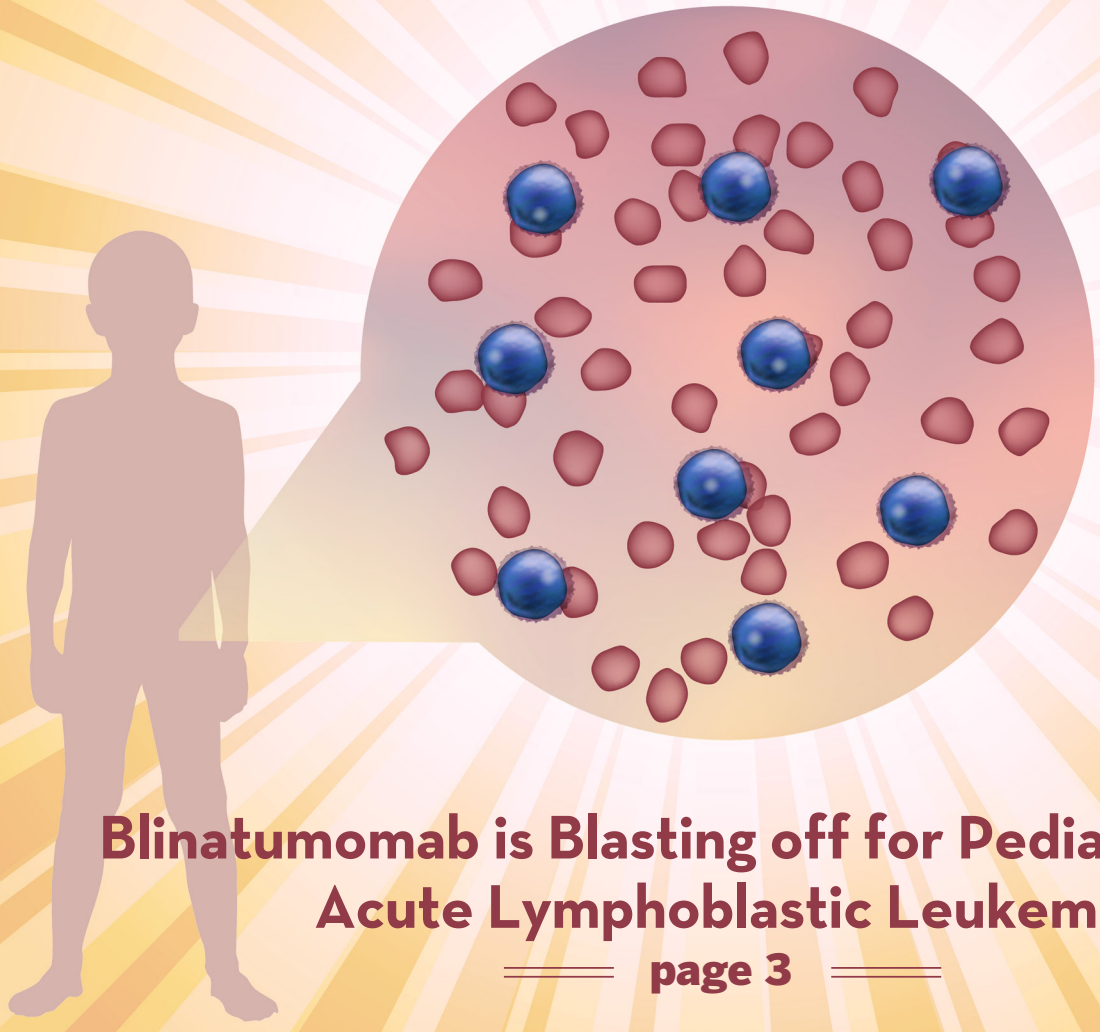
HOPA NEWS

Pharmacists Optimizing Cancer Care

VOLUME 22 | ISSUE 2



Blinatumomab is Blasting off for Pediatric B-cell Acute Lymphoblastic Leukemia

page 3

HOPA
Hematology/Oncology
Pharmacy Association

VOLUME 22 | ISSUE 2

Send administrative correspondence or letters to the editor to HOPA, 555 East Wells Street, Suite 1100, Milwaukee, WI 53202, or e-mail info@hoparx.org.

HOPA News is published by the Hematology/Oncology Pharmacy Association.

HOPA-0425-506

HOPA
Hematology/Oncology Pharmacy Association

Pharmacists Optimizing Cancer Care®

CONTENTS

FEATURE

Blinatumomab is Blasting off for Pediatric B-cell Acute Lymphoblastic Leukemia

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Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy.[1] Incredible improvements in treatment have been made in the past several decades that have led to 5-year overall survival (OS) rates in excess of 90% for standard risk B-cell patients, but improvement has stagnated in recent years.[1] Unfortunately, survival rates for patients with relapsed disease are still poor with 5-year OS estimated to be about 50%.[2] Recent frontline trials from the Children's Oncology Group (COG) have aimed to decrease relapse rates and improve survival outcomes. AALL1731, the most recent frontline COG trial for standard risk B-cell ALL (B-ALL), sought to do so with the addition of blinatumomab.[3]

Blinatumomab is a bispecific T-cell engager that targets CD3 on T-cells and directs them to CD19-expressing B cells to induce B cell lysis.[3,4] It was first FDA-approved for adults with relapsed/refractory Philadelphia chromosome (Ph)-negative B-cell ALL in 2014.[5] Since that time, approval has expanded to include Ph-positive relapsed/refractory disease, CD19-positive B-ALL with minimal residual disease (MRD) positivity, CD19-positive B-ALL in the consolidation phase of multiphase chemotherapy, and in pediatric patients 1 month of age and older for the conditions already described.[5] Key trials are summarized in table 1.[6–8]

"Recent frontline trials from the Children's Oncology Group (COG) have aimed to decrease relapse rates and improve survival outcomes."

AALL1731

Children with newly diagnosed standard risk B-ALL [age ≥ 1 year and <10 years, white blood cell count <50,000 per microliter, absence of testicular disease and frank central nervous system (CNS) disease] were eligible for enrollment on AALL1731.[3] Patients were further sub-classified into standard risk-favorable (SR-Fav), standard risk-average (SR-Avg), and standard risk-high (SR-High) groups based on cytogenetics, peripheral blood MRD status at day 8 of induction, and bone marrow MRD status at day 29 of induction.[3] Patients with SR-Avg and SR-High disease were randomized to receive two non-sequential blocks of blinatumomab (15 mcg/m^2/day continuously for 28 days) in addition to standard chemotherapy or chemotherapy alone.[3] Blinatumomab blocks were administered before and after interim maintenance I, and the overall treatment schema is depicted in figure 1.[3] Patients with SR-Fav disease non-randomly received chemotherapy alone.[3]

The primary end point for AALL1731 was disease free survival (DFS), defined as time from randomization to relapse, second malignant neoplasm, or death.[3] At the planned interim analysis in July of 2024, 1440 patients had been randomized. Estimated 3-year DFS was 96% in the blinatumomab arm compared to 87.9% with chemotherapy alone ($p<0.001$).[3] Other key findings include estimated 3-year overall survival (OS) of 98.4% with blinatumomab and 97.1% with chemotherapy alone, and the estimated 3-year incidence of relapse was 3.3% with blinatumomab vs. 11.8% with chemotherapy alone.[3] The DFS results exceeded the prespecified stopping criterion, and the trial was closed early.[3]

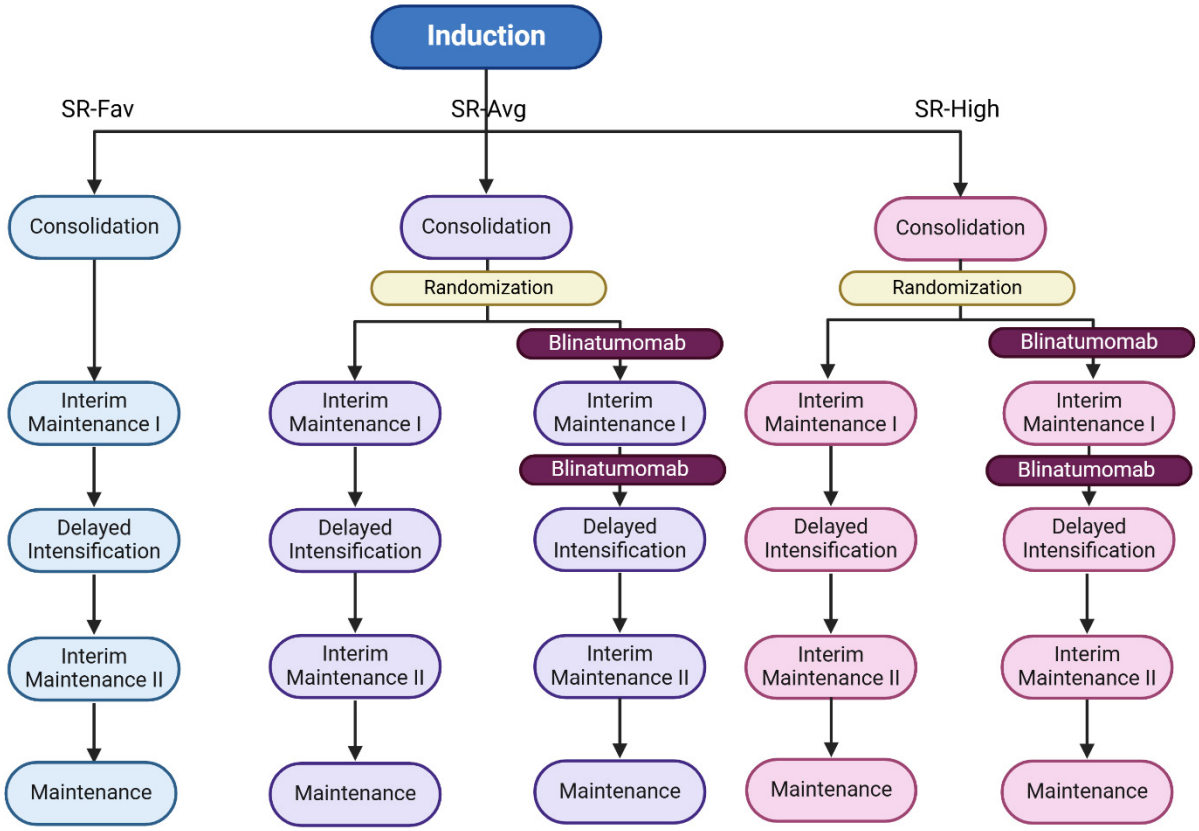
In both arms, DFS and OS were very high.[3] Although the OS was similar in the two groups, the significantly improved DFS and reduction of estimated relapse risk are practice-changing. It is also worth noting that the reduction in relapse risk primarily affects those relapses at the highest risk for poor outcomes: early, isolated bone marrow relapses.[2,3] Blinatumomab benefit was preserved across risk status. In the SR-Avg group, the 3-year DFS was 97.5% vs. 90.2% with 3-year OS 100% vs 98.4% for blinatumomab vs chemotherapy alone, respectively.[3] For the SR-High group, the 3-year DFS was 94.1% vs. 84.8% with 3-year OS 96.1% vs. 95.3% for blinatumomab vs. chemotherapy alone, respectively.[3] In summary, AALL1731 demonstrated a significant improvement in

Table 1: Summary of Blinatumomab in Relapsed/Refractory and MRD+ ALL

Study	Population	Intervention	Results
TOWER (Kantarjian H, et al.)	Adult patients with Philadelphia negative B-cell ALL with relapsed/ refractory disease	Blinatumomab versus SOC chemotherapy	Blinatumomab: Median OS 7.7 months SOC chemotherapy: Median OS: 4 months P-value = 0.01
AALL1331 (Brown PA, et al.)	Children, adolescents, and young adults with B-cell ALL in first relapse	All patients received chemotherapy reinduction therapy. After reinduction, patients were randomized to blinatumomab versus chemotherapy	Blinatumomab: 2-year DFS: 54% Chemotherapy: 2-year DFS: 39% 1-sided p-value = 0.03
BLAST (Gokbuget N, et al.)	Adults who received at least three blocks of chemotherapy with MRD · 0.1%	Single-arm trial Up to four cycles of blinatumomab	78% achieved a complete MRD response after cycle 1

Abbreviations: ALL: Acute lymphoblastic leukemia; DFS: Disease free survival; OS: Overall survival; MRD: Minimal residual disease; SOC: Standard of care

Figure 1: AALL1731 Schema (image created with BioRender.com)



Abbreviations: SR-Avg: Standard risk-average, SR-High: Standard risk-high SR-Fav: Standard risk-favorable

DFS with the addition of blinatumomab for SR-Avg and SR-High childhood ALL.[3] Based on these findings, upfront blinatumomab plus chemotherapy should be considered for patients who meet SR-Avg and SR-High criteria.

