The Oncology Bulletin

SOAP
STUDENT ONCOLOGICAL ADVOCATES IN PHARMACY
COLLEGE OF PHARMACY

Student Oncological Advocates in Pharmacy
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A Focus on Pediatrics

For this issue of the Oncology Bulletin, we chose to focus on pediatric cancers, which account for approximately 1% of all cancers. These patients can suffer unique long-term side effects from their treatments, and pharmacists are integral in monitoring for these complications. Pharmacists in this field often pursue research to improve existing regimens and palliative treatments. In this issue we will examine some of the unique challenges a pharmacist faces in the management of pediatric cancers, as well as exploring survivorship issues, secondary malignancies, and palliative treatment.

INSIDE THIS ISSUE

Career Spotlight: Pediatric Oncology Pharmacy

Pediatric oncology focuses on diagnosis and treatment for cancer patients under 18 years of age. Healthcare providers in this setting face may challenges, including the complexity of these oncologic disease states and their treatments as well as the necessity to understand all the other pediatric considerations which must be incorporated into each patient's care plan. Pediatric patients "don't just have cancer; they get ear infections just like every other 2 year old. And they have GERD and all the other pediatric disease states as well," explains Dr. Cady Ploessl, a specialist in pediatric oncology, who we interviewed to shed some light on this complex field.

Cady Ploessl, Pharm.D.

Dr. Ploessl is a pediatric oncology pharmacist and residency program preceptor at the Virginia Commonwealth University Health System (VCU). After graduating from the University of Iowa College of Pharmacy, she completed a PGY1 residency at Indiana University Health, where she was exposed to pediatric and adult patient populations in both the inpatient and outpatient settings. She then decided to specialize in pediatrics, completing a Pediatric PGY2 residency at Georgia Regents Medical Center.

Her typical day begins with multidisciplinary rounds on both bone marrow transplant and pediatric hematology/oncology patients. She reviews each patient's medication profile and laboratory results before meeting with her "very large", as she described it, pediatric team. "So in pediatrics, it's a pretty large team because not only are we dealing with young patients, but we also have the caregiver's needs to assess as well," she explained. Consequently, her team not only includes traditional members such as physicians and nurses, but may also include chaplains, social workers, school teachers, and specialists in pediatric nutrition and child life. After rounding, she focuses on patients admitted for chemotherapy. In the afternoon, Dr. Ploessl follows up on any items needing clarification from morning rounds and attends various

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Anticipatory Chemotherapy-Induced Nausea and Vomiting in Pediatric Patients

With the impact that chemotherapy-induced nausea and vomiting (CINV) has on the quality of life in cancer patients, attaining better control of this side effect is imperative amongst health care providers. Utilization of evidence-based guidelines for CINV prevention and treatment in adult cancer patients has shown to be effective in improving quality of life and distress reduction. However, adequate guidelines are still lacking in the pediatric population due to insufficient evidence. The lack of quality data is partly due to small sample sizes in reported studies of CINV in pediatric patients, exclusion of pediatric patients from CINV studies for novel drug products, as well as the limited evidence validating pediatric nausea assessment tools (1).

Despite the lack of quality evidence, there is low to moderate quality evidence recommendations available for the pediatric population for the control of CINV. There is a guideline recommendation that the control of acute and delayed CINV should be optimized to minimize the risk of developing anticipatory CINV in pediatric patients. Phases of CINV include acute (within 24hr of chemotherapy), delayed (24hr after chemotherapy and usually within 7 days), and anticipatory which occurs within 24 hours prior to chemotherapy as a conditioned response associated with previous acute and delayed CINV. Guideline-based interventions to control acute and delayed CINV should be followed to help patients avoid this conditioned response from exposure to negative stimuli, which should result in lower rates of anticipatory CINV in pediatric patients (1).

