Hematology/Oncology Pharmacy Association

HOPA Elections are open until December 1, 2011. Visit www.hoparx.org and cast your vote.

HOPA News

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The Impact of Oral Chemotherapy Disparity

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The development of patient-administered oral chemotherapy has changed the landscape of treatment options for providers, as well as the quality of life for patients with hematologic and oncologic malignancies. Prior to the advent of oral agents, chemotherapy was primarily administered intravenously in clinic or hospital settings, necessitating travel and multiple visits per month for most patients. Oral medications, similar to their intravenous (IV) counterparts, have demonstrated efficacy that ranges from an incremental benefit to a complete remission of disease. Similarly, the activity of these agents ranges from total tumor kill to metastasis prevention and can be used throughout the disease spectrum, from induction to maintenance therapy.

During the past 10 years, the development of oral and IV chemotherapy agents aimed at cure and maintenance has exploded. It is estimated that orally administered agents, in particular, comprise more than 25% of the 400 chemotherapy treatments in the development pipeline. In contrast to the rapidly evolving treatment options for cancer patients, our systems for medical and pharmacy benefits in the United States have remained relatively static. IV and oral chemotherapy medications have different dispensing sites, which often dictate which portion of a patient's health insurance provides coverage. An IV medication administered in an outpatient infusion clinic is usually covered through the medical benefit whereas oral medication is covered under the pharmacy benefit. Although treatment outcomes may be similar, a disparity exists in out-of-pocket payments required of patients with cancer. Because the oral agents are covered under the prescription benefit, patients often pay a much larger proportion of the overall cost of treatment compared with IV agents covered under the medical benefit. The higher cost share on the pharmacy benefit side arises when plans have high deductibles or place orally administered chemotherapy into a "specialty tier" or "fourth tier," which may require a cost-sharing responsibility for the patient of anywhere from 25% to 33% . This significant disparity in the financial obligation of patients for oral versus IV chemotherapy has been the impetus

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for legislative efforts at the state and, more recently, the national level, seeking to create parity for patients when orally administered chemotherapy is the most appropriate treatment option.

Many factors affect a patient's success with oral chemotherapy medications, including the quality of initial and follow-up education, severity of adverse effects, efficacy of adverse effect management, and level of adherence with the prescribed regimen. However, affordability of care may be the most significant factor affecting treatment success and should be addressed with patients as soon as a treatment decision is made to include an oral agent. Some patients may qualify for copayment cards and assistance funds as a stop-gap to bridge the disparity in cost for oral medications. However, these funds cannot meet the needs of all patients, and many remain ineligible for assistance based on the type of insurance, income requirements, or availability of copayment program funding. The financial constraints imposed by these out-of-pocket expenses may force patients to choose an alternative IV treatment, which may not be the most effective therapy for their specific type of cancer.

A patient who was recently admitted to The Arthur G. James Cancer Hospital & Richard J. Solove Research Institute at The Ohio State University (The James) was diagnosed with stage IV breast cancer and was prescribed oral capecitabine (Xeloda®) and IV zolendronic acid (Zometa®). Her insurance requires an out-of-pocket deductible of $4,000 before she receives any pharmacy benefits (i.e., she must pay all $4,000 prior to any pharmacy benefit being accessed). The Zometa® is administered in the outpatient clinic, is covered at 100%, and has $0 copay. The cost share of 1 month of Xeloda® is $3,028. The patient has an income of $35,000 for a two-person household and cannot afford the $3,028 copay.

Pharmacists and prescribers alike are affected by the inability of their patients to afford oral chemotherapy medications. "We have had significant delays in initiation of oral chemotherapy due to communication with insurance payers and specialty pharmacies to determine whether or not a patient could afford their copay," stated Jessica Duda, specialty practice pharmacist at The James. "Treatment decisions have been made based on patients' financial responsibility with copays or the availability of programs that could help with high copays."

To ensure selection of therapy is based on scientific evidence rather than route or administration location, it is critical to introduce legislation that will address the oral chemotherapy disparity. Thirteen states (and the District of Columbia) have passed laws requiring parity, and an additional 12 states are considering similar legislation (**Table 1**). However, each state's statutes differ, and coverage can be confusing for patients who may receive care from both a local oncologist and an oncology specialist in another state.

Currently, there are no parity statutes at the national level that could impact the Employee Retirement Income Security Act (ERISA), which governs self-insured health benefit plans. However, on August 1, 2011, Representative Brian Higgins (NY-27) introduced the Cancer Drug Coverage Parity Act (HB-2746), a bill that requires health insurers to provide coverage for IV/injectable and orally administered chemotherapy medications at the same patient cost-sharing benefit.

Table 1. Snapshot of Parity Legislation

Statewide Legislation Passed	Statewide Legislation Proposed
Oregon (2008)	Georgia
Indiana (2009)	Oklahoma
Iowa (2009)	Tennessee
Vermont (2009)	New Jersey
Hawaii (2009)	Wisconsin
District of Columbia (2009)	California
Connecticut (2010)	Missouri
Kansas (2010)	Ohio
Colorado (2010)	Pennsylvania
Minnesota (2010)	South Carolina
New Mexico (2011)	Michigan
Washington (2011)	Massachusetts
Texas (2011)	
Illinois (2011)	
New York (2011)	

With the projected growth in the oral oncology market, this disparity is likely to become more prominent. Becoming involved in advocacy efforts to end this disparate practice is one way for our profession to ensure patients receive the most appropriate medication for their disease rather than just the one that they can afford. Oncology pharmacists should become involved in both state and national initiatives already under way or be the impetus for change in a state where the issue has yet to be addressed.

