Hematology/Oncology Pharmacy Association Newsletter Winter 2011 www.hoparx.org

HOPA News

The National Drug Shortage Crisis: Summary of the ASHP Drug Shortage Summit

Ali McBride, Vice Chair, Legislative Affairs Committee

The subject of drug shortages has become a salient issue with health systems. In 2010 more than 200 drugs were listed in the drug shortage database. Each year academic medical institutions, community hospitals, and infusion centers are hit with drug shortages. The time required to address this issue has been considerable, with 2010 having the worst record for the number of drug shortages (**Figure 1**). The American Society of Health System Pharmacists (ASHP) co-convened a Drug Shortages Stakeholder Executive Session in Bethesda, MD, on November 5 to address the issue. ASHP partnered with the American Society of Anesthesiologists, the Institute for Safe Medication Practices (ISMP), and the American Society of Clinical Oncology for the Drug Shortage Summit and invited participants from the Food and Drug Administration (FDA), health professional organizations, pharmaceutical manufacturers, and supply chain distributors to attend. Because the oncology sector has had to endure shortages without a repertoire of alternative drugs to use in this setting, HOPA was asked to participate in the summit.

The summit started with an overview and detailed history of drug shortages, illustrating potential causes of parenteral drug shortages (i.e., shortage of raw material, manufacturing problems, drug recalls, consolidation of manufacturers, increased global market demands) and providing a review of statistical and survey data. The FDA evaluated its current role in FDA shortages as well as regulations and restrictions the FDA has to address ongoing drug shortages. The opening discussions ended with the evaluation of the ASHP/ISMP Drug Shortage Survey that was completed in August 2010.[1] The survey participants were alarmed by the ever-increasing volume of critically important medications in short supply and the resulting use of less desirable, unfamiliar alternative drugs when available. They felt that shortages have significantly increased the potential for errors and patient harm caused by absent or delayed treatment or preventable adverse drug events associated with alternative drugs or dosage forms. Respondents described more than 1,000 errors and adverse patient outcomes during the past year related to more than 50 drugs on the shortage list that became abruptly unavailable, often without adequate notice.

The summit's afternoon activities focused on evaluating factors that have hampered resolving drugs shortages. Factors that were cited included difficulty obtaining a suitable alternative product and internal hoarding of medications associated with impending shortages. Furthermore, numerous organizations noted manufacturers' and wholesalers' lack of transparency disclosing reasons for drug shortages as a major concern.

HOPA addressed several topics during the meeting that were not outlined by other organizations. First and foremost, HOPA pointed out that in a majority of oncology drug shortages there is a lack of equivalent drugs that can be substituted for front-line regimens. Curative therapies including transplant for both pediatric and adult patients have been delayed due to the etoposide shortage this year. Second, answers about regional drug shortages have remained elusive. HOPA members have been continually hampered by the lack of drugs at their institutional site for the treatment of patients, with numerous infusion centers and community hospitals not being able to acquire an adequate drug supply. These sites have been affected hardest by the situation. Third, the lack of supportive care drugs, including antibiotics and diuretics, has impeded the ability to provide appropriate care to our patients. Last, due to oncology drug shortages, patients who are eligible for studies are not able to proceed on clinical trials.

continued on page 2

CONTENTS

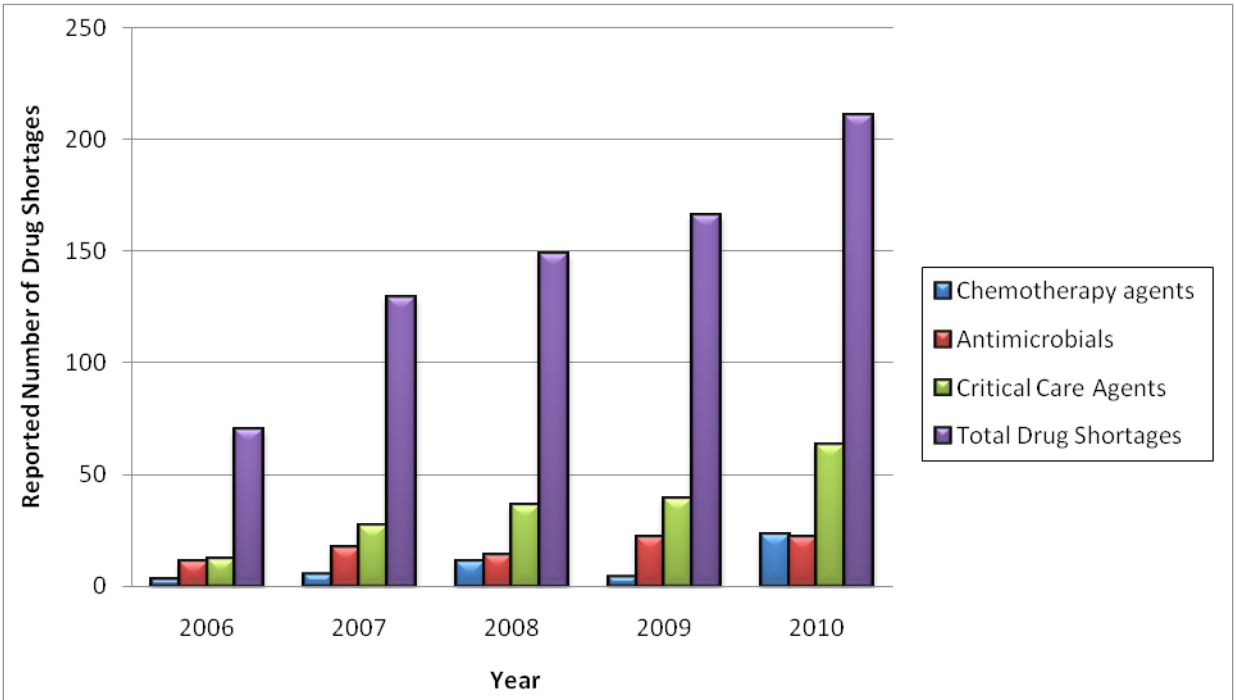
continued from page 1

During the summit, many voices from numerous stakeholders called for transparency of the ongoing causes of drug shortages. The meeting served as a first step in addressing the concerns and causes of drug shortages. At the conclusion of the summit, several recommendations were made, including improving rapid communication between the pharmaceutical supply chain and providers so that providers have more advanced notice and can better understand and manage shortages; removing the barriers faced by drug manufacturers and the FDA to minimize the impact of drug shortages, such as establishing processes for potentially extending the expiration date of a drug in short supply if it still meets safety requirements; and clarifying the definition of *medically necessary*, which is the term that prompts notifications to the FDA about drug shortages to ensure they are aware of shortages like those experienced by the oncology community. With input from numerous organizations, including HOPA, ASHP will continue to study and help resolve the issues related to drug shortages to prevent this problem in the future.

Reference

1. ISMP. ISMP survey on drug shortages. *ISMP Medication Safety Alert!* 2010;15(15):4.

Figure 1. Reported Drug Shortages from 2006–2010



Each column represents the number of new shortages identified during that year.
Data provided by the University of Utah Drug Information Service.

Metastatic Melanoma: New Advances and Recent Updates

LeAnn Norris, PharmD BCPS BCOP
Assistant Professor and Clinical Pharmacy Specialist
South Carolina College of Pharmacy, Columbia, SC

Melanoma is the most aggressive and deadly skin cancer in the United States, killing an estimated 8,700 people in 2010. Unfortunately, the incidence of melanoma continues to increase and treatment continues to be a challenge.[1] Although the disease is potentially curable in the adjuvant setting, there are few effective therapies for treating metastatic disease. Currently, standard systemic therapy has resulted in poor response rates, ranging from 7%–15% with 5-year survival rates <5% and undesirable toxicities.[2] During the past year, ongoing research has shown significant advances in the area of immunotherapy and targeted pathways.

A novel immunologic approach to fighting malignancies involves blocking the cytotoxic T-lymphocytic antigen-4 (CTLA-4) receptor with monoclonal antibodies. The CTLA-4 receptor is a molecule on T-cells that is believed to play a critical role in regulating natural immune response. The absence or presence of CTLA-4 can augment or suppress the immune system's T-cell response in fighting disease.[3] Ipilimumab, an IgG1 isotype, is a fully human antibody that, when administered, binds to the CTLA-4, thereby allowing unrestrained T-cell proliferation.[4] Hodi and colleagues conducted a double-blind, randomized, phase 3 study that enrolled 676 unresectable stage 3 or 4 patients who had been treated previously. The primary endpoint was overall survival (OS) with secondary endpoints, including best overall response rate, duration of response, and progression-free survival. Patients were randomized 3:1:1 to receive ipilimumab at 3 mg/kg + gp100 (a melanosomal protein cancer vaccine; $n = 403$), ipilimumab alone ($n = 137$), or gp100 alone ($n = 136$). Treatment was given once every 3 weeks for four cycles. Median OS for the ipilimumab + gp100 arm was 10 months compared to 6.4 months in the gp100 alone arm ($p < .001$). There were no differences in survival between the two ipilimumab arms ($p = .76$). Median OS for ipilimumab alone was 10.1 months ($p = .003$); this p-value represents the hazard ratio for death in the comparison with gp100 alone. At 24 months, response rates were 43.6% for the ipilimumab + gp100 arm, 45.6% for the ipilimumab alone arm, and 25.3% for the gp100 alone arm. Median progression-free survival at 12 weeks was similar between all three groups (2.76 in ipilimumab plus gp100 and gp100 alone groups and 2.86 in ipilimumab alone group. Immune-related adverse events (IRAEs) occurred in 60% of the patients treated with ipilimumab versus 30% in the gp100 arm. The most common side effects were dermatologic and gastrointestinal in nature. More grade 3 and 4 events occurred in the ipilimumab arms than the gp100 alone arm (10%–15% vs. 3%, respectively). Of the 14 deaths in the study, seven were related to IRAEs. Ipilimumab (Yervoy) was been granted priority review by the Food and Drug and Administration (FDA) and was approved on March 25 for the treatment of unresectable or malignant melanoma. This is the first agent to offer potential OS benefit. However, due to the unusual and potentially fatal side effects of this agent, it was approved with a Risk Evaluation and Mitigation Strategy to help with monitoring and informing healthcare providers about the potential side effects.

