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Game of Clones: Oncologic Drugs Advisory Committee Decision Crowns Daratumumab, Benches Belantamab

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Game of Clones: Oncologic Drugs Advisory Committee Decision Crowns Daratumumab, Benches Belantamab

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The Oncologic Drugs Advisory Committee (ODAC) is an independent panel of experts that advises the FDA on cancer therapies.[1] It reviews the clinical trial benefit-risk profile of data submitted by pharmaceutical companies for new treatments, expanded indications, or labeling changes. Members include oncologists, hematologists, biostatisticians, pharmacologists, patient representatives, and other specialists. In public meetings, FDA reviewers, drug sponsors, and external experts present evidence for evaluation and discussion. While ODAC's recommendations are not final, they significantly influence the FDA's final decisions. In 2025, two ODAC decisions drew significant attention within the malignant hematology and multiple myeloma communities as they were made against expectations.

"In addition, the prolonged treatment schedule extending over multiple years also contributes to cumulative healthcare costs, logistical burdens, and risks of treatment-related morbidity.[16] These aspects should be discussed with patients at the time of offering treatment for SMM."

Daratumumab for Smoldering Myeloma: FDA's ODAC Votes in Favor of Daratumumab as Treatment for Smoldering Myeloma

On May 20, 2025, ODAC voted 6–2 in favor of daratumumab monotherapy for the treatment of high-risk smoldering multiple myeloma (SMM) based on positive results from the Phase 3 AQUILA trial. Key discussion points included the clinical meaningfulness of the efficacy endpoints evaluated in the trial and the overall benefit–risk profile of daratumumab in the high-risk SMM population. The FDA subsequently approved daratumumab for this indication on November 6th,2025, aligning with ODAC's recommendation.[2]

Treatment for Smoldering Myeloma

SMM is an asymptomatic precursor to multiple myeloma (MM) characterized by a clonal plasma-cell disorder without end-organ damage. Under contemporary International Myeloma Working Group (IMWG) criteria, SMM is defined by a serum M-protein of ≥3 g/dL (or ≥500 mg/24 h in urine or both) and/or ≥10-60% bone marrow plasma cells (BMPCs) without evidence of any SLiM-CRAB symptoms – 60% BMPCs, FLC ≥100, MRI evidence of more than one focal lesion, calcium elevation, renal failure, anemia, or bone disease – that define active MM.[3] The IMWG "2/20/20" model (M-protein >2 g/dL, involved/uninvolved FLC ratio >20, marrow plasma cells >20%) stratifies patients into risk groups, with high-risk patients having a 63% chance of progression within two years.[4]

Historically, observation was the standard of care, reserving therapy for symptomatic MM. Randomized studies such as the Spanish QuiRedex trial (lenalidomide plus dexamethasone vs. observation), and ECOG-ACRIN E3A06 (lenalidomide vs. observation) have shown that early therapy for high-risk SMM delays disease progression.[5,6] However, no overall survival benefit was observed, and approximately 40% patients in each study experienced grade 3 or 4 adverse events, most commonly neutropenia, infections, and hypertension. Proteasome inhibitor combinations such as KRd (carfilzomib, lenalidomide, and dexamethasone) and intensive regimens like GEM-CESAR have shown deep responses but are more toxic.[7,8] Based on this, guidelines view lenalidomide as an acceptable option in carefully selected high-risk patients, but acceptance is based on lower-level evidence. A clinical trial remains the preferred approach in this setting.

Daratumumab is a human IgG1κ monoclonal antibody that targets CD38, a protein highly expressed on plasma cells. Its effects include complement-dependent cytotoxicity, antibody-dependent cytotoxicity, phagocytosis, and direct apoptosis. In addition, daratumumab has also demonstrated immune-modulatory effects through the depletion of regulatory cells, which could contribute to sustained disease control and delay progression in SMM.[9] The phase 2 CENTAURUS trial evaluated daratumumab monotherapy in intermediate/high-risk SMM and showed ~40–60% response rates and durable control.

The phase 3 AQUILA trial enrolled 390 patients who received either subcutaneous daratumumab (QW in cycles 1 and 2, Q2W in cycles 3-6, and Q4W thereafter) in 28-day cycles until cycle 39, 36 months, or disease progression, whichever came first, or were on active surveillance.[10] The trial defined high-risk multiple myeloma as patients with clonal BMPC ≥10% and at least one of the following: serum M-protein of ≥3 g/dL, IgA SMM, immunoparesis with reduced levels of two uninvolved immunoglobulin isotypes, a ratio of involved:uninvolved serum FLCs ≥8 to < 100, or a percentage of clonal BMPC of more than 50%-60%. The primary endpoint was progression-free survival (PFS), defined as progression to active

MM as assessed by an independent review committee and according to IMWG diagnostic criteria for MM (SLiM-CRAB) or death. Major secondary endpoints included complete response (CR), overall response (ORR), PFS on first-line MM treatment (PFS2), and overall survival (OS). Daratumumab significantly improved PFS compared to active surveillance; however, PFS2 or OS were improved but did not reach statistical significance. Grade 3-4 treatment-emergent adverse events (TEAEs) occurred in 40.4% and 30.1% of patients, and serious adverse events (SAEs) occurred in 29% and 19.4% in the daratumumab and active monitoring groups, respectively. The incidence of grade 3-4 was 16.1% in the daratumumab group and 4.6% in the active-monitoring group infections. However, the frequency of TEAEs leading to daratumumab discontinuation was low at 5.7%.

Per FDA analyses presented during the ODAC meeting, the study protocol definition in the AQUILA trial for high-risk SMM did not align with any of the established models including PETHEMA 2007, MAYO 2008, Mayo 2018, or IMWG 2020 models.[4,11,12,13] Rather, the protocol combined criteria from the different models and added on other parameters. When re-classifying the patient population using the established models mentioned above, more than 50% of patients in the trial fell into the low- to intermediate-risk SMM category. This suggests that the study population may not be representative of the currently defined high-risk group, raising concerns about the applicability of the AQUILA trial findings to truly high-risk SMM patients, as the trial claims. Another limitation was clinical meaningfulness of the primary PFS endpoint and secondary PFS2 endpoint. While the study met the primary endpoint, a majority of PFS events were progression in laboratory parameters (SLiM), and there were very few CRAB-related end organ damage events. Additionally, the lack of significance in OS and PFS2, which were key secondary endpoints in the trial, introduce uncertainty regarding the sequencing of therapies and upfront treatment. Use of daratumumab for SMM may also impact later treatment of multiple myeloma where first line treatment now includes CD38 targeted drugs. Molecular studies have shown that treatment with daratumumab reduces CD38 expression on MM cells that endures throughout the entire drug regimen.[14,15] Additionally, while well tolerated overall, daratumumab doubled the risk of infections which may not be favorable for the SMM population who are primarily asymptomatic in their disease.

ODAC recommendation and subsequent FDA approval were based on an unmet need in this population, where some patients and providers would want an option to prevent progression to active myeloma with early treatment versus a watch and wait approach, where active surveillance may not be an effective strategy in a real-world setting.

Implications for Clinical Practice of SMM

According to guidelines, low-risk SMM patients should be enrolled in a clinical trial or observed at 3-6 months intervals. For high-risk patients, a clinical trial is strongly recommended, or other options include observation at 3-month intervals or treatment with single-agent lenalidomide only in carefully selected patients. With the ODAC recommendation and recent FDA approval, single-agent daratumumab has now been incorporated into guidelines for high-risk SMM. However, a head-to-head study comparing daratumumab with lenalidomide utilizing established models for risk-stratification is warranted to better understand which drug should be preferentially used. Based on the results of the AQUILA trial and the discussion in the ODAC committee meeting, daratumumab can be presented as an option for patients with high-risk SMM. It will be important for providers to recognize that treatment with daratumumab could alter CD38 expression which could diminish the efficacy of this critical therapeutic class at the time of symptomatic relapse. This concern is nontrivial as the most effective front-line treatments for multiple myeloma consist of CD38-directed therapies. In addition, the prolonged treatment schedule extending over multiple years also contributes to cumulative healthcare costs, logistical burdens, and risks of treatment-related morbidity.[16] These aspects should be discussed with patients at the time of offering treatment for SMM.

Belantamab Mafodotin for Relapse/Refractory Multiple Myeloma (RRMM): FDA's ODAC Votes Against Belantamab Mafodotin in Combination with Bortezomib and Dexamethasone (BVd) and Pomalidomide and Dexamethasone (BPd) as Treatment for RRMM

On July 17, 2025, ODAC concluded that the risk–benefit profile of belantamab mafodotin, when used in combination with BVd or BPd for the treatment of relapsed multiple myeloma, was unfavorable. This determination was primarily attributed to concerns regarding ocular toxicities and missed opportunities for optimal dosing, as documented in the public record. Despite the favorable efficacy data, ODAC voting outcomes reflected significant concerns regarding the overall benefit–risk profile of belantamab mafodotin at the proposed doses. For the combination with BVd, the committee voted 5 against and 3 in favor, while the combination with BPd yielded a vote of 7 against and 1 in favor.[16,17]

Belantamab Mafodotin as a Treatment for RRMM

Belantamab mafodotin is a BCMA-directed antibody–drug conjugate linked to the microtubule inhibitor MMAF.[18] It was the first BCMA-targeted therapy to receive FDA approval was granted accelerated approval on August 5, 2020 based on DREAMM-2 for adults with RRMM after ≥4 prior therapies.[19] In November 2022, approval was voluntarily withdrawn following the negative DREAMM-3 confirmatory trial. Subsequent phase 3 trials (DREAMM-7, DREAMM-8) demonstrated positive results, supporting its use in later-line MM.[20,21] However, ODAC raised concerns about patient representation (older adults, Black patients, U.S. patients), the relevance of comparator arms (e.g., PVd not being FDA-approved), and significant ocular toxicity including keratopathy and vision changes, as well as uncertainty about the proposed dosing regimen. The ocular toxicity presentation includes corneal changes and alterations in visual acuity, ranging from mild superficial changes to severe epithelial defects and keratopathy, with potential ulceration.

In both phase III studies of DREAMM-7 and DREAMM-8, combinations incorporating belantamab mafodotin showed statistically significant and clinically relevant improvements

Table 1. Efficacy Analysis[20, 21]

DREAMM -7 (August 1, 2024)	DREAMM-8 (June 2, 2024)
Belantamab mafodotin in combination with bortezomib and dexamethasone **(BVd)**	Belantamab mafodotin in combination with pomalidomide and dexamethasone **(BPd)**
RRMM with at least one prior line of therapy	RRMM with at least one prior line of therapy including lenalidomide
Belantamab mafodotin dose: 2.5 mg/kg Q3W	Belantamab mafodotin dose: 2.5 mg/kg on cycle 1 followed by 1.9 mg/kg Q4W starting on cycle 2
Primary endpoint: PFS was met HR=0.41 (95% CI: 0.31, 0.53); p-value <0.0001 Secondary endpoint: OS Statistically significant; HR = 0.58 (95% CI: 0.43, 0.79); p-value 0.0005	Primary endpoint: PFS was met HR=0.52 (95% CI: 0.37, 0.73); p-value = 0.0001 Secondary endpoint: OS not reached No statistical significance; HR 0.77 (95% CI: 0.53, 1.14)

PFS, progression-free survival; OS, overall survival; HR, hazard ratio

over standard comparator regimens. Both trials demonstrated significant improvements in PFS for the belantamab mafodotin arm in the second-line setting. DREAMM-7 showed statistically significant improvement in OS and is the first trial that outperformed daratumumab combination therapy in the RRMM setting. While ocular toxicity remains a notable safety concern, both studies demonstrated that this risk can be mitigated with appropriate dose adjustments.[6,22] Notably, despite the need for less frequent dosing, belantamab mafodotin maintained efficacy when used as part of combination therapy. Lower doses and longer intervals were associated with similar response rates and lower rates of dose modifications.

Implications for Clinical Practice of RRMM

Despite the ODAC discussion, on October 23, 2025, belantamab mafodotin was FDA-approved in combination with bortezomib and dexamethasone under a Risk Evaluation and Mitigation Strategy (REMS) program pertaining to the need for ophthalmic exams prior at the start of treatment and before each dose.[23] Patients should use preservative-free lubricant eye drops at least 4 times a day starting with the initial infusion and continuing until the end of therapy and also avoid contact lenses unless otherwise directed. While REMS is a requirement by the FDA for certain medications with serious safety concerns, REMS cannot compensate for an unfavorable benefit-to-risk ratio of drugs. Approximately 75% of patients in both studies required dose modifications (interruptions or reductions) due to ocular events, and dose modifications proved to be an effective mitigation strategy; however, it remains unclear whether the ocular events are reversible.

The multiple myeloma community is ready to welcome back belantamab mafodotin as a multiple myeloma treatment given the unmet need in the RRMM setting for specific patient populations based on the results of DREAMM-7 and DREAMM-8 studies with the ability to have dose-adjustment strategies. Uncertainty persists regarding what constitutes an optimal dose in the real world, as well as optimal sequencing of BCMA therapies. Certain populations, such as patients rapidly progressing who live in rural areas, those who live far from centers that can administer CAR-T or bispecific therapies, older patients who are unable to tolerate lymphodepletion therapy before CAR-T, or those patients who cannot tolerate bridging therapy and/or the CAR-T treatment itself, are all potential candidates for an off-the-shelf anti-BCMA agent like belantamab mafodotin. Having belantamab mafodotin available as a therapy option after CAR-T and bispecific therapies is beneficial as there has been success when using other BCMA-targeted therapies after BCMA CAR-T. Accessibility is a key advantage, including outpatient administration, with no hospitalization required and no special care needed. Ongoing trials like DREAM-10 and DREAM-14 are expected to answer these questions about optimal safety and tolerability, as well as comparable efficacy.

