HOPA NEWS

Pharmacists Optimizing Cancer Care

VOLUME 17 | ISSUE 3

Pharmacist-Led Oral Oncology Programs

page 3

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Pharmacists Optimizing Cancer Care®

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Correction

See page 19 for the correct version of a table that appeared in the article "Toxicity Management for Immune Checkpoint Inhibitors" in *HOPA News*, Volume 17, issue 2.

FEATURE

Pharmacist-Led Oral Oncology Programs

Oral anticancer agents have become a mainstay for the treatment of both solid tumors and hematologic malignancies. However, the benefit of patient convenience comes with the challenges of nonadherence, monitoring for adverse effects, and insurance restrictions. Establishing an institutional program for oral anticancer agents allows pharmacists the opportunity to provide patient education and support through a formal process. Three well-established pharmacist-led oral oncology programs are highlighted below. The authors provide insight on the formation and structure of the program, patient flow, and lessons learned.

Oral Oncology Medically Integrated Dispensing Program, St. Luke's Cancer Institute, Boise, ID

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The St. Luke's Cancer Institute Oral Oncology Medically Integrated Dispensing Program began as a pilot residency project in 2009. Through the program a small subset of oral oncology prescriptions were reviewed and processed. With improved patient access, the pilot project quickly expanded in the following year to include all providers at the five oncology clinics in the health system. The first full-time oral chemotherapy pharmacist and half-time technician were hired in 2010. Since then, the program has grown to include 4 pharmacist full-time equivalents (FTEs), 5 technician FTEs, and a 0.5 FTE nurse, who manages mail orders for patients at the largest site. Prescriptions are processed in a spoke-and-wheel distribution model.

After a treatment plan has been entered into the Epic electronic health record (EHR) software, new prescriptions are sent to the pharmacy using the software's "Send Plan" functionality. When the new prescription is received, an electronic chart is created for each patient, as well as a tracking sheet that is used for internal pharmacy processes only. The tracking sheet contains patient demographics, prescription details for each cycle of treatment, follow-up appointments, monitoring parameters, drug interactions, dispensing logistics, and other pertinent information that is sometimes not readily available in the EHR.

The pharmacist performs a clinical review of the new prescription, and initial contact is made with the patient to confirm the plan for starting treatment. The pharmacist reviews the details related to processing specialty prescriptions, such as prior authorization, referrals to financial advocates, and insurance contracts with out-of-state specialty pharmacies.

The new prescription is then sent to the pharmacy technician, who begins prior authorization and performs an insurance benefits investigation. The process for prior authorization is completed internally—in most cases, by a technician, a pharmacist, or both. After the prescription has been approved, the technician processes a test claim with the insurance to determine the patient's out-of-pocket cost. If the cost is unaffordable, a referral is sent to the financial advocate to review options for financial assistance or to seek a free supply of the drug directly from the manufacturer.

When the prescription is ready for processing, the pharmacist will again contact the patient to obtain consent to fill it, make arrangements to dispense the medication, and provide medication counseling. A technician will close the loop to confirm that the prescription was received. For patients whose insurance requires the use of a specific specialty pharmacy, the pharmacist will transfer the prescription to the specialty pharmacy and provide contact information to the patient. A referral is then sent to the provider's primary nurse for future refills.

"The pharmacist reviews the details related to processing specialty prescriptions, such as prior authorization, referrals to financial advocates, and insurance contracts with out-of-state specialty pharmacies."

Daily tasks are assigned using the "All Reminders" queue in Epic. Tasks are split between pharmacists and technicians, using standardized wording for a variety of functions that direct the staff member on what needs to be done (e.g., refill, follow up, dispense the prescription at an appointment, give assistance on pending drugs, mail the prescription, counsel the patient).

One of the biggest challenges was the rapid growth of the program. The program currently follows an average of 550 patients. Because the program expanded much more quickly than expected, balancing FTEs and workload has been a constant struggle. The workflow was greatly improved with the expansion of pharmacist services. This was done through another residency project in which a collaborative practice agreement (CPA) was developed for the reordering of oral oncology medications.

Pharmacists sign prescriptions on behalf of providers for specific adjustments outlined in the CPA. The CPA includes clinical activities such as dose rounding to the nearest tablet size; dose adjustments based on renal and hepatic function, toxicities, and specific indications; renewal of prescription refills; and ordering laboratory tests or exams recommended by guidelines. Results from the residency project showed a statistically significant improvement in the mean turnaround times for prescriptions completed per the CPA.[1] Following implementation of the CPA,

it was observed that each pharmacist saves significant time each day by signing prescriptions on behalf of providers per the CPA. Further expansion of pharmacist services is under consideration, given the success of the CPA in this program. Some of the barriers encountered include insurance contracting, with many insurers still requiring contracted specialty pharmacies, and obtaining access to dispense products from pharmaceutical manufacturers. Fortunately, the program does have access to dispense the Celgene Risk Evaluation and Mitigation Strategies program drugs, and each pharmacist is a certified counselor. Since the launch of the pilot project, the program has published more than a dozen peer-reviewed articles and has been referenced by the 2018 Hematology/Oncology Pharmacy Association's oral oncolytic therapy practice standard[2] and the Standards for Medically Integrated Dispensing produced jointly by the American Society of Clinical Oncology and the National Community Oncology Dispensing Association.[3] In addition, the program has won a medication safety award from the American Society of Health-System Pharmacists (2012) and two innovator awards from the Association of Community Cancer Centers (2011 and 2020). The pharmacy department continues to expand and refine the delivery of patient services in its Oral Oncology Medically Integrated Dispensing Program. ●●

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Oral Anti-Cancer Agent Management Clinic, Malcom Randall VA Medical Center, Gainesville, FL

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When the shift from intravenous (IV) to oral anticancer agents began around 2008, concerns about proper utilization and toxicity management surfaced. It was recognized that these patients needed to be properly taught how to take the medications, what the common toxicities were and how to manage them, and when to call for help. The oncology pharmacy staff (three full-time oncology pharmacy specialists) at the Malcom Randall VA Medical Center in Gainesville, FL, approached the oncology physician leadership for a discussion of how the pharmacy staff could assist in managing this patient population.

Leadership buy-in from both the medical oncology and the pharmacy administration is likely the first hurdle of any proposed new clinic. Our oncology leaders were enthusiastic about a pharmacy-led initiative to support patient care. From a pharmacy standpoint, concerns are usually related to staffing. Are there enough hours to devote to clinical activities and still support oncology operations? In an examination of support staffing, we identified the availability of two advanced-practice pharmacy interns per month and several pharmacy residents who were doing oncology rotations and saw a learning opportunity. The idea of using trainees helped us obtain support from the pharmacy leadership, and our plan was bolstered by published research on the potential cost benefits of ensuring appropriate use of these high-cost drugs.[1,2]

Referral to the clinic begins when pharmacy staff are notified through a consultation with oncology providers of the desire to start a patient on oral anticancer agents. The pharmacist reviews the patient's record to ensure that the patient meets the criteria for the use of a given drug. If therapy is determined to be appropriate, a member of the pharmacy team will counsel the patient. In-person counseling is preferable, but video visits or phone calls are acceptable. Pharmacy trainees are educated by oncology pharmacists before they conduct patient education, to ensure their competency. After a patient has been counseled, a weekly follow-up phone or video call is scheduled with pharmacy for the first 3 weeks until the patient returns to the clinic in the fourth week (for monthly regimens). The oncologist orders the anticancer therapy, but the pharmacy staff's scope of practice within federal law and institutional credentialing procedures allows them to order supportive care medications, depending on the medication's toxicity profile.

Pharmacy trainees, when available, conduct most of the follow-up visits, using a templated toxicity assessment form (the form has been previously published in a more comprehensive review of our clinic[3]). The pharmacist then develops a plan for any needed toxicity management and implements any changes to the drug therapy. Additional supportive care medications, monitoring devices such as blood pressure monitors, and lab tests can be ordered by the pharmacist if necessary. If changes to the anticancer therapy regimen are needed, pharmacy staff will instruct patients to withhold their medication and will contact the provider to discuss the plan, making changes as needed.

Following the initial month (which we felt to be the most crucial period for ensuring compliance), the responsibility for follow-up is returned to the oncology provider. Pharmacy may be asked to conduct additional interim follow-up on certain issues. Institutional policy calls for monthly visits and labs for the first 6 months when a patient is taking a new medication. An oncology pharmacy staff member reviews the patient's labs before processing each refill. We are also field testing a population management tool to help track patients on oral chemotherapy agents and identify patients who are overdue for refills, may have abnormal labs, or may have been lost to follow-up. After a patient has been stable on one dose for

6 months, up to two refills are allowed. If a patient is stable on a dose for a year or more, 6-month follow-up may be considered on a case-by-case basis.

The pharmacy-led oral chemotherapy management clinic has been operating since 2009. One lesson learned in the beginning was the importance of formally establishing proper follow-up to help ensure accountability. Adaptations have included increasing the clinical time devoted to management of oral anticancer agents and incorporating video follow-ups to allow for visual assessment of skin toxicities and overall improvement of patient assessment capabilities. As the use of oral anticancer agents continues to expand and evolve, we see a continued future for the clinic. Future directions, if staffing allows, could include the use of oncology pharmacy specialists to conduct follow-up (in lieu of a physician visit) for stable patients receiving oral chemotherapy. ●●

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Comprehensive Oral Chemotherapy Management Program, University of North Carolina, Chapel Hill, NC

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Since the World Health Organization released its landmark analysis of medication adherence, "Evidence for Action," in 2003, the approval of oral chemotherapy drugs (OCs) has exploded.[1] In the wake of that explosion, patients' nonadherence to taking OCs has become a significant barrier to achieving clinical outcomes, creating an opportunity for clinical pharmacy services.[2] For that reason, we implemented our comprehensive OC management program at the University of North Carolina in 2014.

Our first step was to survey 95 patients to understand the patient-perceived barriers to adherence.[3] We found that 30% of respondents forget to take their OC as prescribed, and 21% of patients deliberately cut back on their OC primarily because of adverse effects or specialty pharmacy delays.[3] Subsequently, we established an OC management program with an embedded clinical pharmacist and our own specialty pharmacy. We hypothesized that a closed-loop system where patients received their OCs from an institutional pharmacy would yield better adherence, provide better access, and be financially viable.

Our program is structured to ensure that our clinical pharmacists are involved throughout the continuum of the patients' care. Patients receive education on their OC from a pharmacist after a referral is made by the oncologist. Clinical pharmacists are stationed in the clinic, facilitating a seamless (often informal) referral process. The education encounter contains a comprehensive medication review, discussion of common and serious adverse effects and the importance of medication adherence, and an explanation of the drug access process. The majority of prescriptions are sent by physicians (MDs), nurse practitioners (NPs), and physician assistants (PAs), but clinical pharmacists also occasionally prescribe, as permitted through the Clinical Pharmacist Practitioner licensure by the North Carolina Medical Board. A limited number of refills are given, and patients are followed closely by both specialty and clinical pharmacists for adverse effects.

Initially, patients have frequent visits with the clinical pharmacist so that toxicities from the new OC and adherence can be assessed. Typically, a pharmacist encounter (telephone or in-person) occurs at 2 weeks and 4 weeks after the patient starts the OC. The patient is also often seen by the MD (or NP or PA) at the 4-week visit; the patient's time with the clinical pharmacist is scheduled first. This allows the pharmacist to address OC-related concerns so that the MD, NP, or PA can focus on follow-up of disease status. A satisfaction survey of our physicians showed that they appreciated the involvement of the pharmacist in this follow-up approach.[4]

Based on the first 3 months of treatment, patients are given a more intensive or a less intensive follow-up plan. Patients who have a medication possession ratio <80%–90%, who experience adverse drug reactions or have abnormal laboratory values, or who have an MD request for more frequent follow-up are followed closely with pharmacist visits every 1–2 weeks. Patients deemed to be at lower risk of nonadherence (not falling within any of the high-risk parameters) would have a visit with the pharmacist every 3–6 months while they were on therapy.

Our comprehensive OC management program improved patient outcomes. During the first 10 months, 107 patients were enrolled, for a total of 350 pharmacist encounters during which 318 adverse events were reported and 235 interventions were implemented. We observed increased rates of patient understanding of OCs, high rates of adherence, and high rates of patient and provider satisfaction. In addition, major molecular response rates increased in our chronic myeloid leukemia patients compared with those in our historical control (pre: 58% vs. post: 83%).[4]

After implementation, we faced notable challenges in ensuring the sustainability of the program. First, because pharmacists were embedded in the clinic, they became core members of the clinical team and were addressing not only concerns with OC, but also concerns about supportive care, anticoagulation, transitions of care, infectious complications, and more. This expanded field of responsibility may have contributed to less intensive follow-up of patients

on OC in some clinics. The continued increase in the approval of OCs also makes it challenging for the clinical pharmacy staff to own the entire drug-access program. Our institution has therefore embedded disease-specific medication access specialists who work alongside clinical pharmacists to expedite prior authorizations and applications for copay assistance. Significant challenges have also occurred with reimbursement and contracting. Unfortunately, limited distribution models sometimes prevent our pharmacy from serving our own patients.[5] To deal with this problem, staff members are currently developing a more comprehensive workflow addressing the needs of patients who have their drugs filled through external channels.

Overall, implementation of a structured OC management program has yielded positive clinical, humanistic, and financial outcomes for our patients. We continue to modify our internal processes in order to adapt to the increasing number of OC approvals and a challenging limited-distribution landscape. ●●

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Off the Beaten Path

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Growing up in the Pacific Northwest, I would sometimes hike the many trails in the area. I enjoyed the solitude and the time to reflect. That love for the outdoors continues today, and one of our family's favorite vacation activities is to go on a hike, particularly one that leads to a beautiful scenic spot. One of the most memorable (and difficult) hikes was Angel's Landing in Zion National Park in Utah. I didn't fully appreciate the beauty of the mountains and water until I moved away.

A long career is like a long hike. You never know exactly where the trail is going to take you. I enjoy reading the reflections of "young" practitioners in the Hematology/Oncology Pharmacy Association (HOPA) newsletter, and Susie Liewer, a former student who works at my institution, encouraged me to write one from the perspective of a "mature" practitioner. Next year, I will celebrate 40 years since the completion of my training. In this column I share a few of the lessons learned from my career. I won't repeat many of the usual lessons shared in these columns—work hard, have a plan, never stop learning, learn from your failures, etc. They are timeless, and I agree with them.

Know Yourself

I know you hear this repeatedly, but it is not emphasized enough. We are often told to never stop learning, but we sometimes forget to learn about ourselves. Why is this so important? In the book *On Becoming a Leader*, Warren Bennis tells us that our assumptions (values) cause us to select certain behaviors, and those behaviors have consequences.[1] Our values are determined in part by our childhood and culture. As a proud Asian American, I have grown to accept and embrace the values of my culture. That wasn't always the case. When I was growing up, I was embarrassed by my Chinese middle name, which according to tradition was given to me by my paternal grandfather. Then my parents told me that my name literally meant "above the crowd," that I would be outstanding among my peers. I didn't think too much about it at the time, but it now inspires me to strive for excellence in everything that I do. What do you care about? Take time to reflect, not just when you fail or face adversity. As a Christian, I developed a habit of regular reflection, usually during Bible study or prayer. That habit of regular reflection has helped me with every major decision.

What are your strengths? Take advantage of one of the many available tools to learn about your strengths. When I took StrengthsFinder (now called CliftonStrengths)[2] several years ago as part of a leadership development program at the university, I was surprised at how accurately it explained my strengths.

Expect the Unexpected

Trails can take unexpected turns. It's great to have a plan and goals. When I was an undergraduate pharmacy student, I worked in a cancer research laboratory and liked it. I later realized that I liked research because I was analytical and enjoyed solving problems (I played chess in high school and competed in state and national tournaments). When I completed my Doctor of Pharmacy degree, oncology pharmacy was an emerging specialty, and few role models existed. Even fewer specialty residencies (most were referred to as fellowships) were available. I was fortunate to have great mentors such as Bill Evans who inspired me to dream big. I wanted to have my own laboratory supported by research grants. I wanted to publish in the very best medical journals. Things started well, and I was on track to meet my goals. Then the unexpected happened—twice. In each case, key physician collaborators and mentors moved, and my research program was adversely affected. My plan and goals were shattered. Reflection is important during times of disappointment. I remember feeling like a failure and wondering what I was going to do. One of the important lessons learned during those times was that what I did (as an oncology pharmacist, a professor, a researcher)—my professional identity—did not define who I was (a person, a husband, a father, and now a grandfather).

During a long career, unexpected events will occur, and some will have a personal impact. It could be a change in leadership or your responsibilities. It could be a larger global event such as the COVID-19 pandemic. Many will be outside of your control, but some could also be the direct result of something you said or did. You will be disappointed and may feel like a failure. Adopt a growth mindset. Be thankful for those difficult times; learn from them, and don't let them define who you are.

Explore New Paths

Don't be afraid to explore a new path. Shortly after returning from a 1-year sabbatical, I decided to pursue a department chair position in a college of pharmacy. My decision surprised others because I had stated earlier that I had no desire to be an administrator. I wanted to make a difference by helping and mentoring others. After serving in that position for about 7 years, I decided to step down and return to the faculty. About 2 years later, I was asked by our new dean to become an associate dean. Between my

(continued on p. 14)

FIRST AND ONLY mUC TREATMENT FDA-APPROVED FOLLOWING BOTH A PD-1 OR PD-L1 INHIBITOR AND A PLATINUM-CONTAINING CHEMOTHERAPY[1-10]

SET A COURSE FOR RESPONSE

For adult patients with locally advanced or metastatic urothelial cancer who have previously received a PD-1 or PD-L1 inhibitor, and a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting[1]

INDICATION

PADCEV (enfortumab vedotin-ejfv) is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC) who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting.

This indication is approved under accelerated approval based on tumor response rate. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hyperglycemia occurred in patients treated with PADCEV, including death and diabetic ketoacidosis (DKA), in those with and without pre-existing diabetes mellitus. The incidence of Grade 3-4 hyperglycemia increased consistently in patients with higher body mass index and in patients with higher baseline A1C. In one clinical trial, 8% of patients developed Grade 3-4 hyperglycemia. Patients with baseline hemoglobin A1C ≥8% were excluded. Closely monitor blood glucose levels in patients with, or at risk for, diabetes mellitus or hyperglycemia. If blood glucose is elevated (>250 mg/dL), withhold PADCEV.