Additional Studies of Upfront Blinatumomab

AALL1731 is the first trial to show benefit from the addition of blinatumomab in the upfront setting in childhood ALL, although there have been exciting results in the infant and adult populations. In 2023, van der Sluis and colleagues published the results of blinatumomab plus chemotherapy for infant ALL.[9,10] Infant ALL is defined as a diagnosis of ALL in patients less than one year of age and historically has had much worse outcomes when compared to childhood ALL.[10,11] Many groups have attempted to improve outcomes through intensification of treatment or through the addition of novel agents.[12–17] Unfortunately, despite several attempts, outcomes still remain poor with 6-year OS estimates around 60%, especially in infants with *KMT2A*-rearranged disease.[10,11]

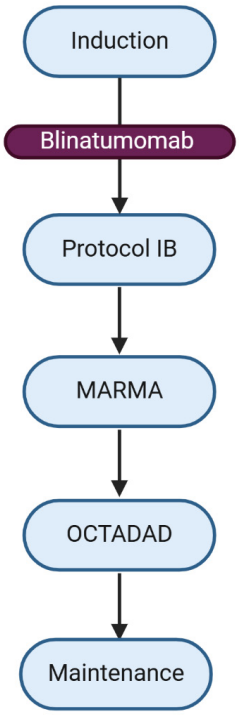
Infants with *KMT2A* rearrangement were eligible for the phase 2 trial reported by van der Sluis and colleagues.[10] This trial utilized the Interfant-06 chemotherapy backbone (figure 2) and added a single block of blinatumomab (15 mcg/m^2/day continuously for 28 days) between induction and protocol IB.[10,13] This was a small study that included 30 patients and did not have a comparator arm.[10] The primary outcome was clinically relevant toxic effects.[10] The 2-year DFS was 81.6% and 2-year OS was 93.3%.[10] While not a direct comparison, Interfant-06 reported a 2-year event free survival (EFS) of 42.4% and a 2-year OS of 54.5%.[10,13] The addition of a single block of blinatumomab to infants with *KMT2A*-rearranged ALL seems to lead to major improvements in the treatment of infant ALL. Data was only collected for 2 years, but infants with *KMT2A*-rearranged disease tend to have early relapses.[11] Long-term and real-world data are still needed to confirm these promising results.

The other major publication that has evaluated blinatumomab in the upfront setting for Ph-negative B-ALL is E1910. Briefly, the results of E1910 were published in 2024 by Litzow and colleagues.[9] Patients between the ages of 30 and 70 with Ph-negative ALL were eligible for this trial.[9] Patients who were MRD-negative after induction and intensification chemotherapy were randomized to receive chemotherapy alone vs. chemotherapy plus four cycles of blinatumomab.[9] The primary end point was OS.[9] At a prespecified interim analysis, 3-year OS was 85% with blinatumomab vs. 68% with chemotherapy alone (p=0.002).[9]

Safety and Practical Considerations

In addition to the promising efficacy data, blinatumomab is also generally well tolerated.[4] Blinatumomab has well-known, potentially severe, adverse effects of cytokine release syndrome (CRS) and neurotoxicity.[4] For these reasons, patients should be monitored closely, especially at initiation of blinatumomab. In AALL1731, one

Figure 2: Blinatumomab plus Chemotherapy for Infant ALL Schema



Agents used in each phase:

- Induction: prednisone prophase, dexamethasone, vincristine, cytarabine, daunorubicin, pegaspargase, intrathecal chemotherapy
- Protocol IB: cyclophosphamide, mercaptopurine, cytarabine, intrathecal chemotherapy
- MARMA: mercaptopurine, high-dose methotrexate, high-dose cytarabine, pegaspargase, intrathecal chemotherapy
- OCTADAD: dexamethasone, thioguanine, vincristine, daunorubicin, pegaspargase, cytarabine, cyclophosphamide, intrathecal chemotherapy
- Maintenance: mercaptopurine, methotrexate, intrathecal chemotherapy

SR-Avg patient (0.3%) and one SR-High patient (0.4%) developed CRS in the blinatumomab arms.[3] Additionally, 14 (2.2%) blinatumomab treated patients experienced a seizure and five (0.8%) experienced a non-seizure central nervous system (CNS) event compared to 14 (2.1%) and seven (1.1%) in the chemotherapy alone arms, respectively.[3] SR-Avg patients randomized to blinatumomab had a higher incidence of sepsis or catheter related infections with 52 patients (14.8%) in the blinatumomab cohort compared to 19 patients (5.1%) in the chemotherapy alone arm ($p<0.001$).[3] Interestingly, this significant difference was not seen in the SR-High arms.[3] There were no deaths during the blinatumomab cycles.[3]

In the infant trial, blinatumomab was similarly well-tolerated.[10] All 30 infants were able to complete the blinatumomab cycle, although one patient had a two-day interruption due to hypertensive crisis.[10] Three patients experienced grade one fever, and no patients experienced neurotoxicity.[10] Additionally, there were no deaths during the blinatumomab cycle.[10]

With these practice-changing results, there are some practical considerations. These studies all added blinatumomab to existing chemotherapy backbones, meaning that addition of blinatumomab may result in a longer total duration of treatment—though AALL1731 did truncate the duration of maintenance in the blinatumomab arms to maintain same total duration of therapy.[3] Additionally, intrathecal chemotherapy administration schedules may require minor adjustments. In AALL1731, intrathecal methotrexate was administered at the beginning of each of the blinatumomab blocks.[3] To deliver the same total number of intrathecal chemotherapy doses across study arms, two intrathecal methotrexate doses were removed from maintenance.[3] There have also been numerous changes in recommendations for compounding/administration of blinatumomab. Blinatumomab can be administered via 24-hour, 48-hour, 72-hour, 96-hour, and 7-day preparations.[5] Previously, preservatives were only recommended for the 7-day preparations, and due to the addition of preservatives, 7-day bags were initially not recommended for patients who weighed less than 22 kilograms.[5] Recent package insert updates include preservatives in the 72-hour and 96-hour preparations, with the weight requirement now lowered to 5.4 kilograms.[5] Therefore, patients who weigh less than 5.4 kilograms are now limited to the 24-hour and 48-hour preparations, likely resulting in more frequent appointments for bag changes.[5] Due to the risk for CRS, dexamethasone is often recommended prior to initiation of a blinatumomab cycle, however, this is not always the case. For example, E1910 required dexamethasone at the beginning of each cycle, but AALL1731 only required dexamethasone at the beginning of the first blinatumomab cycle.[3,9] One final consideration is that continuous cycles of blinatumomab have been reported to result in T-cell exhaustion and decreased blinatumomab efficacy.[18] AALL1731 spaced out the two blinatumomab blocks by several weeks with a chemotherapy cycle (interim maintenance I) between the two blocks of therapy.[3] E1910 grouped cycles 1 and 2 and cycles 3 and 4 together but provided a 2 week break between blinatumomab cycles.[9] For patients who are midway through treatment who would likely benefit from the addition of blinatumomab but are past the timepoints used for blinatumomab blocks in AALL1731, this should be considered when determining the best place in treatment to add blinatumomab if multiple blocks will be used.

As with all new data, we are left with some remaining questions. First, what is the optimal number of blinatumomab cycles? The infant trial included one, AALL1731 included two, and E1910 included four, but all were compared to zero. Blinatumomab use certainly comes with a high price tag, and while it is generally well-tolerated, it also still comes with a risk for adverse effects and logistical burden.[19] It would be ideal if fewer blocks could be used without affecting efficacy, but at this point in time, we do not have comparative data. On a similar note, with the addition of blinatumomab, can we remove more toxic chemotherapy without sacrificing DFS and OS? The hope is that use of upfront blinatumomab will reduce the risk for relapse, but how will upfront blinatumomab affect its use in the relapsed refractory setting? Finally, these studies are still limited in their long term follow up data – will these results stand in the setting of longer follow up?

Questions specifically for infants: Should blinatumomab be explored in the *KMT2A*-wildtype setting? Are the results promising enough in the *KMT2A*-rearranged setting to justify extrapolating the data? Outcomes tend to be more favorable in patients with *KMT2A*-wildtype disease with Interfant-99 finding a 4-year EFS of 74%, but these are still far less ideal than outcomes in childhood ALL.[12]

Question specifically for childhood ALL: How do we best treat our high-risk children? There have been recommendations that high-risk pediatric patients be treated with blinatumomab based on the findings of E1910 and AALL1731, but at this point, we do not have upfront blinatumomab data for these patients.

In conclusion, blinatumomab previously made a name for itself in the relapsed/refractory and MRD+ settings but has now expanded to the upfront settings. Blinatumomab plus chemotherapy for infant ALL and AALL1731 are practice-changing studies, and as a result blinatumomab should be included in treatment of KMT2A-rearranged infant ALL and SR-Avg and SR-High childhood ALL. ●●

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No Higher Calling: Reflections on a Career in Higher Education

Amber B. Clemmons, Pharm.D., BCOP, FHOPA
Clinical Professor, University of Georgia College of Pharmacy

When most people think of academia, they imagine a professor standing in front of a classroom or quietly writing grants and papers alone in an office. But the reality is far more dynamic – and for me, more fulfilling.

During rotations as a student and resident, I found deep satisfaction and joy in the clinical and interpersonal aspects of direct patient care. But I also found excitement in the behind-the-scenes work—the policies, research projects, and in-service presentations that shaped healthcare on a larger scale. As an admittedly introverted and Type-A person, I realized that these "deliverables" weren't just fulfilling to work on— they were making a lasting difference. I was drawn to the intellectual challenge of shaping systems with immense satisfaction in knowing that my contributions had a broader impact.

"Pursuing a career in academia doesn't mean abandoning your passion for patient care— it means integrating it with teaching and research to shape the future of pharmacy."

In these early years, I heard from many mentors and preceptors who offered the same advice: "Practice for a few years, then transition into academia." While this sentiment was well-meaning, I have come to realize it reflects a misconception: that you cannot be a 'real' clinician if you are in academia. Even now, when we interview residency candidates, it's common to hear, "I want to work as an oncology pharmacy specialist and then move into academia," with the assumption that one must first 'complete' a clinical role before transitioning into academia. However, here's the truth I have learned; it is possible, even advantageous, to start your career in academia and still be integrated into clinical practice. Furthermore, the sentiment offered by my mentors also failed to recognize that many clinical specialists not in academia contribute substantially to teaching and scholarly efforts.

Starting out in academia was one of the best decisions I ever made. My role allowed me to have the so called 'off service' protected time to pursue research and scholarly activities and to focus on creating and assessing teaching content. Non-faculty certainly can pursue these same activities but often are limited in the amount of time allotted within their work hours. Another unique advantage of starting a career in academia is the ability to apply for early-career grants—opportunities that become less available as you gain years of clinical experience. Clinical faculty such as myself are a part of daily patient interactions usually through clinic or inpatient service assignment that requires ~30-60% of time commitment (e.g., two clinic days a week or on-service for 25 weeks of a year). Remaining closely connected to patient care enhances scholarly pursuits to be relevant, timely, and responsive to the current needs of patients and oncology practice. While some pharmacists transition into academia later in their careers to focus solely on teaching or administration, this can unintentionally deprive students of the opportunity to learn from instructors who bring real-world insights into the classroom. Oncology pharmacists who are considering transitioning to academia should not be discouraged by my advice for current residents to consider academia immediately. Many successful clinical faculty come to universities after working for years in a hospital-based position. The benefit of doing this is that they already possess the real-world clinical knowledge to impart on students, offer unique insight into curricular design aligned with the current and future practice of pharmacy, and leverage their prior scholarship, leadership, and service experience (e.g., organizational involvement) to advance through academic ranks more quickly.

You may be thinking, "Why not leverage clinical pharmacists to volunteer as adjunct faculty?" While their contributions are undoubtedly invaluable, focused teaching time for volunteer faculty often gets squeezed between already demanding clinical responsibilities. Developing quality content, creating assessments, and keeping up with the latest teaching methodologies takes more time than most adjuncts can offer. Dedicated clinical faculty members overseeing the courses and content have the focused time to ensure courses are structured and executed effectively. Teaching isn't just about knowledge— it's about how we impart it, how we assess student progress, and how we continuously improve as educators. Clinical faculty members, embedded throughout the curriculum, have the time and focus to engage in ongoing scholarship of teaching and learning. They can integrate new technologies, enhance assessment methods, and contribute

Reflection on Personal Impact and Growth

in meaningful ways that adjunct faculty—with their already full schedules—understandably may not be able to prioritize. However, these adjunct faculty can 'follow the lead' of a dedicated full-time faculty member who has completed those tasks on their behalf, structuring the courses accordingly.

As of February 2025, there are 4,519 board-certified oncology pharmacists (BCOP). However, there is a growing need for more oncology pharmacists to assume faculty positions. Out of the thousands of registered HOPA members, only 93 self-identify as faculty members across the nation. We need more oncology pharmacists to take on faculty positions. The future of oncology pharmacy begins with the next generation of students. To increase the number of oncology pharmacists, we must first ignite their passion for the field. Dedicated oncology faculty are essential—not only to inspire students to pursue oncology pharmacy, but also to ensure that every pharmacist, whether they specialize in oncology or not, is equipped to understand the rapidly evolving therapies and their monitoring needs. As we know, our colleagues in other areas (e.g., emergency medicine, cardiology, infectious diseases, etc.) require baseline oncology knowledge when providing comprehensive care for cancer patients too.

Reflecting on my own journey, I have a few key pieces of advice for anyone considering a career in academia.