Table 2. Adverse Events Analysis[20, 21]

	DREAMM -7		DREAMM-8	
	BVd n=243	Daratumumab, Bortezomib, and Dexamethasone **(DVd)** n=251	**BPd** n=155	Pomalidomide, Bortezomib, and Dexamethasone **(PVd)** n=147
Grade 3 or higher adverse events	95%	78%	94%	76%
Infection	70%	67%	82%	68%
Ocular events	79%	29%	89%	30%
Grade 3 or 4 ocular toxicity	34%	3%	43%	2%
Discontinuation	26%	15%	15%	12%
Ocular events leading to treatment discontinuation	9%	0	9%	0

Conclusion

Although ODAC decisions historically align with FDA final decisions, we can see that this does not always happen based on the belantamab mafodotin example. However, the decision has not yet been made on biologics license application for daratumumab. The manufacturer is currently submitting additional data, and final decision is pending. Both FDA approval and guideline recommendations are influencing treatment paradigms and insurance approvals. Regardless, with both drugs available to patients, it is up to the treating physicians to determine how they will be utilized in practice and what role they will play. ●●

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Rejection as Redirection: My Path in Pharmacy

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Pharmacy is more than a career; it is a calling. Look closer inside a pharmacy, and you'll see it's not just about filling prescriptions. It is a place where stories are shared, fear finds a voice, and solace is found in an unspoken connection. Today, as I reflect on my journey, I feel pharmacy chose me as much as I chose it. While I can't claim my decision was the product of meticulous deliberation, the rollercoaster that followed was navigated successfully thanks to the unwavering support of the strong relationships and invaluable networks I was fortunate to have.

My introduction into the world of pharmacy began in the bustling environment of retail. While grateful for the experience of offering unique learning opportunities and the chance to connect with people from all walks of life, I felt a nagging sense that something was missing. The daily rhythm of dispensing medications, though punctuated by moments of connection and challenge, didn't fully align with my growing desire to delve deeper into the clinical aspects of the profession. However, transitioning away from retail with no prior hospital experience proved more challenging than anticipated. The perceived gap in my resume often led to closed doors and discouraging rejections. It became clear that I couldn't wait for an opportunity to appear – I had to create one myself.

"There's no denying that being a pharmacist demands a delicate balance: the scientific expertise to understand complex concepts and the genuine compassion to connect with patients on a personal level."

Ultimately, securing my position in hospital pharmacy was the culmination of a deliberate, multi-pronged strategy fueled by resolve. I began by actively building relationships, leveraging pharmacy associations as a platform to connect with hospital pharmacists and administrators. My goal wasn't just to ask for job leads, but to listen, learn, and understand the specific challenges and needs of their institutions. Simultaneously, I focused on proactively bridging the clinical knowledge gap between retail and clinical practice. I invested in myself by obtaining disease-specific certifications and completing advanced training such as Basic Life Support, ensuring I had the credentials to match my ambition. Finally, I maintained a mindset of flexibility, staying open to any role regardless of location, shift, or initial responsibilities, and that would provide the crucial foot in the door. Through a combination of networking, continuing education, and sheer determination, I finally found my way into the world of oncology, a specialty that I can now say has not only fulfilled my professional aspirations but also ignited a sense of purpose I hadn't experienced before.

My transition out of the retail environment was a welcome challenge, but the invaluable foundation for my success was undoubtedly built during my time in community pharmacy. It was there I learned to master high-efficiency multitasking, communicate complex drug information clearly, and foster the essential teamwork that underpins every successful transaction. Above all else, retail pharmacy taught me one crucial lesson: know your customer. The only thing that changes in the setting from retail to hospital pharmacy is the customer themselves—moving from the patient at the counter to the nurse, doctor, or family member on the unit.

Nevertheless, pivoting from retail pharmacy to oncology was indeed a dramatic shift. Fortunately, this new environment immersed me in a supportive network of colleagues who freely shared their expertise and were instrumental in bridging the gap between my retail background and the specialized knowledge required for oncology pharmacy. They patiently demystified complex concepts, explained intricate treatment protocols, and guided me through the nuances of patient care in this dynamic area of practice. More than just training, their mentorship fostered a sense of belonging, making me feel supported and valued in a field that had initially felt so foreign. This welcoming environment was crucial in my transition and fostered a deep appreciation for the collaborative spirit of oncology care. While my colleagues provided the foundation for my success, leadership within the institution played a pivotal role in my professional growth. They actively cultivated my role by opening doors to diverse and impactful opportunities, revealing strengths in myself even I hadn't fully recognized, offering guidance and support through challenging times, and championing my achievements, ultimately shaping my career in ways I could never have imagined.

Reflection on Personal Impact and Growth

My oncology pharmacy career has come full circle, from novice and eager to learn, to educator and sharing my knowledge with both patients and fellow pharmacists starting their own careers. At the heart of my institution's philosophy is a deep commitment to patient-centered care, and they recognize the invaluable contributions pharmacists can make in achieving this goal through their unique skillset and knowledge base. Leadership within my facility has actively championed breaking down traditional barriers and expanding the pharmacist's role beyond the confines of the pharmacy department by encouraging pharmacists to engage directly in patient care through activities such as comprehensive medication management, participating in collaborative practice with physicians and other healthcare professionals, and targeting patient education initiatives. This forward-thinking approach is perfectly exemplified by our pharmacist-led patient education program, an initiative I had the privilege of both helping to develop and participate in currently. Pharmacist-led patient education empowers patients to become informed stewards in their own health management by providing resources and tools to make thoughtful decisions, ultimately leading to more effective, safer, and integrated care. My institution's commitment to education extends beyond patient care to fostering the next generation of pharmacists, a role I deeply value. There's a unique sense of fulfillment that comes from helping others navigate the path you once traveled. Having faced my own challenges early in my career, I find it incredibly rewarding to now serve as a preceptor for both sixth-year pharmacy students during their clinical rotations as well as for pharmacy residents in our comprehensive PGY-2 program.

When I consider my winding path through pharmacy, I am filled with gratitude because my career has given me an important source of motivation and a deep commitment to serving others through engaging in challenging yet impactful work. Amidst the day-to-day demands, it's easy to lose sight of the deeply personal nature of oncology pharmacy. With every compounded chemotherapy bag, verified medication order, and patient encounter, we are given a tangible reminder of a person, their network of relationships, and a life upended by cancer. We must remember that our patients are more than just diagnoses; they are mothers, fathers, partners, children, friends. They are individuals whose lives have been irrevocably changed. They entrust us with their hopes and fears, relying on our expertise to guide them through this challenging time. Oncology pharmacy offers the extraordinary privilege of supporting them through their darkest days and celebrating their remarkable victories. There's no denying that being a pharmacist demands a delicate balance: the scientific expertise to understand complex concepts and the genuine compassion to connect with patients on a personal level. I'm incredibly proud to be part of this profession, which continually pushes boundaries and adapts to the changing needs of our patients. The challenges are certainly significant, but the ability to make a difference in people's lives is a reward beyond measure. And, as with any journey in life, it's important to remember that rejection can become a redirection toward your true calling.

Operationalizing Precision Medicine: How Pharmacists Can Support Practices Across the Oncology Ecosystem

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Precision medicine has moved from a visionary concept to a practical reality in oncology. By tailoring treatment strategies to the molecular and genetic profile of each patient's cancer, clinicians can deliver therapies that are more effective, less toxic, and increasingly aligned with patient-centered care.[1] Yet, the promise of precision medicine is not self-executing. It requires infrastructure, coordination, and expertise to translate scientific advances into routine practice.[1,2]

Oncology pharmacists are uniquely positioned to bridge the gap between innovation and implementation. From identifying patients who should undergo testing, to ordering and coordinating the test with the appropriate laboratory, through interpretation of results and ultimately program design, pharmacists are central to ensuring that precision medicine is not only available but also sustainable, equitable, and impactful.[3]

Precision Medicine in Oncology: A Brief Primer

In oncology, precision medicine is built on the ability to identify biomarkers that inform treatment decisions and patient outcomes. Biomarkers can be broadly categorized as prognostic or predictive. Prognostic biomarkers provide information about the overall cancer outcomes, regardless of therapy. Predictive biomarkers indicate the likelihood of response or resistance to a specific therapy. Understanding the distinction is critical: prognostic biomarkers help clinicians counsel patients and stratify risk, while predictive biomarkers directly guide therapeutic selection.[2]

Testing is the foundation of precision medicine. Without timely and accurate biomarker identification, targeted therapies cannot be deployed effectively. Yet despite clear guideline recommendations, testing rates remain low across many cancer types. For example, up to 40% of patients with advanced non–small cell lung cancer (NSCLC) do not receive comprehensive biomarker testing before treatment initiation, and fewer than half of eligible colorectal cancer patients undergo RAS or BRAF testing.[4,5] Even when testing is performed, gaps persist. A 2024 study found that 24% of patients with actionable driver mutations in NSCLC began non-targeted therapy before results were available, and many patients with identified mutations never received the corresponding targeted therapy.[5,6] These missed opportunities undermine the promise of precision oncology and highlight the need for system-level program design.

These gaps are not simply clinical oversight; rather, they reflect deeper system-level challenges in how testing is ordered, processed, and acted upon. Addressing them requires not only awareness of testing guidelines, but also a working knowledge of the laboratory methods used to detect and characterize predictive and prognostic biomarkers.[1] Each technique has unique strengths and limitations, and pharmacists must understand these nuances to contribute effectively as integral members of the multidisciplinary oncology team. Table 1 highlights some of these nuances.

> **"Unlike traditional tumor boards, MTBs focus on genomic data, helping teams distinguish between prognostic and predictive alterations, prioritize clinically actionable findings, and identify opportunities for targeted therapies or clinical trial enrollment."**

A previous volume of HOPA News is a critical resource that comprehensively covered select solid tumor biomarkers including NCCN testing recommendations and Food and Drug Administration (FDA) approved therapies.[10]

The Role of Oncology Pharmacists in Precision Medicine Programs

Oncology pharmacists are essential partners in precision oncology, contributing expertise that spans biomarker testing, therapy selection, toxicity management, and long-term program sustainability. Their role is not limited to interpreting molecular reports – they also help design and operationalize the systems that make precision medicine feasible in practice.[2,3]

Program design begins with mapping the patient journey to determine when testing should occur based on cancer type and clarifying responsibilities across the care team. Pharmacists can establish governance by securing representation on pathway committees, formulary teams, and, critically, tumor boards. Defining measurable outcomes such as turnaround time, therapy alignment with biomarkers, and appropriate delays in treatment until results are available creates accountability and supports continuous improvement.[1,3,11]

Implementation brings these plans to life. Pharmacists collaborate with IT to embed order sets, electronic medical record (EMR) alerts, and documentation templates that prompt appropriate testing and streamline interpretation. Increasingly, AI-enabled decision support tools are being integrated into EMRs to identify patients who meet criteria for testing and alert providers when results are missing. Pharmacists play a key role in configuring these tools to ensure relevance and reduce alert fatigue. They also lead genomic education for providers and coordinate with laboratories to ensure timely, interpretable results.[2,3,11]

Once designed and implemented, sustainability depends on demonstrating value. Pharmacists track key metrics, conduct cost-benefit analyses, and engage payers to support reimbursement. They also advocate for standardized testing protocols and equitable coverage, ensuring precision medicine is accessible across diverse settings.[3,11]

Molecular Tumor Boards: A Cornerstone of Precision Oncology

Within this broader programmatic framework, molecular tumor boards (MTBs) represent one of the most visible and impactful venues for pharmacist leadership. MTBs are specialized forums that bring together oncologists, pathologists, genetic counselors, pharmacists, and other experts to interpret molecular profiling results and translate them into actionable treatment strategies. Unlike traditional tumor boards, MTBs focus on genomic data, helping teams distinguish between prognostic and predictive alterations, prioritize clinically actionable findings, and identify opportunities for targeted therapies or clinical trial enrollment.[3,12]

For instance, in a case of metastatic colorectal cancer, a traditional tumor board might focus on imaging findings, surgical options, and systemic chemotherapy regimens. In contrast, an MTB would delve into the patient's next generation sequencing results, discussing the implications of a *KRAS* mutation, *BRAF V600E* status, or microsatellite instability (MSI). The team might debate whether the *BRAF* mutation warrants targeted therapy, or whether MSI-high status opens the door to immunotherapy.[12,13]

Pharmacists are indispensable in these discussions. Beyond matching molecular alterations with guideline-based therapies, they assess the feasibility of proposed options by evaluating toxicity profiles, prior lines of therapy, drug-drug interactions and access barriers such as payer coverage or patient assistance programs. They also anticipate resistance patterns, advise on sequencing strategies, and keep the team current on new approvals and evolving guidelines, ensuring that MTB recommendations are both evidence-based and implementable in practice.[3,12]

The Managed Care Connection

The complexity of biomarker testing extends beyond the clinic and into the payer landscape. Each test carries unique requirements for tissue handling, assay selection, turnaround time, and interpretation. These variables intersect with payer policies, coding systems, and coverage criteria, creating a landscape that is often fragmented and difficult for practices to navigate. Without deliberate coordination, patients may face delays, denials, or incomplete testing that compromise the promise of precision oncology.[14]

To address these complexities, managed care organizations (MCOs) are increasingly recognized as critical partners in addressing these challenges. By aligning coverage policies with evidence-based guidelines, MCOs can help ensure that patients receive the right test, at the right time, from the right laboratory. Coverage alignment, reflex testing policies, and preferred laboratory networks can streamline workflows and reduce redundant biopsies.[14] Equally important, payer engagement can address disparities by supporting testing in community settings, reducing out-of-pocket costs, and ensuring equitable access to advanced diagnostics.[15]

