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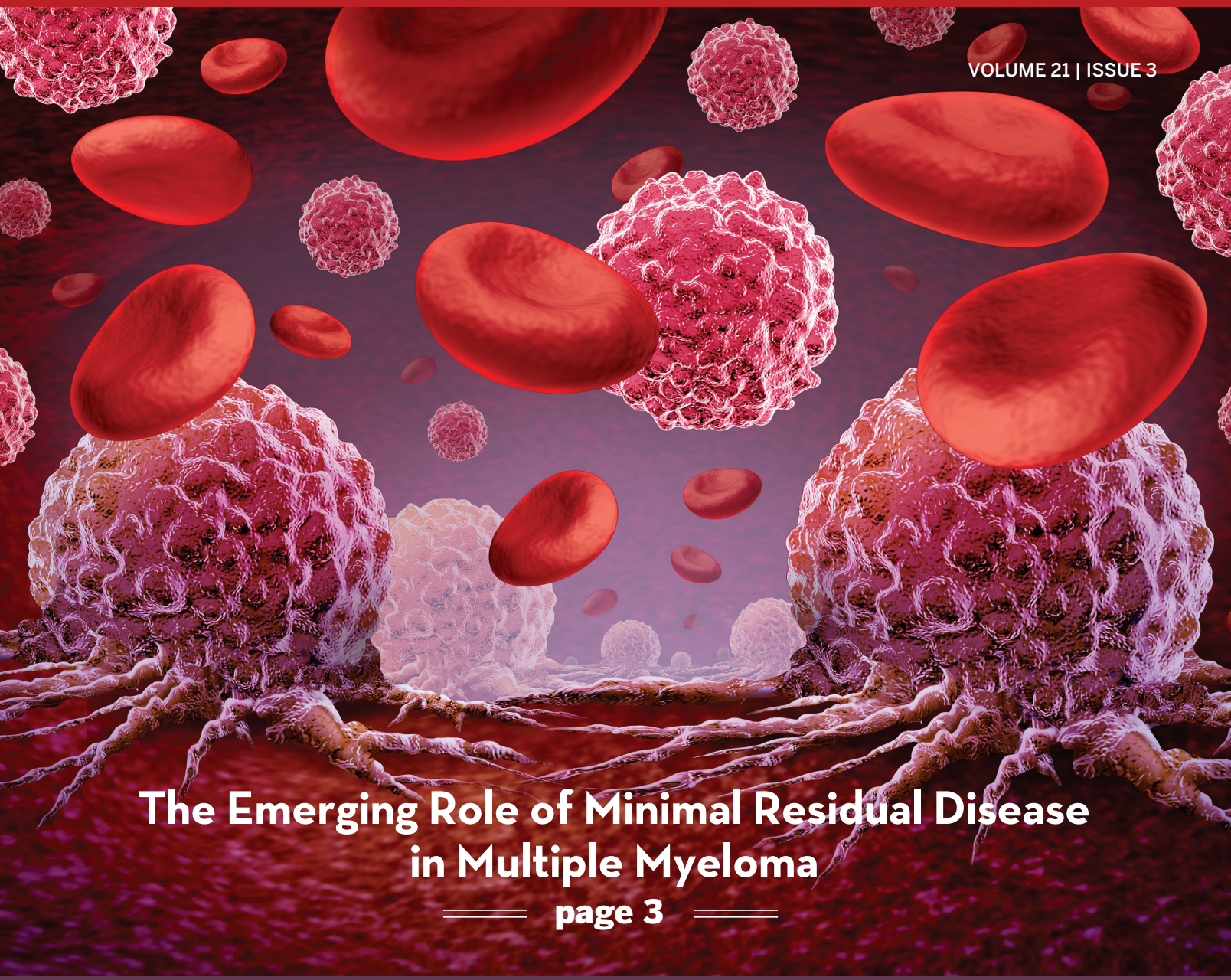

The Emerging Role of Minimal Residual Disease in Multiple Myeloma

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FEATURE

The Emerging Role of Minimal Residual Disease in Multiple Myeloma

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Multiple myeloma (MM) is the second most common hematologic malignancy, and it remains an incurable malignancy despite significant advances in treatment. Clinically meaningful clinical trial outcomes including progression free survival (PFS) and overall survival (OS) take an extended time to mature due to the chronicity of the disease; this can delay treatment approvals and, consequently, patient access to novel treatments. Though PFS has been a United States (US) Food and Drug Administration (FDA) validated endpoint for MM, it may take many years to show a statistically significant benefit for PFS with a novel therapy or therapeutic combination. These time barriers may be overcome through the FDA accelerated approval pathway which requires the use of surrogate endpoints that are 'reasonably likely' to predict clinical benefit in clinical trials.[1]

Surrogate, or intermediate, endpoints may be used to find a therapeutic benefit quicker, though use in oncology clinical trials is limited by weak associations with clinically meaningful outcomes. To date, overall response rate (ORR) has been the accepted, clinically relevant surrogate endpoint for use in accelerated approval MM trials, but this is limited by the range of responses including partial response (PR), which only requires 60% reduction of disease, and the growing challenge to show clinically significant benefit. Due to therapeutic advancements, the sample size necessary to show a significant benefit and the duration of follow up to show survival benefit continue to increase. Additionally, ORR does not always correlate with survival benefit. One example of this was the BELLINI trial that evaluated venetoclax, bortezomib, and dexamethasone versus bortezomib and dexamethasone in patients with relapsed or refractory multiple myeloma (RRMM). Although early results of PFS and ORR showed benefit with the addition of venetoclax, a decrease in OS was observed.[2]

"MRD, as a measurement of depth of response, has been associated with improved PFS and OS as a secondary and exploratory endpoint in both NDMM and RRMM patient populations."

Minimal Residual Disease (MRD)

Minimal residual disease (MRD) is a measurement of a deeper level of response beyond conventional methodology that identifies patient specific clonal rearrangements of tumor cells from the bone marrow.[3] MRD may show improved differentiation of treatment effect with smaller samples sizes needed to show a benefit sooner, making it an ideal surrogate endpoint. MRD is often used in patients with a complete response (CR) to quantify depth of response, and it has grown in popularity as a prognostic indicator in the treatment of both newly diagnosed multiple myeloma (NDMM) and RRMM. It is now included in the International Myeloma Working Group (IMWG) Consensus Criteria for Response and MRD Assessment in MM.[3] Current technology utilizes flow cytometry-based or sequencing-based platforms. Both are acceptable methods according to the FDA as long as they are validated for the context of use, thresholds are predetermined, and procedures for sample collection and processing are standardized within the trial protocol or clinical practice.

MRD, as a measurement of depth of response, has been associated with improved PFS and OS as a secondary and exploratory endpoint in both NDMM and RRMM patient populations (Table 1).[4-15] This association with survival outcomes has increased interest in MRD as an endpoint to support regulatory decisions. This association has also been described in multiple meta-analyses. Landgren and colleagues evaluated four studies that assessed MRD at various early time points ranging from 6-8 cycles of therapy to 3-6 months post autologous stem cell transplant (ASCT) in NDMM patients. The investigators found that MRD positivity, evaluated with a threshold of 10^{-4}, was associated with worse prognosis including worse PFS (HR = 2.85, p<0.001) and OS (HR = 2.08, p<0.001) compared to MRD negative patients.[16] A similar meta-analysis of trials including NDMM found that MRD negativity was associated with improved PFS (HR = 0.41, p<0.001) and OS (HR = 0.57, p <0.001).[13] For patients who achieved a CR and MRD negativity, similar benefit was seen for both PFS (HR = 0.44, p<0.001) and OS (HR = 0.47, p<0.001).[17] A limitation of both meta-analyses was the exclusion of RRMM patients and the limited number of patients who were transplant ineligible. A pooled analysis of four phase 3 trials of daratumumab including newly diagnosed transplant ineligible and RRMM patients found that patients who achieved a CR or better and MRD negativity had a longer PFS than those who did not achieve a CR or who were MRD positive (HR = 0.20, p<0.0001).[18]

The MRD data available to date is notably limited for patients with RRMM as well as patients receiving cellular therapies including chimeric antigen receptor (CAR) T-cells and bispecific antibodies (BiAbs). However, recent early phase trials for these therapies have included MRD as an exploratory outcome. Emerging pooled analyses including patients who received either CAR T-cell or BiAbs suggest that MRD negativity with novel immunotherapies improved PFS (HR = 0.11, p<0.001) and OS (HR = 0.16, p<0.001).[19]

FDA Submission and Review

On April 12, 2024 the US FDA convened the Oncologic Drugs Advisory Committee (ODAC) to assess the use of MRD as a

Table 1: Phase 3 Clinical Trials of Small Molecules and Monoclonal Antibodies Evaluating MRD as Secondary or Exploratory Endpoint[4-15]

Trial	Patient Population	Intervention	MRD-ve + ≥ CR	MRD-ve + Any Response	Median PFS (mo)
PERSEUS	NDTE	Dara-VRd v VRd	75.2% v 47.5%	–	48 mo PFS: 84.3% vs 67.7%
CASSIPOEIA	NDTE	Dara-VTd v VTd	34% v 20%	64% v 44%	59.1 vs 41.4
DETERMINATION	NDTE	VRd + ASCT vs VRd	13% vs 12%	–	67.5 vs 46.2
IFM 2009	NDTE	VRd + ASCT vs VRd	–	21 vs 15%	50.0 vs 36.0
ATLAS	NDTE, maintenance	KRD vs R	53% v 31%	–	59.1 vs 41.4
ALCYONE	NDTIE	Dara-VMP v VMP	–	28% v 7%	36.4 vs 19.3
MAIA	NDTIE	DaraRd v Rd	31% v 10%	–	62.0 vs 34.3
POLLUX	RRMM	DaraRd v Rd	33.2% v 6.7%	–	45.0 vs 17.5
CASTOR	RRMM	DaraVd v Vd	15.1% v 1.6%	–	16.7 vs 7.1
CASTOR	RRMM	DaraKd vs Kd	18% v 4%	–	28.6 vs 15.2
APOLLO	RRMM	DaraPd v Pd	9% v 2%	–	12.4 vs 6.9
IKEMA	RRMM	IsaKd v Kd	20% v 11%	30% v 13%*	NR vs 19.2

All reported data was statistically significant; *: included patients with a VGPR or better
MRD-ve: minimal residual disease negative, CR: complete response, PFS: progression free survival, mo: months, NDTE: newly diagnosed transplant eligible, NDTIE: newly diagnosed transplant ineligible, RRMM: relapsed/refractory multiple myeloma, Dara: daratumumab, Isa: isatuximab, V: bortezomib, K: carfilzomib, T: thalidomide, R: lenalidomide, d: dexamethasone, M: melphalan, P: prednisone.

surrogate accelerated approval endpoint in MM clinical trials. To validate surrogacy, the ODAC reviewed two recent meta-analyses addressing this question. Though there were minor differences in the patient populations and statistical analysis, both trials assessed correlations between MRD and clinically relevant outcomes of PFS or OS at the individual patient level and the trial level in order to evaluate whether the treatment effect on survival may be predicted by the observed treatment effect on the surrogate endpoint.

The first analysis conducted by The University of Miami included eight phase 2-3 randomized, controlled trials that enrolled 4,907 patients with NDMM and performed validated MRD assays at an *a priori* defined time point as a primary, secondary, or exploratory endpoint. The primary objective of this analysis was to evaluate whether MRD negativity during CR is a reasonably likely endpoint for clinical benefit by PFS in newly diagnosed transplant eligible and transplant ineligible patients. The investigators also evaluated whether sustained MRD negativity was associated with improved PFS and if it is 'reasonably likely' to predict OS benefit. The analysis demonstrated individual-level association between 12-month MRD negativity and PFS (OR 4.72, 95% CI 3.53-5.90) as well as OS (OR 4.02, 95% CI 2.57-5.46) in the NDMM population. Similar results were seen for both the transplant eligible and transplant ineligible subgroups. Trial level associations varied based on patient population and linear regression model used. MRD had a moderate to strong association with PFS in the transplant eligible (R^2 0.67-0.84) and transplant ineligible population (R^2 0.83-0.85). The association with OS was moderate to strong with transplant ineligible patients (R^2 0.63-0.83) and weak to moderate in the transplant eligible population (R^2 0.21-0.33).[20]

The second meta-analysis conducted by the i2TEAMM included 20 randomized, controlled, phase 3 trials. The heterogeneous population of 12,316 patients included newly diagnosed transplant eligible, newly diagnosed transplant ineligible, and RRMM patients. The investigators conducted 34 two-arm comparisons, and the principal surrogate endpoint evaluated was the proportion of patients who achieved a CR with at least one MRD negative sample at 9 months (+/- 3 months). Of note, this analysis included trials that assessed 10^{-4}, 10^{-5} and 10^{-6} MRD thresholds, but the majority included 10^{-5} based on the IMWG response criteria. The investigators found a strong correlation between 9-month and 12-month MRD negative CR and PFS at the individual patient level, and this correlation was stronger with higher levels of MRD sensitivity. This finding was supplemented by moderate correlations that were demonstrated for trial-level assessments for both PFS (R^2 0.66-0.70) and OS (R^2 0.64-0.69).[21]

The third analysis was conducted by the FDA to pool the heterogeneous data submitted by both applicants and to evaluate whether inclusion of all available data would impact conclusions. This analysis included 25 two-arm comparisons including 11,019 patients from 18 trials. The FDA investigators demonstrated strong individual-level correlation with MRD for PFS and OS, supporting the prognostic value of MRD negativity. Similarly to the two applicant analyses, the trial-level associations were weak to moderate for both PFS and OS, and the greatest association was seen for the newly diagnosed transplant ineligible population.[22] Though the lack of strong trial-level associations limits the ability for validation of MRD as a surrogate endpoint, the strong individual-level association supports its utility.

The ODAC voted unanimously to recommend MRD as an accelerated approval endpoint in MM clinical trials. This is already being put into practice as demonstrated in the ISKIA trial which is the first phase 3 trial to assess MRD as a primary outcome.[23] Future considerations for implementation of MRD testing include: timing and frequency of MRD testing, preferred MRD assay and sensitivity level, reimbursement, durability of MRD, impact of sustained

MRD on survival outcomes, and ability to use MRD to drive clinical decisions. Though the final FDA approval has not yet been announced as of the time of writing, it is expected that MRD as a surrogate endpoint for accelerated approvals in MM clinical trials will expedite drug development and continue to push treatment aims of myeloma from control to cure. ●●

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Reflections on Presentations: Lessons Learned

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My presentation skills are a topic I come back to time and again in my career.

