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Advances in Multiple Myeloma Treatment with Lenalidomide and Bortezomib

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Multiple myeloma accounts for approximately 1% of all cancers and 13% of hematologic cancers worldwide.[1,2] The management of multiple myeloma has evolved since the introduction of autologous stem-cell transplantation and the availability of medications such as thalidomide, lenalidomide, and bortezomib.[1,3] Treatment strategies for active disease are directly based on the patient's age, transplant eligibility, risk-stratification, and coexisting conditions, and usually include induction regimens followed by maintenance treatment. Patients younger than 65 years without substantial organ dysfunction should be considered for treatment with an induction regimen containing thalidomide, lenalidomide, or bortezomib plus autologous transplant.[1] Conventional therapy with melphalan and prednisone combined with thalidomide, lenalidomide, or bortezomib should be considered for patients older than 65 years of age or otherwise ineligible for stem-cell transplantation.[1,6] Less intensive treatment with melphalan plus prednisone, thalidomide plus dexamethasone, or lenalidomide plus dexamethasone should be considered in patients older than 75 years of age or in younger patients with coexisting conditions because these drug combinations limit toxic effects and prevent treatment interruptions. Consolidation therapy after autologous transplantation with bortezomib- or lenalidomide-based regimens significantly improves the rate of complete response.[1] Maintenance treatment historically contained thalidomide; however, severe peripheral neuropathy often occurred. Currently, lenalidomide has been shown to have improved progression-free survival (PFS) in younger and elderly patients due to the ability to control the proliferation of residual malignant cells after transplantation.[1,4]

Lenalidomide, an analogue of thalidomide, is an immunomodulatory agent. In vitro, lenalidomide is up to 50,000 times more potent than thalidomide at inhibiting TNF-α (tissue necrosis factor). Lenalidomide's main adverse effects are less common than with thalidomide and include myelosuppression and venous thromboembolism (VTE).[4] There are currently three phase 3, randomized, placebo-controlled trials that explore lenalidomide as maintenance treatment. Two of the trials introduced lenalidomide maintenance in patients postautologous stem-cell transplant and one trial in patients postinduction.[4-6] Bortezomib is a proteasome inhibitor that is indicated in both newly

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diagnosed and relapsed multiple myeloma patients. Previously, only the intravenous route was approved for treatment, but one phase 3 trial explored the efficacy and safety of bortezomib administered subcutaneously. The main adverse effect associated with bortezomib is peripheral neuropathy.[3]

Lenalidomide Data

The IFM 2005-02 trial was a randomized, double-blind, placebo-controlled, multicenter, phase 3 trial conducted in 614 patients younger than 65 years of age with nonprogressive multiple myeloma after first-line autologous transplantation. Patients were randomized 1:1 to either consolidation treatment with lenalidomide 25 mg per day on days 1 to 21 of each 28-day cycle, for two cycles followed by maintenance therapy with lenalidomide 10 mg daily for the first 3 months and increased to 15 mg if tolerated, or the same consolidation treatment with lenalidomide, followed by maintenance therapy with placebo. Lenalidomide and placebo were both continued until disease relapse. The baseline characteristics were similar between the two groups except the lenalidomide maintenance group had more patients with adverse cytogenetic profiles ($p = .006$). The primary end point was PFS and secondary end points included the response rate (RR), event-free survival (EFS), and overall survival (OS). At 45 months follow-up the PFS was 41 months in the lenalidomide maintenance group compared with 23 months in the placebo group ($p < .001$), and OS was 73% in the lenalidomide maintenance group and 75% in the placebo group. There was an improved rate of complete response (CR) or very good partial response (VGPR) in the lenalidomide maintenance group: 58% before consolidation versus 69% after consolidation. Lenalidomide maintenance improved the rate of CR and VGPR as compared with placebo (84% versus 76%, respectively; $p = .009$). Treatment was discontinued because of adverse effects in 27% of those receiving lenalidomide maintenance and 15% of those receiving placebo. Thromboembolic events were more frequent in the lenalidomide maintenance group (6%) compared with the placebo group (2%; $p = .01$); the incidence of second primary cancers was also more frequent (7.5% versus 2.9%, respectively). The incidence of second primary cancers (hematologic malignancies and solid tumors) was 3.1 per 100 patients in the lenalidomide maintenance group versus 1.2 per 100 patients in the placebo group ($p = .002$).[4]

The CALGB 100104 trial was a randomized, double-blind, placebo-controlled, phase 3 trial conducted in 460 patients ages 18 to 70 years who had stable multiple myeloma or a documented response 100 days after undergoing stem-cell transplantation. Patients were randomized 1:1 to either lenalidomide with a starting dose of 10 mg per day or placebo continued until disease progression. The primary end point was time to progression, and secondary end points included OS, response after transplantation, and feasibility of long-term treatment. At 18 months follow-up 20% of the lenalidomide group and 44% of the placebo group had disease progression or had died ($p < .001$). The study was unblinded after the primary end point was met, allowing 86 of the 128 eligible patients in the placebo group to cross over to receive lenalidomide maintenance treatment. At 34 months follow-up, 37% of the patients in the lenalidomide group and 58% of the placebo group had disease progression or had died. The median PFS was 46 months in the lenalidomide group and 27 months in the placebo group ($p < .001$). The 3-year OS was 88% in the lenalidomide group and 80% in the placebo group ($p = .03$). More patients in the lenalidomide group had grade 3 or 4 neutropenia and grade 3 or 4 hematologic adverse effects overall ($p < .001$). Thromboembolic events were more frequent in the lenalidomide group (1.3%) in comparison with the placebo group (0.4%). Treatment was discontinued due to adverse effects in 10% of the lenalidomide group, 1% of the placebo group, and 6% of the group that crossed over to lenalidomide. The incidence of second primary cancers was 7.8% in the lenalidomide group versus 2.6% in the placebo group ($p = .002$).[5]

The MM-015 trial was a randomized, double-blind, placebo-controlled, phase 3 trial conducted in 459 patients with newly diagnosed multiple myeloma who were 65 years of age or older and ineligible for transplant. Patients were randomized 1:1:1 to receive MPR-R, MPR, or MP. The MPR-R regimen consisted of induction with nine 28-day cycles of melphalan 0.18 mg/kg on days 1–4, prednisone 2 mg/kg on days 1–4, and lenalidomide 10 mg on days 1–21 each 28-day cycle, followed by lenalidomide maintenance with 10 mg on days 1–21 of each 28-day

cycle. The MPR group received the same MPR induction, followed by placebo maintenance, and the MP group received MP induction with placebo during induction and maintenance. After disease progression, the MPR and MP groups were allowed to cross over to receive lenalidomide maintenance treatment. Baseline characteristics were similar between the three groups, except the MP group had a higher Karnofsky performance-status score, which was not statistically significant. The primary end point was PFS. Secondary end points included OS, RR, time to response, duration of response, CR rates, VGPR rates, and adverse effects. MPR-R significantly improved PFS (31 months) in comparison with MPR (14 months, $p < .001$) and MP (13 months, $p < .001$). Among patients 65 to 75 years of age, MPR-R significantly prolonged PFS (31 months) in comparison with MPR (15 months, $p < .001$) and MP (12 months, $p < .001$). In patients older than 75 years of age, median PFS was 19 months with MPR-R, 12 months with MPR, and 15 months with MP, none of which were statistically significant. A VGPR or better was reported in 33% of the MPR-R and MPR groups and 12% in the MP group. The median time to the first evidence of a response was 2 months with MPR-R and MPR and 3 months with MP ($p < .001$ for both in comparison to MP). The 3-year OS rate was 70% in the MPR-R group, 62% in the MPR group, and 66% in the MP group. Treatment was discontinued due to adverse effects in 16% of patients in the MPR-R group, 14% in the MPR group, and 5% of the MP group. In the MPR-R group, maintenance discontinuation occurred in 8% of those 65 to 75 years old and in 17% of those older than 75 years. Grade 4 thromboembolic and neutropenic events were more frequent in the MPR-R group (32% and 35%) in comparison with the MPR group (12% and 32%) and MP group (4% and 8%), respectively. The 3-year rate of invasive second primary tumors was 7% with MPR-R, 7% with MPR, and 3% with MP.[6]

Bortezomib Data

Based on the results of a randomized, open-label, multicenter, phase 3 trial conducted in 222 patients with relapsed multiple myeloma after one to three previous treatments, bortezomib administered subcutaneously was approved for use in multiple myeloma. Patients were randomized 2:1 to bortezomib 1.3 mg/m^2 on days 1, 4, 8, and 11 by either subcutaneous injection or intravenous infusion for up to eight 21-day cycles. The baseline characteristics were similar between the two groups, except the subcutaneous group had more patients with a Karnofsky Performance Status of 80% or less (73% versus 49%), creatinine clearance <60 mL/min (41% versus 32%), more patients from Eastern Europe (66% versus 45%), fewer males (50% versus 64%), and more patients with standard risk cytogentics (86% versus 81%), none of which were statistically significant. The median age in both groups was 64.5 years. In the subcutaneous group, 38% had more than one previous treatment and received the last line of therapy 3.4 months prior to enrollment compared with 35% of patients in the intravenous group having more than one previous treatment, with the last treatment administered 5.8 months prior to enrollment. The median treatment duration for both the subcutaneous and intravenous groups was eight cycles with the cumulative bortezomib doses in the subcutaneous group of 33.76 mg/m^2 compared with 31.46 mg/m^2 in the intravenous group. Dexamethasone use was similar after cycle 4 in the subcutaneous and intravenous groups (56% and 53%, respectively). The primary end point was to show that subcutaneous administration is not inferior to intravenous administration in terms of overall response rate (ORR) after four cycles of single-agent treatment. Secondary end points included CR, near CR, and VGPR rates after four cycles, ORR after eight cycles, time to response, duration of response, time to progression, PFS, and 1-year OS. The median time to first response was 3.5 months in both groups ($p = .772$). ORR after four cycles was 42% in both groups ($p = .002$ for noninferiority) with both groups having 12% and 14% of patients with CR or near CR, respectively. After eight cycles of single-agent bortezomib or in combination with dexamethasone, the ORR was 52% in both groups with 20% of the subcutaneous and 22% of the intravenous patients achieving CR or near CR and 25% in both groups achieving at least VGPR. Median duration of response was 9.7 months in the subcutaneous group and 8.7 months in the intravenous group. There was no significant difference in time to progression, PFS, or OS after a median follow-up of 11.8 months in the subcutaneous group and 12 months in the intravenous group.[3]