- ✓ First, *don't wait* to start your career in academia. You can be (or continue to be) an exceptional clinician and an impactful educator and researcher at the same time. Being in academia doesn't mean stepping away from patient care. In fact, the two complement each other. The role of a faculty member is similar to that of a clinical pharmacy specialist, but with a different balance of teaching, research, and patient care responsibilities. This mix is what makes being a faculty member so dynamic and rewarding. You don't have to wait for years of clinical practice to begin making a difference in the classroom, and you do not have to sacrifice your love of patient care to teach either.
- ✓ Second, it is crucial to establish a clear arrangement between your college of pharmacy and your patient care institution. Having precise written agreements stating your patient care responsibilities, time commitments, and additional duties (such as hospital committees, policy work, staffing or cross-coverage duties) is essential and should be reviewed regularly. A successful practice site should meet both the needs of the institution and allow ample time for teaching, research, and other scholarly endeavors. Finding the right balance is key, and there is no one-size-fits-all model for what a practice site should look like. But when it works, it's incredibly fulfilling for both you and the institution, which ultimately benefits students and patients alike.
- ✓ Be aware of the "other" workload in academia. While patient care, teaching, and research are the commonly recognized components, a significant amount of other behind-the-scenes work exists. Faculty must carry administrative and service workloads beyond what a non-academic pharmacist will be required to complete. Course management (oh the volume of student emails!), college or university committees, promotion and tenure reviews, accreditation tasks, instructor evaluations, etc. can take up a fair amount of time. There is little glory, accolades, or often personal satisfaction in these more mundane tasks, but they are essential for the student experience and functioning of a college/school of pharmacy.
- ✓ Lastly, focus on building strong, supportive relationships with your colleagues and with the managers at the practice site. Relationships must be built on transparency, mutual respect, give and take, and understanding of each party's needs and restrictions. Solid relationships are invaluable in helping you balance your academic responsibilities with clinical duties.
- ✓ In terms of research, I have found that successful clinical faculty often focus on a narrow area within their portfolio. This focus should align with the promotion and tenure criteria at your college and with your own professional goals. If you're not inclined toward research, find a college that supports your other areas of interest where research may not be a central component of your promotion criteria.

For those of you considering this path, don't let the idea that academia is "for later" hold you back. Pursuing a career in academia doesn't mean abandoning your passion for patient care— it means integrating it with teaching and research to shape the future of pharmacy. You don't have to choose between being a dedicated clinician and a passionate educator. You can be both—and in doing so, you'll inspire the next generation of oncology pharmacists to do the same. ●●

Development of Clinical Support Decision Pathways for Symptom Management

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Clinical decision support (CDS) pathways create a framework to optimize symptom management. Dr. Leila Rostamnjad, Clinical Pharmacy Manager at Dana-Farber Cancer Institute provided the Dana-Farber experience with implementation of symptom management CDS during the March 2025 HOPA Virtual Practice Management Series webinar. This webinar series is a new opportunity for the HOPA community to develop leadership skills and share practice management-related educational content. This article highlights the importance of the role of pharmacy leadership and the strategies utilized by Dr. Rostamnjad to ensure successful implementation of symptom management pathways into existing clinical treatment pathways.

CDS pathways promote evidence-based interdisciplinary practice and can offer the advantages of reducing cost, enhancing efficiency, and improving standardization of care. Three important aspects of oncology patient care must be considered when creating and implementing CDS symptom management pathways. First, cancer patients experience a variety of symptoms caused by their disease and/or the treatment modalities used. Second, symptom control impacts patient quality of life. And third, clinical pathways may improve adherence by optimizing chemotherapy treatments, reducing complications, and improving symptom management, patient survival, and quality of life.[1]

A national healthcare trend of increased clinic staff turnover is problematic and leads to fragmentation of patient care. Many cancer programs are comprised of different practice locations across a geographic region, adding to the likelihood of practice variability. As cancer programs expand to additional sites, documentation practices within the electronic health record (EHR) may become more varied, leading to staff confusion regarding charted patient information. The incorporation of CDS pathways may help overcome these barriers by guiding the end user to apply the correct institutional standard as the grade of toxicity is assessed, thus enhancing the quality of patient care via standardization and improved efficiency.

The oncology patient population frequently requires symptom management interventions from either a drug toxicity or a disease state complication. Ideally, the oncology team works to maximize the ability of the patient to remain in the outpatient setting, in part by intervening early. The benefit realized from CDS pathway implementation is the creation of standardized workflows, which can reduce practice variability and improve time to intervention. CDS pathways are known to facilitate improvement in quality of care, provide measurable results, and increase adherence to evidence-based practice models. An additional benefit seen with some CDS pathway models is increased clinical trial enrollment, as the pathway will identify open clinical trials as treatment options.[2]

For organizations that want to create a symptom management CDS pathway platform, a multi-step process is required that includes development of a structured, multidisciplinary approach; creation of an institutional algorithm with a stepwise treatment approach; and identification of target population. The institution can facilitate the development process by eliminating possible barriers such as staff conflicts of interest and by clearly identifying the methodology to be used for pathway creation, including cost considerations. The appeals process for off-label pathways and complex patient scenarios should also be considered. The incorporation of pathways for rare cancers and inpatient chemotherapy regimens is also important to the process. The supportive care medications for treatment plans in the acute care settings can vary, and incorporation of appropriate treatment algorithms into the process is required.

"The benefit realized from CDS pathway implementation is the creation of standardized workflows, which can reduce practice variability and improve time to intervention."

In the Practice Management webinar, Dr. Rostamnjad described the importance of developing symptom management pathways anticipated to be required for specific treatment regimens as well as pathways for recurrent or chronic symptom management. The Dana-Farber pathway project aimed to improve patient outcomes and support clinical operations by developing standardized clinical and patient decision support pathways to manage symptoms or triage interventions. Each pathway is based on levels of evidence in the literature combined with patient access to the intervention, including over-the-counter medications, non-pharmacologic treatments such as heat or ice, and prescription medications. Prior to implementation, each pathway is approved by the medical staff interdisciplinary committee. For consistency, pathways are built from templates using structured language and input entry points, standardized assessment rating scales, and defined patient

evaluation frequencies. The pathways are configured to evaluate each patient's risk and to define an intervention specific to that patient. The planned intervention will indicate the optimal patient setting including home management, outpatient treatment, or escalation to a higher-level assessment that includes transfer of the patient from the outpatient setting to the acute care setting.

Dana-Farber has built two evidence-based supportive care pathways in their EHR (EPIC): 1) a pre-emptive pathway to avoid symptoms from treatment regimens, and 2) a pathway for the treatment of disease-induced symptoms. Cancer patients routinely require symptom management for anxiety, constipation, diarrhea, nausea and vomiting, dermatologic adverse events, fatigue, headache, insomnia, mucositis, and pain. As the pathways are created, a development prioritization schedule is identified. Once the pathways are approved, staff education and training will be required and included in the institution's implementation plan.

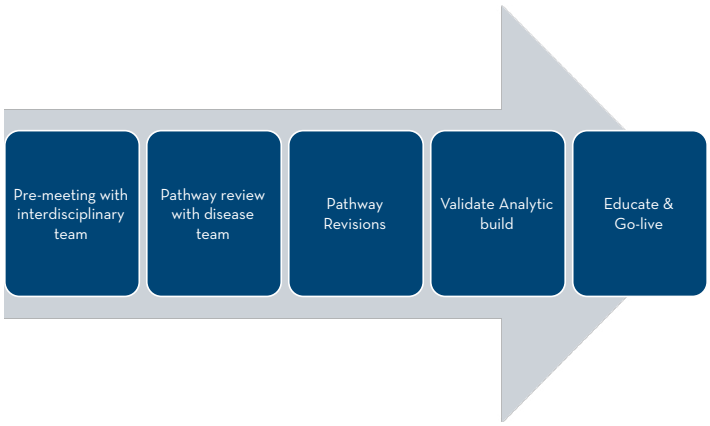
The EHR can be configured to improve efficiency. Dr. Rostamnjad shared that Dana-Farber's pre-emptive pathway is automatically triggered when a treatment plan is ordered, and the provider exits the plan. A best practice alert (i.e. a pop-up message or inbox message) then fires with the pathway recommendations and links to education material, prescriptions, and an order set in the EHR. A clinical note template can be created to optimize the documentation process. The implementation of pathways has been shown to improve team member satisfaction and morale.[3,4]

A symptom management treatment pathway should be utilized for ease of symptom reporting, symptom assessment/triage, treatments/interventions, and monitoring. An EHR data-driven algorithm guides assessment of the symptom and grading of the toxicity, treatments, and interventions (e.g. patient education videos, teaching sheets for counseling, and embedded prescriptions). The clinical staff utilizes the pathway in real-time during the patient encounter and the pathway directs the institutional intervention. Since patient symptoms are discussed regardless of visit setting (virtual vs. in-person), treatment pathways may be used even for patients seen virtually.

Clinical pharmacists play an integral role on the multidisciplinary team developing clinical content for treatment pathways. Dr. Rostamnjad collaborated with a team that included advanced practice practitioners, oncology nurse navigators, and an oncologist to develop several symptom management clinical pathways at Dana-Farber. Her scope focused on the development of clinical guidance for prevention, treatment, and medication counseling for each symptom; standardization of content for both pharmaceutical and non-pharmaceutical interventions; and application of symptom management algorithms for pre-emptive and treatment of both hematological and solid tumor diseases.

In the webinar, Dr. Rostamnjad explained that the first step in CDS pathway development is review of established guidelines, clinical trials, and published literature that become the backbone of the pathway. Feedback from the multidisciplinary team can then be incorporated. During algorithm development, an evidence key for each treatment and/or intervention is assigned. Evidence keys include options for tier 1 (high level evidence), tier 2 (moderate level evidence), tier 3 (low level evidence), and secondary treatment. The level of evidence assigned is primarily based on the robustness of the clinical trial for that treatment or intervention. Once the algorithm and level of evidence is validated by the team, the content is then standardized across disease centers and implemented into clinical practice (Diagram 1).

Pathway Development Process: Diagram 1



In conclusion, symptom management is an important aspect of oncology patient care. The development of institutional CDS pathways has been shown to improve outcome-based care by optimizing cancer treatment selection, improving symptom management approaches, reducing complications, and improving overall patient survival and quality of life. The pharmacist is a key member of the pathway development team. The institutional EHR system is a tool used to facilitate the symptom management pathways and standardization.

The HOPA Practice Management Committee recognizes the high quality of the webinar "Designing Comprehensive Symptom Management Pathways: A Roadmap for Optimizing Clinical Decision Support and Improved Patient Outcomes" and the broad application for many cancer programs. The committee would like to thank Dr. Rostamnjad for the detailed slides showcasing pathway templates, information system guidance and build recommendations, and outcome data analysis recommendations. ●●

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Navigating the Path to Successful Pharmacy Driven Quality Improvement Projects: Strategies to Promote Project Adoption, Implementation and Sustainability

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Pharmacists are well positioned to identify gaps and opportunities to advance patient care and safety. Creating medication-related quality projects that yield successful and sustainable processes can be challenging. Organizations such as the American Society of Clinical Oncology, Centers for Medicare and Medicaid Services, and the National Comprehensive Cancer Network set up quality standards for institutions to demonstrate quality of services provided; these may affect reimbursement.

Dr. Benyam Muluneh, from University of North Carolina (UNC) and UNC Health, works to optimize adherence to oral anticancer agents (OAA). To implement the program across UNC Health System, Community Cancer Center, and rural Cancer Center and Clinics, he adapted Consolidated Framework for Implementation Research (CFIR) and Implementation Science (IS) and Mapping (IM) to aid in program success and sustainability. He introduced us to these in HOPA 2023 poster "Strategies for Implementing an Oral Medication Adherence Intervention"[1] and resulting publications.[2,3] Both methods can help with successful adoption, implementation, and sustainability of pharmacy projects. With these tools we can help our institutions to gain competitive advantage by implementing successful, quality programs unique to our institution and practice.

> **"I learned that it is very important to have intellectual curiosity and be open-minded, trying to avoid bringing our own experiences, biases, and assumptions."**

What was the inspiration for this project?

Dr. Muluneh:
We designed a pilot Pharmacist-Led Oral Chemotherapy Management Program about 10 years ago, which was successful,[4] but not sustainable. I received a grant from the National Institute of Health (NIH) to refine our intervention using IS methods. The goal was to develop and to implement a project to reach patients across the health system, help patients with adherence to OAA, be sustainable, and help us to determine outcomes that we can measure.

Why was your original project not sustainable?

Dr. Muluneh:
It was Pharmacy-based and did not involve outside stakeholders. Although Cancer Center directors and physicians knew about our program it was not considered "official." At that time, novel oral and intravenous treatments were exploding and bringing more complexity and treatment lines to patient care. As a result, pharmacists were being asked to do more and prioritizing the Oral Chemotherapy Program became challenging. Additionally, increased co-pays and access to medications were becoming a bigger barrier to care. This required pharmacists to shift from clinical management of drug therapies to helping patients with medication access.

Which quality measure did you decide to focus on and why?