Peripheral neuropathy (PN), predominantly sensory, occurred in 49% of the 310 patients treated with PADCEV in clinical trials; 2% experienced Grade 3 reactions. In one clinical trial, peripheral neuropathy occurred in patients treated with PADCEV with or without preexisting peripheral neuropathy. The median time to onset of Grade ≥2 was 3.8 months (range: 0.6 to 9.2). Neuropathy led to treatment discontinuation in 6% of patients. At the time of their last evaluation, 19% had complete resolution, and 26% had partial improvement. Monitor patients for symptoms of new or worsening peripheral neuropathy and consider dose interruption or dose reduction of PADCEV when peripheral neuropathy occurs. Permanently discontinue PADCEV in patients that develop Grade ≥3 peripheral neuropathy.

Ocular disorders occurred in 46% of the 310 patients treated with PADCEV. The majority of these events involved the cornea and included keratitis, blurred vision, limbal stem cell deficiency and other events associated with dry eyes. Dry eye symptoms occurred in 36% of patients, and blurred vision occurred in 14% of patients, during treatment with PADCEV. The median time to onset to symptomatic ocular disorder was 1.9 months (range: 0.3 to 6.2). Monitor patients for ocular disorders. Consider artificial tears for prophylaxis of dry eyes and ophthalmologic evaluation if ocular symptoms occur or do not resolve. Consider treatment with ophthalmic topical steroids, if indicated after an ophthalmic exam. Consider dose interruption or dose reduction of PADCEV for symptomatic ocular disorders.

Skin reactions occurred in 54% of the 310 patients treated with PADCEV in clinical trials. Twenty-six percent (26%) of patients had maculopapular rash and 30% had pruritus. Grade 3-4 skin reactions occurred in 10% of patients and included symmetrical drug-related intertriginous and flexural exanthema (SDRIFE), bullous dermatitis, exfoliative dermatitis, and palmar-plantar erythrodysesthesia. In one clinical trial, the median time to onset of severe skin reactions was 0.8 months (range: 0.2 to 5.3). Of the patients who experienced rash, 65% had complete resolution and 22% had partial improvement. Monitor patients for skin reactions. Consider appropriate treatment, such as topical corticosteroids and antihistamines for skin reactions, as clinically indicated. For severe (Grade 3) skin reactions, withhold PADCEV until improvement or resolution and administer appropriate medical treatment. Permanently discontinue PADCEV in patients that develop Grade 4 or recurrent Grade 3 skin reactions.

Infusion site extravasation Skin and soft tissue reactions secondary to extravasation have been observed after administration of PADCEV. Of the 310 patients, 1.3% of patients experienced skin and soft tissue reactions. Reactions may be delayed. Erythema, swelling, increased temperature, and pain worsened until 2-7 days after extravasation and resolved within 1-4 weeks of peak. One percent (1%) of patients developed extravasation reactions with secondary cellulitis, bullae, or exfoliation. Ensure adequate venous access prior to starting PADCEV and monitor for possible extravasation during administration. If extravasation occurs, stop the infusion and monitor for adverse reactions.

Embryo-fetal toxicity PADCEV can cause fetal harm when administered to a pregnant woman. Advise patients of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during PADCEV treatment and for 2 months after the last dose. Advise male patients

EV-201 TRIAL: PRIMARY (ORR) AND SECONDARY (DOR) ENDPOINTS[1,11,12]*

- PADCEV™ is an **antibody-drug conjugate** that requires **no biomarker testing**[1,11,12]

*The EV-201 trial is a single-arm, multicenter trial of 125 patients with locally advanced or metastatic urothelial cancer who had previously received a PD-1 or PD-L1 inhibitor and a platinum-containing chemotherapy. Patients received 1.25 mg/kg of PADCEV via IV infusion over 30 minutes on days 1, 8, and 15 of every 28-day cycle and continued to receive treatment until disease progression or unacceptable toxicity. The major efficacy outcome measures, confirmed ORR and DOR, were assessed by BICR using RECIST v1.1. ORR consisted of confirmed CR and PR. CR was defined as the disappearance of all target lesions. PR was defined as a ≥30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Median duration of follow-up was 10.2 months.[1,11,12]

with female partners of reproductive potential to use effective contraception during treatment with PADCEV and for 4 months after the last dose.

ADVERSE REACTIONS

Serious adverse reactions occurred in 46% of patients treated with PADCEV. The most common serious adverse reactions (≥3%) were urinary tract infection (6%), cellulitis (5%), febrile neutropenia (4%), diarrhea (4%), sepsis (3%), acute kidney injury (3%), dyspnea (3%), and rash (3%). Fatal adverse reactions occurred in 3.2% of patients, including acute respiratory failure, aspiration pneumonia, cardiac disorder, and sepsis (each 0.8%).

Adverse reactions leading to discontinuation occurred in 16% of patients; the most common adverse reaction leading to discontinuation was peripheral neuropathy (6%). Adverse reactions leading to dose interruption occurred in 64% of patients; the most common adverse reactions leading to dose interruption were peripheral neuropathy (18%), rash (9%) and fatigue (6%). Adverse reactions leading to dose reduction occurred in 34% of patients; the most common adverse reactions leading to dose reduction were peripheral neuropathy (12%), rash (6%) and fatigue (4%).

The most common adverse reactions (≥20%) were fatigue (56%), peripheral neuropathy (56%), decreased appetite (52%), rash (52%), alopecia (50%), nausea (45%), dysgeusia (42%), diarrhea (42%), dry eye (40%), pruritus (26%) and dry skin (26%). The most common Grade ≥3 adverse reactions (≥5%) were rash (13%), diarrhea (6%) and fatigue (6%).

LAB ABNORMALITIES

In one clinical trial, Grade 3-4 laboratory abnormalities reported in ≥5% were: lymphocytes decreased (10%), hemoglobin decreased (10%), phosphate decreased (10%), lipase increased (9%), sodium decreased (8%), glucose increased (8%), urate increased (7%), neutrophils decreased (5%).

DRUG INTERACTIONS

Effects of other drugs on PADCEV Concomitant use with a strong CYP3A4 inhibitor may increase free MMAE exposure, which may increase the incidence or severity of PADCEV toxicities. Closely monitor patients for signs of toxicity when PADCEV is given concomitantly with strong CYP3A4 inhibitors.

SPECIFIC POPULATIONS

Lactation Advise lactating women not to breastfeed during treatment with PADCEV and for at least 3 weeks after the last dose.

Hepatic impairment Avoid the use of PADCEV in patients with moderate or severe hepatic impairment.

Please see Brief Summary of full Prescribing Information on adjacent page.

BICR=blinded independent central review; CI=confidence interval; CR=complete response; DOR=duration of response; FDA=US Food and Drug Administration; IV=intravenous; NE=not estimable; ORR=objective response rate; PD-1=programmed death receptor-1; PD-L1=programmed death-ligand 1; PR=partial response; RECIST=Response Evaluation Criteria in Solid Tumors.

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The following is a brief summary of full Prescribing Information. **Please see the package insert for full prescribing information.**

INDICATIONS AND USAGE

PADCEV is indicated for the treatment of adult patients with locally advanced or metastatic urothelial cancer (mUC) who have previously received a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, and a platinum-containing chemotherapy in the neoadjuvant/adjuvant, locally advanced or metastatic setting.

This indication is approved under accelerated approval based on tumor response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

DOSAGE AND ADMINISTRATION

Recommended Dosage

The recommended dose of PADCEV is 1.25 mg/kg (up to a maximum of 125 mg for patients ≥100 kg) administered as an intravenous infusion over 30 minutes on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxicity.

Dose Modifications

Adverse Reaction	Severity*	Dose Modification*
Hyperglycemia	Blood glucose >250 mg/dL	Withhold until elevated blood glucose has improved to ≤ 250 mg/dL, then resume treatment at the same dose level.
Peripheral Neuropathy	Grade 2	Withhold until Grade ≤1, then resume treatment at the same dose level (if first occurrence). For a recurrence, withhold until Grade ≤1 then, resume treatment reduced by one dose level.
	Grade ≥3	Permanently discontinue.
Skin Reactions	Grade 3 (severe)	Withhold until Grade ≤1, then resume treatment at the same dose level or consider dose reduction by one dose level.
	Grade 4 or recurrent Grade 3	Permanently discontinue.
Other nonhematologic toxicity	Grade 3	Withhold until Grade ≤1, then resume treatment at the same dose level or consider dose reduction by one dose level
	Grade 4	Permanently discontinue.
Hematologic toxicity	Grade 3, or Grade 2 thrombocytopenia	Withhold until Grade ≤1, then resume treatment at the same dose level or consider dose reduction by one dose level.
	Grade 4	Withhold until Grade ≤1, then reduce dose by one dose level or discontinue treatment.

*Grade 1 is mild, Grade 2 is moderate, Grade 3 is severe, Grade 4 is life-threatening.

WARNINGS AND PRECAUTIONS

Hyperglycemia

Hyperglycemia occurred in patients treated with PADCEV, including death, and diabetic ketoacidosis (DKA) in those with and without pre-existing diabetes mellitus. The incidence of Grade 3-4 hyperglycemia increased consistently in patients with higher body mass index and in patients with higher baseline A1C. In EV-201, 8% of patients developed Grade 3-4 hyperglycemia. In this trial, patients with baseline hemoglobin A1C ≥8% were excluded. Closely monitor blood glucose levels in patients with, or at risk for, diabetes mellitus or hyperglycemia. If blood glucose is elevated (>250 mg/dL), withhold PADCEV.

Peripheral neuropathy (PN)

Peripheral neuropathy, predominantly sensory, occurred in 49% of the 310 patients treated with PADCEV in clinical trials; 2% experienced Grade 3 reactions. In study EV-201, peripheral neuropathy occurred in patients treated with PADCEV with or without preexisting peripheral neuropathy. The median time to onset of Grade ≥2 was 3.8 months (range: 0.6 to 9.2). Neuropathy led to treatment discontinuation in 6% of patients. At the time of their last evaluation, 19% had complete resolution, and 26% had partial improvement. Monitor patients for symptoms of new or worsening peripheral neuropathy and consider dose interruption or dose reduction of PADCEV when peripheral neuropathy occurs. Permanently discontinue PADCEV in patients that develop Grade ≥3 peripheral neuropathy.

Ocular disorders

Ocular disorders occurred in 46% of the 310 patients treated with PADCEV. The majority of these events involved the cornea and included keratitis, blurred vision, limbal stem cell deficiency and other events associated with dry eyes. Dry eye symptoms occurred in 36% of patients, and blurred vision occurred in 14% of patients, during treatment with PADCEV. The median time to onset to symptomatic ocular disorder was 1.9 months (range: 0.3 to 6.2). Monitor patients for ocular disorders. Consider artificial tears for prophylaxis of dry eyes and ophthalmologic evaluation if ocular symptoms occur or do not resolve. Consider treatment with ophthalmic topical steroids, if indicated after an ophthalmic exam. Consider dose interruption or dose reduction of PADCEV for symptomatic ocular disorders.

Skin Reactions

Skin reactions occurred in 54% of the 310 patients treated with PADCEV in clinical trials. Twenty-six percent (26%) of patients had maculopapular rash and 30% had pruritus. Grade 3-4 skin reactions occurred in 10% of patients and included symmetrical drug-related intertriginous and flexural exanthema (SDRIFE), bullous dermatitis, exfoliative dermatitis, and palmar-plantar erythrodysesthesia. In study EV-201, the median time to onset of severe skin reactions was 0.8 months (range: 0.2 to 5.3). Of the patients who experienced rash, 65% had complete resolution and 22% had partial improvement.

Monitor patients for skin reactions. Consider appropriate treatment, such as topical corticosteroids and antihistamines for skin reactions, as clinically indicated. For severe (Grade 3) skin reactions, withhold PADCEV until improvement or resolution and administer appropriate medical treatment. Permanently discontinue PADCEV in patients that develop Grade 4 or recurrent Grade 3 skin reactions.

Infusion Site Extravasation

Skin and soft tissue reactions secondary to extravasation have been observed after administration of PADCEV. Of the 310 patients, 1.3% of patients experienced skin and soft tissue reactions. Reactions may be delayed. Erythema, swelling, increased temperature, and pain worsened until 2-7 days after extravasation and resolved within 1-4 weeks of peak. One percent of patients developed extravasation reactions with secondary cellulitis, bullae, or exfoliation. Ensure adequate venous access prior to starting PADCEV and monitor for possible extravasation during administration. If extravasation occurs, stop the infusion and monitor for adverse reactions.

Embryo-Fetal Toxicity

Based on the mechanism of action and findings in animals, PADCEV can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of enfortumab vedotin to pregnant rats during the period of organogenesis caused maternal toxicity, embryo-fetal lethality, structural malformations and skeletal anomalies at maternal exposures approximately similar to the clinical exposures at the recommended human dose of 1.25 mg/kg.

Advise patients of the potential risk to the fetus. Advise female patients of reproductive potential to use effective contraception during PADCEV treatment and for 2 months after the last dose of PADCEV. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with PADCEV and for 4 months after the last dose.

ADVERSE REACTIONS

Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The data in the **WARNINGS AND PRECAUTIONS** section reflect exposure to PADCEV as a single agent at 1.25 mg/kg in 310 patients in EV-201, EV-101 (NCT02091999), and EV-102 (NCT03219333). Among 310 patients receiving PADCEV, 30% were exposed for ≥ 6 months and 8% were exposed for ≥12 months.

The data described in this section reflect exposure to PADCEV from EV-201, a single arm study in patients (n=125) with locally advanced or metastatic urothelial cancer who had received prior treatment with a PD-1 or PD-L1 inhibitor and platinum-based chemotherapy. Patients received PADCEV 1.25 mg/kg on Days 1, 8 and 15 of a 28-day cycle until disease progression or unacceptable toxicity. The median duration of exposure to PADCEV was 4.6 months (range: 0.5-15.6).

Serious adverse reactions occurred in 46% of patients treated with PADCEV. The most common serious adverse reactions (≥3%) were urinary tract infection (6%), cellulitis (5%), febrile neutropenia (4%), diarrhea (4%), sepsis (3%), acute kidney injury (3%), dyspnea (3%), and rash (3%). Fatal adverse reactions occurred in 3.2% of patients, including acute respiratory failure, aspiration pneumonia, cardiac disorder, and sepsis (each 0.8%).

Adverse reactions leading to discontinuation occurred in 16% of patients; the most common adverse reaction leading to discontinuation was peripheral neuropathy (6%). Adverse reactions leading to dose interruption occurred

in 64% of patients; the most common adverse reactions leading to dose interruption were peripheral neuropathy (18%), rash (9%) and fatigue (6%). Adverse reactions leading to dose reduction occurred in 34% of patients; the most common adverse reactions leading to dose reduction were peripheral neuropathy (12%), rash (6%) and fatigue (4%).

The most common adverse reactions (≥20%) were fatigue, peripheral neuropathy, decreased appetite, rash, alopecia, nausea, dysgeusia, diarrhea, dry eye, pruritus and dry skin. The most common Grade ≥3 adverse reaction (≥5%) were rash, diarrhea, and fatigue.

Table 1 summarizes the all grade and Grade ≥3 adverse reactions reported in patients in EV-201.

Table 1. Adverse Reactions Reported in ≥15% (Any Grade) or ≥5% (Grade ≥3) of Patients Treated with PADCEV in EV-201

Adverse Reaction	PADCEV n=125	
	All Grades %	Grade ≥3 %
Any	**100**	**73**
General disorders and administration site conditions		
Fatigue*	56	6
Nervous system disorders		
Peripheral neuropathy†	56	4
Dysgeusia	42	0
Metabolism and nutrition disorders		
Decreased appetite	52	2
Skin and subcutaneous tissue disorders		
Rash‡	52	13
Alopecia	50	0
Dry skin	26	0
Pruritus§	26	2
Eye disorders		
Dry eye¶	40	0
Gastrointestinal disorders		
Nausea	45	3
Diarrhea#	42	6
Vomiting	18	2

*Includes: asthenia and fatigue

†Includes: hypoesthesia, gait disturbance, muscular weakness, neuralgia, paresthesia, peripheral motor neuropathy, peripheral sensory neuropathy and peripheral sensorimotor neuropathy.

‡Includes: dermatitis acneiform, dermatitis bullous, dermatitis contact, dermatitis exfoliative, drug eruption, erythema, erythema multiforme, exfoliative rash, palmar-plantar erythrodysesthesia syndrome, photosensitivity reaction, rash, rash erythematous, rash generalized, rash macular, rash maculo-papular, rash papular, rash pustular, rash pruritic, rash vesicular, skin exfoliation, stasis dermatitis, and symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) and urticaria.

§Includes: pruritus and pruritus generalized

¶Includes: blepharitis, conjunctivitis, dry eye, eye irritation, keratitis, keratopathy, lacrimation increased, limbal stem cell deficiency, Meibomian gland dysfunction, ocular discomfort, punctate keratitis, tear break up time decreased.

#Includes: colitis, diarrhea and enterocolitis

Other clinically significant adverse reactions (≤15%) include: herpes zoster (3%) and infusion site extravasation (2%).

Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or other enfortumab vedotin products may be misleading. A total of 365 patients were tested for immunogenicity to PADCEV; 4 patients (1%) were confirmed to be transiently positive for anti-therapeutic antibody (ATA), and 1 patient (0.3%) was confirmed to be persistently positive for ATA at any post-baseline time point. No impact of ATA on efficacy, safety and pharmacokinetics was observed.

DRUG INTERACTIONS

Effects of Other Drugs on PADCEV

Strong CYP3A4 Inhibitors

Concomitant use with a strong CYP3A4 inhibitor may increase free MMAE exposure, which may increase the incidence or severity of PADCEV toxicities. Closely monitor patients for signs of toxicity when PADCEV is given concomitantly with strong CYP3A4 inhibitors.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Based on the mechanism of action and findings in animals, PADCEV can cause fetal harm when administered to a pregnant woman. There are no available human data on PADCEV use in pregnant women to inform a drug-associated risk. In an animal reproduction study, administration of enfortumab vedotin-ejfv to pregnant rats during organogenesis caused maternal toxicity, embryo-fetal lethality, structural malformations and skeletal anomalies at maternal exposures approximately similar to the exposures at the recommended human dose of 1.25 mg/kg. Advise patients of the potential risk to the fetus.

Lactation

Risk Summary

There are no data on the presence of enfortumab vedotin-ejfv in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in a breastfed child, advise lactating women not to breastfeed during treatment with PADCEV and for at least 3 weeks after the last dose.

Females and Males of Reproductive Potential

Pregnancy testing

Verify pregnancy status in females of reproductive potential prior to initiating PADCEV treatment.

Contraception

Females

PADCEV can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during PADCEV treatment and for 2 months after the last dose.

Males

Advise male patients with female partners of reproductive potential to use effective contraception during treatment with PADCEV and for 4 months after the last dose.

