Toxicity is a common concern in most cancer regimens. Patients often undergo extensive treatments that affect their quality of life. However, the packaging of the medication might enhance the drug delivery while reducing toxicity. By encapsulating the medication, the frequency of drug administration can be minimized, as seen in certain extended release tablets. Similarly, intravenous chemotherapy drugs can be encased to improve stability, enhance bio distribution and reduce potential toxicity. An example of this approach is Doxil® (Centocor OrthoBiotech, Horsham, PA), which is currently the only clinically approved cytotoxic chemotherapy utilizing nanoparticle-encapsulation to enhance bio distribution.\(^1\)

Within the University of Georgia’s College of Pharmacy, Dr. Cummings, along with Dr. Shenoy, are working to utilize sterically-stabilized liposomes (SSL) in order to study the ability of a p21 activated kinase type 1 (PAK-1) inhibitor called IPA3 to inhibit prostate cancer growth.\(^1\) PAK-1 is a mediator of cell growth and proliferation that is abundantly expressed in prostate tumor biopsies and metastasized colonies in lung tissue.\(^2\) IPA3 is a highly specific but metabolically unstable inhibitor of PAK-1.\(^3\) PAK-1 expression is ubiquitous within the body, presenting a challenge for using IPA3 therapeutically. The unstable nature of IPA3 combined with the extensive expression of PAK-1 leads to serious toxic side effects when using free form IPA3.\(^1\) Therefore, encapsulation of the metabolically unstable IPA3 in liposomes was used to evaluate a probable prostate cancer treatment on tumor growth within athymic nude mice.

Liposome-mediated drug delivery is known to improve drug stability and decrease the frequency of drug administration. Moreover, SSL’s can sometimes facilitate drug delivery without decreasing drug efficacy by accumulating passively in solid tumors.\(^4\) Within healthy circulation, the vasculature membrane permeability is lower compared to tumor vasculature. The maintenance of tight junctions within healthy tissues decreases the penetration of the liposomes in the healthy tissue. However, the vasculature in tumors can become ‘leaky’ and lacks functional lymphatics, allowing for the permeation and accumulation of liposomes in tumor tissues. This buildup of SSL-IPA3 in solid tumor growth allows for a level of specificity in the therapy.\(^5\)
Pharmacogenomics is the study of the impact of genes in response to medication therapies. One of the most powerful applications of this information is the ability to create specific drug regimens for patients with various diseases, including cancer. Understanding the patient’s genome can allow healthcare providers the opportunity to create safer and more effective therapies by closely examining how genetic variants influence drug efficacy and toxicity. Personalized oncology may not be too far in the future if the ability to predict how a cancer patient will respond to a particular treatment regimen is solidified (1). Publications of materials related to pharmacogenomic cancer treatments have seen a 250% increase in the past 10 years, highlighting the growing interest in this promising field of research (2).

The US Food and Drug Administration have published specific materials to help patients understand this information. Further, the FDA recommended that drug manufacturers begin printing pharmacogenomics information on package-insert labeling for more than 120 drugs, which are associated with mutations in 50 or more genes (2). By embracing pharmacogenomics research involving cancer therapy, the FDA aims to enhance appropriate selection of regimens and reduce toxicity. Additionally, pharmacogenomics driven clinical trial designs may improve the success of the drug development process by assisting with appropriate patient selection for trials. The FDA also hopes to use this data to make new headway in cancer drug development.

MUCOSITIS

Mucositis, painful inflammation and damage in various regions of the gastrointestinal tract, such as the oral cavity and esophagus, is a common complication associated with certain radiation therapies and chemotherapies. Oral mucositis typically presents as erythematous lesions that may progress to extremely painful ulcerations that penetrate the submucosa (1). Patients can have significantly decreased quality of life due to dysphagia, dysarthria, odynophagia, and increased occurrence of opportunistic infections (2). Most patients receiving head and neck or total body irradiation therapy also develop mucositis in the pharyngeal, laryngeal, and esophageal regions, which presents with symptoms such as pain, nausea, vomiting, and diarrhea. This can further complicate a patient’s health status by impairing nutritional intake, facilitating dehydration, and necessitating opioid analgesic use, which carries its own risks (3). Mucositis has considerable economic impacts as a result of hospitalization and management of symptoms, secondary infections, and requirement for nutritional support. Importantly, the impact of mucositis may necessitate breaks in radiation therapy, lead to chemotherapy dose reductions, and/or require changes in antineoplastic drug choices; therefore, mucositis can be a serious drug-limiting toxicity that threatens the optimization of otherwise efficacious therapies (1).