Dr. Muluneh:
We used IM a 5-step process to structure the program:[3]

1. Assess barriers and facilitators, decide on key adopters, implementers, and sustainers
2. Identify program adoption, implementation, and sustainment objectives and outcomes
3. Select and refine change methods and distinct implementation strategies
4. Produce the protocols and materials for the strategies identified in #3
5. Evaluate implementation outcomes

The heart of IM is engaging stakeholders early on in co-creating implementation strategies and applying an evidence-based approach to ensure selected strategies are matched up with identified barriers. To identify implementation barriers and facilitators, we conducted semi-structured interviews and used the CFIR toolkit.[5]

What was your process for identifying and engaging stakeholders?

Dr. Muluneh:
There are three phases to any project: **adoption**, **implementation**, and **sustainability**. With some overlap, in principle, each of them is distinct and requires specific roles. With the **adoption phase** the stakeholders will be Pharmacy Director, Clinical Manager, Physician Cancer Center Leader, and other decision makers whose approval and support are required to proceed with a project and their early engagement in program design. For all institute

leaders it is critical to have a competitive advantage, and it is important to make a value proposition, why and how the proposed program is unique and might bring the competitive advantage to the Institute or Health System.

Next phase, **implementation**: these are end users including nurses, pharmacists, physicians. We work with them on developing processes, program adaptability into current practice, and prioritizing patients that might benefit from our program the most.

Moving to the **sustainability phase,** quality assurance of the program, and involvement of the institute QI Committee in establishing endpoints and processes for tracking and reporting outcomes. This may require updates or new EHR templates to document interventions and outcomes.

We looked at stakeholder experiences: experiences with piloting new programs, innovators, those not afraid to make bold decisions, also having representatives from various clinics and practices, social workers, nurses, IT, etc. We also identified the need for a methodologist, to support us throughout the project.

We also added a patient representative from the Cancer Center Patient Engagement Advisory Group. Although I was nervous about it, it was the best decision because they were so honest and helpful! It is essential to be intentional in selecting stakeholders and ensure they are diverse and representative.

Which struggles did you encounter during the project and how did you overcome them?

Dr. Muluneh:

This is an intensive process requiring several hours every day, working with the research and stakeholder team. Initially, I was a full-time clinician, trying to implement this program on the side. It was very hard. This is a reality for most pharmacists. I received grant support from the NIH for this program, therefore I gained more time to invest in this project, 2-3 days a week. We also worked with trainees to be more efficient in synthesizing feedback we received from our stakeholders.

What did you learn from working on this project?

Dr. Muluneh:

This process yielded things I expected to be deliverable such as a standard operating procedure and clear workflows for our program. However, the evidence-based barriers-matching with potential solution approach (2) yielded deliverables such as marketing materials for the program and presentations for leadership which I did not anticipate. I learned that the first step to build an intervention is clear understanding of existing gaps and barriers using a systematic framework like CFIR.[5]

It is a slow process to identify strategies and then adopt and implement them into practice. People want change, so we worked on small changes to our workflows, and we are trialing them, and adjusting as we keep building the entire program.

I learned that it is very important to have intellectual curiosity and be open-minded, trying to avoid bringing our own experiences, biases, and assumptions.

Any recommendations on using IM and CFIR when working on pharmacy programs?

Dr. Muluneh:

They are valuable and adaptable to any project by incorporating elements that can add to your clinical experience and help you to reach your goal. Approach them as tools that you can leverage for a successful outcome of your project.

Any key points to share with other pharmacists working on their projects?

Dr. Muluneh:

1. Clear definition of scope and desired outcomes, staying focused
2. Identifying how your program can bring competitive advantage to your institute, create a value proposition
3. Engage leadership and stakeholders early on
4. Patient stratification and identification of those that can benefit from the program the most (understanding your patients' social determinants of health, their financials, education, literacy level, their primary language, comorbidities, polypharmacy, their caregiver situation, etc.)

Where are you with your project now?

Dr. Muluneh:

We completed Phase I of our project[3] where interprofessional experts focused on developing strategies for the program implementation using IM. In Phase II, we worked on identifying barriers and facilitators to aid in implementation of OAA Adherence Program, across UNC Health System, our Community Cancer Center and in our rural Cancer Center and Clinics, using CFIR.[2] Currently we are working on preparations for launching a pilot program within six of our clinics, a goal for July.

Our ultimate goal is to help our pharmacists to provide high quality care, to be able to reach the sickest patients and those that might need our services the most. In addition, we would like to show how pharmacists might be able to leverage IS methods, which play well with our strengths of being detail oriented, logical and being practice focused in developing clinical research programs to advance our patients care.

Conclusion:

Quality improvement projects in oncology pharmacy require strategic adoption, implementation, and sustainability to ensure lasting impact. By leveraging multiple tools highlighted above and on HOPA's quality page, pharmacists can create evidence-based, patient-centered projects that enhance care. With continued collaboration with stakeholder engagement and commitment to quality, pharmacists can drive meaningful advancements in oncology patient outcomes.

For those of you interested in learning more about Implementation Science and other quality improvement tools, Dr. Muluneh recommends:

Training Institute for Dissemination and Implementation Research in Cancer (TIDIRC) OpenAccess | Division of Cancer Control and Population Sciences (DCCPS)

HOPA's Quality Oversight Committee (QOC) website: https://www.hoparx.org/resources/oncology-quality-resources/ offers information on quality in healthcare, training programs, and tools that pharmacists can use to develop quality projects. ●●

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Executive Director Update: Reflections on the 2025 Annual Conference

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Executive Director

It was a pleasure to see so many of our members at the HOPA 2025 Annual Conference (HOPA 2025) in Portland, OR! I'm excited to share that this was a record-breaking and highly successful year for HOPA on many fronts.

We welcomed 1,702 registrants to the conference — a 10% increase over 2024 in Tampa. Attendees shared positive feedback about the Oregon Convention Center (OCC), where networking, collaboration, and relaxation all found a home. Many thanks to the city of Portland and the OCC for their warm hospitality!

This year's conference featured 32 educational sessions offering 41 CE credits, including 8 BCOP credits. The most popular sessions included the Wednesday and Thursday BCOP presentations, the Platform Research session, the General Session on Multiple Myeloma, and the Hematology updates breakout. CE session proposals increased by 5.7%, with more panels and debates offered than ever before. Feedback from our post-event survey will guide future programming — thank you to all who contributed.

We showcased 40 digital e-posters and 476 traditional posters, including a 13% increase in Industry Encore submissions and a 5% increase in Trainee poster evaluators. Two Trainee Award winners were selected, and our poster sessions enjoyed strong attendance and engagement.

We were thrilled to have 11 sponsors, 27 symposia (15 non-CE and 12 CE), 60 exhibitors (up from 57 in 2024), and 82 Industry Encore Posters (up from 63). Engagement was strong — 287 attendees participated in our exhibitor Scavenger Hunt. Thank you to our sponsors and exhibitors for your continued support.

Our social media presence soared with over 93,000 impressions during conference week, and we were proud to see HOPA featured in Pharmacy Times, JHOP, and Pharmacy Practice News, among other oncology and pharmacy publications.

Beyond education and science, HOPA 2025 provided ample opportunities to network and have fun. From lively receptions and food trucks to the Board Meet & Greet (with coffee and donuts!) and therapy llamas Beni and Panda, the conference atmosphere was warm, connected, and energizing. Special thanks to our Wellness Advisory Group for the chair massages and llama magic — we're already thinking about next year!

Overall satisfaction was high: 93% of attendees reported being "satisfied" or "highly satisfied," and 68% said they're likely or highly likely to attend AC26 — up from 59% last year. We're grateful for your feedback and are already working on improvements for next year.

Thank you to all our annual conference committee volunteers, moderators, and speakers and thank YOU for being part of this milestone year. (On pages 20-21, read a snippet from Robert Mancini's Incoming President's Address.) I look forward to what we'll accomplish together in 2026 to continue to support and educate pharmacy practitioners to optimize the care of individuals affected by cancer. I hope to see you in New Orleans March 25-28, 2026.

False Alarm: Navigating Pseudo-AKI with Oral Anticancer Medications

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Introduction

Targeted oral anticancer medications (OAM) have revolutionized the management of cancer patients by targeting molecular pathways for all types of cancers. This shift from traditional intravenous chemotherapy to oral chemotherapy has allowed patients to receive treatment at home. While safe for home use, OAMs still come with potentially serious adverse effects including possible acute kidney injury (AKI), tubular necrosis, and nephritis. Renal toxicity monitoring for many OAMs include checking serum creatinine (SCr) periodically to ensure appropriate dosing and toxicity monitoring. While SCr is a widely utilized tool to assess renal function and monitor for serious adverse events, it can be impacted by medications that affect tubular secretion.[1-17] Several OAMs used today impact tubular secretion, leading to artificially elevated SCr and underestimating eGFR.[1-17] These false elevations in SCr may lead clinicians to be suspicious for AKI, but may also lead to inappropriate dose modification or interruption. We will review the mechanism of SCr elevation seen with many OAMs and suggest alternative measures of renal function based on current literature and guideline recommendations.

Mechanism of Creatinine Elevation with Oral Anticancer Medications

Clinical assessment of renal function is required for routine medical care, as well as for monitoring for potential toxicity in many therapies in oncology. Estimated glomerular filtration rate (eGFR), calculated using SCr with the Cockcroft-Gault or the Modification of Diet in Renal Disease (MDRD) formula, is widely used in clinical practice to assess renal function.[18-19] These equations are also utilized to determine appropriate renal dosing for medications in everyday practice. SCr is a waste product generated from both the breakdown of creatine phosphate in muscle tissues and digestion of foods containing creatine.[18-21] One of the major limitations to using SCr in estimating true renal function is that it is affected by age, muscle mass, diet, sex, and certain medications.[19-20] SCr is primarily excreted from the body through glomerular filtration, but active tubular secretion also accounts for a portion of creatinine removal.[21]

Glomerular filtration consists of the small creatinine molecule in the blood being filtered through the glomerulus into the glomerular filtrate.[20] This glomerular filtrate is then eventually excreted from the body through urine. Active tubular secretion occurs primarily through the proximal tubules of the nephron, where there are many creatinine transporters and binding proteins present. Some of these creatinine transporters and proteins include organic cation transporter 2 (OCT2), multidrug and toxin extrusion protein 1 (MATE1), and MATE2-K. OCT1 is present on the basolateral membrane of the proximal tubule and plays a role in uptake of endogenous substrates, like creatinine, into the proximal tubule epithelial cells. MATE1 and MATE2-K are present on the brush border membrane of the proximal tubule epithelial cells and exchange protons and cations to facilitate transcellular transport with OCT2 of creatinine into the tubule lumen.[20] Several OAMs that are utilized in oncology can have inhibitory effects on OCT1, MATE1, and MATE2-K, as listed in Table 1.[1-17] When this inhibition occurs, creatinine cannot undergo tubular secretion, leading to SCr elevations and "pseudo-acute kidney injury" (pseudo-AKI).[1-17] Distinguishing between pseudo-AKI and true nephrotoxicity when there is a SCr elevation for patients receiving these OAMs can be challenging.

Table 1. Oral Anticancer Medications Impacted by Tubular Secretion

Tubular Secretion Transporter/ Protein Inhibited/Affected	Oral Anticancer Medication
MATE1	Abemaciclib[5] Brigatinib[2] Cabozantinib[7] Capmatinib[7] Crizotinib[2,3,7] Dasatinib[13] Entrectinib[7] Gefitinib[2] Imatinib[2,10, 16] Lorlatinib[7] Pazopanib[2,9] Pralsetinib[7] Selpercatinib[7,14] Sorafenib[2] Sunitinib[2] Tepotinib[7, 15] Tucatinib[12]
OCT2	Abemaciclib[5] Bosutinib[17] Crizotinib[2,3] Dasatinib[13] Gefitinib[2] Imatinib[2,10,16] Pazopanib[2,9] Sunitinib[2] Tucatinib[12]
MATE2-K	Abemaciclib[5] Dasatinib[13] Imatinib[10,16] Pazopanib[9] Selpercatinib[14] Tucatinib[12]

Assessment of Cystatin C as a Measure of Renal Function

Due to the variation that can be seen with SCr, alternative markers to measure renal function, like cystatin C, have been proposed.[18-19] Unlike SCr measurements, cystatin C is freely filtered by the glomerulus and not secreted by tubules making it a favorable alternative to measure eGFR. Cystatin C is a cysteine protease inhibitor present in all nucleated cells in the body. It is not affected by muscle mass, diet, sex, or tubular secretion in the proximal tubules like creatinine.[18-19] In the setting of chronic kidney disease (CKD), the 2024 KDIGO Clinical Practice Guideline for the Evaluation and Management of CKD recommends using the eGFRcys equation with cystatin C to determine renal function if a patient is taking a mediation that decreases tubular secretion.[19] Cystatin C concentration is inversely correlated with eGFR – when cystatin C increases in concentration in the blood, it suggests a more accurate representation of kidney impairment (See Equation 1 and Equation 2).[4,18] The normal reference range for cystatin C is 0.67-1.21 mg/L.

$$eGFRcys = 133 \times \left(\frac{Scys}{0.8}\right)^{-1.328} \times 0.996^{Age} [\times 0.932 \; if \; female]$$

Equation 1. 2012 CKD-EPI Serum Cystatin C Equation (Cystatin C >0.8) (both female and male)[18]

Scys = standardized serum cystatin C in mg/dL

$$eGFRcys = 133 \times \left(\frac{Scys}{0.8}\right)^{-0.499} \times 0.996^{Age} [\times 0.932 \; if \; female]$$

Equation 2. 2012 CKD-EPI Serum Cystatin C Equation (Cystatin C ·0.8) (both female and male)[18]

Acute kidney injury is defined by KDIGO as an increase to at least 1.5 times baseline SCr in 7 days, an increase of at least 0.3 mg/dL in SCr in 48 hours, or urine volume < 0.5 mL/kg/hour for 6 hours.[22] While KDIGO does not provide recommendations for use of cystatin C in AKI, several studies have outlined the use of cystatin C when assessing for pseudo-AKI versus true AKI with medications that can affect SCr.