Infertility

Males

Based on findings from animal studies, PADCEV may impair male fertility.

Pediatric Use

Safety and effectiveness of PADCEV in pediatric patients have not been established.

Geriatric Use

Of the 310 patients treated with PADCEV in clinical studies, 187 (60%) were 65 years or older and 80 (26%) were 75 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

Hepatic Impairment

Avoid the use of PADCEV in patients with moderate or severe hepatic impairment. PADCEV has not been studied in patients with moderate or severe hepatic impairment. In another ADC that contains MMAE, the frequency of ≥Grade 3 adverse reactions and deaths was greater in patients with moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment compared to patients with normal hepatic function. No adjustment in the starting dose is required when administering PADCEV to patients with mild hepatic impairment.

Renal Impairment

No dose adjustment is required in patients with mild (CrCL >60-90 mL/min), moderate (CrCL 30-60 mL/min) or severe (CrCL <30 mL/min) renal impairment.

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Leadership Strategy During Challenging Circumstances: Lessons from a Roman Emperor

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Leading a healthcare team is inherently challenging because of the many complex, high-risk tasks and competing priorities involved and the rapidly evolving changes to our landscape. Now imagine the stakes being amplified during times of adversity, when situational outcomes are dependent on the key tactics we employ in response to challenging circumstances. Some of the most successful strategies are encompassed in what is known as Stoic leadership.

Stoicism is an ancient Greco-Roman philosophy founded in the fourth century BC, and its principles can be applied to our personal and professional lives. Stoicism teaches us how to keep a calm and rational mind no matter the circumstances and to focus on what we can control, rather than letting events outside our control dominate our actions.

The Roman emperor Marcus Aurelius, the last of the five great emperors, ruled from 161 to 180 AD. The most powerful man in the world at the time, he was a stout proponent of Stoic philosophy and was renowned for his humanistic, level-headed leadership. He recorded his thoughts and observations in a journal, now known as *Meditations*.[1] These journal writings have inspired some of the greatest leaders in history. Stoicism gave Aurelius a guidebook for living a virtuous life, focusing on what mattered, and persevering despite setbacks—and he had quite a few during his reign. It was a time of impending wars; famine; threats to the throne; and, most relevant to us in this day, the Antonine Plague. This pandemic spanned the Roman Empire, persisted for 15 years, and claimed approximately 5 million lives in Europe. Yet this period was also a time of an expansion of power for the Roman Empire largely because of Aurelius's leadership during adversity. Marcus Aurelius faced unprecedented challenges head on, with total composure and endurance.

Recently, our healthcare community has experienced challenges strikingly similar to those faced by the Romans more than 2,000 years ago. The COVID-19 pandemic tests our resilience daily. With restricted resources, conflicted governmental leadership, and limited relevant experience, we have battled a virus with the potential to cause mass casualties. As leaders, we control our response and set the stage for how others respond to adversity. Similar to Aurelius, by using the tenets of Stoicism, such as setting priorities, taking decisive action, and adapting and planning for the future, we are able to persevere during challenging times.

Setting Priorities

"If you seek tranquility, do less. Or (more accurately) do what's essential. Do less, better. Because most of what we do or say is not essential."—Marcus Aurelius, *Meditations*[1]

Leaders face various sources of pressure that threaten to pull their attention in different directions. It takes skill to separate the distractors from the priorities. It is crucial to focus your energy on tasks that move your team forward, on what Aurelius called "the essential." When you begin doing that, you are much more likely to hit your goals.

In our health system, it was determined that these things would be our priorities during the COVID-19 pandemic:

- minimizing disease spread and transmission to patients, healthcare personnel, and the community
- maximizing efficient use of resources, including staff, personal protective equipment (PPE), and medications
- maintaining the highest level of care, quality, and service for our patients and families.

Our primary tactic to achieve these goals was to accelerate the transition of digitization and automation. Fortunately, we were able to leverage our previously implemented telehealth platform enabled by our electronic medical record (EMR) system in selected areas within our system. The rapid expansion of that platform to include all oncology providers required the building of new appointment types and clinic schedules in the EMR and a massive preparation of devices and the physical space where the visits would occur. Physicians and staff had to be trained, and new workflows were created and implemented in an extremely short timeframe.

Our hospital system implemented large-scale community drive-through testing in collaboration with the National Guard. Staff members were retrained to provide testing and support the community. As the need for flexible space escalated, we converted conference rooms and other spaces to allow for additional capacity.

With physical-distancing recommendations in full effect, we still needed to maintain accurate medication histories and reconciliation services. We implemented a medication reconciliation call center to limit face-to-face interactions. By using an open flow of communication and collaboration, this method allowed pharmacy technicians to assess patients in the emergency department and on COVID isolation units without additional exposure risk. The leadership, physicians, and information technology and care teams collaboratively tackled this challenge with expedience, knowing that they were helping us care for our patients while protecting our teams.

Taking Action

"You have power over your mind—not outside events. Realize this, and you will find strength."—Marcus Aurelius, *Meditations*[1]

This is the most prominent principle in Stoic leadership. There are things we control and things we don't. We should focus on the things we control, devoting our energy and actions to them. Identifying areas that we can control allows us to begin making plans, taking into account the multitude of possibilities justified by current evidence. Action requires courage, not brashness—creative application, not brute force. We need to act with deliberation, boldness, and persistence.

We researched our decisions meticulously, taking note of experiences in other parts of the world. We examined best practices as well as cautionary tales to devise the best approach. With flexibility, we relied less on traditional organizational structures and started locking in practices that sped up decision making and execution during the crisis.

We took action by forming systemwide collaborative groups, each with a specific purpose. A multidisciplinary infectious disease work group composed of physicians and pharmacists designed and continuously updated treatment algorithms. Criteria for the use of interleukin-6 inhibitors were developed in collaboration with cellular therapy teams, who were familiar with cytokine release syndrome. Another systemwide task force was initiated to maintain adequate inventory of PPE and critical drugs and help coordinate care between campuses, including patients' access to newly initiated clinical trials.

Oncology patients were stratified into three categories: those who had life-threatening conditions that required immediate treatment (e.g., newly diagnosed acute leukemia patients), patients with serious conditions for whom treatment was not urgent but could not be delayed until the end of the pandemic (e.g., breast cancer patients undergoing active treatment), and patients with a disease stage for which treatment could wait until the pandemic subsided without adversely affecting outcomes (e.g., those in long-term follow-up). Each group was assigned appropriate levels of care based on the risk category. Our stem cell transplant program conducted a similar assessment, deferring consolidative transplant for conditions such as multiple myeloma. By setting priorities in patient management and system strategies, we were able to limit interruptions in patient care while mitigating risks.

Communication

A low-key, practical, and democratic communication style is crucial in times of adversity. Throughout his *Meditations*, Aurelius promoted the belief that no matter what happens, individuals should maintain control of the mind at all times, giving thought to the consequences of their words instead of reacting to their impulsive natures.[1] Effective communication during times of crisis is powerful because it reduces emotional distress caused by the unknown, provides tactical guidance, and demonstrates to team members that their leaders are genuinely concerned and involved in the situation.

Our institution implemented team huddles regarding workflow changes, resources, inventory management, treatment guidelines, staffing, and daily assignments, using a variety of communication channels. The system's chief nursing officer sent out a daily Coronavirus Watch Board e-mail that included the current numbers of active cases, persons under investigation, mortalities, and discharges. The Watch Board communication also reported on the status of PPE supply, current guidelines regarding patient flow, masking protocols, etc. Communicating in a consistent, transparent manner was instrumental in maintaining the proper flow of information and getting necessary initiatives implemented.

A systemwide focus on communicating how we were keeping our team members safe was maintained. In several areas of the country, large numbers of front-line healthcare employees were infected. Reassuring our team, especially our front-line staff, that their safety was a top priority created a culture of camaraderie. Having this trust between leaders and team members is crucial during difficult times. Team members who feel that they are valued and appreciated will seek to provide high-quality work and find solutions to obstacles that may arise.

Turning Obstacles into Advantage

"The impediment to action advances action; what stands in the way becomes the way."—Marcus Aurelius, *Meditations* (Book 5.20)[1]

Massive changes such as those associated with the novel coronavirus could and should foster the strengthening of key values like collaboration, flexibility, inclusion, and accountability. We needed to continue to deliver service as usual, but in the most unusual of circumstances. We needed to be open to frequent and constant change in order to operationalize services as new information became available—thus forcing us to evolve our means as a consequence of rapidly morphing events. The need to operate differently gave our organization the opportunity to grasp new opportunities, embrace never-before-thought-of abilities, and expand our horizons and operations beyond previous limitations.

Newfound ideas that previously may not have been considered became a way of the future. Innovative ideas implemented in our system included new services, telephonic medication histories, patient counseling, and telepharmacy appointments and consultations. We also adjusted the operating hours of our dispensing pharmacy to be more convenient for patients. Our community pharmacy service line implemented home and mail delivery and developed a way to offer curbside pickup. This not only kept our volumes steady (we expanded ways to deliver our offerings for the meds-to-beds program) but also minimized potential COVID-19 exposure to discharged patients.

Planning for the Future

"Let no one rob me of a single day who is not going to make me an adequate return for such a loss."—Seneca (Roman Stoic philosopher), *On the Tranquility of the Mind*, 1.11b[2]

Health care may never be the same again. However, we cannot let our short-term focus distract us from our long-term vision and plans, and we can't dismiss the opportunity to capitalize on lessons learned.

One must plan and prepare for unexpected events. As we build new facilities, the experience of needing social distancing will enable us to think beyond what we know today and work on improving our emergency-preparedness through design, construction, and strategy development. Risk stratification, the development of new services, the removal of barriers, and shifts to telehealth will remain permanent tactics for facilitating access to care. The learnings regarding the importance of open communication and teamwork must pave the way for a higher-functioning system, making a better return on the time spent managing recent events.

Conclusion

Leadership during times of adversity can teach us about the types of leaders we want to be, no matter the circumstances. Leaders—with their own unwavering focus—must motivate others to see the tough times through, not just navigate through calm waters. As any crisis transitions from its urgent phase, the time pressure will ease, as will the need for split-second decisions. At that point, the plan must evolve into a more complex system that looks at recovery and getting things back to normal—whatever the new normal looks like.

An important tenet of Stoicism is that time must not be wasted and every day must be lived as though it is one's last. Each day is a new opportunity to make a lasting impact. Maintaining this mindset helps us guide others to accomplish a shared vision. By paying attention to our own emotions, needs, and behaviors, we will be better prepared to handle times of crisis. Consequently, we will be more capable of containing the impact of a crisis, regaining control, and effectively preventing, or reducing the duration of, an extremely difficult leadership situation. ●●

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Off the Beaten Path *(continued from p. 7)*

time as department chair and associate dean, I reflected on what I wanted to do in the last chapter of my career. I decided to improve the profession through service in professional organizations. Service has always been part of my DNA, but I was so focused early in my career that I didn't actively pursue service opportunities. Since that time, I have served on the HOPA Board of Directors, the American College of Clinical Pharmacy (ACCP) Board of Regents (as president), and the ACCP Research Institute Board of Trustees. I currently serve on the Board of Pharmacy Specialties Board of Directors.

After serving as associate dean for about 10 years, I decided to step down because I wanted to do something different. While the college recruited for my replacement, the position of associate vice chancellor for academic affairs became available at my institution. I wasn't ready to retire, so I reflected on whether to pursue this new opportunity. I enjoyed academic administration and saw this as an opportunity to get out of my comfort zone and learn new skills. I decided to apply and accepted the position in July 2019. After nearly 1 year into my new position, I can say that the change has been positive. It is always uncomfortable doing things for the first time, but I have learned so much from that experience. And I am able to continue to teach and interact with pharmacy students, residents, and faculty.

In contrast to our parents or grandparents, few of us will do the same thing in the same institution for several decades. I could have remained in my associate dean position until retirement. During your career, you will know when it is time for a change. It is different for every person, but for me, it was persistent feelings of restlessness and lack of peace. It usually occurred after about 7–10 years in my position. The timing reminds me of Simone's Maxims, based on a Grand Rounds presentation at MD Anderson Cancer Center.[3] Dr. Joe Simone was a pediatric oncologist and senior administrator at several major academic medical centers, including St. Jude Children's Research Hospital, Stanford University Medical Center, and Memorial Sloan Kettering Cancer Center, and most recently at Huntsman Cancer Center. Although he gave his presentation more than 20 years ago, his comments are just as relevant today. In his article, Dr. Simone states that "with rare exceptions, the appropriate maximum term for an academic leader/administrator is 10 years, plus or minus 3 years."[3]

Exploring new paths can be scary. When I decided to step down, I didn't have a backup plan, although I knew I still had a satisfying job (one of the advantages of being a tenured professor). Leslie Hendeles, a former colleague at the University of Florida, used to say that being a professor was the best job in the world. And I knew that I was the same person regardless of my position title.

Enjoy the journey. And don't forget to stop and smell the roses. ●●

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Making an Impact: Research Highlights from Recipients of the First Annual Certificate of Recognition for Exemplary Research on Quality of Care in Oncology

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The Quality Oversight Committee of the Hematology/Oncology Pharmacy Association (HOPA) would like to congratulate the recipients of the first annual Certificate of Recognition for Exemplary Research on Quality of Care in Oncology. A work group of the committee developed an evaluation process and reviewed each of the completed research and trainee research abstracts. Criteria for evaluating the submitted abstracts included the focus of the research on quality and value metrics in the care of patients with cancer using a nationally recognized oncology or pharmacy quality metric and the potential impact of the results on current practice.

Four certificates were awarded for abstracts presented at the HOPA Ahead 2020 conference in Tampa, FL: one was for completed research by Rachel McDevitt, PharmD BCOP (University of Michigan Rogel Cancer Center); and three were for trainee research by Jacqueline Majeski, PharmD (Maine Medical Center); Bianka Patel, PharmD (University of North Carolina Medical Center); and Michelle Azar, PharmD candidate (Michigan Oncology Quality Consortium and University of Michigan).

Evaluation of an Oncology Transitions of Care Pilot Program, presented by Rachel McDevitt, PharmD BCOP

Transition-of-care coordination led by pharmacists has been associated with a decrease in patient readmissions and an improvement in quality of care; however, implementation has been a nationwide challenge, and oncology patients are often excluded from these programs. To further study the feasibility of implementing such a program for patients with cancer, McDevitt and colleagues conducted a 3-month pilot program to investigate the effectiveness of an oncology pharmacist-led transition-of-care program on clinical outcomes at hospital transitions.[1] Of the 29 patients enrolled, 15 patients received outpatient pharmacist follow-up, and 14 patients did not. A total of 42 interventions were observed in a group of 15 patients with gastrointestinal cancers enrolled in the intervention cohort. The most common action items were related to symptom management, antibiotics, oncologic treatment, issues related to other comorbidities (e.g., diabetes), diet, anticoagulation, and medication reconciliation. In this prospective study, the 30-day readmission rate was reduced by 50% for patients who received outpatient pharmacist follow-up compared to patients who did not receive follow-up. Given the successful establishment of the program at the current institution, expansion to other oncology specialties is planned.

> **"In this prospective study, the 30-day readmission rate was reduced by 50% for patients who received outpatient pharmacist follow-up compared to patients who did not receive follow-up."**

Impact of a Pharmacist Managing Outpatient Oral Oncolytics, presented by Jacqueline Majeski, PharmD

Oncology pharmacists have been instrumental in providing high-quality care to patients with cancer. In multidisciplinary teams, their role has expanded from providing patient education to leading clinically meaningful interventions measured by various quality metrics including symptom improvement, clinical outcomes, and patient satisfaction.[2] Now greater opportunities exist for pharmacists to enhance care through interprofessional collaboration.

Majeski and colleagues evaluated the impact of having a pharmacist managing outpatient oral oncolytics. They reported that pharmacists' involvement in managing oral cancer therapy had a positive impact on the quality of patient care, as shown in a retrospective chart review.[3] Their primary objective was to assess adherence to the 2016 American Society of Clinical Oncology (ASCO)/Oncology Nursing Society Chemotherapy Administration Safety Standards for oral oncolytics in a pharmacist-led oral oncolytic management program. A total of 193 interventions were made on 96 oral prescriptions, of which 45% involved dosing recommendations. The most common interventions involved medication procurement assistance. The results showed greater opportunities related to preventing prescribing errors and promoting patient safety and further highlighted the impactful interventions of oncology pharmacists.

Characterization of Testing for Targeted Therapy in Advanced Non–Small Cell Lung Cancer (NSCLC), presented by Bianka Patel, PharmD

Oncology pharmacists are increasingly being integrated into precision medicine programs to identify actionable mutations and apply specific targeted therapies to treat cancer.[4] The service that they provide in this area demonstrates the important role of pharmacists in personalized medicine and opportunities for their integration.

The completion of molecular testing and testing turnaround time (TAT) for patients with stage IV NSCLC with adenocarcinoma histology are included as metrics in ASCO's Quality Oncology Practice Initiative (QOPI) recommendations.

To assess TAT for molecular testing, Patel retrospectively reviewed patients with stage 4 NSCLC with adenocarcinoma histology and identified 66 patients.[5] Testing was completed in most patients (89.4%). The median time from diagnosis to receipt of sample at the vendor was 13 days, and the median time from vendor's receipt of sample to testing results was 13 days, which exceeded ASCO QOPI recommendations that test results be available within 10 working days. The most common reasons for prolonged TAT were delays in samples being sent to the vendor and insufficient tissue samples. Results from this study identified specific opportunities for process improvement to be consistent with published guidelines. The authors made several recommendations for improvement of TAT, including the use of reflex molecular testing at the time of diagnosis and measures to ensure adequate sample quality.

Statewide Quality Improvement Addressing Overutilization of Neurokinin-1 (NK-1) Receptor Antagonists, presented by Michelle Azar, PharmD candidate

QOPI became available to ASCO members and their practices in 2006, with the goal to assess practice performance for a series of evidence- and consensus-based process measures.[6] Practices that participated in QOPI demonstrated improved performance in self-reported process measures, with the greatest improvement demonstrated in initially low-performing practices.[7] Symptom management, including the appropriate use of antiemetic therapy, is one of the medication-related QOPI measures. The use of NK-1 receptor antagonists or olanzapine administered for low or moderate emetic risk is classified as one of the top five test measures in QOPI. To evaluate this metric, Azar and colleagues conducted a statewide quality improvement evaluation addressing overutilization of NK-1 receptor antagonists.[8] Following development of a framework for assessing the lack of concordance with guidance recommendations, a survey was developed to gain an understanding of the patterns of usage. Education on chemotherapy-induced nausea and vomiting was provided to participating practices, with the goal of decreasing inappropriate NK-1 receptor antagonist usage to less than 30%. The state average in fall 2018 was 34% and decreased to 19% in spring 2019, compared to the national average of approximately 29%. Reassessment of practice performance is planned following program completion. This study further demonstrated an opportunity for improvement through the use of prepopulated antiemetic order sets and evidence-based education led by oncology pharmacists.