Pharmacists are uniquely positioned to bridge the clinical and payer perspectives. In MTBs, they not only interpret molecular results but also contextualize recommendations within the realities of coverage, reimbursement, and patient access. At the program level, they collaborate with managed care teams to design testing pathways that balance clinical utility with cost-effectiveness while monitoring utilization and outcomes data to demonstrate value.[14,15]

In this way, pharmacists serve as the connective tissue across the precision medicine ecosystem, linking laboratory science, multidisciplinary decision-making, and managed care strategy. By

Table 1: Precision Medicine Tests in Oncology[7-9]

Testing Modality	Primary Use	Examples in Oncology	Strengths	Limitations
IHC	Protein expression	ER/PR in breast cancer; PD-L1 for immunotherapy	Widely available; Relatively low cost	Semi-quantitative; Inter-observer variability
ISH (FISH/CISH)	Gene amplification for rearrangement	HER2 in breast cancer; ALK/ROS1 in lung cancer	High specificity; Visual confirmation	Labor-intensive; Limited to single targets
PCR	Hotspot mutation detection	BRAFV600E in melanoma; KRAS in colorectal cancer	Fast; Sensitive; Cost effective	Limited to know mutations; Not comprehensive
NGS	Comprehensive genomic profiling	EGFR, KRAS, MET, RET, NTRK, etc.	Broad coverage; Detects multiple mutations simultaneously	Higher cost; Longer turnaround time; Requires bioinformatics support
ctDNA	Non-invasive mutation detection; MRD monitoring	EGFR T790M in NSCLC; MRD in hematologic malignancies	Minimally invasive; Allows serial monitoring	Lower sensitivity in low tumor burden: Not yet standardized
ddPCR/Multiplex assays	Highly sensitive mutation detection; multi-marker panels	Rare mutation detection; MRD monitoring	Very sensitive; Quantitative	Limited availability; Specialized expertise required

IHC = immunohistochemistry, ER/PR = estrogen receptor/progesterone receptor, PD-L1 = program death-ligand 1, ISH = in situ hybridization, FISH = fluorescence in situ hybridization, CISH = chromogenic in situ hybridization, HER2 = human epidermal growth receptor 2, ALK = anaplastic lymphokinase, ROS1 = proto-oncogene tyrosine -protein kinase, PCR = polymerase chain reaction, BRAFV600 = B-raf proto-oncogene valine 600, EGFR = epidermal growth receptor factor, KRAS = Kirsten rat sarcoma viral oncogene homolog, MET = mesenchymal epithelial transition factor, RET = rearranged during transfection, NTRK = neurotropic tyrosine receptor kinase, ctDNA = circulating tumor DNA, NSCLC = non-small cell lung cancer, MRD = minimal residual disease, ddPCR = droplet digital polymerase chain reaction

integrating these domains, they help ensure that patients are more likely to receive the right test, have that test be interpreted in the right context, and be linked to the right therapy, fulfilling the true promise of precision oncology.[15]

Conclusion

Precision medicine in oncology cannot succeed without deliberate systems, collaboration, and accountability, and pharmacists are central to making that vision become a reality. By guiding biomarker testing, shaping program design, and contributing to molecular tumor boards, pharmacists ensure that genomic insights translate into actionable, patient-centered care. Their ability to bridge clinical practice with managed care strategy positions them as indispensable leaders in building sustainable and equitable precision medicine programs. Ultimately, pharmacists serve as the linchpin that connects science, policy, and practice to deliver the right test and the right therapy to every patient. ●●

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The Rest is Still Unwritten: Quality Improvement Projects - Path from Concept to Publication

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Quality improvement (QI) plays a vital role in advancing patient care by streamlining clinical workflow and optimizing the use of resources.[1] Quality initiatives also support healthcare organizations in meeting regulatory requirements and core measures, assuring high quality patient care and services. Pharmacists are often integral members of interprofessional teams working on QI initiatives, yet only a few of these projects make it to publication. A study conducted between 2016 and 2019 found that only 6% of local QI projects submitted for an internal presentation were eventually published in peer-reviewed journals.[2] While this only represents a small sample of projects, it highlights the broader gap in QI publication. As pharmacists who have personally faced challenges in publishing QI work, we aim to share common barriers and provide practical strategies leading to successful QI project publication. These strategies can increase pharmacists' effectiveness in publishing their QI projects, sharing their meaningful contributions to advancements in oncology practice and optimizing patient care.

Why should you publish your QI project?

Sharing your QI project is essential for extending improvements in patient care beyond your local setting. Published QI initiatives allow other healthcare organizations to adopt successful strategies or avoid repeating mistakes in the improvement process. Compared with word-of-mouth communication or local presentations, publication also offers a more efficient way to disseminate your results on a broader scale. It helps to strengthen the evidence base for QI in healthcare and adds credibility to your work, reinforcing its value to both your institution and the healthcare community.

Setting an early goal for publishing when discussing QI initiatives could also motivate interprofessional teams to persist through inevitable project challenges. Additionally, publication provides opportunities for further professional networking, collaboration, and career development, allowing healthcare professionals to learn from each other's improvement efforts.[3]

What are barriers to QI publication?

QI manuscripts substantially differ from traditional research manuscripts. Many healthcare professionals are accustomed to the familiar structure of research articles, which can make it challenging to adapt to the unique writing style for QI initiatives. While both research and QI projects share the goal of advancing patient care, research seeks to generate new knowledge and is typically hypothesis-driven, measured with pre- and post-assessments. QI aims to improve a process with continuous measurement through Plan, Do, Study, Act (PDSA) cycles to demonstrate sustained improvement. Because of these differences, authors must be clear in their writing when describing their QI project.[4] By recognizing distinctions between research and QI, pharmacists can better tailor their writing to meet journal expectations and maximize their publication's impact.

"It is important to remember that QI initiatives with negative or unexpected outcomes are still valuable to share. While some multidisciplinary teams may hesitate to publish projects that did not go as planned, these experiences provide critical insights."

It is important to remember that QI initiatives with negative or unexpected outcomes are still valuable to share. While some multidisciplinary teams may hesitate to publish projects that did not go as planned, these experiences provide critical insights. Sharing such results can help others understand potential challenges, encourage discussions on why interventions may not have worked, and provide insight to those considering similar initiatives.

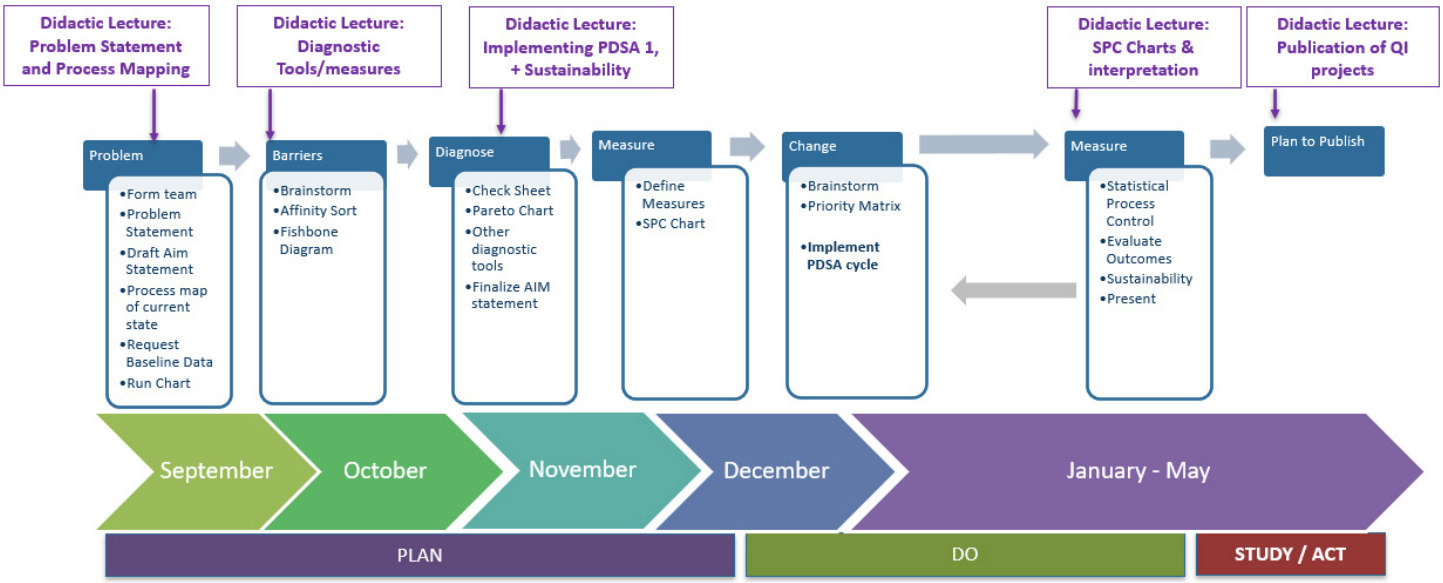
Another common barrier includes time constraints for project completion with so many competing priorities. If pharmacy residents are participating, completing at least one full PDSA cycle within the limited timeframe of a residency year can be challenging. To overcome this, it is important to establish strict timelines early on and adhere closely to project milestones. Figure 1 shows an example of a timeline that the University of Virginia uses with coordinated didactic lectures to help pharmacists stay on track with their QI projects.

How can you strengthen your QI manuscript?

When preparing your QI manuscript, be sure to involve the full interprofessional team throughout the writing process. Diverse perspectives from all team members can enhance clarity, improve accuracy, and emphasize the collaborative nature behind the project. Additionally, the team should utilize available resources to ensure the manuscript meets high standards and effectively demonstrates your work.

One such resource is the Standards for Quality Improvement Reporting Excellence (SQuIRE), which was originally published in 2008 and updated in 2015 (SQuIRE 2.0). Table 1 summarizes these

Figure 1. Example of Project Timeline from the University of Virginia Health System Pharmacy Department



Adapted from American Society of Clinical Oncology (ASCO) Quality Training Program (QTP)

standards, which provide a structured framework for QI publications and helps increase their credibility.[5]

As QI initiatives continue to evolve, the committee is working to ensure the standards are user-friendly and aligned with the needs of the healthcare improvement community. SQuIRE 3.0 updates are in process and are expected to be released in the near future.[6] Once published, it is recommended to review the new guidelines to ensure your QI manuscript aligns with the most current standards before submitting to a journal.

Another great reference with detailed explanation of QI publication components was published in *Journal of Graduate Medical Education*: "How to Write up Your Quality Improvement Initiatives

Table 1. SQuIRE 2.0 Summary for Manuscript Publication

Manuscript Section	Description
Title and Abstract	• Indicate manuscript is about an initiative to improve healthcare • Provide adequate summary of key information in the abstract to assist in searching and indexing
Introduction	*Why did you start this project?* • Provide a problem description, available knowledge, rationale, and specific aims
Methods	*What did you do to complete this project?* • Report context, description of intervention(s), approach used to assess impact of interventions, measures chosen for studying processes and outcomes • Analyze qualitative and quantitative methods used to draw conclusions from the data and provide methods for understanding variation within the data • Incorporate ethical considerations and how they were addressed, including formal ethics review and potential conflicts of interest
Results	*What did you find in this study?* • Report initial steps of the intervention(s) and their evolution over time, details of the process measures and outcome, and contextual elements that interacted with the intervention(s) • Elaborate on observed associations, unintended consequences (such as unexpected benefits, problems/failures), or missing data
Discussion	*What does it all mean?* • Summarize key findings, including relevance to rationale and specific aims, and discuss strengths and limitations • Interpret results and compare findings to other publications • Explain project impact on healthcare system • Conclude sustainability, potential spread of processes to other contexts, implications on practice/generalizability to other areas, and suggested next steps
Other Information	• Report funding sources • Cite SQuIRE if used to write a manuscript

Table 2. Recommended Elements for QI Publication and Common Pitfalls

Manuscript Section	Elements	Common Pitfalls
Introduction	• Describe relevance of QI initiative being assessed • Explain gap between existing knowledge and information needed to attain QI outcomes • Add problem and aim statements	• Too long • Relevance review is longer than evidence gap discussion • Aim statement not clearly included
Methods	• Provide details about project context to connect details on intervention choice, plans for implementation, and how outcomes may be affected • List multiple intervention steps (could discuss using PDSA cycle description) • Provide a family of measures (may include outcome, process, and balancing measures)	• Superficial description with lack of context • No theory supporting reported intervention • Steps reduced to single intervention and single measure to track project impact
Results	• Use statistical process control (run or control charts) to demonstrate data presented over time	• Data displayed as simple before-after comparisons
Discussion	• Describe a brief summary of most important findings • Place study in context of other similar QI initiatives • Reflect on result implications • Describe lessons learned • Discuss how limitations may impact results • Review future steps	• Limited to implications for local institution/setting only • Results repeated without analyzing and providing a deeper reflection on their implications • Lessons learned during the process omitted instead of included • Listing limitations without providing thoughtful consideration for their potential effects
Conclusion	• Summarize key take-aways from study	• Simply suggest "further research is needed" • Overgeneralize study findings to all settings

for Publication." The authors' recommendations incorporate SQuIRE 2.0 guidelines but provide further explanation for each outlined section. Table 2 summarizes these recommended elements and common pitfalls for QI manuscripts.[7]

Another strategy to improve the likelihood of publication is selecting the most appropriate journal for your work. Choosing a journal with a focus on QI initiatives may increase the chance that reviewers will understand and appreciate the unique aspects of your project. The Institute for Healthcare Improvement (IHI) provides guidance on potential journals that commonly publish QI work. Additional examples of oncology-focused journals that more frequently feature QI initiatives include:

- Journal of Hematology Oncology Pharmacy (JHOP)
- Journal of Clinical Oncology (JCO) Oncology Practice – Quality in Action
- Journal of Oncology Pharmacy Practice

Prior to submitting your manuscript, review examples of published QI literature to ensure your organization and flow align with the selected journal's preference. The journals listed above provide several excellent examples of QI publications that can serve as templates to guide your submission.