I had given didactic lectures as a pharmacy student and thought of myself as having above average experience. So, without hesitation, to showcase my exuberant personality and unconventional thinking, I presented on mental math strategies during a "choose your own topic" prompt for a residency interview. Another candidate spoke on an unusual medical case he encountered during rotations. Upon reflection, I should have considered my audience and their rationale for the request.

During residency, a preceptor informed me that my frenetic handwaving during my lecture made me look like I was dancing. That was the first time I was told about my tendency to overly gesticulate. Another time I was instructed to remove the animations and cartoons that festooned my presentations, to increase their professional look and feel for the audience. That was the first time I thought about professionalism in the context of a slide presentation. Towards the end of my post-graduate year (PGY)-1 residency, I perfected the strategy of adding questions throughout the presentation to engage the audience. At this point, my preceptors told me I was ready.

"This has led me to the revelation that in previous presentations and meetings, I failed to give enough consideration to what the other person wanted from the interaction.".

So, it was with great gusto, that I created and presented briefs as an Army Officer. Even as a pharmacy officer, we created and presented countless PowerPoint presentations on metrics, standard operating procedure updates, and process improvements for our department chiefs and hospital executives. I learned to memorize my slides and regurgitate the material, zooming through the information to impress my audience via overwhelming data. As a field grade Officer in military school, we critiqued each other on presentation styles and whether we hit all the needed metrics within the allotted time. We officers were alike in the way we excelled at this procrustean task.

As a clinical pharmacist working on a national presentation, I received a list of objectives. I spent several weeks crafting a lecture that would adequately address those objectives. For the first time, I seriously worked with a set of objectives from scratch, rather than creating the points from a presentation I had already made, which had been my modus operandi all throughout my PGY-1 and PGY-2 residencies.

Finally, as a Medical Science Liaison, I learned about the concept of telling a cohesive story rather than just data dumping the information on each slide. More importantly, I learned to summarize the slides into pithy takeaways. Nowadays, I start with the objectives of a meeting, visualize an ideal conversation based on my objectives, and practice a few times prior to each meeting. I am learning more each day that my role is less about delivering data than it is about adjusting the flow of dialogue to concentrate on what is of interest to my audience.

This has led me to the revelation that in previous presentations and meetings, I failed to give enough consideration to what the other person wanted from the interaction. Throughout my pharmacy career I had conflated communication with presentation, but I am beginning to appreciate that presentation is a form of communication, and I didn't understand either technique fully. In pharmacy school I merely absorbed information from my professors, with objectives being a slide I promptly skipped over. In residency, most critiques came after presentations were made and habits formed. As clinical pharmacists, the expectation is that we've learned communication sometime along the way, perhaps prior to pharmacy school.

As I reread books on presentation in all its forms and reflect on my experiences with communication in general, I am reminded of many tips. Below are suggestions I find most valuable:

- Do not fidget: Whether on the podium or in a one-on-one, fidgeting decreases the credibility and professionalism of the speaker and distracts from the topic. This also applies to excessive head bobbing when in dialogue.
- Visualize: Imagine yourself giving the talk, where you pause, where you point out data, where you ask a question, etc. Practice and visualize the response.
- Eye contact: I used to "scan" the room thinking I was superb at making eye contact, but giving each pair of eyes a sentence before moving on to the next brings this interaction to the next level.

Reflection on Personal Impact and Growth

- Begin with what your audience wants out of the interaction: The earlier I parsed out what my audience sought, the faster I pivoted to a more useful topic. This involves knowing your information, figuring out as much as you can about your audience, and listening for keywords when in conversation.
- Minimize extemporaneous information on a slide: Your audience generally cannot listen and read at the same time. Expound on context and keep your audience engaged in dialogue with you as opposed to focusing on your slides.

Everyone maintains their opinions on the best presentation styles. I inform my students of this before they attempt to make sense of the barrage of disparate recommendations from even one rotation. If I were to restart my presentation journey, I would begin with the audience's perspective, learn to engage them in presentation, and have enough command of the material to pivot to where audience interest lies. So, I reflect on my presentations and daily conversations time and again and do my best to become a better communicator. Communication is a dance between the involved parties, and I've found it can be fun.

A Primer on Pharmacoeconomic Evaluations in Hematology/Oncology

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Pharmacoeconomics and Formulary

Pharmacoeconomics is the science of measuring the costs and outcomes associated with drug therapies and interventions in health care delivery.[1] Pharmacoeconomic research, also referred to as health economics and outcomes research (HEOR), seeks to describe and analyze the costs of consequences of pharmaceuticals. Such studies encompass both the economic and humanistic value of a health care intervention. Economic evaluations often include assessment of cost effectiveness or cost benefit, while humanistic outcomes include quality of life (QoL), patient preferences, and patient satisfaction. In an era of increasing costs for cancer therapeutics, financial toxicity, and a need for oncology stewardship, understanding economic and humanistic outcomes has become more important than ever before.

Pharmacoeconomics can be very important for us in hematology/oncology practice management as it can be a valuable asset in formulary decision-making.[2,3] It is important to understand that pharmacoeconomic evaluations are *decision-making tools* but are not *decision makers*. Whether a drug therapy is cost effective is not the end-all-be-all or sole point of evaluation for that drug, but rather an additional factor to consider in formulary evaluation along with clinical efficacy, safety, and level of evidence. In hematology/oncology we are frequently faced with having multiple drugs in the same class, with the same or similar indication, but no direct comparative clinical trials assessing for efficacy and safety. I like to often think of pharmacoeconomic evaluations as a great "tie-breaker" in these types of scenarios.

"It is important to understand that pharmacoeconomic evaluations are decision-making tools but are not decision makers."

With clinical trials, we learn how to break these down during pharmacy school and become more adept at doing so in clinical practice; however, we are often not exposed to the same concepts with pharmacoeconomic studies. When evaluating a clinical trial, we need to be cognizant of specific aspects such as study design, randomization, blinding, stratification, inclusion and exclusion criteria, and choice of appropriate primary and secondary outcomes; there are several core principles of pharmacoeconomic studies that are analogous to these aspects. In pharmacoeconomic studies we need to consider costs, consequences, analysis perspective, study design, and decision modeling. A fundamental understanding of such principles will be vital for successfully incorporating such data into a formulary review at your Pharmacy and Therapeutic (P&T) Committee. Herein, I will review some of the core principles of pharmacoeconomic studies.

Costs, Consequences, and Perspectives

Costs refer to the resources consumed when providing a treatment or service. There are direct costs and indirect costs.[1] Direct costs are just that: costs directly related to providing care. Examples include the costs of drugs, laboratory testing, facilities, practitioners, and equipment. Indirect costs are less tangible, and often focus on the time or productivity cost associated with treatment, such as time off work, leisure time lost, or being less productive or effective at work.

Consequences are essentially the outcomes with providing a treatment or service. Common consequences, especially in hematology/oncology pharmacoeconomic analyses, include quality adjusted life years (QALYs), life years gained, length of remission, and cure. In a pharmacoeconomic study, the probability of each consequence or outcome must be identified. These probabilities are often obtained from external data sources such as published literature, clinical trials, and health plan databases.

Another important aspect in reviewing pharmacoeconomic studies is the analysis perspective. If a cost-effectiveness analysis is being conducted for a new drug, the perspective tells us *who* the new drug could be cost-effective for. Common perspectives for such studies include society, payers, patients, and health care providers. The analysis perspective can often be found in the Methods section of a pharmacoeconomic study manuscript. The other components of the Methods of such a study can be influenced by the perspective including the analysis questions, study design, data variables to be included, and the source of the cost data.

Pharmacoeconomic Study Designs and Outcomes

There are several different types of pharmacoeconomic analyses, including cost-of-illness, cost minimization, cost effectiveness, and cost utility.[1] It is important to know that cost minimization, effectiveness, and utility studies require a comparison for the intervention in question. Cost minimization studies are conducted on the basis of treatment alternatives having equal outcomes (ex. brand versus generic) with the objective of determining the least costly way to achieve an outcome, rather than to compare benefits. Cost effectiveness analyses compare costs and benefits between interventions to determine if it is of reasonable or sufficient value to adopt. In comparing cost and benefit, the incremental cost-effectiveness ratio (ICER) is often calculated and includes inputs of the difference in both costs and effects between alternatives. The ICER can be interpreted as the cost to achieve a single unit increase in an outcome between treatment options. An example of a unit in this scenario could be one additional life year saved.

A cost utility analysis (CUA) is similar to a cost effectiveness analysis in that there are inputs and outputs; however, the difference here is that the outputs incorporate quality and quantity of life. As QoL can be a difficult concept to measure, CUAs incorporate utility estimates, which is the desirability that individuals exhibit for a condition, as measured on a scale of 0 (death) to 1 (perfect health).[1,4] This is an important concept for us in hematology/oncology, as we have treatments with adverse events that can impact QoL. While we may have some treatments that prolong survival, it is also important to incorporate the utility of those additional life years and factor that into the equation to determine the QALYs. Often the ICER in a CUA will be the cost per QALY gained. An important tip for when you are evaluating a CUA: there should be a willingness-to-pay (WTP) threshold described in the Methods section. An ICER that exceeds the WTP is likely to mean that the treatment is not cost-effective. A common WTP for the United States is $150,000 per QALY.

Decision Modeling

Decision modeling methodologies can be very complex to understand, but for the sake of simplicity, they are where all the inputs, such as costs, probabilities, and utilities, get put into place to compare the likelihood of various events occurring between treatment options.[4] Probabilities of events occurring for patients in a decision model often come from clinical trials. There are various resources and literature available for utilities that will be used in modeling. And then of course, costs – cost for the drugs, adverse events, health care resource utilization, etc. will be factored into the decision analysis. It is also important to note that decision analyses often have a time horizon for how long the simulation would run for a given patient. Often, when we have short-term follow-up for a new drug therapy, there can be extrapolations on survival outcomes and probabilities.[5]

Incorporating Pharmacoeconomics into Formulary Evaluations

Some form of a pharmacoeconomic evaluation or financial analysis should be included in a formulary review for new drugs we are considering for formulary addition. When including formal pharmacoeconomic evaluations, such as a CUA, into the formulary evaluation it will be important to critically appraise all the above components of such a study and understand the limitations of such data in our own institutions. For example, an analysis perspective can differ from the perspective of our own institutions. Many pharmacoeconomic studies have assumptions for situations and extrapolations on data that are applied to decision models to provide a degree of simplicity; it should be noted that conclusions based on such studies are indeed made on assumptions. Additionally, many of the cost-related inputs into a pharmacoeconomic model may differ from institution-specific costs.[3]

Sometimes when we are evaluating a new drug to be considered for addition to formulary, we may not yet have a pharmacoeconomic analysis published in the literature to add to our presentation. In lieu of having published literature available for a formulary evaluation, the next best thing could be comparison of direct drug costs between drugs across a class or a new drug compared to other potential treatment options or standards of care. This can include the direct drug costs, site of care where the drug needs to be administered (inpatient or outpatient), non-medication-related costs such as laboratory testing, and any other additional financial consequences to the health-system or pharmacy.[3]

Conclusion

In summary, pharmacoeconomic evaluations can be very helpful as an adjunct to evaluating efficacy and safety in formulary decision making in hematology/oncology, especially when we have data gaps and multiple agents in the same drug class that have not been directly compared. While there can be some limitations to formal pharmacoeconomic evaluations in the literature, including their complexities and their perspectives being not readily applicable to our practice settings, there are other considerations we can include in a financial analysis when evaluating new drugs for our formularies, such as direct drug costs and differences in health care resource utilization between the new drug and any potential comparators. ●●

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Recipients of the Certificate of Recognition for Exemplary Research on Quality of Care in Oncology

Chris Parish, PharmD
PGY2 Oncology Pharmacy Resident
Atrium Health Wake Forest Baptist Comprehensive Cancer Center

Shraddha Kansagra, PharmD, BCOP
Clinical Pharmacy Specialist - Medical Oncology
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The Hematology/Oncology Pharmacy Association (HOPA) would like to congratulate the three recipients of the Certificate of Recognition for Exemplary Research on Quality of Care in Oncology that were awarded during the 2024 HOPA Annual Conference. Awardees were selected by a subgroup of HOPA's Quality Oversight Committee, and projects were graded based on their innovativeness, potential for broader implementation in oncology care, and utilization of broadly recognized oncology or pharmacy quality metrics. Whether through the application of technology or through novel pharmacy practice models, this year's winners demonstrated the ability of oncology pharmacists to employ quality improvement frameworks to optimize the care of cancer patients.

> **"Whether through the application of technology or through novel pharmacy practice models, this year's winners demonstrated the ability of oncology pharmacists to employ quality improvement frameworks to optimize the care of cancer patients."**

The Impact of Virtual Education on Veteran and Caregiver Understanding of Chemotherapy (TEACH)[1]

Presenter: Lauren E. Johnson, PharmD

Patient counseling upon initiation of chemotherapy is a cornerstone of oncology pharmacy practice and is a vital first step in ensuring that patients are comfortable and confident with their oncology treatment. However, initial counseling sessions can be overwhelming for patients and subsequent reinforcement of information is commonly provided through educational handouts or other resources. This project sought to modernize the provision of educational handouts through the development of educational videos for cancer patients that reinforce key chemotherapy-related topics.

The TEACH project was conducted at the William S. Middleton Memorial Veterans Hospital in Madison, Wisconsin and involved the development, dissemination, and effectiveness assessment of two chemotherapy educational videos for Veterans receiving oncology care. The videos were entitled "Chemotherapy: What to Expect" and "Oral Chemotherapy: How to Safely Take, Store, and Dispose" and can be viewed at the following links: (https://youtu.be/LrzmO4mXizg?si=ikbycxhilyxyBk3F, https://youtu.be/Fbj_-wLcIPo?si=wIEHjMzRxqABN85A). These videos were created in collaboration with the Veterans Health Administration's (VHA) Patient Education Resources Center and posted to the VHA's YouTube Channel. Veterans and their caregivers were directed to the YouTube site upon initiation of chemotherapy and were provided surveys to complete regarding the effectiveness of the educational content.