Tremelimumab, an IgG2 isotype, is the second anti-CTLA-4 agent being investigated. Ribas and colleagues evaluated the role of chemotherapy (temozolamide or dacarbazine) versus tremelimumab alone as first-line therapy.[5] In a large, randomized trial that included 655 patients with stage 3c–4 melanoma, tremelimumab 15 mg/kg IV was administered every 90 days in the treatment group compared to temozolamide 200 mg/m^2 PO on d1-5 q28d or dacarbazine 1,000 mg/m^2 IV q21d in the chemotherapy arm. Primary endpoints included OS with secondary endpoints evaluating response, durable tumor response, 6-month progression-free survival, and safety. Unfortunately, tremelimumab failed to demonstrate a significant improvement in OS compared to standard chemotherapy. OS with tremelimumab was 11.76 months versus 10.71 months for chemotherapy (with overlapping confidence intervals and HR = 1.04). Therefore, the data and safety monitoring board recommended early discontinuation after two-thirds of the events had occurred. Response rates were similar at 9.1 months versus 10.1 months. In addition, 6–month progression-free survival showed similarity between the two arms (18.6 and 14.1). Diarrhea (43% overall), pruritus (25%), and rash (23%) were the most common toxicities in the tremelimumab arm. Furthermore, the authors concluded that tremelimumab failed to show OS benefits in stage 3c–4 melanoma patients as first-line therapy.[5]

CTLA-4 inhibition is an exciting therapy but has resulted in an emerging class of toxicities. Although the mechanism behind IRAEs is still being investigated, early data suggest these effects are a result of tissue damage associated with inflammatory T-cell infiltrates involving the skin and gastrointestinal tract.[6] Furthermore, IRAEs may represent a breaking of tolerance to self-antigens, but are considered mild and self-limiting.[7] The most commonly documented IRAEs include rash, colitis, hepatitis, and other rare effects including hypophysitis. Grade 3–4 events have been observed in several trials. However, most events resolve with the initiation of high-dose steroids or cessation of drug. Severe IRAEs occur infrequently, but without the proper precautions, life-threatening effects such as diarrhea and colitis can lead to bowel perforation. Hypophysitis is perhaps the most irreversible toxicity, but can be managed appropriately with endocrine replacement therapy. Prevention of IRAEs may be difficult because the onset of these events is extremely variable, ranging from days to weeks after CTLA-4 administration.[7] Weber and colleagues conducted a phase 2 trial evaluating the safety and efficacy of ipilimumab (anti-CTLA-4) with or without budesonide for prevention of IRAEs.[8] This study was in treatment-naïve and previously treated patients with advanced melanoma. Study endpoints included OS, response rates, and grade 2 diarrhea or higher. OS at 10.5 months was not reached, but 1-year survival rates were 58% (ipilimumab + budesonide) and 59.1% (ipilimumab + placebo). Treatment-naïve patients had a 1-year survival rate of 71%. Response rates were seen in both groups (ipilimumab + budesonide: 12.1%; ipilimumab + placebo: 15.8%), but no differences were seen in the incidence of grade 2–4 diarrhea between the two groups.[8] Therefore, budesonide is not effective in preventing grade 2 or higher diarrhea and should not be used prophylactically with ipilimumab therapy. Supportive management should be initiated on Day 1 of presentation of symptoms, including antimotility agents for diarrhea. If symptoms do not resolve, steroids should be initiated immediately and continued for a sustained period of time. In addition, liver function tests should be assessed at baseline and periodically after starting CTLA-4 therapy.[8]

continued on page 4

continued from page 3

The most interesting characteristic associated with anti-CTLA-4 therapy is the relationship between IRAEs and tumor regression. Freedom from relapse and antitumor responses have been associated with serious IRAEs or grade 3–4 events.[9,10] In a study by Attia and colleagues, 14 patients with metastatic melanoma who received anti-CTLA-4 therapy experienced grade 3 or 4 IRAEs and 5 (36%) had tumor regression compared with 2 of 42 patients (5%) without immune toxicity.[9] Recently, Pavlov and colleagues found a trend toward improved survival in all grades of IRAEs ($p = .14$) with anti-CTLA4 therapy, but the incidence of grade 3–4 events specifically was inconclusive.[11] More importantly, Beck and colleagues reported that treating IRAEs with steroid therapy does not appear to have an effect on efficacy or tumor responses.[12] These data confirm that if needed, supportive care agents can be used to treat IRAEs without affecting tumor response. Additional studies to better understand the pharmacokinetics of anti-CTLA-4 agents, incidence of IRAEs, and the relationship between toxicities and anti-CTLA-4 therapy on tumor cells are ongoing. Currently, algorithms have been developed to help physicians treat and recognize IRAE symptoms.[7]

In the area of targeted therapies, understanding the importance of melanoma and the mitogen-activated protein kinase (MAPK) pathway is essential because the MAPK pathway regulates cell growth, proliferation, and differentiation.[13] A mutation in the gene that encodes the serine-threonine protein kinase B-RAF (BRAF) in the MAPK was recently discovered to occur in 40%–60% of melanomas. The majority of BRAF mutations result in a substitution of glutamic acid for valine at amine acid 600 (V600E mutation), resulting in increased initiation and progression of disease.[14] PLX4032 (Roche Pharmaceuticals) is a selective BRAF inhibitor and the first agent in the class to be tested. Flaherty and colleagues conducted a multicenter, phase 1, dose-escalation trial followed by an extension phase. Patients received PLX4032 twice daily until they had disease progression.[14] Fifty-five patients were initially enrolled in the study; 49 of these patients had melanoma. The phase 2 dose was determined to be 960 mg twice daily. Additional increases in dose were limited by rash, fatigue, and arthralgias (grade 2 or 3). Of the 16 patients with melanoma who were receiving 240 mg or more of PLX4032 twice daily as part of the dose-escalation phase, one patient had a complete response and 10 patients had partial responses. As part of the extension phase, 32 additional patients were enrolled with metastatic melanoma with confirmed V600 mutation. Two of the patients had a complete response and 24 patients had a partial response. The median progression-free survival was 7 months. The most common grade 2–3 events included nausea, rash, arthralgias, photosensitivity, fatigue, pruritus, and palmar-plantar dysesthesias.[14] PLX4032 is currently being studied in several ongoing phase 2 and 3 studies.

Additional tyrosine kinase inhibitors are currently undergoing investigation for the treatment of melanoma. Valatinib (PTK787) is an oral tyrosine kinase inhibitor of vascular endothelial growth factor receptor (VEGF) 1 and 2. In a phase 2 study of 29 patients with metastatic melanoma, treatments were escalated weekly beginning at 250 mg twice daily, then 500 mg twice daily, and finally 500 mg in the morning and 750 mg in the evening (maximum daily dose).[15] Therapy was continued until disease progression or unacceptable toxicity. Of the 44% of patients who received the maximum daily dose, one patient experienced a partial response and eight patients experienced stable disease. Median survival rates were 2.6 to 11.6 months. Grade 3 adverse events included hypertension, vomiting, diarrhea, disorientation, fatigue, and neutropenia. Axitinib (AG-013736) is an investigational oral tyrosine kinase inhibitor that inhibits both VEGF and platelet-derived growth factor (PDGF).[16] In a phase 2 study of 32 metastatic melanoma patients, treatment with Axitinib 5 mg twice daily resulted in an overall response rate of 15.6% and a duration of response of 2.3 to 10.2 months. The most common adverse events included fatigue, hypertension, hoarseness, and diarrhea. Responses were associated with blood pressure changes, specifically in patients with diastolic blood pressure >90 mmHg. The median OS was 3.2 months in 13 patients and 6.2 months in 9 other patients.[17]

Recently, multiple clinical advances have been discovered in the area of melanoma. Additional anti-CTLA-4 therapies are currently being developed, and multiple tyrosine kinase inhibitors are under investigation. The use of ipilimumab and its resulting OS benefit in the area of metastatic melanoma is the most promising; however, it can be associated with severe adverse events. Pharmacists may have a major role in managing the side effects of these newer therapies and educating patients and caregivers about the importance of recognizing their effects.

References

1. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics 2010. *CA: Cancer J Clin.* 2010;60:277-300.
2. National Comprehensive Cancer Network. NCCN clinical guidelines: melanoma 2011. Available at: www.nccn.org/index.asp. Accessed on January 15, 2010.
3. Egen J, Kuhns MS, Allison JP. CTLA-4: new insights into its biological function and use in tumor immunotherapy. *Nat Immunol.* 2002;3:611-618.
4. Hodi SF, O'Day SJ, McDermott DF, et al. Improved survival in ipilimumab in patients with metastatic melanoma. *N Engl J Med*. 2010;363:711-723.
5. Ribas A, Hauschild A, Kefford R, Gomez-Navarro J, Pavlov D, Marshall M. Phase III, open-label, randomized, comparative study of tremelimumab (CP-675,206) and chemotherapy (temozolomide [TMZ] or dacarbazine [DTIC]) in patients with advanced melanoma. *J Clin Oncol.* 2008;26:485s.
6. Peggs KS, Quezada SA, Korman AJ, Allison JP. Principles and use of anti-CTLA4 antibody in human cancer immunotherapy. *Curr Opin Immunol.* 2006;18:206-213.
7. Weber J. Review: anti-CTLA-4 antibody ipilimumab: case studies of clinical response and immune-related adverse events. *Oncologist.* 2007;12:864-872.
8. Weber JS. Safety and efficacy of ipilimumab with or without prophylactic budesonide in treatment-naive and previously treated patients with advanced melanoma. *J Clin Oncol.* 2009;15(17):5591-5599.
9. Attia P, Phan GQ, Maker AV, et al. Autoimmunity correlates with tumor regression in patients with metastatic melanoma treated with anti-cytotoxic T-lymphocyte antigen-4. *J Clin Oncol.* 2005;23:6043-6053.

continued on page 5

continued from page 4

10. Sanderson K, Scotland R, Lee P, et al. Autoimmunity in a phase I trial of a fully human anti-cytotoxic T-lymphocyte antigen-4 monoclonal antibody with multiple melanoma peptides and Montanide ISA 51 for patients with resected stages III and IV melanoma. *J Clin Oncol.* 2005;23:741-750.
11. Pavlov D, Bulanhagui C, Wallis N, et al. Immune-related adverse events in patients with melanoma treatment with tremlimumab (CP-675, 206). Presented at: International Society for Biological Therapy of Cancer 22nd Annual Meeting; November 2-4, 2007; Boston, MA.
12. Beck KE, Blansfield JA, Tran KQ, et al. Enterocolitis in patients with cancer after antibody blockade of cytotoxic T-lymphocyte-associated antigen 4. *J Clin Oncol.* 2006;24:2283-2289.
13. Arkenau HT, Kefford R, Long GV. Targeting BRAF for patients with melanoma. *Br J Cancer.* 2011;104:392-398.
14. Flaherty KT, Puzanov I, Kim KB, et al. Inhibition of mutated, activated BRAF in metastatic melanoma. *N Engl J Med*. 2010;363:809-819.
15. Corrie P. A phase II study of PTK787 in metastatic melanoma patients. Poster presented at: American Society of Clinical Oncology Annual Meeting; May 30–June 3, 2008; Chicago, IL.
16. Choureiri TK. Axitinib, a novel anti-angiogenic drug with promising activity in various solid tumors. *Curr Opin Investigl Drugs.* 2008 Jun;9(6):658-671.
17. Fruehauf JP, Lutzky J, McDermott DF, et al. Axitinib (AG-013736) in patients with metastatic melanoma: a phase II study. *J Clin Oncol.* 2008;26:484s.