The four recipients of the inaugural certificate of recognition addressed quality in cancer care using validated quality metrics, and their research further supports the roles of oncology pharmacists.

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Pharmacists Bridging the Gap Between Oncology Care and Primary Care

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Over the past several years cancer treatments have changed from classic cytotoxic therapies to molecular targeted treatments. With this change in target, we've seen more oral anticancer agents (OAAs) approved and integrated into standard treatment protocols.[1] In addition to the type of systemic therapy changing, the duration of treatment has been extended. The average duration of cancer treatment in the late 1990s (1994–1999) was 4 months, with the median duration more than doubling to 9 months just a decade later (2010–2014).[1] Extending the median duration of cancer treatment, and moving to OAAs that are generally taken daily at home, increases the interaction of systemic cancer treatment and comorbid conditions caused by drug-drug interactions and potentially worsening side effects.[2]

Among Medicare beneficiaries age 65 years and older with cancer, 40% have at least one comorbid condition, and 15% have two or more. The most common of these comorbidities are cardiovascular disease, diabetes mellitus, and mental health disorders.[2] We know that cancer has effects on comorbidities—particularly related to the worsening of diabetes or cardiovascular disease seen with certain systemic therapies like tyrosine kinase inhibitors, endocrine therapy, and steroids. We also know that comorbidities can affect cancer outcomes, given their impact on treatment toxicities, treatment effectiveness, and overall survival. Given the significant proportion of patients who are managing a chronic condition in addition to their cancer diagnosis, a collaboration between oncologists and primary care providers is necessary to ensure the patient's overall health.[2-5] Unfortunately, the literature is replete with evidence of lapses in communication between oncology specialty providers and primary care providers. These lapses provide multiple opportunities for improvements in care and, ultimately, in patient outcomes.[3,6,7]

We believe that pharmacists are well suited to help bridge the gap between oncology care and primary care. Pharmacists are well versed in adverse-effect management and in identifying and resolving drug-drug interactions. Studies estimate that drug-drug interactions affect one-third of patients treated for cancer. Pharmacists can screen medication lists, assess clinical significance, and recommend alternatives. In addition, pharmacists can also recognize treatment-related adverse effects and arrange for proper management and follow-up.[8-10]

In an effort to enhance the collaboration between oncology and primary care, we developed the Primary Care Oncology Model (PCOM) pilot program in the Michigan Oncology Quality Consortium (MOQC).[11] The MOQC-PCOM pilot used a primary care pharmacist to conduct comprehensive medication reviews (CMRs) via phone visits for patients with cancer who were receiving active systemic cancer treatment and had at least one of the following pre-existing chronic conditions: diabetes, hypertension, heart failure, depression, and anxiety. Results of the CMR and management recommendations were communicated to the patient's primary care physician (PCP) and oncologist and/or oncology pharmacist. Although the CMR was the responsibility of the primary care pharmacist in this model, the oncology pharmacist was heavily involved when the primary care pharmacist identified any medication issues related to the patient's cancer care or when the primary care pharmacist had questions related to the plan for the patient's cancer treatment. The goals of MOQC-PCOM were to improve management of the chronic disease state, decrease unplanned healthcare utilization, decrease drug-drug interactions, and decrease cancer therapy toxicity.

A total of 96 patients met our inclusion criteria of having a PCP at one Michigan Medicine General Medicine clinic, having an oncologist at the Michigan Medicine Rogel Cancer Center, receiving active cancer treatment, and having at least one of the chronic conditions listed above. Of those 96, a total of 55 had completed CMRs conducted by the primary care pharmacist. The median age was 66 years (range 32–87), 59% were female, 27% were Black, and 67% were White. The median number of medications the patients took was 11 (range 2–23). The following were incidences of comorbid conditions: hypertension, 73%; diabetes, 26%; congestive heart failure, 13%; and psychiatric illness, 42%.

Results from the CMRs included the findings that 77% of patients had changes made to their medication list, 18% were referred to a primary care pharmacist for ongoing chronic disease state management, 22% were referred to a physician for needed follow-up, and 22 medication-related problems (MRPs) were identified.[12] In addition, there were 66 instances of patient education provided related to a medication, disease, or lifestyle. Of the MRPs identified, 32% were related to adherence, 23% to safety, 14% to an indication, and 9% to treatment effectiveness; the remaining 23% were in the "other" category.

The results of this pilot highlight the opportunity that pharmacists have to improve the coordination of care and enhance clinical outcomes for patients with cancer and comorbid conditions. Future work following this pilot will include expansion across the state of Michigan with involvement of other sites, modification to real-time (rather than retrospective) referral, and ultimately the development of a risk model to identify those patients most likely to benefit from the pharmacist's CMR. ●●

Acknowledgment

The authors wish to recognize and thank the following co-investigators for the MOQC-PCOM pilot: Michelle Azar, PharmD candidate; Karen Farris, PhD; and Emily Joehengen, PharmD.

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Correction to *HOPA News*, Volume 17, issue 2

In the printed edition of *HOPA News*, Volume 17, issue 2, an incorrect version of Table 1 appeared on page 15 of the Clinical Pearls article, "Toxicity Management for Immune Checkpoint Inhibitors." The information on pembrolizumab as a U.S. Food and Drug Administration–approved PD-1 inhibitor was inadvertently omitted. We regret the error.

The correct version of the table appears below and can be found in the electronic version of the article at hoparx.org/hopa-news/volume-17-issue-2-2020.

Table 1. FDA-Approved PD-1/PD-L1 Inhibitors[3-8]

Class	Medication Name (Generic, Brand)	FDA-Approved Indication(s)*
PD-1 Inhibitors	pembrolizumab (Keytruda)	• Cervical cancer (recurrent or metastatic) • Endometrial cancer (advanced) • Esophageal cancer (recurrent locally advanced or metastatic) • Gastric cancer (recurrent locally advanced or metastatic) • Head and neck, SC (unresectable/recurrent or metastatic) • HCC • HL, classical (relapsed or refractory) • Melanoma (adjuvant and unresectable or metastatic) • Merkel cell carcinoma (recurrent or metastatic) • MSI-high cancer (unresectable or metastatic) • NSCLC • Primary mediastinal large B-cell lymphoma (relapsed or refractory) • RCC (advanced) • SCLC (metastatic) • Urothelial carcinoma (locally advanced or metastatic)
	nivolumab (Opdivo)	• CRC, MSI-high, or mismatch repair deficient (metastatic) • Head and neck, SC (recurrent or metastatic) • HCC • HL, classic (relapsed or refractory) • Melanoma (adjuvant and unresectable or metastatic) • NSCLC • RCC (advanced) • SCLC (metastatic) • Urothelial carcinoma (locally advanced or metastatic)
	cemiplimab (Libtayo)	• Cutaneous squamous cell carcinoma (locally advanced or metastatic)
PD-L1 Inhibitors	atezolizumab (Tecentriq)	• Breast cancer, triple negative (locally advanced or metastatic) • NSCLC (metastatic) • SCLC, extensive stage • Urothelial carcinoma (locally advanced or metastatic)
	avelumab (Bavencio)	• Merkel cell carcinoma (metastatic) • RCC (advanced) • Urothelial carcinoma (locally advanced or metastatic)
	durvalumab (Imfinzi)	• NSCLC, stage III unresectable • Urothelial carcinoma (locally advanced or metastatic)

*As of February 17, 2020; detailed information on the specific place in therapy in these indications can be found in the drugs' prescribing information.
Note. CRC = colorectal cancer; FDA = Food and Drug Administration; HCC = hepatocellular carcinoma; HL = Hodgkin lymphoma; MSI-high = microsatellite instability-high cancer; NSCLC = non-small-cell lung cancer; PD-1 = programmed death 1; PD-L1 = programmed death-ligand 1; RCC = renal cell carcinoma; SC = squamous cell; SCLC = small-cell lung cancer.

DARZALEX *Faspro*™
(daratumumab and hyaluronidase-fihj)
Injection for subcutaneous use | 1,800mg/30,000units

Introducing DARZALEX *FASPRO*™ (daratumumab and hyaluronidase-fihj): subcutaneous administration in ~3 to 5 minutes[1]

SAME POWERFUL EFFICACY. *FASTER ADMINISTRATION.*[1,2*]

Approved across 5 indications spanning a wide range of multiple myeloma patients[1]

INDICATIONS

DARZALEX *FASPRO*™ is indicated for the treatment of adult patients with multiple myeloma:

- in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant
- in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy
- in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy
- as monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DARZALEX *FASPRO*™ (daratumumab and hyaluronidase-fihj) is contraindicated in patients with a history of severe hypersensitivity to daratumumab, hyaluronidase or any of the components of the formulation.

WARNINGS AND PRECAUTIONS

Hypersensitivity and Other Administration Reactions

Both systemic administration-related reactions, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX *FASPRO*™.

Systemic Reactions

In a pooled safety population of 490 patients who received DARZALEX *FASPRO*™ as monotherapy or in combination, 11% of patients experienced a systemic administration-related reaction (Grade 2: 3.9%, Grade 3: 1.4%). Systemic administration-related reactions occurred in 10% of patients with the first injection, 0.2% with the second injection, and cumulatively 0.8% with subsequent injections. The median time to onset was 3.7 hours (range: 9 minutes to 3.5 days). Of the 84 systemic administration-related reactions that occurred in 52 patients, 73 (87%) occurred on the day of DARZALEX *FASPRO*™ administration. Delayed systemic administration-related reactions have occurred in less than 1% of the patients.

Severe reactions included hypoxia, dyspnea, hypertension and tachycardia. Other signs and symptoms of systemic administration-related reactions may include respiratory symptoms, such as bronchospasm, nasal congestion, cough, throat irritation, allergic rhinitis, and wheezing, as well as anaphylactic reaction, pyrexia, chest pain, pruritis, chills, vomiting, nausea, and hypotension.

Pre-medicate patients with histamine-1 receptor antagonist, acetaminophen and corticosteroids. Monitor patients for systemic administration-related reactions, especially following the first and second injections. For anaphylactic reaction or life-threatening (Grade 4) administration-related reactions, immediately and permanently discontinue DARZALEX *FASPRO*™. Consider administering corticosteroids and other medications after the administration of DARZALEX *FASPRO*™ depending on dosing regimen and medical history to minimize the risk of delayed (defined as occurring the day after administration) systemic administration-related reactions.

Local Reactions

In this pooled safety population, injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 0.6%. The most frequent (>1%) injection-site reaction was injection site erythema. These local reactions occurred a median of 7 minutes (range: 0 minutes to 4.7 days) after starting administration of DARZALEX *FASPRO*™. Monitor for local reactions and consider symptomatic management.

DARZALEX *FASPRO*™: For a strong start to their treatment journey

~3 to 5 minute administration

- Subcutaneous injection is **substantially faster** than intravenous daratumumab[1,2]

The recommended dose of DARZALEX *FASPRO*™ is 1,800 mg daratumumab and 30,000 units hyaluronidase administered subcutaneously over ~3 to 5 minutes. **DARZALEX *FASPRO*™ is for subcutaneous use only. Do not administer intravenously.**[1]

See the Dosage and Administration section of the Prescribing Information for dosing considerations and dosing schedules for approved regimens.

See **Important Safety Information** below for hypersensitivity and administration reactions, pre-medication and post-medication requirements, and other important considerations for use of DARZALEX *FASPRO*™.

Get the latest data and information at darzalexhcp.com/faspro

Contact your Oncology Specialist to learn more about DARZALEX *FASPRO*™

Efficacy consistent with intravenous daratumumab

- **DARZALEX *FASPRO*™** demonstrated a **non-inferior overall response rate (ORR)** vs intravenous daratumumab in an open-label, randomized study assessing monotherapy in 522 patients[1]
  - ORR was 41% (95% CI: 35%, 47%) for DARZALEX *FASPRO*™ (n=263) and 37% (95% CI: 31%, 43%) for intravenous daratumumab (n=259)[1]
  - Eligible patients were required to have relapsed or refractory multiple myeloma who had received ≥3 prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who were double-refractory to a PI and an immunomodulatory agent[1]
- In a single arm of a multicohort, open-label trial, **DARZALEX *FASPRO*™ with lenalidomide and dexamethasone (DRd)** was evaluated in 65 patients with multiple myeloma who had received ≥1 prior multiple myeloma therapy. The **ORR was 91%** (95% CI: 81%, 97%)[1]
- In a single arm of a multicohort, open-label trial, **DARZALEX *FASPRO*™ with bortezomib, melphalan, and prednisone (DVMP)** was evaluated in 67 patients with newly diagnosed multiple myeloma who were ineligible for a transplant. The **ORR was 88%** (95% CI: 78%, 95%)[1]

Fewer systemic ARRs vs intravenous daratumumab

- Nearly **3x reduction in systemic administration-related reactions**† (ARRs) with DARZALEX *FASPRO*™ vs intravenous daratumumab observed in the COLUMBA trial (13% of patients on DARZALEX *FASPRO*™ had a systemic ARR of any grade vs 34% with intravenous daratumumab)[1,3]
- Both systemic ARRs, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX *FASPRO*™. See Important Safety Information for more details[1]

*For intravenous daratumumab, median durations of 16 mg/kg infusions for the first, second, and subsequent infusions were approximately 7, 4, and 3 hours, respectively.[2]

†In clinical trials of DARZALEX *FASPRO*™, DARZALEX® (daratumumab), and the Prescribing Information for DARZALEX®, the term "infusion reactions" was used instead of "systemic administration-related reactions."

Neutropenia

Daratumumab may increase neutropenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX *FASPRO*™ until recovery of neutrophils. In lower body weight patients receiving DARZALEX *FASPRO*™, higher rates of Grade 3-4 neutropenia were observed.

Thrombocytopenia

Daratumumab may increase thrombocytopenia induced by background therapy. Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Consider withholding DARZALEX *FASPRO*™ until recovery of platelets.

Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX *FASPRO*™ can cause fetal harm when administered to a pregnant woman. DARZALEX *FASPRO*™ may cause depletion of fetal immune cells and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive potential to use effective contraception during treatment with DARZALEX *FASPRO*™ and for 3 months after the last dose.

The combination of DARZALEX *FASPRO*™ with lenalidomide is contraindicated in pregnant women, because lenalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide prescribing information on use during pregnancy.

Interference with Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab administration. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum. The determination of a patient's ABO and Rh blood type are not impacted. Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX *FASPRO*™. Type and screen patients prior to starting DARZALEX *FASPRO*™.

Interference with Determination of Complete Response

Daratumumab is a human IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. This interference can impact the determination of complete response and of disease progression in some DARZALEX *FASPRO*™-treated patients with IgG kappa myeloma protein.

ADVERSE REACTIONS

The most common adverse reaction (≥20%) with DARZALEX *FASPRO*™ monotherapy is: upper respiratory tract infection. The most common adverse reactions with combination therapy (≥20% for any combination) include fatigue, nausea, diarrhea, dyspnea, insomnia, pyrexia, cough, muscle spasms, back pain, vomiting, upper respiratory tract infection, peripheral sensory neuropathy, constipation, and pneumonia.

The most common hematology laboratory abnormalities (≥40%) with DARZALEX *FASPRO*™ are: decreased leukocytes, decreased lymphocytes, decreased neutrophils, decreased platelets, and decreased hemoglobin.

Please see Brief Summary on adjacent pages.

cp-143279v1

References: 1. DARZALEX *FASPRO*™ [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** DARZALEX® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **3.** Mateos M-V, Nahi H, Legiec W, et al. Subcutaneous versus intravenous daratumumab in patients with relapsed or refractory multiple myeloma (COLUMBA): a multicentre, open-label, non-inferiority, randomised, phase 3 trial. *Lancet Haematol*. 2020. doi: 10.1016/S2352-3026(20)30070-3. [Epub ahead of print]

janssen Oncology
PHARMACEUTICAL COMPANIES OF Johnson & Johnson

DARZALEX FASPRO™ (daratumumab and hyaluronidase-fihj) injection, for subcutaneous use

Brief Summary of Full Prescribing Information

INDICATIONS AND USAGE

DARZALEX FASPRO is indicated for the treatment of adult patients with multiple myeloma:

- in combination with bortezomib, melphalan and prednisone in newly diagnosed patients who are ineligible for autologous stem cell transplant.
- in combination with lenalidomide and dexamethasone in newly diagnosed patients who are ineligible for autologous stem cell transplant and in patients with relapsed or refractory multiple myeloma who have received at least one prior therapy.
- in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy.
- as monotherapy, in patients who have received at least three prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory agent or who are double-refractory to a PI and an immunomodulatory agent.

CONTRAINDICATIONS

DARZALEX FASPRO is contraindicated in patients with a history of severe hypersensitivity to daratumumab, hyaluronidase or any of the components of the formulation *[see Warnings and Precautions* and *Adverse Reactions].*

WARNINGS AND PRECAUTIONS

Hypersensitivity and Other Administration Reactions

Both systemic administration-related reactions, including severe or life-threatening reactions, and local injection-site reactions can occur with DARZALEX FASPRO.

Systemic Reactions

In a pooled safety population of 490 patients who received DARZALEX FASPRO as monotherapy or in combination, 11% of patients experienced a systemic administration-related reaction (Grade 2: 3.9%, Grade 3: 1.4%). Systemic administration-related reactions occurred in 10% of patients with the first injection, 0.2% with the second injection, and cumulatively 0.8% with subsequent injections. The median time to onset was 3.7 hours (range: 9 minutes to 3.5 days). Of the 84 systemic administration-related reactions that occurred in 52 patients, 73 (87%) occurred on the day of DARZALEX FASPRO administration. Delayed systemic administration-related reactions have occurred in less than 1% of the patients.

Severe reactions included hypoxia, dyspnea, hypertension and tachycardia. Other signs and symptoms of systemic administration-related reactions may include respiratory symptoms, such as bronchospasm, nasal congestion, cough, throat irritation, allergic rhinitis, and wheezing, as well as anaphylactic reaction, pyrexia, chest pain, pruritis, chills, vomiting, nausea, and hypotension.