Upon presentation of this project at the 2024 HOPA Annual Conference, 22 survey responses had been collected— 12 from Veterans and 10 from their caregivers. All Veterans and caregivers that completed the survey stated that they either agreed or strongly agreed to survey questions regarding the helpfulness, understandability, and overall positive impact that the educational videos had on their oncology care experience. After conducting the project, the authors concluded that the creation and use of educational videos to improve chemotherapy understanding for Veterans and caregivers was feasible and well-received. Future directions for the TEACH project include expansion of video topics to immunotherapy and specific chemotherapy regimens and disseminating the video content to other VHA pharmacists and providers.

Improving Post-Transplant Vaccination Compliance via Implementation of a Clinical Pharmacist-Managed Service[2]

Presenter: Christopher Clayton, PharmD, BCOP

Vaccinations after hematopoietic stem cell transplant (HSCT) are key to the prevention of post-transplant infections. However, guideline-recommended vaccine schedules after transplant are complex. Effective completion requires coordination from several members of the healthcare team. Upon recognition of potentially suboptimal vaccine compliance rates after transplant at Aurora St. Luke's Medical Center in Milwaukee, Wisconsin, the HSCT pharmacist team was tasked with ownership of the post-transplant vaccine process, including immunization plan entry in the electronic medical record (EMR), coordination of appointments with clinic staff, and quarterly vaccine compliance tracking. The transplant group's goal for vaccine compliance was >90% for inactive vaccines.

After implementation of the pharmacist-led post-transplant vaccination service, the transplant team at Aurora St. Luke's conducted a pre/post-implementation study to evaluate the effectiveness of the pharmacist-led process. This was a retrospective review that

used data from the institutional EMR and the Wisconsin immunization registry from December 2017 to September 2021. The analysis included patients who were at least 24 months post-transplant, coinciding with the timeframe for the final recommended vaccinations. The primary outcome evaluated in this analysis was overall inactive vaccine compliance during the study period, and secondary outcomes included on-time administration of all vaccines and active vaccine compliance.

Overall inactive vaccine compliance was 95.4% in the pharmacist-managed vaccination group and 88.3% in the non-pharmacist-managed ("baseline") group ($p<0.01$). On-time vaccine administration increased from 43% in the baseline group to 67% in the pharmacist-managed group, and live vaccine administration was also higher in the pharmacist-managed group (71% vs 44%; $p<0.01$).

This study demonstrated a significant improvement in vaccine compliance rates through a pharmacist-driven process, and the investigators attained their institutional goal of >90% inactive vaccine compliance post-transplant. The authors attributed the increase to improved care coordination and regular compliance review by the transplant pharmacist team. Authors recommend that institutions with HSCT programs perform a similar internal analysis of vaccine compliance rates to determine the potential utility of enhanced pharmacist involvement in the post-transplant vaccination process.

Implementation of Pharmacy Medication Counseling Services for Phase I Investigational Agents[3]

Presenters: Seonga Song, PharmD and Jonathan Want, PharmD

While patient counseling by oncology pharmacists is a common practice among patients receiving standard-of-care therapies, a 2017 survey published in the American Journal of Health-System Pharmacy showed room for increased uptake in pharmacist involvement in counseling patients on early-phase clinical trials.[4] While investigational drug service (IDS) pharmacists have traditionally been focused on logistical operations of clinical trials, their expertise on investigational agents positions them well to provide medication-related education to patients regarding early phase clinical trials. Therefore, investigators at Roswell Park Comprehensive Cancer Center developed a prospective pilot study to evaluate the impact of an IDS pharmacist's involvement in patient education during early phase clinical trials.

Key metrics evaluated in this study were patient satisfaction and patient comprehension of the trial on which they were enrolled. Secondary endpoints included qualitative descriptions of services provided by the IDS pharmacist when embedded in the early phase research clinic setting. This study was conducted from September 2023 to March 2024. Outcomes were derived from a patient satisfaction survey, and an eight-question knowledge assessment administered to patients at three time points during their treatment on a clinical trial: after physician counseling, after subsequent pharmacist counseling during their first treatment cycle, and finally on the first day of cycle 2 of treatment.

Twenty-six patients were evaluated after their initial pharmacist counseling session, and 24 patients were evaluated on cycle 2 day 1 of therapy. There was a statistically significant improvement in the number of correct answers on the patient knowledge assessment after pharmacist counseling sessions, both at first cycle follow-up (5.6 correct answers at baseline, 7.3 correct answers after pharmacist counseling; $p<0.0001$) and upon follow-up on cycle 2 day 1 (5.5 correct answers at baseline, 7.0 correct answers after pharmacist counseling; $p<0.0001$). Over 80% of patients agreed or strongly agreed to survey items regarding the importance, value, and effectiveness of pharmacist counseling after participation in this pilot study. When present in the early phase research clinic, the most common pharmacist interventions included answering drug information questions, assisting in side effect management, and identifying drug interactions with study medications.

As a result of this study, investigators concluded that counseling services by IDS clinical pharmacists in phase 1 clinical trials were associated with improvement in patients' comprehension of clinical trials and their satisfaction with phase 1 trial enrollment. As a result of this study, Roswell Park Comprehensive Cancer Center will seek to embed a full-time IDS pharmacist in their early phase research clinic to provide patient counseling and other pharmacy-related services.

In conclusion, these projects showcase the diverse and impactful quality improvement initiatives undertaken by oncology pharmacists. From developing educational videos for veterans, to implementing pharmacist-managed vaccination services and integrating pharmacist counseling into early-phase clinical trials, these award-winning projects demonstrate the expanding role of pharmacists in optimizing patient care and outcomes in oncology. ●●

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QTc Measurements and Chemotherapy: Practical Advice for Oncology Pharmacists

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Background

Many cancer treatments and supportive agents carry the risk of QT prolongation. The QT interval represents the time required for the heart to repolarize after onset of depolarization, measured via electrocardiogram (ECG). Abnormalities in myocardial ion channels can disrupt the balance between sodium influx and potassium efflux, leading to a prolonged repolarization phase and prolonging QT interval. This can lead to torsades de pointes (TdP), a potentially life-threatening ventricular arrhythmia.[1,2]

The duration of repolarization is influenced by heart rate (HR), with faster rates shortening the QT interval. To normalize for heart rate, the corrected QT interval (QTc) is calculated using various formulas. However, multiple studies have identified a lack of standardization in QTc calculation methods and problems that are associated with this.[3,4]

Each QTc formula uses a unique method; common formulas include Bazett, Framingham, and Fridericia. While commonly used, the Bazett formula - developed in the 1920s - tends to overestimate QTc compared to others, particularly at higher heart rates.[3] Given a QT of 400 milliseconds (ms) and HR of 95 beats per minute (bpm), Bazett calculates QTc to be 503 ms, while Framingham and Fridericia calculate QTc as 457 ms and 466 ms, respectively. These differences are significant enough that in the example, QTc calculated with Bazett's would be considered significantly prolonged and would likely result in a change in care.

Differences in QTc can be explained by reviewing formula development. These formulas were designed to correct QT to a HR of 60 bpm, equivalent to RR (R interval to R interval) of 1000 ms. The Bazett (QTcB=QTRR) and Fridericia formula (QTcF=QT3RR) both rely on the presumption of an exponential connection between QT and RR interval, thus reducing precision with fast heart rates. However, the Framingham formula (QTcFram=QT+0.1541-RR) presumes a linear relationship between QT and RR interval, making it more accurate, especially when HR is greater than 90 bpm.[5,6] Although both Bazett and Fridericia can overestimate QT with a faster heart rate - as seen in the example above - Fridericia remains more accurate.

Our team reviewed a total of 142 patients receiving potentially QT prolonging-chemotherapy.[3] While no episodes of TdP were identified, 28 encounters required clinical intervention due to prolonged QTc (using Bazett). Interventions included electrolyte supplementation (9 patients), discontinuation of concomitant medications (8 patients), withholding chemotherapy (7 patients), reducing chemotherapy dose (2 patients), discontinuing chemotherapy (1 patient), and adjusting dosing schedules (1 patient). Of these changes, 5 were inappropriate (4 – not in accordance with FDA labeling, 1 – no change needed with Fridericia or Framingham). The study also highlighted the Bazett formula's association with clinically significant differences in QTc values compared to the Fridericia or Framingham formulas, with mean differences of 26.3 ms and 29.3 ms, respectively.[3]

"Ongoing research efforts continue to unravel the mechanisms of how medications impact QTc, demonstrating that not all medications impact QT via the same mechanism."

Mechanisms of QT Prolongation

Ongoing research efforts continue to unravel the mechanisms of how medications impact QTc, demonstrating that not all medications impact QT via the same mechanism. For instance, oxaliplatin enhances the I_{NA} channel while imatinib inhibits the I_{KR} channel.[7] Many supportive medications can also impact QTc in various ways, such as altering electrolyte levels or affecting potassium channels in the heart. Acknowledging differences in mechanism can better guide treatment decisions and medication combinations. Managing QT prolongation in cancer patients requires consideration of multiple factors, including standardizing QTc measurement and understanding the limitations of different methods, recognizing the diverse mechanisms causing QTc prolongation, and accounting for patient-specific factors.

Not all QT prolonging medications pose the same risk, underscoring the importance of thorough evaluation. The QT interval as reported on ECG represents the summation of action potential in ventricular myocytes. Specialized channels facilitate ion currents across the cell membrane, and the net decrease in repolarization current results in action potential. Mutations in genes encoding these ion channel proteins lead to congenital long QT syndrome (cLQTS). Conversely, drug-induced QT prolongation likely occurs due to the blockage of the inward potassium rectifier (I_{Kr}) channel, commonly known as the hERG channel. Other mechanisms include disruption of channel trafficking and reduction in the number or rate of mature potassium channels in the cell membrane.[8]

Understanding which cardiac ion channels are specifically blocked via different medications can assist pharmacists in mitigating the risk of excessive prolongation. Multiple potassium, sodium, and calcium channels have suggested involvement in the QT prolongation. I_{Na} determines phase 0 of the action potential, which is then followed by the rapid partial repolarizing potassium current (I_{to}). The plateau period is determined by a current created through calcium (I_{ca1}, I_{ca2}) and sodium entry, and exit of potassium through I_{Kr} (rapidly activating delayed rectifier potassium current) and I_{Ks} (slowly activating delayed rectifier potassium current). The I_{Ks} and I_{Kr} are the main repolarizing currents and are where most drug blockages are observed. Lastly, the I_{K1} (the inward rectifier potassium current) becomes activated during the late part of repolarization and maintains the negative resting potential.[8]

The unique structural features of I_{Kr} channel may explain why it is more susceptible to block compared to other channels. While blocking either I_{Kr} or I_{Ks} can cause lengthened repolarization, a previous study has shown that blocking both I_{Kr} and I_{Ks} simultaneously may lead to an excessive lengthening of cardiac repolarization and QT.[9] This suggests that increased caution may be required when using multiple drugs that prolong QT in order to avoid combining medications that block I_{Kr} and I_{Ks}.

Although other channels appear to be less susceptible, blocking them has been shown to affect QT as well. For example, early afterdepolarizations (depolarizing currents occurring early during the period of repolarization) result from inward calcium currents and can lead to a prolonged repolarization and QT by increasing long type calcium channels. The unique structural features of the I_{Kr} channel, particularly the large number of aromatic residues in the hERG potassium channels, seem to be linked to its increased susceptibility to drug-block compared to other channels.[8]

Even with this knowledge, the clinical impact on the degree of QT prolongation and risk of TdP remains challenging. For example, verapamil is known to block I_{Kr} but does not prolong QT interval to the expected extent.[10] Areas of continued research include better clarifying additional changes in repolarization as a risk factor for TdP, improved understanding of the interplay between different myocardial cells, and understanding which cell type carries the biggest impact regarding medication selection.

Patient Assessment Pearls

One of the most comprehensive and accessible resources for QT prolonging medications is "CredibleMeds".[11] This Internet resource is managed by the nonprofit AZCERT (The Arizona Center for Education and Research on Therapeutics), and is frequently updated with clinical evidence to support the medication categorizations. Patients can also use the website to understand the QT prolonging risk of many medications. CredibleMeds use 4 risk categories: known risk of TdP ("these drugs prolong QT interval AND are clearly associated with known risk of TdP; even when taken as recommended"), possible risk of TdP ("these drugs can cause QT prolongation BUT currently lack evidence for a risk of TdP when taken as recommended"), conditional risk of TdP ("these drugs are associated with TdP but only under certain conditions of their use or by creating conditions that facilitate or induce TdP."), and cLQTS (medications known to increase risk in congenital long QT syndrome). Table 1 includes a list of che-

Table 1

Name	Class	Known QTc prolonging method	Risk of QTc prolongation
Anti-Cancer/Chemotherapy			
Oxaliplatin	Platinum-based alkylating agent	Inhibit hERG (enhance Ina: increasing Na+ influx)[12]	Known Risk of TdP
Vandetanib	EGFR inhibitor; VEGF inhibitor; TKI	Inhibit hERG K+ channels[12]	Known Risk of TdP
Quizartinib	TKI	Inhibit hERG (IKs only)[12]	Known Risk of TdP
Arsenic Trioxide	Antineoplastic	Inhibit hERG (IKr and IKs)[13]	Known Risk of TdP
Rucaparib	PARP inhibitor	Exact mechanism unknown (no evidence yet that it is related to hERG)[14]	Known Risk of TdP
Fluorouracil (5-FU)	Pyrimidine Analog	Exact mechanism unknown[15]	Possible Risk of TdP
Capecitabine	Pyrimidine Analog	5-FU oral prodrug, specific mechanism unknown	Possible Risk of TdP
Trifluridine/Tipiracil	Pyrimidine Analog; Thymidine Phosphorylase Inhibitor	Exact mechanism unknown	Possible Risk of TdP
Epirubicin	Anthracycline; Topoisomerase II inhibitors	Can increase sensitivity to IKr, blocking drugs and reducing re-depolarization reserve. Can increase patient susceptibility to other drugs that can prolong QT[16]	Possible Risk of TdP
Inotuzumab Ozogamicin	Anti-CD22; monoclonal antibodies	Very low inhibition of potassium channel current on hERG[17]	Possible Risk of TdP
Midostaurin	FLT3 inhibitor; TKI	Drug metabolite inhibits hERG current[18]	Possible Risk of TdP
Ivosidenib	IDH1 inhibitor	Inhibit hERG K+ channels[19]	Possible Risk of TdP
Glasdegib	Hedgehog pathway inhibitor	Dose dependent inhibition of hERG K+[20]	Possible Risk of TdP
Ribociclib	Cyclin-Dependent Kinase Inhibitor	Down regulating expression of KCNH2 (encoding for potassium channel hERG) and up-regulate SCN5A and SNTA1, in total 3 genes associated with long QT syndrome[21]	Possible Risk of TdP
Tamoxifen	SERM	Inhibit hERG (IKr), possibly effects calcium channel[7]	Possible Risk of TdP

