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Emerging BCMA-Directed Therapies in Multiple Myeloma: Bispecific Antibodies and CAR T-Cell Therapies

AMIR ALI, PHARMD, BCOP; KEVIN LE, PHARMD, BCOP; TANJIA TOMA, PHARMD CANDIDATE; SOUMAR HADDAD, PHARMD CANDIDATE; FLEURI DINDAR, PHARMD CANDIDATE; AND BRYAN CEBALLOS, PHARMD CANDIDATE

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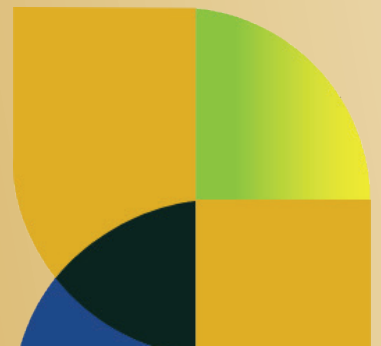
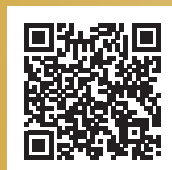
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Publisher's Note

Advancements in Multiple Myeloma Therapies and Operational Insights in Oncology Clinical Trials

MULTIPLE MYELOMA (MM) is characterized by abnormal plasma cell proliferation and monoclonal immunoglobulin production, often presenting with hypercalcemia, renal dysfunction, anemia, and bone lesions. The introduction of proteasome inhibitors, immunomodulatory agents, and anti-CD38 monoclonal antibodies has revolutionized treatment, extending survival rates. Among recent advances, bispecific antibodies (bsAbs) and chimeric antigen receptor (CAR) T-cell therapies have reshaped the treatment landscape, offering new options for relapsed/refractory (R/R) MM.

In the cover feature on page 10, Amir Ali, PharmD, BCOP; Kevin Le, PharmD, BCOP; Tanjia Toma, PharmD candidate; Soumar Haddad, PharmD candidate; Fleuri Dindar, PharmD candidate; and Bryan Ceballos, PharmD candidate, provide an updated overview of the role of BCMA-directed therapies following the 2024 American Society of Clinical Oncology Annual Meeting and 29th European Hematology Association Congress, particularly looking at bsAbs and CAR T-cell therapies for R/R MM. Among BCMA-directed bsAbs, BCMA-targeting bsAbs teclistamab (Tecvyli; Janssen Biotech) and elranatamab (Elrexfio; Pfizer) demonstrate similar efficacy and safety profiles. However, elranatamab offers logistical advantages, including shorter hospitalization and fixed dosing. Talquetamab, with its unique GPRC5D target, provides high response rates and flexibility for sequential or combination use. While CAR T-cell therapies show unprecedented efficacy, their one-time administration contrasts with the continuous nature of bsAbs. Optimal sequencing between bsAbs and CAR T-cell therapy remains an area of ongoing research to maximize therapeutic benefit.

In original research on page 15, Kaycey Pearce, PharmD; and Jennifer Murphy, PharmD, BCOP, BCPS, focus on operational challenges within oncology clinical trials. The authors analyze factors influencing infusion appointment duration and arrival-to-chair time for oncology clinical trial patients at UC Davis Comprehensive Cancer Center in Sacramento, California, from 2019 to 2022. Despite initial hypotheses, most intrinsic and extrinsic variables, such as study type, pharmacokinetic requirements, and AM/PM scheduling, showed no statistically significant impact on appointment duration or wait times. However, phase 3 trials and appointments involving multiple investigational products (IPs) significantly increased duration, highlighting these as key areas for improvement. Age was inversely associated with appointment duration, possibly reflecting less intensive protocols for older patients. The findings underscore the need for targeted strategies in multi-IP trials and advanced trial phases to enhance efficiency.

The treatment landscape for MM continues to evolve with the integration of innovative therapies such as bsAbs and CAR T-cell therapies. Continued research is essential to optimize the use and sequencing of these therapies, ensuring maximum patient benefit in this dynamic treatment era. Further, operational improvements in oncology clinical trials, particularly for complex protocols, remain critical to advancing patient care.

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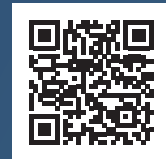
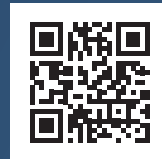
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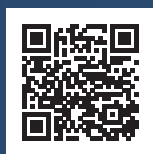
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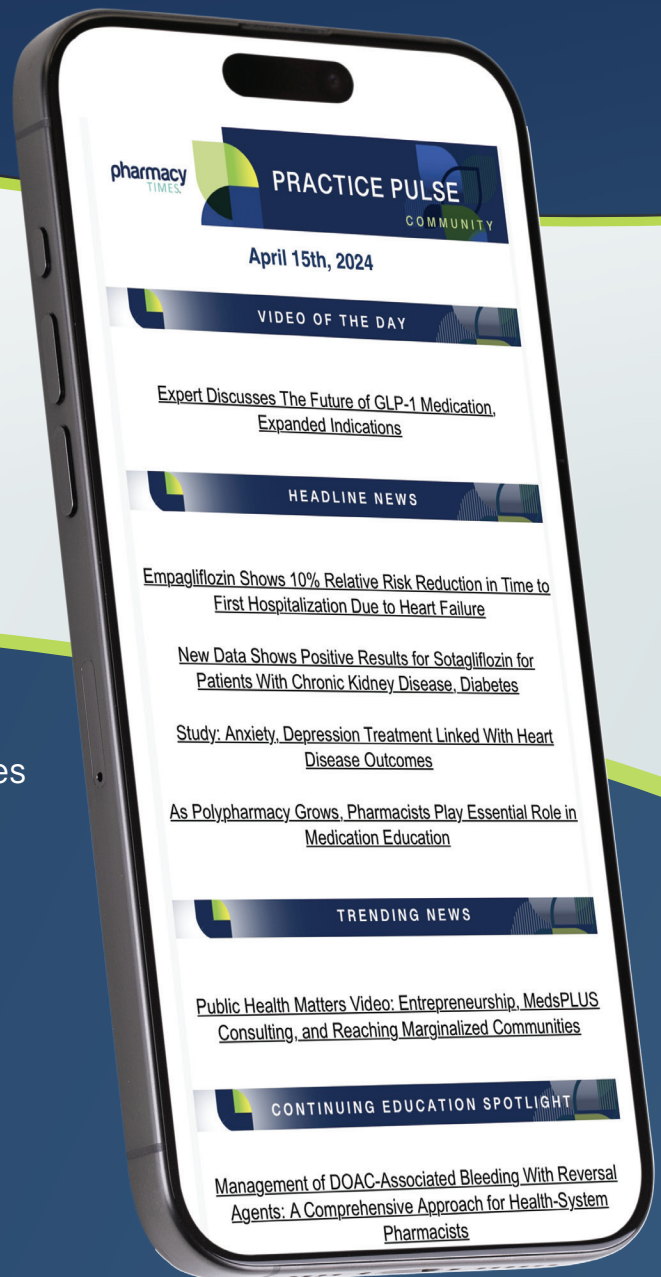
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Advocacy in Action: Opportunities for Oncology Pharmacists in 2025

Zahra Mahmoudjafari, PharmD, MBA, BCOP, FHOPA

ABOUT THE EDITOR IN CHIEF

Zahra Mahmoudjafari, PharmD, MBA, BCOP, FHOPA, is a clinical pharmacy manager in the Blood and Marrow Transplant Program in the Division of Hematologic Malignancies and Cellular Therapeutics at the University of Kansas Cancer Center in Kansas City, Kansas. Mahmoudjafari is a board-certified oncology pharmacist involved in several oncology-pharmacy organizations, such as the Hematology/Oncology Pharmacy Association (HOPA), currently serving as secretary on the HOPA board of directors. She has also been the chair or cochair of conferences such as Advanced Topics for Oncology Pharmacy Professionals and Oncology Pharmacists Connect. In 2022, she was the recipient of the American Society for Transplantation and Cellular Therapy Pharmacy Special Interest Group Lifetime Achievement Award and received the American Society of Clinical Oncology's 40 Under 40 in Cancer Award.

Mahmoudjafari has presented nationally on her experience with managing high-cost therapies and on clinical topics such as cell and gene therapies, acute and chronic graft-vs-host disease, and the management of fungal infections in hematopoietic stem cell transplantation. Mahmoudjafari completed her pharmacy training at the University of Missouri-Kansas City (UMKC) and her PGY-1 pharmacy practice residency at The Ohio State University Wexner Medical Center. She completed her PGY-2 oncology residency at Huntsman Cancer Institute at the University of Utah and most recently received her MBA from Henry W. Bloch School of Management, which is affiliated with UMKC.



As we close out 2024, I cannot help but reflect on the past year. One of my best memories was attending the Hematology/Oncology Pharmacy Association (HOPA) Hill Day in September. Hill Day is when we, as pharmacists, step out of our usual roles in clinics, hospitals, or research settings to engage directly with policy makers. Walking into a congressional office to discuss complex health care policies can feel intimidating for many participants,

including me. Sometimes, this is not second nature, and distilling nuanced pharmacy and oncology issues into concise, compelling messages for a nonexpert audience can be challenging. Yet, as I stood alongside my HOPA colleagues and shared our collective passion for improving oncology care, the initial nervousness gave way to empowerment.