- Your local branch of the American Cancer Society can provide information on any state parity legislation that has been introduced and how you can get involved in the state's coalition.
- Join the Patients Equal Access Coalition (PEAC). PEAC can assist with coordination of efforts in your state with those of other state coalitions and promote federal legislation. (PEAC is a national coalition with goals that include raising awareness about parity and forwarding legislation on the federal level.)
- Consider inviting state and federal legislative leaders to your practice site to share a more personal view of the impact of this disparity on patients and providers.
- Encourage colleagues to write letters to state and federal leaders that include real-life patient examples, if permitted by the patient.

Advocating for our patients is one of the most important things we can do as pharmacists With a little effort, we can make a difference.

Summary of FDA Drug Shortage Workshop

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Drug shortages are one of the most significant challenges hematologist/oncologist pharmacists face today as we strive to provide optimal care for our patients. In the past year, HOPA has worked to identify issues that affect our members and to be active and visible on the national level. Prior to the most recent forum, we asked you to provide your thoughts and concerns regarding drug shortages on the HOPA Listserv. Recently, we also launched a membership survey to assess the scope and impact of these shortages. Armed with this information, we are hopeful that we will be better positioned to provide your perspective to our patients, the public, our elected officials, commercial and government insurance providers, and the pharmaceutical industry.

On September 26, 2011, members of HOPA participated in a workshop hosted by the U.S. Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER). The workshop brought together many of the drug shortage stakeholders and provided an opportunity for open dialogue with government officials, industry, healthcare providers, and patients and family members. **A prepared statement representing HOPA members' key concerns was presented and is provided in the sidebar following this article.** This statement focused on concerns impacting both pharmacy practice and patient care that have resulted from the current handling of drug shortages. The predominant message focused on the urgent need for policymakers and other stakeholders to determine the causes of recent drug shortages and to provide better strategies for notifying people about them and, if possible, preventing them.

HOPA and oncology pharmacy were well represented at this discussion. Ali McBride, PharmD MS BCPS, and James Hoffman, PharmD MS BCPS, participated in the panel discussion on perspectives from the point of care. McBride opened the panel by reading HOPA's prepared statement. Hoffman discussed the impact of drug shortages on specialty settings, focusing mainly on St. Jude Children's Research Hospital and similar pediatric institutions. Other HOPA members at the proceedings included Charlie Lucarelli, MS, director of pharmacy at Memorial Sloan-Kettering Cancer Center; Dwight Kloth, PharmD, director of pharmacy at Fox Chase Cancer Center; William Greene, PharmD BS, chief pharmaceutical officer, also from St. Jude; and Moe Schwartz, PharmD BCOP, director of oncology pharmacy at Johns Hopkins Hospital.

Workshop Agenda

Douglas Throckmorton, MD, deputy director of CDER, began the meeting with introductory comments regarding CDER's perspective on drug shortages. The public health impact of drug shortages was also discussed. Edward Cox, coordinator of the CDER Drug Shortage Program, described the current FDA strategies for identifying and managing drug shortages. He provided examples of how the FDA has used its regulatory discretion to help alleviate shortages. He stressed that the strategies have been partially successful; the FDA was able to avoid 38 drug shortages in 2010 and avoided 99 shortages due to manufacturer notification in 2011.

Reason for Recent Increase in Drug Shortages

Many factors contribute to drug shortages, including limited access to raw materials. More frequently, according to members of the FDA Drug Shortage Group, the shortages have been related to significant issues with product quality, such as identifying glass particulates or mold in injectable products. Unfortunately, when a product is predominantly from a single source, manufacturers are unable to rapidly increase production.

The Impact of Drug Shortages on Patients

During the meeting, several patients spoke eloquently regarding their personal experiences with shortages. One patient with metastatic colon cancer spoke about treatment delays due to the 5FU shortage, and a young patient with acute myeloid leukemia expressed concern about chemotherapy changes in her treatment. A patient on long-term total parenteral nutrition (TPN; about 30 years) discussed how the electrolyte and TPN component shortages have negatively impacted her quality of life.

The Impact of Drug Shortages on Healthcare Providers

Healthcare practitioners spoke on behalf of their organizations and practice sites regarding the challenges resulting from drug shortages. The shortages have affected hospitals, homecare agencies, community physician practices, and community pharmacies. The American Hospital Association, American Society of Health System Pharmacists, American Society of Clinical Oncology, American Society of Anesthesiologists, American Society of Parenteral and Enteral Nutrition, Institute for Safe Medication Practices, Child Healthcare Association of America, and Oncology Nursing Society were among the healthcare professional groups represented at the meeting.

Growing Concern

An increasingly important issue identified during the meeting is the growth of a gray market, where alternative distributors obtain short-supply drugs with the intent of selling products at a grossly inflated

price. There is concern that products from these suppliers may be of poor quality and their cost may be escalated 1,000-fold. Wholesalers and manufacturers stated they had discontinued selling product to specific distributors that participate in these gray markets. Unfortunately, many unanswered questions remain regarding these suppliers, including how they can be appropriately monitored and regulated.

Hope for the Future

In addition to the news that the FDA has avoided 99 shortages in 2011, the Generic Pharmaceutical Association and companies that manufacture generic injectable drugs provided some optimism for further improvements in the future. Representatives from industry, including Hospira, Bedford, TEVA, and APP, participated in a panel discussion and made recommendations and proposed solutions. The generic industry representatives stated that they want to continue manufacturing generic medications and do not plan to walk away from the market. Several generic injectable companies stated they are actually increasing capacity, but that it can take years for a new facility to come online.