Table 1 continued

Toremifene	SERM	Inhibit hERG (IKr)[7]	Possible Risk of TdP
Eribulin Mesylate	Microtubule dynamics inhibitor	Exact mechanism unknown	Possible Risk of TdP
Lapatinib	EGFR inhibitor; TKI	Inhibit hERG channel (IKr) in transfected HEK293 cell and prolong action potential[22]	Possible Risk of TdP
Osimertinib	EGFR inhibitor; TKI	Inhibit hERG K+[12]	Possible Risk of TdP
Sunitinib	TKI	Inhibit hERG K+[12]	Possible Risk of TdP
Dasatinib	TKI	Inhibit hERG K+[12]	Possible Risk of TdP
Bosutinib	TKI	Inhibit hERG K+[12]	Possible Risk of TdP
Nilotinib	TKI	Inhibit hERG K+[12]	Possible Risk of TdP
Gilteritinib	TKI	Low in vitro potency shown at blocking hERG currents[20]	Possible Risk of TdP
Imatinib	TKI	Inhibit hERG (IKr)[12]	Possible Risk of TdP
Ceritinib	TKI	Inhibit hERG K+[12]	Possible Risk of TdP
Sorafenib	VEGF inhibitor; TKI	Inhibit hERG K+[12]	Possible Risk of TdP
Cabozantinib	VEGF inhibitor; TKI	Inhibit hERG K+[12]	Possible Risk of TdP
Pazopanib	VEGF inhibitor; TKI	Inhibit hERG K+[12]	Possible Risk of TdP
Lenvatinib	VEGF inhibitor; TKI	Inhibit hERG K+[12]	Possible Risk of TdP
Entrecitinib	TRK inhibitor; TKI	Inhibit hERG K+[12]	Possible Risk of TdP
Necitumumab	EGFR inhibitor; monoclonal antibody	Inhibit hERG K+[23]	Possible Risk of TdP
Vorinostat	Histone deacetylase inhibitor	Transcriptional changes of gene caused by medication that is required for ion channel trafficking[24]	Possible Risk of TdP
Romidepsin			Possible Risk of TdP
Pralsetinib	RET inhibitor; TKI	Exact mechanism unknown, did not inhibit in vitro hERG at relevant concentrations in animal study[25]	Possible Risk of TdP
Encorafenib	BRAF inhibitor	Not well known but maybe cardiotoxicity through interfering Ras-Raf-MEK-ERK pathway[26]	Possible Risk of TdP
Dabrafenib			Possible Risk of TdP
Vemurafenib			Possible Risk of TdP
Cobimetinib	MEK inhibitor		Possible Risk of TdP
Bortezomib	Proteasome inhibitors	Exact mechanism unknown	Possible Risk of TdP
Crizotinib	MET inhibitor; TKI	Inhibit hERG K+	Possible Risk of TdP
Pacritinib	JAK inhibitor; TKI inhibitor	Inhibit hERG K+	Possible Risk of TdP
Relugolix	GnRH Antagonist	Hormone imbalance changing potassium and calcium currents[27]	Possible Risk of TdP
Leuprolide	GnRH Agonist		
Degarelix	GnRH Antagonist		
Bicalutamide	Antiandrogen	Testosterone levels inversely related to QTc due to changes in potassium and calcium currents[28]	Possible Risk of TdP
Apalutamide	Antiandrogen		Possible Risk of TdP
Panobinostat	HDAC inhibitor	Inhibit hERG (IKr)[24]	Possible Risk of TdP
Adagrasib	KRAS inhibitor	Exact mechanism unknown	Possible Risk of TdP
Bendamustine	Nitrogen Mustard Analogue	Exact mechanism unknown	Possible Risk of TdP
Abiraterone	Antiandrogen	Testosterone levels are inversely related to QTc due to changes in potassium and calcium currents[28]	Conditional Risk of TdP
Supportive Medication			
Antimicrobials			
Levofloxacin	Fluoroquinolone	Inhibit hERG (IKr), stimulate B1-receptor8	Known Risk of TdP
Ciprofloxacin	Fluoroquinolone		Known Risk of TdP
Moxifloxacin	Fluoroquinolone		Known Risk of TdP
Azithromycin	Macrolide	Inhibit hERG (IKr)[29]	Known Risk of TdP
Clarithromycin	Macrolide		Known Risk of TdP
Erythromycin	Macrolide		Known Risk of TdP
Gemifloxacin	Fluoroquinolone	Inhibit hERG IKr, stimulate B1-receptor[8]	Possible Risk of TdP
Piperacillin/Tazobactam	Beta-lactamase inhibitor	Cause hypokalemia, and possible block of IKr[30]	Conditional Risk of TdP

Table 1 continued

Antifungal[8]			
Fluconazole	Azole (tri) Antifungal	Inhibit hERG IKr, stimulate B1- receptor	Known Risk of TdP
Pentamidine	Antiprotozoal	Inhibition of hERG K+ channel trafficking	Known Risk of TdP
Ketoconazole	Azole Antifungal	Inhibit hERG IKr, stimulate B1- receptor	Conditional Risk of TdP
Amphotericin B	Antifungal	Possibly through extreme potassium depletion	Conditional Risk of TdP
Antidepressant			
Mirtazapine	Alpha-2 Antagonist; TeCA	Inhibit hERG IKr[31]	Possible Risk of TdP
Antiemetic[8]			
Ondansetron	Selective 5-HT3 receptor antagonists	Inhibit hERG IKr, stimulate B-1 receptor	Known risk of TdP
Granisteron			Possible Risk of TdP
Dolasetron			Possible Risk of TdP
Promethazine	1st Generation Histamine H1 antagonist; Phenothiazine	Inhibit hERG K +	Possible Risk of TdP
Metoclopramide	Serotonin 5-HT4 receptor agonist; Dopamine antagonist	Inhibit hERG K +	Conditional Risk of TdP
GERD			
Famotidine	Histamine H2 antagonist	Affected by electrolyte imbalance (hERG channel inhibition might not be the underlying mechanism)[32]	Conditional Risk of TdP
Other			
Methadone	Opioid	Inhibition of hERG (IKr, INaL, ICaL)[33]	Known Risk of TdP
Tramadol	Opioid	Blocking sodium and potassium channels[34]	Possible Risk of TdP
Hydrocodone-ER	Opioid	Low affinity for hERG channel, but can prolong based on dose[34]	Possible Risk of TdP
Buprenorphine	Opioid	Exact mechanism unknown, cannot be explained entirely by hERG inhibition[33]	Possible Risk of TdP
Loperamide	Antidiarrheal	Indirectly increase risk by electrolyte imbalance	Conditional Risk of TdP

BRAF: v-raf murine sarcoma viral oncogene homolog B1, EGFR: epidermal growth factor receptor, FLT3: fms related receptor tyrosine kinase 3, GnRH: gonadotropin releasing hormone, HDAC: histone deacetylase, IDH1: isocitrate dehydrogenase 1, JAK: Janus kinase, K+: potassium, MEK: mitogen-activated extracellular signal-regulated kinase, MET: mesenchymal epithelial transition factor receptor, Na+: sodium, PARP: poly (ADP-ribose) polymerase, RET: rearranged during transfection, SERM: selective estrogen receptor modulator, TeCA=tetracyclic antidepressant; TKI: tyrosine kinase inhibitor, TRK: tropomyosin receptor kinase, VEGF: vascular endothelial growth factor

motherapy and supportive care medications particularly relevant for Oncology pharmacy practice, excluding cLQTS medications.[11]

As pharmacists, it is important to screen for other mechanisms contributing to QT prolongation such as severe electrolyte disturbances. Hypokalemia, a complication of uncontrolled chemotherapy-induced nausea and vomiting (CINV) and of some chemotherapy agents, can reduce I_{Kr} currents via enhanced inactivation or exaggerated competitive block by sodium. Hypokalemia can prolong QT interval even in the absence of QT prolonging drugs or in the presence of low-risk QT prolonging drugs. This emphasizes the importance of continuous monitoring and assessing risk and benefit based on patient risk factors.[10]

A Clinical Approach

Figure 1 depicts a simplified, literature-based approach for clinicians navigating use of QT prolonging medications.[35] As shown, Tisdale QT prolongation risk factor scoring helps to determine risk level. Medium/high risk corresponds to a score ≥7 and low risk is a score <7. In situations of structural heart disease, history of QT prolongation, electrolyte disturbance, presence of cardiac symptoms, or QTc ≥500 ms, a cardiology consult would be recommended. It is important to understand that many different patient factors come into play when making decisions regarding initiating QT prolonging drugs. Rather than reflexively discontinuing medications, utilizing multiple monitoring factors and determining the patient's exact risk is crucial.

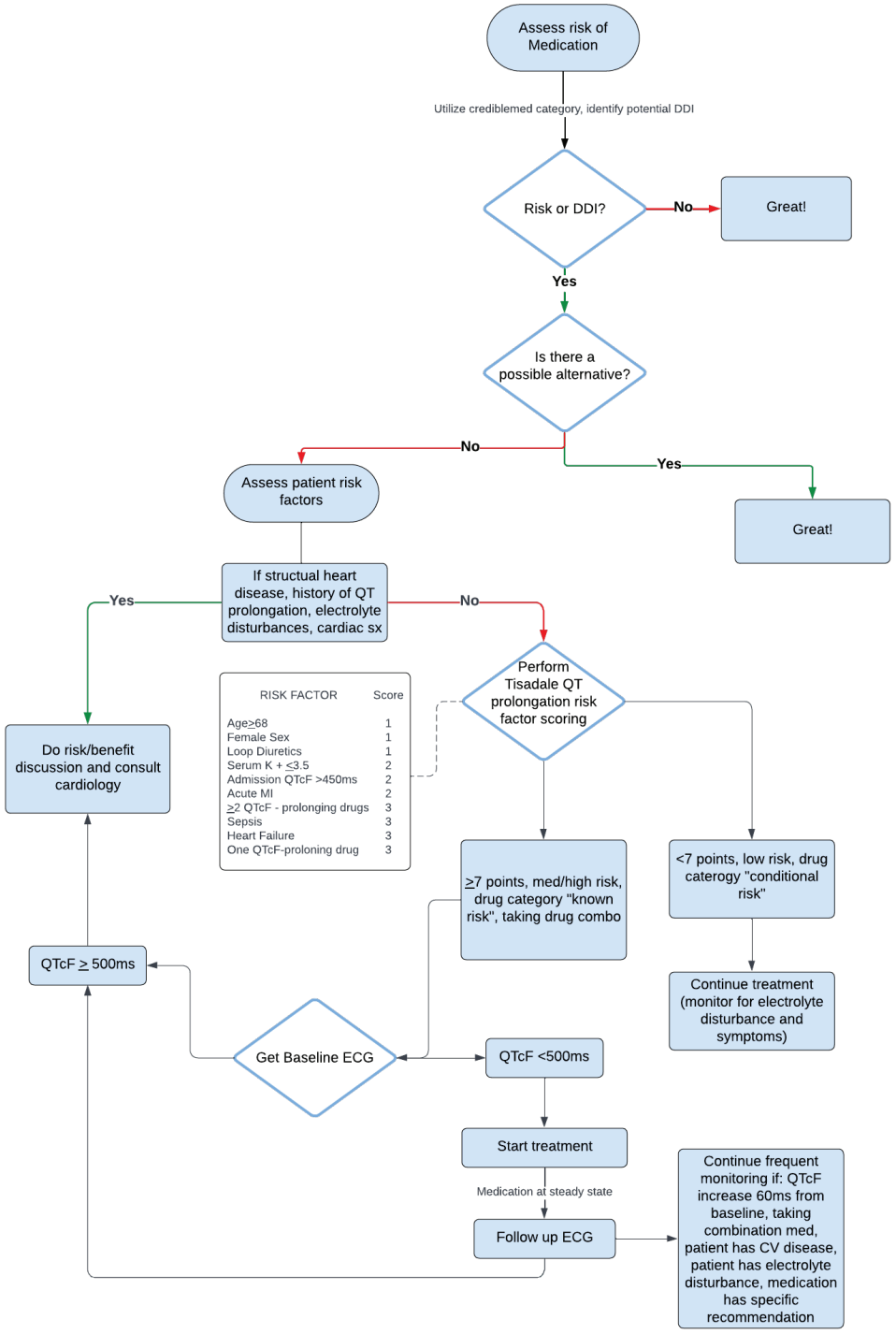
Conclusion

Challenges in managing care persist, as many drug-information resources lack standardized recommendations for QTc calculations. This ambiguity can be especially vexing when faced with patients with cancer and elevated QTc, potentially jeopardizing access to optimal treatments. These complexities highlight the urgent need for a deeper understanding of the mechanisms underlying medication induced QT prolongation, to assist clinical teams in navigating the use of multiple QT prolonging medications.

Ongoing research should elucidate more QT prolonging mechanisms to improve the precision of clinical guidelines and therapeutic strategies. Until then, pharmacists can improve the care of Oncology patients by conducting thorough medication reviews, ensuring the selection of the most appropriate QTc formula, and identifying appropriate interventions. ●●

CLINICAL PEARLS (continued)

Figure 1: QTc Risk Assessment Flowchart



This QTc flowchart, derived from Zolezzi and Chung35, demonstrates QTc risk assessment.
CV: cardiovascular, DDI: drug-drug interaction, ECG: electrocardiogram, K+: potassium, ms: milliseconds, sx: symptoms

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Oncology Pharmacists Know No Borders – A French Adventure to Côte d'Ivoire

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Doors. I've always been fascinated by doors! Not actual doors, although I fell in love with all the doors I saw and took pictures of while walking in Paris after my visit to Côte d'Ivoire. The doors I'm talking about are the opportunities that have presented themselves to me in life, not knowing what was behind those doors.