Overall rates of gastrointestinal, respiratory, thoracic, mediastinal, and nervous system disorders; diarrhea; and peripheral neuropathy were all at least 10% lower in the subcutaneous group in comparison with the intravenous group. Grade 3 or higher adverse events were noted in 57% of the subcutaneous group and 70% of the intravenous group. In the subcutaneous and intravenous groups, peripheral neuropathy of any grade occurred in 38% and 53% of patients ($p = .044$), grade 2 in 24% and 41% of patients ($p = .012$), and grade 3 or worse in 6% and 16% of patients ($p = .026$), respectively. Treatment was discontinued due to adverse effects in 22% of the subcutaneous group and 27% of the intravenous group, and dose reductions were needed in 31% of the subcutaneous group and 43% of the intravenous group. Subcutaneous administration had acceptable injection site tolerability with the most common reaction being redness in 57% of the patients.[3]

Conclusion

The addition of lenalidomide and subcutaneuous bortezomib to the treatment options for patients with multiple myeloma has improved care during all stages of therapy. Lenalidomide maintenance prolongs response, but OS benefit is less obvious and it has toxicities. It is important to inform patients before starting lenalidomide about the risks of adverse effects and benefits of possible OS. The IFM 2005-02 and MM-015 trials showed no improvement in OS, whereas the CALGB 100104 trial did show an OS benefit. These trials do provide data on PFS, supporting the use of lenalidomide in maintenance therapy after careful assessment of the risks and benefits to the patient. It is important to note that two of the trials allowed patients to cross over from placebo to active treatment with lenalidomide. Overall, these new data show improved PFS with lenalidomide maintenance, but OS results are mixed.[4-6]

Bortezomib administered subcutaneously has an improved systemic safety profile compared with intravenous administration, with lower rates of grade 3 or greater adverse effects, fewer dose reductions, and fewer discontinuations due to adverse effects. Subcutaneous administration might be a good option for patients at higher risk for peripheral neuropathy and patients with poor venous access because it eliminates the need for repeated intravenous access or insertion of long-term central venous access devices, which might improve convenience for patients and physicians.[3]

Survey of Interest in Future HOPA Standards/Guidelines: Summary of Results

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From November 2012 through January 2013, a survey was sent to HOPA members to gauge their interest on topics for future standards or guidelines to be developed by HOPA. This survey was prepared and reviewed by members of the Standards Committee. The survey asked participants about standard demographic data, their use of national oncology-related guidelines, and their interest in a list of topics for future standards development. Survey participants also had the opportunity to identify additional topics of interest not specifically listed in the survey.

Results

A total of 227 members responded to this survey, a return rate of 12%. The majority of respondents (72.2%) classified themselves as oncology clinical pharmacists who had been in practice for either fewer than 5 years (30%) or 5–10 years (27%). Approximately 30% of survey participants listed their primary practice setting as hospital inpatient, while an additional 30% listed their practice setting as an ambulatory infusion center. Survey participants identified that they most frequently utilize National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) guidelines.

Given a list of potential topics for standards development, survey participants rated standards for pharmacist involvement in managing oral chemotherapy and standards for pharmacists in oncology community practice as the highest priority topics (58.5% and 35.9%, respectively). The lowest priority topics were identified as standards for oncology survivorship programs and oncology clerkship rotations for pharmacy students (14.8% and 14.3%, respectively). When asked to select two topics for potential standards development, 70% of respondents selected pharmacist involvement in managing oral chemotherapy, 35% selected pharmacist involvement in oncology community practice, and 29% selected oncology residency training clinical experiences. There were 41 additional suggestions for standards development beyond the list provided on the survey, which could be grouped into several categories: training/competency of oncology pharmacists (10 responses), electronic prescribing of chemotherapy (4 responses), dosing of chemotherapy (8 responses), and miscellaneous suggestions (19 responses). Standards for carboplatin dosing, oncology curriculum for schools of pharmacy, and handling of hazardous drugs were among the topics suggested by multiple survey respondents.

Conclusions

The survey indicates that HOPA members view development of standards for pharmacist management of oral chemotherapy as the highest priority topic followed by standards for pharmacists in oncology community practice. The Standards Committee will meet to discuss the future direction of standards development based on the feedback provided by this survey.

Several of the additional topics suggested for standards development have been covered by other national organizations. The American Society of Health System Pharmacists (ASHP) provides information on oncology residency clinical experiences, which can be accessed on its website (www.ashp.org). Guidelines for handling hazardous drugs have been published by ASHP and the National Institute for Occupational Safety and Health, which can be accessed on their websites (www.ashp.org and www.cdc.gov/niosh).

We thank you for your responses to this survey and thank the individuals who developed, reviewed, and summarized the survey.

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Renewed Inspiration and Excitement for Clinical Oncology Practice

The Experience of a Pharmacy Resident's First Time Attending the HOPA Annual Conference

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A pharmacy residency can be one of the most exciting, fast-paced, and educational times in a clinical pharmacist's career. It is also known for its heavy (and continually increasing) workload. As residents, we are taught to always pursue knowledge and continually push the boundaries of our expectations to refine our skills as future practitioners and, ultimately, to advance the profession of clinical pharmacy. But 9 months into my second year of residency, my usual high-energy and motivated attitude was being weighed down by the ever-growing list of tasks and administrative details stacked on top of additional staffing responsibilities and weekend trips to interview for jobs. Needless to say, when I boarded my transcontinental flight to Los Angeles, CA, to attend my first HOPA Annual Conference, I was feeling less than inspired about the trip ahead of me.

My expectation was based on the very large general pharmacy conferences I had attended in the past. I was anticipating a similar atmosphere and structure, only with continuing education topics that were a bit more interesting to me. My experience turned out to be so much more than that. The first surprise was the many familiar faces I encountered at the conference. Typically when I attend conferences, the only people I know are the people who came with me and maybe a classmate here or there. However, for the first time I began to understand this "small world" of pharmacy that everyone has been talking about. I not only recognized people and names from numerous places, but always seemed to be running into someone and striking up engaging conversations. From catching up with an old friend I met on a rotation at the Indian Health Service as a student to making new friends with a fellow pharmacist from Utah while having lunch in the sun, opportunities to network and strengthen connections were abundant.

The next surprising aspect was that not only were the educational sessions interesting to me, but they were applicable to clinical practice. There were disease state topics geared toward new practitioners that provided a great refresher and overview to prepare for future Board Certified in Oncology Pharmacy (BCOP) certification. I also found myself extremely interested in the sessions relating to practice management, drug shortage reimbursement issues, establishment of new monitoring programs, and creating new residency learning experiences. I was able to go beyond just taking notes on the slides to already thinking of how I could incorporate certain ideas into my practice site and jotting down topics that sparked my interest for new research projects and quality improvement strategies. This conference inspired me to evolve my way of learning from stockpiling as many facts as possible to using the ideas presented to develop my own vision of how to mold the knowledge I had gained into meaningful outcomes for patients.

The last major unexpected facet of my attendance at this meeting was the pride I felt in being part of such a progressive and empowered group. The individuals within this organization have put in countless hours of work to ensure that they are at the clinical forefront of oncology pharmacy practice and encourage active collaboration among us at our various institutions and across disciplines by expressing the desire to reach out to medical and nursing organizations to unify our approach to better patient care. Also, it is inspiring to see how far this relatively young organization has come and its plans for continued growth and increased prominence in the healthcare community. The increasing number of new pharmacy jobs in the field of oncology makes it evident that this specialty area is in for an exciting time of rapid growth and expansion. HOPA members will be pioneers in the field as we face unique issues and challenges. I am fortunate to have become involved in this organization early in my career, and I look forward to working with this dynamic group of colleagues and mentors for years to come.

Sitting on the plane heading back east into what would surely be another frigid snowstorm, I felt very different than I did when I boarded my outbound flight. I think I would most closely relate the feeling I had to that of a child returning home from a week at summer camp. Transplanted away from my daily life within my familiar cubicle, I was able to refresh my ambitious drive for excellence as a clinical practitioner, mentor, preceptor, and pharmacy practice leader. I know those words seem slightly above someone on the brink of completing her residency, but the confidence and skills I gained during this conference have allowed me to set those as goals for myself—goals that I will keep throughout my entire career.

Highlights from the HOPA Annual Conference Oncology Boot Camp 101

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The Oncology Boot Camp 101 session was presented during the HOPA Annual Conference to interested pharmacists and students, providing a basic overview of oncology in addition to a review of four of the most common cancers that affect the adult population (breast, colorectal, lung, prostate). The session included a discussion of the overall management of cancer patients and the goal of achieving the best possible outcomes for patients. This lecture was a great reminder that "while we are doctors of pharmacy, we are also doctors of therapies in practice." Basic treatment modalities, including surgery, radiation, and chemotherapy, and safe handling of chemotherapy by both patients and pharmacists also were reviewed.

A discussion regarding breast cancer was presented in a case-based style, emphasizing both early stage and metastatic breast cancer. Involvement from patients, family members, and pharmacists in supportive care groups and the pharmacist's role in survivorship also were highlighted. The presentation ended with a brief glimpse into the future of breast cancer treatment.

During the lung cancer presentation, summary charts and slides provided easy-to-follow treatment algorithms for both non-small-cell and small-cell lung cancer. The main pivotal trials were discussed for colorectal cancer, explaining each of the treatment options available. Specific toxicities associated with epidermal growth factor receptor inhibitors, regorafenib, and ziv-aflibercept were discussed with treatment options.

The pivotal trials for prostate cancer were also discussed, focusing on four new medications for castration-resistant prostate cancer (sipuleucel-T, cabazitaxel, abiraterone acetate, enzalutamide).

Overall, the Oncology Boot Camp 101 session was a great learning opportunity that provided specific cancer-related disease state overviews, discussion of pivotal trials, and outlines of treatment algorithms for breast, lung, colorectal, and prostate cancers.

Nominations for HOPA Membership Awards Now Being Accepted

Hematology/Oncology Pharmacy Association

hoparx.org

The HOPA Nominations & Awards Committee is now accepting nominations for the 2013 Membership Awards Program. Learn more and nominate a qualified candidate today at www.hoparx.org. The deadline for nominations is October 1, 2013.