In a retrospective trial review of CDK 4/6 inhibitors in breast cancer, 16.8% (24 of 143) of patients experienced pseudo-SCr elevation while on CDK 4/6 inhibitors with abemaciclib having the highest incidence.[6] The median time to onset was 27 days and SCr increased by median of 0.69 mg/dL from baseline.[6] In the 3 patients receiving ribociclib that were evaluated using cystatin C, one of these patients was deemed to have a pseudo-SCr elevation, while the other two were deemed to have true renal injury that required further workup including biopsy.[6] The authors concluded that cystatin C was a useful tool to assess renal function prior to invasive interventions like hospitalization and renal biopsy.[6] True kidney toxicity including acute tubular necrosis, tubular injury, and tubulo-interstitial nephritis can also occur with CDK 4/6 inhibitors, highlighting the need for assessment of renal function in these patients to prevent missing a true toxicity.

In a retrospective trial reviewing tyrosine kinase inhibitors used in lung cancer, the incidence of any-stage AKI was 10% with a median onset of 4 months and median change in SCr of 0.7 mg/dL.[7] In the patients that had both cystatin C and serum creatinine measured, cystatin C levels were lower than creatinine levels with a median difference in estimated GFR of 16 mL/min, with eGFRcys estimating higher GFR.[7] This study concluded that eGFR is often underestimated in patients on MATE-1 inhibitors used in lung cancer and that using cystatin C can identify patients with pseudo-AKI, reducing unnecessary dose adjustments.[7]

In a retrospective monocentric study of vemurafenib, a BRAF inhibitor commonly used in advanced melanoma, found 97% of patients (68/70 patients) had a significant increase in SCr levels (>5%) one month after vemurafenib initiation with a median variation of 22.8%.[4] However, after the initial increase, they found the SCr remained stable at that level while continuing therapy without any modifications or interruptions. The investigators also measured cystatin C levels to further define the underlying mechanism of SCr elevation in 11 patients. In this group, the decrease in eGFR after vemurafenib initiation measured by cystatin C had a median 9.4% decrease in GFR, whereas SCr levels indicated a median reduction of 16.7% in GFR. The authors hypothesized this was due to an inhibition of the normal tubular secretion of creatinine leading to this elevation.[4]

Limitations of Cystatin C

Several studies have suggested cystatin C as a reasonable alternative marker of renal function when elevations in SCr are observed due to inhibited tubular secretion from OAMs. While cystatin C offers certain benefits of measuring kidney function, cystatin C also comes with several limitations. Similarly to SCr differences observed between special populations (sex, age, race, muscle mass, diet), levels of cystatin C can be affected by comorbidities including thyroid disorders, underlying inflammation, malignancy, steroid use, and even patients who recently underwent chemotherapy treatment.[19,23,24] In a prospective study including 1,200 adult patients with solid tumors comparing eGFRcr-cys to Cockcroft-Gault equation, the authors concluded that eGFRcr-cys is preferred compared to other measures of renal function in patients with malignancy.[23] Another study evaluating cystatin C as an alternative biomarker for eGFR in oncology found significantly higher concentrations of cystatin C in the oncology cohort both prior to and during chemotherapy treatment. Their findings were suggestive of a malignancy-mediated effect on cystatin C, although the mechanism wasn't fully detailed.[24] While the eGFRcr-cys equation may represent the most accurate renal function in oncology patients for routine renal assessment, these studies did not incorporate patients on medications known to inhibit tubular secretion. Therefore, utilizing cystatin C for eGFRcys is still recommended in assessment of pseudo-AKI versus true kidney damage from OAMs

while eGRcr-cys may be beneficial in routine renal function assessment in oncology patients.

Logistic barriers to widespread use of cystatin C also exist, which include increased expenses associated with running and maintaining the assays, as well as additional time required for cystatin C lab processing compared to SCr.[19] While cystatin C processing can be done the same day it is collected, the turnaround time compared to SCr may be unfavorable in facilities that do not have the capability to run the lab in-house.[19]Furthermore, additional costs are incurred when sending samples to an outside laboratory.[19] KDIGO optimistically suggests that with the increased utilization of cystatin C, laboratories offering cystatin C tests may be further encouraged to provide to institutions, making them more accessible to optimize patient care.[19]

Alternative Methods for Assessment of Renal Function

If cystatin C is unavailable or if eGFRcys and eGFRcr results significantly differ, additional methods to further evaluate for AKI include discontinuing agents that are known to cause kidney damage outside of the OAM, measuring urine output for oliguria, obtaining urinary markers, performing a renal ultrasound, utilizing a nephrology consult, or obtaining a renal biopsy.[22] While it may be uncommon for a case to require this additional work-up, these options must be considered when clinically appropriate to ensure no true kidney damage is occurring. Some notable limitations of these options include increased cost, the need for holding OAMs surrounding renal biopsies, and complications that can arise from invasive procedures, including hematomas, pain at biopsy site, and hematuria.[25] Additionally, an unfortunate reality of nephrology consults include the potential prolonged wait time for scheduling an appointment for patients. Depending on the patient's geographical location, this process may take up to weeks or months to get arranged. It should also be noted that the KDIGO 2024 guidelines recommend against the use of nuclear renal scans as they have been reported to be highly prone to errors.[19]

"Several OAMs used today impact tubular secretion, leading to artificially elevated SCr and underestimating eGFR.[1-17]"

Conclusions and Future Directions

There is currently a lack of standardized guidelines for accurately assessing renal function in cancer patients on OAMs that affect tubular secretion, which can lead to uncertainty in maintaining drug efficacy. As new OAMs continually emerge each year, it is crucial to distinguish true nephrotoxicity from pseudo-AKI prior to making any adjustments in cancer treatment. When elevations in SCr are observed while a patient is on a medication that is known to cause tubular secretion, cystatin C levels should be utilized to estimate GFR. If cystatin C levels are elevated and eGFRcys is representative of kidney injury, patients should undergo further workup for AKI including holding the OAM, obtaining urine output, urinary markers, performing renal ultrasound, and potentially referring patient to a nephrologist. In facilities where cystatin C cannot be obtained due to cost or accessibility, these measures can also be utilized for AKI workup and nephrology should be consulted. While there are still many institutions that lack the capability of running cystatin C in-house, anecdotal evidence suggests that cancer centers should invest in a process for running cystatin C to assess kidney function given the growing number of OAMs that are introduced each year. Cystatin C is a reasonable alternative to measuring kidney function in the setting of OAMs that affect tubular secretion, but further research is needed to determine the true utility of cystatin C, renal imaging, and renal biopsies in the setting of SCr elevations from OAMs. ●●

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“Don’t Stop Believing — Putting the Person Back into Practice”

Robert Mancini
PharmD, BCOP, FHOPA

Below you will find excerpts from Robert Mancini’s Incoming President’s Address during HOPA Annual Conference 2025 in Portland, Oregon on April 11, 2025. The following has been edited for length and clarity.

Thank you for being here. I may get a little choked up—because what we do matters deeply to me.

At my daughter’s kindergarten graduation last year, they sang “Start a Wave” from Disney’s World of Color. The lyrics stayed with me:

But someone has to start.
Start the motion,
Throw the stone,
Stir the ocean,
Be the hand that reaches out for the unknown.
Sometimes just one drop is all it takes,
See the ripples, watch them turn the waves
Right before your eyes.
You never know who it might touch,
And soon, it might be all of us.

That’s how I see our work as oncology pharmacists. We might not always see the impact of our actions but they ripple out, touching more lives than we know. We all have our own journeys, and that is what makes HOPA a great community. I want to show you what has inspired me in the hopes that it will continue to inspire you. Along with my family and my training, I am where I am today because of many of you.

So, who am I?

There is nothing extraordinary about me; I am just another person who answered the call to help move HOPA forward. But I do think it is important to understand who I am and where I am from. I hope hearing my story will make you feel comfortable coming to talk to me about yours.

I grew up in Southern California and studied pharmacy at the University of California San Diego. The program was so new that my early classes were held in trailers—no glamorous start here. My journey took me to Boise, Idaho, where I completed my PGY1 and PGY2 at St. Luke’s Cancer Institute.

With a nudge from my PGY1 residency director, Catherine Gundlach, I have stayed there ever since, helping build something meaningful in our community program.

Along the way, I’ve had plenty of ordinary jobs—Baskin Robbins (yes, I got fired), Taco Bell (which gave me Chalupa nightmares)—but every role, including those early missteps, shaped me. That’s something I want every member of HOPA to know: your story matters, no matter how it starts. My path through leadership started locally with the Idaho Society of Health-System Pharmacists and eventually led to serving as Grand Regent of Kappa Psi. That experience helped prepare me to serve you now, as HOPA President.

And I stand here today because of people who shaped me—especially my family.

My grandpa, a WWII vet who lived to almost 102, once joked about me taking care of him when I became a doctor. I said, “You’ll be gone by then”—fortunately, I was wrong. He lived to see me become an oncology pharmacist.

My dad, a four-time cancer survivor, and my mom, a four-time caregiver, have taught me as much about patient communication and empathy as any course or rotation. I have seen firsthand how some outcomes are positive, like my Aunt Arlene’s lymphoma being in remission, while others are not, like in the case of my Uncle Steve who succumbed to a rare form of leukemia T-PLL.

My Aunt Jeri’s recent diagnosis reminds me: it’s not always about the treatment plan—it’s about respecting the person. We offer knowledge, but patients choose their paths.

My daughters, Lia (10) and Livia (7), have helped shape me too. They have taught me patience (mostly) and helped me remember what matters most in life. While I dedicate my career to helping my patients, I dedicate my life accomplishments to doing everything I can to make them proud.

"There is a fine line between succeeding in careers and not sacrificing your time with family. I have walked that line."

That's why my three presidential priorities are rooted in creating space for all of us to thrive:

1. Reimagining Volunteerism
Not everyone can commit to a year-long committee. That's okay. We're working to diversify volunteer opportunities—more micro-volunteering, project-based roles, and new ways to engage that fit different schedules and energy levels. Your time matters, and we want to make it work for you.

2. Elevating Early Education
We're launching a HOPA-sponsored virtual residency and fellowship showcase—a new way to reach students and trainees earlier and more equitably, especially those who can't travel to Midyear. We're also exploring APPE and residency exchange opportunities to broaden exposure to oncology practice.

3. Championing Our Stories
Our stories have power. We're launching a storytelling initiative to highlight the human side of our work, with support from a task force led by Kristen McCullough and Latha Radhakrishnan. Inspired by powerful pieces like "Do You See Me?" by Kristen McCollough and "The Chemotherapist," by Joe Kalis, we're building a member-authored book, which will be available in time for HOPA 2026 in New Orleans!

Finally, I want to thank my residents, students, and colleagues. You all keep me going. As Morrie Schwartz wrote in Tuesdays with Morrie, "Devote yourself to loving others, to your community, and to something that gives you purpose and meaning." That's what HOPA has become for me. And I hope it's that for you, too.

Thank you. And as my walk-up song reminds us:

Don't Stop Believing.
-Robert

More Money, More Choices: Pharmacist Perspectives on Financial Success After Residency

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Perspective from Amy Seung

Approximately 82% of pharmacy students graduating in 2024 borrowed money to help pay for college expenses, with an average debt of $170,000.[1] As we transition from training into our careers, our financial situations and goals will inevitably evolve. No two financial journeys are the same, so creating an individualized plan that aligns with your personal and professional aspirations is key.

> **"A little planning and discipline now can create financial freedom and security for the future."**

Finishing residency is a major adjustment—not just professionally but financially. A pharmacy school professor once told me, **"Live at your resident's salary for as long as you can."** That advice stuck with me, especially as I suddenly had more time and money to spend after residency. I quickly realized that having a financial strategy in place early on would set the foundation for long-term success.

One of the best decisions I made was meeting with a financial advisor before earning my full salary. They helped me understand the balance between paying off student loans, covering moving expenses, and planning for future savings. If you haven't set financial goals before, this is a great place to start. I also learned that budgeting was crucial—I mapped out my fixed expenses each month, which gave me a clear picture of my disposable income and allowed me to prioritize financial goals.