Conclusions and Available Resources

Publishing QI initiatives helps oncology pharmacists contribute to a culture of continuous improvement and ensures that meaningful advancements are recognized and adopted more widely. By understanding common barriers and applying practical strategies, interprofessional teams can increase the likelihood of a successful QI publication. For more information on QI projects and access to other quality tools, please visit HOPA's Quality Oversight Committee (QOC) website: https://www.hoparx.org/resources/oncology-quality-resources/

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Following the Roadmap of our Current Strategic Plan

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As we move toward the close of HOPA's current three-year strategic plan, it's a fitting moment to reflect on how far the organization has come—and how our strong foundation continues to position HOPA for the future. This has been a period of thoughtful growth, steady progress, and deep commitment to the mission that guides our work every day.

Since its launch, the strategic plan has provided a roadmap for strengthening the organization, enhancing member value, and ensuring that our operations are aligned with HOPA's long-term vision. Through this work, we have sharpened our focus, strengthened our structure, and enhanced our ability to deliver meaningful impact. Thanks to the dedication of our staff team, the guidance of the board, and the engagement of HOPA's members and partners, the organization is well-positioned for continued success.

Operational excellence is at the heart of how we deliver on HOPA's mission. While much of this work happens behind the scenes, it is what allows your organization to remain responsive, resilient, and forward-focused. Whether it's improving service delivery, optimizing resources, or strengthening partnerships, we approach each effort with a focus on stewardship and impact.

As we look ahead to the next chapter, we do so from a place of stability, strength, and momentum. HOPA's foundation remains solid as we expand our reach, deepen our impact, and prepare to launch the next strategic plan. Together we are poised to tackle new opportunities, adapt to new challenges, and continue building meaningful change together while we chart a course for continued excellence.

We invite you to stay engaged as we transition into the next chapter — your support, input, and partnership continue to be vital as we set new operational priorities and deliver on HOPA's mission and vision. ●●

Primary Prophylaxis for Cancer Therapy-Related Cardiac Dysfunction – Adding SGLT2i to Our Arsenal

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It is well established that besides cancer recurrence, the second most common cause of mortality for the oncology patient population is cardiovascular disease. Given this concern and the increased knowledge on cardiovascular complications attributed to anti-cancer medications, the cardio-oncology subspecialty has continued to grow over the years.[1] Furthermore, given that these cardiovascular (CV) toxicities commonly occur secondary to anti-cancer medications, it can be argued that the role of the pharmacist in minimizing these complications is paramount. It is critical that the oncology pharmacy community is up to date on risk, patient assessment, recommended monitoring, and potential cardio-toxicity prophylaxis when initiating anti-cancer agents.

When considering oncologic therapies and their potential CV toxicities in question, the primary class that has been investigated to-date is anthracyclines, in particular doxorubicin.[1,2] However, other high-risk classes that have been identified by the International Cardio-Oncology Society (IC-OS) and European Society of Cardiology (ESC) include HER2 targeted therapies, VEGF inhibitors, RAF/MEK inhibitors, BCR-ABL inhibitors, proteasome inhibitors, immunomodulatory drugs, and immune checkpoint inhibitors, with Table 1 listing CV toxicities commonly seen with these agents.[3] A patient's individual risk for cancer therapy-related cardiac dysfunction (CT-RCD) can be calculated, and depending on baseline risk factors (e.g. comorbidities, biomarkers, age, prior therapy, etc.), monitoring standards have been recommended by IC-OS as well.[1,3] Notably, the utility of this calculation is still heavily debated in clinical practices given the lack of robust prospective trials validating the tool for comprehensive use. However, there have been several retrospective validation studies demonstrating successes with the use of this calculator for CV toxicity prediction and a potential future role in CT-RCD estimation.[4-7] Prospective validation studies are ongoing.

"Ultimately, given the majority of data and the focus on patients with baseline T2DM, it is best to initially implement these agents in this group. SGLT2i use could be considered for patients who are warrant therapy for a different indication in which a benefit has been seen (e.g. HFrEF or CKD); however, the benefit of SGLT2i for CT-RCD prophylaxis in this space is uncertain, concluding that risk/benefit analyses should be considered."

Following the identification of risk and proper monitoring, it then becomes warranted to consider if tactics can be used as primary prophylaxis, especially for patients at a high or very high risk of CT-RCD. In the 2022 IC-OS and ESC Cardio-Oncology guidelines, multiple prophylactic approaches were proposed including the administration of dexrazoxane, substitution of standard anthracyclines for liposomal counterparts, extension of the chemotherapy infusion duration, and implementation of prophylactic agents including beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), or statins.[1] Besides optimizing baseline CV health based on primary prevention guidelines (without regard for chemotherapy), the above recommendations were classified as a Category IIb recommendation, instructing readers that these interventions 'may be considered', with either a B or C level of evidence. In this guideline, a B level of evidence was defined as 'data derived from a single randomized clinical trial or large non-randomized studies' and C was defined as 'consensus of opinion of the experts and/or small studies, retrospective studies, registries.' Since this publication, there have yet to be significant changes to these recommendations, with two primary exceptions. The first exception is statins - two prospective,

Table 1. Anti-Cancer Agents and Associated CV Toxicities

Cancer Treatment Class	Treatment Related CV Toxicity
Anthracycline chemotherapy	Heart failure, asymptomatic LVSD, atrial and ventricular arrhythmias
HER2-targeted therapies	Heart failure, asymptomatic LVSD, hypertension
VEGF inhibitors	Hypertension, heart failure, asymptomatic LVSD, myocardial ischemia and infarction, QTc prolongation
Second and third generation BCR-ABL tyrosine kinase inhibitors	Arterial thrombosis, venous thromboembolism, hypertension, heart failure, asymptomatic LVSD, atherosclerosis, QTc prolongation
Proteasome inhibitors	Heart failure, asymptomatic LVSD
Immunomodulatory drugs	Myocardial ischemia and infarction, trial and ventricular arrhythmias, venous thromboembolism, arterial thrombosis, hypertension
RAF and MEK inhibitors	Heart failure, asymptomatic LVSD, hypertension, QTc prolongation
Androgen deprivation therapies	Atherosclerosis
GnRH agonists	Myocardial ischemia and infarction
Antiandrogens	Diabetes mellitus, hypertension
Immune checkpoint inhibitors	Myocarditis, pericarditis, non-inflammatory heart failure, ventricular arrhythmias, AV block, acute coronary syndromes

CV, cardiovascular; GnRH, gonadotropin-releasing hormone; LVSD, left ventricular systolic dysfunction; VEGF, vascular endothelial growth factor

randomized trials published after the ESC guidelines provide conflicting results on the true benefit of statins for CT-RCD prophylaxis.[8,9] The other is the addition of sodium-glucose co-transporter-2 inhibitors (SGLT2i), primarily empagliflozin or dapagliflozin, to the list of potential prophylactic agents.

The SGLT2i class was developed to inhibit the reabsorption of glucose from the glomerular filtrate in the proximal tubule.[2,10,11] Through this mechanism, these agents reduce renal reabsorption of filtered glucose and increase urinary glucose excretion. Given this mechanism, SGLT2i were originally approved for type 2 diabetes mellitus (T2DM), acting as an effective agent for insulin-resistant patients.[11] However, in the analyses of the T2DM-focused studies, secondary endpoints demonstrated CV safety benefits indicating SGLT2i have potential use as 'Swiss Army Knives' of the primary care practice setting. Multiple further studies have confirmed these findings. Initially, this expansion occurred in heart failure with reduced ejection fraction (HFrEF), with the DAPA-HF and EMPEROR-Reduced trials demonstrating a reduction in risk of worsening heart failure, heart failure-related hospitalizations, and death from CV causes for patients with or without diabetes. Investigations then continued into the heart failure with preserved ejection fraction (HFpEF) or moderately reduced ejection fraction (HFmrEF) spaces with the EMPEROR-Preserved and DELIVER trials, again demonstrating a benefit in CV death with SGLT2i beyond T2DM.[11] One key take-away from those publications was the preservation of renal function in patients on SGLT2i which highlighted a potential role in chronic kidney disease (CKD). Both the DAPA-CKD and EMPA-KIDNEY trials investigated the role of dapagliflozin and empagliflozin in CKD, respectively, again demonstrating benefit from SGLT2i in decline of kidney dysfunction or death from CV or renal causes and further expanding the indications for these agents.[11] Given the potential for CV benefit beyond patients with T2DM, a seed was planted indicating that these medications could also have a role in the cardio-oncology space.

The mechanisms by which SGLT2i protect against CT-RCD is believed to be multi-factorial involving anti-inflammatory effects, antioxidant effects, minimizing endo-reticular (ER) stress, increasing ketogenesis, enhancing energy metabolism and autophagy, and inhibiting ferroptosis.[2,11] These mechanisms can ultimately be organized into two categories – mitigating inflammation/myocardial stress or optimizing function of myocardial tissue. All of the above mechanisms are believed to have a role in the pathogenesis of CT-RCD. However, increased inflammation and promotion of reactive oxygen species can especially impact myocytes negatively. SGLT2i are thought to work against this primarily by decreasing the activation of nuclear factor κB and nod-like receptor pyrin domain-containing 3 (NLRP3), ultimately attenuating the synthesis of proinflammatory cytokines.[2,11] Concurrently, SGLT2i minimize other cellular stressors including reactive oxidative species, reducing expression of ER-related proteins and reducing ferroptosis. In addition to inflammation mitigation, SGLT2i work to increase the contractility and function of the myocardium. This is primarily driven by an increase in the AMP-activated protein kinase (AMPK) pathway and shifting β-hydroxybutyrate oxidation, increasing ketogenesis. With an increase in glucosuria, SGLT2i trigger a state that resembles starvation, increasing the use of β-hydroxybutyrate and thus increasing myocardial contractility and reducing inflammation. Given this function, it is also believed that SGLT2i could have an anti-tumor effect in addition to being cardioprotective. Additionally, upregulation of the AMPK pathway and restoration of autophagy (following dysregulation by anti-cancer agents) helps to increase ATP production in the myocardium and decrease buildup from autolysosomes, allowing myocytes to restore their baseline metabolic function.[2,11]

While the potential for SGLT2i and the proposed mechanisms sound promising, applying them to current cardio-oncology practices can be difficult given a lack of robust evidence in humans to-date. Notably, many murine models or in-vitro studies have

described the aforementioned mechanisms, particularly elucidating a potential role in CT-RCD mitigation; however, current human trials are limited to retrospective studies and case series described in Table 2.[2,10-19] Given that these trials are subject to biases and have heterogeneous cohorts, there also have been two notable meta-analyses investigating the true benefit of SGLT2i by compiling these data.[20,21] The first of these was by Novo, et al. and pooled 11 observational, retrospective studies that assessed CV toxicities in patients with cancer and T2DM who were undergoing therapy with cardiotoxic chemotherapy.[20] Overall, this analysis included 104,327 patients with various malignancies receiving a variety of agents (e.g. anthracyclines, anti-HER2 therapies, alkylating agents, anti-metabolites, platinum agents, tyrosine kinase inhibitors, immune checkpoint inhibitors, VEGF inhibitors, EGFR inhibitors, anti-microtubule agents, aromatase inhibitors, proteasome inhibitors, and radiation). The average study period was from 2010-2022, with a total number of 29,212 patients receiving SGLT2i. The average age of patients in each trial was 56-77 years, and the average follow up duration was 1-4.8 years. The primary outcome assessed in this meta-analysis was all-cause mortality, finding a benefit with the SGLT2i arm [RR 0.47, 95% confidence interval (CI) 0.33-0.67, $p<0.0001$] and a reduction in heart failure hospitalization (RR 0.44,

Table 2. Clinical Trials Supporting Use of SGLT2i for CT-RCD Prophylaxis[2,10-19]

Study (Year)	Study Type	Population	Groups	Treatments	Key Takeaways
Gongora, et al. (2022)	Observational, retrospective cohort study	• Adults with T2DM and cancer (anthracycline-based therapy • Patients with prior HF	• Cases (n=32): SGLT2i during therapy • Controls (n=96): not SGLT2i exposed	CANA (34%), DAPA (16%), EMPA (50%)	• SGLT2i group demonstrated decreased CV events including decreased HF admissions and decreased rate of CV dysfunction • No new CT-RCD cases observed in SGLT2i cohort
Abdel-Qadir, et al. (2023)	Observational cohort study using medical record data	• Patients ≥ 65Y with T2DM (no HF) • Receiving anthracycline-based therapy	• SGLT2i exposed arm (n=99) • SGLT2i unexposed arm (n=834)	CANA, EMPA, DAPA	• SGLT2i use decreased risk of HF hospitalization but no difference in incidence of new HF • SGLT2i use was not associated with significant mortality benefit
Chiang, et al. (2023)	Retrospective cohort analysis	• Patients with T2DM treated for any cancer	• SGLT2i exposed arm (n=878) • SGLT2i unexposed arm [propensity score matched] (n=878)	CANA, EMPA, DAPA	• SGLT2i use reduced risk for hospitalization from HF and increased OS • Safety data also favored SGLT2i arm
Giangiacomi, et al. (2023)	Prospective, single arm case series	• Patients with anthracycline induced CT-RCD	• SGLT2i exposed [added to other GDMT] (n=7)	EMPA, DAPA	• Improvement in NYHA class, LVEF • No discontinuations or major adverse effects
Hwang, et al. (2023)	Observational cohort study using medical record data	• Adults receiving anthracycline-containing chemotherapy (non-metastatic)	• Patients with T2DM and SGLT2i (n=779) • Patients with T2DM not SGLT2i exposed (n=2337) • Patients wiithoutT2DM (n=7800)	CANA, EMPA, DAPA	• SGLT2i cohort demonstrated improved composite outcome of HF hospitalization, acute MI, ischemic stroke, and death
Avula, et al. (2024)	Retrospective cohort analysis	• Adults with T2DM and exposure to an anti-cancer agent associated with CT-RCD and had subsequent diagnosis of HF or cardiomyopathy	• SGLT2i exposed arm (n=640) • SGLT2i unexposed arm [propensity score matched] (n=640)	CANA, EMPA, DAPA	• SGLT2i arm had decreased risk of HF exacerbation and all-cause mortality • SGLT2i demonstrated benefit in reducing all-cause hospitalizations, ED visits, arrythmias, AKI, and need for renal replacement therapy
Bhatti, et al. (2024)	Retrospective cohort analysis	• Adults with T2DM, cancer, exposure to cardiotoxic therapies, and no HF PMH	• SGLT2i exposed arm (n=8675) • SGLT2i unexposed arm [propensity score matched] (n=8675)	CANA, EMPA, DAPA	• SGLT2i cohort had lower risk of developing CT-RCD, decreased incidence of HF exacerbations, decreased incidence of all-cause mortality, and decreased all-cause hospitalization/ER visit rate
Henson, et al. (2024)	Retrospective cohort analysis	• Patients with HF previously treated with anthracyclines	• SGLT2i exposed arm (n=1323) • SGLT2i unexposed arm [propensity score matched] (n=1323)	CANA, EMPA, DAPA	• SGLT2i use was associated with significantly reduced risk of cachexia, malnutrition, failure to thrive, and all-cause mortality

95% CI 0.27-0.72, p=0.001). Notably for these outcomes, the heterogeneity between the findings was high, with the I^2 for all-cause mortality and hospitalizations being 98% and 84%, respectively.