Obesity: A Poor Prognosis for Early-Stage Breast Cancer

Laura R. Bobolts, PharmD
The Center for Women's Oncology Clinical Pharmacist
Moffitt Cancer Center and Research Institute, Tampa, FL

As we advance our knowledge of breast cancer, the apparent association between obesity and breast cancer increases in complexity. Obesity, defined as a body mass index (BMI) of 30 kg/m^2 or more, is an established risk factor for the development of breast cancer in postmenopausal women, as well as an indicator of poor clinical outcomes and worse survival compared to nonobese patients who are newly diagnosed with breast cancer.[1]

Ewertz and colleagues recently explored the effect of obesity on the risk of breast cancer recurrence and death as a result of breast cancer or all causes. This study linked obesity effectiveness to adjuvant treatment for early-stage breast cancer. Data were collected from the Danish Breast Cancer Cooperative Group database, which contains information on the BMI for nearly 19,000 women treated for early breast cancer in Denmark between 1977 and 2006 with 10 years of follow-up data for recurrence and up to 30 years for mortality. Patients with a BMI of greater than or equal to 30 kg/m^2 were more likely to be postmenopausal, be older, have larger tumors, have more ductal grade 3 tumors, and have more positive lymph nodes than leaner women with a BMI less than 25 kg/m^2. Keeping in mind many of these factors are associated with a poorer prognosis for women with breast cancer, this study adjusted for age, menopausal status, tumor size, nodal status, deep fascia invasion, histologic type and grade, estrogen receptor status, systemic adjuvant therapy, and protocol year to determine the impact of obesity on breast cancer recurrence or death.[2]

After adjusting for the variables described, obesity was identified as an independent prognostic factor for the development of distant metastases and death as a result of breast cancer. The risk for distant metastases increased with increasing BMI after approximately 3 years from the diagnosis of breast cancer. This translated to a 46% (hazard ratio, 1.46; 95% CI, 1.11 to 1.92; p = .007) increase in the risk of distant metastases after 10 years and a 38% (hazard ratio, 1.38; 95% CI, 1.11–1.71; p = .003) increase in the risk of dying from breast cancer in women with a BMI of 30 kg/m^2 or more compared to women with a BMI of 25 kg/m^2 or less. Of note, BMI had no affect on locoregional recurrences at 10 years in this population, nor did it increase the risk of contralateral breast cancer, other primary nonbreast cancers, or death as first event.[2]

Many mechanisms have been considered to explain why obese women with breast cancer experience poorer outcomes. Because adipose tissue is the main source for estrogen production through aromatization of androgens in postmenopausal women,[3] one such explanation is that obese postmenopausal women have elevated levels of circulating estrogen from excess adipose tissue, which may increase the risk of breast cancer progression in estrogen receptor-positive disease. In contrast, premenopausal women mainly synthesize estrogen in the ovaries, indicating that alternative mechanisms must be influencing the prognosis for premenopausal women with breast cancer.[4] Obesity is also associated with decreased sex hormone-binding globulin, a glycoprotein that binds to sex hormones and increases the bioavailability of free estradiol, which may lead to increased estrogen receptor-positive tumor growth.[5] Other plausible mechanisms support obesity as an independent prognostic factor for distant metastases and death from breast cancer regardless of estrogen receptor status. Obese women demonstrate high fasting insulin levels and insulin-like growth factor-1 (IGF-1) that act as a potent inhibitor of apoptosis,[6] adipocytokines such as leptin and adiponectin promote tumor growth, and proinflammatory mediators may contribute to tumor progression,[7] irrespective of estrogen levels.

It is not clear whether lifestyle interventions implemented to reverse obesity or pharmacological manipulation of obesity mediators postdiagnosis will improve breast cancer outcomes. Lifestyle modifications such as weight loss or increased physical activity may affect nonbreast cancer mortality, which is beneficial given the curative intent of early breast cancer; however, there is insufficient evidence to recommend lifestyle interventions to improve the prognosis of breast cancer in obese patients.[8] An interesting pharmacological intervention for obese patients that may have some

continued on page 6

continued from page 5

promise in the future is metformin, a biguanide antidiabetic agent. Metformin works to reverse hyperinsulinemia to indirectly affect cancer cells and exert antiproliferative effects via mammalian target of rapamycin (mTOR) inhibition.[9] In a study by Jiralerspong and colleagues, diabetic breast cancer patients receiving neoadjuvant chemotherapy and metformin experienced significant increased pathological complete responses compared to diabetic patients not receiving metformin (24% vs. 8%; $p = .007$).[10]

In Ewertz and colleagues' study, adjuvant chemotherapy and endocrine therapy were less effective for obese women. Interactions between BMI, adjuvant therapy, and follow-up time were analyzed separately to assess the efficacy of adjuvant treatment in lean versus obese women. After 10 years from diagnosis of breast cancer, obese patients with a BMI more than 30 kg/m^2 who received adjuvant chemotherapy had a 77% significant increase in the risk of death from all causes compared to women with a BMI less than 25 kg/m^2. No significant difference was observed for all-cause mortality based on BMI for the first 10 years of follow-up after adjuvant treatment.[2]

A limitation of the study is that the specific chemotherapy regimens were not listed for obese patients versus nonobese patients. A possible imbalance in systemic treatment regimens may have influenced the long-term outcomes following adjuvant therapy in obese women.

Another shortcoming involves the fact that the doses of chemotherapy or method of dosing such as utilizing actual, ideal, or adjusted body weight were not described. This opens the door for the probability that obese patients may have been underdosed, resulting in a poorer outcomes compared to nonobese patients. Alternatively, obese patients may have been overdosed, leading to poor tolerability and reduced relative does intensity. In the retrospective cohort study by Griggs and colleagues,[11] 9,672 women were treated with adjuvant doxorubicin and cyclophosphamide for breast cancer treatment between 1990 and 2001. In this cohort study, a preemptive first-cycle dose reduction of more than 10% of standard published doses occurred in 20% of obese patients (BMI of 30 to less than 35 kg/m^2) and 37% of severely obese patients (BMI greater than or equal to 35 kg/m^2), compared to only 9% of patients with a BMI of less than 25 kg/m^2 ($p < .001$), signaling a dosing apprehension in obese patients. Interestingly, severely obese patients were significantly less likely to be hospitalized for febrile neutropenia, even when full-dose chemotherapy was administered (odds ratio, 0.61; 95% CI, 0.38–0.97) compared with women with a BMI less than 25 kg/m^2 when full-dose chemotherapy was administered at actual body weight. This is a step toward dismissing the fear of increased toxicity in obese patients treated at full dose.[11] Moreover, the Cancer and Leukemia Group B study 8541 randomized almost 1,600 women with stage II breast cancer and positive regional lymph nodes to cyclophosphamide, doxorubicin, and fluorouracil (CAF) at various doses classified as low, moderate, or high. Patients treated with chemotherapy of moderate or high-dose intensity experienced a significantly better disease-free survival and overall survival versus patients treated with a low dose of the same chemotherapeutic regimen when using actual body weight for calculating body surface area. Patients classified in this study as obese (BMI greater than or equal to 27.3 kg/m^2) treated with CAF dosed on actual body weight experienced similar failure-free survival (defined as death or relapse) and no significant increase in first-cycle toxicity compared to nonobese patients. In addition, obese patients who began CAF at a reduced relative dose intensity of less than 95% of the planned weight-based dose experienced shorter failure-free survival.[11,12] Obese patients benefit significantly from full-dose adjuvant chemotherapy administered on actual body weight, and the result of adjuvant chemotherapy being less effective in obese patients in the study by Ewertz and colleagues[2] may have been skewed if the obese women did not receive a similar relative dose intensity compared to nonobese women.

The efficacy of endocrine therapy in obese versus nonobese early breast cancer patients was explored in the study by Ewertz and colleagues. After 10 years from the diagnosis of breast cancer, obese women with a BMI more than 30 kg/m^2 who received adjuvant endocrine only therapy had a 57% significant increase in the risk of death from all causes compared with women with a BMI less than 25 kg/m^2. Limited data were available regarding the duration, type of endocrine therapy, or BMI in relation to endocrine therapy used, but therapy primarily consisted of tamoxifen for 1 to 5 years and only about 3,000 patients received an aromatase inhibitor. Keeping in mind increased adipose tissue leads to elevated circulating estrogen, 59% of the obese patients were postmenopausal, compared to only 39% of nonobese patients ($p < .001$).[2] This difference in baseline characteristics is also significant because postmenopausal women should receive an aromatase inhibitor versus tamoxifen for adjuvant treatment of breast cancer. The lack of aromatase inhibitor use in this population could certainly have contributed to a worse outcome in obese women solely based on the fact that more obese women were postmenopausal and thus, did not receive optimal endocrine therapy. Alternatively, aromatase inhibitors were approved for the adjuvant treatment of breast cancer in early- to mid-2000, trailing the approval of tamoxifen for this patient population and limiting its use in the Danish database that contained information on adjuvant endocrine therapy implemented between 1977 and 2006.