HOPA Annual Conference Bone Marrow Transplant Boot Camp Review

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Prior to the start of the HOPA 9th Annual Conference in downtown Los Angeles, CA, attendees had the opportunity to participate in one of two unique boot camp curriculums, Oncology 101 or Bone Marrow Transplant (BMT). A considerable amount of hard work went into coordinating, preparing, and presenting these two events, which paid off in excellent attendance.

Building on the excitement generated from the American Society of Bone Marrow Transplant (ASBMT) meeting in Salt Lake City, UT, in February, the first HOPA BMT boot camp was designed to introduce hematology/oncology pharmacists to several fundamental concepts within BMT. The session was moderated by vice chair of the HOPA Education Committee Laura Wiggins, PharmD BCOP, and got off to a great start with an introduction to hematopoietic stem cell transplantation (HSCT) from Jeanne McCarthy-Kaiser, PharmD BCOP. McCarthy-Kaiser described the essential differences between autologous and allogeneic transplants, the various sources of stem cells used in transplantation, and the situations in which a myeloablative or nonmyeloablative regimen would be employed. While providing a basic depiction of the major concepts of HSCT, McCarthy-Kaiser also detailed issues such as mobilization, apheresis, and donor selection and matching.

To those members who specialize in BMT, providing a summary of graft-versus-host disease (GVHD) in 1 hour is a difficult task, but Ryan Bookout, PharmD BCPS BCOP, presented a wonderful overview of several import aspects. Bookout covered the pathology and differentiation of acute and chronic GVHD, patient-specific risk factors for the development of GVHD, clinical manifestations, and current strategies for the prevention and treatment of acute and chronic GVHD. His presentation provided a strong foundation for clinicians to build upon.

An equally daunting task to tackle within the confines of a 1-hour presentation is reviewing the common infections that occur in patients undergoing HSCT. Kaci Wilhelm, PharmD BCOP, explained why this unique population is susceptible to infection and the common pathogens that present. Wilhelm discussed bacterial, viral, and fungal infections, reviewing the risk factors, prophylaxis, and treatment of each and providing a comprehensive summation of available literature to support these practices. Wilhelm concluded by looking at some of the more rare infections that can occur and the appropriate vaccination practices.

During the final hour of the boot camp, all three expert lecturers participated in 20-minute discussions that delved more deeply into BMT concepts. During "A Day in the Life of an HSCT Pharmacist," Wilhelm touched on one of the hot topics of this year's conference—drug shortages. She encouraged us to work to reduce waste, develop drug allocation policies to fairly distribute available supplies and, more importantly, to communicate with transparency to both providers and patients. The second of these short sessions, led by Bookout, brought us all back to the days of pharmacy school with a review of pertinent drug interactions common in the BMT population. McCarthy-Kaiser ended the session with a presentation on screening and preventative practices for long-term survivors after HSCT. This topic is crucial for anyone practicing in this field because "80%–90% of all 2-year survivors of HSCT will survive to 10 years."

The goal of this exciting preconference session was to encourage our pharmacy colleagues to seek additional experience in specialized practice area of BMT. It also set the tone for the rest of the annual conference, which was packed with educational sessions, networking, and collaboration.

Highlights from the 2013 American Society for Blood and Marrow Transplantation Tandem Meeting

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The American Society for Blood and Marrow Transplantation (ASBMT) Tandem Meeting was held in Salt Lake City, UT, in February. The 5-day meeting was busy with concurrent plenary sessions, scientific sessions, workshops, and symposia highlighting the progress made during the past year in basic science, translational research, and clinical studies relating to all aspects of blood and marrow transplantation. Notable sessions included discussions on minimal residual disease in adult acute lymphoblastic leukemia, treatment of multiple myeloma in patients who are and are not transplant candidates, influence of reduced-intensity conditioning regimens on leukemia and lymphoma, and the impact of mutational analysis on treatment of myelodysplastic syndrome and acute myeloid leukemia (AML). Below is a review of selected oral abstracts from the meeting.

Abstract 2: Targeting Deacetylases as a Novel Strategy for Prevention of Acute GVHD

Histone deacetylase inhibitors (HDACi) possess activity to mitigate graft-versus-host disease (GVHD) in murine models. This was the first in-human clinical trial with a HDACi (vorinostat 100 mg PO BID) to assess safety and efficacy in reducing GVHD severity in patients undergoing reduced-intensity conditioning (RIC) for a matched related donor (MRD) transplant. Forty-five patients were enrolled in this phase 1/2 study. Patients received conditioning with fludarabine 40 mg/m^2 for 4 days and busulfan 3.2 mg/kg for 2 days. Vorinostat was added to standard immunosuppression of tacrolimus and mycophenolate mofetil. The primary endpoint of incidence of day 100 grade 2–4 GVHD was 22% (grade 3–4 4%) compared with historical control of 42%. Vorinostat was deemed as safe, tolerable, and feasible to administer after MRD RIC transplant.

Abstract 4: Improved Survival with Intravenous Busulfan (IV BU) Compared to Total Body Irradiation (TBI)-Based Myeloablative Conditioning Regimens: A CIBMTR Prospective Study

In general, IV busulfan is better tolerated than oral busulfan. There is mixed data regarding the superiority of cyclophosphamide (Cy) + TBI compared with oral busulfan–based myeloablative conditioning regimens. This abstract highlights the results of a prospective multicenter cohort study comparing these approaches in patients with myeloid malignancies undergoing matched related or unrelated donor transplant. Patients received conditioning with IV BU (>9 mg/kg) plus Cy (≥60 mg/kg) or fludarabine (Flu) (≥80 mg/m^2) or TBI (≥500 cGy in a single fraction or ≥800 cGy fractionated) plus Cy (≥60 mg/kg) or etoposide (≥30 mg/kg). Both groups received calcineurin inhibitor–based GVHD prophylaxis. The study's primary endpoint was the noninferiority of overall survival after IV BU compared with TBI. Almost 1,500 patients (IV BU, n = 1,025; TBI, n = 458) were enrolled in the trial from 120 centers. The two groups were similar with most patients having AML (68% IV BU, 78% TBI). Two-year probabilities of overall survival (95% confidence interval [CI]) were 56% (53%–60%) for IV BU+CY (59%) and IV BU+Flu (41%) compared with 48% (43%–54%) for TBI (p = .02). Probabilities of progression-free survival were 49% (45%–52%) for IV BU and 44% (40%–49%) for TBI (p = .17). Outcomes were not significantly different for treatment-related mortality, relapse, or treatment failure.

Abstract 6: Competitive TNF Inhibitor (ETANERCEPT) for the Treatment of Idiopathic Pneumonia Syndrome (IPS) Following Allogeneic Stem Cell Transplantation (SCT). A Joint Pediatric Blood and Marrow Transplantation Consortium (PBMTC) and Children's Oncology Group (COG) Study

Idiopathic pneumonia syndrome (IPS) is a rare but serious complication occurring acutely post-SCT. Mortality rates are reported as greater than 50% within 28 days of IPS diagnosis. TNF-α has an established role in the pathogenesis of IPS being elevated in plasma and bronchoalveolar lavage (BAL) fluid. A multicenter, phase 2, single-arm, open-label study in children evaluated using etanercept 0.4 mg/kg/dose given twice weekly for eight doses with standard therapy of corticosteroids at 2mg/kg/day. Steroids were tapered per investigator discretion after 7 days. Between 2006 and 2011, 39 patients were enrolled (median age, 11 years; range, 1–17 years), with 28 patients receiving study therapy (11 were excluded due to evidence of infection on BAL). Complete response was defined as survival to day 28 with complete discontinuation of supplemental oxygen support for >72 hours within the 28-day period. Complete response occurred in 71% of patients with a median time to response of 10 days (range 1–24). Patients not requiring mechanical ventilation had significantly higher response rates (100% versus 53%, p = .01). The treatment intervention compared to historical controls resulted in a higher overall response at day 28 (89%; 95% CI: 70–96) and at 1 year (63%; 95% CI: 42–79). Complications from infections occurred in five patients, and six patients experienced grade 3–5 organ toxicities. The results of this study are encouraging and require further evaluation. *(Note: Abstract 108 assessed etanercept added to corticosteroids for treatment of IPS in adults with no improvement in response or survival.)*

Abstract 50: A Multi-Center, Randomized, Double-Blind, Phase III Clinical Trial Comparing Steroids/Placebo Vs. Steroids/Mycophenolate Mofetil as Initial Therapy for Acute Graft-Verus-Host Disease. Blood and Marrow Transplant (BMT) Clinical Trials Network (CTN) Study 0802

Steroids are the current standard of care for treatment of acute GVHD (aGVHD), but durable responses are uncommon. The BMT CTN 0302 trial tested one of four different agents with steroids and

determined mycophenolate mofetil (MMF) to be the most promising. The 0802 trial was a phase 3, multicenter, randomized trial conducted by the BMT CTN to test the addition of MMF (1,000 mg PO/IV Q 8H or 20 mg/kg for patients <60 kg) or placebo to steroids (prednisone 2 mg/kg/day or equivalent) as initial aGVHD treatment. Steroids could be tapered after at least 3 days per the treating physician, but the study required patients to be on at least 0.25 mg/kg/day of prednisone until day 28. MMF was continued until day 56 or until steroids were discontinued if this occurred sooner. The primary endpoint was GVHD-free survival at day 56 after therapy initiation. The predetermined futility rule for GVHD-free survival at day 56 was met at a planned interim analysis after 236 patients (out of 372) were enrolled (MMF, *n* = 117; placebo, *n* = 119). At randomization, 65% of patients had grade I/II GVHD, 28% had grade III, and 6% had grade IV. At day 56, GVHD-free survival occurred in 69 MMF patients (60.5%; 95% CI: 51.6–69.5) and 60 placebo patients (52.2%; 95% CI: 43–61.3; *p* = .78). Chronic GVHD, nonrelapse mortality, and overall survival at 6 months were not significantly different. Cytopenias occurred more often in the MMF group and hyperglycemia was more common in the placebo group. The addition of MMF to steroids unfortunately did not show an improvement in GVHD survival.