CDER FDA Drug Shortage Workshop

The CDER Drug Shortage Workshop was webcast. An archive of the webcast and slides from the meeting are available on the FDA website (www.fda.gov/Drugs/NewsEvents/ucm265968.htm). The Federal Register Notice for this meeting has been reopened and is available at www.regulations.gov/#!documentDetail;D=FDA-2011-N-0690-0001. Public comments are open until December 23, 2011. We encourage HOPA members to submit their comments.

HOPA's Statement Regarding Drug Shortage Issues Presented at the FDA Drug Shortage Workshop September 26, 2011

The Hematology/Oncology Pharmacy Association (HOPA) is a nonprofit professional organization of 1,650 members that launched in 2004. HOPA's purpose is to optimize the care of individuals affected by cancer through the support and advancement of oncology pharmacy practice. HOPA is the leading oncology pharmacy association focusing on efforts to maintain quality and safety in cancer care in an interdisciplinary, collaborative practice setting including, but not limited to, hospitals, clinics, physician offices, community pharmacy, and home health. The roles of our membership span from direct patient care, to education, to research. HOPA leads efforts to ensure that the needs and perspectives of cancer patients and their families are maintained regardless of practice setting and that all cancer patients have access to high0 quality and safe cancer care.

The growing number of drug shortages is presenting serious challenges to the efforts of HOPA members to provide optimal care to individuals affected by cancer. As has been discussed, the number of drugs in critically short supply is increasing at an alarming rate. These shortages threaten the safety and quality of patient care in hospitals and clinics nationwide. In many cases, equivalent therapeutic alternatives are not available, or alternatives have not been tested for the intended use or carry increased potential for drug-related complications and increased costs.

The potential harm to patient safety is of paramount concern. These shortages contribute to disruptions in patient care including the delay of chemotherapy treatment, cancellation of chemotherapy, changes to different dosing or chemotherapy regimens, and unintended adverse effects. The time and resources focused on the management of these shortages pull healthcare resources away from patient care.

Oncology drug shortages have slowed or prevented access to medications with curative intent in a number of cancers. A total of 23 chemotherapy drugs were in short supply in 2010, and 22 shortages were reported by August 2011. This was the highest number of anticancer agents in short supply since national data collection started in 2003. Chemotherapy shortages have included drugs that are integral for first-line treatment for diseases in which cure is the goal. In addition, patients who are being maintained on treatments that have provided a response are now being changed to different therapies (without the proven benefit in the individual patient).

- The lack of several medications in pediatric acute lymphocytic leukemia regimens, a disease with a greater than 95% cure rate, hinders patient treatment when an institution is unable to obtain half the drugs in a regimen including vincristine, daunorubicin, and cyclophosphamide.
- Patients with acute myeloid leukemia have also had curative treatment delayed or transferred to other institutions due to the lack of cytarabine for administration in first-line induction chemotherapy or consolidation treatment.
- Breast cancer patients have been switched to alternative regimens because of the lack of doxorubicin.
- Recently paclitaxel has been in short supply; the aftereffects of this shortage have led to numerous patients with different diagnoses having their chemotherapy delayed or halted because of the drug's unavailability.
- Bone marrow transplantations have been put on hold because of an inadequate supply of chemotherapy drugs for conditioning regimens.
- Cancer clinical trials are being affected for both adult and pediatric cancer patients. Clinical trials are being suspended, patient accrual is being halted, and drug substitutions are resulting in potential problems with the data analysis of clinical trials.
- Patients, either through the direct loss of their chemotherapy regimen or through a supportive care medication being in short supply, are feeling the consequences of these drug shortages.
- Drug shortages have led to a change in chemotherapy regimens, which have the potential for increased side effects and unintended consequences.

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The lack of medication for curative purposes in the treatment of care is simply unacceptable. HOPA is concerned about the effects of oncology drug shortages and continued patient care.

Recommendations

HOPA recommends that the FDA and all relevant stakeholders consider the following actions to reduce and eventually prevent drug shortages:

- Advocate for transparency on all issues surrounding drug shortages, including the reported causes of drug shortages.
- Consider distribution options for products in short supply (with increased information exchange among supply chain members).
- Enhance communication among manufacturers, health professional associations, and the FDA to support product distribution and maintain adequate supplies for institutions based on need.
- Incentivize manufacturing redundancies as part of the FDA approval process for drugs that are deemed vulnerable to provide an overlay of drugs that are medically necessary.
- Require confidential notification of the FDA when there is a single active pharmaceutical ingredient (API) or manufacturing source.
- Notify the FDA of an interruption in the supply of raw materials, APIs, or manufacturing processes.
- Increase collaboration with industry, the Drug Enforcement Administration, and the FDA to establish a process that would more readily modify API quotas in response to drug shortages of controlled substances.
- Develop efficient and equitable access programs when drugs are in short supply and allocated to qualified patients on a per patient basis.
- Maintain adequate reimbursement for the use of brand-name drug therapies or alternative therapies when an existing drug is in short supply.
- Develop guidelines for oncology regimens when there is a shortage of a drug in that regimen.

REMS in the Oncology Setting: Time for a Change?