Pre-medicate patients with histamine-1 receptor antagonist, acetaminophen and corticosteroids *[see Dosage and Administration (2.3) in Full Prescribing Information].* Monitor patients for systemic administration-related reactions, especially following the first and second injections. For anaphylactic reaction or life-threatening (Grade 4) administration-related reactions, immediately and permanently discontinue DARZALEX FASPRO. Consider administering corticosteroids and other medications after the administration of DARZALEX FASPRO depending on dosing regimen and medical history to minimize the risk of delayed (defined as occurring the day after administration) systemic administration-related reactions *[see Dosage and Administration (2.3) in Full Prescribing Information].*

Local Reactions

In this pooled safety population, injection-site reactions occurred in 8% of patients, including Grade 2 reactions in 0.6%. The most frequent (>1%) injection-site reaction was injection site erythema. These local reactions occurred a median of 7 minutes (range: 0 minutes to 4.7 days) after starting administration of DARZALEX FASPRO. Monitor for local reactions and consider symptomatic management.

Neutropenia

Daratumumab may increase neutropenia induced by background therapy *[see Adverse Reactions].*

Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Monitor patients with neutropenia for signs of infection. Consider withholding DARZALEX FASPRO until recovery of neutrophils. In lower body weight patients receiving DARZALEX FASPRO, higher rates of Grade 3-4 neutropenia were observed.

Thrombocytopenia

Daratumumab may increase thrombocytopenia induced by background therapy *[see Adverse Reactions].*

Monitor complete blood cell counts periodically during treatment according to manufacturer's prescribing information for background therapies. Consider withholding DARZALEX FASPRO until recovery of platelets.

Embryo-Fetal Toxicity

Based on the mechanism of action, DARZALEX FASPRO can cause fetal harm when administered to a pregnant woman. DARZALEX FASPRO may cause depletion of fetal immune cells and decreased bone density. Advise pregnant women of the potential risk to a fetus. Advise females with reproductive potential to use effective contraception during treatment with DARZALEX FASPRO and for 3 months after the last dose *[see Use in Specific Populations].*

The combination of DARZALEX FASPRO with lenalidomide is contraindicated in pregnant women, because lenalidomide may cause birth defects and death of the unborn child. Refer to the lenalidomide prescribing information on use during pregnancy.

Interference with Serological Testing

Daratumumab binds to CD38 on red blood cells (RBCs) and results in a positive Indirect Antiglobulin Test (Indirect Coombs test). Daratumumab-mediated positive indirect antiglobulin test may persist for up to 6 months after the last daratumumab administration. Daratumumab bound to RBCs masks detection of antibodies to minor antigens in the patient's serum *[see References].* The determination of a patient's ABO and Rh blood type are not impacted *[see Drug Interactions].*

Notify blood transfusion centers of this interference with serological testing and inform blood banks that a patient has received DARZALEX FASPRO. Type and screen patients prior to starting DARZALEX FASPRO *[see Dosage and Administration (2.1) in Full Prescribing Information].*

Interference with Determination of Complete Response

Daratumumab is a human IgG kappa monoclonal antibody that can be detected on both the serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein *[see Drug Interactions].* This interference can impact the determination of complete response and of disease progression in some DARZALEX FASPRO-treated patients with IgG kappa myeloma protein.

ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Hypersensitivity and Other Administration Reactions *[see Warning and Precautions].*
- Neutropenia *[see Warning and Precautions].*
- Thrombocytopenia *[see Warning and Precautions].*

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Newly Diagnosed Multiple Myeloma

In Combination with Bortezomib, Melphalan and Prednisone

The safety of DARZALEX FASPRO with bortezomib, melphalan and prednisone (D-VMP) was evaluated in a single-arm cohort of PLEIADES *[see Clinical Studies (14.1) in Full Prescribing Information].* Patients received DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously once weekly from weeks 1 to 6, once every 3 weeks from weeks 7 to 54 and once every 4 weeks starting with week 55 until disease progression or unacceptable toxicity (N=67) in combination with bortezomib, melphalan and prednisone. Among these patients, 93% were exposed for 6 months or longer and 19% were exposed for greater than one year.

Serious adverse reactions occurred in 39% of patients who received DARZALEX FASPRO. Serious adverse reactions in >5% of patients included pneumonia and pyrexia. Fatal adverse reactions occurred in 3.0% of patients.

Permanent discontinuation of DARZALEX FASPRO due to an adverse reaction occurred in 4.5% of patients. The adverse reaction resulting in permanent discontinuation of DARZALEX FASPRO in more than 1 patient was neutropenic sepsis.

Dosage interruptions (defined as dose delays or skipped doses) due to an adverse reaction occurred in 51% of patients who received DARZALEX FASPRO. Adverse reactions requiring dosage interruptions in >5% of patients included thrombocytopenia, neutropenia, anemia, and pneumonia.

The most common adverse reactions (≥20%) were upper respiratory tract infection, constipation, nausea, fatigue, pyrexia, peripheral sensory neuropathy, diarrhea, cough, insomnia, vomiting, and back pain.

Table 1 summarizes the adverse reactions in patients who received DARZALEX FASPRO with bortezomib, melphalan and prednisone (D-VMP) in PLEIADES.

Table 1: Adverse Reactions (≥10%) in Patients Who Received DARZALEX FASPRO with Bortezomib, Melphalan and Prednisone (D-VMP) in PLEIADES

	DARZALEX FASPRO with Bortezomib, Melphalan and Prednisone (N=67)	
Adverse Reaction	**All Grades (%)**	**Grades ≥3 (%)**
Infections		
Upper respiratory tract infection[a]	39	0
Bronchitis	16	0
Pneumonia[b]	15	7[#]

Table 1: Adverse Reactions (≥10%) in Patients Who Received DARZALEX FASPRO with Bortezomib, Melphalan and Prednisone (D-VMP) in PLEIADES (continued)

Adverse Reaction	DARZALEX FASPRO with Bortezomib, Melphalan and Prednisone (N=67)	
	All Grades (%)	Grades ≥3 (%)
Gastrointestinal disorders		
Constipation	37	0
Nausea	36	0
Diarrhea	33	3#
Vomiting	21	0
Abdominal pain[c]	13	0
General disorders and administration site conditions		
Fatigue[d]	36	3
Pyrexia	34	0
Edema peripheral[e]	13	1#
Nervous system disorders		
Peripheral sensory neuropathy	34	1#
Dizziness	10	0
Respiratory, thoracic and mediastinal disorders		
Cough[f]	24	0
Psychiatric disorders		
Insomnia	22	3#
Musculoskeletal and connective tissue disorders		
Back pain	21	3#
Musculoskeletal chest pain	12	0
Metabolism and nutrition disorders		
Decreased appetite	15	1#
Skin and subcutaneous tissue disorders		
Rash	13	0
Pruritus	12	0
Vascular disorders		
Hypertension	13	6#
Hypotension	10	3#

[a] Upper respiratory tract infection includes nasopharyngitis, respiratory syncytial virus infection, respiratory tract infection, rhinitis, tonsillitis, upper respiratory tract infection, and viral pharyngitis.
[b] Pneumonia includes lower respiratory tract infection, lung infection, pneumocystis jirovecii pneumonia, pneumonia, and pneumonia bacterial.
[c] Abdominal pain includes abdominal pain, and abdominal pain upper.
[d] Fatigue includes asthenia, and fatigue.
[e] Edema peripheral includes edema, edema peripheral, and peripheral swelling.
[f] Cough includes cough, and productive cough.
[#] Only grade 3 adverse reactions occurred.

Clinically relevant adverse reactions in <10% of patients who received DARZALEX FASPRO with bortezomib, melphalan and prednisone (D-VMP) include:

- **General disorders and administration site conditions:** infusion reaction, injection site reaction, chills
- **Infections:** herpes zoster, urinary tract infection, influenza, sepsis
- **Musculoskeletal and connective tissue disorders:** arthralgia, muscle spasms
- **Nervous system disorders:** headache, paresthesia
- **Metabolism and nutrition disorders:** hypocalcemia, hyperglycemia
- **Respiratory, thoracic and mediastinal disorders:** dyspnea, pulmonary edema
- **Cardiac disorders:** atrial fibrillation

Table 2 summarizes the laboratory abnormalities in patients who received DARZALEX FASPRO with bortezomib, melphalan and prednisone (D-VMP) in PLEIADES.

Table 2: Select Hematology Laboratory Abnormalities Worsening from Baseline in Patients Who Received DARZALEX FASPRO with Bortezomib, Melphalan and Prednisone (D-VMP) in PLEIADES

Laboratory Abnormality	DARZALEX FASPRO with Bortezomib, Melphalan and Prednisone[a]	
	All Grades (%)	Grades 3-4 (%)
Decreased leukocytes	96	52
Decreased lymphocytes	93	84
Decreased platelets	93	42
Decreased neutrophils	88	49
Decreased hemoglobin	48	19

[a] Denominator is based on the safety population treated with D-VMP (N=67).

Relapsed/Refractory Multiple Myeloma

In Combination with Lenalidomide and Dexamethasone

The safety of DARZALEX FASPRO with lenalidomide and dexamethasone (D-Rd) was evaluated in a single-arm cohort of PLEIADES *[see Clinical Studies (14.2) in Full Prescribing Information].* Patients received DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously once weekly from weeks 1 to 8, once every 2 weeks from weeks 9 to 24 and once every 4 weeks starting with week 25 until disease progression or unacceptable toxicity (N=65) in combination with lenalidomide and dexamethasone. Among these patients, 92% were exposed for 6 months or longer and 20% were exposed for greater than one year.

Serious adverse reactions occurred in 48% of patients who received DARZALEX FASPRO. Serious adverse reactions in >5% of patients included pneumonia, influenza and diarrhea. Fatal adverse reactions occurred in 3.1% of patients.

Permanent discontinuation of DARZALEX FASPRO due to an adverse reaction occurred in 11% of patients who received DARZALEX FASPRO. Adverse reactions resulting in permanent discontinuation of DARZALEX FASPRO in more than 1 patient were pneumonia and anemia.

Dosage interruptions due to an adverse reaction occurred in 63% of patients who received DARZALEX FASPRO. Adverse reactions requiring dosage interruptions in >5% of patients included neutropenia, pneumonia, upper respiratory tract infection, influenza, dyspnea, and blood creatinine increased.

The most common adverse reactions (≥20%) were fatigue, diarrhea, upper respiratory tract infection, muscle spasms, constipation, pyrexia, pneumonia, and dyspnea.

Table 3 summarizes the adverse reactions in patients who received DARZALEX FASPRO with lenalidomide and dexamethasone (D-Rd) in PLEIADES.

Table 3: Adverse Reactions (≥10%) in Patients Who Received DARZALEX FASPRO with Lenalidomide and Dexamethasone (D-Rd) in PLEIADES

Adverse Reaction	DARZALEX FASPRO with Lenalidomide and Dexamethasone (N=65)	
	All Grades (%)	Grades ≥3 (%)
General disorders and administration site conditions		
Fatigue[a]	52	5#
Pyrexia	23	2#
Edema peripheral	18	3#
Gastrointestinal disorders		
Diarrhea	45	5#
Constipation	26	2#
Nausea	12	0
Vomiting	11	0
Infections		
Upper respiratory tract infection[b]	43	3#
Pneumonia[c]	23	17
Bronchitis[d]	14	2#
Urinary tract infection	11	0
Musculoskeletal and connective tissue disorders		
Muscle spasms	31	2#
Back pain	14	0
Respiratory, thoracic and mediastinal disorders		
Dyspnea[e]	22	3
Cough[f]	14	0
Nervous system disorders		
Peripheral sensory neuropathy	17	2#
Psychiatric disorders		
Insomnia	17	5#
Metabolism and nutrition disorders		
Hyperglycemia	12	9#
Hypocalcemia	11	0

[a] Fatigue includes asthenia, and fatigue.
[b] Upper respiratory tract infection includes nasopharyngitis, pharyngitis, respiratory tract infection viral, rhinitis, sinusitis, upper respiratory tract infection, and upper respiratory tract infection bacterial.
[c] Pneumonia includes lower respiratory tract infection, lung infection, and pneumonia.
[d] Bronchitis includes bronchitis, and bronchitis viral.
[e] Dyspnea includes dyspnea, and dyspnea exertional.
[f] Cough includes cough, and productive cough.
[#] Only grade 3 adverse reactions occurred.

Clinically relevant adverse reactions in <10% of patients who received DARZALEX FASPRO with lenalidomide and dexamethasone (D-Rd) include:

- **Musculoskeletal and connective tissue disorders:** arthralgia, musculoskeletal chest pain
- **Nervous system disorders:** dizziness, headache, paresthesia
- **Skin and subcutaneous tissue disorders:** rash, pruritus
- **Gastrointestinal disorders:** abdominal pain
- **Infections:** influenza, sepsis, herpes zoster
- **Metabolism and nutrition disorders:** decreased appetite
- **Cardiac disorders:** atrial fibrillation
- **General disorders and administration site conditions:** chills, infusion reaction, injection site reaction
- **Vascular disorders:** hypotension, hypertension

Table 4 summarizes the laboratory abnormalities in patients who received DARZALEX FASPRO with lenalidomide and dexamethasone (D-Rd) in PLEIADES.

Table 4: Select Hematology Laboratory Abnormalities Worsening from Baseline in Patients Who Received DARZALEX FASPRO with Lenalidomide and Dexamethasone (D-Rd) in PLEIADES

	DARZALEX FASPRO with Lenalidomide and Dexamethasone[a]	
Laboratory Abnormality	**All Grades (%)**	**Grades 3-4 (%)**
Decreased leukocytes	94	34
Decreased lymphocytes	82	58
Decreased platelets	86	9
Decreased neutrophils	89	52
Decreased hemoglobin	45	8

[a] Denominator is based on the safety population treated with D-Rd (N=65).

Monotherapy

The safety of DARZALEX FASPRO as monotherapy was evaluated in COLUMBA *[see Clinical Trials (14.2) in Full Prescribing Information].* Patients received DARZALEX FASPRO 1,800 mg/30,000 units administered subcutaneously or daratumumab 16 mg/kg administered intravenously; each administered once weekly from weeks 1 to 8, once every 2 weeks from weeks 9 to 24 and once every 4 weeks starting with week 25 until disease progression or unacceptable toxicity. Among patients receiving DARZALEX FASPRO, 37% were exposed for 6 months or longer and 1% were exposed for greater than one year.

Serious adverse reactions occurred in 26% of patients who received DARZALEX FASPRO. Fatal adverse reactions occurred in 5% of patients. Fatal adverse reactions occurring in more than 1 patient were general physical health deterioration, septic shock, and respiratory failure.

Permanent discontinuation due to an adverse reaction occurred in 10% of patients who received DARZALEX FASPRO. Adverse reactions resulting in permanent discontinuation of DARZALEX FASPRO in more than 2 patients were thrombocytopenia and hypercalcemia.

Dosage interruptions due to an adverse reaction occurred in 26% of patients who received DARZALEX FASPRO. Adverse reactions requiring dosage interruption in >5% of patients included thrombocytopenia.

The most common adverse reaction (≥20%) was upper respiratory tract infection.

Table 5 summarizes the adverse reactions in COLUMBA.

Table 5: Adverse Reactions (≥10%) in Patients Who Received DARZALEX FASPRO or Intravenous Daratumumab in COLUMBA

	DARZALEX FASPRO (N=260)		Intravenous Daratumumab (N=258)	
Adverse Reaction	**All Grades (%)**	**Grade ≥3 (%)**	**All Grades (%)**	**Grade ≥3 (%)**
Infections				
Upper respiratory tract infection[a]	24	1[#]	22	1[#]
Pneumonia[b]	8	5	10	6[@]
Gastrointestinal disorders				
Diarrhea	15	1[#]	11	0.4[#]
Nausea	8	0.4[#]	11	0.4[#]
General disorders and administration site conditions				
Fatigue[c]	15	1[#]	16	2[#]
Infusion reactions[d]	13	2[#]	34	5[#]
Pyrexia	13	0	13	1[#]
Chills	6	0.4[#]	12	1[#]
Musculoskeletal and connective tissue disorders				
Back pain	10	2[#]	12	3[#]
Respiratory, thoracic and mediastinal disorders				
Cough[e]	9	1[#]	14	0
Dyspnea[f]	6	1[#]	11	1[#]

DARZALEX FASPRO™ (daratumumab and hyaluronidase-fihj) injection

[a] Upper respiratory tract infection includes acute sinusitis, nasopharyngitis, pharyngitis, respiratory syncytial virus infection, respiratory tract infection, rhinitis, rhinovirus infection, sinusitis, and upper respiratory tract infection.
[b] Pneumonia includes lower respiratory tract infection, lung infection, pneumocystis jirovecii pneumonia, and pneumonia.
[c] Fatigue includes asthenia, and fatigue.
[d] Infusion reactions includes terms determined by investigators to be related to infusion.
[e] Cough includes cough, and productive cough.
[f] Dyspnea includes dyspnea, and dyspnea exertional.
[#] Only grade 3 adverse reactions occurred.
[@] Grade 5 adverse reactions occurred.

Clinically relevant adverse reactions in <10% of patients who received DARZALEX FASPRO include:

- **General disorders and administration site conditions:** injection site reaction, peripheral edema
- **Musculoskeletal and connective tissue disorders:** arthralgia, musculoskeletal chest pain, muscle spasms
- **Gastrointestinal disorders:** constipation, vomiting, abdominal pain,
- **Metabolism and nutrition disorders:** decreased appetite, hyperglycemia, hypocalcemia, dehydration
- **Psychiatric disorders:** insomnia
- **Vascular disorders:** hypertension, hypotension
- **Nervous system disorders:** dizziness, peripheral sensory neuropathy, paresthesia
- **Infections:** bronchitis, influenza, urinary tract infection, herpes zoster, sepsis, hepatitis B reactivation
- **Skin and subcutaneous tissue disorders:** pruritus, rash
- **Cardiac disorders:** atrial fibrillation
- **Respiratory, thoracic and mediastinal disorders:** pulmonary edema

Table 6 summarizes the laboratory abnormalities in COLUMBA.

Table 6: Select Hematology Laboratory Abnormalities Worsening from Baseline in Patients Receiving DARZALEX FASPRO or Intravenous Daratumumab in COLUMBA

	DARZALEX FASPRO[a]		Intravenous Daratumumab[a]	
Laboratory Abnormality	**All Grades (%)**	**Grades 3-4 (%)**	**All Grades (%)**	**Grades 3-4 (%)**
Decreased leukocytes	65	19	57	14
Decreased lymphocytes	59	36	56	36
Decreased neutrophils	55	19	43	11
Decreased platelets	43	16	45	14
Decreased hemoglobin	42	14	39	16

[a] Denominator is based on the safety population treated with DARZALEX FASPRO (N=260) and Intravenous Daratumumab (N=258).

Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other daratumumab products or other hyaluronidase products may be misleading.