Advocacy is about connection—with lawmakers and with each other, as well as connecting our knowledge to the broader health care landscape. During Hill Day, we focused on critical issues impacting oncology care, including access to affordable medications, the role of the pharmacist in interdisciplinary teams, and the importance of funding for cancer research. Our collective goals were not only to educate but also to inspire action. Hill Day reinforced the importance of advocating for policies that elevate the role of pharmacists in oncology care. We shared with lawmakers how pharmacists contribute to better patient outcomes by managing complex medication regimens, mitigating adverse effects, and providing critical education. Yet, despite our expertise, many of us still face barriers to practicing at the top of our license due to state and federal regulations. I was pleasantly surprised to see the engagement of the various staffers in both the US House of Representatives and the US Senate, and I am already looking forward to participating in future Hill Day events.

As we look ahead to 2025, the Inflation Reduction Act (IRA) is set to impact our oncology patients significantly. The IRA's measures to cap out-of-pocket costs for Medicare beneficiaries, enable price negotiation for certain high-cost drugs, and

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Pharmacists can influence change, not just for our profession but for the patients we serve.

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redesign the Medicare Part D benefit structure represent monumental shifts in how patients access and afford their medications. These changes hold promise for reducing the financial toxicity often experienced by patients with cancer. However, these changes also come with challenges that require careful navigation. As oncology pharmacists, we must stay informed and proactive, ensuring that these policies benefit patients without compromising access to innovative therapies. Additionally, the new out-of-pocket caps for Medicare beneficiaries will necessitate a recalibration of how we support patients clinically and financially. Many of us are already familiar with the hurdles patients face when navigating co-pays, deductibles, and insurance approvals. The IRA's reforms offer an opportunity to ease these burdens, but only if we adapt our practices to the new landscape. This might mean collaborating more closely with financial navigators, advocating for institutional resources to support medication access, or engaging directly with payers to ensure coverage aligns with clinical needs. Oncology pharmacists are pivotal in caring

for our patients, and understanding the IRA is no exception.

As we move forward, I encourage you to find ways to engage in advocacy. Pharmacists bring a unique perspective to health care that bridges clinical knowledge, patient-centered care, and operational expertise. When we step into advocacy roles, we amplify this perspective, shaping policies that directly impact the lives of our patients and the sustainability of our health care system. This might mean attending Hill Day, writing to your elected officials, or starting conversations about policy within your workplace. Advocacy does not require perfection or expertise—it requires passion and a willingness to act.

Pharmacists can influence change, not just for our profession but for the patients we serve. As the oncology care landscape evolves, let us commit to actively shaping its future. Our work today will lay the foundation for more equitable, accessible, and effective care tomorrow.

I wish you all a happy and healthy New Year and look forward to seeing you at a pharmacy conference event in 2025. 🌍



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Emerging BCMA-Directed Therapies in Multiple Myeloma: Bispecific Antibodies and CAR T-Cell Therapies

Here is an updated overview of the role of BCMA-directed therapies following the 2024 ASCO Annual Meeting and EHA Congress.

Amir Ali, PharmD, BCOP; Kevin Le, PharmD, BCOP; Tanjia Toma, PharmD candidate; Soumar Haddad, PharmD candidate; Fleuri Dindar, PharmD candidate; and Bryan Ceballos, PharmD candidate

ABOUT THE AUTHORS

Amir Ali, PharmD, BCOP, is a clinical pharmacist specialist at USC Norris Comprehensive Cancer Center and an adjunct assistant professor of pharmacy practice at USC Alfred E. Mann School of Pharmacy and Pharmaceutical Sciences in Los Angeles, California.

Kevin Le, PharmD, BCOP, is an inpatient oncology and bone marrow transplant pharmacist at USC Norris Comprehensive Cancer Center in Los Angeles, California.

Tanjia Toma is a PharmD candidate at USC Alfred E. Mann School of Pharmacy and Pharmaceutical Sciences.

Soumar Haddad is a PharmD candidate at USC Alfred E. Mann School of Pharmacy and Pharmaceutical Sciences.

Fleuri Dindar is a PharmD candidate at USC Alfred E. Mann School of Pharmacy and Pharmaceutical Sciences.

Bryan Ceballos is a PharmD candidate at USC Alfred E. Mann School of Pharmacy and Pharmaceutical Sciences.

Multiple myeloma (MM) is a hematologic malignancy involving an abnormal clonal proliferation of plasma cells in the bone marrow, along with their excess production of monoclonal immunoglobulin (M protein).¹ Malignant plasma cells on biopsy and M protein in serum and urine are required for diagnosis, with a decrease from baseline indicating a positive response to treatment.¹ Myeloma-defining features include hypercalcemia, renal insufficiency, anemia, and bone lesions.¹ MM is considered incurable yet treatable, and it grows slowly in its earlier Revised International Staging System (R-ISS) stages. At diagnosis of R-ISS stage I, the median 5-year survival rate is 77% and declines to 47% in R-ISS stage III.¹

The substantial improvement in survival rates since the approval of the first proteasome inhibitor and immunomodulatory agent in the 2000s is due to advancements in the treatment landscape, notably combination regimens and newer generations of treatment options. At diagnosis, assessing a patient's candidacy for autologous hematopoietic stem cell transplantation is standard of care, as it influences the choice of initial combination regimen. In transplant-eligible patients, the first-line treatment regimen includes a combination of a proteasome inhibitor, an immunomodulatory agent, and a corticosteroid. The most used regimen is known as RVd or VRd (injectable bortezomib [Velcade; Takeda], oral lenalidomide [Revlimid; Bristol Myers Squibb], dexamethasone [Decadron; Pfizer]).¹

In patients who are transplant ineligible, preferred primary therapy options

include VRd-based regimens or DRd (daratumumab [Darzalex; Johnson & Johnson], lenalidomide, dexamethasone).² Anti-CD38 monoclonal antibodies, such as daratumumab, have become a mainstay in the combination regimens due to their demonstrated ability to improve outcomes.² Several clinical trials, including PERSEUS (NCT03710603), IMROZ (NCT03319667), and MAIA (NCT02252172), have shown benefits in terms of progression-free survival (PFS) with the addition of anti-CD38 monoclonal antibodies to lenalidomide and dexamethasone-based regimens in the frontline setting.²⁻⁴

According to National Comprehensive Cancer Network (NCCN) guidelines, there is no clear consensus on the treatment of relapsed/refractory (R/R) MM with multiple agents and/or regimens. The main goal of treatment is to prolong overall survival (OS), ideally accompanied by improvements in quality of life. Although these combination regimens have extended OS, it is commonly shorter in R/R MM compared with patients newly diagnosed with MM. Novel therapies such as chimeric antigen receptor (CAR) T-cell therapies and bispecific antibodies (bsAbs) demonstrate significant and ongoing advancements in treating R/R MM.

There have been 3 approvals of bsAbs since 2022, including teclistamab (Tecvayli; Janssen Biotech), talquetamab (Talvey; Janssen Biotech), and elranatamab (Elrexfio; Pfizer). These bsAbs can be further separated. Teclistamab and elranatamab target B-cell maturation antigen (BCMA); talquetamab targets G protein-coupled receptor, class C, group 5, member D (GPRC5D). In addition, the field has grown with the expanded

indications for 2 FDA-approved BCMA-targeted CAR T-cell therapies, idecabtagene vicleucel (Abecma; Bristol Myers Squibb) and ciltacabtagene autoleucel (Carvykti; Johnson & Johnson). With updated clinical evidence, the NCCN guidelines now place CAR T-cell therapies in earlier lines of therapy, and they remain a fourth line alongside the 3 bsAbs.

In April 2024, ciltacabtagene autoleucel moved from the fifth line to include an option as a second line for patients who are refractory to lenalidomide and have been exposed to a proteasome inhibitor.⁵ In April 2024, the FDA also announced an expanded indication for idecabtagene vicleucel to be included as a third-line option for R/R MM.⁶ With this, there is a need to reassess the role of bsAbs in therapy, particularly bsAbs that also target BCMA. Whether bsAbs offer significant benefits if introduced earlier as monotherapy similar to CAR T-cell therapy or in combination regimens remains an area of ongoing investigation.

With the rapid emergence of new agents with similar mechanisms and overlapping indications, there is a need to discuss their potential unique roles in our growing landscape, given the absence of head-to-head trials. By integrating emerging evidence and practical considerations and outlining key differences, we aim to provide an updated overview of the role of BCMA-directed therapies that can be used to facilitate clinical decision-making. We will also closely compare the BCMA-directed bsAbs and their optimal timing relative to CAR T-cell therapy to provide nuanced insights into the implications of any observed differences with a focus on efficacy and safety. The practical considerations will consider factors such as cost-effectiveness and pharmacy operational efficiency, as these are often incorporated decision-making when there may be optimal usage of 1 of 3 available bsAbs across institutions.

Examining Efficacy and Safety Between the BCMA-Directed bsAbs

Teclistamab and elranatamab are structurally similar bsAbs that target BCMA and CD3, recruiting T cells to attack the abnormal plasma cells. With both having symmetrical BCMA-binding Fab domains, their main structural distinction lies in their Fc backbone. Based on our literature search, no biochemical structural analyses demonstrate differences in BCMA epitope binding or binding affinities. Therefore, it is difficult to predict differences in efficacy grounded on any potential variations in their mechanism or drug properties. In the absence of head-to-head trials, it is crucial to closely compare and critically appraise nuanced differences to inform clinical decision-making on the optimal use of each.