BMI was also examined in relation to outcomes in postmenopausal women with early-stage breast cancer in the Arimidex, Tamoxifen, Alone, or in Combination (ATAC) trial. A BMI greater than 35 kg/m^2 was associated with a significant increase in the risk of recurrence (adjusted hazard ratio, 1.39; 95% CI, 1.06–1.82; $p = .03$) and significantly more distant recurrences (adjusted hazard ratio, 1.46; 95% CI, 1.07–1.61; $p = .01$) compared with women with a low BMI of less than 23 kg/m^2 irrespective of endocrine therapy. Of note, the efficacy of tamoxifen was not dependent on BMI, while anastrozole was significantly less effective in obese women with a BMI higher than 30 kg/m^2 compared to women with a BMI less than 28 kg/m^2 (pheterogeneity = .01). The study concluded that aromatase inhibitors were more effective in thinner women than tamoxifen and higher circulating estrogen levels in obese postmenopausal women may have led to incomplete inhibition by anastrozole.[14] Ewertz and colleagues[2] noted diminished long-term benefits for obese patients treated with adjuvant endocrine therapy, with the majority of the patients receiving tamoxifen independent of BMI for efficacy.

continued on page 7

continued from page 6

In summary, Ewertz and colleagues' study[2] was instrumental in identifying obesity as a negative independent prognostic factor for the development of distant metastases and death as a result of breast cancer in early-stage disease. Although the evidence from this study demonstrated that chemotherapy and endocrine therapy were less effective in the long-term for obese patients, this conclusion would have been strengthened by more explicit details on the systemic treatment regimen used and the dosing method, if applicable. Pharmacists are an ideal healthcare provider to educate physicians about the importance of dosing adjuvant chemotherapy on actual body weight to preserve chemotherapy efficacy in obese and nonobese patients. The oncology field will continue to explore the complex relationship between adjuvant therapy and clinical outcomes in obese breast cancer patients. One can only hope to have more answers in the future to specifically tailor chemotherapy and endocrine therapy to a patient's BMI to improve outcomes.

References

1. Protani M, Coory M, Martin JH. Effect of obesity on survival of women with breast cancer: systemic review and meta-analysis. *Breast Cancer Res Treat.* 2010;123:627-635.
2. Ewertz M, Jensen MB, Gunnarsdottir KA, et al. Effect of obesity on prognosis after early-stage breast cancer. *J Clin Oncol.* 2011;29:25-31.
3. Cleary MP, Grossman ME. Minireview: obesity and breast cancer: the estrogen connection. *Endocrinology.* 2009;150:2537-2542.
4. Vrieling A, Buck K, Kaaks R, Chang-Claude J. Adult weight gain in relation to breast cancer risk by estrogen and progesterone receptor status: a meta-analysis. *Breast Cancer Res treat.* 2010;123:641-649.
5. Dal Maso L, Zucchetto A, Talamini R, et al. Effect of obesity and other lifestyle factors on mortality in women with breast cancer. *Int J Cancer.* 2008;123:2188-194.
6. Goodwin PJ, Ennis M, Pritchard KI, Trudeau ME, Koo J, Madarnas Y, et al. Fasting insulin and outcome in early-stage breast cancer: results of a prospective cohort study. *J Clin Oncol.* 2002;20:42-51.
7. Van Kruijsdijk RC, van der Wall E, Visseren FL. Obesity and cancer: the role of dysfunctional adipose tissue. *Cancer Epidemiol Biomarkers Prev.* 2009;18:2569-2578.
8. McTiernan A, Irwin M, Von Gruenigen V. Weight, physical activity, diet, and prognosis in breast and gynecologic cancers. *J Clin Oncol.* 2010;28:4074-4080.
9. Goodwin PJ, Pritchard KI, Ennis M, Clemons M, Graham M, Fantus G. Insulin-lowing effects of metformin in women with early breast cancer. *Clin Breast Cancer.* 2008;8:501-505.
10. Jiralerspong S, Palla SL, Giordano SH, Meric-Burnstam F, Liedtke C, Barnett CM, et al. Metformin and pathologic complete responses to neoadjuvant chemotherapy in diabetic patients with breast cancer. *J Clin Oncol.* 2009;27:3297-3302.
11. Griggs JJ, Sorbero ME, Lyman GH. Undertreatment of obese women receiving breast cancer chemotherapy. *Arch Intern Med.* 2005;165:1267-1273.
12. Budman DR, Berry DA, Cirrincione CT, Henderson IC, Wood WC, Weiss RB, et al. Dose and dose intensity as determinants of outcome in the adjuvant treatment of breast cancer. The cancer and leukemia group B. *J Natl Cancer Inst.* 1998;90:1205-1211.
13. Rosner GL, Hargis JB, Hollis DR, Budman DR, Weiss RB, Henderson IC, et al. Relationship between toxicity and obesity in women receiving adjuvant chemotherapy for breast cancer: results from cancer and leukemia group B study 8541. *J Clin Oncol.* 1996;14:3000-3008.
14. Sestak I, Distler W, Forbes JF, Dowsett M, Howell A, Cuzick J. Effect of body mass index on recurrences in tamoxifen and anastrozole treated women: an exploratory analysis from the ATAC trial. *J Clin Oncol.* 2010;28:3411-3415.

CONGRATULATIONS

to the 2011 HOPA Travel Grant Recipients!

Amanda Agnew
Kiran Avancha
Justin Balko
Claire Boomershine
Amber Bradley
Rachelle Carter
Vivian Chow
Amber Diaz
Natalie Dickmeyer
Morgane Diven
Carina Dolan
Kathy Galus
Joanna Ghayad
Katherine Jennings
Natalie Lee
Philip Lubanski
Michael Madsen
Zahra Mahmoudjafari
Nicole McMullen
Tanja Monroe
Jennifer Neal
D. Van Nguyen
Christina Radcliffe
Ashli Rasmussen
Ivan Reveles
Ann Schwemm
Mahsa Sharifi
Sarah Shockley
Patrick Skeffington
Tania Stewart
Angela Urmanski
Brandon Vakiner
Jennifer Wagner
Mark Walsh
Kathryn Wheeler
Amy Williams
Krystal Wilson
Hanna Zaghloul

BOARD AND COMMITTEE UPDATES

Board Update

Rowena (Moe) Schwartz, Past President, HOPA

It has been more than a year since the 2010 HOPA Annual Conference in New Orleans. Since that meeting HOPA has experienced significant growth and change, and I look forward to the opportunity to discuss this progress with HOPA members. The 2011 HOPA Annual Conference in Salt Lake City, UT, from March 23–26 provided a forum to speak with members about some of the most important changes. Unfortunately, not all of our members were be able to attend this meeting, so I wanted to outline several of the topics that were on the agenda for the Annual Members' Meeting. I also wanted to share where you will be able to obtain updated information.

HOPA Committee Reports

HOPA's committees continue to contribute to the growth and development of the organization. Each year during the Annual Conference we provide an opportunity for the committees to highlight their efforts. Because the available time for each committee is limited, we have decided to publish the HOPA committee reports in the next edition of *HOPA News*. The work and successes of the committees are very much appreciated, and we want to provide an opportunity for HOPA members to learn about each committee's achievements.

HOPA Strategic Plan

The HOPA Strategic Plan was presented during the Annual Members' Meeting in Salt Lake City. The HOPA Board is excited to have developed a dynamic and focused plan for the organization that we believe will help HOPA transition as healthcare changes. The full document is available on the HOPA website for your reference. Please take a minute to read this document.

Some key points include the following:

- Core purpose: The Strategic Plan describes the core purpose of HOPA: to support pharmacy practitioners and promote hematology and oncology pharmacy to optimize the care provided to individuals affected by cancer. It is from this purpose that the goals for HOPA were developed.
- Goal efforts: In the next few years, there will be three main goal areas for HOPA. These goals focus on oncology pharmacy education, development and implementation of standards for oncology pharmacy practice, and the establishment of an advocacy effort for the organization. We would like to expand our current efforts in each of these areas. In addition, we would like to develop new strategies to meet these goals of our large and diverse membership.
  - We look forward to working with both the Education and Program Committees to look for additional strategies to provide member education.
  - The Standards Committee has worked on a defined process for developing standards, and the next anticipated step is to develop standards to support oncology pharmacy practitioners.
  - The Legislative Committee will work with HOPA leadership to move forward on a strategy to implement an advocacy plan for the organization.
- Putting the plan into action: To turn to the goals from the Strategic Plan into actions, we are now working with the committees to operationalize the goals. HOPA will need to evaluate resources to better support the work needed to achieve our identified goals. The plan for restructuring has been developed in collaboration with committee leadership.

HOPA Foundation

HOPA has moved forward with plans for establishing the HOPA Foundation. The HOPA Foundation will focus its effort on supporting oncology pharmacy research.

HOPA Website Redesign

The HOPA website has been redesigned. Thanks to all of the HOPA members who provided ideas and advice for this effort. The new website was launched at the HOPA meeting.

As we move into the first year of a new strategic plan, we expect to have many opportunities for members to use their talents to support the goals and purpose of HOPA. Committees remain an important component of this organization, but there is a very real need to develop work groups for projects that extend beyond one committee or individual committee charges. Watch for these calls for volunteers—we need your expertise as we continue our efforts to provide optimal pharmacy care to those individuals affected by cancer.

Education Committee

Susannah Kootz, Chair
Helen Marshall, Vice Chair

As the new year gets under way, the Education Committee continues to work diligently on several initiatives to meet the needs of our organization's growing membership. Our immediate focus has turned to drafting patient education sheets and planning for a virtual meeting to follow the HOPA Annual Conference.

Our committee has resumed work started by previous members of the Education Committee to create patient education sheets designed to enhance patients' understanding of side effects attributable to a particular chemotherapy regimen as opposed to individual drug effects. Common adult and pediatric regimens have been identified, and work continues on identifying toxicities associated with particular regimens as well as drafting standard language to be used to describe toxicities. The board has since determined that the scope of this project may require additional resources and will consider its options when the board meets in July.