Additionally, Reshadmanesh, et al published a meta-analysis earlier this year.[21] Similarly, the patient population evaluated all had T2DM, cancer, and received an assortment of agents including anthracyclines, alkylating agents, anti-metabolites, immune checkpoint inhibitors, and others that were not specified in the trial publications. These authors also evaluated 11 studies and included 88,096 patients between 2022-2024, with 20,538 receiving a SGLT2i. The mean age in the SGLT2i arm was 61.68 ± 10.7 years versus 68.24 ± 9.48 years, with most patients in the investigational arm having gastrointestinal malignancies. Like the previous meta-analysis, these data demonstrated a favorable all-cause mortality (RR 0.46, 95% CI 0.34-0.63, p<0.0001) and even cancer-associated mortality with SGLT2i use (RR 0.29, 95% CI 0.27-0.30, p<0.0007), potentially either attributable to anti-tumor effects of SGLT2i or a relatively low patient population, and thus overestimating the impact SGLT2i have on cancer outcomes. Other endpoints also favored SGLT2i including heart failure-associated hospitalizations (RR 0.44, 95% CI 0.27-0.70; p=0.00067) and lower risk of arrhythmias (RR 0.38, 95% CI 0.26-0.56, p<0.0001). When considering the impact these meta-analyses can have on practice, the primary limitation relates to the generalizability of these data. While these publications are broad, incorporating a wide variety of malignancies and cardio-toxic agents, it is difficult to know when to apply SGLT2i interventions to optimize patient outcomes. From these publications, it can be discerned that despite high heterogeneity, there is likely some benefit that SGLT2i have for CT-RCD prevention; however, when to apply these prophylactically is still under question. In addition to these two published meta-analyses, several other meta-analysis abstracts by Shahid, et al, Shafique, et al, and Wannaphut, et al, have also been presented at ASCO Annual Conferences both in 2024 and 2025, demonstrating similar findings for both patients with and without diabetes and again favoring the use of SGLT2i for primary prophylaxis of CT-RCD.[22-24]

With this data confirming a potential use for SGLT2i in this space, the question then becomes where and when this should be implemented into practice. Like previously discussed, implementation is difficult to discern given the limitations of the retrospective and heterogeneous nature of the current data. Ultimately, given the majority of data and the focus on patients with baseline T2DM, it is best to initially implement these agents in this group. SGLT2i use could be considered for patients who are warrant therapy for a different indication in which a benefit has been seen (e.g. HFrEF or CKD); however, the benefit of SGLT2i for CT-RCD prophylaxis in this space is uncertain, concluding that risk/benefit analyses should be considered. Similarly, most of the data primarily focus on anthracycline-based CT-RCD, which again implies it could be best to focus on this patient population for SGLT2i implementation. Other considerations prior to initiation include other baseline cardiovascular risk factors, CT-RCD risk, place in ongoing therapy, risk of adverse events or barriers to SGLT2i care, and monitoring plans, all of which allow for continued expansion of the pharmacist role in care and potential collaboration with other multi-disciplinary teams.[11]

Nonetheless, SGLT2i are a growing class in which their role for CT-RCD primary prophylaxis will potentially become a standard in years to come. At least two meta-analyses have found all-cause mortality benefits in patients receiving these agents while on cardiotoxic chemotherapy. There are a myriad of retrospective analyses demonstrating SGLT2i could play a part in our prophylactic measures for those at increased CT-RCD risk. There is one randomized, prospective analysis, the EMPACT (NCT05271162) trial, currently investigating the role of empagliflozin in anthracycline-associated cardiomyopathy prevention as well as others (e.g. NCT06341842, NCT06427226, NCT06304857, NCT06103279) assessing dapagliflozin or spanning across other CT-RCD associated therapies. As these data and others continue to be published, a greater clarity of SGLT2i's benefit will be discerned. Furthermore, other cardiovascular agents, including sacubitril/valsartan, are continuing to be evaluated in this prophylactic space, further expanding the possibility of the use of additional agents alongside cardiotoxic anti-cancer therapy. Until this is elucidated, the role of SGLT2i should be limited to those with current FDA-approved indications (e.g. T2DM); however, as pharmacists, continued evaluation for eligibility and potential patient benefit is key for optimizing patient care and potentially impacting overall mortality. ●●

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The Path Less Traveled

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The first few years of my pharmacy career went almost perfectly according to plan. So perhaps no one was more surprised than myself when I chose to walk away from clinical practice to pursue a more nontraditional path. I had rigorously followed the typical "clinical pharmacy plan": two years of residency, BCOP, a clinical role, and a sprinkle of academics. I always knew I wanted to teach, and I had fallen in love with outpatient care during my training; so, I was over the moon when I took a faculty role with an ambulatory oncology clinical appointment. Three years later, I had built an oral chemotherapy clinic and established outpatient clinical pharmacy services at my cancer center. At my college of pharmacy, I had developed an entire hematology-oncology curriculum and even created an oncology elective course. I was filled with pride when I considered these accomplishments, but increasingly I wondered, "What next?"

The easy and straightforward path was more of the same: expand ambulatory oncology pharmacy services, create more oncology scholarship, precept more students and residents, take on more committee assignments, etc. However, I saw other pharmacists taking on nontraditional roles, using their clinical expertise to advance care delivery in innovative ways. What if I, too, could impact cancer patients on a greater scale than one patient and one clinic at a time? For me, this change in mindset came with a great deal of anxiety; it required tearing up my plan and leaving behind the "dream" role that I thought would see me through to retirement.

My first steps into exploring alternative roles were deliberately cautious. I began by speaking with classmates and mentors who had already moved into nonclinical work: entrepreneurship, startups, industry, and more. Job boards and blogs became research materials as I considered how different roles would suit my experience and passions, and I critically evaluated my own professional and personal priorities. After much research and self-reflection, I was ready to make a change. With some trepidation, I started applying for nonclinical roles. It took me about 9 months of applying, interviewing, and coming tantalizingly close a few times before I landed a medical science liaison role (MSL) – the quintessential nontraditional oncology pharmacist position.

"One barrier that seems to hold pharmacists back from choosing nontraditional roles is a fear (usually unfounded) that we lack applicable experience in these roles or that the experience we bring may not translate outside healthcare settings. Personally, I had to reframe my accomplishments, both to prepare for the application process, but also to counter my own sense of imposter syndrome."

Pivoting away from clinical practice was a big change; I missed seeing patients, but I gained schedule flexibility, travel opportunities, engagement with respected thought leaders, and a little compensation advantage. In my MSL role, I found satisfaction in familiar elements: staying on the cutting edge of oncology science, creating innovation in cancer care, and collaborating with (and sometimes challenging) interprofessional colleagues. I participated in two new drug launches, bringing novel therapies to patients and engaging providers on optimal sequencing and combinations. Later, I moved into a training role, leveraging my background in education to teach a field medical team. Even in pharma, the teaching certificates I earned in residency and my time directing curricula proved valuable.

After a few years, I once again found myself thinking, "What next?" This time, the fork in the road seemed to be whether to continue in medical training/medical excellence, or to pivot again. As much as I loved running a field medical training program, I began to feel limited to a narrow niche of oncology; I was spending about 90% of my time working on multiple myeloma, in contrast to my time running an oral chemo clinic when I had interacted with patients and providers across almost all tumor types. I also felt that I had moved away from making improvements to cancer workflows and processes. Once more, I returned to researching and reflecting on career options. I wanted to use both my clinical and industry experience while developing new skills in emerging technologies.

When a clinical role opened at a large diagnostics company for an oncology subject matter expert to work on clinical decision support tools for precision oncology, I aggressively pursued it – even after the hiring team told me honestly that they had never thought about recruiting a pharmacist. Landing the job gave me the chance to become a leader in digital health and improve processes across the oncology care journey. Now, a typical day might include meeting with UX/UI engineers to refine dashboard designs, joining sales reps in customer discussions to understand workflow challenges, answering medical information questions about pharmacogenomics, or advising on business strategy for oncology partnerships. Importantly, leadership protects time for patient care, recognizing how clinical practice enriches our work. With this flexibility, I maintain a PRN role at an NCI-designated cancer center, staffing the infusion pharmacy twice a month. Keeping one

foot in practice strengthens my contributions as a subject matter expert on the technology team.

As a pharmacist working outside a typical health care setting, I enjoy a unique opportunity to advocate for the profession of oncology pharmacy, both inside and outside of my company. In an organization of over 70,000 employees, but only a handful of pharmacists, I have become a champion for the voice of the pharmacist designing healthcare solutions. I feel a responsibility to educate the public on the incredible contributions of pharmacists and, equally, to encourage pharmacists to be bold in using their expertise to break new ground in care delivery. Both in industry and in my current role, I have continued to precept pharmacy students. This serves as an outlet for my passion for education and exposes students to creative ways to use their degree. I love showing students that although I may not work in a hospital, I am still a part of an interprofessional team impacting patient care. Maybe not so nontraditional after all.

One barrier that seems to hold pharmacists back from choosing nontraditional roles is a fear (usually unfounded) that we lack applicable experience in these roles or that the experience we bring may not translate outside healthcare settings. Personally, I had to reframe my accomplishments, both to prepare for the application process, but also to counter my own sense of imposter syndrome. Journal club presentations and P&T monographs became evidence of my ability to provide medical insights and respond to drug information requests. Interprofessional teamwork translated to "cross-functional collaboration." Creating curricula and patient education prepared me to lead training programs. Even reviewing Computerized Provider Order Entry chemotherapy order sets proved relevant to partnering with engineering teams on new technology.

For pharmacists open to exploring nontraditional roles, I would encourage beginning with conversations. I engaged with nontraditional pharmacists in my network, reached out to others through social media, and sought out HOPA members working in unique spaces. Before leaping straight into a new role, stretch projects on the job or committee work through an organization like HOPA can offer opportunities to try tasks outside the normal pharmacist job description and deepen one's resume. Reviewing chemotherapy order build sets and volunteering to run a college social media account provided me with digital health practice. Leading working groups on HOPA committees gave me confidence in my project management capabilities. Finally, when it comes to applying to nontraditional roles, expand the search criteria beyond PharmD-required job descriptions.

As I consider my meandering path through pharmacy, which I fully expect will have more twists and turns in the future, I find myself amazed at the versatility of a PharmD degree. Looking around, I see so many creative colleagues pushing the boundaries of what pharmacists are expected to do. Across industry, health technology, diagnostics, medical education, public policy, and more, pharmacists are redefining how we practice. Particularly in oncology, where therapeutic innovation depends on clinical expertise, pharmacists have countless opportunities to contribute. I believe the best innovations emerge when diverse viewpoints are included, and pharmacists are instrumental members of the care team, whether in a cancer center or a nontraditional setting. ●●

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Digesting the Data: Updates in Gastric and Gastroesophageal Cancer

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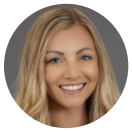

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Background

Globally, gastric and gastroesophageal junction (GEJ) adenocarcinomas rank among the most frequently diagnosed cancers worldwide and are a leading cause of cancer-related mortality.[1] Established risk factors include *Helicobacter pylori* (*H.pylori*) infection, Epstein-Barr virus (EBV), chronic gastritis, obesity, smoking history, and inherited genetic predispositions.[2] Incidence varies markedly by geography, with the highest rates observed in East Asia, Eastern Europe, and South America, while North America reports some of the lowest rates.[3] These differences are largely attributed to variations in diet, living conditions and *H.pylori* prevalence. Adenocarcinomas account for approximately 95% of gastric cancers and are further subdivided based on anatomical location, histology, and molecular profile.[2-4]

Surgical or endoscopic resection remains the standard of care treatment for patients with curative, localized disease.[3] In resectable cases, perioperative FLOT (fluorouracil, oxaliplatin, and docetaxel) followed by surgery has significantly improved overall survival (OS) rates, as demonstrated in the FLOT4 trial.[5] Nonetheless, recurrence after resection remains common, and the global acceptance of perioperative chemotherapy has been inconsistent.[4]

Because gastric cancer is often asymptomatic in early stages, nearly 60% of patients present with advanced or metastatic disease, where curative-intent treatment is no longer feasible.[4] The standard first-line approach includes a platinum and fluoropyrimidine doublet, although prognosis remains poor with median survival typically under one year.[3] Amplification and/or overexpression of Human Epidermal Growth Factor Receptor 2 (HER2) occurs in 17-20% of patients with gastric cancer.[3,6] Based on the TOGA trial, addition of trastuzumab to cisplatin and fluoropyrimidine doublet improved median OS and is now first-line standard of care for HER2 3+ immunohistochemistry (IHC) or HER2 2+ IHC and fluorescence in situ hybridization (FISH)-positive disease.[6] In the second-line setting, ramucirumab plus paclitaxel is widely used, while trastuzumab deruxtecan has emerged as a key option for HER2-positive disease, as supported by the phase 2 DESTINY-Gastric02 trial.[7,8]

Three recently published studies sought to improve outcomes for patients with gastric and GEJ adenocarcinomas. The MATTERHORN trial evaluated the addition of durvalumab, an anti–programmed death ligand 1 (PD-L1) inhibitor, to perioperative FLOT in resectable disease.[9] PRODIGE 51- FFCD-GASTFOX compared a modified FLOT regimen (TFOX) against FOLFOX for first-line treatment in patients with HER2-negative advanced disease.[10] Additionally, the DESTINY-Gastric04 trial directly compared trastuzumab deruxtecan to ramucirumab plus paclitaxel as second-line therapy after a trastuzumab-based regimen for HER2-positive metastatic disease.[11] In the following review, we will summarize the efficacy and safety findings from these three trials and discuss their implications for the treatment of gastric and GEJ adenocarcinomas.