Abstract 80: Phase I/II Multicenter Clinical Trial of Lenalidomide Maintenance After Allogeneic Hematopoietic Cell Transplant (alloHCT) in Patients with High Risk (HR) Multiple Myeloma (MM)

Patients with HRMM are in danger of relapse and need new methods to prevent this complication. AlloHCT utilizes graft-versus-myeloma to help control the disease posttransplant. Reduced-intensity conditioning (RIC) alloHCT provides a treatment option with low transplant-related mortality (TRM). Despite graft-versus-myeloma effect with RIC alloHCT, patients are at risk of relapse and maintenance therapy may improve outcomes. The primary study outcome was to determine the tolerability and safety of lenalidomide (Len) maintenance for 1 year post-alloHCT in patients with HRMM. HRMM was defined as relapse after autologous HCT or plasmablastic morphology > 2%, β2M ≥ 5.5 mg/L, hypodiploidy, del 13 by standard karyotyping, t(4;14), t(14;16) or del 17p. Len was started at 10 mg/day on days 21 of a 28-day cycle. The dose was increased by 5 mg monthly to a maximum of 25 mg/day. Due to toxicity, doses could be reduced to 5 mg/day or 5 mg every other day. Twenty-nine patients were available for evaluation who had completed 177 cycles completed, average of 6.1 cycles per patient. Len doses were >10 mg/day in 17%, 10 mg/day in 45%, 5 mg/day in 17%, and 5 mg every other day in 21% of patients. Maintenance Len was discontinued for various reasons, including aGVHD (37%), MM progression (33%), neutropenia (10%), skin rash (10%), and infection (10%). The most common reason for lowering doses or interrupting therapy was grade 3-4 neutropenia. Fifty-five percent of patients achieved a complete response (CR), with 4 of 14 patients achieving CR after 2–5 cycles. Patients were evaluated from the start of maintenance therapy with Len and the results concluded the cumulative incidence of MM progression was 28% (95% CI: 12%–48%), TRM was 3% (0%–12%), and 17% (6%–33%) grade ≥3 aGVHD. Twelve-month probabilities for progression-free survival were 68% (95% CI: 46%–83%) and overall survival was 88% (95% CI: 67%–96%). Len therapy was completed in 34% of patients but appears to be generally well tolerated despite dose reductions. Lowering starting doses and utilizing growth factor support may be needed in this setting. Survival outcomes do suggest a benefit of maintenance Len for HRMM patients after alloHCT.

The Pharmacy Special Interest Group (SIG), in partnership with the National Donor Program System Capacity Initiative, hosted a 2-day Fundamentals of Hematopoietic Stem Cell Transplantation Training Course geared toward new practitioners of all disciplines, including pharmacists, nurses, advanced practice professionals, and medical oncology fellows. The printed material from this meeting is available for purchase (www.asbmt.org). The Pharmacy SIG also coordinated a 2-day Pharmacists Conference for more seasoned practitioners, presenting updates on areas of practice ranging from the role of regulatory T cells in GVHD to iron chelation posttransplantation. The pharmacy meeting also included highlights from the American Society of Hematology meeting, updates on infectious diseases, and a review on new literature for GVHD prevention and treatment.

The meeting concluded with several pharmacy abstracts being accepted as poster presentations. The top four pharmacy abstracts submitted were selected for oral presentations during the Pharmacists Conference to compete for the "Best Pharmacy Abstract." Andrea Faison and Eric Chow, from the University of North Carolina Hospitals and Clinics, presented their research regarding their institution's use of an algorithm for chemomobilization and filgrastim-based mobilization with plerixafor (Abstracts 121 and 122). Olga Miltano, from the New York Medical College, presented research on utilizing mycophenolate mofetil in combination with tacrolimus for the prevention of acute and chronic GVHD in pediatric allogeneic stem cell transplant recipients (Abstract 124). Ashley Teusink, from Cincinnati Children's Hospital Medical Center, presented data on the impact of pharmacogenetics and therapeutic drug monitoring on optimizing voriconazole dosing in pediatric patients undergoing hematopoietic stem cell transplantation (Abstract 123). Dr. Teusink's oral abstract was selected as the winner of the prestigious Best Pharmacy Abstract award.

All abstracts from the 2013 Tandem Meetings are available in the February issue of *Biology of Blood and Marrow Transplantation* (Volume 19, Number 2, Supplement 2). Audio and slide recordings may also be ordered from the ASBMT website (www.asbmt.org).

Highlights from the December 2012 San Antonio Breast Cancer Symposium

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Ten-Year Tamoxifen Better than 5-Year at 15 Years Follow-Up[1]

One of the most exciting findings presented at the San Antonio Breast Cancer Symposium came from the ATLAS (Adjuvant Tamoxifen—Longer Against Shorter) trial: the duration of tamoxifen therapy in the adjuvant setting may further improve survival in early-stage breast cancer patients. Some studies have suggested that the optimal duration of tamoxifen in the adjuvant setting is 5 years and that longer duration would increase the risk of endometrial cancer without bringing any additional benefit. The ATLAS study was an international randomized clinical trial designed to determine the optimal duration of adjuvant tamoxifen in early-stage breast cancer. This study was initiated in the mid-1990s and randomized 6,846 women with early-stage estrogen receptor-positive (ER+) disease who had already completed 5 years of tamoxifen to either stop therapy or continue for 5 additional years to compare mortality rates over 15 years after diagnosis. These patients represented a diverse population, with 25% from Asia or the Middle East, 28% from Latin America, and 47% from Europe/United States/Australia-New Zealand/South Africa. More than 50% of the patients were node-negative at the time of enrollment. Analyses done between 5 to 10 years after diagnosis showed little benefit for tumor recurrence rate (13.1% versus 14.5%) and breast cancer mortality (5.8% versus 6.0%) from continuing tamoxifen when compared with stopping after 5 years. However, at the 15-year analysis, the additional 5 years of adjuvant tamoxifen therapy brought about a 4% reduction in tumor recurrence rate (21.4% versus 25.1%) and an approximate 3% reduction in breast cancer mortality (12.2% versus 15.0%); both were statistically significant. The death rate ratio was 0.97 in the first decade after diagnosis, but decreased to 0.71 in the second decade with a *p*-value of .0016. Although 5 additional years of tamoxifen was associated with 0.2% extra mortality (0.4% versus 0.2%) from endometrial cancer, the 3% gain in breast cancer mortality shifts the benefits to risk ratio in favor of 10-year tamoxifen. The patients are still being followed for evaluation of benefit at a later time point. These findings now change the standard of care in younger patients with ER+ breast cancer who remain premenopausal at the end of 5-year tamoxifen therapy. It is still unclear whether 10-year tamoxifen is superior to tamoxifen followed by aromatase inhibitors or to extended use of aromatase inhibitors in postmenopausal women.

Promising Role of PD0332991, a CDK4/6 Inhibitor, in Combination with Letrozole in ER+/HER2- Breast Cancer[2]

Because of promising preclinical and clinical phase 1 data, PD0332991, a cyclin-dependent kinase (CDK) 4/6 inhibitor, was investigated for efficacy in combination with letrozole in patients with ER+/HER2- breast cancer. In this randomized phase 2 study, postmenopausal women with stage 3B or stage 4 ER+/HER2- disease were randomized to PD0332991 + letrozole 2.5 mg/day (*n* = 84) or placebo + letrozole (*n* = 81). The results of the interim analysis were reported at the symposium. The overall clinical benefit rate (defined as complete response + partial response + stable disease ≥ 24 weeks) was higher with PD0332991 compared with placebo (7% versus 44%). Furthermore, the median progression-free survival time was 26.1 months with PD0332991 + letrozole compared with only 7.5 months with placebo + letrozole. Remarkably, PD0332991 showed a very moderate toxicity profile with manageable uncomplicated neutropenia and leukopenia as its most common adverse effects. Exploratory analyses to identify predictors of response to PD0332991 were unsuccessful, with ER positivity as the only biomarker required for therapy.

500 mg Versus 250 mg Fulvestrant: Higher Dose Still Better in Advanced ER+ Breast Cancer[3]

The CONFIRM (Comparison of Faslodex in Recurrent or Metastatic Breast Cancer) trial investigating the optimal dose of fulvestrant confirms previous findings by showing that a higher dose of fulvestrant (500 mg) is better than 250 mg in postmenopausal women with locally advanced or metastatic ER+ breast cancer that either recurred or progressed following prior endocrine therapy. In this randomized, double-blind, multi-center, phase 3 study, more than 700 patients participated and received either one intramuscular (IM) injection of 250 mg fulvestrant plus one placebo injection or two IM injections of 250 mg fulvestrant (trial arm) on day 1, day 14, day 28 and every 28 days thereafter. A final analysis at 75% maturity revealed that the higher dose of fulvestrant was associated with a median overall survival of 26.4 months versus 22.3 months with the lower dose (HR 0.81; 95% CI: 0.69, 0.96; nominal *p* = .016). Furthermore, the 4.1 month median survival advantage and 19% reduction in relative risk of death associated with the high dose fulvestrant were not accompanied by clinically important differences in the toxicity profiles. Thus, 500 mg is the recommended fulvestrant dose in ER+ postmenopausal patients with advanced breast cancer.

Letrozole Better than Tamoxifen in Lobular Carcinoma[4]

The Breast International Group (BIG) 1-98 trial compared the efficacy of tamoxifen and letrozole in postmenopausal women with invasive lobular carcinoma (ILC) and invasive ductal carcinoma (IDC). This

study also took into consideration the distribution of Luminal A (approximately 77% of the study population, defined as Ki-67 < 14%) versus Luminal B (approximately 19%, defined as Ki ≥ 14%) subtypes. In this randomized phase 3 trial, 324 ILC and 2599 IDC patients were enrolled. In patients with ER+/HER2- ILC, letrozole showed significantly higher rates of both 5-year disease-free survival (89% versus 75%; hazard ratio [HR] 0.48; p = .03) and overall survival (96% versus 86%; HR 0.40; p = .045) than tamoxifen. Treatment efficacy was not dependent on Luminal gene expression subtype. On the other hand, in patients with IDC, letrozole was associated with significantly improved overall survival rate compared with tamoxifen only in the Luminal B subtype, and the HR for overall survival was only 0.73. This significant extra survival benefit with letrozole adjuvant monotherapy may lead to an evaluation of letrozole in premenopausal ILC patients even though tamoxifen has so far been the standard choice in this population. Letrozole should be considered over tamoxifen for the upfront treatment of patients diagnosed with ILC regardless of proliferation status.