Cytotoxic mucosal effects are subtle during the beginning of chemotherapeutic treatment but gradually increase after the first week (2). The pathogenesis of mucositis is complex and is commonly divided into five steps: initiation of tissue injury by radiation and/or chemotherapy, upregulation via messenger signals, cytokine signaling and amplification of mucosal injury, inflammatory ulceration, and healing. Reactive oxygen species, tumor necrosis factor-alpha, and colonization of oral microflora are believed to be among the key contributors in this process (4). Notably, lesions often undergo spontaneous resolution, typically within two weeks of ending treatment (2). A better understanding of the pathobiology of mucositis and the identification of targets for treatment is needed to further develop therapies against this drug-induced problem.

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An additional innovation to the liposomes is that they are engineered to contain lipids selective for an enzyme called secretory phospholipase A₂ (sPLA₂) which is overexpressed at the cell surface of prostate cancer cells. These modified liposomes (called SRPL-IPA3) may allow for enhanced degradation of these nanoparticles at the tumor site, facilitating drug release. In contrast, the SPRL-IPA3 that penetrates healthy tissue, where sPLA₂ is not as highly expressed, will be protected, and the liposomes will not be broken down as easily. This has the benefit of allowing even more of the medication to be administered at the site of the solid tumor. This second level of specificity results in an increase in efficacy alongside a potential reduction of adverse reactions.

Developments in the use of nanoparticles such as sterically-stabilized liposomes have major implications on the advancement of chemotherapy. With the rapid evolution of cancer therapies and constant development of new treatment innovations, it is exciting to see the University of Georgia on the cutting-edge of pharmaceutical advances. To read more about the work that Dr. Cummings and Dr. Shenoy are currently doing, “Liposomal-mediated delivery of the p21 activated kinase-1 (PAK-1) inhibitor IPA-3 limits prostate tumor growth in vivo,” is available at: http://www.nanomedjournal.com/article/S1549-9634(16)00073-3/fulltext.

Contributed by Brielle Scutt, Pharm.D. Candidate

SOAP members had the opportunity to attend the annual Hematology/Oncology Pharmacy Association (HOPA) conference this year. HOPA is a professional pharmacy organization that ultimately seeks to optimize the care of cancer patients through supporting, educating, and empowering hematology/oncology practitioners. The organization also partners with other organizations to increase awareness of the importance of oncology pharmacy and advocates on behalf of patients, the pharmacy profession, and the oncology specialty. The annual HOPA conference is an informational event that connects hematology/oncology pharmacy practitioners in exploring emerging therapies and medicinal developments, as well as discussing and sharing clinical practices and applications. It also provides a great opportunity for practitioners to gain Board Certified Oncology Pharmacist (BCOP) continuing education (CE) credit.

The 2016 HOPA conference was held March 16th-19th at the Marriot Marquis in Atlanta, GA. Events and activities included a large variety of general and breakout sessions, pre-conference events, research/poster sessions, and exhibition hall. Health policy and advocacy sessions covered topics such as interacting with elected officials, the usage of herbs, and HOPA’s health policy and legislative agenda. Topics relating to practice management included techniques to improve patient adherence, incorporating medication therapy management (MTM) into oncology practice, and chemotherapy safety. Many other topics were discussed,
LUNG CANCER

Lung cancer is one of the most common types of cancer in the world (1). In 2015 over 221,000 people were newly diagnosed and over 158,000 people died from lung cancer in the US alone. (2). Lung cancer can be categorized as non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). NSCLCs include squamous cell carcinoma, large cell carcinoma, and adenocarcinoma. While NSCLC is linked to cigarette smoke adenocarcinomas have been found to also develop in non-smokers. NSCLCs are generally less responsive to chemotherapy and radiation than SCLCs, highlighting the importance of novel therapies in this area (3).