Following this year's annual conference, we will provide HOPA members who are unable to travel to Salt Lake City the opportunity to view select presentations. We plan to make as many as eight sessions (1 for CPE and 7 for non-CPE) available to provide members a chance to enhance their clinical practice skills and broaden their understanding of key issues faced by pharmacists in their daily practice. Programming is expected to be posted to HOPA U in late spring.

Finally, I would like to take this opportunity to thank the outstanding efforts of Helen Marshall (Vice Chair), Michael Vozniak (Board Liaison), Lori Goodnow (Education Manager), and the other Education Committee members: David Gregornick, Anthony Jarkowski, Daniel Sageser, Geoff Saunders, Stephanie Minich, Marc Takemoto, Katie Tipton, Angela Urmanski, Mallika Weant, Laura

COMMITTEE UPDATES

Wiggins, Poppy Wilson, and Lisa Zambito. The many achievements of our committee would not have been possible without the invaluable practice experiences and sustained contributions each member provided on every task. It was a great privilege to collaborate with this group of professionals over the past year to advance the educational mission of HOPA.

Finance Committee

Antoinette Lavino, Chair
Caren Hughes, Vice Chair

During the final months of the calendar year, the Finance Committee focused on developing a recommendation to the HOPA Board for selection of an independent auditor. Since its inception in 2004, HOPA has not had an independent audit of the association's finances. With the growth of the organization and advent of new regulations, it is important to retain the services of an independent auditor for a 2010 fiscal year review.

Our work began with the development of a list of potential auditors. With the assistance of our management company, Association Management Center, we narrowed the potential financial firms to those meeting selection criteria, which included membership in certain certified public accountant organizations (indicating audit expertise), firm size (10–50 employees), proximity to HOPA headquarters, and experience working with not-for-profit organizations. Request for proposals (RFPs) describing independent audit services for HOPA covering a 3- to 5-year period were sent to potential bidders.

Eight companies were explored after the receipt and review of the initial RFPs. The key information compared in the returned bids was services included, price, timeline (target completion of audit for presentation to the board), and references. The committee developed a set of additional questions to understand the quotes, and two references supplied by each bidder were personally contacted by a committee member.

At our final meeting prior to the New Year, a recommendation was finalized for presentation to the HOPA Board. The Finance Committee proposed SS&G to audit the 2010 financials and prepare the required federal and state tax forms. During their January meeting, the board accepted the proposal.

Membership Committee

Karen Smethers, Chair
Meredith Toma Moorman, Vice Chair

The Membership Committee is pleased to announce that this year 38 travel grants have been awarded to HOPA members to offset the cost of travel to the Annual Conference. Membership Committee members Jennifer LaFollette, Ashley Newland, Cindy O'Bryant, and Kristopher Zepeda lead the evaluation and review of the travel grant applications, which was supported by board assessment of the eligibility, scoring, and final applicants. Congratulations to the pharmacy residents, students, practitioners, and pharmacy technicians who received grants. All applicants will be asked to participate in a survey to assess how to improve the award process for next year.

Thank you to all who have encouraged your colleagues to join HOPA—our membership has exceeded 1,700 clinicians, representing 50 states and 17 countries and provinces. Do not forget to take advantage of our new rolling membership renewal and membership discount programs. A 5% discount is given for 2-year memberships, and a 25% discount is offered for members new to HOPA. Group discounts are available for institutions with 10 or more members. For more information, contact HOPA at 877.467.2791.

Nominations and Awards Committee

Karen Fancher, Chair
Laura Jung, Vice Chair

The Nominations and Awards Committee is pleased to announce the winners of the 2010–2011 HOPA Membership Awards. We had many outstanding nominees this year, and our selection process was very difficult. We extend our congratulations to the following recipients.

HOPA Award of Excellence

Jim Koeller, MS
Clinical Professor, Department of Medicine & Oncology
University of Texas Health Science Center at San Antonio
Nominated by Phil Johnson

HOPA New Practitioner Award

Trevor McKibbin, PharmD MS BCPS
Assistant Professor, College of Pharmacy
University of Tennessee Health Science Center
Nominated by Julianna Burzynski

HOPA Technician Award

Tanja Monroe, CPhT
University of California–Davis Medical Center
Nominated by Andrea Ianucci

HOPA Oncology Pharmacy Practice Literature Award

Jacob Kettle, PharmD
Kansas VA Medical Center
Kettle, JK, Grauer D, Folker TL, et al. Effectiveness of exogenous albumin administration for the prevention of ifosfamide-induced encephalopathy. *Pharmacotherapy.* 2010;30(8):812-817.
Nominated by Casey Williams

The recipients were presented with their awards at the 2011 Annual Conference in Salt Lake City.

Program Committee

Lauren Decloe, Chair
Jill Rhodes, Vice Chair

HOPA's 7th Annual Conference was held at the Grand America Hotel in Salt Lake City from March 23–26. Dr. Tito Fojo from the National Institutes of Health kicked off the meeting with "The Cost of Cancer Therapy." The meeting had more than 25 hours of programming and included BCOP lectures, plenary sessions, symposia, and workshops. Plenary sessions covered topics such as nutrition and geriatrics and also featured the popular "Controversies in Care" series, which, for the first time, was expanded to include supportive care topics. The 2011 conference also hosted the First Annual Speaker Exchange Program, during which HOPA partnered with the British Oncology Pharmacy Association (BOPA) to increase collaboration with our international colleagues.

The following were additional conference highlights from 2011.

- The preconference morning workshop, "Accomplishing Meaningful Research in 1 Year," was hosted by the Research Committee on Wednesday, March 23, from 9–11 am.

COMMITTEE UPDATES

- Oncology Interest Groups were led by the Professional Affairs Committee on Friday, March 25, from Noon–1 pm. New practitioners, technicians, pediatrics, bone marrow transplant, administration, and ambulatory care were the interest group topics for this year.
- The 3rd Annual Rays of Hope charity yoga event was held during two sessions on Saturday, March 26, at 6:15–6:45 am and 7–7:30 am. A $40 donation entitled participants to entry into one of the two sessions and included a T-shirt, towels, fruit, and water. Proceeds from the event benefited Camp Hobé, a summer camp for children with cancer and their siblings.
- Expandable folios were provided to attendees to store meeting materials.
- Slide presentations are available on the HOPA U website for download and printing indefinitely.
- Evaluations are accessible online for 30 days following the conference.

This year's annual conference was a resounding success and we want to thank everyone for their hard work in putting the event together.

Professional Affairs Committee

Dan Zlott, Chair
Marjory Curry, Vice Chair

HOPA Booth

The HOPA booth was successfully exhibited at the American Society of Health System Pharmacists Midyear Meeting and enjoyed higher than expected traffic during the exhibition. It is estimated that approximately 200 HOPA membership brochures were handed out during the exhibition. Based on estimates provided by the booth volunteers, approximately 30%–40% of those who stopped by the booth were students, 10%–20% were PGY1 or PGY2 residents, and the remainder were pharmacists. In addition, several vendors visited the booth and expressed interest in exhibiting during HOPA's Annual Conference.

APhA Collaboration

The Committee has received confirmation from the American Pharmacists Association (APhA) that HOPA and APhA will be cosponsoring an oncology session at the APhA Annual Meeting. The session, "The Role of the Community Pharmacist in Caring for Patients with Cancer," will cover new options for drug delivery for patients with cancer and how community pharmacists can help patients receive the most benefit from their outpatient cancer therapy.

At the completion of this program, participants will be able to

1. list the oral oncology medications that are currently available and describe their indications
2. identify common medication errors associated with oral oncology medications
3. list the common adverse effects, drug-drug interactions and food-drug interactions, and important counseling information associated with oral oncology medications
4. discuss emerging therapies and ongoing research in outpatient oncology medications.

In addition, the Professional Affairs Committee met with the National Executive Committee (NEC) of the APhA Academy of Student Pharmacists (APhA-ASP) in early January to explore opportunities for partnership. APhA-ASP currently has more than 30,000 student pharmacist members, making it the largest student pharmacy organization in the world. Some potential ideas include creating a national oncology pharmacy mentor list for students interested in pursuing a career in oncology and creating oncology tools for student pharmacists to use on rotations. Through this potential partnership, the Professional Affairs Committee hopes

New HOPA Volunteer Activity Center Now Open!

Members interested in becoming involved in association activities can now visit the HOPA Volunteer Activity Center. After you click this link, you will be first directed to log in, then given access to the **Volunteer Activity Center.**

This new site is where you can review current volunteer opportunities and provide a list of skills and interests that the association can use when seeking volunteers for future volunteer opportunities.

Visit today and tell us how you would like to be more involved!

COMMITTEE UPDATES

to increase awareness of HOPA's purpose and mission within the pharmacy profession and increase awareness of oncology as a career option within pharmacy.

HOPA Traineeship

The Committee has formed a working group to generate a proposal for a scholarship program, which we are tentatively calling the "Diversity Initiative for Pharmacy Students pursuing Careers in Oncology." We are in the process of refining the initial recommendations now and hope to have a draft version ready for board consideration soon.

Publications Committee

Brooke Bernhardt, Chair
Stacy Shord, Vice Chair

We hope you were able to join us for the February Webinar, "New Cytotoxic Chemotherapy Agents Approved for Metastatic Breast Cancer and Hormone Refractory Prostate Cancer." We would like to thank our speakers, Michael Berger and Sherry Mori Vogt, and our moderator, Brandy Strickland, for an excellent presentation. A summary of the Webinar will be included in the next issue of *HOPA News*. If you were not able to participate, please let us know how we can better meet your educational needs. Please refer to page 12 of this newsletter for a summary of November's HOTopic webinar, which covered pharmacogenomics.

We would like to thank those of you who participated in the survey regarding the Listserv. We recently closed the survey and will summarize the results in the next issue of *HOPA News.* In the meantime, we hope that you will enjoy a new added feature: FDA news blasts, which will be provided to you through e-mails from HOPA. These news blasts will include new drug approvals and other news as provided by the FDA.

Last, the Publications Committee and AMC staff have worked diligently to identify topics, select contributors, and review the contributions for each issue of *HOPA News.* It is a time-consuming task and we hope you enjoy this and other issues of *HOPA News.* If you have any suggestions for future newsletter content or formatting, please do not hesitate to let us know.