Two- Versus One-Year Adjuvant Trastuzumab: No Additional Benefit of Longer Treatment Duration[5]

One year of adjuvant trastuzumab is the standard of care for patients with HER2+ early stage breast cancer. The HERA (herceptin adjuvant) trial, which compared the efficacy and safety of 1 year and 2 years of adjuvant trastuzumab, found no significant survival advantage to the longer treatment. In this international, multicenter, phase 3, randomized trial, 5,102 women with HER2+ early stage breast cancer were randomized to observation, 1 year of trastuzumab, or 2 years of trastuzumab after completion of their elected surgery, chemotherapy, and/or radiotherapy. At 8 years of median follow-up, 1,552 patients in the 1-year arm and 1,553 patients in the 2-year arm remained disease-free for longer than 1 year from randomization. Similarly, overall survival was comparable between the two treatment arms. As expected, 1 year of trastuzumab treatment improved disease-free survival (DFS) and overall survival (OS) when compared with observation in this setting regardless of hormone receptor status (DFS: hazard ratio [HR] 0.76, p < .0001; OS: HR 0.76, p = .0005). The incidence of symptomatic congestive heart failure was comparable in both 1- and 2-year arms, but the rate of asymptomatic cardiac dysfunction was higher in the 2-year arm (7.2%) compared with the 1-year arm (4.1%). Cardiac events occurred primarily during trastuzumab therapy and most were reversible after treatment cessation. One year of adjuvant trastuzumab remains the standard of care for patients with HER2+ early stage breast cancer.

Activating HER2 Mutations in HER2-Negative Breast Cancer: Possible Role for Anti-HER2 Therapy[6]

It is believed that breast cancer patients with activating HER2 mutations may benefit from anti-HER2 therapy. In total, eight genome-sequencing studies that included approximately 1,500 patients were reviewed. Twenty-five patients were identified to have HER2 mutations; nearly all the patients lacked HER2 gene amplification, a hallmark of HER2+ breast cancer. Thirteen HER2 mutations were identified; common mutation sites were at amino acids 309 or 310 (20%) and at amino acids 755–781 (68%), and most were considered activating mutations. Trastuzumab and lapatinib were tested in vivo for their anti-HER2 efficacy against seven activating HER2 mutations: V777L, D769H, V842I, L755S, del. 755–759, R678Q, and G309A. All seven mutations were resistant to trastuzumab, two (L755S and del. 755–759) were resistant to lapatinib, and, surprisingly, all were susceptible to an irreversible HER2 inhibitor, neratinib. The majority of HER2 mutations occur in HER2 gene amplification-negative patients. Due to resistance patterns with trastuzumab and lapatinib, neratinib, which shows activity against all mutations, is a potential treatment option to target these mutations. A multicenter, phase 2 trial has been launched to look at the efficacy of neratinib treatment for metastatic breast cancer with HER2 somatic mutations.

No Clinical Benefit of Bevacizumab for Operable Primary Triple-Negative Breast Cancer[7]

Efficacy and safety of 1-year adjuvant chemotherapy with or without bevacizumab was evaluated in an open-label, multinational, randomized, phase 3 trial that included 2,591 patients with triple-negative operable primary invasive breast cancer. Disease-free survival (DFS) rates at 3-year follow-up were similar for the two treatment arms (83.7% for chemotherapy plus bevacizumab versus 82.7% for chemotherapy alone). Ninety-three deaths (7.1%) were reported for the chemotherapy plus bevacizumab versus 107 (8.3%) for the chemotherapy alone arm. In addition, patients in the bevacizumab arm experienced more serious (grade 3 or higher) adverse events of hypertension (7% versus <1%) in the chemotherapy phase compared with chemotherapy alone. The toxicity profiles for both treatment arms were comparable to those seen in previous trials. The results of this trial suggest a limited role for the use of bevacizumab in the treatment of early stage triple-negative breast cancer, and chemotherapy remains the only standard of care systemic treatment.

Eribulin Versus Capecitabine for Metastatic Breast Cancer: Comparable Efficacy[8]

A phase 3, open-label, multicenter trial evaluated the efficacy of eribulin compared with capecitabine as first-, second-, or third-line therapy. The study enrolled 1,102 patients with metastatic breast cancer who had previously received anthracycline- and taxane-based chemotherapy. Median progression-free survival for the capecitabine arm was 4.2 months versus 4.1 months for the eribulin arm, and median overall survival for capecitabine and eribulin were 14.5 months and 15.9 months (p = .056), respectively. An exploratory subset analysis showed favorable hazard ratios with eribulin in subgroups of patients with triple-negative, ER-, and HER2- breast cancer. Grades 3/4 neutropenia were more common with eribulin (46%) compared with capecitabine (5%); however, the frequency of febrile neutropenia was comparable between the two treatment arms. Nonhematologic adverse events were similar to those reported in previous trials with these agents. Higher rates of hand-foot syndrome (45% versus <1%), diarrhea (29% versus 14%), and vomiting (17% versus 12%) occurred in the capecitabine treatment arm, while peripheral neuropathy (13% versus 7%) and alopecia (35% versus 4%) occurred more frequently in those who received eribulin. In summary, eribulin had similar efficacy while possessing a different toxicity profile compared with capecitabine.

Adjuvant Chemotherapy in Patients with Local and Regional Recurrence of Breast Cancer[9]

A randomized controlled trial evaluated the efficacy of providing adjuvant chemotherapy in patients with isolated local or regional recurrence (ILRR) of breast cancer in combination with surgery and radiation therapy. Patients with ILRR of breast cancer generally have a poor prognosis with a disease-free survival (DFS) of only 50% at 5 years. This was the first trial to show the benefit of adjuvant chemotherapy in patients with ER-negative recurrent breast cancer. Patients were randomized to either the adjuvant chemotherapy arm or the observation arm. Patients in the chemotherapy arm were treated with two agents for 3 to 6 months. At 5-year follow-up, the DFS was 69% versus 57% for chemotherapy versus observation, respectively (hazard ratio [HR] 0.59, p = .045). In ER-negative patients, the DFS was 67% for patients receiving chemotherapy and 35% for those in the observation arm (p = .007). In contrast, no significant difference in DFS rates between the two arms was found (70% versus 69%) in ER-positive patients. Overall survival at 5 years was 88% and 76% for those who received chemotherapy and those who did not, respectively (p = .02). The overall survival lacked statistically significant differences in the ER-positive and ER-negative subgroups. The use of adjuvant chemotherapy is highly recommended in patients with ILRR of breast cancer regardless of ER status. Although the data are strongest in ER-negative patients, the findings for ER-positive patients may be premature and may require longer follow up to achieve similar benefit.

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Board Update

Niesha Griffith, RPH MS FASHP, HOPA President

Accomplishments to Highlight

As we embark on HOPA's 10th year as an organization, HOPA members have much to be excited about and look forward to in the coming year. Our annual meeting was a tremendous success with a record number of conference attendees (727!). As in previous years, attendees were provided with a variety of clinically stimulating and practice management–focused sessions. An addition to this year's conference was the advocacy-focused session, featuring Jeremy Scott and Erin Morton, our health policy representatives from Drinker Biddle & Reath. They were able to impart humor to the often confusing and frustrating topic of healthcare reform. (Check out the Legislative Tracker on the HOPA website to stay in touch with the issues throughout the year.) The preconference research workshop and two boot camps were also well attended, further emphasizing the continued importance of this type of programming for our membership.

During the meeting, outgoing HOPA President Lisa Holle had the pleasure of announcing that the HOPA Drug Shortage Survey had been released on that very day (March 21) and would be published in the April 1, 2013, issue of *American Journal of Health-System Pharmacy*. It is the first published national drug shortage survey that focuses specifically on oncology drug shortages and how they impact the care of cancer patients.

Lisa also announced the approval of the first document created by the Pharmacy Practice Standards Task Force: the *Scope of Practice Document for Hematology/Oncology Pharmacy*. The document was recently released for HOPA membership review and comment. The purpose of this document is to describe the evolution of hematology/oncology pharmacy; address the knowledge, skills, and functions of a hematology/oncology pharmacist; and promote a better understanding of the profession. Once finalized, this document will serve as a valuable resource for our organization as we continue to promote the importance of our role to both patients and political decision makers. In addition, the *Scope* will provide members with a tool to define or create job descriptions and responsibilities, educational offerings, standards, certifications, and quality improvement activities, and even assist with efforts to increase the number of oncology pharmacist positions within their organizations.

On behalf of myself and the HOPA Board Members, I want to thank every HOPA member who contributed to this meeting, including program planners, session speakers and moderators, and HOPA professional staff who supported all of these various activities. HOPA's success is a direct result of the involvement and dedication of our members.

Speaking of success, HOPA's membership has reached an all-time high, with more than 2,000 members as of April 2013! This marks an important milestone for us, but one we should aspire to rapidly surpass. As we continue to improve our visibility through the success of our meetings, advocacy initiatives, research awards, publications, and engagement with social media, this number will only grow.

Exciting Things to Come

Fall Practice Management Meeting

During the HOPA Board Meeting in March, the board voted to support the development of a Fall Practice Management Meeting. This will be our first live educational offering outside of the annual conference. A successful conference is one means of expanding our membership base by attracting new members; however, additional educational offerings are necessary to meet specific needs that may not be as effectively conveyed through a broadly focused meeting. In an era of healthcare reform and cost minimization, our goal is to equip oncology pharmacists and pharmacy leaders with the tools necessary to meet contemporary and future challenges. The meeting will be held September 27, 2013, in Chicago and will cover the following topics aimed at providing many of those necessary tools: implementing clinical services and new technologies, facility and staff compliance with USP 797/NIOSH regulations, reimbursement essentials, managing high-cost medications, formulary considerations for biosimilars, and communicating pharmacy's message to the C-suite (hospital leaders). The day will culminate in a "networking with the experts" cocktail reception for additional interaction with speakers from each of the day's sessions.

Leadership Development

The board also voted to use a facilitator to assist with incorporating leadership development into all aspects of the organization. The first steps in this journey involve making the necessary enhancements to our strategic plan during our summer board meeting. Our intent is to develop a foundation that supports incorporation of leadership development into (1) the selection of all HOPA leaders, (2) on-boarding and development of board members, and (3) educational programming for all HOPA members (including the development of a formal mentorship program). This is a necessary and important step for us to take as an organization as we consider the aforementioned societal changes as well as an anticipated pharmacy leadership gap.