Another piece of advice that resonated with me was to **start saving for retirement immediately.** With my first paycheck, I began contributing to my organization's 403(b)/401(k) plan, and I've consistently contributed the maximum amount possible every year. The earlier you start, the more time your money has to grow, thanks to compound interest.

Additional Practical Tips

1. Figure out your loan repayment strategy. Whether it's standard repayment, income-driven plans, or refinancing, take time to understand your options. Federal loan forgiveness programs may also be worth exploring, depending on your career path.
2. Minimize credit card debt. Credit cards can be helpful tools if used wisely, but high-interest debt can quickly become overwhelming. If you carry a balance, prioritize paying it off as soon as possible.
3. Set up an emergency fund. Unexpected expenses—car repairs, medical bills, or job changes—can happen at any time. Having at least three to six months' worth of living expenses in a separate, easily accessible account provides financial security.
4. Take advantage of employer benefits. Many employers offer financial wellness programs, loan repayment assistance, and matching contributions for retirement savings. Make sure you're maximizing these opportunities to strengthen your financial future.

Managing your finances may feel overwhelming at first, but building good habits early on will pay off in the long run. A little planning and discipline now can create financial freedom and security for the future. However, financial goals aren't set in stone—life changes, and so should your financial plan. Reassessing your budget, savings, and investment strategies at least once a year ensures that your financial approach continues to align with your evolving career, personal goals, and unexpected life events.

Perspective from Kuan Vogel

I am almost two years out from residency training and the best advice I can give for financial success when transitioning from being a resident to a new practitioner is starting as early as possible. When I was in pharmacy school, I had the option to take a personal finance elective which was taught by a financial advisor who worked with a lot of healthcare (particularly pharmacy) clients. Because she had a lot of experience with helping former students with the financial transition between resident and new practitioner, I trusted her to become my financial advisor even before graduating college. Having a financial advisor has helped me because I was able to discuss both my short- and long-term goals and we developed a plan together to help achieve them. I knew I was interested in diversifying my funds and she was very helpful in explaining the different types of individual savings and retirement accounts, including investment strategies, which have helped me grow my money. When it came to starting my first full-time position after residency, she was also able to help review the various insurance plans and supplemental additives offered by my employer to advise which options

would work best for me. More recently, she has greatly assisted with financially planning for a wedding and buying a house. Another financial strategy I have used throughout residency and into becoming a new practitioner is continuing to live below my means. This has not only allowed me to quickly achieve my financial goals but has also provided a greater sense of financial freedom.

Perspective from Jordanne Adolphsen

Benjamin Franklin often gets credit for the phrase, "If you fail to plan, you plan to fail." This quote holds particularly true when transitioning from a resident to a new practitioner, where planning is essential for success. My top tip for financial success is to create a financial plan. Start by assessing where you currently stand, defining your financial goals, and determining how to reach them. There are countless books, podcasts, apps, blogs, and courses that can help you develop a strategy. Financial planning isn't a one-time task, but a continuous, lifelong process that requires regular evaluation and adjustment. As Henry Kissinger wisely said, "If you don't know where you are going, every road will get you nowhere."

Once you've identified where you want to go, the next step is determining how to get there. My second tip for financial success is simple: budget, budget, and budget some more. All the way down to zero; income minus your expenses, investments, and savings should equal zero in what is aptly termed a zero-based budget.[2] Think of it like creating the blueprint for a house, the script for a play, or my personal favorite, the recipe for a chocolate cake. A budget serves as the foundation that guides you toward achieving your financial goals. Create your budget and track your expenses/investments/savings on an app, Excel, or grab a pen and paper. To stay focused, review and revise your budget monthly, adjusting it as necessary. When you lose focus, revisit tip number one. Similar to the residency grind you just endured; remember why you started. ●●

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A Path to Personalized Treatment: How MRD Assessment via ctDNA Can Improve Clinical Outcomes in Diffuse Large B-cell Lymphoma

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B-cell non-Hodgkins lymphoma are one of the most common malignancies in the United States, accounting for upwards of 60% of all lymphoid based malignancies.[1] B-cell lymphomas are comprised of various subtypes with unique treatment modalities and disease monitoring strategies. Traditionally, invasive tissue biopsies, bone marrow biopsies and imaging through PET-CT are the standard to assessing minimal residual disease (MRD).[2] These conventional approaches have several limitations which include accessibility and sensitivity. This has significantly increased the demand for precision- based tools to evaluate and stratify risk when managing patients with B-cell lymphomas. The advent of liquid biopsies, particularly circulating tumor DNA (ctDNA), has provided a minimally invasive, highly sensitive alternative for disease monitoring and prognostication. ctDNA is single- or double-stranded DNA fragments released by the tumor cells into the blood containing tumor-specific genetic alterations. The mutations can be identified and quantified using next-generation sequencing (NGS) or polymerase chain reaction (PCR)- based assays. The ability to detect finite amount of ctDNA makes it a powerful tool for MRD assessment.[3]

"The advent of liquid biopsies, particularly circulating tumor DNA (ctDNA), has provided a minimally invasive, highly sensitive alternative for disease monitoring and prognostication."

In 1948 it was discovered that hematologic cells can release DNA fragments known as cell-free DNA (cfDNA) into the blood when they undergo apoptosis. However, it was not until 1977 that increased cfDNA levels were detected in cancer patients leading to further investigation as a potential biomarker. The cfDNA detected in cancer patients is now known as ctDNA. The tumor cells can release ctDNA into bloodstream through several mechanisms of cell death which include necrosis, apoptosis, phagocytosis, pyroptosis, oncosis and ferroptosis. In addition, there are non-cell death mechanisms like senescence or active secretion in extracellular vesicles and mitochondrial DNA egestion.[4-6] All of which allow the use of ctDNA analysis to provide clinical information regarding the tumor. ctDNA liquid biopsy has been proposed in clinical practice to provide a non-invasive approach to detect early cancer cells, detect resistance, molecular profiling to allow targeted treatment, monitor response, detect minimal residual disease and monitor relapse. Early investigations primarily were focused on solid tumors, like non-small cell lung cancer (NSCLC), colorectal, breast, head, neck and skin cancers. Currently, there are only a handful of FDA approved liquid biopsy tests which detect ctDNA for various types of malignancies. Common examples of these tests include Cobas® epithelial growth factor receptor (EGFR) Mutation Test v2, Guardant360® CDx and FoundationOne® Liquid CDx. The first FDA approved ctDNA test was Cobas® in 2016 and it detects EGFR mutations in patients with NSCLC. This testing is utilized to determine if patient with NSCLC will benefit from an EGFR-tyrosine kinase inhibitor (TKI). Guardant360® CDx is more comprehensive as it provides information for NSCLC, breast, prostate and colorectal cancer. It has the capability to assess 74 genes with a 5-day turnaround of actionable results. Finally, FoundationOne® CDx is FDA approved to analyze 311 genes in NSCLC, breast, prostate, and ovarian cancer. There has been significant development of ctDNA liquid biopsies in the world of solid tumors, but its role in hematologic malignancies has emerged as an interest in investigation.[4-6]

Numerous studies have demonstrated prognostic significance of ctDNA in B-cell lymphomas. For instance, in diffuse large B-cell lymphoma (DLBCL) the dynamic changes in ctDNA levels have been shown to correlate with treatment response. Patients with undetectable ctDNA after front-line therapy have significantly better progression-free survival (PFS) and overall survival (OS) compared to those with detectable ctDNA.[3] Moreover, rising ctDNA levels during remission can serve as an early indicator of relapse, often preceding clinical or radiographic evidence of disease recurrence. Incorporating ctDNA into clinical practice does have its challenges like standardization of assays, sensitivity thresholds and validation across different B-cell lymphomas. In addition, the ctDNA analysis needs to be a cost-effective and accessible option. Despite these challenges, the growing body of evidence supporting ctDNA's role in MRD assessment highlights its potential to transform the management of patients with B-cell lymphomas.

The field of precision medicine in oncology continues to evolve, and ctDNA-based MRD assessment represents a promising advancement in the personalized care of patients with B-cell lymphomas. Several clinical trials that are currently ongoing are expected to further elucidate its role in refining treatment strategies, improve patient outcomes and mitigate the need for invasive monitoring procedures. The inclusion of ctDNA in NCCN guidelines

for PET-positive DLBCL post-first line treatment is a category 2B recommendation, as an option for those in which a biopsy is not feasible. This is a significant step forward in implementing this technology into routine clinical practice.

When attempting to replicate the success of MRD seen in other hematologic malignancies, lymphoma does not commonly circulate in the peripheral blood. The presence of ctDNA is more readily detectable in comparison to circulating lymphocytes, making it the best option for liquid biopsy specimens in lymphoma[3]. Given the complex tumor heterogeneity, which differs between patients, making use of a single genetic abnormalities inadequate for this assessment. For this reason, polymerase chain reaction (PCR) amplification is not unanimously effective in lymphoma. While PCR use is effective in follicular and mantle cell lymphoma due to the highly recurrent translocations universally seen, aggressive large cell lymphoma lack this genetic homogeneity and therefore cannot appropriate assess disease status.[7] For this reason the use of NGS-based methods is most appropriate for ctDNA assessment in DLBCL. NGS is able to use rearrangements in the immunoglobulin (Ig) receptors that are clonally unique in lymphomas. With continued advancements in the use of NGS, two different methods have been developed and studied in the lymphoma space. The first to be used in liquid tumor response assessment in lymphoma was *cancer personalized profiling by deep sequencing* (CAPP-Seq). With a higher background error rate, CAPP-Seq is only able to detect as few as 1 cancer cell in 10,000 non-cancer DNA-sequences, with 40-50% clinical sensitivity in B-cell lymphomas. In contrast, the most recent NGS method is called *phased variant enrichment and detection by sequencing* (PhasED-Seq). This approach significantly lowered background error rates by tracking multiple somatic variants and increased tumor reporters on the same cfDNA molecule. Although this test has the ability to detect 1 cancer cell in 1,000,000 non-cancer DNA-sequences, this increasing clinical sensitivity takes anywhere from 1-3 weeks to deliver results to providers and patients.[3] Table 1 outlines the differences between CAPP-Seq and PhasED-Seq in terms of sensitivity, specificity and clinical limitations of use.

While the use of ctDNA as a prognostic predictor of poor outcomes prior to treatment is being studied, the only approved clinical application is in end of treatment (EOT) to determine degree of surveillance needed to assess for relapse. The accuracy of MRD has been compared to PET response assessment in various reports. The highest quality assessment comes from an active, prospective clinical trial, in which patients who received front-line induction chemotherapy for DLBCL were assessed by both PET and MRD via PhaseED-Seq at EOT in 54 patients. The 2-year progression free survival (PFS) for those who experienced remission via PET (blindly interpreted) was 90% vs. 67% in patients who did not have remission via PET. When looking at MRD via PhasED-Seq, 2-year PFS was 98% vs. 33% in patients with detectable MRD. It is important to note that no patients with undetectable MRD experienced progression, but one patient died from a myocardial infarction.[8] Furthermore, another report prospectively compared both traditional response assessment and MRD by PhasED-Seq in 99 patients who received frontline induction therapy with R-EPOCH or R-CHOP. MRD demonstrated a greater degree of association to clinical outcomes when compared to PET, as the median PFS and overall survival (OS) were worse for those with detectable MRD at EOT (PFS: P=0.004, HR=2.7; OS: P=0.0004, HR=5.1).[9] It is important to note that the clinical correlation of PET was statistically significant, but MRD assessment showed a stronger correlation.[3,8]

As understanding of clinical utility of MRD assessment via ctDNA continues to expand, further applications could help enhance care at different time points in treatment. It is proposed based on the data above, that patients undergoing treatment for DLBCL who present as MRD negative in a complete remission at EOT may be permitted to be placed on longer interval surveillance. Despite this recommendation, there is no data to support at what interval patients should repeat MRD testing to ensure the deep remission is maintained. Some of the earlier NGS testing saw MRD positivity reappear 3-6 months prior to relapse, but there is no clinical data to support therapeutic intervention at first detection of MRD versus at first sign of clinical relapse.[3] Despite validated clinical trials, it is also theorized that MRD testing via NGS could act a confirmatory test in patients who are PET-positive prior to salvage therapy. This may help avoid overtreatment in patients with false-positive follow up PET scans. Finally, further expansion of MRD assessment into a risk-adapted approach to treatment may help increase survival rates for patients undergoing treatment for DLBCL. Interim assessment of MRD after 2 cycles of induction chemotherapy via NGS would allow physicians to understand individualized response to treatment, providing either abbreviated or intensified therapy to minimize toxicity and maximize clinical outcomes.[3]

As a result of the increased sensitivity and specificity with NGS testing using the PhasED-Seq technology, the National Comprehensive Cancer Network (NCCN) guidelines incorporated ctDNA testing for MRD assessment in PET-positive patients at EOT after first-line therapy (CLARITY™). The addition of CLARITY™ to the NCCN guidelines comes as a result of demonstrating a greater than 90% clinical accuracy rate with a 96% reproducibility rate in comparing cancer-free and tumor-derived cfDNA samples from healthy donors and patients with DLBCL.[10] The addition of this test to the guidelines is the first step towards minimizing the need for invasive procedures and testing, while maximizing clinical tools

Table 1: MRD Assessment Assays for DLBCL

Assay	Clinical Sensitivity (%)	Analytical Specificity (%)	Limitations
CAPP-Seq	40-50	>95	Background error rate
PhasED-Seq	80-90	>95	Limited geographic availability

to ensure safe and appropriate delivery of chemotherapy in the relapse/refractory setting.