In pediatric patients who develop anticipatory CINV, the interventions currently available are hypnosis, systematic desensitization, and the administration of lorazepam in a dose of 0.04 to 0.08 mg/kg/dose with a max of 2 mg/dose (2). Suggested administration of lorazepam includes one dose at bedtime the night before chemotherapy and one dose the next day prior to the administration of chemotherapy. Hypnosis and systematic desensitization techniques are not standardized. Therefore, all of these interventions are classified as weak with low quality evidence by the Children's Oncology Group (COG) (2).

Due to the deleterious effects of CINV on quality of life, health care providers should strive to prevent this side effect while receiving chemotherapy. Although available guidelines suggest the administration of hypnosis, systematic desensitization, and lorazepam, the current evidence supporting this is of poor strength and needs to be evaluated further. Therefore, more pediatric-focused studies are needed on prevention measures for anticipatory CINV.

1.Dupuis, L. L., Robinson, P.D., Boodhan, S., Holdsworth, M., Portwine, C., Gibson, P., Sung, L. (2014). Guideline for the prevention and treatment of anticipatory nausea and vomiting due to chemotherapy in pediatric cancer patients. *Pediatric Blood and Cancer, 61*(8), 1506-1512. doi:10.1002/pbc.25063

2.Children's Oncology Group (2015). *COG Supportive care endorsed guidelines*. Retrieved from https://childrensoncologygroup.org

Contributed by Sherriel Padua, Pharm.D. Candidate

Survivorship Issues in Pediatrics

With the rise in survival rates for various cancers it is essential that current therapy not only focus on curing the malignancy but also improving the quality of life of patients both during and after treatment. It is estimated today that there are 14 million survivors in the United States with nearly half a million being childhood cancer survivors. These patients may experience an array of late effects in the years to decades after cure of their malignancy. The risk of late effects correlate with patient, treatment, and tumor related risk factors. Although most late effects may not be life threatening, they can have a significant affect on morbidity and quality of life (1).

Late effects are commonly caused by surgery, chemotherapy, radiation, and stem cell transplantation and can significantly impact a survivor's medical, reproductive, and psychosocial health. Medical concerns include the risk of major cardiac events, atherosclerotic and stroke risks, secondary primary thyroid cancer, radiation-related risk of basal-cell carcinoma, and fractures. Reproductive concerns include infertility, congenital abnormalities, stillbirth and neonatal death, as well as early menopause. Psychosocial concerns include psychological distress, cognitive delays or deficits, and impaired psychological status (1). These late effects are responsible for a decrease in quality of life and increased morbidity and mortality compared to the general population.

Late effects in the brain can have dramatic impacts on the quality of life of a patient, particularly pediatric patients. Children who experienced brain tumors or acute lymphoblastic leukemia often experience treatment related effects to the central nervous system in a variety of manifestations. Currently, physicians avoid using

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CLINICAL PEARL: Anti-CD20 Monoclonal Antibodies

The FDA has issued a boxed warning for anti-CD20 monoclonal antibodies concerning the reactivation of Hepatitis B virus, which can result in fulminant hepatitis, hepatic failure, or death. These drugs [rituximab (Rituxan®), ofatumumab (Arzerra®), and obinutuzumab (Gazyva®)] are used in the treatment of certain adult and pediatric diseases such as non-Hodgkin lymphoma, autoimmune hemolytic anemia, chronic lymphocytic leukemia, and rheumatoid arthritis. All patients receiving these medications should be screened via the Hepatitis B Surface Antigen (HbsAg) and Hepatitis B Core Antibody (HBV Core IgM Ab) laboratory tests. Appropriate antiviral prophylaxis should be administered when indicated. At Georgia Regents Medical Center the oncology pharmacists have educated other practitioners on this boxed warning and have added a pop-up alert in the pharmacy verification system to remind pharmacists to ensure Hepatitis B screening has been performed prior to dispensing the first dose of these monoclonal antibodies. Through interventions such as these, pharmacists can play a vital role in the safe administration of medications.