Oncology Interest Groups

In the previous issue of the newsletter we encouraged members to join one of the five new specialty Listservs (Administration, Ambulatory, BMT, New Practitioner, Pediatrics). We are currently looking for volunteers to serve as cofacilitators for each of these groups and liaisons to the Membership Committee. These forums will provide opportunities to continue many of the important

discussions that began during the various special interest group meetings at the annual conference. Although this is an exciting start to an anxiously awaited member benefit, this is likely just the beginning phase for these groups. It will be exciting to watch them grow and contribute to the future development of the organization and its educational programming.

Industry Relations Council (IRC)

Our industry partners were presented with revisions to both IRC membership levels and benefits during the annual conference. We received positive feedback regarding these changes and look forward to the growth of the council over the next year. On behalf of myself and the board, I want to thank Amgen, Bristol-Meyers Squibb, Eisai, Millennium: The Takeda Oncology Company, and Teva Oncology for their support of the HOPA IRC.

Research Award

The HOPA Foundation Board recently announced the opening of a call for proposals for the 2013 HOPA Foundation Research Award. A total of $50,000 in funding is available to be awarded in 2013 through a competitive peer-review process. A letter of intent must be submitted electronically by June 14, 2013. Visit the HOPA website for a full description of the application process.

Preserving HOPA History

As I prepared my incoming-president remarks for the conference, I thought it would be interesting to look back through HOPA's history. Information about the founding members, past presidents' remarks, meeting agendas, and annual accomplishments from the previous 10 years were just some of the things I was interested in reviewing. To my surprise, much of this information is not readily available on the website. Photos from past meetings are also noticeably absent. I see this both as an opportunity and a challenge. The opportunity is for HOPA to begin to collect and archive these important items from our past. The challenge is to all of *you* to share what you have saved. We will be creating a separate task force specifically for this purpose, so start looking under beds, in closets and drawers, and on office bookshelves for any information you may have saved!

Becoming a Part of HOPA's Future

During my incoming remarks, I made a point to talk about my path to the HOPA presidency. I am going to summarize some of what I said that day because I believe that building interest in a leadership path within HOPA is critical to the future success of this organization.

There is really nothing terribly special about any of us who have volunteered to serve on the board. We are in these positions because of our dedication to the care of cancer patients and the organization whose core purpose is to support hematology/oncology pharmacy practitioners. We are also committed to the promotion and advancement of our profession to optimize the care of individuals affected by cancer.

My interest and passion for improving the care of cancer patients originated when I was assigned to manage the James Cancer Hospital Pharmacy Services. More than 12 years later, I can't imagine working anywhere else.

Following the inaugural HOPA Annual Conference in La Jolla, CA, I made a conscious decision to stay involved with HOPA and volunteer for a committee. After I was appointed to a committee (Legislative Affairs, now Health Policy), I became an active participant. I had become active in health policy issues in Ohio, and this committee gave me the chance to expand those skills to the national level. Because of my active involvement, I was asked to be vice chair and then chair of the committee.

I have been fortunate to have great mentors throughout my career. Effective mentorship was a key component of my path to a HOPA leadership position. I honestly believe that I would not be in this position today if it wasn't for the personal and professional influence of those individuals.

If you are new practitioner, find a mentor. Don't be shy about it. Ask someone you look up to or someone who can provide you with valuable learning experiences. If you are a seasoned practitioner, offer to be a mentor—both to new practitioners and to those you believe still have opportunities to meet their full potential. With a looming leadership gap facing the pharmacy profession, strong mentors are vital to the leadership development of our future hematology/oncology pharmacy leaders.

Ultimately, I believe that it was a combination of my early and active involvement in HOPA, strong mentorship, and passion for advocacy that led me to run for the board and ultimately pursue the HOPA presidency.

Therefore, my message to all of you who might someday envision yourself as a committee chair, board member, or president is: volunteer (via the Volunteer Activity Center), stay active, select a mentor, and eventually become one yourself. As we create our leadership development agenda for the organization, I can assure you that these will be key components of our plan!

Please feel free to reach me directly with your thoughts about anything I have mentioned in this update or any thoughts or ideas you have for HOPA in general (niesha.griffith@osumc.edu). Although I have met many of you, I look forward to meeting many more of you during the next year. Have a safe and happy summer!

Cabozantinib (Cometriq®)

Class: Tyrosine kinase inhibitor

Indication: Treatment of patients with progressive, metastatic medullary thyroid cancer

Dose: 140 mg by mouth once daily without food

Dose modifications: Hold therapy for any grade 4 hematologic adverse reactions, ≥ grade 3 nonhematologic adverse reactions, or intolerable grade 2 adverse reactions. Upon resolution, reduce the dose from 140 mg to 100 mg daily, or from 100 mg to 60 mg daily. If the previous dose was 60 mg daily, resume at 60 mg if tolerated, otherwise discontinue treatment.

Common adverse effects (>30% incidence): Diarrhea, stomatitis, nausea, oral pain, fatigue, decreased weight and appetite, dysgeusia, palmar-plantar erythrodysesthesia, hair color changes, hypertension, elevated liver function tests, hypocalcemia, lymphopenia, neutropenia, thrombocytopenia

Serious adverse effects: Black box warnings for perforations, fistulas, and hemorrhage

Drug interactions: Substrate of CYP3A4; avoid strong CYP3A4 inhibitors and inducers.

Cabozantinib for Metastatic Medullary Thyroid Cancer

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Thyroid cancer is the fifth most common malignancy in women and affects approximately three times as many women as men. It has been estimated that 60,220 new cases of thyroid cancer will be diagnosed in 2013 and approximately 1,850 will die from this malignancy.[1] There are three main histologic subtypes of thyroid carcinoma, including differentiated, which accounts for the majority of cases, anaplastic, and medullary.[2-4] Medullary thyroid cancer (MTC) constitutes approximately 4% of all thyroid cancers and is most often sporadic in nature, although up to a quarter of cases worldwide can be attributed to a hereditary disorder.[4] MTC is a cancer of the thyroid parafollicular C cells which are responsible for hormone secretion, particularly calcitonin.[5]

Initial therapy for MTC is a total thyroidectomy. Surgical resection of the neck and radiation may be utilized in select patients based on tumor size and surgical margins.[4,6] Approximately half of patients present with limited disease that has a low recurrence risk and a 10-year survival rate of 95.6%.[4,7] Those with metastatic disease on diagnosis have worse outcomes. Their 10-year survival rate is much lower (40%), which represents approximately 13% of patients.[7] This patient population is being targeted for new therapeutic strategies.

Historically, traditional chemotherapeutic agents have not been shown to produce adequate response rates or duration of response in MTC.[5,8] The search for targeted therapy began with the discovery of a mutation in the tyrosine kinase rearranged during transfection (RET), a proto-oncogene, which is found in almost all hereditary MTC and as many as 50% of sporadic MTC.[4,9] Current treatment recommendations for unresectable or metastatic disease from the National Comprehensive Cancer Network include two tyrosine kinase inhibitors (TKIs) that target RET, vandetanib and cabozantinib. Other treatment options, dependent on prior response and symptoms, include radiation, best supportive care, clinical trial, and two other TKIs, sorafenib and sunitinib, in select patients.[6]

Cabozantinib (Cometriq®, Exelixis, Inc) is an oral TKI that was approved by the U.S. Food and Drug Administration (FDA) on November 29, 2012, for the treatment of patients with progressive metastatic MTC.[10] Cabozantinib inhibits the tyrosine kinases RET and vascular endothelial growth factor receptor (VEGFR) 1, 2, and 3, as well as many others including MET, KIT, TRKB, FLT-3, AXL, and TIE-2. The result of this inhibition is interruption of cellular signaling leading to the impairment of tumor angiogenesis, disruption of the tumor microenvironment, and decreased tumor invasiveness and metastasis.[11,12]

Cabozantinib showed activity in a phase 1 dose-escalation study that enrolled 37 patients with MTC. Ten patients (29% of 35 evaluable patients) achieved a partial response and 41% had stable disease for at least 6 months. Interestingly, the authors reported that they did not find a relationship between mutations in RET and clinical response, indicating that the drug may be efficacious in the absence of this mutation.[12]

The safety and efficacy of cabozantinib in MTC was evaluated in the phase 3 EXAM trial.[10,13] This study was an international, double-blind, randomized, controlled clinical trial of 330 patients with locally advanced or metastatic MTC with documented disease progression within 14 months of enrollment. Participants were randomized to cabozantinib 140 mg orally daily or placebo in a 2:1 ratio, and were treated until intolerable toxicity or progression; no crossover was permitted. The primary endpoint was progression-free survival (PFS), documented by an independent review facility according to response evaluation criteria in solid tumors (RECIST), and secondary endpoints included overall response rate (ORR) and overall survival (OS). Median patient age was 55 years, 67% were male, 21% of patients had previously received therapy with a TKI, and 48% were positive for the RET mutation. PFS was significantly longer in the cabozantinib arm versus placebo (median 11.2 months vs. 4.0 months; hazard ratio [HR] 0.28, 95% confidence interval [CI] 0.19–0.40, $p < .0001$). The ORR was 27% in patients who received cabozantinib and 0% given placebo ($p < .0001$). At the time of a planned interim analysis, there was no difference in OS between the two groups. As of this writing, the full results of the EXAM trial have not been published.