Growing up in a small country, a dot on the world map: "Lebanon"; I always heard that America was the land of opportunities. And where I was, I saw great minds, infectious passion, insane drive; but no opportunities. I therefore wanted to jump at every opportunity that was presented to me. I saw a big opportunity as a pharmacy student and founded the first Lebanese Pharmacy Student Association, then applied to become a member of the International Pharmaceutical Student Federation (IPSF) and connect with pharmacy students around the world. I remember traveling to Portugal to attend my first IPSF Congress, and the most fascinating thing I learned was that pharmacy students around the world had a lot in common. Many students had an interest in clinical practice yet the only country that offered residency was the United States (US).

As an international pharmacy student, I knew that it was near impossible to get matched for a pharmacy residency in the US, as the competition is high for US citizens already, and most programs do not hire internationals. Oncology was always my dream and passion, and I promised myself that if I ever matched, and specialized in Oncology, let alone practiced in the US, I would serve in every possible way.

Fast forward to 2023, HOPA puts out a call for French speaking oncology pharmacists needed to serve as trainers for an African Access Initiative led by Bio Ventures for Global Health (BVGH). I did not know all that it would entail, but being a French speaking oncology pharmacist, I was inclined to respond. They needed me to complete training in French for oncology practitioners for an online course, with the potential for an in-person training in Côte d'Ivoire. I decided to take on the challenge of teaching oncology in French. All my college and residency training have been in English, and it then occurred to me that I never thought in French when it came to medicine, pharmacy, or clinical practice. I was also fascinated by African cancer epidemiology and guidelines, which I needed to investigate, research, and learn just to be able to teach the online training.

> **"I've always dreamt of helping places that lack access to high quality health care, so this was the opportunity of a lifetime."**

Being an oncology pharmacist is incredibly rewarding and something to look forward to if you are currently a resident. I have learned over the years that we are educators first and foremost. We educate patients, students, healthcare providers, and the public. I have had tears of joy leaving work many times, not believing that this is what I get to do for a living. Every day is a good day to impact a chance at life and improve quality of life! And that's what we do, and not everyone can say that! For that, I am forever grateful. Little did I know that my choice of path would open a door to Africa. Coming from a country that is stranded in resources, especially when it comes to cancer treatments, coupled with the promise I made to myself if I ever made it to where I am today, I felt that I had to answer this call and take part in this online training and in-person training.

Completing my slides for the online oncology course was a challenge. I focused on global epidemiology and highlighted cancer statistics in Africa. I introduced principles of cancer screening and prevention and compared these to best practices in the US. I then delved into diagnostics, treatments, guidelines, side effect management and monitoring. It was quite a brain exercise to think of all of that in French, and it took me over two weeks to meticulously complete. Unbeknownst to me, this would be attended by participants from 16 countries, who stayed on the call and asked questions for ninety minutes after my lecture. I had not seen students this passionate for knowledge, for better serving their patients. Their thirst for learning lit a fire in me to work on an in-person training and I felt like I had to go. I felt that this is me paying it forward and using my expertise in areas where I am needed. I work in academia because I feel that I can impact more cancer patients by passing on my knowledge to my students. I've always dreamt of helping places that lack access to high quality health care, so this was the opportunity of a lifetime.

For the in-person training I worked for weeks in tandem with a fellow oncology pharmacy colleague that had also been in-person before me. We had daily debriefs about his onsite observations. I was asked to train pharmacists on consults I do at my practice, such as developing an oral chemotherapy clinic, educating patients, monitoring patients, and clinical trials. We learned very fast during my colleague's visit that much more was needed before developing clinical services, and that basic infrastructure was missing. I had to tweak and tailor my training accordingly, right until my travel date, and made continuing changes based on personal observations.

I learned that pharmacists have little oncology training in pharmacy schools, despite the high cancer rates in the country, and various pharmacy positions in oncology centers. Pharmacy departments in hospitals are completely separated from medical

offices. Pharmacists have no access to medical records, history, pathology, or labs. I saw people mixing chemotherapy on a table with no protective equipment, no hood, nothing! It was amazing what pharmacists were doing to help cancer patients, even if it meant risking their own safety. I walked into storage rooms that contained targeted cancer therapies that typically require genomic testing, yet no tumor profiling or next generation sequencing took place. I feared asking, "how do you determine the right drug if the patient's tumor was never tested for HER-2, or PD-L1, or EGFR…?". I learned that pharmacists and physicians don't communicate regularly. Pharmacists received chemotherapy orders that only included medication and final dose, no labs, no area under the curve (AUC), no body surface area (BSA), or height or weight or anything of that sort. I found out that they don't know National Comprehensive Cancer Network (NCCN) guidelines, and unfortunately don't have access to any drug databases like Lexicomp or Micromedex. I was fascinated by what they were doing without access to any resources. After all these observations, I was inclined to start my training by discussing sterile compounding, and safe handling of chemotherapy. I subsequently dissected every aspect of order verification and introduced them to NCCN Harmonized Guidelines for Sub-Saharan Africa. We navigated various resources and discussed how they can be translated to French. We spent nine hours daily in a classroom, did didactic lectures followed by discussions and practice. After covering basics, we delved into developing clinical services, starting with communication with physicians and access to more patient information. I felt like what I learned in years, I taught in days to some brilliant minds wanting to learn it all. I felt like I deserved my match into oncology, and recalled the many people who took a chance on me to have the expertise I have today. I wanted to take a chance on each and every one of them, and advocate to advance oncology pharmacist practice in Côte d'Ivoire.

My visit concluded with an invitation to attend a meeting with stakeholders from all over the country, consisting of healthcare department heads and stakeholders who worked in the health ministry. After hearing everyone's perspective, I was asked to share my observations during my visit and make suggestions to improve the observed gaps. I was able to advocate for pharmacists and share how they can have a seat at the table and make a big difference. My voice was heard, and they asked for a detailed report with all my suggestions to act on those points. This was again, one of those days where I felt like, through hard work, I earned the privilege of being an oncology pharmacist and I hope that I made pharmacy practice a little better for my international colleagues and hopefully helped cancer patients' outcomes overseas.

To future oncology pharmacists, I hope this gives you a small snapshot into what an amazing career you have chosen, an idea of how much difference you can make, and that oncology pharmacists know no border and can impact patients globally, with their training and expertise.

FEATURE

The Science and Art of Mobilization: Aphexda® and Mozobil®

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Background

Multiple myeloma (MM), a malignant neoplasm of plasma cells that accumulate in the bone marrow leading to bone destruction and marrow failure, is the second most common hematologic malignancy in the United States (US). In 2021, there were an estimated 179,063 people living with multiple myeloma in the US and in 2024, there are an estimated 35,000 new cases, with an increasing number of new cases every year.[1] High-dose chemotherapy followed by autologous hematopoietic stem cell transplant (ASCT) results in high response rates and is the standard of care after primary induction therapy for transplant-eligible patients.[2] Hematopoietic stem cell (HSC) mobilization is utilized to mobilize HSC to the peripheral blood for collection and subsequent autologous stem cell transplant. The American Society of Transplantation and Cellular Therapy (ASTCT) consensus guidelines recommend a minimum collection of 2 x 10^6 CD34+ cells/kg with a target for a single ASCT of 3-5 x 10^6 CD34+ cells/kg or 8-10 x 10^6 CD34+ cells/kg to store for a potential second transplant.[3] The number of ASCT for MM increases every year, increasing the burden on the healthcare system to mobilize patients for transplant.

"As there is no head-to-head trial comparing plerixafor and motixafortide it is difficult to comment on differences in their efficacy. Both agents are promising options to improve mobilization success rates, demonstrating success in achieving target collection in >70% of patients within two apheresis sessions and within one apheresis session in over 50% of patients."

Overview of Mobilization Strategies

Growth colony stimulating factor (GCSF) based HSC mobilization strategies have historically been the standard of care; however, mobilization failures with traditional strategies of GCSF monotherapy are common and result in delays in treatment as well as increased cost and resource utilization.[3] Therefore, GCSF is typically combined with other mobilizing agents such as chemotherapy and/or plerixafor (Mozobil®) or motixafortide (Aphexda®).[4] GCSF is administered daily for four days prior to initiation of plerixafor or motixafortide, as seen in Figure 1.[4] Plerixafor was US Food and Drug Administration (FDA) approved in 2008, and motixafortide was FDA approved in 2023 to be used in combination with GCSF for HSC mobilization.[5,6]

Plerixafor and motixafortide are inhibitors of C-X-C Motif chemokine receptor 4 (CXCR4) receptors and prevent the binding of stromal cell-derived factor-1α (SDF-1α). CXCR4 and SDF-1α play an important role in retaining HSCs in the bone marrow; preventing their interaction results in mobilization of HSC and progenitor cells from the bone marrow into peripheral blood to allow for collection via apheresis.[5,6]

Plerixafor is administered as a subcutaneous injection at a 24 mg fixed dose or 0.24 mg/kg approximately 11 hours prior to the initiation of each apheresis session for up to four consecutive days.[5] Motixafortide is dosed at 1.25 mg/kg and administered as a slow (~2 minutes) subcutaneous injection 10 to 14 hours prior to initiation of apheresis. A second dose can be administered prior to the third apheresis session, if needed.[6]

Overview of Clinical Trials

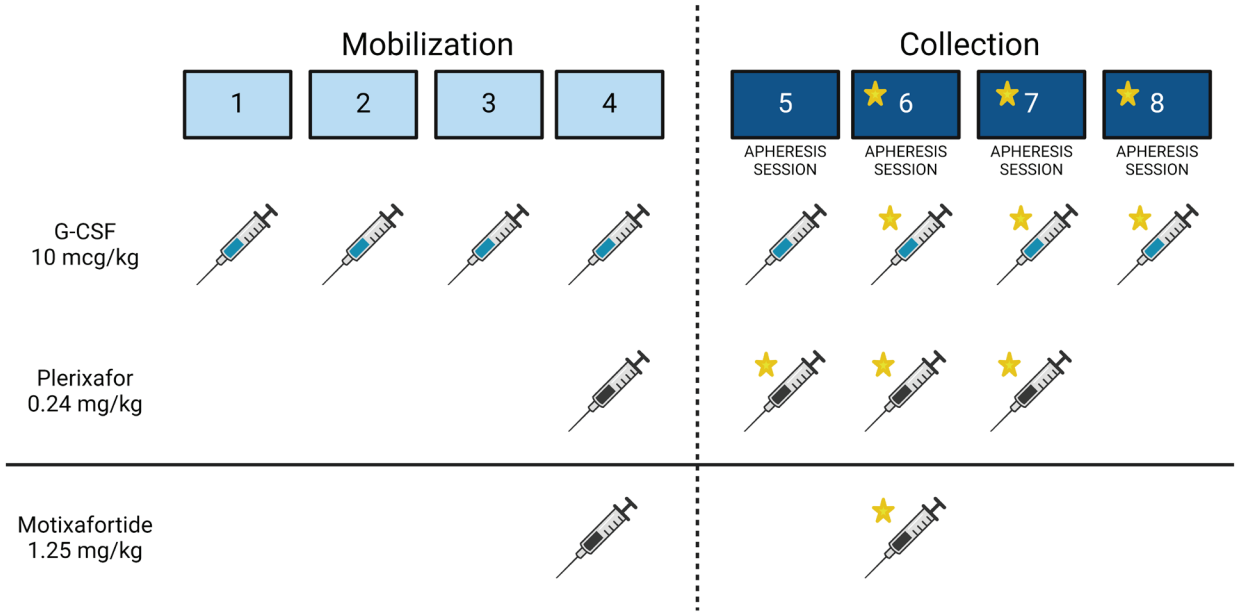
Plerixafor

Plerixafor is indicated in combination with filgrastim to mobilize HSCs to the peripheral blood for collection and subsequent autologous transplantation in patients with non-Hodgkin's lymphoma or multiple myeloma.[5] This was FDA approved in 2008 based on a phase III, multicenter, randomized, double-blind, placebo-controlled study. One hundred and forty-eight patients received GCSF and plerixafor for HSC mobilization compared with 154 patients who received GCSF and placebo. The primary endpoint of percentage of patients who collected ≥6 x 10^6 cells/kg in ≤2 apheresis sessions was achieved in 71.6% of patients who received plerixafor versus 34.4% who received placebo ($p < 0.001$). The majority (54%) of patients who received plerixafor reached the target after one apheresis session, while 56% of patients in the placebo group required four apheresis sessions. The most common adverse events were gastrointestinal (diarrhea 18%, nausea 25%, vomiting 5%) and injection site erythema (20%).[7]

Motixafortide

Motixafortide is indicated in combination with filgrastim to mobilize hematopoietic stem cells to peripheral blood for collection and

Figure 1: Mobilization and apheresis schedule [5,6]



subsequent autologous transplantation in patients with multiple myeloma. This was FDA approved in September 2023 based on the GENESIS trial.[6] Eighty-eight patients received GCSF and motixafortide for HSC mobilization compared with 42 patients who received GCSF and placebo. The primary endpoint of percentage of patients who collected ≥6 x 10^6 cells/kg in ≤2 apheresis sessions was seen in 67.5% of patients who received motixafortide versus 9.5% who received placebo (P < 0.0001) in the central laboratory assessments, which was a validated single platform method which provided standardization across countries and states. The central laboratory assessments were performed 24 hours to several days after collection and used for efficacy results. In the local laboratory assessment, which was readily available to guide clinical decision-making to determine further apheresis sessions, 92.5% of patients who received motixafortide versus 21.4% who received placebo collected ≥6 x 10^6 cells/kg in ≤2 apheresis sessions. The vast majority (88% in central laboratory assessments) of patients mobilized ≥2 x 10^6 cells/kg in one apheresis session compared with 38% of patients in the placebo group (p < 0.0001). The most common adverse events were injection site reactions (73% of patients total: pain 50%, erythema 28%, pruritis 21%) and systemic reactions (flushing 33%, pruritis 34%, urticaria 13%) with approximately one-third being grade 3.[8]

Clinical Implications

As a pharmacist, it is important to understand the similarities and differences between plerixafor and motixafortide including mechanism, administration, adverse events, cost, and efficacy, which are summarized in Table 1.