1. Lexicomp Online®, Lexi-Drugs, Hudson, Ohio: Lexi-Comp, Inc.; July 2015.

2. Villadolid J, LaPlant KD, Markham MJ, *et al*. Hepatitis B Reactivation and Rituximab in the Oncology Practice. *The Oncologist*. 2010;15(10):1113-1121. doi:10.1634/theoncologist.2010- 0106.

Contributed by
Hayley Hodgson, Pharm.D. Candidate, and
Stephen Michael Clark, Pharm.D., BCOP

CAREER SPOTLIGHT (CONTINUED FROM PAGE 1)

hospital-wide meetings. Additionally, Dr. Ploessl works on longitudinal research projects, very recently submitting a review on the new pediatric chemotherapy agent dinutuximab for publication. Previous publications focused on her research in depression among pediatric cystic fibrosis patients and the assessment of vancomycin troughs in pediatric patients.

Dr. Ploessl stated she always desired to practice clinical pharmacy; thus, she had always planned to complete residencies after graduating from pharmacy school. During her 4th year of pharmacy school, she had a pediatric oncology rotation which sparked her initial interest in pediatrics. Her PGY1 and PGY2 residencies solidified her interest in this sub-specialty. Dr. Ploessl's advice to aspiring clinical pharmacists is to be careful, yet open, in choosing rotations and residencies. "Don't let go of certain opportunities...once you get into a certain field, it will open your eyes to what it is actually like, instead of what it may appear to be like," she explained. Dr. Ploessl also advises students to not be afraid of talking to clinical preceptors or professors about their specialty. "Pharmacy is a very small world so having that close mentor can really help you figure out and achieve your career goals."

Dr. Ploessl expressed that there was not much she would change about her job and that she loved being a pediatric oncology pharmacist. She explained that despite it being a very challenging field, with overall pediatric cancer cure rates near 80-90%, it was also an extremely rewarding field.

Contributed by Baotram Van, Pharm.D. Candidate

CLINICAL CASE STUDY: TEST YOUR KNOWLEDGE

A 3 year old male patient with high-risk acute lymphoblastic leukemia (ALL) has completed induction therapy with successful remission. He is now beginning consolidation therapy: 8 weeks of vincristine, pegaspargase, cyclophosphamide, and cytarabine. What long-term issues will our patient be at risk for with cyclophosphamide exposure?

A. Infertility

B. Pulmonary fibrosis

C. Cataract

D. Rash

Find the correct answer at the end of the newsletter!

Contributed by Andrea Clarke, Pharm.D. Candidate

THE ONCOLOGY BULLETIN

NEW DRUG UPDATE: PALBOCICLIB

Approximately 12% of women in the United States will be diagnosed with breast cancer during their lifetime and of those approximately 6% have distant metastases at presentation. While outcomes for breast cancer patients have improved overall, only 1 in 4 patients with metastatic breast cancer survive five years after diagnosis, which keeps us searching for new and improved treatments (1). One such recent improvement was granted accelerated approval by the FDA in February 2015.

Palbociclib (Ibrance®) is an oral drug used in the treatment of ER-positive, HER2-negative advanced metastatic breast cancer. The proliferation of hormone-receptor-positive tumor cells is dependent on cyclin-dependent kinases 4 and 6 (CDK4 & CDK6), which are vital for the cell cycle to progress from G_1 to S phase. Palbociclib acts as a first-in-class inhibitor of CDK4/6, halting DNA synthesis and decreasing tumor growth (Figure 1). (2)

Palbociclib was originally approved for use in combination with an aromatase inhibitor, letrozole, based on a randomized open-label phase 2 study comparing palbociclib plus letrozole to letrozole alone in postmenopausal women with ER-positive, HER2-negative advanced breast cancer who had not received previous systemic treatment for their advanced disease. The primary endpoint of progression-free survival (PFS) was 20.2 months and 10.2 months in the palbociclib-letrozole arm and the letrozole alone arms, respectively. This improvement in median PFS by 10 months gained palbociclib its accelerated approval for use in combination with letrozole for initial endocrine-based therapy in advanced breast cancer. (2)