The most common adverse effects reported with cabozantinib (≥20% of patients) include diarrhea, stomatitis, nausea, oral pain, constipation, abdominal pain, vomiting, fatigue, asthenia, decreased weight and appetite, dysgeusia, dysphonia, palmar-plantar erythrodysesthesia, hair

color changes, and hypertension. Laboratory abnormalities associated with cabozantinib include elevations in liver function tests (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and bilirubin), reductions in numerous electrolytes (calcium, phosphate, magnesium, potassium, and sodium), neutropenia, lymphopenia, and thrombocytopenia. Sixteen percent of patients discontinued treatment due to adverse effects and the majority of patients receiving cabozantinib required a dose reduction during treatment (79%). As expected with an inhibitor of VEGFR, cabozantinib causes hypertension, proteinuria, and wound complications and carries a black box warning for perforations, fistulas, and hemorrhage. Thrombotic events, osteonecrosis of the jaw, and reversible posterior leukoencephalopathy syndrome have also been reported. Cabozantinib does not appear to affect the QTcF (Fridericia) interval as significantly as the similar drug vandetanib. A QTcF interval increase was found to be 10–15 ms (mean) after 4 weeks of drug exposure; however, no significant cardiac changes were observed and no patient had a QTcF > 500 ms.[11]

The FDA-approved dose of cabozantinib is 140 mg orally once daily. Therapy should be held in patients with any grade 4 hematologic, grade 3 or above nonhematologic, or any intolerable grade 2 adverse reactions. Upon resolution to baseline or grade 1 adverse reactions, the dose should be reduced to 100 mg or 60 mg, respectively, daily in those previously receiving 140 mg or 100 mg daily, respectively. Cabozantinib should be held at least 28 days prior to surgical procedures due to the risk of wound dehiscence and impaired healing. In vitro data suggests cabozantinib is metabolized by CYP3A4. It has varying degrees of inhibition on CYP2C8, 2C9, 3A4, and p-glycoprotein and has demonstrated induction of 1A1. Because of this, it is recommended to avoid using strong CYP3A4 inhibitors or inducers concurrently; however, dose reduction recommendations are available in the package insert if use cannot be avoided. The pharmacokinetics of cabozantinib in renal or hepatic impairment has not been formally studied. The half-life is predicted to be 55 hours.[11]

Cabozantinib is available as 20-mg and 80-mg capsules, necessitating the standard daily dose of 140 mg to be given as one 80-mg capsule and three 20-mg capsules. The capsules should not be opened and should not be taken with food; it is recommended to avoid food for at least 2 hours before or 1 hour after the dose.[11] Cabozantinib has limited distribution and is only available through Diplomat Specialty Pharmacy (855.253.3273).[14]

Patients with progressive metastatic MTC have poor long-term outcomes and limited effective treatment options. Cabozantinib is a newly FDA-approved TKI for the treatment of patients with this rare cancer. The EXAM trial demonstrated an improvement in PFS and ORR as compared to placebo, although the effect on OS is still unknown. Cabozantinib has many reported adverse effects and three black box warnings for perforations, fistulas, and hemorrhage. Further studies are needed to assess differences in efficacy between cabozantinib and vandetanib (Caprelsa®), which was approved by the FDA in 2011, and how each will be utilized in MTC.

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Pomalidomide (Pomalyst®)

Class: Thalidomide analog/immunomodulatory drug

Indication: Patients with multiple myeloma who have received at least two prior therapies including lenalidomide and bortezomib and have demonstrated disease progression on or within 60 days of completion of the last therapy

Dose: The recommended starting dose is 4 mg once daily orally on days 1–21 of repeated 28-day cycles until disease progression.

Dose modifications: Dose should be reduced for hematologic toxicity; pomalidomide should be avoided in patients with a serum creatinine greater than 3 mg/dL, serum bilirubin greater than 2 mg/dL, or aspartate aminotransferase (AST)/alanine aminotransferase (ALT) greater than three times the upper limits of normal.

Common adverse effects: Fatigue, asthenia, neutropenia, anemia, dizziness, confusion, constipation, diarrhea, nausea, upper respiratory tract infection, back pain, dyspnea

Serious adverse effects: Pneumonia, sepsis, neutropenic fever

Drug interactions: Coadministration with strong inhibitors of CYP1A2, CYP3A4, or P-glycoprotein could increase exposure to pomalidomide and should be avoided. Coadministration with strong inducers (including cigarette smoking) of these enzymes could decrease exposure and also should be avoided.

Pomalidomide

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The introduction of immunomodulatory drugs (IMiDs) and proteasome inhibitors for the treatment of multiple myeloma (MM) has provided multiple therapeutic options that have favorably affected survival.[1] Thalidomide or lenolidamide, combined with dexamethasone, produce response rates (partial response [PR] or better) of 40%–50% and 55%–60%, respectively, in patients with relapsed disease. Response rates are further improved when thalidomide or lenolidamide are combined with bortezomib or traditional cytotoxic agents. However, MM remains incurable secondary to the eventual resistance to available agents. Newer therapies are needed for patients with relapsed, refractory disease. Pomalidomide was developed as a more potent IMiD than those that are currently available. In addition to its cytotoxic and immunomodulatory actions, pomalidomide inhibits cyclooxygenase-2 (COX-2) production, which is highly expressed in patients with MM and is associated with poor outcomes. Pomalidomide also inhibits osteoclast production and function, which may prove to have benefits with respect to prevention of myelomatous bone disease.[1]

Phase 1 studies of pomalidomide demonstrated a maximally tolerated dose (MTD) of 2 mg/day or 5 mg every other day when given to patients with relapsed MM exposed to a median of 3–4 prior regimens (excluding bortezomib or lenalidomide).[2,3] In a more heavily pretreated sample (median of six prior regimens, including bortezomib and lenalidomide), the MTD was 4 mg daily for 21 days of a 28-day cycle.[4] The dose-limiting toxicity was grade 4 neutropenia. The incidence of peripheral neuropathy and venous thromboembolism was <5%.

Sixty patients with relapsed or refractory myeloma were enrolled in a phase 2 study to evaluate the safety and efficacy of pomalidomide in combination with low-dose dexamethasone.[5] Pomalidomide was administered orally at a dose of 2 mg daily on days 1–28 of a 28-day cycle, and dexamethasone 40 mg was given weekly. The primary endpoint was the proportion of confirmed responses > PR as defined by the International Myeloma Working Group. Sixty-three percent of patients met this endpoint with response rates of 37%, 40%, and 60% in patients refractory to thalidomide, lenalidomide, and bortezomib, respectively. These data imply noncross resistance with other IMiDs. Patients with high-risk cytogenetic and molecular features demonstrated a 74% response rate. Myelosuppression was the most common toxicity, with 32% of patients experiencing grade 3 or 4 neutropenia; thrombocytopenia and anemia were less common. One patient had a thromboembolic event and one patient died of pneumonia. Among 33 patients without neuropathy at baseline, 30% reported neuropathy during treatment (all grade 1). The median progression-free survival was 11.6 months.

In follow-up to the above study, the same investigators from the Mayo Clinic evaluated the efficacy of two different dosing strategies of pomalidomide in combination with dexamethasone in MM patients who were refractory to lenalidomide and bortezomib.[6] In two sequential phase 2 trials, either 2 mg or 4 mg of pomalidomide was given daily on days 1–28 along with weekly dexamethasone (40 mg) to a total of 70 patients (35 in each dosing cohort). Overall response rates were similar between the two dosing cohorts (49% in the 2-mg group and 43% in the 4-mg group), suggesting a lack of advantage with the 4-mg dose. As with other studies, myelosuppression was the most common toxicity. Response rates were promising given the refractory nature of the disease being treated.

To further elucidate the optimal dosing regimen of pomalidomide, the Intergroupe Francophone du Myelome reported results from a randomized phase 2 study (2009–02).[7] Eighty-four patients with relapsed/refractory MM (median of five prior regimens) were randomized to receive either 4 mg daily on days 1–21 or days 1–28 of a 28-day cycle. Dexamethasone 40 mg was given orally once weekly to all patients. Overall response rates were 35% in the group receiving drug days 1–21 and 34% in patients who received drug days 1–28. Median duration of response and progression-free survival were also similar. Overall survival at 1 year for both cohorts was 57%. Toxicity was primarily myelosuppression. Results indicate that the combination of pomalidomide plus dexamethasone is a safe and effective combination for the treatment of very advanced MM, including those treated with prior IMiDs, bortezomib, or alkylating agents. The authors

recommended further study of the 21-day regimen (followed by a week off of drug) based on a theoretical minimization of acute and cumulative toxicity.

In addition to MM, pomalidomide is being evaluated in myelofibrosis. In a phase 2 randomized study, 84 patients were assigned to pomalidomide 2 mg/day, pomalidomide 0.05 mg/day or 2 mg/day with prednisone, or prednisone alone.[1] Response rates were 23%, 36%, 16%, and 19%, respectively. Grade 3 or 4 toxicity occurred in fewer than 15% of patients and included myelosuppression, pneumonia/sepsis, and venous thrombosis. Investigators from the Mayo Clinic treated 58 patients with 0.5 mg/day of pomalidomide alone.[1] Patients with JAK2V617F, drug-induced basophilia, and absence of significant splenomegaly were more likely to have a response.

As reported from the studies summarized above, myelosuppression is the most common dose-limiting toxicity with grade 3 or 4 neutropenia occurring in 26%–66% of patients; thrombocytopenia and anemia are less common.[1] Patients should be advised to report signs and symptoms of infection or bleeding immediately. Fatigue, asthenia, constipation, diarrhea, nausea, back pain, and dyspnea were also reported in more than 10% of study participants. Thromboembolic complications are infrequent (<5%) when appropriate prophylaxis or antithrombotic treatment is administered; so is neuropathy, unless patients are heavily pretreated. Dizziness and confusion have been reported (18% and 12%, respectively); grade 3 or 4 events occurred in fewer than 5% of patients.[8] Patients should be counseled to avoid driving or operating dangerous machinery until they know how pomalidomide will affect them. Serious toxicities include both infectious and noninfectious pneumonia. The noninfectious events are rare and have been reported to respond to corticosteroids.[1] Cases of acute leukemia have occurred in patients for diseases other than MM.[8]

Doses should be adjusted for neutropenia and thrombocytopenia per the manufacturer's recommendations.[8] For other grade 3 or 4 toxicities, pomalidomide should be held until resolution to grade 2 or less, then resumed at a dose of 1 mg less than the previous dose. Pomalidomide should be avoided in patients with serum creatinine greater than 3 mg/dL because these patients were excluded from clinical trials. Likewise, patients with bilirubin greater than 2 mg/dL and AST/ALT greater than 3 times the upper limit of normal were also excluded and the manufacturer discourages administering pomalidomide to these patients.

Peak concentrations of pomalidomide occur approximately 2–3 hours after oral administration, and the systemic exposure increases in an approximately dose proportional manner.[8] Pomalidomide has a mean apparent volume of distribution between 62–138 L and plasma protein binding ranges from 12%–44%. It is primarily metabolized in the liver by CYP1A2 and -3A4, is a substrate of p-glycoprotein, and its metabolites are excreted renally. The median plasma half-life is approximately 7.5 hours in patients with MM with a mean total body clearance of 7–10 L/hr. No formal drug interaction studies have been conducted but in vitro studies have not demonstrated inhibition or induction of CYP450 enzymes by pomalidomide.[8] However, coadministration with strong inhibitors of CYP1A2, CYP3A, or P-glycoprotein could increase exposure to pomalidomide and should be avoided. Coadministration with strong inducers (including cigarette smoking) of these enzymes could decrease exposure and also should be avoided.