Atezolizumab (Tecentriq) is a treatment option approved by the FDA in October 2016 for patients who have metastatic NSCLC with disease advancement despite platinum-containing chemotherapy (4). The drug was originally granted accelerated approval in May 2016 to treat some bladder cancers that were unresponsive to platinum chemotherapy (5). October approval was given as a result of two clinical trials, both of which showed improvement in overall survival when compared to docetaxel, a drug commonly used to treat several cancers. One study demonstrated overall survival (OS) of 13.8 months with atezolizumab and OS of 9.6 months with docetaxel. The second study indicated OS of 12.6 months with atezolizumab and 9.7 months of OS with docetaxel (4).

Atezolizumab is a humanized monoclonal antibody called an “immune checkpoint inhibitor”. The immune system uses checkpoints on cells to differentiate “self” cells from foreign cells. Some cancer cells can use these checkpoints to trick the immune sys-

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PHARMACOGENOMICS IN ONCOLOGY TREATMENT (CONTINUED FROM PAGE 2)

which can often be a slow process and ends up in 90% of drugs that get to the clinical trial phase becoming failures (2).

Medical experts at the UT MD Anderson Cancer Center are utilizing pharmacogenomics for their current patients. The experts at MD Anderson claim that due to the quickly evolving genomic profiling technology, the problem is not getting the patient’s genomic history, but rather learning how to use it to help the patient. They urge health care providers to determine if genomic alterations found in their patients are considered “actionable” (3). They suggest a model for health care providers to follow in order to determine this. Providers must predict a therapy response, know how the alteration affects the function of a cancer-related gene, know if the alteration contains specific eligibility criterion, demonstrate if the alterations can influence prognosis of the patient, and demonstrate if the alteration has germ line evidence of changing drug metabolism (3). They hope that if medical practitioners can learn to manage and decipher the data that comes from pharmacogenomics, it will give them a clear view into their patients’ disease states and allow them to fine the most effective way of treating them.

Oncology pharmacy is a growing and emerging specialty for those interested in pharmacy practice. With the adoption of pharmacogenomic testing for oncology patients and the development of novel therapeutics with proper implementation of genomic data, pharmacists and healthcare providers can make a substantial effect on the lives of many patients.


Contributed by Aasna Patel, Pharm.D. Candidate
Currently, there are several modalities available to combat this condition in clinical settings. In 2014, the Multinational Association of Supportive Care in Cancer (MASCC) and International Society of Oral Oncology (ISOO) collaborated in publishing the MASCC/ISOO Clinical Practice Guidelines for the Management of Mucositis Secondary to Cancer Therapy, which is based on systematic reviews of evidence for different interventions. Guidelines for gastrointestinal mucositis favor use of amifostine, octreotide, sucralfate enemas, sulfasalazine, hyperbaric oxygen, and *Lactobacillus*-containing probiotic agents in specific treatment settings.

Palifermin, keratinocyte growth factor-1, is the only FDA approved agent (cite specific population indicated for please – not for all mucositis inducing regimens!!) for oral mucositis. However, oral care protocols, other growth factors and cytokines, anti-inflammatory agents (e.g. benzodamine hydrochloride mouthwash), analgesics (e.g. patient-controlled morphine, morphine and doxepin mouth rinse, and transdermal fentanyl), natural agents (e.g. zinc), low-level laser therapy, and oral cryotherapy are all favored recommendations or suggestions provided by the MASCC/ISOO guidelines in specified therapeutic situations (3). Additionally, these guidelines provide recommendations against the use of certain therapies that have not produced positive results in clinical studies. Notably, guideline recommendations apply only to very specific treatment situations which have published evidence; therefore, these recommendations cannot be extrapolated to all populations. Despite this limitation, the MASCC/ISOO guidelines provide concise, specific guidelines for healthcare professionals to utilize in making decisions regarding drug-induced mucositis.

Alleviating discomfort caused by mucositis is critical in improving nutritional status, hydration, and general quality of life in cancer patients. Left untreated, lesions may result in temporary or permanent treatment discontinuation and, ultimately, compromised cancer control (2). Pharmacists are well positioned to make guideline-based recommendations to treat drug-induced mucositis in cancer patients.