Standards Committee

Mike Green, Chair
Jamie Poust, Vice Chair

The HOPA Standards Committee remains hard at work creating standard operating procedures and laying the groundwork for current and future committees. As the mission and strategic plan for HOPA has emerged, the Standards Committee has started to focus more on creating clinical practice guidelines and partnering with outside oncology-related organizations to broaden HOPA's influence. During the new committee year, we are poised to create clinical practice guidelines. We strongly encourage each HOPA member to consider lending his or her skills and experience to the HOPA Standards Committee and become part of the future of HOPA and oncology pharmacy.

HOPA Has a Brand New Website!

- Fresher Look
- Better Navigation
- Enhanced Career Center
- Drug Updates with Advanced Search
- Sharing Functions

Visit **www.hoparx.org** and take a tour!

Pharmacogenomics: November's HOTopic

Lisa M. Savage, PharmD BCOP
Medication Safety Clinical Specialist
The James Cancer Hospital at The Ohio State University

As the field of oncology progresses toward personalized medicine, it is no surprise that pharmacogenomics has become a topic of interest for practitioners. During November's HOTopics Webinar, two HOPA members, Christine Walko, PharmD BCOP (University of North Carolina, Eshelman School of Pharmacy), and Kristine Crews, PharmD BCPS (St. Jude Children's Research Hospital), shared examples of practical applications of pharmacogenomics.

Not all patients respond to standard therapies. Pharmacogenomics offers the potential to customize therapy for those patients who have excess toxicities or who do not respond to standard therapies because of genetic polymorphisms. Two prime examples of treatments for which these circumstances can occur are warfarin and tamoxifen. Only 6% of patients are started on optimal doses of warfarin because of polymorphisms in the cytochrome P450 2C0 (CYP2C9) genotype and vitamin K epoxide reductase complex subunit 1 (VKORC1) haplotype, while 35% of estrogen receptor-positive breast cancer patients are nonresponders to tamoxifen because of variations in cythocrhome p450 2D6 (CYP2D6) and the resulting levels of endoxifen, the active metabolite. In 2010 a labeling change to Coumadin adjusted recommended doses based on pharmacogenomic values. Walko explained, "This is actually one of the few examples of a drug where the package insert actually gives you specific dosing recommendations based on the VKORC1 and the CYP2C9 genotypes."

As a result, companies like CVS Caremark and Medco Health Solutions are offering genetic testing because "it's optimizing the drugs they're giving to their patients," said Walko. The Medco-Mayo Warfarin Effectiveness Study (MM-WES) hypothesized that genetic testing of CYP2C9/VKORC1 will reduce hospitalization risk during the first 6 months of warfarin therapy.[1] Statistically significant decreases at 180 days favored the intervention group (dosed by pharmacogenomics) in terms of all-cause hospitalization rate and hospitalization rate for bleed or venous thromboembolism; these translated into rate reductions of 31% and 28%, respectively. Moreover, 75% of physicians adopted genotype testing. Medco is also partnering with LabCorp to determine the prevalence of 2D6 inhibitor prescribing with tamoxifen and physician willingness to change therapy on the basis of specific lab results. As of November 2010, data were still being collected. In addition, patient survey results suggested a demand for additional education regarding the purpose of pharmacogenomic testing (presented at ASCO, 2010).

The second half of the seminar featured Crews, who discussed the role of genetic testing in the community pharmacy and in the prevention of adverse events, using 6-mercaptopurine (6-MP) and codeine as examples. 6-MP is a substrate for the polymorphic enzyme thiopurine methyltransferase (TPMT); mutations may lead to an increase in myelosuppression and risk of secondary malignancies, but the drug's overlapping toxicities with other agents makes it difficult to titrate clinically. At Dr. Crews's practice site, St. Jude Children's Research Hospital, a TPMT genotype is one of five pharmacogenetic tests offered through the clinical pharmacokinetics laboratory. After the test is ordered, a consult note with dosing recommendations is placed in the patient's chart and the enzyme mutation is added to the problem list. Unlike other therapeutic drug monitoring programs, the genotype testing offered is preemptive, with the goal of testing each patient before the first dose is administered. A similar process is in place for CYP2D6 genotype testing, which ultimately provides an electronic alert to the prescriber when a CYP2D6 substrate is ordered.

Pharmacists will have increased roles in education and patient testing as pharmacogenomics expands; it may even be coming to a community pharmacy near you.

Reference

1. Epstein RS, Moyer TP, Aubert RE. Warfarin genotyping reduces hospitalization rates results from the MM-WES (Medco-Mayo Warfarin Effectiveness Study). *J Am Coll Cardiol.* 2010 June 22;55(25):2504-2812. Epub 2010 Apr 8.

	Medications	Services Offered
Medco Health Solutions		
	Warfarin (partnership with Mayo Clinic) Tamoxifen (partnership with LabCorp) Clopidogrel Abacavir	Six therapeutic research centers; prescriptions routed to specific location based on disease state. Pharmacist contacts patient to discuss genetic testing Patients sent test kit for saliva; results mailed to MD with interpretation
CVS Caremark		
	Azathioprine Thioguanine Carbamazepine Clopidogrel Tamoxifen Abacavir	Generation Health: manages testing through Best Test™ Genetics Network

DRUG UPDATES

Eribulin (Halaven™)

Class: Microtubule inhibitor

Indication: Metastatic breast cancer patients who have received at least two chemotherapeutic regimens for the treatment of metastatic disease including an anthracycline and a taxane in either the adjuvant or metastatic setting

Dose: 1.4 mg/m^2 intravenously over 2 to 5 minutes on Days 1 and 8 of a 21-day cycle

Serious adverse effects: Peripheral neuropathy, neutropenia, thrombocytopenia, QTc prolongation

Drug interactions: None listed

Treating Breast Cancer with Eribulin

Adam Peele, PharmD BCPS
Clinical Hematology/Oncology Pharmacist
Moses Cone Regional Cancer Center, Greensboro, NC

Breast cancer is the most commonly diagnosed malignancy in women throughout the United States with an expected 1 in 8 developing invasive breast cancer in her lifetime.[1] Only lung cancer is responsible for more cancer-related deaths in women with approximately 15% of deaths resulting from breast cancer. As much as 10% of women initially present with metastatic breast cancer with approximately 1 in 5 patients treated for early-stage breast cancer relapsing with distant metastases within 5 years of the original diagnosis.[2] The 5-year survival rate of women with metastatic disease is approximately 15% and most deaths are due to chemotherapy-resistant disease.[3]

In 2010 an estimated 207,090 women were expected to be diagnosed with a new breast cancer, resulting in approximately 39,840 deaths.[1] Newer therapies and targeted agents to control the disease are being researched.

On November 15, 2010, the Food and Drug Administration (FDA) granted eribulin (Halaven™) approval for the treatment of patients with metastatic breast cancer who have previously received at least two chemotherapeutic regimens for the treatment of metastatic disease.[4] Patients must have had further diesase progression on therapy, including an anthracycline and a taxane in either the adjuvant or metastatic setting.

Eribulin is a nontaxane synthetic analog of halichondrin B, a microtubule inhibitor extracted from the *Halichondria okadia* sea sponge.[5] Most microtubule inhibitors, including the taxanes, inhibit the shortening and growth phases of malignant cells. In contrast, eribulin restricts the growth of microtubules without affecting the shortening phase by sequestering tubulin into nonfunctional aggregates.[6] The effects are exerted via a tubulin-based antimitotic mechanism leading to cell-cycle blockage, which ultimately disrupts mitotic spindles and apoptosis. Early preclinical trials showed evidence of activity in paclitaxel-resistant cell lines in vitro.[7]

The recommended dose of eribulin is 1.4 mg/m^2 IV bolus over 2–5 minutes on Days 1 and 8 of a 21-day cycle.[8] Dosage modifications are recommended for patients with mild (Child Pugh A) and moderate (Child Pugh B) hepatic impairment due to pharmacokinetic studies reveailng increased exposure. Although no formal pharmacokinetic studies were conducted in patients with renal impairment, it is recommended that patients with moderate renal insufficiency (creatinine clearance of 30–50 mL/min) be dose reduced prior to initiating therapy because the geometric mean dose-normalized systemic exposure is being increased twofold. Studies were not conducted in patients with creatinine clearance less than 30 mL/min. Dosage recommendations are available for neutropenia, thrombocytopenia, and nonhematologic toxicities. Eribulin does not undergo metabolism and the unchanged form is the major circulating metabolite after administration. The half-life is approximately 40 hours. Eribulin inhibits cythochrome P450 3A4 (CYP3A4) activity in human liver microsomes, but it is unlikely that a substantial drug interaction will occur in patients taking CYP3A4 substrates. Eribulin is eliminated unchanged via the feces. No contraindications are listed and eribulin is a pregnancy category D.[8]

Eribulin can be administered undiluted as an IV push over 2 to 5 minutes or diluted in 100 mL of 0.9% sodium chloride.[8] Administering, mixing, or diluting eribulin in dextrose or intravenous lines with dextrose is not recommended due to lack of compatibility. Undiluted eribulin is stable in the syringe for up to 4 hours at room temperature or 24 hours under refrigeration. Diluted solutions in 100 mL of 0.9% sodium chloride are also stable for up to 4 hours at room temperature and 24 hours under refrigeration. Eribulin is available in a 1 mg/2 mL (0.5 mg/mL) vial.[8]

Neutropenia was reported in approximately 28% of patients who received eribulin in early studies with febrile neutropenia occurring in 5% of patients. The mean time to nadir was 13 days. Granulocyte colony-stimulating factor (G-CSF) was used in 19% of patients who received eribulin.[8] Grade 1 peripheral neuropathy was reported in 17% of patients; however, dose reductions only occurred in 3% of patients receiving eribulin. Peripheral neuropathy was the most common reason for discontinuation.[8]

Electrocardiogram (ECG) monitoring is recommended in patients with congestive heart failure, bradyarrhythmias, electrolyte abnormalities, and patients receiving medications prolonging QTc intervals. ECG monitoring is recommended in these patients because of an open-label study of 26 patients reporting QT prolongation on Day 8 not present on Day 1 independent of eribulin concentration.[8] It is recommended to correct underlying electrolyte abnormalities before initiating therapy and avoid eribulin in patients with congenital long QT syndrome. A study evaluating the QT prolongation in patients with advanced solid tumors is ongoing but not actively recruiting patients.[9] Approximately 18% of eribulin-treated patients experienced grade 2 or higher ALT elevation; however, these elevations were transient.[8]

Early phase 2 trials showed that eribulin provided some clinical activity in patients with metastatic breast cancer, which led to the phase 3 registration trial.[10] Eribulin was FDA approved based on the results of the Eisai Metastatic Breast Cancer Study Assessing

continued on page 14

DRUG UPDATES

Physician's Choice versus Eribulin (EMBRACE) study presented at the American Society of Clinical Oncology 2010 Annual Meeting.[11] Women with locally recurrent or metastatic breast cancer were eligible for this phase 3, open-label, randomized, multicenter trial. Enrolled patients had received anywhere from 2 to 5 chemotherapy regimens, including an anthracycline and a taxane unless a contraindication to either was present.