Pomalidomide can cause fetal harm when administered to a pregnant woman and is contraindicated in this setting.[8] Women of child-bearing potential must be counseled to avoid pregnancy while taking pomalidomide and for at least 4 weeks after completing therapy. Women must commit to either abstaining from sexual intercourse or to using two methods of reliable birth control beginning 4 weeks prior to initiating pomalidomide therapy continuing for at least 4 weeks after discontinuation (including during dose interruptions). Two negative pregnancy tests (one within 10–14 days and one within 24 hours) must be obtained prior to starting therapy. Pregnancy testing should continue weekly during therapy for the first month, then monthly thereafter if menstrual cycles are regular or every 2 weeks if they are not. It is not known if pomalidomide is excreted in human milk; it is excreted in the milk of lactating rats. Lactating women should be told to discuss with their physicians the risks and benefits of breast feeding and continuing therapy with pomalidomide. Due to the significant distribution of the drug into the semen, men should be advised to always use a latex or synthetic condom during sexual contact with women of childbearing potential while taking pomalidomide and for up to 4 weeks after discontinuing the drug.[8]

Because of the embryo-fetal risk, pomalidomide is only available through a REMS program. Required components include

- certification of prescribers and pharmacists
- a signed patient-prescriber agreement and compliance with the REMS requirements (as summarized above for prevention of pregnancy and embryo-fetal exposure).

The safety and effectiveness of pomalidomide in pediatric patients (younger than 18 years of age) have not been established. No dosage adjustments are required for geriatric patients; however, patients older than 64 years were at a higher risk of pneumonia in clinical studies than younger patients and should be closely monitored.[8]

Pomalidomide is supplied as 1-, 2-, 3-, and 4-mg oral capsules that should be stored at room temperature. The recommended dose is 4 mg daily by mouth on days 1–21 of a 28-day cycle until disease progression. In addition, dexamethasone may be added to this regimen. Pomalidomide may be taken with water but at least 2 hours before or 2 hours after a meal. Patients should be informed not to break, chew, or open the capsules. Patients should be instructed to take their dose at approximately the same time every day. If they miss a dose, they can take it up to 12 hours after the time they would normally have taken it; otherwise, they should skip the dose for that day.[8]

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Oncology Medication Safety Update: January–May 2013

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High-profile events, drug shortages, and new governmental regulations have pushed medication safety to the forefront in many institutions. Multiple organizations publish medication safety–related information and materials; however, the task of sifting through this breadth of information can be a daunting task for the practitioner who is simply searching for oncology-related safety information.

This quarterly column summarizes some of the medication safety notifications released by The Institute for Safe Medication Practices (ISMP), the U.S. Food and Drug Administration (FDA), and other organizations.

This Oncology Medication Safety Update covers January–May 2013.

Recalls, Withdrawals, and Safety Alerts from the FDA

- **1/10/13, updated 5/14/13:** Zolpidem labeling change to recommend lower doses for women, as well as prescribing the lowest effective dose (www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm334738.htm).
- **3/21/13:** Clinical Specialties voluntarily recalled all lots of its repackaged and distributed sterile ophthalmic products, distributed between October 19, 2012, and March 19, 2013, due to the development of endophthalmitis infections. One of the products in question was compounded bevacizumab for ophthalmic use.
- **4/11/13:** Green Valley Drugs issued a recall of all lots of sterile compounded, repackaged, and distributed medications. A full list can be obtained on the Green Valley Drugs website (www.greenvalleymed.com/wp-content/uploads/2013/04/Green-Valley-Recall-Statement-FINAL.pdf).
- **4/13:** Additional recalls on compounded products have been issued by ApotheCure, Inc., NuVision Pharmacy, Balanced Solutions, and Nora Apothecary and Alternative Therapies (www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm333878.htm).
- **5/6/13:** The FDA notified health professionals regarding the possible confusion and potential for medication errors between Kadcyla (**ado-trastuzumab emtansine**) and Herceptin (**trastuzumab**). It was noted that some third-party publications, electronic health information systems, compendia references, and Internets sites displayed the truncated nonproprietary name, which omitted "ado" and the hyphen. Recommendations from both the FDA and ISMP include using both the proprietary name *and* the complete nonproprietary name in all orders, communications, and electronic health records. Although no medication errors have been reported to the FDA at this time, medication errors were reported in clinical trials (www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm350817.htm).

Changes in Safety Labeling (See Details on FDA Website)

- **December 2012:** www.fda.gov/Safety/MedWatch/SafetyInformation/ucm332340.htm
  - Abiraterone, eculizumab, nilotinib. peginterferon alfa-2b
- **January 2013:** None
- **February 2013:** www.fda.gov/Safety/MedWatch/SafetyInformation/ucm342027.htm
  - Denosumab, epirubicin, everolimus, exemestane, imatinib, leuprolide acetate
- **March 2013:** www.fda.gov/Safety/MedWatch/SafetyInformation/ucm346535.htm
  - Bevacizumab, cetuximab, glucarpidase, panitumumab

ISMP Medication Safety Alert!

- **February 7, 2013 (Volume 18, Issue 3):** Be aware of potential confusion between Neulasta (pegfilgrastim) and Nudexta (a dextromethorphan-quinidine product for treatment of a neurological condition called pseudobulbar affect; www.ismp.org/newsletters/acutecare/issues/20130207.pdf).
- **February 21, 2013 (Volume 18, Issue 5):** Be aware of potential confusion between iso-tretinoin and Tretinoin (used exclusively for acute promyelocytic leukemia; www.ismp.org/newsletters/acutecare/issues/20130221.pdf).
- **March 7, 2013 (Volume 18, Issue 5):** ISMP initially recommends differentiation strategies for ado-trastuzumab emtansine and trastuzumab (www.ismp.org/newsletters/acutecare/issues/20130307.pdf).

IT, as an abbreviation for intrathecal, may be confused with multiple obscure routes of administration (e.g., intratumor), as well as the common abbreviation for information technology.

- **April 4, 2013 (Volume 18, Issue 7):** Discussed strategies for risk reduction with high-alert medications (www.ismp.org/newsletters/acutecare/issues/20130404.pdf)
- **April 18, 2013 (Volume 18, Issue 8):** www.ismp.org/newsletters/acutecare/issues/20130418.pdf
  - **National Alert Network (NAN)** activated by the American Society of Health-System Pharmacists and ISMP regarding the potential confusion with ado-trastuzumab emtansine and trastuzumab
  - **QuarterWatch** segment on glucagon-like peptide-1 (GLP-1) therapies and the need for additional investigation surrounding the concerns of the link between use of these agents and the development of pancreatic and thyroid cancers
  - **Safety brief:** Approximately 1,110 Canadian patients may have received lower than anticipated doses of chemotherapy due to miscommunication between a compounding pharmacy and hospital. The issue resulted

from a lack of common understanding about overfill volumes in the intravenous bags.

Because HOPA members play different roles in the continuum of oncology care, the needs for medication safety information will vary greatly. If you have any suggestions for future medication safety topics, or comments on the contents of this issue, please provide feedback to *HOPA News* at info@hoparx.org, with "Medication Safety Column" in the subject line.

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HOPA's 9th Annual Conference Goes to LA

More than 750 hematology/oncology pharmacists attended this year's annual conference in Los Angeles, making it the highest attended conference in HOPA's history. The conference boasted an array of impressive educational sessions, poster presentations, BCOP review sessions, and networking opportunities for new and experienced pharmacists. Sessions focused on current screening and treatment options for patients and explored recent developments in and updates to the medical literature. Attendees learned about new and emerging therapies and reviewed important principles for hematology/oncology pharmacy practice.

This year, early arriving attendees were offered three excellent preconference education session options. The popular Oncology Boot Camp, developed for pharmacy practitioners who do not focus solely on hematology/oncology, was once again well attended. The Bone Marrow Transplantation Boot Camp was added to this year's roster of preconference sessions and was developed for new practitioners, residents, and nontransplant pharmacists who care for patients being treated for hematopoietic stem cell transplantation (bone marrow transplantation) and are seeking a better understanding of the transplantation process. The final preconference offering was the Research Workshop: Healthcare Quality Improvement Research—Methods and Opportunity, which showcased HOPA's continued commitment to oncology pharmacy research.

The Drug Updates sessions (another new addition to the annual conference) discussed marketed and investigational products and the role of these agents in the treatment of patients affected by cancer. During the popular Practice Issues Panel, panelists from pharmacy practice, academia, and the U.S. Food and Drug Administration discussed oral oncology agents and clinical, administrative, and other pharmacy issues related to oral antineoplastic agents.

Other highlights included the Reimbursement Challenges in Oncology session, which discussed recent federal government–enacted changes in reimbursement for cancer care. The Carboplatin Debate addressed hot topics related to methods used to evaluate renal function as well as controversial issues surrounding dosing of carboplatin.

The exhibit hall hosted 43 booths, providing attendees access to state-of-the-art products, services, and information pertinent to the demands of this year, and a Career Fair with eight participating facilities.

Robert J. Ignoffo, PharmD FASHP FCSHP, was awarded the 2013 HOPA Award of Excellence for his contributions to the field of hematology/oncology pharmacy. Other award recipients included Steve Stricker, PharmD MS BCOP, for the New Practitioner Award, and Kamakshi V. Rao, PharmD BCOP CCP, for the 2013 Oncology Practice Literature Award.

It was wonderful to see so many members connecting with colleagues and forging new relationships during this year's conference. We look forward to seeing you next year at HOPA's 10th Annual Conference in New Orleans.

"The carboplatin session was very good in terms of discussing what is currently happening in our clinics and where we might be going in standardizing."

"I really enjoyed all of the sessions and felt like I learned a lot."

"Impressive quality of speakers in terms of knowledge base and presentation skills."

"The clinical controversy discussions in both hematology and oncology were very interesting. I found those sessions to be very useful as a new practitioner."

"I always appreciate the opportunity to reconnect and network with new colleagues."

"I thoroughly enjoyed all of the lectures. I feel they all helped with my knowledge base and increased my confidence."

"I liked the gastroesophageal and MM lectures, but the best was the keynote speaker (Dr. Mark Pelham)."