Administration

Plerixafor must be dosed before each apheresis session for up to four consecutive days while motixafortide is administered prior to the first apheresis session and then prior to the third apheresis session, if needed. While plerixafor and motixafortide have the same mechanism of action, motixafortide has a significantly higher binding affinity with receptor occupancy maintained for over 72 hours, allowing for less frequent dosing than plerixafor.[5,6]

As plerixafor has been on the market for over a decade, many centers have explored optimization of mobilization strategies utilizing plerixafor. Substituting daily filgrastim with a one-time dose of pegfilgrastim has been shown to be equally efficacious and, while not FDA-approved, is an NCCN category 2A recommendation.[4,9] Similarly, as the constraints of infusion center staffing and hours can be a limitation, plerixafor administration beyond 11 hours (up to ~17 hours) prior to an apheresis session and/or at-home are appealing options that have shown to be effective.[10,11] Similarly, in the GENESIS trial, motixafortide was intended to be administered 10 to 14 hours prior to apheresis, however in approximately half of the patients it was administered beyond 14 hours. There was no correlation between the timing of apheresis and cell yield in patients who collected 10 to 14 hours vs 14 to 16 hours following motixafortide injection.[12] At this time, motixafortide must be administered in a health care facility due to the risk of reactions described below.[6]

Adverse events

Plerixafor has an acceptable safety profile with the main adverse events of gastrointestinal distress and injection site erythema.[5] It has also demonstrated safety when administered at home by the patient or a caregiver.[11] As mentioned previously, motixafortide must be administered in a facility with adequate personnel and treatments immediately available for the treatment of a hypersensitivity reaction and monitored for one hour post injection.[6] The initial GENESIS trial protocol required premedication with a H1

		Plerixafor (Mozobil®)	Motixafortide (Aphexda®)
Cost Considerations	Generic Available?	Yes	No
	Insurance Coverage	Pharmacy[a]	Medical
	Cost per vial[b]	$600 per 24 mg vial	$7,080 per 62mg vial
	Dose	24 mg flat dose (if > 83 kg, then 0.24 mg/kg)	1.25 mg/kg
	Cost per dose[c]	$600	$11,419
	Max total doses	4	2
Administration Considerations	Site of injection	At home or infusion center	Infusion center
	Preparation	Vial to be drawn up	Vial requiring reconstitution
	Pre-medications	No	Yes[d]
	Concomitant GCSF[e]	Peg-filgrastim x 1[a] OR filgrastim daily	filgrastim daily
	Timing prior to apheresis	11-17 hours	10-16 hours
	Administration	Subcutaneous	Subcutaneous (over 2 min)
	Recommended Monitoring	30 minutes	1 hour

Table 1. Comparison of plerixafor and motixafortide[5,6]

a. Dependent on insurance and caregiver support
b. Average wholesale price. Auromedics generic plerixafor
c. Utilizing flat dose for plerixafor and assume 80-kilogram patient for motixafortide dose
d. H1 antagonist (diphenhydramine), H2 antagonist (famotidine), leukotriene-receptor antagonist (montelukast) and consideration for addition of analgesic (acetaminophen)
e. Concomitant GCSF use starts 4 days prior when used with either agent

antagonist, but was then amended to require additional premedications including an H2 antagonist, a leukotriene inhibitor, and acetaminophen which reduced the incidence and severity of reactions. Any grade injection site reactions and systemic reactions with single agent premedication were reduced from 95.5% and 90.9% respectively to 90% and 20% respectively with combination premedications. The package insert requires an H1 and H2 antagonist, a leukotriene inhibitor, and the consideration to add an analgesic such as acetaminophen.[13]

Cost

In July 2023, plerixafor became generic, significantly lowering the cost of this medication that previously cost ~$10,000 per vial.[5] The cost depends on the manufacturer but is now approximately $500 to $1,700 per 24 mg vial. Motixafortide is not available as a generic and costs $7,080 per 62 mg vial and with weight-based dosing, the majority of patients (patients >50 kg) would require more than one vial.[6] It is worth noting that the goal of plerixafor and motixafortide is to reduce the number of apheresis sessions needed and prevent failed mobilizations, which are significant costs to the healthcare system. Therefore, utilization of these agents, even with added medication costs, may be a cost-savings measure in the reduction of resource utilization.

Efficacy

As there is no head-to-head trial comparing plerixafor and motixafortide it is difficult to comment on differences in their efficacy. Both agents are promising options to improve mobilization success rates, demonstrating success in achieving target collection in >70% of patients within two apheresis sessions and within one apheresis session in over 50% of patients.[7,8] There is data demonstrating the efficacy of plerixafor after induction regimens that contain an anti-CD38 monoclonal antibody, which is a risk factor for mobilization failure.[14] However, the GENESIS trial with motixafortide only included one patient in the placebo arm who had received an anti-CD38 monoclonal antibody.[8] Also of note, while our focus is on HSC mobilization for autologous transplants for patients with multiple myeloma, it is worth noting that plerixafor is also approved for this indication in patients with non-Hodgkin's lymphoma.[5] Motixafortide is only approved for HSC mobilization in patients with multiple myeloma.[6]

Conclusion

HSC mobilization continues to be a challenge when planning for an autologous transplant in patients with multiple myeloma. It is exciting to now have two CXCR4 inhibitors, plerixafor and motixafortide, on the market to improve mobilization success rates. At this time, plerixafor has the benefit of being available as a generic, being studied with pegfilgrastim instead of daily filgrastim, and the ability to administer at home or in a short infusion slot due to the safety profile. In comparison, motixafortide has comparable success in improving stem cell collection yields and decreasing the number of apheresis sessions, however current challenges include price, adverse events, and additional constraints on the healthcare facility that requires premedication prior to administration and observation time to monitor for reactions. Overall, the decision to utilize plerixafor or motixafortide will be based on patient factors, institution capabilities, and provider discretion. ●●

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Health Literacy

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Background

Navigating cancer treatment and care is a complex process across many departments, and includes navigating multiple appointments from a variety of these health care departments. Patients are expected to understand complicated terminology about their diagnoses, make treatment decisions with their oncologists, schedule appointments, comprehend how to take pre-medications and other medications correctly, and learn how to contact their treatment teams when they are not feeling well. More than one-third of United States adults have limited health literacy, which can negatively affect their access to high-quality health care and may contribute to poorer health outcomes.[1] Health literacy is integral to ensuring a patient receives optimal care.

Health literacy is described as "the combination of personal competencies and situational resources needed for people to access, understand, appraise, and use information and services to make decisions about health. It includes the capacity to communicate, assert, and act upon these decisions."[2] Many factors affect health literacy, including gender, age, education, ethnicity, and income level.[2-4] Patients with lower education status and income are more likely to have lower health literacy.[3,4] A lack of understanding of health risks, the importance of routine cancer screening, and cultural beliefs regarding health and medicine may lead to delayed time to seek care and worse outcomes.[5-7]

Studies have demonstrated that low health literacy is associated with poor health status and outcomes, higher premature mortality rates, lack of adherence to medical recommendations, increased hospitalizations, greater utilization of emergency services, less shared decision-making, and more medication errors.[2,4-8] A study on health literacy in patients diagnosed with human papillomavirus (HPV)-related cancers at the University of South Florida found that patients who understood their HPV status were more likely to "initiate conversations with current sexual partners, use condoms during future sexual encounters, and/or encourage their loved ones to get the HPV vaccine."[9] Another study in patients with stage III/IV colorectal cancer concluded that adequate health literacy was associated with an increased likelihood of patients receiving chemotherapy as compared to patients with low health literacy.[10] While there is no conclusive evidence that links health literacy to improvement in cancer-related outcomes, the current sentiment is that adequate health literacy can increase a patient's capacity to take responsibility for their own health, which may in turn result in improved clinical outcomes.[2]

> **"Meet patients where they are and come to the encounter with an open perspective."**

Perspectives from Healthcare Team Members

Dr. Fátima Reyes (Gynecologic Oncology Fellow)

Dr. Reyes speaks about her experiences with health literacy: "My motivation to become a physician was rooted in seeing my mom interface with healthcare as a Mexican immigrant. Health literacy is important because it frames the way Spanish-speaking women interface with healthcare." She explains that it can be difficult for patients with low health literacy to ask for help due to education and cultural components, including not wanting to bother others, fear of being perceived as unintelligent, and distress about not having access to resources.

Dr. Reyes shares about her recent experience taking care of a patient with cervical cancer who had recently immigrated to the United States. The patient did not speak English, was unable to read or write, and had also broken her glasses. Not only did this patient endure a difficult immigration process in coming to the United States, but she also had to deal with the trauma of being diagnosed with cervical cancer in a foreign country and interacting with a healthcare team that does not speak her native language. For this patient, the disparities in healthcare were palpable and difficult to navigate. It was hard for her to make doctor's appointments, get directions to the oncology clinic, learn about the side effects of chemotherapy, and understand the pharmacy refill process, among many other aspects of healthcare. Dr. Reyes was able to begin bridging the gap for this patient by requesting an interpreter for her visits, translating medication instructions on her pill bottles,

coordinating medication delivery with the pharmacy, and spending extra time with the patient to understand the patient's full history and learn how to best help her. This patient continues under Dr. Reyes's care today with stable disease.

Dr. Reyes provides the following advice for taking care of patients with low health literacy:

- Meet patients where they are and come to the encounter with an open perspective. Some patients cannot read. Some patients feel that asking for help would be a burden. Some patients feel shame that they do not understand English and do not know they can ask for an interpreter.
- Be respectful in the way you ask questions. For example, instead of asking "how many years of school did you complete?" instead ask "how do you like to receive information?" or "how much reading and writing do you do?"
- Think outside of the box to help patients. Dr. Reyes writes notes for her non-English speaking patients to bring to their pharmacies. The notes let the pharmacy know which medications the patients need refilled if they cannot communicate this to the pharmacy. She also creates medication calendars for patients to help them remember which medications are to be taken at what times of day.

Patricia Tong (Chinese Patient Navigator)

Patricia helps Chinese-speaking patients navigate all aspects of their cancer care. She says, "every patient is different in their situation and condition" and so she helps them "with any little problem, which includes handling medication prescription refills, scheduling appointments, and even personal feelings about how things are going."

One of the tasks Patricia spends a significant amount of time on is teaching non-English speaking Chinese patients about the medication refill process. Due to many patients' monolingual Chinese statuses, they feel very anxious about how to obtain refills and fear running out of their medications. Some patients are even unaware that medications can be refilled. Many think that once they finish a one-month supply or three-month supply of their medication, they are done with treatment, and do not reach out to refill their medications. Patricia takes the time to call pharmacies with each patient and walk them through the refill process so that patients can initiate the refill process on their own in the future and stay adherent to their medications.

Patricia's biggest piece of advice to help patients with low health literacy is to take the extra time with patients to understand what they are going through. Once we understand where a patient is coming from and how much they know about the United States healthcare system, we can better understand their needs and help them obtain the best care.

Sam Schauer (PGY2 Oncology Pharmacy Resident)

Health literacy is such a complex issue that Sam thinks pharmacists are uniquely trained to handle. Pharmacists are often involved in many facets of patient care and with their training, can provide crucial education to patients on a variety of topics. Sam always strives to provide concise, accurate, and pertinent information, but what good is that information if the patient cannot fully understand or benefit from it?

This skill can certainly be a challenge to young practitioners as it is often difficult to conceptualize and relay information to patients when you are still learning that information yourself. Albert Einstein was quoted, "If you can't explain it simply, you don't understand it well enough." This quote serves as a constant reminder to continue the ever-ongoing pursuit of learning and striving to meet his patients where they are.

Sam's biggest piece of advice to new pharmacists is to talk to preceptors, mentors, and coworkers to see how they operate. "Shadow anyone that you can and see how they talk to patients and navigate tricky situations. I love getting input and advice from several sources so you can take all the good parts of each and make it your own. Don't be afraid to ask questions either! If you don't know a topic as well as you should, reach out to an expert and learn more. As pharmacists, we owe it to our patients to come prepared, knowledgeable, and ready to help wherever and whoever we can."

Patient Resources to Improve Cancer Health Literacy

National Comprehensive Cancer Network (NCCN) Guidelines for Patients[11]	Expert information presented in plain language with visuals, charts, and definitions to empower people with cancer and caregivers to talk with their clinicians about the best treatment options
American Cancer Society Patient Educational Materials[12]	Comprehensive information on common types of cancers, navigating cancer care, and coping with cancer to help patients and families make informed healthcare decisions
Hematology/Oncology Pharmacy Association (HOPA) Patient Education[13]	Resources on intravenous and oral medications to help patients better understand the various types of cancer treatments
OncoLink[14]	Tools and educational materials on cancers, treatment, psychosocial support, and survivorship care plans
Leukemia and Lymphoma Society Patient and Caregiver Resources[15]	Disease, treatment, and support resources to help patients make informed decisions
Triage Cancer[16]	Free education on the legal and practical issues that may impact individuals diagnosed with cancer and their caregivers
ChemoExperts[17]	Free education created by oncology pharmacists on treatment regimen, side effects, and oncology disease states

Conclusion

Health literacy plays an essential role in cancer care, with patients with lower health literacy facing greater difficulties in navigating the cancer care continuum, higher risks of poorer access to care, and worse clinical outcomes.[2] Striving to understand the patients' needs and meeting patients where they are in terms of their health literacy level is paramount to improving their health literacy by increasing the accessibility and usability of information and services available to them in an effort to decrease disparities in cancer-related health outcomes. ●●

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Real-World Data of Cardio-oncologic Interventions for Cardiovascular Adverse Events with Oral Oncolytics

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Background

The development of oral oncolytics continues to exponentially increase as research elucidates the cellular signaling pathways responsible for malignant cell transformation.[1] However, the widespread utilization of oral oncolytics has led to increased attention to survivorship care and management of potentially associated deleterious adverse effects.[2] Several oral oncolytics, such as tyrosine kinase inhibitors (TKIs), target cellular signaling pathways that are implicated in oncogenesis but are also essential for normal physiological function of some organs, including the cardiovascular (CV) system.[2] Cancer-therapy-related cardiac dysfunction (CTRCD) ranges from asymptomatic decrease in the left ventricular ejection fraction (LVEF) to overt heart failure (HF).[3] Other CV toxicities include acute coronary syndromes (ACS), arrhythmias, pericardial disease, and venous thromboembolism.[2,4]

Although a few consensus documents and position articles regarding monitoring and management of CV toxicity exist, the lack of defined CV endpoints in clinical trials, low level of evidence, and heterogeneity in recommendations have complicated applying a practical approach in clinical practice, especially in relation to oral oncolytics.[3-6] It remains unclear whether the oral oncolytic dose should be temporarily withheld or reduced, treatment should be discontinued, or the oral agent should be continued with initiation of cardioprotective medications. The purpose of this study is to describe real-world cardio-oncologic interventions for patients who have experienced CV adverse events after initiating oral oncolytics.