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On July 26, 2011, more than 75 participants were invited to gather at the American Society of Clinical Oncology (ASCO) headquarters in Alexandria, VA, for an oncology Risk Evaluation and Mitigation Strategies (REMS) workshop. Participants included members of the U.S. Food and Drug Administration (FDA), ASCO, Oncology Nursing Society (ONS), American Society of Hematology (ASH), HOPA, patient advocacy groups, industry, and other hematology/oncology healthcare professionals. The purpose of the workshop was to initiate a discussion between hematology/oncology healthcare providers and the FDA regarding hematology/oncology-related REMS programs and REMS-related issues specific to the discipline. In addition, the group discussed possible strategies that could be developed to minimize these issues, such as working with the FDA to develop new REMS programs, carve out oncology products from REMS requirements, or change the requirement of REMS. Because hematology/oncology healthcare providers are familiar with prescribing, managing, and mitigating the risks and toxicity profiles of the various cancer therapies, the implementation of additional REMS programs to newly approved cancer drugs seems unnecessary and only adds to the complexity of care by requiring additional time, resources, and effort for REMS compliance. Furthermore, the lack of prospective data on the ability of REMS to improve safety outcomes has not been documented.

Key REMS stakeholders presented topics and then participated in a panel discussion. Topics included (1) REMS history, logistics, and current clinical practice safety measures; (2) an overview of current oncology-related REMS programs, REMS experiences, and implementation in clinical practice; and (3) current initiatives in patient safety initiated by the FDA and existing in practice. The panels were multidisciplinary and comprised members of the FDA and industry, healthcare providers (physician, nurse, or pharmacist), and one patient representing a patient advocacy group. HOPA Past President Phil Johnson, MS RPh, presented the REMS experience and implementation in clinical practice within the oncology community. He discussed operational issues, practitioner feedback from the National Comprehensive Cancer Network REMS survey, the pharmacy perspective (including HOPA member concerns from a July 2011 Listserv request), and essential metrics that should be used to determine the effectiveness of REMS programs. The goal of his presentation was to present a model in which the need for REMS is waived based on the established practice of managing drug toxicity as part of the overall drug management protocol developed for each disease. Johnson also participated in a panel discussion. Following the *Current Initiatives in Patient Safety* presentations, HOPA Board Member Niesha Griffith, MS RPh FASHP, represented HOPA as a panelist and provided a pharmacy perspective on how to best streamline the system and the current barriers. HOPA President-Elect Lisa Holle, PharmD BCOP, also participated as a workshop attendee. The information presented by HOPA representatives was integral to the panel discussions.

The workshop ended after a full day of discussions. All who attended enthusiastically agreed to continue the discourse with the FDA. The FDA recognized that those working in the area of hematology/oncology have processes in place for managing medication toxicities and seemed willing to keep dialogue open. A white paper is being developed to summarize this meeting and is expected to be published in the *Journal of Clinical Oncology.* ASCO is also assessing whether a survey to characterize various safety measures currently in place for all practice settings that administer oncology medications would be useful in furthering discussions about oncology medication REMS programs with the FDA.

Board Update

R. Donald Harvey, PharmD BCPS BCOP FCCP, HOPA President

Advocacy means many things to many people. For HOPA, our strategic plan guides our advocacy agenda, and efforts for patients and members have been a substantial focus for the board as we continue to establish HOPA as a recognized leader in medication-related concerns in hematology/oncology. From collaborations with the American Society of Clinical Oncology (ASCO) to high-profile publications and engagement with U.S. Food and Drug Administration (FDA) Center for Drug Evaluation and Research (CDER) workshops, HOPA continues to have a growing voice in the field thanks to the efforts of members.

Advocacy

Our work with Drinker, Biddle, & Reath continues, and a final advocacy agenda is being developed. We are grateful to staff and the Legislative Affairs Committee for their continued help and input as we refine our areas of legislative and policy focus during the coming months.

Drug Shortages

Thanks to those who completed the recent drug shortage survey, the perspectives of our members will continue to add to a comprehensive understanding of the effects of shortages on patient care. The recent executive order is one step toward a solution; however, much work remains. HOPA has endorsed both Senate and House legislation addressing the shortage crisis. If you haven't done so already, I encourage you to read the Perspective column on the shortage crisis in the November 3 issue of the *New England Journal of Medicine*. In it, HOPA member Mandy L. Gatesman addresses broad economic concerns with oncology drug shortages and potential ramifications of solutions. In addition, many HOPA members were engaged in the recent FDA CDER workshop and have commented in the media on local and national approaches to coping with shortages. Two key messages from this workshop are that the FDA has prevented a number of shortages already and that manufacturing quality concerns contribute substantially to currently limited supplies.

REMS Programs

Phil Johnson, Niesha Griffith, and Lisa Holle also participated in an ASCO-sponsored summit with the FDA on the current and future role of REMS programs. Please see the article on page 3 for more details, and be on the lookout for a follow-up publication from the proceedings.

Standard Development

A plan to create the Hematology/Oncology Pharmacy Practice Definition and Scope of Practice document has been developed, the first step in a herculean effort to define who we are and what we do. This work is fundamental to a number of potential secondary efforts aimed at ensuring hematology/oncology pharmacy is identified as integral to the treatment of individuals affected by cancer.

HOPA Foundation

Chair Susan Goodin continues to lead the Foundation in defining our scope of research and funding opportunities for hypothesis-driven evaluations that align with the foundation's strategic plan, which can be found at www.hoparx.org/foundation.html. A call for proposals will follow a refined grant process and identified funding focus. Stay tuned for the announcement.

Nominations

As a reminder, HOPA elections are upon us. Please take the time to vote before December 1.

Committee Updates

BCOP Recertification Committee

Ryan Bookout, Chair
Debbie Blamble, Vice Chair

The six 2011 Oncology Pharmacy Specialty Sessions for BCOP recertification were offered for the second time this year at the 2011 American College of Clinical Pharmacy (ACCP) Annual Meeting in Pittsburgh, PA, October 16–19. If you missed the HOPA Annual Conference or the ACCP Annual Meeting, the Oncology Pharmacy Specialty Sessions will be presented once more at the 2011 American Society of Health System Pharmacists Midyear Clinical Meeting in New Orleans, LA, December 4–8. The Oncology Sessions will be offered in two parts on Tuesday, December 6. Part 1 will be offered at 8–11 am, and Part 2 will be offered at 2–5 pm.