In the EMBRACE trial, women were randomized patients 2:1 to eribulin 1.4 mg/m^2 IV bolus over 2 to 5 minutes on Days 1 and 8 of a 21-day cycle or treatment of physician's choice (TPC). The TPC was defined as any monotherapy agent including hormonal, cytotoxic, or biologic or supportive care. Overall survival (OS) was the primary endpoint with secondary endpoints including objective response rate (ORR), progression-free survival (PFS), and duration of response.

Seven hundred sixty-two (762) patients were enrolled in EMBRACE; 508 patients were randomized to eribulin and 254 patients were randomized to TPC. The average age of the patient was 55 years. The patients had been exposed to an average of four previous chemotherapy regimens prior to enrollment. Approximately 19% of patients were estrogen receptor negative and HER-2 neu negative.

The median OS was 13.1 months (eribulin) versus 10.7 months for TPC (p = .04; HR = 0.81). ORR was 12% (0.4% complete response [CR], 11.5% partial response [PR]) with eribulin comparted with 5% ORR (0% CR, %5 PR) for PC (p = .005). Median PFS was 3.7 months (eribulin) versus 2.3 months for TPC (p = .09). The average duration of response favored TPC (4.1 months vs. 6.7 months). No difference in PFS was observed (p = .14; HR = 0.87). The most frequently cited adverse events of the trial related to eribulin included neutropenia (44%), peripheral neuropathy (8.4%), and fatigue (7.6%).

Eribulin, a nontaxane microtubule inhibitor, gives practitioners another treatment option for metastatic breast cancer. It shows benefit when being compared to other advanced treatments and offers a unique mechanism of action. Eribulin is recommended by the 2011 National Comprehensive Cancer Guidelines[12] for the treatment of breast cancer. Eribulin is now currently being evaluated in comparison to capecitabine for patients who have received up to three previous chemotherapy regimens for breast cancer.[3] Eribulin is also being evaluated in numerous studies of advanced malignancies not limited to non-small cell lung, bladder, pancreatic, ovarian, and prostate cancers.[13-17]

References

1. American Cancer Society. *Key statistics about breast cancer.* Available at: www.cancer.org/Cancer/BreastCancer/DetailedGuide/breast-cancer-key-statistics. Accessed February 11, 2011.
2. Arriagada R, Spielmann M, Koscielyn S, et al. Patterns of failure in a randomized trial of adjuvant chemotherapy in postmenopausal patients with early breast cancer treated with tamoxifen. *Ann of Oncol.* 2002;13:1378-1386.
3. Cortes J, Vahdat L, Blum J, et al. Phase II study of the halichondrin B analog eribulin mesylate in patients with locally advanced or metastatic breast cancer previously treated with an anthracycline, a taxane, and capecitabine. *J Clin Oncol.* 2010;28:3922-3928.
4. FDA/CEDR resources page. Food and Drug Administration Website. Available at: www.fda.gov/AboutFDA/CentersOffices/CDER/ucm234527.htm. Accessed December 30, 2010.
5. Jackson K, Henderson J, Phillips A. The halichondrins and E7389. *Chem Rev.* 2009;109:3044-3079.
6. Jimeno A. Eribulin: rediscovering tubulin as an anticancer target. *Clin Cancer Res.* 2009;15:3903-3905.
7. Cigler T, Vahdat L. Eribulin mesylate for the treatment of breast cancer. *Expert Opin Pharmacother.* 2010;11(9):1587-1593.
8. Halaven™ [package insert]. Woodcliff Lake, NJ: Eisai Pharmaceuticals, Inc.; November 2010.
9. Wanders J. QT interval prolongation study of eribulin mesylate (E7389) in patients with advanced solid tumors. Clinical Trials.gov [internet]. Bethesda, MD: National Library of Medicine (US). 2000–[cited 2001 Jan 19]. Available from: http://clinicaltrials.gov/ct2/show/NCT01106248 NLM Accessed March 11, 2011.
10. Vahdat L, Pruitt B, Fabian C, et al. Phase II study of eribulin mesylate, a halichondrin B analog, in patients with metastatic breast cancer previously treated with an anthracycline and a taxane. *J Clin Oncol.* 2009;27:2954-2961.
11. Twelves C, Loesch D, Blum JL, et al. A phase III study (EMBRACE) of eribulin mesylate versus treatment of physician's choice in patients with locally recurrent or metastatic breast cancer previously treated with an anthracycline and a taxane. *J Clin Oncol.* 2010;28(Suppl);18s.
12. 2011 NCCN guidelines for breast cancer. Available at: www.nccn.org. Accessed January 6, 2011.
13. Eisai Inc, PharmaBio Development. Eribulin mesylate administered in combination with pemetrexed versus pemetrexed alone as second line therapy in patients with stave IIIB or IV nonsquamous non small cell lung cancer.Clinical Trials.gov [internet]. Bethesda, MD: National Library of Medicine (US). 2000–[cited 2011 Jan 19]. Available at: http://clinicaltrials.gov/ct2/show/NCT01126736.
14. National Cancer Institute, Memorial Sloan-Kettering Cancer Institute. Phase II study of E7389 in patients with recurrent ovarian epithelial, primary peritoneal cavity, or fallopian tube cancer. Clinical Trials.gov [internet]. Bethesda, MD: National Library of Medicine (US). 2000–[cited 2011 Jan 19]. Available at: http://clinicaltrials.gov/ct2/show/NCT00334893.
15. Quinn D, Aparicio A, Tsao-Wei D, et al. Phase II study of eribulin (E7389) in patients with advanced urothelial cancer (UC) [abstract 4539]. *J Clin Oncol.* 2010;28(Suppl);15s.
16. National Cancer Institute, Princess Margaret Hospital. Phase II study of E7389 as second-line therapy in patients with locally advanced, unresectable, or metastatic pancreatic cancer. Clinical Trials.gov [internet]. Bethesda, MD: National Library of Medicine (US). 2000–[cited 2011 Jan 19]. Available at: http://clinicaltrials.gov/ct2/show/NCT00383760.
17. Eastern Cooperative Oncology Group. E7389 in treating patients with metastatic prostate cancer that did not respond to hormone therapy. Clinical Trials.gov [internet]. Bethesda, MD: National Library of Medicine (US). 2000–[cited 2011 Jan 19]. Available at: http://clinicaltrials.gov/ct2/show/NCT00337077.

DRUG UPDATES

Ipilimumab (Yervoy™)

Class: Human monoclonal antibody directed against cytotoxic T lymphocyte antigen 4 (CTLA-4)

Indication: Unresectable or metastatic melanoma

Dose: 3 mg/kg administered intravenously over 90 minutes every 3 weeks for a total of four doses

Common adverse effects: Skin rash, hepatitis, colitis, endocrinopathies, injection site reactions, vitiligo, uveitis

Serious adverse effects: Black-boxed warning for severe immune-mediated reactions including enterocolitis, hepatitis, dermatitis (toxic epidermal necrolysis), neuropathy, and endocrinopathy; grade 3 or 4 diarrhea, colitis, abdominal pain, fever, nausea and vomiting, leukocytosis

Drug interactions: Has not been evaluated

Ipilimumab for Metastatic Melanoma

Sarah K. Shockley, PharmD
Oncology Pharmacy Resident
Hospital of the University of Pennsylvania

During the past 30 years the incidence of melanoma has been steadily increasing. In 2010 the American Cancer Society estimated that there were approximately 68,130 new cases of melanoma diagnosed and approximately 8,700 deaths in the United States. For patients who develop distant metastases the median survival is less than 1 year.[1,2]

The National Comprehensive Cancer Network (NCCN) currently lists dacarbazine, temozolomide, high-dose interleukin-2, paclitaxel (alone or in combination with cisplatin or carboplatin), or enrollment in a clinical trial as first-line options for treating metastatic melanoma. Objective response rates reported for these treatments range from 7%–20% and have a median duration of response of 6 to 8 months.[4,10-12] At this time, current treatment options are limited and often unsuccessful.

Ipilimumab (Yervoy) is a new cytotoxic T lymphocyte antigen 4 (CTLA-4) inhibitor recently approved by the FDA on March 25, 2011, for the treatment of unresectable metastatic melanoma. The mechanism of CTLA-4 is to allow the maintenance of immune homeostasis by exhibiting an inhibitory role in the control of T-cell activation. Inhibition of CTLA-4 promotes T-cell activation with subsequent enhancement of the immune response against tumors.[4]

Ipilimumab's safety and efficacy were evaluated in a randomized, double-blind, phase 3 study that enrolled 676 patients between September 2004 and August 2008. Patients had unresectable stage 3 or 4 melanoma with disease that had progressed while receiving therapy. Previous therapeutic regimens included one or more of the following: dacarbazine, temozolamide, fotemustine, carboplatin, or interleukin-2. Patients were randomly assigned to receive an induction course of ipilimumab plus gp100 peptide vaccine (n = 403), ipilimumab alone (n = 137), or gp100 alone (136). Ipilimumab was administered at a dose of 3 mg/kg intravenously with or without gp100 every 3 weeks for up to four treatments. The primary end point was overall survival (OS).[5] Patients receiving ipilimumab plus gp100 had a median OS of 10 months (95% CI, 8.5–11.5 months) versus 6.4 months (95% CI, 5.5–8.7 months) in those receiving gp100 alone ($p < .001$). Median OS for ipilimumab alone was 10.1 months (95% CI, 8–13.8; $p = .003$). At 12 months the OS rates in the ipilimumab plus gp100, gp100 alone, and ipilimumab alone group was 43.6%, 25.3%, and 45.6%, respectively. At 24 months, OS was 21.6%, 13.7%, and 23.5%, respectively. There was a 19% reduction ($p < .05$) in risk of progression in the ipilimumab plus gp100 group versus a 36% reduction ($p < .001$) in the ipilimumab group alone.[5]