"Unfortunately, no studies on preventive cardioprotective strategies have yet been performed for attenuation of CV toxicity with oral oncolytics."

Methods

This institutional review board-approved, retrospective study included patients in a multi-hospital system who had at least one electronic medical record (EMR) of oral oncolytics, excluding cytotoxic medications, considered to have cardiotoxic potential. The cohort included patients who had an ICD-10 code for arrythmias, HF or cardiomyopathy, myocardial infarction, pericardial disease, and venous/and or arterial thrombosis added to their EMR after the start of oral oncolytics between June 2016 and July 31, 2021. The primary endpoint was the characterization of cardio-oncologic and medication-related interventions such as dose reduction, treatment interruption, treatment discontinuation, and initiation of cardioprotective medications. In addition, the FDA Event Reporting System (FAERS) was queried on May 16, 2022 for terms related to heart failure or cardiomyopathy secondary to aromatase inhibitors (AIs) (given the frequency observed during chart review) and all other drugs. Adverse events were obtained from January 1, 1996 to March 31, 2022. All terms were grouped together for analysis, and a signal disproportionality analysis was calculated by using the reporting odds ratio (ROR). The precision of the ROR was determined by 95% confidence intervals (95% CI). P-values were calculated by using chi-squared or Fisher's exact test, and a p-value <0.05 was considered statistically significant.

Results

A total of 1146 patients were identified to have an ICD-10 code for a cardiotoxic event added to their EMR after initiating oral oncolytics. After accounting for exclusion criteria, 67 patients were included in the final analysis. Baseline characteristics are summarized in Table 1. The mean age was 69 ± 15 years. Preexisting CV risk factors were prevalent in the cohort as 97% had at least one CV risk factor or established CV disease (CVD). The most common baseline comorbidities were hypertension (n=48; 71.6%), hyperlipidemia (n=27; 40.3%), and obesity (n=26; 38.8%). Prior chest radiation, anthracyclines, or trastuzumab was documented in 25.4%, 22.4% and 4.5% of patients, respectively. AIs (n=25;46%), BCR-ABL inhibitors (n=11;16%), and vascular endothelial growth factor receptor (VEGFR) inhibitors (n=9;13%) were the three principal classes of oral oncolytics associated with CV adverse events.

The identified cardiotoxic manifestations were HF/cardiomyopathy (31 events), arrhythmias (30 events), acute coronary syndromes (ACS) (14 events), pericardial disease (5 events), and deep vein thrombosis (DVT) (5 events). The three most common classes of oncolytic agents associated with HF were AIs (10 events), VEGFR inhibitors (6 events), and BCR-ABL inhibitors (6 events). With comparison to all reported events in the FAERS database, a significant ROR for HF and cardiomyopathy was found with AIs (ROR 2.45 [95% CI 2.31, 2.61], $p<0.0001$) (Table 2). The median time to onset of CV adverse events ranged from 29 to 343 days and was shortest for pericardial disease and longest for deep vein thrombosis. At presentation, 31 patients (46.2%) had elevated troponins.

Table 1. Baseline Characteristics for Evaluable Patients (N=67)

Mean age, years (SD)	69 (ffl 15)
Mean body-mass index, kg/m² (SD)	28.34 (ffl 6.73)
Gender (%)	
Female	45 (67.2)
Male	22 (32.8)
Race (%)	
Caucasian	44 (65.7)
African American	18 (26.9)
Asian	3 (4.5)
Other	2 (3)
Smoking status (%)	
Never smoker	43 (64.2)
Former smoker	21 (31.3)
Current smoker	3 (4.5)
Alcohol use (%)	
No alcohol use	38 (56.7)
Infrequent to light use	21 (31.3)
Moderate use	7 (10.4)
Heavy use	1 (1.5)
Cancer Diagnosis (%)	
Breast cancer	26 (38.8)
Hematological malignancies	22 (32.8)
Other solid tumors	19 (28.4)
Past Medical History (%)	
Hypertension	48 (71.6)
Hyperlipidemia	27 (40.3)
Obesity	26 (38.8)
Diabetes	20 (29.9)
Arrhythmias	20 (29.9)
Heart failure	17 (25.3)
Coronary artery disease	14 (20.9)
Treatment History (%)	
History of chest radiation	17 (25.4)
History of anthracyclines	15 (22.4)
History of trastuzumab	3 (4.5)
Baseline Cardiovascular Disease (CVD) or CVD Risk Factor (%)	
At least one risk factor	65 (97)
None	2 (3)
Classification of Oral Oncolytics (%)	
Aromatase inhibitors	25 (36)
BCR-ABL inhibitors	11 (16)
VEGFR inhibitors	9 (13)
Immuno-modulators	7 (10)
Antiandrogens	5 (7)
EGFR inhibitors	4 (6)
mTOR inhibitors	4 (6)
BTK inhibitors	3 (4)
FLT3 inhibitors	1 (2)

SD: standard deviation; VEGFR: vascular endothelial growth factor receptor; EGFR: epidermal growth factor receptor; mTOR: mammalian target of rapamycin; BTK: Bruton tyrosine kinase; FLT3: fms like tyrosine kinase 3

Table 2. HF and cardiomyopathy events reported with AI and associated ROR

	HF Reactions	Other ADRs	ROR (95% CI) for AIs vs. full database, p value
AIs	1,084	49,229	2.45 (2.31-2.61), p<0.0001
Other drugs	215,754	24,036,165	

HF: Heart failure; ROR: Reporting odds ratio; AI: Aromatase inhibitor; ADR: Adverse drug reaction; CI: Confidence interval

CV adverse events were managed by initiation of cardioprotective medications (n=44), treatment interruption (n=18), treatment discontinuation (n=14), and/or dose reductions (n=7). In 15 (22.4%) patients, no particular intervention was identified. Among the 19 (61.3%) heart failure with reduced ejection fraction (HFrEF) or heart failure with mid-range ejection fraction (HFmrEF) cases, angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs)/angiontensin receptor neprilysin inhibitors (ARNI), beta blockers, and mineralocorticoid receptor antagonists (MRAs), were initiated in 15 (78.9%), 13 (68.4%), and 4 (21%) patients, respectively. Among 12 (38.7%) heart failure with preserved ejection fraction (HFpEF) cases, ACEIs/ARBs/ARNI, beta blockers, and MRAs, were initiated in 6 (50%), 7 (58.3%), and 1 (8.3%) patients, respectively. Sodium-glucose transport protein 2 inhibitors were not initiated in any HF patients.

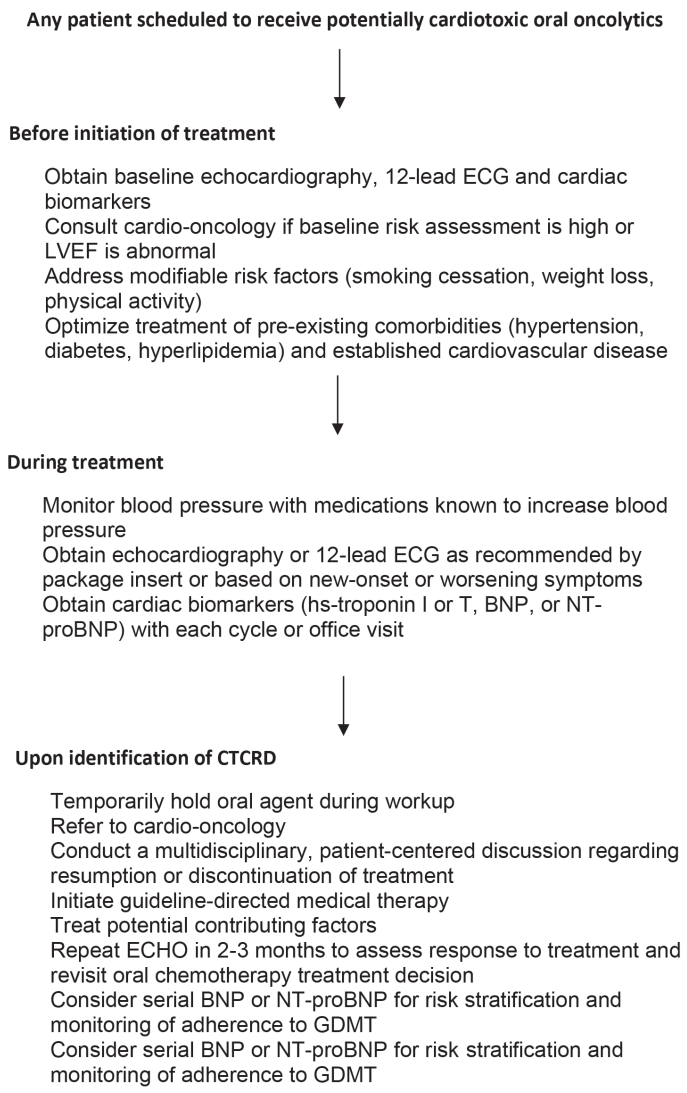
Discussion

In this cohort of 67 patients, HF was the most common CV adverse event with 31 events occurring at a median of 148 days (IQR 43-476). Roughly a third (32.2%) of the HF/cardiomyopathy events occurred in patients taking AIs. Of note, three prior meta-analyses of randomized controlled trials have shown an increased risk of CVD, mainly ischemic events, with AIs compared with tamoxifen, especially upon longer exposure.[7-10] AIs have also been associated with an increased risk of HF, CV mortality, and hypercholesterolemia.[10-12] The antioxidant and cardioprotective effects of tamoxifen may justify its relatively lower risk of association with CV adverse events.[9,10,13] In a recent matched-control study, breast cancer survivors treated with endocrine therapy appeared to have a higher risk of hypertension and diabetes.[14] The aforementioned association with ischemic heart disease and cardiometabolic risk factors could explain the indirect mechanism through which AIs may lead to HF. A signal disproportionality analysis was conducted based on a query of the FAERS pharmacovigilance database and revealed a significant association of AIs with HF (ROR 2.45 [95% CI 2.31, 2.61], p<0.0001). This perceived association of AIs with HF and/or cardiomyopathy bolsters prior findings and warrants further investigation in prospective studies for AIs' association with both symptomatic and asymptomatic CTRCD.

In this cohort, 97% of the patients had pre-existing CVD or at least one risk factor for CVD.[15,16] The results of this study highlight the fact that such patients are at an elevated risk for CV adverse events and emphasize the need for close monitoring and proactive management of any pre-identified CV risk factors. Pre-treatment

risk assessment using recognized risk assessment tools such as Heart Failure Association–International Cardio-Oncology Society (HFA-ICOS) baseline CV toxicity risk assessment tool is recommended. Patients deemed to be at moderate-to-high risk would benefit from close surveillance, strict management of traditional CV risk factors, and a cardio-oncology referral. Unfortunately, no studies on preventive cardioprotective strategies have yet been performed for attenuation of CV toxicity with oral oncolytics. In our study, the development of CV adverse events in these patients despite early cardioprotective strategies underscores the high-risk nature of the cohort and reinforces the need for more effective preventive strategies that are validated with oral oncolytics.

Figure 1. Algorithm for monitoring and treating patients for oral chemotherapy-induced cancer-therapy-related cardiac dysfunction (CTRCD)



The 2022 American Heart Association (AHA)/American College of Cardiology (ACC)/Heart Failure Society of America (HFSA) Guideline for the Management of Heart Failure recommends discontinuing cardiotoxic therapy in patients who develop overt HF while a diagnostic workup is undertaken to establish the etiology and initiate guideline-directed medical therapy (GDMT).[17] The guideline also promotes a collaborative, patient-centered approach, including a CV specialist in cardio-oncology and primary oncologist, when determining whether to resume, modify, or permanently discontinue therapy. The severity of HF, potential reversibility based on mechanism of toxicity, response to GDMT, and availability of alternative oncolytics can aid in decision-making. To date, there is no guidance for discontinuation or resumption of therapy with other types of cardiotoxicities. Based on the observed real-world cardio-oncologic interventions in this study, treatment was notably continued in 80% of the cases. Treatment was discontinued solely due to CV toxicity in only 3 cases. The most common causes for discontinuation included transition to hospice or death as well as progression shortly after development of the CV adverse events. In addition, pharmacological treatment of the CV adverse events was initiated in 65% of the cases in lieu of therapy discontinuation. Notably, interruption of anti-HER2 agents because of CV adverse events was found to be associated with worse outcomes in patients with breast cancer.[18,19] The aforementioned observation led to the emergence of the concept of permissive cardiotoxicity, which favors aggressive management of cardiotoxicity to enable continuation of life-prolonging oncolytic.[20] In the current study, adherence to GDMT was suboptimal; therefore, cardio-oncology referral may help optimize outcomes. A proposed algorithm for monitoring and management of patients who present with CTCRD associated with oral oncolytics is outlined in Figure 1.

Our study was limited by the small population size which did not allow description of medication class-specific cardiotoxicities and consequent interventions and prohibited regression analysis to investigate correlation of individual risk factors with incidence of CV adverse events. The observational and non-controlled nature of this study can only show association of oral oncolytics with CV adverse events and precludes ascertaining causality of agents in inducing CV toxicity.

Conclusion

A multidisciplinary approach to treatment that includes appropriate monitoring of imaging and cardiac biomarkers, temporary interruption of treatment for CV adverse events, and initiation of GDMT is recommended. ●●

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DPYD Testing: Is it finally time to implement?