There are currently more than 10 clinical trials open, evaluating the use of ctDNA at various points of treatment for patients with DLBCL. With continued use, improvements in testing abilities, and better understanding of the utility of the test elicited through these clinical trials, ctDNA will continue to expand its scope of use in all types of malignancies, especially aggressive lymphomas. ●●

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The Right Dose for Every Patient

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Breakthroughs in medicine are often touted for their ability to improve survival and response rates in patients with various medical conditions, but the equally important component of safety is often evaluated as medications undergo development, research, and commercial access. Traditionally, dose-finding oncology trials are designed to establish a maximum tolerated dose (MTD) using a 3+3 design. This methodology is intended to maximize cytotoxicity while pushing the limits of tolerability in clinical research subjects. The Clinical Reassessment Method (CRM) is an alternative approach that utilizes interim data to reevaluate the next dose level. The Bayesian Optimal Interval (BOIN) design improves upon 3+3 design in that consecutive dose levels are chosen by analyzing and incorporating data collected from the current dose level to determine subsequent levels. While all these designs are credible and applicable to cytotoxic chemotherapy, with the latter two decreasing the chance of overdosing subjects, these methods may fall short of providing ideal dosing for certain targeted agents or predicting long-term cumulative side effects that may impact a patient's quality of life for months or years. Patients with metastatic breast cancer (MBC), for example, may be on multiple drugs for decades to prevent recurrence and prolong survival.

In 2020, an organization called the Patient Centered Dosing Initiative (PCDI) conducted a survey to gauge the impact of treatment related adverse events on individuals with MBC. Presented at ASCO in 2021, the survey revealed that over 90% of the 1221 respondents were willing to discuss dosing options with their provider that would enhance their quality of life (QOL).[1] In 2021, the Friends of Cancer Research published a White Paper stressing the need for dose optimization of new cancer therapies.[2] One literature review revealed that 48% of subjects in Phase III clinical trials of molecularly targeted agents required some form of dose modification.[3]

"Presented at ASCO in 2021, the survey revealed that over 90% of the 1221 respondents were willing to discuss dosing options with their provider that would enhance their quality of life (QOL).[1]"

We had an opportunity to talk to PCDI co-founder, Julia Maues (JM), and team member, Jo Lynn Collins (JLC), to discuss the initiative.

Can you share about Anne Loeser, her journey, and the impetus for starting PCDI?

JM: Anne was the creator of PCDI, and I was involved from the start when she first had the idea and began the work to make it happen. Anne was a very educated patient advocate. She lived with MBC for several years. She had a deep commitment to improving cancer care—not just for herself, but for all patients. She kept a running list of challenges patients face and called it her manifesto. Dosing became her focus, and she brought together a group of like-minded people who shared her vision and wanted to help push it forward. Before PCDI, she wrote *The Insider's Guide to Metastatic Breast Cancer*. She self-published it as a patient-centered resource covering life with MBC, treatments, side effects, and key questions to ask doctors.

How did your journey with MBC lead you to Anne and PCDI?

JM: Anne lived in Salt Lake City, and I live in Washington, DC. We are members of the Metastatic Breast Cancer Alliance and so were several other patient advocates. I knew Anne from her book and through Alliance meetings .

It was really important because my own experience was shaped by conversations that prioritized both length and quality of life, and included dosing. The more I met other patients on treatment, the more I saw that I was privileged to have a doctor who had those conversations [with me] and the more I wanted to be loud and help others be able to have those conversations.

JLC: There are advocates within the MBC community who do amazing things, and Anne was one of those people and her reputation has infiltrated and blossomed throughout the community.

I was diagnosed in 2019 and was initially on a treatment that was causing side effects that were very unwelcome, very unpleasant. In these advocacy spaces, her book was mentioned to me. It didn't specifically talk about dosing, but it did talk about QOL with respect to side effects. I started doing a bit more digging and trying to understand what other patients' experiences were and I found that people, like Julia, were following in the footsteps of others who had done dose reductions and were having success with it. It gave me the courage to broach that subject with my oncologist, and fortunately, I was also privileged that my oncologist was open and receptive and that helped me to stay on that medication longer. My third line treatment automatically started at a reduced dose because I learned that people had success with a ramp up [dose] approach instead of starting at the maximum dose and waiting for side effects to become too toxic. I was able to stay on my third line treatment for three years and had almost no side effects. It was unbelievable, because a lot of people have terrible side effects.

I'm on my fourth line of treatment, which is a newer medication, and a lot of people have had significant side effects. I've been very fortunate not to experience any of those [side effects] because I've started on a reduced dose, and it's made a huge impact on my

QOL. I'm a single mom. I work. So, being able to feel good and take care of the things that I need to do for my children and my job is extremely important. I'm very grateful and passionate about sharing my experience with others which is why I joined the PCDI team.

What's next for PCDI?

JM: We are in the process of designing version 2.0 of the survey, creating marketing materials and submitting for IRB approval for exemption. Two PCDI patient members are leading it, Dr. Amy Beumer and Martha Carlson. It's a collaboration between PCDI, a medical oncologist, Dr. Maryam Lustberg, and a social epidemiologist, Dr. Mya Roberson. It will be launched in April.

We recently did a smaller survey of patients on antibody-drug conjugates because an informal poll in an online group had shown that most weren't on the full dose, highlighting a key issue. With over 200 responses, we're analyzing the data and plan to submit findings to conferences and journals. These drugs are unique, yet their dosing may still rely on outdated principles.

What can we, as pharmacists, and members of the healthcare team, do to help?

JM: We launched the [first] patient survey in 2020. Twenty percent of patients had to go to the ER because of a side effect from a cancer drug, and over 40% had to skip a treatment. What good is a therapy you have to skip? Things started to change in 2021, particularly after Anne's talk at ASCO in June of 2021.

Instead of defaulting to the maximum tolerated dose, drug development should prioritize exposure-response, efficacy, and safety data to find the right balance. For metastatic patients who rely on these treatments for life, a more tolerable approach isn't just ideal – it's necessary.

In October, [the] FDA launched Project Optimus and published an opinion piece in the NEJM emphasizing that the long-standing assumption—higher doses mean better efficacy—doesn't always hold, especially with newer treatments. It's hard to disagree with the idea that patients, especially metastatic patients who are going to be on these treatments for life, deserve to live not just longer, but also well.

I will tell you that even back when it was not a popular topic to bring up, pharmacists were on our side. I remember talking with pharmacists in academia and the government and them saying "Thank you, we have been trying to scream this from the rooftops." There are people we've had to convince, and we've come a long way, but the pharmacists have been in agreement from the very beginning.

Any closing thoughts?

JM: We're working on a new website and trying to find ways to keep resources up to date. It's frustrating that some patients only hear about these options from our website or other patients instead of their own doctors. People with cancer shouldn't have to be the ones bringing up quality of life or different dosing strategies—that should be part of the conversation with their care team. We want to make sure this information is easier to find so patients don't have to figure it out on their own.

As pharmacists who care for and advocate for patients in our daily practice, we can continue to support research that evaluates efficacy of more tolerable doses of cancer therapy and discuss dose modifications with the healthcare team that balance efficacy with quality of life. As Julia mentioned, pharmacists have consistently understood the value of finding the right dose. Our perspective into patient routines, adherence, and toxicities lends itself to better advocate for optimizing quality-of-life. While the team at PCDI encourages patients to ask the right questions of their healthcare team, they also recognize that reduced dose intensity therapies are not for all patients, diseases, and therapies. In some scenarios, reducing the dose of cancer treatment may not result in non-inferior outcomes, so research needs to continue investigating what doses and schedules would optimize the balance of safety and efficacy. To read more about the Patient-Centered Dose Initiative, visit https://www.therightdose.org. ●●

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Hedgehog Pathway Inhibitors for Locally Advanced and Metastatic Basal Cell Carcinoma: A Real-World Single-Center Retrospective Review

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Background

Basal cell carcinoma (BCC) is the most common skin cancer in people of Caucasian ancestry.[1] It is highly curable by surgical excision or radiation therapy. In rare cases, BCC can be locally destructive, difficult to surgically remove, and develop distant metastases.[2] Hedgehog pathway inhibition with vismodegib or sonidegib is considered to be the standard-of-care first line therapy.[3] Hedgehog inhibitors (HHI) can induce a 50–60% response rate in patients with locally advanced basal cell carcinoma (laBCC) or metastatic basal cell carcinoma (mBCC).[4,5] However, tolerability can be a challenge, and dose adjustment strategies are not provided in the manufacturer labeling. The most common adverse event experienced with HHI treatment is muscle spasm, affecting nearly half of patients. BCC oncogenesis is linked to activating mutations that lead to the stimulation of the hedgehog pathway.[6] The stimulation of this pathway can result in an influx of calcium through the activation of coreceptors. Through hedgehog inhibition, there can be a depletion of calcium in muscle cells, inducing muscle spasms. Thus, calcium replacement might prevent muscle spasms, and coenzyme Q10 (CoQ10) may play a role in supporting muscle health.[7-9] There is limited evidence regarding real-world management of HHI toxicity and the use of calcium and CoQ10 supplementation to mitigate adverse events.

"There is limited evidence regarding real-world management of HHI toxicity and the use of calcium and CoQ10 supplementation to mitigate adverse events."

Methods

This is a single-center retrospective study, with institutional board approval, evaluating the efficacy and safety of HHIs for the treatment of laBCC & mBCC. Patients with locally advanced or metastatic BCC who received vismodegib or sonidegib from January 2012 to June 2021 were included with minimum of a 6 month follow up period. Patients were identified using pharmacy treatment plans and prescription records indicating receipt of vismodegib or sonidegib. Patients who were incarcerated, pregnant, receiving a HHI through a clinical trial, or receiving treatment prescribed by providers from outside institutions were excluded.

Results

Of 71 patients screened, 60 patients started on a HHI for BCC. Patient characteristics are described in Table 1. Most patients were white males with a median age of 65 years. Of the 60 patients, 37 patients were treated with vismodegib and 23 with sonidegib. Approximately 30% of patients started therapy with an empiric dose reduction. Table 2 shows the initial dosing regimen for all patients. Seventy percent and 83% of patients were started on FDA approved once-daily dosing of vismodegib and sonidegib respectively, while 18% and 9% were started on five-times-per-week frequency, respectively. Dose reductions occurred in 85% of patients. Only 9 patients (15%) were able to maintain daily dosing. Nineteen patients (32%) continued taking the HHI for more than 6 months. Due to toxicities, 7 patients were crossed over to the alternate HHI.

Of 60 patients, 55 patients were assessable for the primary outcome. The median progression-free survival (PFS) was not reached (95% CI, 34.7 months-not reached for sonidegib and 34.4 months-not reached for vismodegib). The median overall survival was not reached either (Fig 1. and Fig 2.). Twenty-five patients (45%) had a complete response and 9 (16%) had partial response. The overall response rate was 62%. Fourteen (25%) patients had stable disease, and 7 (13%) patients had disease progression.

The most common treatment-related adverse events (ADEs) with the initial treatment were myalgia/muscle spasm (46%), dysgeusia (37%), fatigue (30%), gastrointestinal effects (28%), weight loss (15%), and alopecia (15%). The toxicities were similar in the crossover group as well with myalgia/muscle spasm (43%), fatigue (29%), and weight loss (28%) being the most common. Treatment interruption occurred in 63% of patients due to ADEs. More patients in the vismodegib group (59%) required dose reduction compared to the sonidegib group (24%). The rate of treatment discontinuation was also higher with vismodegib (30%)

Table 1. Baseline characteristics

Characteristic	Vismodegib N=37 (62%)	Sonidegib N=23 (38%)	Total N=60
Median age, years (range)	60 (29-86)	68 (49-88)	64 (29-88)
Gender, n (%)			
Male	24 (65)	12 (52)	36 (60)
Race, n (%)			
Asian	0 (0)	0 (0)	0 (0)
Black or African American	0 (0)	1 (4)	1 (1.7)
White	36 (97)	21 (92)	57 (95)
More than one race	0 (0)	1 (4)	1 (1.7)
Unknown	1 (3)	0 (0)	1 (1.6)

than with sonidegib (9%). A total of 7 patients were switched from one HHI to the other. Of those patients, 71% were switched for intolerance and 29% for progression. Calcium supplementation was used in 19 patients for either prevention (63%) or treatment (37%) for HHI-induced myalgia. Eight patients also received CoQ10 along with calcium supplementation. Fewer dose reductions (17%) were required in patients who received prophylactic calcium and/or CoQ10 supplementation compared to patients who did not receive prophylaxis (42%). However, despite supplementation, the incidence of myalgia/muscle spasm did not differ between the prophylaxis and no prophylaxis groups (42% and 46%, respectively).