Teclistamab was the first bsAb to receive approval in 2022, followed by elranatamab in 2023.^{7,8} In the phase 1 MajesTEC-1 trial (NCT03145181), the overall response rate for teclistamab was 63% with a complete response (CR)

rate or better of 39.4%.⁹ The median time to response was approximately 1 month.⁹ After a median follow-up of 14.1 months, the median PFS was 11.3 months.⁹ The median OS of 18.3 months and median duration of response (DOR) of 18.4 months were both immature.⁹ Long-term follow-up data from MajesTEC-1 were presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting. At an extended follow-up period of 30.4 months, the overall response rate remained at 63%; however, the CR rate was 46.1%.¹⁰ The median PFS remained the same at 11.4 months.¹⁰ Consequently, an increased median OS of 22.2 months and an increased median DOR of 24 months were seen for all responders.¹⁰ The extended follow-up confirms that the responses are durable and deepened over time.

In a multi-institutional real-world study with a patient population comprising a higher proportion of high-risk MM and a significantly higher proportion with penta-drug refractoriness, teclistamab maintained a very good partial response (PR) rate or better of 51% compared with 58.8% in MajesTEC-1.¹¹ Teclistamab showed similar efficacy with an overall response rate of 66% in a second study composed of a heavily pretreated patient population with a significantly high portion of penta-drug refractory disease.¹² Whereas the extended follow-up strengthens the reliability of the observed data, the real-world evidence provides complementary data showing how teclistamab may perform in practice, suggesting comparable efficacy in a heavily pretreated, high-risk patient population.

The study design of the phase 2 MagnetisMM-3 trial (NCT04649359) for elranatamab was similar to MajesTEC-1, which included comparable methodologies with minor differences in the participant selection criteria.¹³ Among the notable key differences was the inclusion of triple-class exposed participants in MajesTEC-1 compared with triple-class refractory participants in MagnetisMM-3. In MagnetisMM-3, after a median follow-up of 14.7 months, the objective response rate was 61%, with a CR rate of 35%.¹³ The median time to response was approximately 1 month.¹³

Long-term follow-up data from MagnetisMM-3 were presented at the 2024 ASCO Annual Meeting. With an extended follow-up of 28.4 months, the objective response rate remained at 61%, with a CR at 37.4%.¹⁴ The median OS was 24.6 months, with a median PFS at 17.2 months.¹⁴ A comparison between the 2 studies demonstrated that teclistamab had a higher stringent CR rate at more than 2-fold that of elranatamab.^{9,13} It is also important to recognize the differences in the characteristics of participants at baseline, which may limit this takeaway. In addition to slight differences across the proportions of ISS risk stage, cytogenetics risk profile, median number of lines of previous therapy, and penta-drug refractoriness, the percentage of extramedullary disease (EMD) was 17% for teclistamab vs 31.7% for elranatamab. However, EMD was strictly defined

as true soft tissue plasmacytomas for teclistamab, whereas this was broadened to include extramedullary and/or paramedullary disease with a soft tissue component for elranatamab. Based on this information, it is difficult to conclude whether elranatamab may be more efficacious in patients with poor prognostic features.

The direct comparison of tolerability and safety profiles in MagnetisMM-3 and MajesTEC-1 is complicated by differing criteria for discontinuation across the trials. Treatment-emergent adverse events (AEs), notably infections, constituted a smaller proportion of all discontinuations. Overall, discontinuation rates were 58% for teclistamab compared with 67% for elranatamab, and the trend was consistent with interruptions in dosing, which were 63% for teclistamab compared with 77% for elranatamab.^{9,13} Disease progression constituted the largest proportion of all discontinuations, representing 64% for teclistamab compared with 59% for elranatamab.^{9,13}

Matching could clarify the inconsistencies in the trends observed. It is easier to match safety profiles given that the same criteria are used to evaluate outcomes such as infection, cytokine release syndrome (CRS), and immune effector cell–associated neurotoxicity syndrome (ICANS). For teclistamab, 76% of participants experienced all-grade infections, with 45% experiencing grade 3 or 4 infections.⁹ For elranatamab, 70% of participants experienced all-grade infections, with 40% experiencing grade 3 or 4 infections.¹³ A meta-analysis demonstrated that more than half of all patients experienced all-grade infections, with a quarter experiencing grade 3 or 4 infections.¹⁵ There was significant heterogeneity in the percentage of infections across trials.¹⁵ This variability is attributable to differences in the approaches to anti-infective prophylaxis and management. Although specific guidelines are lacking, unique recommendations include universal *Pneumocystis jirovecii* pneumonia prophylaxis and intravenous immunoglobulin as indicated. Given the higher risk of severe infection with BCMA-directed therapies compared with non-BCMA therapies, a comprehensive approach to anti-infective prophylaxis and management is necessary, irrespective of institutional variations.^{15,16} Among all participants, CRS and ICANS occurred in 72% and 3% of cases for teclistamab compared with 56% and 3% for elranatamab, respectively.^{9,13} This trend aligns with the use of tocilizumab (Actemra; Genentech) and corticosteroids for managing CRS. Tocilizumab and corticosteroids were administered in 36% and 9% of participants receiving teclistamab compared with 23% and 8% of participants receiving elranatamab, respectively.^{9,13}

The onset and severity of CRS and ICANS observed followed a consistent pattern. Grade 1 or 2 CRS occurred mostly during step-up dosing with a median onset of 2 days and duration of 2 days.^{9,13} Given that the pattern is

highly predictable, the step-up dosing is administered in an inpatient setting, whereas the maintenance dosing is administered in an outpatient setting. Based on the current evidence, no other tolerability or safety differences clearly distinguish one BCMA-directed bsAb from another.

Other Practical Considerations

Because current literature leads us to believe that the efficacy and safety profiles of the BCMA-directed bsAbs are proportionate, pharmacoeconomic considerations should be made to establish a preference for one bsAb over another (**Online Table**).^{10,14,17-19} For a typical patient with MM weighing 85 kg, lower cumulative drug acquisition costs are provided by teclistamab. Specifically, our calculations show that over 12 months, the total cost of teclistamab is \$427,210 compared with \$543,171 for elranatamab, which results in a 27% wholesale acquisition cost (WAC) savings. Looking closer at cost per treatment vial, the cost for teclistamab is lower, with a weighted average of \$10,521 compared with \$13,051 for elranatamab, yielding a 24% drug cost premium for elranatamab per vial. The average WAC price of teclistamab for a weekly dose is \$9478 compared with \$13,051 for elranatamab. Given the similar efficacy and safety profiles, the economic advantage of teclistamab discussed gives a potential benefit as a more long-term, cost-effective treatment option. The total cost of care over 12 months for weekly and biweekly talquetamab administration is \$521,567 and \$551,350, respectively.¹⁸

Patients receiving teclistamab should be hospitalized for 48 hours after all doses within the step-up dosing schedule. In contrast, elranatamab requires hospitalization for 48 hours after the first step-up dose and 24 hours after the second. This translates to a hospital stay of 7 to 9 and 5 days for teclistamab and elranatamab, respectively.^{9,13}

The Centers for Medicare & Medicaid Services offers a new technology add-on payment (NTAP) program that provides additional payments to hospitals above the standard Medicare severity diagnosis-related group payment amount. Teclistamab received NTAP approval in October 2023; elranatamab was approved in October 2024. Hospitals can receive add-on payments until September 2025 for teclistamab and elranatamab.²⁰ Additionally, Pfizer offers a free drug program for inpatient step-up doses of elranatamab. The program is available only to inpatient hospital pharmacies that certify they are supplying pharmacy services to an inpatient hospital. Hospitals may not seek or obtain reimbursement for the product directly or indirectly from any party.

Elranatamab offers the convenience of a fixed dosing schedule, an earlier transition to biweekly dosing for those sustaining PR for 2 or more months starting at week 25,

and a shorter hospital stay when initiated in an inpatient setting. Although elranatamab offers the advantage of a free drug program for inpatient step-up doses from the manufacturer, teclistamab's cumulative drug acquisition cost after 12 months of treatment is lower. Reimbursement for outpatient administered drugs may vary based on the institution. The considerable cost-savings programs available for teclistamab can mitigate the operational complexities, making it a financially reasonable choice for organizations. Furthermore, a longer study follow-up period, higher CR rates, and lower discontinuation rates are key points to consider for teclistamab.²¹ Another benefit for teclistamab to consider is that it is managed under the same risk evaluation and mitigation strategy (REMS) program as another bsAb, talquetamab; both are developed by Johnson & Johnson. This consolidated REMS program can reduce the complexity of the management process.

Harnessing a bsAb That Targets a Novel Mechanism

Talquetamab is a bsAb with a unique target, GPRC5D; talquetamab received approval in 2023.²² In the phase 1 MonumenTAL-1 trial (NCT03399799), the objective response rate for talquetamab was 73.6% with a CR or better of 33%.²² The median time to response was approximately 1 month.²² Long-term follow-up data from MonumenTAL-1 were presented at the 29th European Hematology Association (EHA) Congress in 2024. With an extended follow-up period of 29.8 months for the weekly dosing cohort and 23.4 months for biweekly, the objective response rate was 74.1% and 69.5%, respectively, with CR of 32.9% and 40.3%, respectively. With the recent update from the trial, a PFS of 7.5 and 11.2 months, respectively, was also reported.¹⁹ For talquetamab, patient preferences should be incorporated into shared decision-making as the on-target, off-tumor effects may compromise quality of life. The most common of these, affecting more than half of all participants, included dysgeusia and dermatologic-related events, most of which were low-grade and manageable.²² Given its unique target, talquetamab could be used sequentially without dampening the BCMA effect or in combination with BCMA-directed bsAbs to provide a synergistic effect.