Contributed by Baotram Van, Pharm.D. Candidate

**SAFE PRACTICES FOR HEALTHCARE PROVIDERS IN DEALING WITH ORAL CHEMOTHERAPY AGENTS**

Oral chemotherapy has many advantages over intravenous (IV) chemotherapy including increased convenience of use, reduced travel costs, and reduced use of healthcare resources, but it requires appropriate handling to reduce administration errors, contamination of surfaces, and exposure to other individuals. Oral chemotherapy has the same exposure risk as intravenous infusion chemotherapy to health care practitioners, patients, and their caregivers; however, in practice, oral chemotherapy is often perceived to be safer than IV chemotherapy. Because exposure to oral chemotherapeutic agents can occur in several parts of the process including manufacturing, storage, handling, administration, and disposal, following recommendations regarding safe practices is imperative.¹

Healthcare providers, especially specialty pharmacists, may handle oral chemotherapeutic agents frequently, so appropriate training and instruction in guidelines for safe handling are important for ensuring their safety. Available training includes competencies, training programs, and licensure to assess knowledge and ability to follow safe practices. Recommendations for health care providers from an international panel of pharmacists include proper storage and handling of these agents in a designated area per manufacturer’s

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including Hepatitis C management, information about conducting clinical trials, oral chemotherapy and anticoagulants, pharmacogenomics, and medical marijuana. Research conducted by practicing pharmacists as well as trainees was presented through research/poster sessions and general or breakout sessions, covering a wide variety of oncology states and therapies. The keynote speaker for the conference was Siddhartha Mukherjee, MD PhD, a leading cancer physician and researcher and author of The Laws of Medicine and Pulitzer Prize winner The Emperor of All Maladies: A Biography of Cancer.

Students from the University of Georgia College of Pharmacy were able to attend the HOPA conference for the first time this year. This was the first professional conference for many of the students and provided great exposure to the workings of a national organization and the specialty field of oncology pharmacy. Conferences provide pharmacy students with networking opportunities, experience in membership to professional organizations, and exploration of various areas of pharmacy. Despite not yet being practitioners, students are able to perceive how pharmacy is advancing and can readily make connections between what they learn in the classroom setting to what is happening in practice. SOAP hopes to continue sending members to the annual HOPA conference in the future to improve members’ knowledge and stay active in oncology advocacy efforts.

Atezolizumab is dosed as a 1200 mg IV infusion over 60 minutes every 3 weeks. It can be used until the disease worsens or until unbearable adverse reactions occur. Because PD-L1 proteins are present on a number of cells in the body as well as some cancer cells, the drug also binds to the normal cells and can cause the immune system to attack healthy organs, leading to undesirable side effects. Common adverse drug reactions of atezolizumab include fatigue, rash, anorexia, dyspnea, myopathy, and constipation. More serious, but less common drug reactions can cause problems with the liver, kidneys, and lungs (4,6).

Harnessing the immune system via checkpoint inhibitors is an exciting advancement within the oncology field. Medications such as atezolizumab offer survival advantage compared to cytotoxic chemotherapy in patients with metastatic NSCLC but require monitoring for adverse events. Further studies will continue to describe the optimal place in therapy for patients with NSCLC and other diseases.


Contributed by Baotram Van, Pharm.D. Candidate

Contributed by Samantha Basco, Pharm.D. Candidate
SOAP UPDATE: RECENT AND FUTURE EVENTS

The Student Oncological Advocates in Pharmacy (SOAP) kicked off the 2016-2017 school year with our annual welcome back BBQ Pool Party at the lovely home of our advisor, Dr. Tackett. This was a great chance for new members to meet other new and older members. It also served as a preview for all the things SOAP had planned for the school year. This past fall semester, we had the chance to listen to two fantastic speakers, Dr. Nancy Nix and Dr. David Deremer, both of whom provided real insight into life as a new graduate, residencies, and the life of an Oncology Pharmacist. SOAP also held a percentage night at Pauley’s Crepe Bar, where we raised over $300. All of the proceeds went directly to Winship Cancer Institute at Emory, our philanthropic organization. In October, we participated in the College of Pharmacy’s annual health fair, where we educated patients on ways to decrease their risk of cancer. We also partnered with another UGA COP organization, CPNP, to host the first ever bra pong activity to help spread breast cancer awareness. Our November meeting was very special. This year, all the members designed handmade holiday cards for cancer patients at Winship. We were able to deliver over 50 cards for the carolers to distribute. In December, we hosted a Christmas Party where we collected toy donations to give to the children at CHOA. In January, we made Valentine’s Day gift bags for the patients at Winship. We were actually able to hand deliver our gift bags to the patients during our visit to the facility. This gave our members a chance to interact with patients as well as

SAFE PRACTICES FOR IN DEALING WITH ORAL CHEMOTHERAPY AGENTS (CONTINUED FROM PAGE 5)

instructions. These agents should be stored separately from the non-cytotoxic agents to avoid contamination. For handling of these agents, personal protective clothing and equipment should be used to reduce exposure and health risks. An important practice should be to not dispense oral chemotherapy agents via automatic dispensing systems. Usage of disposable gloves and hand washing before and after handling the oral chemotherapeutic agents should also be employed. Use of a biological safety cabinet to compound, crush, cut or split oral chemotherapy agent has been employed in several hospitals which reduces exposure.