"While final OS data in the MATTERHORN trial is still pending, the improvement in EFS and pathological complete response rate, in addition to a trend towards favorable OS outcomes with minimal differences in toxicity, supports the addition of durvalumab to perioperative FLOT chemotherapy."

MATTERHORN

The MATTERHORN trial was a phase 3, double-blind, multinational, randomized clinical trial evaluating the addition of durvalumab versus placebo to standard FLOT chemotherapy in patients with stage II-IVA resectable gastric or GEJ adenocarcinoma. Notable exclusion criteria included presence of peritoneal dissemination or distant metastasis, squamous-cell or adenosquamous-cell carcinoma, or gastrointestinal stromal tumors. Overall, 948 patients were randomized 1:1 to receive durvalumab 1,500 mg intravenously (IV) or placebo on day 1 in combination with FLOT administered on days 1 and 15 of each 4-week cycle. FLOT treatment consisted of docetaxel 50 mg/m^2, leucovorin 200 mg/m^2, oxaliplatin 85 mg/m^2, and fluorouracil 2,600 mg/m^2 over 24 hours. Treatment consisted of two neoadjuvant and two adjuvant cycles followed by durvalumab or placebo monotherapy every 4 weeks for up to 10 additional cycles. Surgery was to be performed within 4 to 8 weeks after completing neoadjuvant therapy.

Baseline characteristics were comparable between groups; the median age was 62 years, 19% of patients were from Asia, 67.5% had gastric cancer, and 90% had PD-L1 expression ≥1%. The primary outcome was event-free survival (EFS). At the data-cutoff, with a median duration of follow-up of 31.5 months, the median EFS was not reached in the durvalumab arm versus 32.8 months in the placebo arm (hazard ratio [HR] of 0.71; 95% CI 0.58 to 0.86; p<0.001). Secondary outcomes included OS, which at two years was

75.7% in the durvalumab arm and 70.4% in the placebo arm. This difference has not yet reached statistical significance. The percentage of patients with a complete pathological response was 19.2% in the durvalumab arm versus 7.2% in the placebo arm (relative risk, 2.69 [95% CI, 1.86 to 3.90]). Of patients who completed surgery, 91.5% of patients in the durvalumab arm versus 92.3% of patients in the placebo arm had an R0 resection. Additionally, reported adverse event rates were similar between both treatment arms, with the most commonly reported grade 3 or greater adverse events being neutropenia (21.3% with durvalumab versus 22.2% with placebo), diarrhea (6.3% versus 6.0%), and anemia (5.1% versus 5.1%). Immune-mediated side effects occurred in 23.2% of patients in the durvalumab arm (7.2% grade 3 or higher) and 7.2% in the placebo arm (3.6% grade 3 or higher). Adverse effects that trended higher in the durvalumab arm included diarrhea, rash, pruritus, stomatitis, hypothyroidism, hyperthyroidism, dry skin, infusion related reactions, hyperglycemia, pneumonitis, and adrenal insufficiency.

The authors concluded that the addition of durvalumab to FLOT in the perioperative setting significantly improved event-free survival and pathological response rates compared to FLOT alone in patients with resectable gastric or GEJ cancers.[9]

PRODIGE 51-FFCD-GASTFOX

PRODIGE 51-FFCD-GASTFOX was an open-label, randomized, phase 3 trial in France that compared TFOX versus FOLFOX in HER2-negative advanced unresectable or metastatic gastric or GEJ cancer. Key exclusion criteria included peripheral neuropathy of grade 2 or higher at baseline, cerebral or meningeal metastases, known deficit of dihydropyrimidine dehydrogenase, and prior docetaxel treatment. The FOLFOX arm received folinic acid 400 mg/m^2, oxaliplatin 85 mg/m^2, 5-fluorouracil bolus 400 mg/m^2 and 5-fluorouracil 2,400 mg/m^2 over 46 hours every 2 weeks. The TFOX arm received docetaxel 50 mg/m^2, folinic acid 400 mg/m^2, oxaliplatin 85 mg/m^2, and 5-fluorouracil 2,400 mg/m^2 over 46 hours every 2 weeks.

Baseline characteristics between the two arms were well matched with 79% male, 43% gastric cancer, and 58% with an Eastern Cooperative Oncology Group (ECOG) score of 1. The primary endpoint of the trial was progression free survival (PFS) with secondary endpoints of OS, objective response rate (ORR), and safety. Overall, 507 patients were randomized 1:1 to TFOX versus FOLFOX. At a median follow-up of 42.8 months, the median PFS in the intention-to-treat (ITT) population was 7.59 months versus 5.98 months, respectively. However, during this analysis the assumption of proportional hazards was violated so a 12-month restricted mean survival time was published showing 7.52 months in the TFOX arm versus 6.62 months in the FOLFOX arm (p=0.007). The OS in the ITT population was 15.08 months in the TFOX arm versus 12.65 months in the FOLFOX arm, and the proportional hazards assumption was confirmed (HR 0.82, 95% CI 0.68-0.99; p=0.048). ORR was 62.3% in the TFOX arm and 53.4% in the FOLFOX arm. Patient subgroups that favored TFOX for OS benefit included age <70, ECOG 0, metastatic disease, diffuse classification, and liver metastases. No new safety signals were found in this trial, but almost all patients had a treatment-emergent adverse event during treatment. Some adverse events that trended higher in the TFOX versus FOLFOX arm were diarrhea (61% versus 34%), vomiting (41% versus 29%), alopecia (42% versus 11%), palmar-plantar erythrodysesthesia syndrome (21% versus 13%), pyrexia (13% versus 7%), and nail changes (12% versus 0%). Over 40% of the patients in both arms discontinued docetaxel, oxaliplatin or both due to cumulative neurotoxicity and continued 5-fluorouracil alone.

The PRODIGE 51-FFCD-GASTFOX trial demonstrated that TFOX can have superior survival rates versus FOLFOX but may be more appropriate for younger, more fit patients based on subgroup analyses.[10]

DESTINY-Gastric04

DESTINY-Gastric04 was a phase 3, randomized, international trial that compared second-line trastuzumab deruxtecan with ramucirumab plus paclitaxel in patients with HER2-positive unresectable or metastatic gastric cancer or GEJ adenocarcinoma who had progression during trastuzumab-based therapy. Key exclusion criteria were history of noninfectious interstitial lung disease (ILD) or pneumonitis (both confirmed and suspected cases that could not be ruled out). Overall, 494 patients were randomized in a 1:1 ratio to trastuzumab deruxtecan 6.4 mg/kg on day 1 every 21 days or ramucirumab 8 mg/kg on days 1 and 15 plus paclitaxel 80 mg/m^2 on days 1, 8 and 15 of a 28-day cycle.

Baseline characteristics between arms were well matched with a median age of 64 years, 50% white, 61% gastric cancer, and over 80% HER2 IHC 3+. The primary end point for the trial was OS with secondary endpoints of PFS, confirmed objective response, disease control, and duration of response. At a median duration of follow-up of 16.8 months, median OS was significantly longer in the trastuzumab deruxtecan arm at 14.7 months versus 11.4 months in the ramucirumab plus paclitaxel arm (HR 0.70, 95% CI, 0.55-0.90; p=0.004). PFS was also significantly longer in the trastuzumab deruxtecan arm with a median PFS of 6.7 months versus 5.6 months (HR 0.74, 95% CI 0.59-0.92; p=0.007). Patients with a confirmed objective response resulted as 44.3% versus 29.1% (p<0.001). In the trastuzumab deruxtecan arm versus the ramucirumab plus paclitaxel arm, disease control rate was 91.9% versus 75.9% and the median duration of response was 7.4 versus 5.3 months, respectively. There were no new safety signals in this study, but drug-related adverse events were reported in 93% of patients in the trastuzumab deruxtecan arm and 91.4% in the ramucirumab and paclitaxel arm. Some common adverse effects (all grade) are listed in Table 1.

The DESTINY-Gastric04 study showed that trastuzumab deruxtecan had superior survival without sacrificing safety when compared to ramucirumab plus paclitaxel in HER2-positive gastric cancer or GEJ adenocarcinoma.[11]

Discussion

These three trials have resulted in important changes to treatment recommendations for patients with gastric or GEJ adenocarcinomas. While final OS data in the MATTERHORN trial is still pend-

Table 1. Common Adverse Events in DESTINY-Gastric04[11]

Adverse Event, %	Trastuzumab Deruxtecan (n = 244)	Ramucirumab + Paclitaxel (n = 233)
Fatigue	48.0	37.8
Neutropenia	48.0	48.9
Nausea	44.3	14.2
Anemia	31.1	33.0
Decreased appetite	29.1	18.0
Thrombocytopenia	26.6	13.7
Aminotransferase level increased	21.7	9.4
Vomiting	20.1	6.9
ILD/Pneumonitis	13.9	1.3
Neuropathy	2.5	29.2

ing, the improvement in EFS and pathological complete response rate, in addition to a trend towards favorable OS outcomes with minimal differences in toxicity, supports the addition of durvalumab to perioperative FLOT chemotherapy.[9] Cancer guidelines now list FLOT plus durvalumab as a preferred regimen for perioperative systemic therapy for patients with PD-L1 combined positivity score (CPS) >/1 or tumor area positivity (TAP) >/1%. The preference for PD-L1 positivity comes from the subgroup analysis of EFS that showed a lack of statistically significant benefit with durvalumab in tumors with <1% PD-L1 expression, although this was a small, underpowered subgroup.[9] This subgroup analysis also showed a lack of statistical benefit in patients with diffuse gastric or GEJ tumors. Reported toxicity from durvalumab was similar to previously reported immunotherapy-related adverse events and did not result in an increase in surgical delays or decrease in R0 resection.

One of the limitations of the MATTERHORN trial was its inability to distinguish the impact of neoadjuvant versus adjuvant immunotherapy. The ATTRACTION-5 trial, which evaluated the addition of nivolumab to adjuvant chemotherapy after surgery without preoperative treatment, found that there was no improvement in relapse-free survival compared to chemotherapy alone.[12] The KEYNOTE-585 trial, which evaluated the addition of pembrolizumab to perioperative fluoropyrimidine and cisplatin followed by adjuvant pembrolizumab, did not result in a statistically significant improvement in primary endpoints of EFS or OS; however, it did result in a numerical improvement in OS, with median OS of 71.8 months with pembrolizumab versus 55.7 months with placebo.[13] A key limitation to note in this trial was its use of a sub-optimal chemotherapy backbone, which may have contributed to the lack of statistical benefit.[14] Finally, the phase II/III DANTE/IKF-s633 trial found that the addition of atezolizumab to perioperative FLOT resulted in a higher proportion of patients achieving complete histopathologic regression (24% with atezolizumab versus 15% without) and improved postoperative stage T0 (23% versus 15%, respectively) and N0 disease (68% versus 54%, respectively).[15] The results of the MATTERHORN trial, coupled with the numerical improvement in OS in the KEYNOTE-585 trial and improved pathologic response rates in the DANTE/IKF-s633 trial, support the addition of immunotherapy in resectable gastric and GEJ tumors.

When evaluating treatment options for patients with unresectable or metastatic gastric or GEJ cancer, it is important to take into consideration the limitations of the other two studies mentioned above. The PRODIGE 51-FFCD-GASTFOX trial only included patients from France, which limits the applicability of the trial to a global population.[10] There is a previously published study documenting the lack of efficacy of docetaxel in Asian populations so the results from this trial would be difficult to extrapolate to that patient group specifically.[14] At the time this study was conducted, FLOT had not yet become standard of care for perioperative treatment in resectable disease. Since this trial excluded patients with prior docetaxel exposure, it limits the applicability to patients who have not received FLOT treatment in the perioperative setting and now require treatment for recurrent/relapsed disease. Finally, TFOX may be best reserved for patients who are younger with a good performance status based on the subgroup analyses. The study only had significance for patients age < 65 years and with an ECOG performance status of 0. For patients who do not fit into those categories, it is likely best to initiate a less intense chemotherapy regimen with or without targeted treatment, if appropriate.