The data from MonumenTAL-1 further support the use of talquetamab before BCMA-directed therapies.²² Its suitability for earlier use is rooted in its high response rates and manageable safety profile. Talquetamab serves as an alternative when BCMA-directed therapies have been exhausted or are being reserved for later use. It has been proposed that talquetamab could significantly improve response rates when combined with teclistamab.²³

Using talquetamab in combination regimens may become an option.

Regarding practical considerations, talquetamab was associated with the highest objective response rate of 73.6% when compared with teclistamab and elranatamab. Further, its hospitalization requirements are similar to teclistamab. There is also an immediate transition to biweekly dosing with talquetamab, which makes it the most convenient of the bsAbs in terms of dosing frequency. Talquetamab will likely be included in most formularies due to its unique target and advantageous practical considerations.

Role of BCMA-Directed bsAbs and Optimal Timing Relative to CAR T-Cell Therapy

Adopting earlier use of CAR T-cell therapy in clinical practice depends on several factors. First, the patient must be fit enough to tolerate the conditioning regimen and meet the criteria cited by the NCCN for previous treatments. Given the slow progression of MM in its early stages, it may not be preferred to use CAR T-cell therapy after the first relapse in all eligible patients, given the high associated costs and potential for AEs. Efforts are underway to develop prediction models that can accurately identify the subgroups of patients most likely to benefit from the earlier CAR T-cell therapy.²⁴ However, there is a need for more sophisticated and robust models. The value of having such models lies in their ability to guide the clinical decision-making process for pursuing the expanded indication of second-line therapy for ciltacabtagene autoleucel.

In the phase 3 CARTITUDE-4 trial (NCT04181827), ciltacabtagene autoleucel demonstrated a significant improvement in CR with a rate of 73.1% compared with 21.8% for standard care following 1 to 3 lines of therapy.²⁵ Such deep responses are unprecedented and higher than its competitor idecabtagene vicleucel, which had a CR rate of 39% following 2 to 4 lines of therapy in the phase 3 KarMMa-3 trial (NCT03651128).²⁶ Albeit indirect comparisons, ciltacabtagene autoleucel also had a more favorable HR for progression of disease of 0.26 compared with 0.49 indicating longer periods without disease progression.^{25,26} The decision to place ciltacabtagene autoleucel in a higher place of therapy reflects the overall interpretation of its higher efficacy by the FDA's Oncologic Drugs Advisory Committee. Nevertheless, both CAR T-cell therapies received expanded indications for earlier use due to their proven ability to reduce the risk of disease progression and death. Although CAR T-cell therapy is significantly more costly, it is important to consider that it is a one-time treatment vs bsAbs, which require continuous therapy courses. One disadvantage this treatment holds, however, is a lengthy manufacturing process.

Therefore, CAR T-cell therapy should be assessed against other options, including off-the-shelf bsAbs.

The recently expanded indication for earlier use of CAR T-cell therapy may impact the adoption of bsAbs as further investigation is needed to clarify whether bsAbs can be used as earlier lines of therapy. Furthermore, although CAR T-cell therapy and bsAbs demonstrated continued efficacy after prior BCMA-directed therapy, they both exhibited a blunted response, complicating the role of bsAbs if a patient had previously received CAR T as an earlier treatment option.^{11,27} After progression beyond at least 4 lines of therapy, there is no clear guidance on whether BCMA-directed bsAbs should be used before or after CAR T-cell therapy. However, there are competing reasons for selecting one sequence over the other. We anticipate that the experts will lean toward prioritizing ciltacabtagene autoleucel as the initial treatment when it is accessible, given its unprecedented efficacy and convenient one-time administration. However, accessibility is limited to large tertiary medical centers.

Due to their greater accessibility and lower risk for acute toxicities, bsAbs are also suitable as a first choice in the treatment sequence, specifically in the setting of progression beyond at least 4 lines of therapy. This approach aims to manage disease progression initially with bsAbs while reserving the more efficacious option of CAR T-cell therapy for use after relapse or when it becomes accessible. Further investigation is necessary to elucidate the extent to which the response is blunted and how it compares across the sequence selected. The blunted response may be attributable to intrinsic resistance mechanisms, such as selective pressures for BCMA-negative clones.²⁸ It is unclear whether the ongoing administration of bsAbs applies greater selective pressures over time compared with the one-time administration of CAR T-cell therapy. This temporal aspect should be considered in future investigations to guide the optimal sequencing strategy. It will ascertain whether CAR T-cell therapy should be prioritized before bsAbs, or whether such considerations are necessary.

Exploring how to use bsAbs as a bridge to CAR T-cell therapy will allow for more flexible use, enabling their use during the manufacturing process and beyond. Fully investigating the optimal sequence is necessary to maximize the therapeutic benefit of BCMA-directed therapies. Currently, ongoing clinical

trials are investigating the use of bsAbs as earlier lines of therapy and/or use in combination regimens.

Conclusions

Amid a shifting treatment paradigm for MM, bsAbs have a promising role. We closely compared the 3 available bsAbs, focusing on the 2 BCMA-directed bsAbs. Teclistamab and elranatamab have been game-changing therapies for patients with R/R MM, demonstrating remarkable efficacy in improving patient outcomes. From our analysis, any difference in efficacy seen is balanced by the differences in patient population and results comparisons with matched length of follow-up. Therefore, we conclude that neither BCMA-targeted therapy has an advantage in safety or efficacy. However, teclistamab offers more real-world experience with a longer trial follow-up period of 30.4 months compared with 28.4 months for elranatamab and providers, which may still favor the advantages shown in outcomes with the extensive amount of real-world data for teclistamab.

On the other hand, elranatamab holds potential logistical advantages in terms of the convenience of fixed dosing, fewer hospitalization requirements when initiated inpatient, and the potential of an earlier switch to biweekly dosing, which patients may prefer. From an economic standpoint, we found that the WAC pricing of teclistamab, as well as the cumulative 12 months cost of treatment, is considerably lower than elranatamab. Although institutional contracting and reimbursement modeling may show differing financial benefits, the clinical decision of teclistamab vs elranatamab will likely come down to balancing the advantage in longer-term data with teclistamab and potential cost savings versus the potential logistical benefits of elranatamab. More insights regarding safety, efficacy, and cost-benefit considerations may be found with a longer follow-up period for elranatamab.

Determining the most effective sequence for BCMA-directed therapies—particularly the sequence of bsAbs relative to CAR T-cell therapy, especially considering the advancement in CAR-T cell therapies—will require more investigation. Finally, talquetamab's unique target, which alleviates the concern for blunting of effect on BCMA-targeted therapies, supports the unique role of talquetamab in the treatment landscape of MM. 🌱

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ORIGINAL RESEARCH

Optimizing Infusion Chair Time for Oncology Trials: Follow-Up Study

Kaycey Pearce, PharmD; and Jennifer Murphy, PharmD, BCOP, BCPS

AUTHORS

Kaycey Pearce, PharmD, is a clinical oncology pharmacist in the Department of Pharmacy and Investigational Drugs Services at Samuel Oschin Cancer Center at Cedars-Sinai in Los Angeles, California, and a former PGY-2 investigational drugs and research pharmacy resident at UC Davis Health in Sacramento, California.

Jennifer Murphy, PharmD, BCOP, BCPS, is a senior pharmacist in the Oncology & Investigational Drug Service at UC Davis Health in Sacramento, California.

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DISCLOSURES

None.

PRÉCIS

This study evaluated factors affecting the duration of the infusion appointment times for 392 clinical trial patients. We found no significant correlations, although further research is needed.

ABSTRACT

OBJECTIVES

This study identified variables significantly affecting the duration of appointment times for oncology clinical trial patients. Additionally, researchers sought to differentiate between intrinsic and extrinsic delays to determine areas needing optimization.

STUDY DESIGN

Conducted as a single-center, retrospective quality improvement initiative, the study looked at data from adult patients enrolled in oncology clinical trials at UC Davis Comprehensive Cancer Center in Sacramento, California, from July 1, 2019, to July 1, 2022.

METHODS

The analysis involved descriptive statistics and multiple linear regression to evaluate factors affecting infusion appointment duration and arrival-to-chair time. Variables included patient age, number of investigational products administered, appointment time (morning vs afternoon), type and phase of the study, pharmacokinetics at chair time, and the use of interactive response technology kit assignment.

RESULTS

The study examined 392 individuals and found no significant correlations between the analyzed variables and infusion appointment duration ($P = .085-.53$) or arrival-to-chair time ($P = .085-.93$).

CONCLUSION

Although this analysis did not yield definitive results, it highlights the complexity of delays in oncology infusion chair times. The lack of significant correlations suggests intricate interactions among various factors, emphasizing the need for further research to uncover these complexities and optimize appointment efficiency for patients in clinical trials.

INTRODUCTION

The UC Davis Comprehensive Cancer Center (UCDCCC) in Sacramento, California, is a National Cancer Institute–designated comprehensive cancer center that conducts early-phase clinical trial research, operating hundreds of oncology clinical trials annually. UCDCCC is the main hub for cancer treatment in the Central Valley region. High patient volume has affected the infusion center schedule, leading to a long wait list. Patients who travel long distances, such as from Southern California or out of state, need to complete multiple care-related activities in a single day, including obtaining laboratory tests and seeing their provider, all on top of receiving their cancer treatment. This is especially the case for clinical trial patients seeking care at UCDCCC because their local institution may

not conduct clinical trials or be permitted to conduct study-related activities for the trial on which they are enrolled.