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Fluorouracil and capecitabine (fluoropyrimidines) are often used in combination with other agents in curative-intent regimens for solid tumor malignancies. Common fluoropyrimidine adverse effects include mucositis, hand and foot syndrome, diarrhea, and neutropenia.[1-2] These usually manageable side effects can potentially be fatal if enzymatic allelic variants alter how fluoropyrimidines are metabolized and prevent clearance from the body.[3] Fluoropyrimidines are metabolized, in large part, by dihydropyrimidine dehydrogenase (DPD). Pathogenic allelic variants in the *DPYD* gene that encodes for DPD (which are associated with reduced enzymatic activity) occur in roughly 5% of the population and have been linked to a >25 times increased risk of fluoropyrimidine related mortality.[4]

The Clinical Pharmacogenomics Implementation Consortium (CPIC) and Dutch Pharmacogenetics Working Group (DPWG) have created testing and dosing recommendations due to *DPYD*-related pharmacokinetic differences.[5-6] The Institution for Safe Medication Practices (ISMP) supports *DPYD* testing, and United States (US) Food and Drug Administration (FDA) package insert updates included *DPYD* testing discussions for capecitabine in December 2022 and fluorouracil in March 2024.[7-9] Fluoropyrimidine fatalities are rare and overdoses are preventable with proper testing and monitoring of these patients. Given the significance and utility of these medications, preemptive *DPYD* testing and close monitoring is warranted due to the variability in metabolization and potentially fatal toxicities of these medications.[5] Ultimately, it is our responsibility as healthcare professionals to conduct *DPYD* testing prior to fluoropyrimidine utilization in order to do no harm to these patients.

Testing for *DPYD* and monitoring patients harboring pathogenic allelic variants has become an increasing topic of conversation for pharmacists since the FDA approved fluoropyrimidine package inserts now state to "consider" *DPYD* testing.[8-9] Institutions face considerable challenges in *DPYD* testing implementation, including: lack of consensus amongst official guidelines, potential lack of financial reimbursement, lack of key stakeholder support, lack of provider/patient knowledge, limited access to testing, potential extensive turnaround times for results, and limited access to clinical decision support (CDS).[10] However, numerous institutions have proven that building a sustainable *DPYD* testing/monitoring system is possible despite these challenges, and the American Society of Health-System Pharmacists (ASHP) even offers a Pharmacogenomics Accelerator Program to help institutions address these barriers and initiate pharmacogenomics testing/adoption.[11-13]

Perhaps the largest barrier for *DPYD* testing adoption is lack of a consensus amongst guideline recommendations for *DPYD* testing. A 2021 survey showed that only 20% of providers had ordered preemptive *DPYD* testing and only 3% of providers tested ≥10% of their fluoropyrimidine patients largely due to lack of clinical practice guideline recommendations.[14] The National Comprehensive Cancer Network (NCCN) guidelines and FDA package inserts only state to "consider" testing.[1,2,15] The primary concern within the NCCN is the potential for underdosing with preemptive dose reductions. However, many argue that there is not evidence to support claims of decreased efficacy and that both the NCCN and FDA guidelines should recommend testing, require testing, and add a black box warning in fluoropyrimidine package inserts.[16-19] Any decreased efficacy concerns can be addressed by following updated CPIC recommendations to quickly escalate 5-FU with the second and third doses as long as the patient's toxicities are manageable (less than grade 3 leading to hospitalizations).[20] Numerous other organizations seem to agree as the British National Health Service, Cancer Care Ontario, European Medicines Agency, European Society of Medical Oncology, French National Agency for the Safety of Medicines and Health Products, and the Medicines and Healthcare products Regulatory Agency all support *DPYD* testing.[16,21-23]

> **"It is up to us as pharmacists to be proactive and assertive enough to have the hard conversations with the providers."**

Despite foreign organizational support for *DPYD* testing, US insurance companies may claim *DPYD* testing is elective and refuse coverage since the NCCN does not currently recommend preemptive *DPYD* testing at this time. The Centers for Medicare & Medicaid Services (CMS) uses Medicare Administrative Contractors (MACs), or private entities, to administer Medicare programs across geographical regions. These MACs may or may not cover pharmacogenomics testing based on Local Coverage Determinations. Therefore, Medicare may cover *DPYD* testing in one part of the country, but not another. Third party vendors may also not be covered. Some institutions will absorb the costs of testing as part of the specific regimens or use internal grant funding to cover *DPYD* testing expenses. Other institutions, like the Levine Cancer Institute, may use external grants to cover *DPYD* testing expenses.[11] Still others, like Wentworth-Douglas Hospital, have created a pharmacogenomics consult service and notify patients that *DPYD* testing is available within the third-party panel but may not be covered by their insurance.[24] Patients incurring out-of-pocket expenses by pursuing pharmacogenomics testing may find some financial

relief via vendor sponsored patient assistance programs.[25] However, until the NCCN and FDA mandate preemptive testing and insurance companies acknowledge testing as a necessity, institutions may have to use some creative financing to cover *DPYD* testing.

Key stakeholder support should be garnered using CPIC (and subsequently PharmGkB) evidence along with proposed financial coverage. Strong patient advocates, such as the Advocates for Universal DPD/*DPYD* Testing (AUDT), can also be the catalyst to initiate *DPYD* testing programs, as was the case at Dana-Farber Cancer Institute (DFCI). A member of AUDT inspired DFCI leadership to advocate for *DPYD* testing on behalf of her mother who tragically passed away after receiving a fluoropyrimidine without a *DPYD* test. Other institutions/stakeholders may be motivated by highly publicized legal actions. Oregon Health & Science University settled for $1 million after being sued for medical negligence and wrongful death when a patient passed away after receiving a fluoropyrimidine without being tested for *DPYD*.[26] Once executive stakeholder approval is attained, senior leadership should attend and/or appoint representatives to an advisory committee. The advisory committee should be composed of physicians, pharmacists, advanced practice providers, laboratory services personnel, informational technology services (ITS) for CDS, clinical operations, clinical education, and finance personnel when needed.

A clinical workgroup committee composed of or nominated by the advisory committee is vital for the success of the *DPYD* testing program. The clinical workgroup should first determine the appropriate variants to be assayed to ensure equitable coverage of all populations.[27] This should be done first as it may ultimately change which lab is utilized for *DPYD* testing. In-house laboratory testing may be ideal as it allows control of turnaround time as well as the selection of variants tested. Additional steps include assigning the creation of educational materials to appropriate provider and pharmacist "champions", delegating CDS tasks within the electronic healthcare record (EHR; including hard stops, best practice alerts (BPAs), and dosing guidelines/recommendations) creating/approving appropriate in-house guidelines and workflows, meeting regularly to update in-house guidelines and assess workflow issues, and being accessible for CDS/dosing recommendations.

Third party vendors will have to be utilized if institutions are unable to conduct in-house *DPYD* testing. Institution specific contracts will dictate costs and turnaround times. Additional consideration must be given as to what is to be done with incidental pharmacogenomic information with actionable medication management that does not pertain to the patient's oncology management if a full panel is used.

DFCI currently utilizes a third-party laboratory which guarantees *DPYD* results within 7 days. This allows DFCI providers to receive *DPYD* results prior to initiating therapy. Institutions with longer *DPYD* result turnaround time can potentially submit samples earlier with biopsies in order to receive results prior to treatment initiation.[28]

Active engagement with ITS is also crucial in the development of a successful *DPYD* testing/monitoring program. ITS will be heavily utilized for creating BPAs for suggesting *DPYD* testing, posting pharmacogenomic testing results as discrete data (preferably on a time-independent page within the EHR), alerting providers when *DPYD* activity scores are abnormal subsequently necessitating a fluoropyrimidine dose reduction, posting institutional guidelines and/or dosing/monitoring recommendations, and creating EHR reports to monitor and ensure providers/pharmacists are dose reducing/escalating according to guidelines.

Lastly, consideration must be given as to who is responsible for the daily monitoring of these patients. Who is responsible for reminding providers to dose reduce the initial fluoropyrimidine dose, and equally as important, dose escalate these patients to maintain efficacy when they can tolerate it? The answer is clear. Pharmacists are now being educated in pharmacogenomics prior to licensing. Pharmacists are the dosing experts. Pharmacists are responsible for verifying the appropriate fluoropyrimidine dose according to a patient's related side effects. It is up to us as pharmacists to be proactive and assertive enough to have the hard conversations with the providers. Anyone can dose-reduce chemotherapy due to adverse effects, but how many pharmacists/providers are comfortable dose escalating when it goes against the grain?

There are legitimate concerns associated with *DPYD* testing, however, the preponderance of evidence and the duty to our patients can't be denied. *DPYD* testing can only benefit our patients and it is up to us as healthcare professionals to make it work appropriately. How can we promote "precision medicine" and the use of next generation sequencing without also including pharmacogenomic applications? Pharmacogenomics has been advertised and built up for decades, but providers are still unfamiliar with CPIC and DPWG, the pharmacogenomics experts.[29,30-32] We can't wait for the NCCN and FDA to recognize CPIC and the DPWG as the pharmacogenomics experts or for CMS to initiate a National Coverage Decision to financially cover *DPYD* testing. We need to implement *DPYD* testing immediately to protect our patients, validate that fluoropyrimidine patients require preemptive *DPYD* testing, and confirm that the existing evidence supporting *DPYD* testing is accurate as it stands. ●●

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Board Update

As Summer Turns to Fall, HOPA Continues to Thrive

Jolynn Sessions, PharmD, BCOP, FHOPA
HOPA President (2024-2025)
Oncology Pharmacy Manager, Charles George VA Medical Center
Oncology Clinical Pharmacist Practitioner, Charles George VA Medical Center
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Late-summer greetings from North Carolina! Whether vacationing or simply enjoying longer sunlit days, I hope you all had a chance to rejuvenate.

Here at HOPA fall is always a busy time: HOPA Hill Day will take place around the same time this publication arrives in your mailboxes. The new Virtual Practice Management webinar series starts with "Operationalizing Bispecific T-Cell Engagers" on November 12 – please watch for registration announcements. And October is American Pharmacists Month and a time for us to celebrate you and your commitment to oncology pharmacy.

It is Board Election season and our annual call for nominations for Member Awards and HOPA Fellows closes soon! Also going on now is The Big Idea, featuring innovations submitted – and being advanced – solely by our members. More updates on that to come.

Annual Strategic Snapshot from HOPA Councils

The HOPA Board of Directors recently invited council chairs to provide a synopsis of committee work to help bridge one year of service to the next. I am thrilled to provide a few highlights from 2023-2024 below.

Education Council

HOPA's Education committees again rose to the challenge of providing all levels of oncology pharmacy professionals with the knowledge needed for care optimization and career advancement.

As Core Competency continues to serve as an introduction to oncology pharmacy across healthcare professions, the task force responsible for its most recent update was sunset in early 2024. BCOP programming also had a good year as we exceeded our goal of a 3% increase in revenue in 2023 compared to 2022. In 2023, HOPA provided learners with the opportunity to earn 65 BCOP credit hours. New this committee year, the Oncology Case Series gives residents and clinicians an online space to discuss topics that may not extensively be covered at every institution. The first installment was in August with more being planned throughout the residency year.

Professional Practice Council

There are many examples of how our Professional Practice committees drove momentum in 2023-2024. Emeritus Member has emerged as a new membership designation, and we are always on the lookout for like-minded oncology pharmacy organizations to explore partnerships or dual memberships.

Our well-attended Leadership Roundtable at Annual Conference now serves as a blueprint for leadership learning and networking at each future conference.

The HOPA Mentorship Program continues to grow with a current cohort of seven mentor/mentee pairs, up from five pairs in past years. Expansion of our mentorship program is afoot, so stay tuned. Our Special Interest Groups also continue to expand and conduct much of their knowledge-sharing on the recently updated HOPA Central.

Research & Quality Council

Our Research & Quality committees wrapped up, reported on, and initiated a variety of new projects in 2023-2024. The Oral Chemotherapy Collaborative is writing up the results of the Oral Oncolytic Landscape Survey and updating the 2018 Oral Oncolytic Practice Standards. Practice Outcomes and Professional Benchmarking Committee (POP-BC) completed a manuscript for the Workload Unit Project, in collaboration with Practice and Research Networks (PRNs) from American College of Clinical Pharmacy (ACCP).

Our Quality Oversight Committee trained residents and practitioners in quality improvement and created online resources, including Introduction to Quality, FAQs about Quality Metrics, and Quality Improvement Modules – with more material available at hoparx.org.

Two of our members from the 6-Month HOPA-ASCO QTP program have been invited to train as future coaches for that program. A recent Research Needs Assessment will help us assist members in applying for the HOPA Research Fund Grant.

Advocacy & Awareness Council

While it is difficult to summarize all the accomplishments of our Advocacy & Awareness committees, one theme did emerge this past year: amplifying patient voices.

Many who attended the Advocacy Update at Annual Conference commented on the value of patient perspectives. And, during last committee year, the Patient Outreach and Education Committee developed a plan for our first-ever HOPA Patient Advocacy Summit. At the time of this writing, that event is set to take place in about one month from now in Washington DC.

On the policy side, HOPA's Statement of Support for the National Cancer Plan was approved and submitted to the National Cancer Institute, who included it in a recent newsletter to their email subscribers. This additional reach goes a long way toward moving our strategic pillar of Advocacy & Awareness forward. Congratulations to the statement authors and all those involved.

A big thank you to all HOPA members for your continued dedication to oncology pharmacy and the patients we serve. None of the above is possible without you! ●●

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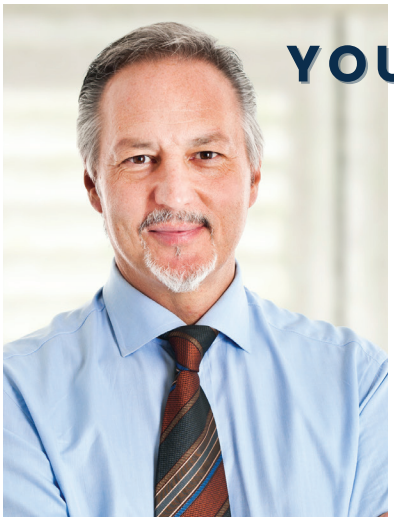

YOUR VOTE IS YOUR VOICE.

HOPA BOARD OF ELECTIONS OPEN SOON!

Your vote will directly impact the direction of HOPA as a leading voice for hematology/oncology pharmacy for years to come.

Cast your vote for these leadership positions:

- President-Elect
- Treasurer
- At-Large Director

Voting is Open November 2 - December 2, 2024.

Learn more at hoparx.org

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