For HER2-positive disease, one limitation of the DESTINY-Gastric04 study is that patients were required to have a repeat biopsy completed to confirm HER2 status after they had progressed on trastuzumab-based therapy.[11] While the potential for HER2 expression loss has been documented, it may not always be feasible for patients to undergo another biopsy prior to initiating a new line of treatment.[17] This may lead to less robust results when applied to a real-world population. Another point to take into consideration is the dose of trastuzumab deruxtecan administered – gastric cancer is the only indication approved at the dose of 6.4 mg/kg whereas the agent is administered at a dose of 5.4 mg/kg for all other approved indications.[18] Providers should be vigilant to monitor for toxicities and note that 31.1% of the patients in the DESTINY-Gastric04 study did require dose reductions of trastuzumab deruxtecan during the trial.

Overall, there have been great strides in the gastric/gastro-esophageal junction cancer landscape in the last several years. The studies provide new treatment options for patients in both the perioperative setting and the unresectable/metastatic setting. When applied appropriately, there is the potential to greatly increase patients' survival rates. ●●

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Patient Perspective: Undergoing Cancer Treatment During the Holidays

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As we approach the winter holiday season, many of us may look forward to some well-deserved time off and constantly think about our shopping and to-do lists. But the end of the calendar year also means it's time to consider not only how to adjust patient treatment schedules for outpatient site closures, but also to recognize how we can help our patients feel their best while continuing to meet treatment goals during this often hectic time of year. Approaching the holiday season with a cancer diagnosis may feel overwhelming to patients and to caregivers. Just hearing the word cancer in conjunction with you or your loved one is a life-changing experience – it brings an extra mental burden or can place a shadow over holiday times spent with family and friends. This month, we spoke with several HOPA Patient Advisory Panelists who wanted to share their experiences with members regarding cancer treatment during the winter holidays.

As a recent Patient Advisory Panelist, this subject matters to me as I was diagnosed with cancer during December of 2013. A week before Christmas, I was given my preliminary diagnosis and had my biopsy. My diagnosis was finalized, and treatment planning began on December 26. While my fresh biopsy site peeks out of my collar prominently in many photographs, I keenly remember soaking up the care and concern of my family during the holiday season. The following week between Christmas and New Years, I will always remember the kindness of my team during the whirlwind of preparing for treatment. From my physician who gave me paper and a pen to take notes, to the pharmacist and co-worker who took the time to answer all my questions, I truly felt that each person was fully tuned in to helping meet my needs and allay my fears.

Kathryn Redden, a 3rd year member of HOPA's Patient Advisory Panel, shared that she was three months into neoadjuvant chemotherapy with her surgery scheduled for the day before Thanksgiving in 2019. Her family was able to shift their holiday celebration to the weekend prior to Thanksgiving to accommodate their beloved mother and grandmother. They brought the holiday to Kathryn, delivering the complete feast to her home, holiday cheer and grandchildren included. Kathryn credits her oncology pharmacist with optimizing her anti-nausea therapy, which helped her be able to relax and enjoy family time. Despite her appetite being low from her chemotherapy, Kathryn remembers "one more family joyful memory" when she thinks back to Thanksgiving 2019. When asked about her experience during the holidays, Kathryn remembers that her care team did a particularly great job managing her pain after surgery. She says that her team communicated with her so well that nothing came as a surprise to her over the course of her chemotherapy and subsequent surgery. Overall, Kathryn says that going through chemotherapy and surgery around the fall holiday festivities was only a minor inconvenience in the scope of her holiday. She feels like the joy of Thanksgiving for her was in the support of her family and knowing that her surgery was eminent to "evict" the cancer burden from her body. The reflections of her blessings, even in the middle of cancer treatment, and the promise of recovery helped her through.

Sandra Zori, a community pharmacist in Michigan and a 4th year member of the Patient Advisory Panel, says that she was able to keep all of her treatments on track during the holidays. With her diagnosis and initial treatment having been in the spring and summer of 2018, she spent her first holiday season taking oral antineoplastics. The following year, she was enrolled in a clinical trial containing immunotherapy. As a patient, Sandra calls herself 100% compliant, dedicated to keeping everything exactly on track. While caring for a young family and with her extended family's presence and support, Sandra was able to maintain what she called "a normal schedule" for her family during the holidays. She and her treatment team had ensured that she was up to date with all of her recommended immunizations, and with her family close by, she didn't plan any traveling for her holiday.

"It's important to listen to and really hear what the patient needs to fully experience their holiday while on treatment. Some patients may prefer a drug holiday with no treatment, while others may prefer to stay on a tight schedule with no deviations."

However, Sandra did recall a time when her specialty pharmacy delivery was delayed by a snowstorm. She came within a few days of running out of her medication, and despite all of her own knowledge and her ongoing communication with her treatment team, that was an especially stressful time. For Sandra, keeping her family on track with their normal holiday traditions and keeping her treatment on schedule was a top priority. She had the support and knowledge of her family (several of whom are pharmacists and other medical professionals!) backing her up, in addition to her care team. As Sandra alluded to, immunization status is an important consideration around the holidays as we think about gathering with family and loved ones. Helping patients understand optimal timing of immunizations in relation to their specific therapy plan and the importance of not only their own vaccination, but also the vaccine history of those they will be close to during holidays can be a critical component of holiday celebrations. Staying well during the holidays is a priority for everyone, and cancer patients may be nervous about family

gatherings or other events. Ultimately, supporting a patient in their desire to participate in their community holiday events helps enable them to feel that cancer is not controlling their life.

Many patients like Sandra may be receiving oral antineoplastic agents as part of their cancer treatment. While oral or home injection therapies are convenient for patients and families, they also come with additional hurdles especially around the holiday season. Medications from specialty pharmacies can be delayed due to holiday closures, weather events, or increased shipping demands surrounding the holidays. As a result, patients and their caregivers may need additional assistance in ensuring timely refill requests and delivery of their anticancer medications. Oncology pharmacists can provide much needed information and peace of mind when it comes to helping patients ensure that all medications are available and avoid delays during a busy holiday season for patients like Sandra who choose to continue therapy during this time.

As a gentle reminder during the holidays, it is critical to focus on what our patients tell us about their needs. Our patient panelists emphasized that not all patients may understand the options available to them when it comes to their treatment during the holidays. It's important to listen to and really hear what the patient needs to fully experience their holiday while on treatment. Some patients may prefer a drug holiday with no treatment, while others may prefer to stay on a tight schedule with no deviations. Exploring all of the suitable options with a patient can help them and their loved ones select the option that works best for them and can provide them with much needed reassurance that all of their treatment choices are centered around them.

Finally, we must acknowledge that the winter holidays are not always warm and cheery for everyone. For those such as myself grappling with a new diagnosis or those who may have a host of feelings and memories linked to either their ongoing therapy or that of a loved one who lost a battle with cancer, the need remains the same. Listening to and hearing the patient is the point of connection that is remembered.

The end of year holidays can be stressful and hectic for everyone, and adding a cancer diagnosis into that adds an extra layer of complexity and demand for patients and caregivers. Our role as pharmacists is critical to helping patients get that extra measure of calmness and comfort to help relieve their minds so they can celebrate with their loved ones. That extra time to listen, the reassuring words, and the attention to details can really make a difference in how a holiday is remembered. ●●

How Long Does It Take to Complete Common Oncology Pharmacist Tasks?

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Background

There is a paucity of published studies quantifying oncology pharmacist scope, workload, and productivity. This deficiency limits both the evaluation of current oncology pharmacist positions and justification of new positions. The few research studies that have attempted to define oncology pharmacy workload are either single-center, observational time-motion studies, or primarily focused on categorizing the type of interventions and quantification of pharmacist tasks.[1-4] These studies have limited generalizability; while oncology pharmacists are performing similar job-related tasks, the distribution of effort tasks for a particular position varies greatly between institutions.[5] This contrasts with other oncology providers whose productivity is often defined by relative value units derived from patient complexity, length of visit, and specific procedures performed.[6] To aid oncology pharmacists and pharmacy leaders, HOPA and ACCP Hematology/Oncology Practice and Research Network (PRN) partnered to survey hematology/oncology pharmacists with the aim of establishing a consensus on the time required to complete specific oncology pharmacy tasks.

"The results, which outline the time and resources required for task completion, can also be easily understood by the non-oncology hiring managers and non-pharmacist leadership, further enhancing their practical value."

Methods

The Practice Outcomes and Professional Benchmarking Committee (POPBC) within HOPA utilized the *Further Defining the Scope of Hematology/Oncology Pharmacy Practice* publication to compile a list of the 24 oncology pharmacist tasks.[7] These tasks were deemed to be common regardless of practice setting or specialty and classified as either patient care or non-patient care tasks. Each task's average time estimation included a range and described the amount of time a pharmacist needs to complete the associated task greater than 80% of the time it is performed. These time averages were then combined to create 24 consensus statements. For each consensus statement, six responses were available: unable to answer, strongly disagree, disagree, neither agree nor disagree, agree, and strongly agree.

To validate the time assigned by POPBC to each pharmacist job task, a Delphi survey was conducted between December 2023 and February 2024 using previously established survey techniques.[8-11] The list of experts who would receive the Delphi Survey was derived from the membership of ACCP Hematology/Oncology PRN. Thirty-three members agreed to participate as the expert panel in the Delphi Survey.

The 33 experts were sent an email asking them to complete the electronic survey. All information collected was analyzed to identify the degree of consensus. Based on previously published studies utilizing this method, an a priori decision was made to consider greater than or equal to 75% agreement (agree or strongly agree) as consensus.[9-11] Statements that fell between 65% and 75% agreement were included unmodified in the next round to confirm borderline consensus. Statements that fell below 65% agreement were modified by the POPBC based on open-ended respondent feedback, and the modified versions were included in the next round of the survey. In subsequent rounds, results from the previous round as well as any modifications were noted for each included statement.

Results

Of the 33 oncology pharmacist experts who agreed to participate in this survey, all participated in round 1, and 29 (87.9%) participated in round 2. The complete consensus statements are summarized in Table 1.

Discussion and Application

This study met its objective and reached consensus regarding the amount of time required for oncology pharmacists to complete common tasks associated with their roles. These findings have been reviewed and endorsed by HOPA and ACCP Hematology/Oncology PRN—two of the largest national organizations representing oncology pharmacists in the US. There are no other published guidelines that can be generalized across practice settings and patient populations to help measure the workload of oncology pharmacists. The use of an expert panel of practicing oncology pharmacists from a variety of settings provides confidence that these results are applicable to different practices.

A large US-based survey of oncology pharmacists found that those with high levels of burnout reported working more hours per week and reported a greater intent to leave their current job as compared to those without burnout.[12] This data may help mitigate the contribution of unrealistic workloads to oncology pharmacist burnout. Utilizing the data herein, practicing oncology pharmacists can evaluate how their expected job tasks may fit within their work hours. The rationale for providing data on the per task level was to account for the heterogeneity that exists between practice sites in the US. This will empower frontline employees and help pharmacy leaders facilitate more informed data-driven conversations.

Table 1: Summary of Consensus Statements

Oncology Pharmacist Task	Consensus Statement of Average Time to Complete
Assess patient suitability for specific oncologic treatment including clinical trials by gathering comprehensive patient information conducting medication reviews and ensuring evidence-based, patient-specific treatment recommendations	15 min ± 5 min per patient
Optimize anticancer therapy orders by reviewing and adjusting them according to patient-specific factors, monitor treatment efficacy, manage toxicities, and ensure accuracy in drug regimen details	15 min ± 3 min per drug regimen
Assess drug complementary or alternative care, drug-disease, drug-drug, and drug-food interactions; **5 drugs or fewer**	5 min ± 1 min per patient
Assess drug complementary or alternative care, drug-disease, drug-drug, and drug-food interactions; **more than 5 drugs**	10 min ± 2 min per patient
Review metabolism-specific pharmacogenetic data for dosing modifications	25 min ± 5 min per patient
Conduct generalized supportive care management for patients with cancer utilizing pharmacologic and non-pharmacologic techniques, including referrals to other disciplines	10 min ± 2 min per intervention
Perform transition planning, including assisting with transitions of care and medication reconciliation	20 min ± 5 min per intervention
Facilitate access to medications (e.g. work with prior authorization coordinators and financial counselors, coordinate with retail of specialty pharmacies)	45 min ± 15 min per intervention
Trainee education and supervisory activities associated with learners	3 hours ± 1 hour per learner per day
Educate patients and caregivers on anticancer therapy, supportive care medications, symptom management, scheduling and administration, coordination with meals, adherence, and safe handling/disposal of medications	30 min ± 6 min per education session
Participate in interprofessional patient care rounds	15 min ± 3 min per patient
Coordinate chemotherapy administration with nursing staff	10 min ± 2 min per administration
Provide ongoing monitoring of efficacy, toxicity, organ function changes, therapeutic drug monitoring, and diagnostic test results. Communicate concerns, supportive care needs, or dose adjustment recommendations to appropriate healthcare provider. Address barriers to adherence and educate on toxicity management and prevention	10 min ± 2 min per intervention
Provide therapeutic drug monitoring and therapy adjustment	10 min ± 2 min per intervention
Practice antimicrobial stewardship including documentation	10 min ± 2 min per intervention
Prepare education for interprofessional healthcare team members and trainees	2 hours ± 30 min per 15 min of planned presentation
Policy, guidelines, and drug monograph development	8 hours ± 4 hours per project
Committee participation	4 hours ± 2 hours per committee per month
Ensure regulatory compliance while actively working, aligning with institutional, state, and federal requirements	1 hour ± 0.25 hour per day
Medication error, adverse event, and safety event reporting	5 min ± 1 min per intervention
Annual competencies, maintenance of certifications, licenses	40 hours ± 8 hours per year
Create a standardized treatment plan in the EMR	2 hours ± 0.5 hours per plan
Validate a standardized treatment plan in the EMR	1 hour ± 0.25 hour per plan
Contribute to institutional and collaborative research and scholarly activities	40 hours ± 8 hours per project

We would recommend that practicing pharmacists track the number of each type of task that they are currently completing on a weekly basis. From this, the data included in this manuscript could then be used to estimate the total amount of time that is recommended to complete these tasks. The variance from a full-time equivalent (FTE) could then be compared to determine if appropriate pharmacist resources were being devoted to the expected workload. On the flip side, when new FTEs are developed pharmacy leaders could determine the number of FTEs that would be required to complete the desired type and number of tasks. One institution has already created an excel document with built-in formulas to track productivity as compared to a standard FTE of 40 hours per week. When creating any such tool, it is important to include non-patient care tasks. Based on these results, it is estimated that for an oncology pharmacist in a direct patient care role, at least 20% of an FTE will need to be devoted to non-patient care tasks. Furthermore, this ties position justification directly to job-specific tasks as opposed to the traditional pharmacist justification method of cost-savings.[13] The results, which outline the time and resources required for task completion, can also be easily understood by the non-oncology hiring managers and non-pharmacist leadership, further enhancing their practical value.