The 2011 topics are Updates in the Treatment of Metastatic Breast Cancer by Michael Berger, PharmD BCOP; The Heart of the Matter: When Targeted Cancer Therapies Cause Off-Target Toxicities by Courtney Bickford, PharmD BCPS; Chronic Lymphocytic Leukemia by Ashley Morris Engemann, PharmD BCOP; Castration-Resistant Prostate Cancer by Rebecca Greene, PharmD BCOP; Immunizations in Cancer Patients: Recommendations for Vaccine-Preventable Diseases in the Immunocompromised Population by Tracey Walsh-Chocolaad, PharmD BCOP; and Germ Cell Tumors: Beyond BEP by Kellie Jones, PharmD BCOP. We would like to take this opportunity to again congratulate and thank the 2011 Oncology Pharmacy Specialty Sessions speakers for their continued commitment and hard work this year.

If you attend all six sessions at any of the three meetings, you will receive an e-mail with a link to the examination to claim BCOP recertification credit. If you have attended all six sessions and have not received this e-mail, please contact info@hoparx.org. **Don't forget that the examination must be successfully completed by 11:59 pm CST on December 31, 2011, to receive BCOP recertification credit.**

The BCOP Recertification Committee has had a busy summer working on the development of the 2012 Oncology Pharmacy Specialty Sessions. The topics have been determined, and the speakers have been selected. Thanks to all HOPA members who took the opportunity to complete an application in response to the call for BCOP speakers. The topics and speakers for the 2012 Oncology Pharmacy Specialty Sessions are

- Trends in Oncology Drug Expenditures and Practical Cost Management Strategies—James Hoffman, PharmD MS BCPS
- Treatment Advances for Advanced Non–Small Cell Lung Cancer—Christine Walko, PharmD BCOP
- Neuroendocrine Tumors: A Focus on Recent Advances in Pharmacotherapy—Julian Hoyt Slade III, PharmD BCOP
- Bone Health in the Oncology Population—Chad Barnett, PharmD BCOP
- Therapy of Cutaneous and T-Cell Lymphomas—Patrick Kiel, PharmD BCPS BCOP
- The Emergence of Adolescent and Young Adult Oncology (AYAO)—Kerry Parsons, PharmD BCOP.

The speakers are already working on their slides and BCOP questions, and we would like to extend our appreciation and gratitude to them for their commitment to the BCOP programming. Thanks in advance to all of the BCOP Recertification Committee members and the BCOP Review Panel for field testing the BCOP lectures and questions this winter and being part of the development process for the 2012 Oncology Pharmacy Specialty Sessions.

CE Accreditation Committee

Carol Balmer, Chair
Jolynn Sessions, Vice Chair

CE Accreditation Committee Chair Carol Balmer and Director of Education Lori Goodnow attended the Accreditation Council for Pharmacy Education's 14th Conference on Continuing Pharmacy Education in Cambridge, MA, in late September. The conference, Building Bridges to Reposition CPE, was productive and offered many valuable opportunities to learn, share, and discuss ideas with CPE colleagues and address CPE issues specific to the needs of HOPA members.

Planning meetings for the CE Accreditation Committee took place in early November.

Education Committee

Helen Marshall, Chair
Laura Wiggins, Vice Chair

The Education Committee has been hard at work during the past few months. We are excited to report that we have finalized plans for the 2012 Oncology Boot Camp, which will be offered prior to the annual conference in March 2012. This year's Boot Camp will focus on the basics surrounding the use of targeted therapies in hematology/oncology.

Much of the committee's recent efforts have focused on evaluating the current educational offerings available on HOPA U as well as how to strengthen HOPA U's position as a resource for oncology pharmacy education. To that end, a member survey is being developed to help us determine how members are using HOPA U. In addition, the committee is in the process of evaluating HOPA U and comparing it to other providers of oncology pharmacy continuing education as part of a strategic program assessment. Our next steps will include the assessment of previously offered HotTopic Webinars and development of future educational offerings.

Membership Committee

Meredith Moorman, Chair
Jennifer LaFollette, Vice Chair

The Membership Committee is pleased to announce that recent new-member recruitment efforts have been successful, and membership is increasing steadily. Thank you to all members who have contributed to this by participating in the new Colleague Recruitment Program. Remember, this program continues until December 1, 2011, so encourage your colleagues to join HOPA and take advantage of our organization's benefits. In addition, the committee recently contacted PGY-2 oncology residency program directors for their assistance in recruiting their residents to participate in HOPA. This was a successful endeavor last year, and the committee hopes to continue to increase the number of resident/fellow memberships and trainee participation within the organization.

Details for the HOPA Travel Grant Program to support member attendance at the 2012 Annual Meeting are currently being finalized. Look for information regarding the application and awards process to be distributed soon. We encourage all members to apply and attend the meeting in Orlando!

HOPA's previous membership discounts are still available. These include

- a 25% discount for new members who join for 2 years
- a 5% discount for current members who renew for 2 years
- group membership discounts for institutions with 10 or more members.

For more information about any of HOPA's membership options or programs, contact HOPA Member Services at 877.467.2791.

Nominations and Awards Committee

Laura Jung, Chair
Jane Pruemer, Vice Chair

Board Elections

The Nominations and Awards Committee has just completed setting the slate for the upcoming HOPA Board election! To better accommodate the timing of the HOPA 8th Annual Conference, HOPA Board elections are occurring earlier this year. **Online election polls opened November 1 and close December 1.**

The HOPA Board positions up for election are

- President-Elect (3-year term)
- Treasurer (2-year term)
- Member-at-Large (2-year term)—two positions available.