Further evidence has demonstrated potential for palbociclib to be used with fulvestrant (Faslodex®) in women with HR+/HER2- metastatic breast cancer following disease progression during or after endocrine therapy. A randomized double-blinded phase 3 study of 521 patients was conducted to evaluate breast cancer progression with a combination of palbociclib with fulvestrant compared to fulvestrant alone. The primary endpoint of median PFS was 9.2 months with palbociclib–fulvestrant and 3.8 months with placebo–fulvestrant, respectively. This study also highlighted some adverse effects of this combination therapy. Grade 3 and 4 neutropenia occurred in 62% and 0.6% in the palbociclib-fulvestrant cohort and placebo-fulvestrant cohort, respectively. Furthermore, grade 3 and 4 leukopenia (25.2% vs. 0.6%), anemia (2.6% vs. 1.7%), thrombocytopenia (2.3% vs. 0%), fatigue (2% vs. 1.2%), and febrile neutropenia (0.6% vs. 0.6%) were noted, respectively. The rate of drug discontinuation due to adverse effects was 2.6% for palbociclib-fulvestrant and 1.7% for fulvestrant alone. This indication is not currently FDA-approved, but the increase in median PFS by 5.2 months is a promising improvement in the treatment of disease progression after endocrine therapy. (3)

Current FDA labeling recommends palbociclib 125 mg administered daily for 21 consecutive days followed by 7 days off treatment and letrozole 2.5 mg administered daily throughout a 28-day cycle. Grade 3 and 4 toxicities may require a reduction in dosage per criteria in the package insert. Palbociclib interacts with other drugs that affect CYP3A, so strong inhibitors and inducers should be avoid-

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SECONDARY MALIGNANCIES

Cancer is the second leading cause of death, following accidents, in children aged 5 to 14 years (1). Survivors of childhood malignancy are at risk for numerous long term complications which can include cancer recurrence as well as late effects from the treatment of the original cancer, such as malignant neoplasms, chronic diseases, and functional impairments (2). These late effects may occur months or years after the primary treatment ended.

The Childhood Cancer Survivor Study (CCSS) reported the incidence of late recurrences for survivors of astrocytoma, Ewing's Sarcoma, medulloblastoma, and “other leukemias” at 20 years of 14.4, 13.0, 9.3, and 9.4%, respectively. The development of secondary malignancies is another area of serious concern for pediatric cancer patients who survive into adulthood. The presence of one benign or malignant neoplasm after a median follow-up of 23 years was 9.6%. Approximately one quarter of survivors developed a second neoplasm. Of those patients nearly forty percent developed a third neoplasm. The development of breast cancer followed by thyroid cancers were the most common subsequent malignant neoplasms. The CCSS also noted that the median latency between the primary cancer diagnosis and subse-

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SURVIVORSHIP ISSUES IN PEDIATRICS (CONTINUED FROM PAGE 2)

radiation therapy, especially in patients younger than three years of age, to avoid brain development issues; however, these development issues may occur in older patients undergoing radiation. Cognitive impairments can include lower IQ scores, low academic achievement, problems with memory and attention, slowed development over time, behavior problems, and poor hand-eye coordination. Seizures and frequent headaches are also possible late effects (2). These complications all influence a patient's ability to perform well at school and thus secure a fulfilling job and future.

Another detrimental late effect of a patient's life includes emotional concerns. Having survived cancer, many patients experience psychological distress. Examples of these include worrying about cancer return, feelings of anger for having cancer while others do not, concerns about being treated differently by classmates, friends, coworkers, etc., and concerns about having a family later in life (2). These psychological issues influence a patient's ability to maintain relationships and overall affects their social wellbeing. Regular mental health check-ups should be part of the follow-up care for childhood cancer due to the risk of depression, suicide, and post-traumatic stress disorder (1).