Discussion

Based on ERIVANCE phase II trial results, vismodegib was the first selective small-molecule inhibitor approved in 2012 for laBCC and mBCC [10, 11]. Followed by sonidegib, approved in 2015 for laBCC based on the results of BOLT trial.[5, 12] Our real-world data showed similar outcomes as the ERIVANCE and BOLT trials with a 62% response rate and a PFS not yet reached as of the data cutoff time point with a 95% CI of approximately 34.5 months to not reached for both drugs. There was no statistical difference found in efficacy between vismodegib and sonidegib (Figs 1-2). However, the adverse events reported in the BOLT and ERIVANCE trials did not align with our real-world data. Our safety analysis showed significant differences in adverse events, with needing fewer dosing changes and rate of treatment discontinuation for sonidegib compared to vismodegib (24% vs. 59% and 9% vs 30%, respectively). Additionally, 63% of patients who remained on therapy for more than six months were taking sonidegib. Our data strongly suggested that sonidegib is better tolerated than vismodegib with equivalent efficacy.

Despite the high incidence of treatment-related ADEs seen in ERIVANCE and BOLT trials, there are no recommendations provided by the manufacturers' labeling for the management of drug-related toxicities.[5, 10-14] Although, in our study the administration of calcium with or without CoQ10 decreased the number of dose reductions needed for HHI-associated muscle spasms, which allowed patients to maintain dose intensity and remain on therapy for a longer duration. Our exploratory analyses also showed that longer durations of treatment exposure were seen in patients with an empiric initial dose reduction without escalation and in patients with lower weekly dosing (3 or 5 times a week), whereas patients on a daily regimen required more interruptions and dose reductions. Hence, longer exposure to HHIs may delay disease progression and prevents exhaustion of subsequent lines of therapy.

Some limitations of our study are that it was a single-center retrospective review, included a small sample size, provider's preference was used for initial drug selection, and dosing for the initial regimen as well as adjustments were not standardized. A larger prospective trial should be conducted to assess the differences in efficacy and tolerability between the two HHIs and to confirm our observations.

Table 2. Initial treatment regimens

Initial Frequency	Vismodegib 150 mg (N= 37) n (%)	Sonidegib 200 mg (N=23) n (%)
Once daily	26 (70)	19 (83)
Five times a week	7 (18)	2 (9)
Other	4 (12)	2 (8)
Every other day	1 (3)	1 (4)
Three times a week	1 (3)	1 (4)
Twice a week	1 (3)	ND
Dose escalationa	1 (3)	ND

a 4 times a week for 2 weeks, then increase to 5 times a week; ND = not done

Fig 2. Overall survival by treatment

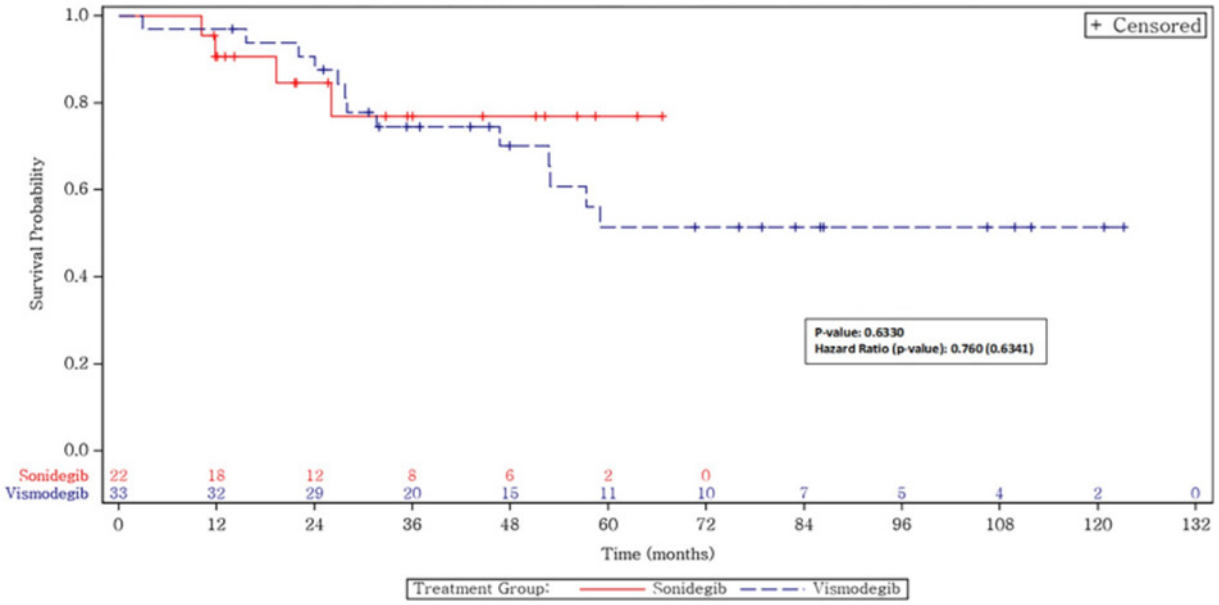
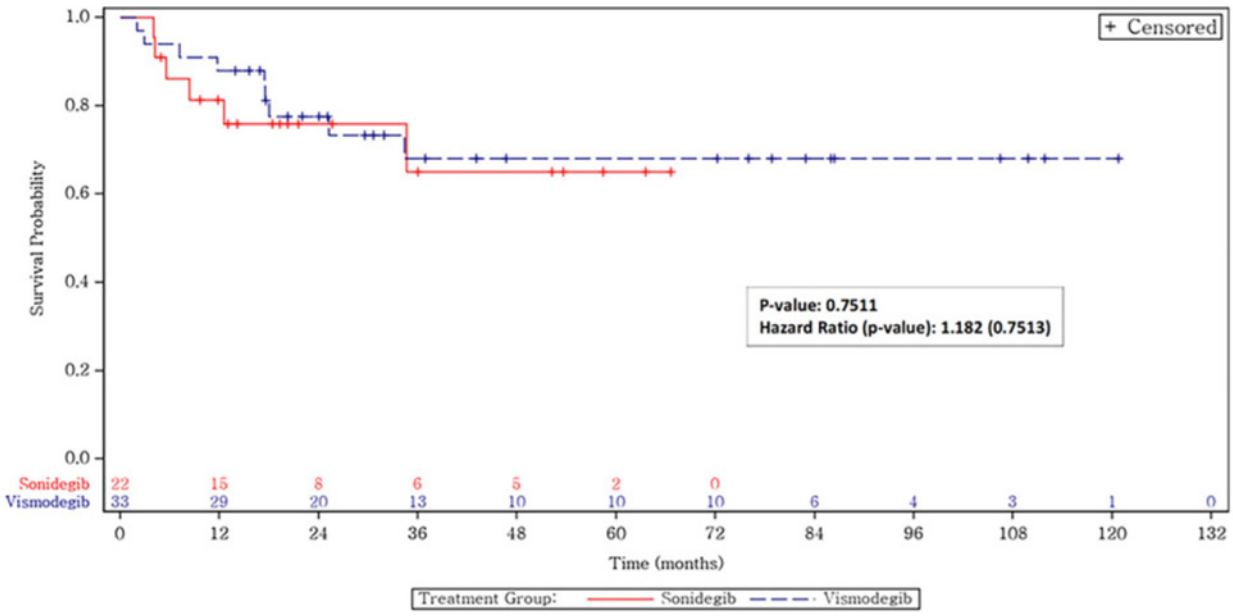


Fig 1. Progression-free survival by treatment



Conclusion

Our real-world safety and efficacy results of HHIs in patients with laBCC or mBCC were consistent with the phase II trial outcomes. Based on our experience, both agents had similar efficacy. However, sonidegib may have better tolerability compared to vismodegib. A less frequent dosing regimen may improve tolerability and allow patients to stay on treatment longer without compromising a response. Furthermore, calcium and/or CoQ10 supplementation may decrease dose reductions due to HHI-associated myalgia or muscle spasm. ●●

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Haste, Waste, & Hope: The Accelerated Approval Pathway

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The accelerated approval (AA) pathway for new medications arose from the AIDS epidemic in 1992, but is now dominated by anti-cancer drugs. This approval pathway aims to speed the approval of medications for unmet medical needs if the drug appears *likely* to provide clinical benefit based on a surrogate marker. For anti-cancer medications, the surrogate marker used as the basis of accelerated approval has often been response rate. Recent reviews of the AA pathway in oncology have found that "only a small portion of indications under the AA program fail to verify clinical benefit"[1] and conversely that "Most cancer drugs granted accelerated approval did not demonstrate benefit in overall survival or quality of life within 5 years of accelerated approval."[2]

There is a delicate balance of unnecessarily delaying patient access to historic treatment advances and ensuring new medications have a safety, dosing, and drug-interaction record of evidence moving them beyond the "experimental" category. To quote one of my favorite movies, "Hindsight is 20/20, my friend" and in retrospect some of the AA decisions seem wiser than others.[3]

"Most cancer drugs granted accelerated approval did not demonstrate benefit in overall survival or quality of life within 5 years of accelerated approval."

Can you imagine if there was no AA pathway prior to imatinib's 2001 approval for blast and accelerated phase CML? One could even argue the chronic phase approval of imatinib in 2002 was an unnecessary delay. Docetaxel, temozolomide, and pemetrexed all reached the market via the AA pathway. The same is true of ibrutinib, pembrolizumab, and nivolumab. While knowledge of pemetrexed's relative inferiority in squamous cell cancers of the lung or the importance of MGMT-methylator status for temozolomide were not known at the time of their accelerated approval, it seems like a wise decision to approve these agents before learning the full weight of their risk-to-benefit profile.

Potential detriments of the AA pathway include widespread use of a drug before the complete safety profile is known, use in a patient population unlikely to benefit (e.g. cetuximab in RAS-mutated colorectal cancer), or use in a disease state where the surrogate marker for approval ends up not correlating to clinical benefit (e.g. overall survival). Duvelisib was granted accelerated approval for follicular lymphoma (FL) in 2018 (at the same time garnering regular approval for CLL/SLL). In 2021, the FL indication was withdrawn and in 2022 an FDA drug safety communication was issued about an increased risk of death.[4]

How is a patient taking duvelisib supposed to feel after learning this? Did the FDA fail me? Or did my oncologist or oncology pharmacist fail me? Such medical reversals surrounding the AA pathway have stirred much debate about how clinicians and the public should discuss and react to new cancer drugs at our disposal thanks to the AA pathway. Is it speed or verification of clinical benefit we want?

A recent and thought-provoking discrete choice experiment suggests the answer to that question is "Yes, both." Forrest and colleagues devised several scenarios where participants with a recent personal (self, relative, or close friend) experience with cancer where they had to choose Drug A or Drug B.[5] Each participant reviewed 12 scenarios and selected between 2 drugs. With almost 900 subjects participating, the researchers were able to glean the motivations of respondents for their choices.

For context here is one such scenario: You are confined to your bed or chair more than 50% of your day and have a life expectancy of 1 year. The two drugs you must choose from both have "substantial improvement" in that they prevented cancer growth for 5 more months than your current treatment.

- Drug A has a "low certainty" you will live 1-5 months longer, but is FDA approved now.
- Drug B has "high certainty" you will live 1-5 months longer, but FDA approval is expected in 6 months.

The researchers found that participants had strong preferences for high certainty of clinical benefit and strong preferences against 1-year delay in FDA approval. They also found respondents faced with a drug with "low certainty" of survival benefit would wait 21.68 months for strong evidence ("high certainty") of survival benefit.

While much has been written about wise or unwise AA decisions, the Forrest experiment gives us much needed insight into public perception of anti-cancer drug approval where both speed and likelihood of benefit are important. Clearly, both are valued.

How does this information help us as clinicians? I believe knowing the AA pathway has had both notable success and notable, ahem, revisions is a requisite place to start. The speed at which cancer drug development and cancer information accrues is fast and getting faster. This means drug use will change over time, and this foresight can be used when discussing use of AA drugs with patients, such as chemotherapy education.

First, it seems reasonable to acknowledge the fact that a drug may only be available because of the AA pathway. This segues nicely into a discussion of the drug's *currently known* adverse event profile, but admitting that both the frequency, severity, and type of drug toxicity may be different. This might mean we will learn quickly how to manage some side effects but may be caught off guard by others.

Second, another way to think of an AA drug is to think of it as a "conditional approval" since AA drugs are required to demonstrate clinical benefit. Telling patients that an AA drug has shown early signs of success, but more evidence is needed for "high certainty" of benefit is also reasonable. The time required to gather additional evidence may be a luxury that some cancer patients cannot afford. This can lead to difficult conversations where we as clinicians are helping to choose the *least bad* option from the *most bad* option.

Finally, these difficult conversations are necessary for good patient care. I have told patients that as an oncology pharmacist, "I speak doctor, and I speak patient." Our ability as pharmacists to connect with patients at their level should allow for such nuanced conversation. While there may be some truth to the old saying "haste makes waste" when it comes to the AA pathway, it also true that the AA pathway brings hope. After all, somewhere in 2001 a patient with no siblings in a CML blast crisis was denied a potentially curative allogeneic stem cell transplant.....then came imatinib....via accelerated approval. ●●

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