A phase 2 multicenter, randomized, double-blind, parallel group study evaluated the efficacy of ipilimumab at three different dose levels. Patients with stage 3 or 4 melanoma who had received at least one previous treatment and progressed after complete or partial response were included. The patients were randomly assigned to receive ipilimumab 10 mg/kg, 3 mg/kg, or 0.3 mg/kg at Weeks 1, 4, 7, and 10. The primary endpoint was best overall response, which was 0%, 4.2%, and 11.1% ($p = .0015$) in ipilimumab 0.3 mg/kg, 3 mg/kg, and 10 mg/kg, respectively.[8]

Most common adverse events reported by Hodi and colleagues[5] include immune-related events that occurred in approximately 60% of patients treated with ipilimumab and 32% of patients receiving gp100.[5] Diarrhea (any grade) occurred in 31%–37% of patients receiving ipilimumab. Grade 3 or 4 immune-related adverse events most often affecting the gastrointestinal tract and skin occurred in 10%–15% of patients treated with ipilimumab and in 3% treated with gp100 alone. The median time to resolution of grade 2, 3, or 4 immune-related events was 6.3 weeks in the ipilimumab plus gp100 group versus 4.9 weeks in the ipilimumab alone group. Other reported adverse events included injection site reactions, vitiligo, and inflammation of the pituitary gland requiring hormone replacement. Hodi and colleagues reported 14 deaths related to the study drugs, of which seven deaths were associated with immune-related adverse events.[5,7]

Few treatment options exist for patients with metastatic melanoma. Ipilimumab is a new CTLA-4 inhibitor that has shown efficacy and improved OS in phase 2 and 3 trials in patients with metastatic melanoma who have failed prior first-line therapy. Hodi and colleagues established that the efficacy of ipilimumab was not improved by the addition of gp100. Hersh and colleagues discovered greater efficacy of utilizing ipilimumab 10 mg/kg in comparison to 0.3mg/kg and 3mg/kg. Immune-related side effects including diarrhea are serious and may limit use.[5] Currently, a phase 3 trial comparing dacarbazine plus ipilimumab versus dacarbazine plus placebo in untreated, unresectable stage 3 or 4 melanoma is underway and may help to better assess ipilimumab's place in therapy.[8]

continued on page 16

DRUG UPDATES

References

1. American Cancer Society. Cancer facts and figures 2010. Available at: www.cancer.org/Cancer/SkinCancer-Melanoma/DetailedGuide/melanoma-skin-cancer-key-statistics. Accessed October 9, 2010.
2. World Health Organization. Skin cancers. Available at: www.who.int/uv/faq/skincancer/en/index1.html. Accessed October 9, 2010.
3. Melanoma. 2010. NCCN clinical guidelines. Available at: www.nccn.org/index.asp. Accessed on October 10, 2010.
4. Movva S, Verschraegen C. The monoclonal antibody to cytotoxic T lymphocyte antigen 4, ipilimumab (MDX-010), a novel treatment strategy in cancer management. *Expert Opin Biol Ther.* 2009;9(2):231-241.
5. Hodi S, O'Day SJ, McDermott DF, et al. Improved survival with ipilimumab in patients with metastatic melanoma. *N Engl J Med.* 2010;363:711-723.
6. O'Day S, Maio M, Chiarion-Sileni V, et al. Efficacy and safety of ipilimumab monotherapy in patients with pretreated advanced melanoma: a multicenter single-arm phase II study. *Ann Oncol.* 2010;21(8):1712-1717.
7. Hersh E, O'Day SJ, Powderly J, et al. A phase II multicenter study of ipilimumab with or without dacarbazine in chemotherapy-naïve patients with advanced melanoma. *Invest New Drugs*. 2010 Jan 16. [Epub ahead of print].
8. A multi-center, randomized, double blind, two arm, phase III study in patients with untreated stage III (unresectable) or IV melanoma receiving dacarbazine plus 10 mg/kg ipilimumab (MDX-010) vs. dacarbazine with placebo. Available at: www.clinicaltrials.gov. Accessed October 9, 2010.
9. Wolchok J, Neyns B, Linette G, et al. Ipilimumab monotherapy in patients with pretreated advanced melanoma: a randomised, double-blind, multicentre, phase 2, dose-ranging study. *Lancet Oncol.* 2010;11(2):155-164.
10. Middleton M, Grob JJ, Aaronson N, et al. Randomized phase III study of temozolamide versus dacarbazine in the treatment of patients with advanced metastatic malignant melanoma. *J Clin Oncol.* 2000;18(1):158-166.
11. Atkins M, Lotze MT, Dutcher JP, et al. High-dose recombinant interleukin 2 therapy for patients with metastatic melanoma: analysis of 270 patients treated between 1985 and 1993. *J Clin Oncol.* 1999;17(7):2105-2116.
12. Rao RD, Holtan SG, Ingle JN, et al. Combination of paclitaxel and carboplatin as second-line therapy for patients with metastatic melanoma. *Cancer*. 2006;106(2):375-382.
13. Ipilimumab. FDA: U.S. Food and Drug Administration. 2011. Available at: www.fda.gov/AboutFDA/CentersOffices/CDER/ucm248478.htm.
14. Ipilimumab [product labeling]. New Brunswick, NJ: Bristol-Myers Squibb Company; 2011.

Introducing Your HOPA Team

HOPA's transition to Association Management Center (AMC) has been an exciting and important time in our organization's growth. We thought it would be helpful to introduce some of the people who have been instrumental in this transition and will be responsible for HOPA's day-to-day business and supporting our members as we move forward. During the next few issues of the newsletter, you will meet the enthusiastic and dedicated staff members who make up your HOPA team.

Karen Nason, Executive Director

Q. What is your role with HOPA? What are some of the specific things you do on a daily basis for the association?

A. I'm the executive director for HOPA. I help my staff team oversee HOPA programs and activities, I work with the board of directors and committees, and I help the leadership envision the future direction of HOPA and move the organization toward that future through the strategic plan.

Q. How long have you been involved in association work? With which other associations have you worked?

A. I've been in association management for about 22 years. I've worked with the Association of Rehabilitation Nurses, Rehabilitation Nursing Certification Board, Rehabilitation Nursing Foundation, American Academy of Hospice and Palliative Medicine, American Society for Bioethics and Humanities, American Association of Legal Nurse Consultants, Midwest Nursing Research Society, American Academy of Aesthetic Dentistry, Society of Automotive Analysts, National Association for Healthcare Quality, National Home Furnishings Association, and Interior Design Society.

Q. How did you get your start working with associations?

A. I started working with the National Home Furnishings Associations and then moved into their affiliate organization, the Interior Design Society. I worked primarily in the membership department and also worked on the newsletter, worked with their chapters, and was the assistant to the executive director.

Q. Where did you grow up?

A. I grew up in Niles, MI, which I tell people is just over the state line from Notre Dame in South Bend, IN. I went to college at Michigan State University and majored in advertising. I worked in marketing for about 8 years before I got into association management.

Q. What is your favorite thing to do in your spare time?

A. What spare time? My yellow labrador, Tanner, wants me to give him undivided attention when I'm not at work. If I do have extra time, my hobbies are sewing and design, glass fusing, and gardening during the limited Midwest growing season.

Q. What is your favorite aspect of working with associations and members?

A. The variety of projects and programs I get to work on is amazing. No 2 days are ever the same, and I come into contact with many different people. I like to learn about what the members and volunteer leaders find exciting, too.

Q. What aspect of working with HOPA is most exciting for you? What are you looking forward to accomplishing this year with HOPA?

A. It has been very exciting to work with this young organization that has already been so successful. I'm looking forward to helping HOPA realize some of its newer goals of developing practice standards and defining the oncology pharmacists' scope of practice, as well as enhancing the HOPA advocacy program and increasing the breadth, quality, and quantity of HOPA's educational initiatives. We've got a lot to do and a very enthusiastic and energetic membership to help us accomplish these goals.

Mary Beth Benner, Director of Operations

Q. What is your role with HOPA? What are some of the specific things you do on a daily basis for the association?

A. As the director of operations, I manage the day-to-day operations of the association, which includes supporting the board of directors' functions and overall committee structure and management, developing the operating budget, and helping with meeting organization and project management.

Q. How long have you been involved in association work? With which other associations have you worked?

A. I started working with associations back in 1992 when I had an internship with the American Heart Association. Since then, I have worked with the United Health Organization (a not-for-profit in Detroit that organized health screenings), the American Massage Therapy Association, and the American Osteopathic Foundation. During the 10 years I have worked with AMC, I have always worked with the Association of Rehabilitation Nurses; I have also served as director of education for the American Academy of Hospice and Palliative Medicine.

Q. How did you get your start working with associations?

A. Shortly before I started my internship with the American Heart Association, my father died of a stroke. That experience helped me learn about associations and how they can help put structure and support around issues and professions for which I had a personal passion. Working with healthcare associations allows me to work behind the scenes to support health and wellness.

Q. Where did you grow up?

A. I grew up in a suburb of Detroit, MI, and attended Central Michigan University. I graduated with a major in public health education.

Q. What is your favorite thing to do in your spare time?

A. I like to stay in shape by running, biking, and going to the gym; read; explore restaurants; and watch plenty of reality TV.

Q. What is your favorite aspect of working with associations and members?

A. Again, working with associations allows me to support the health and wellness of individuals in a very behind-the-scenes way. The most fulfilling part of my job is creating relationships with association members who are passionate about what they do and their profession and helping them to make a difference. I have met many amazing and inspiring people in my work with associations.

Q. What aspect of working with HOPA is most exciting for you? What are you looking forward to accomplishing this year with HOPA?

A. HOPA is a young and energetic organization with great potential. It has been exciting to get to know HOPA's members and hear about their enthusiasm for their profession and concerns for the populations they serve. Working with the board to develop the strategic plan was a solid first step toward helping HOPA realize its goals for the organization. The next year will bring new challenges and accomplishments as we start to work toward those goals.