Treatment-emergent anti-daratumumab antibodies were tested in 451 patients treated with DARZALEX FASPRO as monotherapy or as part of a combination therapy. One patient (0.2%) who received DARZALEX FASPRO as monotherapy tested positive for anti-daratumumab antibodies and transient neutralizing antibodies. However, the incidence of antibody development might not have been reliably determined because the assays that were used have limitations in detecting anti-daratumumab antibodies in the presence of high concentrations of daratumumab.

Treatment-emergent anti-rHuPH20 antibodies developed in 8% (19/255) of patients who received DARZALEX FASPRO as monotherapy and in 8% (16/192) of patients who received DARZALEX FASPRO as part of a combination therapy. The anti-rHuPH20 antibodies did not appear to affect daratumumab exposures. None of the patients who tested positive for anti-rHuPH20 antibodies tested positive for neutralizing antibodies.

Postmarketing Experience

The following adverse reactions have been identified with use of intravenous daratumumab. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System: Anaphylactic reaction

Gastrointestinal: Pancreatitis

DRUG INTERACTIONS

Effects of Daratumumab on Laboratory Tests

Interference with Indirect Antiglobulin Tests (Indirect Coombs Test)

Daratumumab binds to CD38 on RBCs and interferes with compatibility testing, including antibody screening and cross matching. Daratumumab interference mitigation methods include treating reagent RBCs with dithiothreitol (DTT) to disrupt daratumumab binding *[see References]* or genotyping. Since the Kell blood group system is also sensitive to DTT treatment, supply K-negative units after ruling out or identifying alloantibodies using DTT-treated RBCs.

If an emergency transfusion is required, administer non-cross-matched ABO/RhD-compatible RBCs per local blood bank practices.

Interference with Serum Protein Electrophoresis and Immunofixation Tests

Daratumumab may be detected on serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for monitoring disease monoclonal immunoglobulins (M protein). False positive SPE and IFE assay results may occur for patients with IgG kappa myeloma protein impacting initial assessment of complete responses by International Myeloma Working Group (IMWG) criteria. In DARZALEX FASPRO-treated patients with persistent very good partial response, where daratumumab interference is suspected, consider using a FDA-approved daratumumab-specific IFE assay to distinguish daratumumab from any remaining endogenous M protein in the patient's serum, to facilitate determination of a complete response.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

DARZALEX FASPRO can cause fetal harm when administered to a pregnant woman. The assessment of associated risks with daratumumab products is based on the mechanism of action and data from target antigen CD38 knockout animal models *(see Data)*. There are no available data on the use of DARZALEX FASPRO in pregnant women to evaluate drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

The combination of DARZALEX FASPRO and lenalidomide is contraindicated in pregnant women, because lenalidomide may cause birth defects and death of the unborn child. Lenalidomide is only available through a REMS program. Refer to the lenalidomide prescribing information on use during pregnancy.

Clinical Considerations

Fetal/Neonatal Adverse Reactions

Immunoglobulin G1 (IgG1) monoclonal antibodies are transferred across the placenta. Based on its mechanism of action, DARZALEX FASPRO may cause depletion of fetal CD38 positive immune cells and decreased bone density. Defer administering live vaccines to neonates and infants exposed to daratumumab *in utero* until a hematology evaluation is completed.

Data

Animal Data

DARZALEX FASPRO for subcutaneous injection contains daratumumab and hyaluronidase. Mice that were genetically modified to eliminate all CD38 expression (CD38 knockout mice) had reduced bone density at birth that recovered by 5 months of age. Data from studies using CD38 knockout animal models also suggest the involvement of CD38 in the regulation of humoral immune responses (mice), feto-maternal immune tolerance (mice), and early embryonic development (frogs).

No systemic exposure of hyaluronidase was detected in monkeys given 22,000 U/kg subcutaneously (12 times higher than the human dose) and there were no effects on embryo-fetal development in pregnant mice given 330,000 U/kg hyaluronidase subcutaneously daily during organogenesis, which is 45 times higher than the human dose.

There were no effects on pre- and post-natal development through sexual maturity in offspring of mice treated daily from implantation through lactation with 990,000 U/kg hyaluronidase subcutaneously, which is 134 times higher than the human doses.

Lactation

Risk Summary

There is no data on the presence of daratumumab and hyaluronidase in human milk, the effects on the breastfed child, or the effects on milk production. Maternal immunoglobulin G is known to be present in human milk. Published data suggest that antibodies in breast milk do not enter the neonatal and infant circulations in substantial amounts. Because of the potential for serious adverse reactions in the breastfed child when DARZALEX FASPRO is administered with lenalidomide and dexamethasone, advise women not to breastfeed during treatment with DARZALEX FASPRO. Refer to lenalidomide prescribing information for additional information.

Data

Animal Data

No systemic exposure of hyaluronidase was detected in monkeys given 22,000 U/kg subcutaneously (12 times higher than the human dose) and there were no effects on post-natal development through sexual maturity in offspring of mice treated daily during lactation with 990,000 U/kg hyaluronidase subcutaneously, which is 134 times higher than the human doses.

Females and Males of Reproductive Potential

DARZALEX FASPRO can cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations]*.

Pregnancy Testing

With the combination of DARZALEX FASPRO with lenalidomide, refer to the lenalidomide labeling for pregnancy testing requirements prior to initiating treatment in females of reproductive potential.

Contraception

Advise females of reproductive potential to use effective contraception during treatment with DARZALEX FASPRO and for 3 months after the last dose. Additionally, refer to the lenalidomide labeling for additional recommendations for contraception.

Pediatric Use

Safety and effectiveness of DARZALEX FASPRO in pediatric patients have not been established.

Geriatric Use

Of the 291 patients who received DARZALEX FASPRO as monotherapy for relapsed and refractory multiple myeloma, 37% were 65 to <75 years of age, and 19% were 75 years of age or older. No overall differences in effectiveness were observed based on age. Adverse reactions occurring at a higher frequency (≥5% difference) in patients ≥65 years of age included upper respiratory tract infection, urinary tract infection, dizziness, cough, dyspnea, diarrhea, nausea, fatigue, and peripheral edema. Serious adverse reactions occurring at a higher frequency (≥2% difference) in patients ≥65 years of age included pneumonia.

Clinical studies of DARZALEX FASPRO as part of a combination therapy did not include sufficient numbers of patients aged 65 and older to determine whether they respond differently from younger patients.

REFERENCES

1. Chapuy, CI, RT Nicholson, MD Aguad, et al., 2015, Resolving the daratumumab interference with blood compatibility testing, Transfusion, 55:1545-1554 (accessible at http://onlinelibrary.wiley.com/doi/10.1111/trf.13069/epdf).

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Hypersensitivity and Other Administration Reactions

Advise patients to seek immediate medical attention for any of the following signs and symptoms of systemic administration-related reactions: itchy, runny or blocked nose; chills, nausea, throat irritation, cough, headache, shortness of breath or difficulty breathing *[see Warnings and Precautions]*.

Neutropenia

Advise patients to contact their healthcare provider if they have a fever *[see Warnings and Precautions]*.

Thrombocytopenia

Advise patients to contact their healthcare provider if they have bruising or bleeding *[see Warnings and Precautions]*.

Embryo-Fetal Toxicity

Advise pregnant women of the potential hazard to a fetus. Advise females of reproductive potential to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions, Use in Specific Populations]*.

Advise females of reproductive potential to avoid becoming pregnant during treatment with DARZALEX FASPRO and for at least 3 months after the last dose *[see Use in Specific Populations]*.

Advise patients that lenalidomide has the potential to cause fetal harm and has specific requirements regarding contraception, pregnancy testing, blood and sperm donation, and transmission in sperm. Lenalidomide is only available through a REMS program *[see Use in Specific Populations]*.

Interference with Laboratory Tests

Advise patients to inform their healthcare provider, including personnel at blood transfusion centers, that they are taking DARZALEX FASPRO, in the event of a planned transfusion *[see Warnings and Precautions]*.

Advise patients that DARZALEX FASPRO can affect the results of some tests used to determine complete response in some patients and additional tests may be needed to evaluate response *[see Warnings and Precautions]*.

Hepatitis B Virus (HBV) Reactivation

Advise patients to inform healthcare providers if they have ever had or might have a hepatitis B infection and that DARZALEX FASPRO could cause hepatitis B virus to become active again *[see Adverse Reactions]*.

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Staying Current: Advice for New Practitioners

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I still remember starting my very first job after the completion of my hematology/oncology pharmacy residency and feeling like I was on top of the world. I had subscribed to a gazillion journals and website updates, and I was all set to be the living encyclopedia of oncology therapeutics for my team—or so I thought. As the years passed by, the burden of staying up-to-date with oncology practice began to weigh heavily on my shoulders, particularly as I started delving into various roles and activities for professional development all while maintaining high standards for patient care activities. Becoming a mother was a game changer. I had to set boundaries for maintaining a healthy work-life balance, which involved coming up with an effective and efficient system that allowed me to stay current with updates in oncology therapeutics.

New information is coming out at an explosive rate.[1,2] In the 1950s, the amount of medical knowledge was expected to double every 50 years. In 2020, medical knowledge is expected to double every 73 days.[3] At some point in our professional career, each of us has been told that medicine is a lifelong learning journey; however, we must face the reality that comes with this daunting task. It is incredibly challenging to stay up-to-date with one oncology subspecialty, let alone all subspecialties, internal medicine, infectious diseases, and so on. Staying up-to-date involves two tasks: remembering previously acquired information and learning new information. This article offers some tips that can be used to help you stay current with updates in oncology therapeutics.

Tip 1: Remain curious and always challenge yourself.

During pharmacy school or postdoctorate training, remaining curious and challenging yourself is easy just by virtue of being in a training environment. However, this situation can change after training is completed because of the pressure of daily tasks. It is easier to stick to what we know or are familiar with, and given the pace at which oncology therapeutics is transforming, learned information can become outdated fairly quickly. It is important to work in a challenging environment. Curiosity, even about the tasks that have become second nature, is also important. It is an indispensable attribute and is pivotal for sound clinical reasoning.[4,5] Self-reflection, critical thinking, and teamwork become hollow in the absence of curiosity. Challenge yourself to work as a team with colleagues who may practice differently, and establish a nonthreatening environment that will encourage you and everyone around you to be curious and ask questions (e.g., Why is one regimen picked over another?).

Tip 2: Let others curate resources for you.

Researching primary literature to answer questions encountered on a daily basis will keep you up-to-date, but this will not help you proactively identify issues. The amount of information available at our fingertips is overwhelming. It is up to us to create filters. Subscribe to resources that narrow down the many articles published daily to a dozen or so that may be relevant. Subscribing to a Really Simple Syndication (RSS) feed is an easy and efficient way to stay informed about newly published content. Websites create RSS feeds of their content as a strategy to provide continuous updates to subscribers. Subscribing to RSS feeds is a simple process; it requires an RSS feed address and a program that can translate and show content taken from that feed address. There are many different RSS programs that can display and update information from RSS feeds.[6]

- Table of contents (TOC) alerts: Set up an alert for your favorite journal(s) so that you will receive an email or an updated RSS feed when a new issue is published. This can be set up for an individual journal from the journal's website or via search engine websites such as PubMed's MyNCBI feature.[6,7]
- Feedly is a tool that pulls information from all over the Web (e.g., blogs, journals, YouTube videos, Twitter feeds) via RSS feeds. Instead of having to visit webpages every few days to find updates, it delivers the same information to one place. The number of unread articles shows up in the easy-to-read feeds on the main page, allowing you to review everything on one dashboard. Notes can be made in these articles, though this feature requires a fee. You can also save articles to personalized boards. Feedly allows you to integrate with numerous applications and easily share content to social media outlets.
- EvidenceAlerts is an integrated e-mail alerting system for healthcare providers (covering key trials from more than 120 journals) at no charge. All citations are prereviewed by research staff to ensure quality and are subsequently rated by physicians for clinical relevance and interest.
- Read by QxMD, a mobile app, is a digital one-stop shop for medical literature. It allows you to get feeds of the medical journals of your choosing and organize and review your personal collection of articles. A unique feature of this app is that it links with your institution's library account, so you can access full-text articles that your library subscribes to with a single click. You can also make a comment on a paper, save it, share it on social media, or send it to someone.
- Podcasts are an easy way of staying informed if you lack the time to read journals. Several medical journals, including the *Journal of Clinical Oncology* and *Lancet Oncology*, and professional organizations publish podcasts (including the recently launched HOPA Now) to summarize or supplement what is published in journals or is being discussed among healthcare providers.

In addition to journals, numerous other websites (e.g., Medscape, Cancer Network, Clinical Care Options, U.S. Food and Drug Administration, and Journal of National Comprehensive Cancer Network 360) provide e-mail subscription services through which the latest medical news, clinical trial coverage, drug updates, journal articles, continuing education activities, and more are delivered.

Tip 3: Use social media.

Social media (Facebook, Twitter, etc.) are not for everyone, and let's face it—they are not PubMed. However, I personally find it helpful to read what experts and nonexperts alike are talking about, particularly for primary literature. It is important to appreciate opposing perspectives: they may further challenge your viewpoints and cause you to dig deeper. Follow journals or medical/pharmacy organizations on social media to read about the latest updates.

Tip 4: Attend conferences.

Megaconferences such as the American Society of Clinical Oncology or Hematology/Oncology Pharmacy Association annual meetings have attendance numbering in the thousands and are great for accessing a breadth of information and learning about the latest breakthroughs. However, smaller-scale conferences hosted on a local or state level can provide just as much value. Choose conferences that are most relevant to your practice, and try to commit to attending at least one annually.

Tip 5: Use a clinical decision support system.

Clinical decision support systems (e.g., UpToDate) are quickly becoming essential tools for healthcare providers because they provide the most up-to-date evidence-based information (e.g., overview of disease, treatment guidelines) at the point of care. These systems can perform many functions, including, but not limited to, streamlining treatment algorithms based on cancer type.

Tip 6: Teach.

Teaching comes in all shapes and sizes. As pharmacists, we are constantly teaching, whether formally or informally, consciously or subconsciously. We can teach only what we know, so encouraging yourself and all those around you to ask questions is a great way to stay up-to-date. I have found that my best learning comes from teaching. This may be in the form of writing an article, lecturing at a college of pharmacy or at a conference, reviewing mechanisms of action of drugs with a learner, and so much more. We should all consider ourselves both teachers and learners.

Tip 7: Attain board certification.

The Board Certified Oncology Pharmacist program validates that the pharmacist has the advanced knowledge and experience necessary to optimize outcomes for patients with malignant diseases. Attaining board certification and subsequently maintaining it require completion of continuing education and offer you a great way to stay up-to-date.[8]

Tip 8: Interact with peers.

One of the most common and effective ways healthcare providers receive medical updates is from their colleagues. Routine peer-to-peer interaction can be a useful way to stay abreast of changing guidelines and cutting-edge research. Ask fellow pharmacists or providers for their thoughts on a new study or recently updated guidelines, for example.

Tip 9: Engage with pharmacy organizations.

Getting involved in pharmacy organizations, whether at a local, state, or national level, is a great way to stay up-to-date. These organizations offer numerous ways to get involved, ranging from participating on a committee to connecting or collaborating with fellow colleagues. Many organizations also have listservs, which generally involve discussions about issues in clinical practice; pharmacists can submit questions and request feedback from members from various institutions. These are great channels for discussing prominent issues, sharing ideas, and networking with colleagues from across the country.

Although I hope you find some of the tips mentioned in this article useful to you in your efforts to stay current, the most important strategy is to make learning a routine activity rather than limiting it to once or twice a year. I subscribe to numerous TOC alerts, but I graze through most of them to find the most important publications. I carefully choose and pay attention to landmark studies that have led to new drug approvals or have changed treatment strategies. I encourage you to carve out a specific time each day (a few minutes) or week (1–2 hours). The hard part is to not lose motivation and to stay disciplined about finding time. There are many ways to learn, and no single way is ideal for everyone. Regardless of your learning style, embrace the concept of lifelong learning—I assure you that it will make you a better pharmacist![9]

Being an oncology pharmacist is a great privilege. Staying current may seem like a daunting task, but if you make curiosity the foundation of patient care, the task is doable. We make a commitment to serve our patients when we take the pharmacist's oath. We owe it to ourselves and our profession to maintain this commitment. ●●

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Benign Hematology for the Oncology Pharmacist

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Most people think of *hematology* as malignant hematology. This penchant for malignant hematology is reflected in the oncology pharmacy residency standards and the Board Certified Oncology Pharmacist (BCOP) content outline.[1,2] Despite this, hematology/oncology pharmacists are often called upon to care for benign hematology patients in clinical practice. The goal of this review is to familiarize hematology/oncology pharmacists with fundamental benign hematology concepts that can be employed during care for this population.

Meet the Players

Erythrocytes

"Normal" adult hemoglobin (HbA) consists of two α- and two β-globin subunits ($\alpha_2\beta_2$). Fetal hemoglobin (HbF) consists of two α- and two γ-globin subunits ($\alpha_2\gamma_2$) and has greater oxygen-binding affinity than HbA. HbF production nadirs in the postnatal period.[3]

Leukocytes

Hematopoietic progenitors differentiate into either myeloid lineage (neutrophils and other granulocytes) or lymphoid lineage (T and B cells). Both elements are crucial for immune function.[4]

Platelets

Platelets are vital for hemostasis. GPIbα on the platelet surface binds to endothelial-bound von Willebrand factor (vWF) to initiate platelet adhesion.[5,6]

"Hematology/oncology pharmacists are often called upon to care for benign hematology patients in clinical practice."