In order to avoid and manage the various late effects, it is essential that cancer survivors have long-term follow-up care. The *Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers* apply to not only oncologists, but also internal medicine, pediatrics, family practice, gynecology, psychology, and several other specialty fields where care can be provided for cancer survivors (3). While current treatments continue to weigh the benefit of treating the cancer versus the risk of late effects of each treatment intervention, there is an ongoing need for pharmacists to review drug therapy, for example anthracycline cumulative doses, and make interventions regarding the possible long-term complications associated with treatment. After treatment, pharmacists play a crucial role in aggressive patient monitoring, identifying issues, and managing complications.

1. Childhood Cancers. (2015, May 13). Retrieved December 2, 2015, from http://www.cancer.gov/types/childhood-cancers
2. Shad, A. (2015, January 2). Late Effects of Childhood Cancer and Treatment. Retrieved December 2, 2015, from http://emedicine.medscape.com/article/990815-overview#a1
3. Children's Oncology Group, & Children's Oncology Group. (2008). Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. *Arcadia, CA: Children's Oncology Group*.

Contributed by Belinda Li, Pharm.D. Candidate

NEW DRUG UPDATE: PALBOCICLIB (CONTINUED FROM PAGE 4)

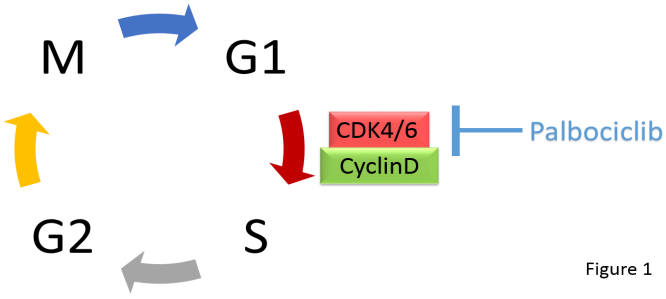

Figure 1

ed. If use of a strong CYP3A inhibitor is necessary, dosage reduction of palbociclib may be required. Due to the common and severe neutropenia seen in trials, bloodwork should be monitored every 2 weeks initially and then before every cycle. The patient should be monitored for signs and symptoms of infection and pulmonary embolism. Palbociclib can also potentially cause fetal harm, so patients should use a contraceptive during treatment and for at least 2 weeks after the most recent dose. (2)

Palbociclib is a promising advancement in the treatment of advanced ER+/HER2- breast cancer with a doubling in PFS when used in combination with letrozole as initial endocrine therapy, and an increase of 5.2 months in PFS when used in combination with fulvestrant as therapy following disease progression after endocrine therapy. As a first-in-class drug, palbociclib is also being evaluated in active and recruiting clinical trials for efficacy in liposarcoma, head and neck cancers, melanoma, acute leukemias, and other cancers (4). As investigation into the potential roles of palbociclib progresses, palbociclib may see expanded indications and improve the lives of more than just those with advanced breast cancer.

1. SEER Cancer Statistics Factsheets: Female Breast Cancer. National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/statfacts/html/breast.html. Retrieved December 23, 2015.
2. IBRANCE(R) (palbociclib) [package insert]. Pfizer Laboratories, Inc., New York, NY; February 2015. http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/207103s000lbl.pdf. Retrieved December 23, 2015.
3. Nicholas C. Turner, M. P. (2015, July 16). Palbociclib in Hormone-Receptor–Positive Advanced Breast Cancer. The New England Journal of Medicine, 10(1056), 209-219. http://www.nejm.org/doi/full/10.1056/NEJMoa1505270. Retrieved November 23, 2015.
4. Search term: palbociclib. ClinicalTrials.gov. U.S. National Institutes of Health. https://clinicaltrials.gov/ct2/results?term=palbociclib&Search=Search. Retrieved December 22, 2015.

Contributed by Pauline Kitolo, Pharm.D. Candidate

SECONDARY MALIGNANCIES (CONTINUED FROM PAGE 4)

quent malignancy ranged from 9 years for a leukemia diagnosis to 23 years for small intestine and colorectal cancer diagnoses (1). These malignant late effects clearly pose long term health consequences for survivors.