Typical reasons for extended infusion appointments, from a patient scheduling perspective, include satisfying trial requirements. Examples include accommodating predose and up to 10 hours postdose pharmacokinetic (PK) blood samples, infusions with durations of several hours, extensive postdose observation and monitoring periods, and numerous infusions. Examples of extenuating circumstances faced by many sites, which are not specific to clinical trials themselves, include patients arriving late, clinic providers experiencing delays in starting at the scheduled time, and other infusion patients utilizing a chair longer than expected. Although some of these reasons are consistent with challenges faced by standard of care, several are unique to clinical trials. Irrespective of the reason for prolonged treatment days, it is important to reduce patient chair time and improve care experiences at UCDCCC.

Many US and international institutions have experienced similar challenges with infusion center efficiency and attempted to create tools to shorten infusion chair wait times and improve patient satisfaction. Examples include developing simulation models, process mapping, and Plan-Do-Study-Act cycles.¹⁻⁵

In 2023, a quality improvement (QI) study was performed at UC Davis Health to identify areas of intervention for increased workflow efficiency and decreased infusion chair time for clinical trial patients. This QI project was completed through EPIC (electronic health record software)-generated reports and examined the current workflow by calculating the time intervals for the following: comprehensive metabolic panel and complete blood count laboratory processing, clinical trial medication orders signed by physician to medication verification by pharmacist, patient arrival to study medication dispense, patient arrival to administration of study medication, and the time of appointment (morning [AM] or afternoon [PM]). No significant findings were identified, aside from the fact that patients with AM appointments waited, on average, 10 minutes longer than patients with PM appointments. It is unclear whether AM appointments happened to be generally longer, or because of the complexity of treatment (eg, the patient had multiple study medications administered at the same visit, multiple PK blood draws), these patients were scheduled in the AM to ensure treatment could be completed during operating infusion hours.

These follow-up study results extend the insights gained from the aforementioned 2023 UC Davis Health study that noted a significant difference between AM and PM appointment delays, confirming trends identified in a 2019 study by the Infusion Efficiency Workgroup under the National Comprehensive Cancer Network.⁶

The study further investigated the variances in infusion chair time optimization for oncology clinical trial patients by comparing the duration of the appointment vs examined variables and arrival-to-chair time vs examined variables to ascertain their impact on the chair time duration.

METHODS

This study was a single-center, retrospective, continuous quality improvement study. An EPIC report was generated for all adult patients with a scheduled infusion clinic appointment between July 1, 2019, and July 1, 2022, who were enrolled in a clinical trial that involved infusion treatment. From the report, the following variables were collected and examined per patient and infusion appointment encounter, with up to the first 3 encounters included for each patient: age, AM or PM appointment, type of study, phase of the study, requiring PK blood draw at chair time, requiring investigational product (IP) supply allocated by interactive response technology (IRT) kit assignment, and number of IPs administered.

The primary objective was to determine any variable(s) that significantly affects the duration of the appointment time for oncology clinical trial patients.

The secondary objective was to determine whether the intrinsic delay from the variable(s) differs from the extrinsic delay that needs optimization. Examples of intrinsic variables include type of study (industry, national, investigator-initiated), phase of study (eg, phase 1, 2, 3, 4), requiring PK blood draw at chair time, requiring IP IRT kit assignment, and number of IPs administered; these are inherent to the clinical trial process and not directly controllable by the clinical team and are not changeable (as is age). Extrinsic variables are AM/PM appointment times and arrival-to-chair time, which reflect elements that may require external optimization. To compare the 2 types of delays, we examined arrival-to-chair time (extrinsic variable) to all mentioned intrinsic variables.

Descriptive statistics were used to summarize the data. This included calculating continuous variables' mean, median, SD, and range. Frequency and percentage were used for categorical variables. These descriptive analyses helped to understand the general characteristics of the data set and the distribution of appointment durations.

A multiple linear regression analysis was used to examine the relationship between the dependent variable (duration of appointment time) and the independent variables (AM/PM appointment, type of study, phase of study, requiring PK blood draw at chair time, requiring IP IRT kit assignment, number of IP administered, and age). This model helped to determine which variables were statistically significant predictors of appointment duration and the extent of

TABLE 1. Basic Demographics of Included Participants and Total Encounters

Characteristic	Number of patients (N = 392)
Age (years) + SD	63.7 + 13
Number of IPs administered	
1 (%)	233 (59.4)
2 (%)	104 (26.5)
3 (%)	30 (7.7)
4 (%)	22 (5.6)
5 (%)	3 (0.8)
PK at chair time	
Yes (%)	146 (37.3)
No (%)	246 (62.7)
IRT	
Yes (%)	68 (17.3)
No (%)	324 (82.7)
Type of study	
Industry (%)	163 (41.4)
IIT (%)	68 (17.3)
Federal (%)	161 (41.3)
Phase of study	
1 and 1/2 (%)	162 (41.2)
2 and 2/3 (%)	150 (38.3)
3 (%)	80 (20.5)
Characteristic	Total number of encounters (N = 964)
Infusion appointment time	
AM (%)	751 (77.9)
PM (%)	213 (22.1)
Average arrival to chair time (min) + SD	16.9 ± 20.4
Average duration of appointment (min) + SD	304.8 ± 149.1

IP, investigational product; IIT, investigator-initiated trial; IRT, interactive response technology, PK, pharmacokinetics.

their impact. A separate regression analysis focused on intrinsic vs extrinsic variables to help identify factors needing optimization through policy changes or additional resources.

RESULTS

For this study, data from the 392 participants included in the final 2023 study analysis were examined. Most patients (59.4%) received 1 IP during their encounter, did not get PK blood draw done at chair time (62.7%), did not get IRT assignment for IP (82.7%), had equal occurrence of industry study (41.4%) vs federal study

(41.3%), and participated in a phase 1 or phase 1/2 study (41.2%). Additionally, 77.9% of appointments were in AM vs PM (22.1%) (Table 1).

For the primary objective, the appointment time (AM/PM) was not significantly associated with the appointment duration ($P = .2776$). The model showed that PM appointments were, on average, 41 minutes shorter, although this difference is not statistically significant. The type of study (ie, industry, investigator-initiated trials [IITs], national) was also not significantly associated with appointment duration (overall model $P = .4475$). Each type of study showed no significant impact on the duration compared with the intercept. The phase of the study showed some indication trending toward association with the duration of the appointment (overall model $P = .0555$), with phase 3 studies being associated with a significant increase in appointment duration by 98.4 minutes ($P = .0433$) (Figure). Whether requiring PK at chair time was performed (Yes [Y]/No [N]) was not significantly associated with the duration of the appointment ($P = .5344$), and whether requiring IP IRT kit was assigned (Y/N) also did not significantly affect the duration of the appointment ($P = .254$). Age was significantly associated with the duration of the appointment ($P = .0443$), with each year increase in age reducing the appointment duration by 2.79 minutes. The number of IPs administered showed some indication of association with appointment duration (overall model $P = .085$), particularly for category 3, which significantly increased the duration by 151.21 minutes ($P = .0127$) (Table 2).

For the secondary objective, the time of the scheduled appointment (AM/PM) showed no significant association with arrival-to-chair time ($P = .2961$). The PM appointments were associated with increased arrival-to-chair time by 5.41 minutes, which was not statistically significant. The type of study (ie, industry, IIT, national) did not significantly affect arrival-to-chair time (overall model $P = .2747$), with no significant differences observed across the types of study mentioned. The phase of the study had a suggestive, yet not universally significant, association with arrival-to-chair time (overall model $P = .0851$). Specifically, phase 2 and phase 3 studies showed a significant increase in arrival-to-chair time by 20.15 minutes ($P = .0322$), indicating some variability based on the study phase. Whether requiring PK at chair time did not significantly influence arrival-to-chair time ($P = .267$), indicating no significant impact of this variable. Requiring IP IRT kit assignment also showed no significant effect on arrival-to-chair time ($P = .6808$). Age was not significantly associated with arrival-to-chair time ($P = .8127$), with a coefficient indicating a negligible

TABLE 2. Primary Outcome: Duration of Appointment

Duration of appointment - variable	Mean (min)	SE	P value	Overall model P value
PK at chair time				.53
No	313.11	21.85	.0	
Yes	290.79	35.75	.53	
IRT kit assignment				.25
No	295.73	18.9	.0	
Yes	347.93	45.4	.25	
Age				.04
	495.68	92.74	.0	
	492.89	1.36	.04	
Number of IPs administered				.08
1	269.79	22.34	.0	
2	327.0	37.55	.13	
3	421.0	59.1	.01	
4	303.0	104.77	.75	
5	453.0	146.47	.21	

IP, investigational product; IRT, interactive response technology; PK, pharmacokinetics.

TABLE 3. Secondary Outcome: Arrival-to-Chair Time

Arrival-to-chair time - variable	Mean (min)	SE	P value	Overall model P value
PK at chair time				.26
No	18.89	2.97	.0	
Yes	13.46	4.85	.26	
IRT kit assignment				.68
No	16.42	2.6	.0	
Yes	19.0	6.25	.68	
Type of study				.27
Number of IPs administered				.93
Phase of study				.08
1	17.18	4.27	.0	
1/2	20.87	8.26	.65	
2	11.09	6.03	.31	
2/3	37.33	9.22	.03	
3	15.0	6.0	.74	

IP, investigational product; IRT, interactive response technology; PK, pharmacokinetic.

