit most from this treatment approach. ●●

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Cancer breakthroughs take time. That's why we work at such a furious pace.

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Board Update

Support, Participate, Achieve, and Celebrate



LeAnne Kennedy, PharmD, BCOP, CPP, FHOPA
HOPA President (2023-2024)
Oncology Clinical Manager
Atrium Health Wake Forest Baptist
Winston-Salem, NC

As a new committee year begins, it's a good time to set the stage for the future – and pause to celebrate recent successes.

First, I want to thank Heidi Finnes, Immediate Past President for her guidance and support and the entire Board of Directors for their continued leadership. I also want to thank Larry Buie, Past President, and Emily Mackler and Lisa Davis, Board Members At Large, for their years of service on the HOPA Board of Directors. Please also join me in welcoming our newest Board Members, Jason Bergsbaken and Sol Atienza.

Mostly, I want to thank all HOPA members for continuing to optimize cancer care amidst unparalleled challenges, from burnout to drug shortages. I'm honored to continue HOPA's commitment to Diversity, Equity, and Inclusion and Wellness and look forward to working alongside members to improve oncology clinical trials and provide recommendations for managing drug shortages.

Looking Back

Although it would be difficult to list all of HOPA's recent success on a single page, here are some highlights from the past year.

- **2023-2026 Strategic Plan.** HOPA's new strategic imperatives were rolled out recently and include: Education, Professional Practice, Quality Research, Advocacy & Awareness, and Organizational Excellence. There is truly a meaningful role for all members to play in driving HOPA forward.
- **Annual Conference 2023 (AC23).** Close to 1,600 (a new record!) of us gathered in Phoenix at the end of March for AC23 and the chance to "Reconnect, Rebuild, and Reimagine" hematology/oncology pharmacy in a post-COVID-19 world.
- **Online Resources for Self- and Group-Improvement.** Toolkits were launched by both the Wellness Task Force and the Diversity, Equity, and Inclusion Committee, making self-assessments and resources available to HOPA members in one, online place.
- **Quality Training Program.** The first set of cohorts for the HOPA/ASCO Quality Training Program are midway through their quality research projects and preparing to present at Practice Management 2023 in Austin on November 9-10.

Moving Ahead

My goals for the coming year focus on providing support and improving member participation, while leaving space for acknowledging and celebrating achievement.

Goal #1: Be the Home for Residents

My vision is for HOPA to create meaning for hematology/oncology residents. We have already begun engaging with strategic partners to create information sessions about both traditional and non-traditional careers. Our Special Interest Group for Residency Program Directors is being reinvigorated so we can better support the RPDs who support the trainees. And, a number of learning and networking sessions geared toward residents are already being planned for Annual Conference 2024.

Goal #2: Build Community

This year, our committee structure makes room for advisory groups and we welcome caregivers to the Patient Advisory Panel. Our inaugural class of HOPAmbassadors will soon be selected and trained to demonstrate the value of hematology/oncology pharmacists within schools of pharmacy and cancer care settings, as well as to patient-advocacy groups and elected officials. We will continue our quarterly Town Halls so you have a chance to see how you can play a role in our strategic plan.

Goal #3: Create Belonging

One of the biggest benefits of a professional membership is the type of support we are all uniquely qualified to lend each other. Networking and mentorship often result in feelings of stability and belonging. That's why more roundtable discussions are planned during conferences and events. It is also why the HOPA Mentorship Program is expanding significantly to encompass members at all career levels.

Thank you, HOPA members, for your ongoing commitment to cancer treatment and patient care. Please save the dates of September 18 for our next Hill Day when our Advocacy team goes to Washington DC, and November 9-10 for Practice Management 2023 in Austin. I look forward to seeing you there. ●●



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A wide-angle photograph of the Austin skyline at dusk. The sky is a mix of orange, yellow, and blue. Numerous skyscrapers are visible, many with their windows lit up. The buildings are silhouetted against the bright sky, and the lights from the buildings create a warm, glowing effect.

HOPA PRACTICE MANAGEMENT 2023 #PM2023

November 9-10, 2023 in Austin, Texas

Two days of CE and networking opportunities in an amazing city
filled with live music.

Early Bird Registration in mid-August!