Factors related to tumor, patient, and treatment interventions can increase the risk of developing late effects. The type of tumor, location, and effects on the tissues and organs determine the likelihood of developing late effects. In addition to the tumor-related factors, the treatment-related factors include the type of surgery, dose and schedule of chemotherapy and/or radiation, stem cell transplant, use of multimodal therapy, blood product transfusion, and chronic graft-versus-host disease. Patient-related factors include the child's gender, pre-existing health problems, age and developmental stage at the time of diagnosis and treatment, length of time since diagnosis and treatment, changes in hormone levels, the ability of healthy tissue to repair itself, changes that occur in the child's genes, family history of cancer or other conditions, and health habits (3). Therefore, the presence of a complex set of variables determine the likelihood of developing late effects.

Due to the possible lifelong implications of late effects, it is important that health care providers identify, educate, and monitor the survivors so their longevity and quality of life can be extended. For example, pharmacists may serve in a role of patient education, monitoring, and direct management of supportive care issues. Pharmacists may review the patient's drug therapy, exposure to the radiation therapy, and make recommendations to physicians regarding the potential complications of cancer treatment. Pharmacists can serve to empower patients and educate themselves about chronic survivor issues (4). In conclusion, pharmacists may contribute significantly in the monitoring and education of survivors as well as provide information to the other healthcare providers in the appropriate care they may provide in improving longevity and quality of life of the survivors.

1. Ward, E., DeSantis, C., Robbins, A., Kohler, B. and Jemal, A. (2014), Childhood and adolescent cancer statistics, 2014. CA: A Cancer Journal for Clinicians, 64: 83–103. doi: 10.3322/caac.21219
2. "Late Effects of Treatment for Childhood Cancer." National Cancer Institute. N.p., n.d. Web. 12 Dec. 2015.
3. "Children Diagnosed With Cancer: Late Effects of Cancer Treatment."Children Diagnosed With Cancer: Late Effects of Cancer Treatment. N.p., n.d. Web. 12 Dec. 2015.
4. "The Importance of Cancer Survivorship Care Plans: A Pharmacist's Perspective." The Journal of Hematology Oncology Pharmacy. N.p., n.d. Web. 23 Dec 2015.

Contributed by Anjali Jarrett, Pharm.D. Candidate

SOAP UPDATE: RECENT AND FUTURE EVENTS

This past fall semester we had to chance to listen to two fantastic speakers, Dr. Julianne Orr and Dr. David DeRemer, both of whom provided insight on residencies/fellowships and what the life of a resident is really like. SOAP also held a percentage night at Your Pie, with all proceeds directly sent to Winship Cancer Institute at Emory. In October, we participated in the College of Pharmacy's annual health fair where we educated patients on ways to decrease the risk of cancer. Our November meeting was also 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 to the patients at Winship.

In January, we plan to make Valentine's Day gift bags for the patients at Winship which we will hand-deliver to patients in our visit to the facility. This will give members a chance to interact with patients as well as see where all our fundraising efforts go toward. On Saturday, February 27th, we will hold our biggest event of the year, the 4th Annual Tina Borg 5K in Athens. This is our longitudinal fundraising event where 100% of our proceeds are donated to Winship Cancer Institute. Last year we were able to raise over $5000! This year with all the

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SOAP UPDATE: RECENT AND FUTURE EVENTS (CONTINUED FROM PAGE 6)

hard work and dedication of our members we hope to top that donation amount. A few weeks after the Tina Borg 5K, the members of SOAP also have the incredible opportunity to attend the HOPA conference in March in Atlanta. I am incredibly excited for the Spring semester as there are many great things in store!

Contributed by Alia Reid, Pharm.D. Candidate
President of Student Oncological Advocates in Pharmacy

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CLINICAL CASE STUDY ANSWER:
A. Infertility

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