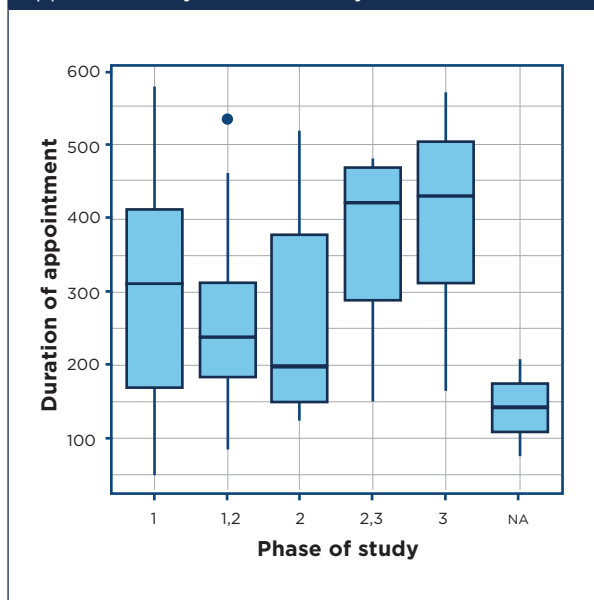
change in arrival-to-chair time per year of age. The number of IPs administered did not show a significant association with arrival-to-chair time (overall model $P = .9305$), indicating no significant impact on arrival-to-chair time delay (**Table 3**).

DISCUSSION

The findings from our comprehensive analysis underscore the complexity of optimizing infusion chair

time for patients with cancer enrolled in clinical trials. Despite initial assumptions about the potential impact of various intrinsic and extrinsic variables, our results suggest that few factors significantly influence the duration of patient appointments and arrival to chair time.

One noteworthy result involved the phase of the clinical trial. Phase 3 studies were associated with significantly longer appointment durations, with an

FIGURE. Primary Outcome: Duration of Appointment by Phase of Study

increase of approximately 98.4 minutes. This finding was unexpected because phase 1 studies usually have many more checks and more extensive data collection with PKs, etc. Furthermore, phase 2 and phase 3 studies showed a significant increase in arrival-to-chair time, particularly reflecting the complexity and resource allocation necessary at these stages. These results highlight the need for targeted strategies to manage the higher demands of advanced trial phases effectively.

Age also emerged as a significant factor, albeit in a somewhat unexpected direction. With each incremental year in age, appointment durations decreased slightly by approximately 2.79 minutes. This counterintuitive finding might be explained by more streamlined or less intensive treatment regimens often prescribed for older patients or perhaps more experienced patient handling by clinical staff. Moreover, this reduction could be reflective of an adjustment in clinical trial protocols or the health care team's more efficiently adapting to older adults.

Interestingly, most other intrinsic variables—including the type of study, requiring PK blood draw at chair time, and requiring IP IRT kit assignment—showed no significant association with either the duration of the appointments or the arrival-to-chair time; this was a surprise. Time is added to the appointment for IRT kit assignment because it requires the pharmacy to wait on the assignment. These findings suggest that such intrinsic factors

might be well managed within current clinical workflows or that their impact is minimal compared with other elements.

As for extrinsic variables, the timing of appointments (AM/PM) was anticipated to influence efficiency potentially, but the data did not support this hypothesis. Although PM appointments were, on average, shorter by 41 minutes, this difference was not statistically significant. It is unclear whether AM appointments happened to be generally longer, or because of the complexity of treatment (eg, the patient had multiple study medications administered at the same visit, multiple PK blood draws, etc), these patients were scheduled in the AM to ensure treatment could be completed during operating infusion hours. Therefore, scheduling adjustments alone might not yield substantial improvements in chair-time efficiency.

The discovery that the number of IPs administered during a visit also significantly extended appointment times by approximately 151.21 minutes when a patient receives 3 IPs underscores the logistical and procedural burdens associated with multidrug protocols. This insight points to the need for specialized processes or additional support for handling multi-IP sessions to reduce inefficiencies.

Although the current study results provide valuable insights into the factors influencing infusion chair time for oncology clinical trial patients, several limitations must be acknowledged.

First, the study duration of approximately 3 years might not be sufficient to capture longer-term trends and variations in clinical trial workflows and infusion times. Seasonal variations, periodic protocol changes, and other temporal factors could play a role in influencing appointment durations, which might not be fully encapsulated within this relatively short time frame.

Second, as a single-center study conducted within the UC Davis Health System, the findings may have limited generalizability to other institutions. The workflows, resources, and patient demographics at our center may differ from those at other comprehensive cancer centers or community treatment facilities. Consequently, the results might not be entirely applicable to different clinical settings with varying operational protocols or patient populations.

Last, the study involved nurses manually inputting time from the patient's arrival to the end of the appointment, which introduced a potential for human error and variability in data accuracy.

Relying on manual recording can lead to inconsistencies in time documentation, which may have affected the precision of our findings. Automated data collection systems could yield more reliable and consistent data, minimizing the risk of inaccuracies in manual entry.

Considering these limitations, future research should aim for longer study durations to better capture temporal variability, multicenter collaborations to enhance generalizability, and the implementation of automated time-tracking systems to improve data accuracy. Addressing these areas will help refine our understanding of infusion chair time optimization and lead to more robust and widely applicable conclusions.

CONCLUSION

Our study results provide valuable insights into the factors influencing infusion chair time among patients with cancer participating in clinical trials. Although the patient's age and the phase of the study were significantly associated with changes in appointment duration, most other intrinsic variables examined, including the type of study, PK at chair time, and IRT kit assignment, did not have a statistically significant impact. Moreover, extrinsic variables such as the time of the appointment (AM/PM) also showed no significant effect on either the overall appointment duration or arrival-to-chair time.

The significant increases in duration for phase 3 studies and appointments involving multiple IPs suggest specific areas where targeted interventions could be effective. For example, additional staffing or dedicated resources during phase 3 trials might help to manage the increased complexity and requirements associated with treatments for these types of trials. Likewise, optimizing processes for multidrug administrations could reduce procedural delays.

The findings emphasize that although

certain intrinsic factors are inherent to treatments associated with clinical trial protocols and may require tailored management strategies, many current workflow components are already optimized to a degree that limits further improvements through changes in those areas alone. Future efforts might focus on refining a standardization for clinical trials to ensure consistent care and remove the risk of error caused by different workflows specific to more complex trial phases, and administration of multiagent regimens to achieve more noticeable enhancements in efficiency and reduction in appointment duration.

This study serves as a foundation for further research and quality improvement initiatives aimed at enhancing the experience and care of oncology trial patients. Continuous assessment and incremental adjustments, particularly focused on the identified significant factors, will be essential in moving toward more efficient and patient-friendly clinical trial processes. 🌐

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Shaping the Future of Oncology Pharmacy Through the NCODA Medically Integrated Oncology Pharmacy Residency Program

The program develops patient-centered oncology pharmacists through comprehensive training.

Nicole Bentivegna, PharmD, BCOP; Gabriela Aponte-Melendez, PharmD; Natalie Kaufman, PharmD; and Cooper Bailey, PharmD

ABOUT THE AUTHORS

Nicole Bentivegna, PharmD, BCOP, is a clinical pharmacy services manager and NCODA MIOP residency program director at Florida Cancer Specialists & Research Institute and Rx To Go, LLC, in Fort Myers, Florida.

Gabriela Aponte-Melendez, PharmD, is a pharmacy resident at Florida Cancer Specialists & Research Institute.

Natalie Kaufman, PharmD, is a clinical staff pharmacist and past MIOP resident at Florida Cancer Specialists & Research Institute.

Cooper Bailey, PharmD, is a manager, Program Development & Strategy at NCODA in Calgary, Alberta, Canada.

The field of oncology pharmacy is constantly evolving, calling for a patient-centered approach that can adapt to its dynamic challenges. The medically integrated oncology pharmacy (MIOP) residency program, accredited by the National Community Oncology Dispensing Association (NCODA) and presented at the 2024 Florida Society of Clinical Oncology (FLASCO) Fall Session, is designed for aspiring oncology pharmacists with comprehensive experience who are ready to navigate these complexities. This residency program aims to shape future oncology pharmacists by combining clinical and business competencies in a medically integrated setting.

Participating Programs and Residency Sites

Key sites nationwide participate in the NCODA MIOP program, including Florida Cancer Specialists & Research Institute in Fort Myers, Texas Oncology in Dallas/Fort Worth, and Tennessee Oncology in Nashville. Each participating institution gives residents hands-on experience in outpatient and infusion-based oncology practices, providing valuable insights into medically integrated pharmacy.

Comprehensive Training Pathway

The NCODA MIOP program is structured into 4 specialized rotations to create well-rounded oncology pharmacists:

1. Oral Outpatient Oncology Practice: This rotation focuses on dispensing oral oncolytic therapies and providing safe and effective oncology care in

collaboration with the medically integrated team to manage oral chemotherapy, emphasizing patient education and adherence strategies.