All HOPA members with voting privileges will receive a postcard with instructions for voting by the end of October and periodic e-mail reminders throughout the month of November.

HOPA Awards

The Nominations Committee also accepted nominations for HOPA awards through November 15. HOPA awards are for HOPA members who have demonstrated outstanding achievement in their field.

The HOPA Award of Excellence recognizes a HOPA member who has made a significant, sustained contribution to or provided excellent leadership in developing or supporting hematology/oncology pharmacy.

The HOPA New Practitioner Award recognizes a HOPA member early in his or her career who has made a significant contribution to developing or supporting clinical hematology/oncology pharmacy services.

The HOPA Hematology/Oncology Technician Award recognizes a HOPA technician member who demonstrates excellence in his or her work and a commitment to hematology/oncology pharmacy practice in an organized healthcare setting.

The HOPA Basic Science and Clinical Research Literature Award recognizes a scientific article describing hematology/oncology basic science and/or translational research or clinical trials evaluating drug efficacy and/or safety published by a HOPA member between November 2010 and November 2011. Examples of eligible articles include basic research studies (i.e., cellular, genetic, or animal studies), clinical trials, or pharmacokinetic or pharmacodynamic studies.

The HOPA Oncology Pharmacy Practice Literature Award recognizes an article, other than scientific research, that contributes to the betterment of the hematology/oncology pharmacy profession and describes innovations in community, hospital, or healthcare system hematology/oncology pharmacy practices published by a HOPA member between November 2010 and November 2011. Articles can describe any aspect of professional practice, including administration, management, technology, pharmacoeconomics, new practice models, clinical services, or drug use control.

If you have any questions regarding board member or award nominations, please contact Mary Beth Benner at mbbenner@connect2amc.com.

Program Committee

Jill Rhodes, Chair
Larry Buie, Vice Chair

This past summer was a very hot time for the HOPA Program Committee! At the beginning of our term, the committee was charged with three major duties: (1) design the HOPA 8th Annual Conference, (2) review and select symposia, and (3) direct research submission and award selection. We are excited to announce that the first of these charges has been completed, and HOPA members can look forward to a dynamic and engaging educational program awaiting them in 2012! The following are just a few highlights of the conference:

- return of the preconference Boot Camp
- an all-new Practice Issue Panel addressing drug shortages
- an all-new Clinical Pearls Session
- an increased number of breakout and general sessions.

HOPA members have been highly active in the planning of the annual program. We had an exceedingly positive response to the call for proposals in the categories of clinical pearls and breakout sessions. We are pleased to have had so many excellent submissions, and each proposal was given careful consideration for selection. HOPA is composed of a truly outstanding group of highly talented and progressive professionals. We appreciate your participation and support in the program planning process. Proposals will be solicited for future programming, so keep an eye out for a call for proposals on the HOPA website next year.

In the upcoming months, the program committee will be completing the remaining charges through the hard work of two dedicated task forces: the Session Proposal Review Task Force and the Research Task Force. Completed research abstract submissions are now being reviewed, and outstanding abstracts are being considered for award and platform presentation at the annual conference. Submissions for Trainee Research in Progress will be accepted until January 4, 2012. For more information, please visit www.hoparx.org/conference/2012-conference/speakerabstracts.html.

The HOPA 8th Annual Conference will be held in Orlando, FL, March 21–24, 2012. Online registration will open soon. Special early-bird registration rates will be posted when registration opens, so mark your calendar to sign up soon and save!

Standards Committee

LeAnne Kennedy, Chair
Barry Goldspiel, Vice Chair

The HOPA Standards Committee is moving forward with the development of our first guideline, which will be a clinical practice guideline for investigational drug services (IDS). The committee has selected the authors for this guideline and will begin working with this group in the coming months. Our goal is to develop this guideline during the next 12 months. We have identified the need for several new standard operating procedures (SOPs), including clinical practice guideline development (which will be used to guide the IDS guideline process) and an SOP to help HOPA when we are asked to collaborate with other organizations to develop guidelines.

Drug Update

Vemurafenib (Zelboraf®)

Class: Rapidly activated fibrosarcoma protein kinase, type B (BRAF) inhibitor

Indication: Unresectable or metastatic melanoma with a V600E mutation on the BRAF gene ($BRAF^{V600E}$)

Dosage form: 240 mg tablets

Dose: 960 mg orally twice daily (four 240 mg tablets)

Common adverse effects: Arthralgias, fatigue, rash, photosensitivity

Serious adverse effects: Cutaneous squamous cell carcinoma (cuSCC), hypersensitivity, dermatologic reactions (including Stevens-Johnson syndrome and toxic epidermal necrolysis), QTc prolongation, ophthalmic reactions

Monitoring: Transaminases, bilirubin and skin evaluation, each at baseline, and monthly during treatment; routine monitoring for ophthalmic changes

Drug interactions: CYP substrate; avoid narrow therapeutic drugs metabolized by CYP1A2, CYP3A4, CYP2D6

Approval date: August 17, 2011

Other: $BRAF^{V600E}$ mutations must be documented by an FDA-approved facility; not indicated for patients with wild-type BRAF status

Vemurafenib for Unresectable or Metastatic Melanoma

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Patients with unresectable or metastatic melanoma face a poor prognosis with average 5-year survival rates ranging from approximately 20% for patients with extensive, unresectable nodal disease to less than 10% in patients with distant metastatic sites of tumor.[1] Treatment of advanced melanoma presents a challenge to healthcare professionals because of its poor response to chemotherapy and radiation. The National Comprehensive Cancer Network (NCCN) guidelines recommend dacarbazine, temozolomide, high-dose interleukin-2, paclitaxel (alone or in combination with cisplatin or carboplatin), clinical trial enrollment, and newly approved agents ipilimumab and vemurafenib as first-line options for the management of metastatic melanoma. Vemurafenib, the newest of these agents, was approved in August 2011 and represents one of the few pharmacologic advances in metastatic melanoma in more than a decade.