A survey of nurses and pharmacists was conducted regarding oral antineoplastic handling at healthcare institutions in the United States. One hundred and twenty-three practitioners responded to the survey, most of whom included pharmacists practicing in a community-based hospital. The results from this survey showed that 76% of responders reported having official policy regarding handling of oral antineoplastics. Personal protective equipment was required by many of the respondents. 70% of institutions required gloves to be worn, and the use of Biological Safety Cabinets were required for compounding of oral antineoplastics in 88% of institutions. Liquid oral antineoplastics were dispensed in single-dose oral syringes in 80% of the institutions and disposal of supplies in designated chemotherapy buckets was required by 78% of institutions. The data showed that safety practices are being employed to limit contamination and exposure of health care workers, but these practices are limited and not all institutions are employing these safe practices.

Increased awareness and training for the handling of oral chemotherapy agents, especially amongst healthcare providers who are dealing with these agents on a daily basis, is necessary. Further, by being aware of the risks, healthcare providers will be better able to ensure that patients and caregivers are similarly equipped with the knowledge to handle oral chemotherapy agents safely at home, preventing unnecessary exposure to potentially dangerous substances.

1. http://jop.ascopubs.org/content/7/1/7.full

Contributed by Meha Shah, Pharm.D. Candidate

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Pain

Due to the pathology of cancer, virtually most patients with cancer will experience pain. When addressing the patient's pain, the golden rule is that pain is subjective, which means that pain is what the patient says it is. Additionally, properly interviewing patients to assess their pain will help determine appropriate treatment options. If opioids are to be used, it is essential to start low and titrate appropriately to ensure the pain is properly managed with minimal adverse effects. There is no maximum dose for opioids so assessing a patient's history of opioid use is essential.

Nausea and Vomiting

Patients undergoing chemotherapy should receive antiemetics to prevent chemotherapy induced nausea and vomiting. The emetogenicity profile of a chemotherapy regimen, route of administration, dose, and other patient specific characteristics can influence course of treatment. As pharmacists, it is important to ensure the appropriate regimen is used based on these parameters.

Infection Risk

The increased risk of infections can be attributed to either the pathology of the cancer or the therapeutic agents that are used to suppress cancer cells. In general, non-specific chemotherapy agents have a higher risk of infection because they target rapidly dividing cells in the body, which include immune cells. Clinicians should be diligently watching for any drops in blood cell counts to determine if antimicrobial therapy should be considered. As a rule of thumb, general infection control practices such as proper hand washing should also be utilized to minimize infection exposure.

Hepatic and Renal Function

Patients can experience renal or hepatic impairment due to cancer metastasis or drug induced toxicity from antineoplastic agents. Clinicians should monitor labs for any signs of renal or hepatotoxicity and dose adjust or discontinue medications appropriately.

Palliative Care

Palliative care addresses the physical, psychological, social and spiritual concerns that can occur in end-stage cancer patients. In addition to providing medications for symptom control related to the cancer, addressing the patient’s mental state and supporting their loved ones can positively impact patient care.

Contributed by Ife Anachebe, Pharm.D. Candidate 2017
SOAP UPDATE: RECENT AND FUTURE EVENTS (CONTINUED FROM PAGE 7)

see where all our fundraising efforts go toward. In March, we held our biggest fundraising event of the year, the 5th Annual Tina Borg 5K in Athens. 100% of the proceeds will be donated to Winship Cancer Institute. With all the hard work and dedication of our members, we were able to raise over $8000. I am incredibly excited for the 2017 Fall semester and all of the great things in store!

*Contributed by Alia Reid, Pharm.D. Candidate*

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*SPECIAL THANKS to all the writers and advisors who helped create this issue and will make future issues of the Oncology Bulletin possible.*