Limitations of this study include the relatively small number of experts who completed the Delphi Survey. These experts also

tended to be experienced clinical pharmacists with 78% having 6 or more years of experience working primarily in academic centers and community centers. New oncology pharmacists or those completing tasks outside of normal job functions may not complete tasks in the same amount of time. While the composition of the expert panel was solicited from a large pool, it is possible that those with strong opinions or those who feel overworked were more likely to volunteer—introducing bias. This may be supported, at least in part, given that to reach consensus, many of the statements were revised to increase the amount of time necessary to complete the associated task.

Conclusion

This project produced the first comprehensive consensus statements for the average time necessary for an oncology pharmacist to complete 24 common patient and non-patient care-related tasks for those practicing in academic and community centers in the US. These statements are endorsed by HOPA and ACCP Hematology/Oncology PRN and may be used to justify, measure, and evaluate oncology pharmacists across the US. ●●

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Serial ESR1 ctDNA Testing: In Need of Prospective Validation

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Background

Hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) advanced or metastatic breast cancer is considered an incurable, chronic disease.[1] Current first-line therapies for this type of cancer include endocrine therapies like selective estrogen receptor modulators (SERMs), selective estrogen receptor degraders (SERDs), and aromatase inhibitors (AIs). Cyclin-dependent kinase 4 and 6 inhibitors (CDK4/6i) are commonly used in combination with AIs in the first-line setting. Unfortunately, many patients eventually experience disease progression, and the median progression-free survival (PFS) on first-line CDK4/6i + AI is approximately 24-28 months.[2-4]

AIs work by reducing the amount of estrogen in the body and preventing activation of hormone receptors. One mechanism of resistance to AIs is through mutations in the estrogen receptor 1 (ESR1) gene. ESR1 mutations (ESR1m) overcome AIs through constitutive activation of estrogen receptors, making them independent of estrogen levels.[5] One way to overcome this mechanism of resistance is to directly target the estrogen receptor instead of reducing estrogen levels by using a SERD.

ESR1m have been found to develop while a patient is on a CDK4/6i + AI. These mutations can be detected by analyzing the circulating tumor DNA (ctDNA) in a patient's blood, so it is possible to detect the emergence of drug resistance prior to any evidence of progression. ESR1m breast cancer can still respond to a CDK4/6i, so there may be a benefit to only changing the endocrine therapy when drug resistance is detected.[6] This may help delay the spread of ESR1m breast cancer at an earlier stage and allow patients to stay on endocrine therapy longer. As a blood draw, ESR1 ctDNA monitoring is also less invasive than the surveillance imaging that patients regularly receive.

To answer this question, the phase III SERENA-6 trial investigated serial monitoring of ctDNA for patients who had been on CDK4/6i + AI therapy for at least 6 months.[7] Patients had their ctDNA regularly monitored, and those who developed ESR1m without other evidence of progression were randomized to either continue on an AI (control arm) or switch to camizestrant 75 mg daily (experimental arm),a next-generation oral SERD. All patients continued taking the same CDK4/6i. SERENA-6 demonstrated a significant median PFS benefit of 16 vs 9.2 months (hazard ratio 0.44; 95% CI, 0.31-0.60; p<0.00001) for patients on the experimental arm. But the question is if these results warrant application of this practice in the everyday clinic setting.

"Given that SERENA-6 did not isolate the benefit of an early change in therapy, this could be an operational lift for clinics without a clear clinical benefit for patients."

Trial Design

One important consideration regarding SERENA-6 is the trial design. The experimental arm in this trial considered the development of ESR1m as a clinically relevant event and switched patients off AI treatment. But developing ESR1m in the absence of clinical or radiographic progression has not been prospectively validated as an event where therapy would need to be changed. Current clinical practice is to wait for radiographic or clinical progression and then test patients for ESR1m. Patients who test positive for ESR1m are then placed on oral SERD monotherapy. In SERENA-6, patients had a median PFS of 9.2 months on CDK4/6i + AI after developing ESR1m. Many patients did not immediately progress after an ESR1m was detected. In addition, while not a perfect comparison, camizestrant 75 mg daily demonstrated a PFS of 6.3 months as second-line therapy in ESR1m patients in a phase II trial.[8] It may have been more beneficial to compare the PFS of two strategies: switching to camizestrant at development of ESR1m versus waiting to switch until radiographic or clinical progression. However, because this trial specifically did not allow crossover, that question was not answered.

Cost

Trial design also impacts our understanding of the costs and benefits of therapy. SERENA-6 planned to enroll 300 patients and ultimately accrued 315 patients. Of 3,325 patients screened, 3,256 underwent at least one ESR1 test, corresponding to approximately 10 patients tested for every patient enrolled. Patients received a ctDNA test every 2 to 3 months alongside regular physician visits and imaging surveillance. Assuming a median PFS of 24 months for patients on CDK4/6i + AI, patients may be tested for one and a half years, never develop an ESR1 mutation, and have a progression event. Patients need to make appointments to have these tests completed, and insurance providers or patients will need to cover the costs of the tests, with the majority never seeing the development of a mutation.

The cost–benefit balance of serial ESR1 ctDNA testing remains uncertain, as its direct contribution to patient outcomes has not been clearly defined. The experimental arm made two interventions in patients: exposing patients to camizestrant and changing therapy prior to clinical or radiographic progression. In the control arm, only a small proportion of patients received a second-line oral SERD, all administered off protocol. Overall, 9.6% of patients were treated with oral SERD monotherapy, while 4.8% of patients received oral SERD in combination with another targeted therapy.

This makes it difficult to isolate the incremental value of the testing strategy itself. Without clarity on how much benefit comes specifically from serial ESR1 monitoring, it is not possible to fully weigh costs against outcomes. Moreover, if approximately ten patients must undergo repeated testing for one to benefit, the key question becomes how much additional PFS is truly being gained per patient tested.

Operational Considerations

There are also operational concerns to implementing serial ESR1 ctDNA testing. Seventy percent of all breast cancer patients are HR+/HER2-, but not all HR+/HER2- breast cancer patients qualify for this testing.[9] In SERENA-6, patients had to have received CDK4/6i + AI for at least 6 months, could not have received any other therapies in the advanced/metastatic setting, and could not have evidence of disease progression. Identifying these patients requires a clinician assessment prior to the ordering of each test, meaning significant changes to clinic workflow might have to be implemented. ctDNA testing may need to be treated like patient imaging, where clinics receive orders from providers, obtain prior authorization, schedule a ctDNA draw, pack and ship ctDNA samples to the lab, receive ctDNA results, and deliver the results to patients and providers.

From this, another question arises – is this level of operational change possible? Yes, it is possible, as we have seen similar workflow changes with the development of outpatient bispecific antibody programs.[10] But these operational changes were made because bispecific antibodies demonstrated PFS and overall survival (OS) benefits against historical controls in a heavily pretreated patient population. Given that SERENA-6 did not isolate the benefit of an early change in therapy, this could be an operational lift for clinics without a clear clinical benefit for patients.

Future Directions

The SERENA-6 trial provides important insights, but it also raises questions about how best to integrate serial ESR1 ctDNA testing into clinical practice. At present, the true clinical value of detecting ESR1m in the absence of radiographic or clinical progression remains uncertain. While early switching to camizestrant demonstrated an improvement in PFS, this effect cannot be cleanly attributed to the testing strategy itself, since the experimental arm combined two interventions: introduction of a next-generation SERD and preemptive therapy change. Without clarity on the independent contribution of testing, broad adoption risks adding cost and complexity without clearly defined benefit.

Continuing therapy in the absence of disease progression is not a concept limited to breast cancer. For example, in chronic lymphocytic leukemia, Bruton's tyrosine kinase inhibitors (BTKi) are a common first or second line treatment. Current standard of care for patients who develop resistance mutations to BTKis in ctDNA, without evidence of disease progression, is to continue BTKi therapy.[11] New clinical decision-making endpoints must be prospectively validated, just as we prospectively validate novel cancer treatments. A clinical trial which exposes both treatment arms to an oral SERD at different clinical time points could help better understand the benefit of serial ESR1 ctDNA monitoring. ●●

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Board Update

Meeting the Demands of the Times with Advocacy and Action

Robert Mancini, PharmD, BCOP, FHOPA
HOPA President (2025-2026)
Oncology Pharmacy Program Coordinator & PGY2 Oncology Residency Program Director, St. Luke's Cancer Institute, Boise, ID
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It has been a busy year for HOPA's Advocacy and Public Policy committees, which reflects both the times and our ongoing commitment to optimizing cancer care for all. Last quarter, I shared with you that our Diversity, Equity, and Inclusion Advisory Group is now the Access, Representation, and Opportunity (ARO) Advisory Group.

This is about far more than replacing an acronym. It is about standing up for the opportunities created by cancer research. It is about fighting for access to life-saving treatments. And it is about advocating for our patients and each other.

Here is a recap of 2025 advocacy and policy efforts. These include position statements and letters that HOPA joined as part of our coalitions, which were led by our policy and advocacy teams.

- February 6 – HOPA Remains Committed to the Oncology Pharmacy Community and All Cancer Patients
- February 19 - One Voice Against Cancer (OVAC) Sign-On Statement Re: Recent executive actions that threaten progress
- April 23 – OVAC Fiscal Year 2026 Funding Request Letter
- April 24 – Coalition for Health Funding Letter on Funding Cuts to Fiscal Year 2026 Budget for Health and Human Services
- April 25 – Statement of the Cancer Leadership Council on elimination of the DCD Division of Cancer Prevention and Control
- May 6 – Virtual HOPA Hill Day
- May 6 – Cancer Leadership Council Statement of Cancer Organizations Regarding Importance of Medicaid as a Critical Part of the Nation's Cancer Care System
- May 27 - American Association of College of Pharmacy (AACP) Statement on Implications of H.R.1 on Pharmacy Education
- June 5 - Research! America Letter on Proposed NIH Cuts in Fiscal Year 2026 Budget
- June 12 – Modern Medicaid Alliance (MMA) Letter to Senate Leadership on Medicaid Cuts
- June 13 – Infectious Diseases Society of America (IDSA) Letter Supporting the Family Vaccine Protection Act
- July 14 - HOPA and Coalition to Improve Access to Cancer Care (CIACC) Commend Reintroduction of Cancer Drug Parity Act
- August 27 – HOPA Officially Registers April 3 of Each Year as National Oncology Pharmacist Day
- September 12 - HOPA Joins the "We're Your Pharmacist" ASHP Campaign
- September 25 – Oncology Pharmacists Urge Responsible use of Leucovorin
- September 30 – Record-Breaking HOPA Hill Day in Washington DC
- October 14 - What Does the Government Shutdown Mean for Oncology Pharmacists and Our Patients?
- October 24 - HOPA Supports FDA Box Label Changes for DPYD Testing
- November 3 – HOPA Endorses ISOPP & UICC Statement on Ensuring International Cancer Drug Quality and Equity
- November 14 – What HOPA Members Should Know About the End of the 2025 U.S. Government Shutdown

As we look forward to the New Year, HOPA remains committed to using our collective voice to fight for access, representation, and opportunity for our patients and profession.

Speaking of the voice of oncology pharmacists, the book, "Healing, Optimism, Pharmacy, and Advocacy: Stories and Perspectives from Oncology Pharmacists," is due to be released this spring. In it, you will find a compilation of more than 30 letters, stories, and reflections from HOPA and ISOPP members. Special thanks to the HOPA Book Task Force and everyone who has contributed!

On behalf of the HOPA Board of Directors, Happy New Year – we look forward to continuing to work toward the vision that all people undergoing cancer treatment will have a pharmacist as an integral member of their care team. ●●

Robert

PS: If you have not already, please mark your calendars for HOPA 2026 in New Orleans on March 25-27! Registration is open.

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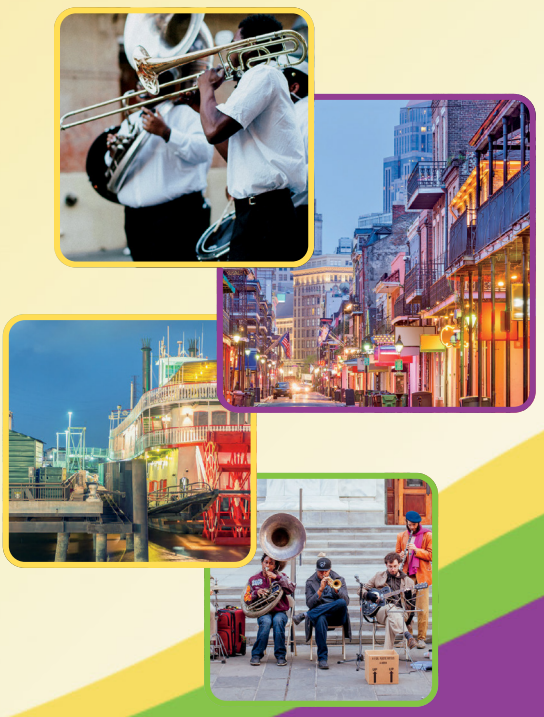

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HOPA2026
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