Vemurafenib is indicated specifically for unresectable and metastatic melanomas harboring the $BRAF^{V600E}$ gene mutation. A component of the mitogen-activated protein (MAP) kinase pathway, this mutation occurs most commonly in melanomas associated with nonchronically sun-damaged skin and is the culprit of 40%–60% of all melanoma cases.[2,3] Mutated BRAF constitutively activates BRAF and downstream signal transduction in the MAP kinase pathway, resulting in cell proliferation. Vemurafenib inhibits mutated serine-threonine kinase $BRAF^{V600E}$, as well as several other tyrosine kinases *in vitro*, thus inhibiting the activation of intracellular tyrosine kinase pathways, which are normally implicated in cellular growth.[2,4]

Pharmacokinetic studies show that steady state concentrations are reached after 15 to 22 days following dosing at 960 mg orally twice daily. Vemurafenib is highly protein bound (99% bound to human albumin and α1 acid glycoprotein) with an estimated volume of distribution of 106 L. Clearance of vemurafenib in patients with mild to moderate hepatic or renal impairment was similar to that in patients with normal organ function. Vemurafenib is metabolized by CYP3A4. Following administration, 94% of the dose was recovered in the feces and approximately 1% recovered in the urine.[4]

The toxicity profile of vemurafenib is unlike that of other therapies approved for use in melanoma. Patients should be counseled about the possibility of anaphylaxis with vemurafenib and educated to immediately seek emergency care in the setting of generalized rash, erythema, and sudden shortness of breath. Vemurafenib therapy should be permanently discontinued in patients who experience anaphylaxis. No premedications or special precautions are required or recommended prior to the first dose of the drug. QTc prolongation was observed in a phase 2 trial of vemurafenib. Monitoring of the QTc interval and electrolytes should be conducted before treatment, 15 days after treatment initiation, monthly for 3 months, and then every 3 months thereafter. QTc interval and electrolyte monitoring should occur more often if clinically indicated. Initiation of vemurafenib therapy is not recommended in patients with QTc > 500 milliseconds (ms). In patients for whom the QTc interval exceeds 500 ms (equivalent to CTC-AE ≥ grade 3) while on therapy, vemurafenib therapy should be interrupted and restarted at a lower dose. Vemurafenib administration is associated with photosensitivity, which, in some cases, can be severe. Patients should be advised to avoid direct sun exposure. If sun exposure is unavoidable, patients should be counseled to wear protective clothing and use a broad spectrum UVA/UVB sunscreen and lip balm (SPF ≥ 30). Dose reductions are recommended for intolerable grade 2 or greater photosensitivity reactions. Vemurafenib has also been associated with more serious dermatologic reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, and should be permanently discontinued if either of these occurs. The appearance of cuSCC (including keratocanthomas) has been reported early in the course of treatment—around 7–8 after vemurafenib has been initiated. Risk factors for cuSCC development include age ≥ 65 years, prior skin cancer, and chronic sun exposure. In clinical trials, cuSCC were managed with excision, and patients were able to continue treatment without dose adjustment.[4] The mechanism behind the development of cuSCC is hypothesized to be the result of potentiation of the MAP kinase pathway in cells with wild-type BRAF in the setting of concurrent mutant BRAF inhibition. Research regarding this adverse

event is currently ongoing.[5-7] Liver function test (LFT) abnormalities have been reported with vemurafenib. These should be monitored at baseline, then monthly during treatment or as clinically indicated. Serious ophthalmologic reactions (uveitis, iritis, retinal vein occlusion) have been reported with vemurafenib, so patients should receive routine monitoring for these side effects.[4]

Vemurafenib is dosed at 960 mg orally twice daily without regard to meals. **Table 1** summarizes the dosage adjustment recommended by package literature based on toxicity grade.

Table 1. Vemurafenib Dose Adjustment Summary

CTC-AE Grade	Recommended Vemurafenib Dose Adjustment
Grade 1 or Grade 2 (tolerable)	No dose adjustment necessary
Grade 2 (intolerable) or Grade 3	
1st Appearance	Hold vemurafenib until toxicity grade is at or below grade 1, then resume at 720 mg twice daily.
2nd Appearance	Hold vemurafenib until toxicity grade is at or below grade 1, then resume at 480 mg twice daily.
3rd Appearance	Discontinue vemurafenib
Grade 4	
1st Appearance	Hold vemurafenib until toxicity grade is at or below grade 1, then resume at 480 mg twice daily.
2nd Appearance	Discontinue vemurafenib

Note: Dose reductions of less than 480 mg twice daily are not recommended.
CTC-AE = Common Terminology Criteria for Adverse Events v4.0

Clinical results demonstrate that vemurafenib is a moderate CYP1A2 inhibitor, a weak CYP2D6 inhibitor, and a CYP3A4 inducer. Vemurafenib should be used cautiously when coadministered with drugs metabolized by these drug classes because it can increase serum concentrations of 1A2 and 2D6 substrates and decrease concentrations of 3A4 substrates. If coadministration is unavoidable, patients should be closely monitored for toxicity or treatment failure, and dose reductions should be considered in patients taking substrates of CYP1A2 and CYP2D6. Vemurafenib is a CYP3A4 substrate, so concomitant administration of strong CYP3A4 inducers or inhibitors should proceed with caution and close patient monitoring.[4] Examples of these drugs are listed in **Table 2.**