Meet the Disorders

Hemostatic disorders

Von Willebrand disease (VWD) is the most common inherited bleeding disorder. In addition to its role in platelet adhesion, vWF also stabilizes circulating factor VIII (FVIII). Types 1 and 3 VWD are quantitative disorders of vWF, and Type 2 is a qualitative disorder.[6,7] Hemophilia is an X-linked disorder that arises from absent or diminished production of FVIII (hemophilia A) or factor IX (FIX; hemophilia B). Hemophilia severity is defined by baseline factor activity level: severe (<1%), moderate (1%–5%), or mild (5%–40%).[8] Severe disease is characterized by spontaneous and potentially life-threatening bleeds. Neutralizing antibodies produced in response to exogenous factors, known as inhibitors, afflict ~30% of patients with severe hemophilia A and ~3%–5% of patients with hemophilia B.[9]

Hemoglobinopathies

Thalassemias are quantitative disorders of hemoglobin, resulting from diminished production of either α- or β-globin. They can be categorized by affected gene, major/intermedia/minor designation, and transfusion-dependent/independent status. Transfusions often begin at a young age, making potentially fatal siderosis a lifelong concern.[10]

Sickle cell disease arises from a point mutation in the β-globin gene. Mutant hemoglobin (HbS, $\alpha_2\beta^S_2$) polymerizes when deoxygenated, which results in the characteristic sickled shape of affected erythrocytes.[11] Clinical sequelae include pain crises, acute chest syndrome, and stroke. In general, patients with HbSS and HbSβ^0 thalassemia tend to have more severe clinical phenotypes than patients with other heterozygous genotypes (i.e., HbSC, HbSβ^+ thalassemia).[11]

Cytopenias

Cytopenias result from either inherent marrow failure or immune destruction. Bone marrow failure syndromes can be inherited or acquired, and they result in either single- (e.g., severe congenital neutropenia) or multi-lineage loss (e.g., aplastic anemia).[12] Common immune cytopenias include immune thrombocytopenia (ITP), autoimmune hemolytic anemia (AIHA), and Evans syndrome (typically coincident ITP + AIHA). Characterization of the causative antibody is particularly useful in AIHA, where thermoreactivity directs treatment approach.[13,14]

Meet the Drugs

Treatment of hemostatic disorders

Possible treatment options for VWD include desmopressin and vWF concentrates. Desmopressin increases vWF and FVIII, also making it useful for treating mild or moderate hemophilia A.[7]

The treatment of choice for severe hemophilia has traditionally been prophylaxis with clotting factor concentrates.[8] Major differentiating features between concentrates include factor (FVIII, FIX, vWF, etc.), source (plasma-derived vs. recombinant), and presence of modifications. Concerns of viral transmission have plagued the plasma-derived concentrates, but modern manufacturing practices minimize the risk of transmission.[15] Recombinant factors carry no risk for viral transmission, but conflicting reports suggest that certain recombinant factors may have a higher risk of inhibitor development than plasma-derived factors containing vWF.[16] Extended half-life (EHL) factors employ various modifications (e.g.,

pegylation, albumin fusion) to reduce the frequency of infusion. EHL FIX products have achieved a 4–6 times half-life extension in contrast to the 1.5–2 times extension of the EHL FVIII products.[17]

Emicizumab is a monoclonal antibody approved for hemophilia A. By binding FIXa and FX, emicizumab mimics the activity of FVIII, making it a therapeutic option for patients with and without inhibitors as evidenced in the HAVEN trials.[18-21] Unlike the intravenous clotting factor concentrates, emicizumab is a subcutaneous injection that can be given one to four times per month.[21,22] Other therapeutic options for patients with inhibitors include bypassing agents (FEIBA and rFVIIa) and immune tolerance induction.[9,23]

Treatment of hemoglobinopathies

Iron chelators are paramount in managing chronic transfusion therapy associated with hemoglobinopathies. Deferoxamine is given as daily subcutaneous infusions, or, less commonly, as intermittent high-dose intravenous infusions.[24] Deferasirox and deferiprone are enteral options, but deferiprone carries a risk for agranulocytosis. Combination chelation can be deployed for refractory cases.[25,26]

Therapeutic options for sickle cell disease have expanded in recent years. Hydroxyurea has been used for several decades; it induces HbF production and reduces the frequency of pain crises, acute chest syndrome, and transfusions.[27,28] The first approved novel agent, L-glutamine, works by maintaining reduction and oxidation balance. L-glutamine was shown to reduce pain crises compared to placebo (three vs. four episodes per year, $p = .005$) in a phase 3 trial.[29] Crizanlizumab is an intravenous P-selectin inhibitor that interrupts adhesion of cells to the vascular endothelium. In the SUSTAIN trial, high-dose crizanlizumab was shown to reduce pain crises compared to placebo (1.6 vs. 3 episodes per year, $p = .01$).[30] Voxelotor is an oral agent that inhibits HbS polymerization. In the HOPE trial, voxelotor increased hemoglobin >1 g/dL from baseline in 51% participants.[31] Studies of voxelotor, crizanlizumab, and L-glutamine included patients with and without concomitant hydroxyurea; however, there is currently no standard for how to sequence these agents in clinical practice.[32]

Treatment of cytopenias

Inappropriate immune system activity can be dampened by various approaches: corticosteroids, intravenous immunoglobin, rituximab, and other immunosuppressants.[13,14] Warm AIHA is typically more responsive to immunosuppressants than cold AIHA.[14] Immunosuppression with equine antithymocyte globulin plus cyclosporine, with or without eltrombopag, is the standard of care for transplant-ineligible patients with severe aplastic anemia.[33,34] Eltrombopag is a thrombopoietin (TPO) receptor agonist thought to have hematopoietic stem cell-stimulatory effects and is approved by the U.S. Food and Drug Administration for refractory aplastic anemia; larger trials are under way to confirm early positive results in front-line therapy.[34,35] In addition to its activity in aplastic anemia, eltrombopag is used to treat chronic ITP, as is the parenteral TPO agonist, romiplostim.[36] Caplacizumab is an anti-vWF antibody with activity in acquired thrombotic thrombocytopenia purpura.[37,38]

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Barriers to the Initiation of Oral Oncolytics

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Oral anticancer therapies are an increasingly prevalent part of cancer treatment. Oral cytotoxic agents, small-molecule inhibitors, and other medications may offer several advantages over parenteral anticancer options. These advantages include the convenience of completing therapy at home and a possible decrease in the frequency of office visits. In addition, some patients may appreciate the enhanced sense of responsibility that stems from administering their therapy at home.[1]

Despite the increasing use of oral anticancer therapy, the process for accessing these medications is often complex and can be time-consuming and confusing for patients and healthcare providers alike. Patients, providers, and other staff members may have to contact an extensive list of organizations, including insurance companies, specialty pharmacies, drug manufacturers, and patient assistance foundations before the patient is ultimately able to access the prescribed medication. Although the particulars of drug procurement, drug cost, and insurance coverage vary from patient to patient, several common barriers to medication access arise, and pharmacists should be aware of these when helping patients who are initiating oral anticancer therapies. In this article, we discuss some of those barriers by using the experience of one patient, PT, as an example.

PT was a 66-year-old female with metastatic estrogen receptor/progesterone receptor-positive, human epidermal growth factor receptor 2–negative breast cancer diagnosed in late 2019. Her oncologist determined that a CDK4/6 inhibitor and anastrozole were the treatment of choice. A prescription for a CDK4/6 inhibitor was sent to the health network's specialty pharmacy. PT had Medicare Part D insurance, which required a prior authorization for the new medication. The prior authorization was submitted by a medication assistance coordinator (MAC), a pharmacy technician working specifically to help patients access oncology medications. PT's health system was very fortunate to have MACs; many health systems do not have such assistance. Fortunately, PT's prior authorization was approved on the same day the prescription was sent. However, the copayment for the CDK4/6 inhibitor was more than $2,000 per month, an unaffordable amount by almost any standard. PT's team also learned that the network specialty pharmacy was not contracted to dispense this specific medication. Therefore, the prescription was sent to another specialty pharmacy. Luckily, the medication's manufacturer offered a voucher program for the first cycle of the drug. The MAC assigned to PT's case registered her for the voucher program and provided the patient and voucher information to the new specialty pharmacy. A few days later, the first cycle of the drug was sent to PT with no out-of-pocket cost.

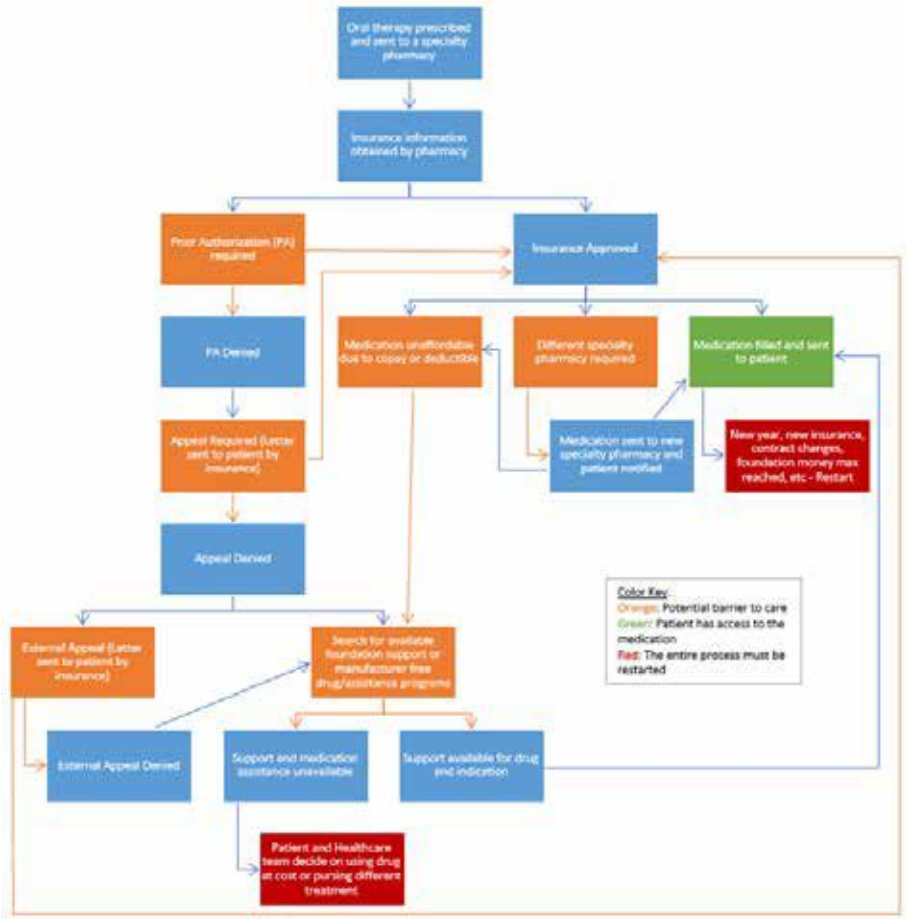
Unfortunately, PT was unable to pay $2,000 monthly for subsequent cycles. PT's MAC filled out an application for foundational support to help cover future copayments. After extensive income information was obtained from PT (including sensitive information like her tax statements from the previous year and Social Security number), the application was filled out, PT's oncologist signed the application, and the MAC faxed the packet of information to the foundation. Five days later, PT's team heard that the foundation was accepting only re-enrollments and that no new patients would be accepted. PT's team then repeated this application process with the drug manufacturer's patient assistance program. Approximately 2 weeks later, PT's team received word that she had been approved to receive the CDK4/6 inhibitor through the patient assistance program until the end of 2020. PT then finally received her second cycle of the drug in the mail, 2 days after she was scheduled to start cycle 2.

PT and her healthcare team ran into some of the most common barriers in oral anticancer therapy access (**Figure 1**). First, as happens with many newly prescribed oral anticancer therapies, PT's insurance company required a prior authorization for the specialty medication. Although the healthcare team did not have to do this in PT's case, an appeal letter, peer-to-peer communication, or both are often required in addition to the initial prior authorization request. If that appeal is denied (typically after a minimum of a 72-hour turnaround time), then an external appeal can sometimes be pursued, with another 72-hour turnaround time. The denial of the external appeal, if it occurs, is often the end of the road for prescription insurance coverage. These processes are time-consuming for healthcare teams and may delay a patient's ability to begin therapy, especially for health systems that lack personnel trained for and designated to the task of coordinating medication assistance.

As seen with PT's copayment, patients may face significant cost sharing when they are prescribed oral anticancer therapies. The case is different with chemotherapy by infusion: drugs given in the infusion center are covered by medical insurance, not the prescription plan. This difference may cause confusion for patients and members of the healthcare team. Providers are often unaware of drug coverage at the point of prescribing and are therefore unable to consider affordability in treatment planning. If a patient is ultimately unable to afford the prescribed medication, the process of repeating treatment planning and prescribing an alternative therapy creates even more delays in treatment.[1] Changing therapy may cause stress for patients who believe that the initially prescribed medication was the best choice for them. Significant delays in therapy resulting from insurance barriers can also lead to psychological harm for patients who believe that their cancer is progressing between treatments.

Patients with commercial insurance may be eligible for a copay card to cover a portion of the out-of-pocket cost of their

Figure 1. A Process for Receiving Oral Anticancer Therapy and Common Barriers to Access



medication, if the manufacturer offers a copay card. However, a large proportion of patients at many cancer centers are 65 years of age or older and have Medicare Part D insurance. These patients, as well as patients with Medicaid, are not eligible for copay cards. Patients with either Medicare/Medicaid or commercial insurance may be eligible for patient assistance programs through manufacturers and foundations. These programs often have specific requirements set by the organization offering the funding. Each program requires a separate application, and some of them have income requirements that may eliminate middle-class or higher-earning patients who still find copayments like PT's challenging to afford. The turnaround time for approval or denial of these programs also varies and may contribute to a delay in starting therapy. Most assistance programs are reserved for products that are still branded, as many oral anticancer therapies are. However, for the few generic options, finding patient assistance can be particularly challenging. For treatments such as capecitabine, healthcare teams may turn to avenues like online coupons to decrease cost, but patients may still be left with a shockingly high copay. Furthermore, at the first of the year many patients must meet a deductible. Usually manufacturer copay cards cover a percentage of the total cost, and the deductible tends to be higher for more expensive therapies.

As PT's story demonstrates, the path to oral anticancer therapy access is often convoluted and time-consuming. Because patients frequently need new prescriptions when dose adjustments are made to the therapies or when insurance coverage changes, the procurement process may need to be repeated during therapy. Many patients are unaware of potential barriers or ways to overcome them, and they may be frustrated and confused when these barriers lead to delays in therapy. In this process, the pharmacy team is often viewed as holding the magic key to drug acquisition. Although unfortunately we can't work magic, pharmacists do play a vital role in drug procurement, education of patients and healthcare providers about the process, and coordination of the many people involved in successfully prescribing and dispensing oral anticancer therapies. As oral therapies become more common in the treatment of cancer, awareness of the long and winding road of access to these therapies must be at the forefront of the oncology pharmacist's practice. ●●

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Deprescribing Interventions for Older Adults with Cancer and Polypharmacy

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Polypharmacy has been called "America's other drug problem."[1] Overuse of medications, especially in older adults, is a multifaceted issue and a large burden to our healthcare system. A diagnosis of cancer adds an additional layer of complexity.[1] A common barrier to evaluating polypharmacy is the heterogeneity of definitions and processes in the current medical literature. The study reviewed here, "Pharmacist-Led Medication Assessment and Deprescribing Intervention for Older Adults with Cancer and Polypharmacy: A Pilot Study," attempted to standardize polypharmacy assessment and subsequent deprescribing interventions in older adults with cancer.[2]

In this study, adult patients age 65 years or older with a diagnosis of cancer (of any type) were assessed in the Geriatric Oncology Clinic at the University of Virginia Health System.[2] Each patient was evaluated by a nurse, physical therapist, pharmacist, and geriatric oncologist. The pharmacist's role on this team was to complete a polypharmacy assessment and add it to the overall comprehensive geriatric assessment (CGA) score. A CGA helps determine existing, treatable health problems in older adults and aims to improve overall care outcomes (a detailed review of the CGA is beyond the scope of this review[3]). The first step to any effective deprescribing intervention is creating an accurate medication list. Therefore, the majority of the time was spent consolidating medication information. This included review of electronic health records, outside pharmacy records, patient reports, and caregiver feedback. All types of medications and supplements were included in the polypharmacy review. A deprescribing process was then applied to each inappropriate therapy.

The following themes were core to the success of the deprescribing interventions in this study:

1. Medication-condition matching

As displayed in **Figure 1** in the study, the medication-condition matching chart helped organize and highlight the specific indications for each therapy. Medications without obvious indications were flagged for further investigation and deemed potential deprescribing candidates. The chart also included "potential problems" in the medication-condition matching chart in order to help identify prescribing cascades or new medication-related adverse effects.

Why is this important?

This visual representation of medications brings to light the extent of medication burden and is often shocking to patients and providers. A missing indication can help prompt the question of whether prescribing cascades or prescribing inertia has occurred.

2. Comprehensive potentially inappropriate medication review (utilizing three assessment tools)

In this study, a three-tool assessment was used in order to be as comprehensive as possible. The Beers Criteria, Screening Tool of Older Persons' Prescriptions, and Medication Appropriateness Index have the strongest data supporting use in older adults with cancer.

Why is this important?

The concurrent, sequential use of these tools was chosen to maximize PIM identification; this combination of implicit and explicit screening tools proved to be effective. This is a novel method of polypharmacy evaluation that had not been evaluated in other studies in older adults with cancer.

3. Determination of medication-related "goals"

In this study, medication-related goals were assessed. This entailed verbal discussions regarding patient and caregiver opinions and attitudes toward general medication use (e.g., minimizing pill burden, optimizing quality of life, focusing on chronic disease state management). The study recognized that a limitation to evaluating medication-related goals was the lack of a well-validated patient-reported goals metric.

Why is this important?

In the course of pursuing deprescribing interventions, it is essential to be person-centric in making decisions. Patients with existing attitudes and opinions about deprescribing can make the action of deprescribing easier and more efficient. Methods to assess patient-reported outcomes related to medication "goals" warrants additional exploration in future studies.

4. Discussion of barriers to deprescribing

Patient and caregiver barriers to deprescribing were informally evaluated during each direct patient encounter. Each patient appointment was on average 15 minutes, and the majority of time was spent directly discussing patient and caregiving questions and fears about deprescribing. Barriers to deprescribing for providers were not assessed in this study.

Why is this important?

A growing body of literature is evaluating patient and provider barriers to deprescribing. It is important to identify barriers to deprescribing as soon as possible—this helps to drive decision making and improves transparency between providers. Since the completion of this pilot, studies looking at a method of assessing barriers to deprescribing has been validated (i.e., the Patients' Attitudes Towards Deprescribing questionnaire).[4-6] Common barriers for providers include reluctance to stop medications initiated by other providers, lack of ownership of the deprescribing process, and underappreciation of the scale of polypharmacy-related harm.

Figure 1. Example of a Pharmacist's Deprescribing Note[2]

89-year-old female who is being seen by pharmacy for assessment of polypharmacy and potentially inappropriate medications (PIMs).