2. Intravenous/Infusion Oncology Practice: This rotation concentrates on preparing, administering, and managing intravenous therapies within a medically integrated oncology team.
3. Pharmacy Business/Leadership: This rotation covers essential skills in operations, management, and leadership, preparing residents for future pharmacy administrative roles.
4. Research (12 months, longitudinal): This is a key component in which residents conduct clinical research and present their findings at the NCODA Spring Forum.

To apply, candidates must hold a doctor of pharmacy degree, demonstrate an interest in oncology pharmacy, and have a strong foundation in patient-centered care. The residency seeks candidates eager to contribute to patient care and pharmacy operations, embodying a strong commitment to the oncology field and continuous learning. The residency structure is patient centered, blending clinical responsibilities with hands-on pharmacy management within a medically integrated practice. Residents play a crucial role in direct patient care, collaborating within a multidisciplinary team to optimize therapeutic outcomes, manage adverse effects, and ensure adherence. This approach has proven highly rewarding, fostering close patient interaction and enabling proactive engagement with evolving treatment needs.



Developing Advanced Oncology Pharmacist Skills

The NCODA MIOP residency offers comprehensive training across diverse oncology pharmacy areas, equipping residents with essential skills in patient counseling, medication management, and business operations. Beyond clinical training, the program offers significant professional growth opportunities in pharmacy leadership. Research and data-driven projects allow residents to positively impact oncology practices. This program encourages innovation by integrating NCODA's quality standards and best practices into pharmacists' daily work. Residents are encouraged to adopt evidence-based practices through NCODA's positive quality interventions and best-practice sharing, fostering a culture

of continuous improvement that is essential in oncology. NCODA's accreditation supports the residency's high standards, assuring a structured approach prioritizing quality and efficiency in patient care. This accreditation provides a valuable foundation, affirming that residents are part of a network dedicated to advancing oncology pharmacy practice.

As the NCODA MIOP residency progresses, each experience reaffirms the impactful role oncology pharmacists play in patients' cancer journeys. In this way, the NCODA MIOP residency program is a pathway that lays the groundwork for a career driven by excellence in clinical knowledge, compassion, and adaptability, which are essential qualities for making a difference in oncology pharmacy. 🌱

Advancing Lung Cancer Treatment With Bispecific Antibodies: A Review of Amivantamab and Tarlatamab

Bispecific antibodies amivantamab and tarlatamab hold promise for patients.

Douglas Braun, PharmD, RPh, CSP

ABOUT THE AUTHOR

Douglas Braun, PharmD, RPh, CSP, is a senior pharmacy director at American Oncology Network, LLC, in Fort Myers, Florida.

Bispecific antibodies (BsAbs) are a class of antibodies that can bind to 2 different sites at the same time. They are a type of next-generation monoclonal antibody (mAb) but, unlike typical mAbs that target only 1 antigen, BsAbs can cause multiple physiological or antitumor responses. Because of the ability to target more than 1 site, BsAbs are proving to be a deeper and more durable treatment option. Currently, there are more than 100 BsAbs in clinical development, most being in the early stages.¹

During the 2024 Florida Society of Clinical Oncology Fall Session in Orlando, Elizabeth Osmon, PharmD, BCPS, BCOP, a medical oncology clinical pharmacy specialist at Memorial Healthcare System, presented a review of BsAbs for lung cancer. In this review, Osmon discussed 2 BsAbs: amivantamab (Rybrevent; Janssen Pharmaceutical Companies) for non-small cell lung cancer (NSCLC) and tarlatamab (Imdelltra; Amgen) for small cell lung cancer (SCLC).

Amivantamab

Amivantamab is a BsAb that binds to receptors on cancer cells for proteins EGF and MET; this prevents the activation of signaling pathways that promote tumor cell growth. Amivantamab is FDA approved:

- in combination with lazertinib (Lazcluze; Janssen Biotech, Inc) for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 19 deletion (Ex19del) or exon 21 L858R substitution mutations;
- in combination with carboplatin and pemetrexed for the treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* Ex19del or exon 21 L858R substitution mutations whose disease has progressed on or after treatment with an EGFR tyrosine kinase inhibitor;
- in combination with carboplatin and pemetrexed for the first-line treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations; and



Considering that SCLC can be a very aggressive disease with a limited PFS, shortened duration of response, and OS in subsequent lines of therapy, [tarlatamab] holds promise for these patients.

- as a single agent for the treatment of adult patients with locally advanced or metastatic NSCLC with *EGFR* exon 20 insertion mutations whose disease has progressed on or after platinum-based chemotherapy.

The approval was based on the results of the phase 3 MARIPOSA trial (NCT04487080), which randomly assigned more than 1000 patients to amivantamab in combination with lazertinib, lazertinib, or osimertinib (Tagrisso; AstraZeneca). The median progression-free survival (PFS) was significantly longer in the amivantamab/lazertinib group than in the osimertinib group (23.7 vs 16.6 months). The median response duration was 25.8 months and 16.8 months, respectively. In a planned interim overall survival (OS) analysis of amivantamab plus lazertinib compared with osimertinib, the HR for death was 0.80.²

Adverse events (AEs) include infusion-related reactions, elevated hepatic enzymes, fatigue, musculoskeletal pain, infection, stomatitis, edema, and constipation. Amivantamab is dosed based on weight and is administered weekly via a peripheral line on week 1 and week 2 to reduce the risk of infusion-related reactions, and with the initial dose as a split infusion on week 1 on days 1 and 2.³

Tarlatamab

Tarlatamab is a BsAb immunotherapy drug used to treat SCLC. Tarlatamab binds to tumor cells and T cells, helping the T cells recognize and destroy cancer cells. It targets the protein DLL3 on the surface of tumor cells and CD3 on T cells.

The FDA approval was based on results of the DeLLphi-301 trial (NCT05060016), which enrolled 220 patients who had previously received a median of 2 lines of prior treatment. At 10 months, a 40% objective response rate was observed. The median duration of response was shown to be 9.7 months,

with 68% of those who responded still on therapy at 6 months and 40% at more than 12 months.⁴

The dosing is 1 mg intravenous (IV) on cycle 1, day 1, followed by 10 mg IV on cycle 1, days 8 and 15. For all subsequent cycles, administer tarlatamab 10 mg IV on days 1 and 15, every 28 days until disease progression or unacceptable toxicity.

However, it is important to monitor patients in an appropriate health care setting for 22 to 24 hours after the start of the tarlatamab infusion on cycle 1, days 1 and 8. It is recommended that patients stay with a caregiver within 1 hour of an appropriate health care setting, for a total of 48 hours from the start of the tarlatamab infusion on cycle 1, days 1 and 8. Common AEs include cytokine release syndrome, fatigue, elevated hepatic enzymes, neurotoxicity, fever, and dysgeusia.⁵

Considering that SCLC can be a very aggressive disease with a limited PFS, shortened duration of response, and OS in subsequent lines of therapy, this treatment holds promise for these patients. 🌟

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Transforming CLL Management: Pharmacists' Impact on Treatment Strategies, Adherence, and Quality of Life

Anthony Perissinotti, PharmD, BCOP, discusses unmet needs and trends in managing chronic lymphocytic leukemia.

Pharmacy Times® interviewed Anthony Perissinotti, PharmD, BCOP, a clinical pharmacist specialist in hematology at Michigan Medicine, on key unmet needs and trends in managing chronic lymphocytic leukemia (CLL), emphasizing the pivotal role of pharmacists. For example, despite the shift away from chemotherapy toward better-tolerated targeted therapies, tolerability challenges persist, particularly for patients with multiple comorbidities who find it difficult to manage Bruton tyrosine kinase (BTK) and B-cell lymphoma 2 (BCL2) inhibitors. High-risk patients with specific mutations, such as *TP53*, still experience poorer outcomes than others. The use of minimal residual disease as a possible end point or marker for guiding therapy is also under investigation. Additionally, despite advancements, CLL remains incurable, often requiring lifelong therapy.

Favored second-generation BTK inhibitors for CLL treatment include acalabrutinib (Calquence; AstraZeneca) and zanubrutinib (Brukinsa; BeiGene) due to their improved tolerability and efficacy. In addition to prolonging patient survival, there is a strong focus on quality of life, with emerging strategies aimed at providing treatment breaks to reduce long-term adverse effects (AEs). Combinations such as venetoclax (Venclexta; AbbVie) with obinutuzumab (Gazyva; Genentech) are becoming standard, and fixed-duration therapies are being explored.

Pharmacists play a critical role in CLL care, moving beyond traditional patient education to advise other health care professionals on treatment guidelines and the latest data. Their role includes supporting AE management, coordinating financial resources, and ensuring medication access.

It is best practice for pharmacists to support shared decision-making with patients regarding treatment, which can lead to improved medication adherence. To further support adherence, pharmacists can address with patients some of the common reasons they may stop medications prematurely, including toxicity, financial burdens, and a misconception that feeling well equates to being free of disease. By providing individualized support and fostering collaborative care, pharmacists are pivotal to advancing the quality and effectiveness of CLL management.

Pharmacy Times: What are some unmet needs in the treatment of patients with CLL?