A randomized, multinational, phase 3 study of vemurafenib compared with dacarbazine was published in June 2011. The results of this study followed promising phase 1 and phase 2 data showing tumor regression and overall response rates greater than 50%, respectively.[3,8] Six hundred seventy-two patients with treatment-naïve BRAF-mutated unresectable or metastatic melanoma were included. The coprimary endpoints of this trial were overall survival (OS) and progression-free survival (PFS). Secondary endpoints included confirmed response rate, duration of response, and time to response. Patients received either vemurafenib 960 mg orally twice daily (n = 336) or dacarbazine 1,000 mg/m^2 intravenously once weekly in each 3-week cycle (n = 336). Two-thirds of patients had an Eastern Cooperative Oncology Group (ECOG) performance status of 0, and more than 95% of patients included had metastatic disease.[9]

At 6 months, OS in the vemurafenib group was 84% (95% CI, 78–89) versus 64% (95% CI, 56–73) in the dacarbazine group. This was

Table 2. Vemurafenib Drug Interactions*

CYP1A2 substrates	Acetaminophen Caffeine Estradiol Haloperidol Olanzapine Tamoxifen Theophylline Tricyclic antidepressants (TCAs; amitriptyline, imipramine) Warfarin
CYP2D6 substrates	Anti-arrhythmics (flecanide, lidocaine, propafenone) Beta-blockers (carvedilol, metoprolol, nebivolol, propranolol) Dextromethorphan Opioids (codeine, oxycodone, tramadol) Metoclopramide Selective serotonin reuptake inhibitors (SSRIs; fluoxetine, fluvoxamine, paroxetine) TCAs Tamoxifen Typical and atypical antipsychotics (chlorpromazine, haloperidol, olanzapine, risperidone)
CYP3A4 substrates	Calcium channel blockers HMG-CoA Reductase inhibitors ("Statins") Immunosuppressants (cyclosporine, tacrolimus, sirolimus) Macrolide antibiotics TCAs Warfarin
CYP3A4 inhibitors	Azole antifungals Clarithromycin Protease inhibitors
CYP3A4 inducers	Anticonvulsants (carbamazepine, oxcarbazepine, phenytoin) Efavirenz Nevirapine Phenobarbital Rifampin

**This is not a comprehensive listing.*

associated with a hazard ratio of 0.37 (95% CI, 0.26–0.55; $p < .001$) in favor of vemurafenib. Median PFS was 5.3 months in the vemurafenib group and 1.6 months in the dacarbazine group. The most common grade 2 or higher adverse events in the vemurafenib group included arthralgias, fatigue, rash (including photosensitivity characterized by blistering), and cuSCC. Fewer than 1% of patients experienced neutropenia in the vemurafenib group, and there were no grade 4 or higher toxicities reported in either arm.[9]

Vemurafenib is the first orally available targeted therapy for the treatment of unresectable and metastatic melanoma. It is FDA approved for use in the first-line setting only for patients with BRAF^{V600E}-mutated melanoma and has significantly improved OS when compared to dacarbazine in this patient population. Phase 2 abstract data have shown vemurafenib responses in more than half of the patients treated after failure of a prior therapy for melanoma. Vemurafenib is an attractive treatment option when compared with traditional chemotherapy, given its oral route of administration and absence of certain toxicities associated with traditional chemotherapeutic agents (e.g., myelosuppression, alopecia). However, this agent is not without adverse effects that require close monitoring and follow-up. Vemurafenib is also associated with several drug interactions. Patients

should discuss their current medications (including over-the-counter and complementary and alternative therapies) with their healthcare provider both prior to initiating vemurafenib and upon initiating any new medications.

References

1. Balch CM, Gershenwald JE, Soong SJ, et al. Final version of 2009 AJCC melanoma staging and classification. *J Clin Oncol.* 2009;27:6199-6206.
2. Curtin JA, Busam K, Pinkel D, Bastian BC. Somatic activation of KIT in distinct subtypes of melanoma. *J Clin Oncol.* 2006;24:4340-4346.
3. Flaherty KT, Puzanov I, Kim KB, et al. Inhibition of mutated, activated BRAF in metastatic melanoma. *N Engl J Med.* 2010;363(9):809-819.
4. Zelboraf™ (vemurafenib) [prescribing information]. South San Francisco, CA: Genentech USA, Inc; August 2011.
5. Poulikakos PI, Zhang C, Bollag G, Shokat KM, Rosen N. RAF inhibitors transactivate RAF dimers and ERK signalling in cells with wild-type BRAF. *Nature.* 2010;464:427-430.
6. Hatzivassiliou G, Song K, Yen I, et al. RAF inhibitors prime wild-type RAF to activate the MAPK pathway and enhance growth. *Nature.* 2010;464:431-435.
7. Heidorn SJ, Milagre C, Whittaker S, et al. Kinase-dead BRAF and oncogenic RAS cooperate to drive tumor progression through CRAF. *Cell.* 2010;140:209-221.
8. Ribas A, Kim KB, Schuchter LM, et al. BRIM-2: an open-label, multicenter phase II study of vemurafenib in previously treated patients with BRAF V600E mutation-positive melanoma. *J Clin Oncol.* 2011;29:Suppl 8509.
9. Chapman PB, Hauschild A, Robert C, et al. Improved survival with vemurafenib in melanoma with BRAF V600E Mutation. *N Engl J Med.* 2011;364(26):2507-2516.