Cancer type: pancreatic (unresectable, metastatic to liver)
ECOG: 1
Current symptoms: Decreased appetite; muscle aches; dizziness

Condition		Drug given for condition	Potential problems	Notes
1	Primary cardiac prevention	Aspirin 81 mg PO daily	GI bleeding; lack of benefit >80 years old per Beers Criteria	
2	HTN	Atenolol 50 mg PO daily	Fatigue; hypotension; orthostasis	BP = 144/64 mmHg
3	HTN	Hydrochlorothiazide 50 mg PO daily	Dehydration; orthostasis; ineffective	
4	Hyperlipidemia	Atorvastatin 40 mg PO daily	Time-to-benefit; myalgias; myopathy; fatigue	
5	Constipation	Docusate 50 mg PO BID	Ineffective therapy	Not taking
6	Hypothyroidism	Levothyroxine 50 mcg PO daily	Drug interactions; proper administration	
7	DM	Metformin 500 mg PO BID	Diarrhea; GI upset	
8	Sleep/appetite	Mirtazapine 15 mg PO HS	Sedation; falls; CNS depression	Nausea
9	Pain	Oxycodone 5 mg PO q4h PRN pain	Constipation; respiratory depression; CNS depression; falls	Not taking
10	Hypokalemia	Potassium chloride 20 meq PO BID	Pill burden; diarrhea; hyperkalemia	
11	**B12 deficiency**	**Vitamin B12 1000 mcg PO daily**		

*__Bold__ denotes a newly added medication.

OTHER MEDS (OTC, herbal, vitamins, etc.): n/a

Total number of medications = 11
Rx: 8 Herbal: 0 OTC: 3 Misc: 0

Medication allergies: NKDA

Drug interactions (Up-to-date; Micromedex)
There are 3 moderately significant drug interactions. Use of oxycodone with hydrochlorothiazide increases risk of orthostasis; a pharmacodynamic interaction is present between oxycodone and mirtazapine, and concomitant use increases the risk of CNS depression; finally, hydrochlorothiazide is known to increase glucose levels and may impair the antidiabetic effect of metformin.

Under use (START): calcium/vitamin D

Medications Assessment (Number of PIMs)
Beers: 1 STOPP: 1 MAI: 3

Time (mins) Medication Review	Time (mins) Patient Encounter	Number of PIMs	Number of Updates/ Changes*
12	17	5	6

***Description of medication changes**
1. Discontinued aspirin
2. Discontinued hydrochlorothiazide
3. Discontinued atorvastatin
4. Discontinued potassium chloride
5. Removed docusate from the med list
6. Removed oxycodone from the med list

(continued)

Pharmacist Recommendations

1. Primary prevention/PVD: The use of aspirin for primary prevention of cardiac disease in patients >80
2. Hypertension: The patient's blood pressure is currently at goal (<150/90 mmHg per JNC 8). Hydrochlorothiazide may be ineffective in elderly patients; there is a potential risk of dehydration and hypotension accompanied by the drug interaction with the patient's metformin. Recommend to discontinue hydrochlorothiazide and to continue to monitor blood pressures.
3. Hyperlipidemia: Statin medications have little utility in elderly cancer patients for primary prevention because of lack of time-to-benefit and the risk of myalgias, myopathies, and fatigue. The patient is also reporting muscle aches that could be caused by this medication. Recommend to discontinue atorvastatin without tapering.
4. Potassium supplementation: Recommend to discontinue potassium chloride tablets because of normal/slightly elevated potassium levels as well as pill burden.

Note. BID = twice daily; BP = blood pressure; CNS = central nervous system; DM = diabetes mellitus; ECOG = Eastern Cooperative Oncology Group; GI = gastrointestinal; HTN = hypertension; HS = at bedtime; MAI = Medication Appropriateness Index; NKDA = no known drug allergies; OTC = over-the-counter; PO = orally; PRN = as needed; PVD = peripheral vascular disease; q = every; Rx = prescription; STOPP = Screening Tool of Older Persons' Prescriptions.

Common barriers for patients include the belief that taking a medicine to prevent or treat a disease is always needed ("pill for every ill"), fear of drug withdrawal, and feeling "abandoned" or not worthy of treatment.

In our study,[2] data were collected for 26 patients during an 8-month period. The 26 patients in this study were taking a total of 312 medications, of which 197 were prescription and 113 were over-the-counter or alternative therapies. The mean number of medications per patient was 12. The Beers Criteria alone identified 38 potentially inappropriate medications (PIMs) compared to 119 PIMs with the three-tool assessment; a mean of 5 PIMs per patient was identified. After the application of the three-tool assessment, 73% of PIMs identified were deprescribed in real time by the pharmacist and geriatric oncologist, resulting in a mean of three medications deprescribed per patient. Based on University Health System Consortium outcomes cost data, healthcare expenditures of $111,390 were potentially avoided as a result of PIM assessment and deprescribing. Fifty-two percent of patients reported no barriers related to stopping medications and felt comfortable with the process. Of the patient-reported barriers to deprescribing, the most common concern was fear of return of symptoms or worsening of the underlying condition being treated.

This is one of the first studies to demonstrate the effectiveness of a standard approach to polypharmacy assessment and deprescribing in older adults with cancer. The three-tool assessment process should be incorporated into interdisciplinary assessments of older patients with cancer and validated in future studies. Deprescribing should be seen as an individualized assessment of medications that is driven by patient and caregiver goals as well as evidence-based medicine. ●●

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Sequencing the Treatment of Metastatic Castration-Resistant Prostate Cancer

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Prostate cancer is the second most common cancer among males, with an estimated 191,130 new cases in 2020, and the second leading cause of cancer-related death in males in the United States.[1,2] Localized and regional disease confers a relatively optimistic prognosis, with 5-year overall survival of 100% versus 30% for patients with advanced disease.[2] Treatment of advanced prostate cancer is driven by androgen deprivation therapy via surgical or medical castration with a luteinizing hormone-releasing hormone (LHRH) agonist or antagonist, with or without an antiandrogen or abiraterone.[2] The goal is to achieve castrate levels of testosterone <50 ng/dL to reduce hormonal stimulation of cancer growth. Eventually, many patients with metastatic disease develop castration resistance, known as metastatic castration-resistant prostate cancer (mCRPC), characterized by cancer progression despite the use of standard androgen deprivation therapy and maintainence of castrate levels of testosterone.[2,3]

"Historically, minimal data were available to guide the sequence of therapies for metastatic castration-resistant prostate cancer."

The recommended treatments used in the mCRPC setting include taxanes (docetaxel and cabazitaxel), androgen-signaling-targeted inhibitors (ASTIs) (abiraterone and enzalutamide), sipuleucel-T, and radium-223 dichloride.[4] Cabazitaxel is a next-generation taxane approved for mCRPC in patients previously treated with a docetaxel-based regimen.[5] It has been shown to retain activity in patients who previously failed treatment with docetaxel or an ASTI.[5-7] Abiraterone inhibits CYP17A1, an essential enzyme involved in androgen synthesis, which is often upregulated in mCRPC and contributes to resistance.[8] Enzalutamide inhibits the androgen receptor and is able to overcome upregulated androgen-receptor expression implicated in resistance and disease progression.[9] Historically, minimal data were available to guide the sequence of therapies for mCRPC. This article summarizes recently published studies evaluating the sequencing of cabazitaxel, abiraterone, and enzalutamide for mCRPC.

Cabazitaxel Versus Abiraterone or Enzalutamide in mCRPC: The CARD Trial

De Wit and colleagues conducted a multicenter randomized open-label trial at 62 sites across Europe, investigating whether cabazitaxel is superior to abiraterone or enzalutamide in mCRPC patients previously treated with docetaxel and an ASTI.[10] Included were mCRPC patients previously treated with at least three cycles of docetaxel with disease progression occurring during 12 months of therapy with abiraterone or enzalutamide before or after the docetaxel. Patients were randomized 1:1 to receive cabazitaxel or an ASTI not previously given, and the treatments continued until imaging-based confirmation of disease progression, unacceptable toxicity, initiation of subsequent therapy, or another request to discontinue. Cabazitaxel was administered as 25 mg/m^2 intravenously (IV) over 1 hour every 3 weeks plus prednisone 10 mg orally daily according to the European drug label. Abiraterone was administered as 1000 mg orally daily plus prednisone 5 mg orally twice daily to patients who had previously received enzalutamide. Enzalutamide was given as 160 mg orally daily to patients who had previously received abiraterone. Crossover to the opposite treatment arm was allowed upon disease progression. Patients were stratified according to Eastern Cooperative Oncology Group (ECOG) performance status 0–1 versus 2, time to disease progression ≤6 months versus >6–12 months, and timing of previous ASTI before docetaxel versus after docetaxel. The primary outcome evaluated was imaging-based progression-free survival (PFS).

Between November 2015 and November 2018, 255 subjects were included in this study, with 129 patients randomized to receive cabazitaxel and 126 randomized to receive either abiraterone (n = 58) or enzalutamide (n = 66). The median duration of treatment was longer in the cabazitaxel group (22 weeks vs. 12.5 weeks), and more patients discontinued therapy in the ASTI group overall (63.5% with cabazitaxel vs. 79.9% with an ASTI), mostly because of disease progression (43.7% vs. 71%, respectively). At median follow-up at 9.2 months, median PFS was 8 months versus 3.7 months in favor of cabazitaxel (hazard ratio [HR] = 0.54, p < .001). Median overall survival (OS) was significantly improved with cabazitaxel (13.6 months vs. 11 months; HR = 0.64, p = .008). Prostate-specific antigen (PSA), tumor, and pain response rates were all improved with cabazitaxel (PSA response, 35.7% vs. 13.5%, p < .001; tumor response, 37% vs. 12%, p = .004; pain response, 45% vs. 19.3%).

In a comparison of safety outcomes, the proportion of patients with adverse effects (AEs) of any grade and serious AEs were similar (38.9% vs. 38.7% serious AEs). AEs leading to discontinuation were more common with cabazitaxel (19.8% vs. 8.9%), but cabazitaxel patients required fewer dose reductions (21.4% vs. 37.9%). The most common grade ≥3 AEs reported for cabazitaxel versus ASTI respectively were infection (7.9% vs. 7.3%), musculoskeletal pain (1.6% vs. 5.6%), fatigue (4% vs. 2.4%), diarrhea (3.2% vs. 0), and peripheral neuropathy (3.2% vs. 0).

The CARD trial concluded that mCRPC patients previously treated with docetaxel and an ASTI achieved significantly longer imaging-based PFS and OS with cabazitaxel versus the alternative ASTI, despite crossover between treatment arms. Statistically significant benefit or trend toward benefit with cabazitaxel was seen across all subgroups, including ECOG performance status 0–1 versus 2, timing of ASTI before or after docetaxel, disease severity, and type of previous progression.[10] These results align with previous data revealing poor outcomes for patients immediately initiating an alternative ASTI after progression, likely because of similar resistance mechanisms between agents.[11] Regarding therapy sequencing, this trial suggests that cabazitaxel should be used before the alternative ASTI in subsequent treatment of mCRPC.[10] Conclusions from this trial are limited by its open-label design, lack of blinding for central review of imaging, and geographic limitation to Europe using the approved European cabazitaxel dosage. In addition, the CARD study lacks a subgroup analysis evaluating efficacy specific to abiraterone followed by randomization to enzalutamide or cabazitaxel. It is unclear whether cabazitaxel would still be favored if this sequence was specified.

Sequencing of Enzalutamide and Abiraterone in mCRPC

Khalaf and colleagues conducted a randomized open-label trial at six centers in British Columbia, Canada, assessing the ideal sequencing of ASTIs in patients with newly diagnosed mCRPC (N = 202).[12] Patients were randomized 1:1 to abiraterone 1000 mg orally daily plus prednisone 5 mg orally twice daily, followed by enzalutamide 160 mg orally daily after PSA progression (abiraterone-enzalutamide, n = 101), or the opposite sequence (enzalutamide-abiraterone, n = 101). Treatment continued until symptomatic or clinical disease progression, unacceptable toxicity, or patient withdrawal. Patients were allowed prior docetaxel treatment for castration-sensitive disease and had to maintain LHRH agonist treatment throughout the study if they had no history of orchiectomy. Patients were excluded if they had previously taken abiraterone, enzalutamide, or another experimental ASTI. Primary outcomes included time to second PSA progression (time from start of first-line treatment to confirmed PSA progression on second-line treatment, or death from prostate cancer before crossover, whichever occurred first) and proportion of patients with PSA response on second-line therapy.

Patients were enrolled from October 2014 to December 2016 and had a median 22.8 months follow-up for analysis of the intention-to-treat population. At data cutoff, 72% and 74% from the abiraterone-enzalutamide group and enzalutamide-abiraterone group, respectively, had crossed over to second-line therapy. For the primary outcomes, median time to second PSA progression was significantly longer in the abiraterone-enzalutamide group (19.3 months vs. 15.2 months; HR = 0.66, p = .036), and PSA response with second-line treatment was significantly higher with abiraterone-enzalutamide (36% vs. 4%; p < .0001). Median time to PSA progression on second-line treatment was also significantly longer with abiraterone-enzalutamide (3.5 months vs. 1.7 months; HR = 0.42, p < .0001). However, no significant difference was seen in median OS (28.8 months vs. 24.7 months; p = .23), nor in median time to first progression (11.2 months vs. 10.2 months; p = .78), although PSA response rate with first-line treatment was significantly higher with enzalutamide-abiraterone (68% vs. 82%; p = .023).

Regarding safety outcomes, serious AEs were more common with enzalutamide-abiraterone (15% vs. 20%), and more patients on enzalutamide required dose reductions (6% vs. 18% with first-line treatment and 19% vs. 5% with second-line treatment).

In summary, enzalutamide showed significantly improved activity as a second-line agent over abiraterone, with prolonged time to second progression and a higher PSA response rate. Each drug was equally effective in the first-line setting according to median time to first PSA progression, despite higher PSA response in the first-line setting with enzalutamide. This study suggests that the greatest clinical benefit comes from the sequencing of agents with abiraterone followed by enzalutamide. Improved time to second PSA progression in the abiraterone-enzalutamide group seems to have been driven by second-line activity of enzalutamide, which was improved compared with abiraterone. A possible mechanism behind the efficacy of enzalutamide in the second-line setting is its ability to overcome abiraterone resistance conferred by progesterone-activated, androgen receptor ligand–binding domain mutations L702H and T878A, found in approximately 15%–20% of mCRPC cases.[13,14]

Conclusion

The CARD study suggests that cabazitaxel followed by an ASTI after relapse on docetaxel and the opposite ASTI is useful.[10] Khalaf and colleagues compared sequences of ASTIs in the upfront setting of mCRPC treatment, with results showing improved outcomes using abiraterone followed by enzalutamide.[12] Combining the results of these studies, new research questions emerge, such as whether cabazitaxel is more efficacious when used before or after abiraterone, and, similarly, whether abiraterone is more efficacious when used before or after docetaxel. ●●

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Board Update

Accelerating to the Next Chapter

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As we move into September, I think of this quotation from Henry David Thoreau: "One must maintain a little bit of summer, even in the middle of winter." I hope that you and your family had the opportunity for some relaxation this summer and that you' ll be able to enjoy the outdoors and observe the colorful autumn foliage despite the challenges of COVID-19.

Member Activity

Our organization was very active in advocacy efforts this past spring. I want to recognize specifically the activity of the Public Policy Committee. Members of this group collaborated with the pharmacy community on the Joint Policy Recommendations to Combat the COVID-19 Pandemic, participated in two meetings with the U.S. Food and Drug Administration/Center for Drug Evaluation and Research regarding COVID-19, met with representatives of the Centers for Medicare and Medicaid Services regarding pharmacists and COVID-19 testing and billing, promoted the addition of pharmacists in the Student Loan Forgiveness for Frontline Health Workers Act (H.R 6720), worked with the Pharmacy Health Information Technology Collaborative to support pharmacists in connection with the 2021 and 2022 Medicare Advantage and Part D Proposed Rule (CMS-4190-P) on telehealth, and created and disseminated an oncology drug shortage survey to our membership. The board is immensely grateful for the efforts of the Public Policy Committee and to HOPA staff member Dominic Sawaya and advocacy consultant Jeremy Scott.

This summer we were unable to gather in person at the American Society of Clinical Oncology (ASCO) annual meeting, but through the virtual format we were able to sift through the abundant information on the valuable efforts of oncology pharmacists. Shannon Hough presented on the efforts of several oncology pharmacists at the University of Michigan in leading a remote care monitoring program for patients with chemotherapy-induced nausea and vomiting. The team's collaborative efforts led to a significant reduction in urgent care visits associated with nausea. Also, an abstract from PGY-1 resident Amin Virani reported that the interventions provided by an oncology pharmacist in a myeloma clinic were associated with a predicted annual value of $757,000. It is wonderful to see the value of the oncology pharmacist presented on national and international platforms.

Virtual Practice Management Program

Speaking of venues promoting the activities of oncology pharmacy, we hope your fall plans included joining us on September 11—just about the time this newsletter reaches your mailbox—for the eighth annual HOPA Practice Management program, to be held as a virtual meeting this year. Our Practice Management Program Committee has been busy converting our traditional meeting into a virtual format to accommodate our members' needs. This program features a presentation on quality- and value-based strategy, practice pearls sessions, and a panel discussion on oncology systems. As all are aware, COVID-19 has dramatically changed the landscape of health care; this meeting will give oncology pharmacy managers and directors the opportunity to discuss their experiences during these challenging times. Additional educational content on practice management will be released following the 1-day meeting and also presented at HOPA's 2021 Annual Conference.

Looking Back, Looking Forward

HOPA members, committees, and task forces continue to be energetically engaged in activities outlined in our new strategic plan (2020–2023). The HOPA board wants to thank you again for your service to the organization, particularly during these unusual times. These groups have also observed our ongoing transition to a new management company. The decision to end our relationship with Association Management Center (AMC) was not easy: HOPA and AMC have had a longstanding partnership that has led to the growth of the organization and many meaningful relationships between staff and volunteers. The board would like to recognize the efforts and leadership of Steve Smith, AMC's CEO, and Stacy Sochacki, who has served as HOPA's interim executive director. Stacy has been a tremendous asset to the organization in providing guidance on strategy and governance. She has fostered a positive culture with the staff and has been essential in our work toward a seamless transition in the past several months. Another person I would like to recognize is Sarah Tiwana, HOPA's director of operations. There isn't enough room on this page for the positive adjectives that describe Sarah's impact on HOPA during the past several years. I would encourage volunteers to communicate with these individuals and thank them for their service to HOPA.

Starting on October 1, HOPA's management company will be Executive Director Incorporated (EDI) in Milwaukee, WI. EDI is one of the top association management companies in the United States, providing counsel and management for 35 national and global medical, health, and scientific associations and certifying bodies. Tara Withington, vice-president of EDI and current executive director for the Society for Immunotherapy of Cancer, has been working with AMC leadership on this transition. At the time of writing, the new HOPA team is being recruited. Announcements about the addition of key personnel will be made at a future time.

HOPA now has more than 3,650 members, and approximately 300 members participate on HOPA committees and task forces. The next chapter for HOPA is about to begin. The board hopes you share our enthusiasm and energy for our future! Much promise lies ahead. ●●

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