Anthony Perissinotti, PharmD, BCOP: During our Clinical Forum, it was really refreshing to hear that all pharmacists within their lifetime, within their career time, [have] been able to see the metamorphosis away from chemotherapy toward some of our targeted therapies. But we all still admitted that there were some unmet needs. So, the first unmet need was the tolerability. Even though these therapies are better tolerated than chemotherapy, in real-world patients with several comorbidities, with the logistical challenges, patients [who] are on several medications; it can be pretty challenging to treat these patients, even with our very well-tolerated BTK inhibitors and BCL2 inhibitor, venetoclax. We have seen that this has improved with our second-generation BTK inhibitors, acalabrutinib and zanubrutinib, but there's still some room for improvement. Another unmet need [is] patients with high-risk molecular or cytogenetic abnormality. So, a patient with a [*TP53*] mutation, although these patients now do tremendously better compared with chemotherapy, they still don't do as well as patients [who] don't have a [*TP53*] mutation. Another unmet need is trying to learn how to use measurable residual disease. Should we use that as an end point? Should we use that as a way to stop therapy? Should we use it as a way to compare therapies? These are things that we're still learning how to apply in the medical community. Another unmet need [is that] patients [who] relapse after our BTK inhibitors and BCL2 inhibitors can be particularly challenging. Lastly, another unmet need is we still can't cure CLL. Despite all the advancements, despite the metamorphosis of the treatments of CLL, we still have chronic lymphocytic leukemia, a chronic disease that requires lifelong therapy for many of our patients.

Pharmacy Times: What are some recent trends of note in CLL management?

Perissinotti: The major trend I've seen in CLL is the complete shift away from chemotherapy. I'll admit I have not used chemotherapy in almost a decade now, and when you speak to pharmacists across the country,

that's also true in their practice, whether it's been a decade or 5 years. The bottom line is none of us are using chemotherapy at all anymore. We're now using our targeted therapies, [which] are either our BTK inhibitors or a venetoclax-based regimen with obinutuzumab or rituximab [Rituxan; Genentech]. And we've also started to move away from even using our first-generation BTK inhibitor, ibrutinib [Imbruvica; Pharmacyclics, Janssen Biotech], in favor [of] our second-generation BTK inhibitors such as zanubrutinib and acalabrutinib. I've also seen more trends toward us emphasizing quality of life. Patients with CLL can now live as long as the general population, but we also want them to live as [well] as the general population.... We've been really focusing on how [we can] not only reduce disease symptoms but how [we can] help patients live a life where they're not having symptoms from their therapy. Other trends [include] how [we are] going to stop therapy. Because it is a lifelong disease, is there a way for us to give our patients a treatment break? So, there have been some emerging combinations with venetoclax. Obinutuzumab with venetoclax is the mainstay, but there's also venetoclax with ibrutinib. That got approved in Europe; it did not get approved in the United States. There are some issues with tolerability because of ibrutinib. We also would like to see some longer follow-up to make sure it's as durable as venetoclax with obinutuzumab. But I think in the future, [we will see] our second generations added to venetoclax. Hopefully, we can see as durable, if not more durable, remissions for those patients.

Pharmacy Times: What are key takeaways from real-world patient cases discussed during the Clinical Forum relating to recent guideline updates and new clinical trial data on BTK inhibitors?

Perissinotti: The major takeaway from the Clinical Forum, and I'm going to sound like a broken record, is none of us are using chemotherapy at all for CLL. And I think that something that might be surprising to some [readers is that] none of us are also using ibrutinib as our first-line treatment. And again, it's because of the favorable toxicity profile of our second-generation BTK inhibitors, whether that's acalabrutinib, and that's based on the [phase 3] ELEVATE-RR relapse/refractory study [NCT02477696], or zanubrutinib, which was based on the [phase 3] ALPINE study [NCT03734016]. Interestingly, ALPINE may show superiority not only in the toxicity profile but also potentially in the efficacy. Many of our cases that we discussed [involved that] we're now going to be picking between either a second-generation BTK inhibitor or a fixed-duration treatment

with BCL2 inhibitor, venetoclax with obinutuzumab. Now, the other thing that I noticed during our real-world discussions was that many of us really would prefer fixed-duration therapy with venetoclax and obinutuzumab, but in the real-world setting, that's not always possible. There are a lot of logistics that impede this. Many patients also don't [prefer] to have frequent lab draws, [having] to come into the hospital. For that reason, many of our patients [about whom] many of us would think, "Oh, we should put them on fixed-duration therapy," they end up on BTK inhibitors. But, I think we all agreed that we have excellent options in the frontline setting. In the second line, we [discussed] some cases. "Well, how do you treat a patient [who] progressed after BTK inhibitor?" And we all agreed that we would use venetoclax with either obinutuzumab or rituximab. And then, if a patient started with venetoclax with obinutuzumab, we discussed 2 potential options. One is [that] we could switch to a BTK inhibitor. But we also discussed that if a patient had a prolonged remission—we're talking years of remission after stopping venetoclax and obinutuzumab—we would consider re-treating them. We would sit down with the patient and talk about the pros and cons. Lastly, we discussed some cases that were relapse or refractory after all those therapies that I discussed, and what options do our patients have now? Some emerging options are pirtobrutinib [Jaypirca; Lilly], a reversible BTK inhibitor. It's much more selective for BTK, and then [we] also [discussed] chimeric antigen receptor therapy.

Pharmacy Times: What is the role of pharmacists in caring for patients with CLL on BTK inhibitors?

Perissinotti: The role of pharmacists in CLL is really advancing, and it's quite diverse. As you all know, there are many different types of pharmacists, and [each] plays an equally important role. So, we have pharmacists [who] are embedded in clinics, [who] are helping with treatment decisions, helping with adverse effect management, and pharmacists at the bedside of patients. We also have pharmacists in specialty pharmacies, and they're helping with their financial coordinators to ensure access for patients. We also have patients within oral chemotherapy programs, where they're doing a lot of virtual care for those patients, following up on patients at certain intervals to ensure that patients are tolerating their therapy, have access to their therapy, and if they have any further questions, they're there to answer those questions. I think what I was most impressed with [in] understanding the advancing role [of] the pharmacist within our Clinical

Forum was they're moving away from the traditional role of educating just the patients, but now pharmacists are really educating others: other health care professionals, our physicians, educating them on the newest data that [have] come out. Whether it's new, published data or abstracts that have been presented at new national or international conferences, and really getting into the nitty-gritty details, critically appraising that literature and coming up with pathways of how to treat patients best. Also, educating our nurses so that [they] are empowered to make some decisions when they are called, when patients have questions.

Pharmacy Times: What are some takeaways around best practices to optimize patient selection, education, and monitoring?

Perissinotti: I believe that shared decision-making is by far the most important best practice we can have in CLL. We have multiple great options. You could put the options in a hat. You can put venetoclax, you can put acalabrutinib, you can put zanubrutinib. Pick one out and it would be a fantastic option, and that option would likely lead to a patient living close to a normal life. That said, because the options are so good, we still need to pick the option. So, who is the best person to pick the option? It's the patient. What is the best option that fits our patient's lifestyle? To do that, we need to sit down with our patients and educate them on the pros and cons of each therapy so that they now have the knowledge to choose their therapy. When you empower patients, they're going to feel like they've now gotten back in control, right? So, they were just given a devastating diagnosis. They now have cancer. So, you feel like you're out of control, but the second that you can get them feeling like they're back in control of their decisions—shared decision-making—you can then get your patient to be a part of their journey, to be a part of their treatment decisions, to be a part of even adverse effect management decisions. When you have a patient [who] is incredibly involved, they're going to be more adherent to their therapy because, ultimately, these are all their decisions, not just us dictating their care. Another best practice is early intervention. So, these therapies can still cause some toxicities, and we want to identify them early. There are a couple of ways to do this. One is, again, educating the patient so that they are empowered to call us. But also, we want to check in on these patients at certain intervals. So initially, many of us are checking in on our patient within a week to make sure that they got access to their therapy. But then we're checking every 2 weeks, monthly, every

3 months thereafter, to ensure patients are still tolerating their medications. And if they have any additional questions, we're there to support them.

Pharmacy Times: What are some strategies to enhance medication access and adherence for patients with CLL on BTK inhibitors?

Perissinotti: Adherence in CLL is important. Obviously, patients are not going to benefit from a therapy that they're not taking, and [because] these therapies are highly effective, we're going to notice when patients are not adherent. The 3 [top] reasons why my patients stop their therapies prematurely would be toxicity, financial, and they feel great, right? They're thinking, "Well, why am I taking this medication when I have absolutely no disease symptoms, my disease is under control, or there's no detectable disease? Why am I still taking this?" So those are the 3 major reasons. So, from a toxicity perspective, it really comes back to empowering the patients with the knowledge of when they should reach out when they're having any toxicity or if they have any questions. It's also involving them in some of the medical management, giving them the option. And many times, there are multiple options. We can do dose holds; we can do drug holidays. We can do dose reductions. Or we can keep the dose the same and medically manage their [adverse] effect. And so ultimately, a lot of times, there is no right or wrong answer, but having the patient help you decide and help them decide as a team can really help with some adherence.

From a financial perspective, I think we're all lucky to have incredible financial counselors within our specialty pharmacy. Having them on the case helps with the financial aspects. It gets tricky when the care gets sent out to third parties where we might lose the patient. So, I think in those cases, even though they're not within our system, we need to keep a close eye on those patients to make sure that they don't fall through the cracks. And lastly, on the issue of patients feeling great, which is not an issue, it's a good thing. We want our patients to feel great. It's super important, and a very traditional role of the pharmacist is to educate patients, not only on the good things about their medications but also potentially some of the misunderstandings of their medication. So, letting patients know that just because you aren't feeling symptoms from your disease anymore does not mean that the disease is gone. We need them to understand that CLL is not curable, and the disease will eventually come back, and the best way to prevent it from coming back is to continue a medication that's still working. 📍