Making time for the multitude of doctors’ appointments is just one of the major lifestyle changes cancer patients must accommodate. For patients receiving myelosuppressive chemotherapy, which results in increased risk of infection from prolonged neutropenia, an additional doctor’s visit is often required to receive granulocyte-colony stimulating factor (GCSF). GCSF medications, such as filgrastim and pegfilgrastim, shorten the duration of neutropenia in effort to prevent infection caused by febrile neutropenia\(^1\). However, these medications must be administered by the healthcare provider 24-72 hours after chemotherapy; therefore, historically patients were required to return to clinic for the injection.

Recently, a novel drug delivery device, Neulasta Onpro\(^\circ\), was approved to deliver the single dose of pegfilgrastim approximately 27 hours after it is placed on the skin. This device utilizes a single use on-body injector that is applied to the patient’s skin at the doctor’s office following administration of chemotherapy. It is programmed to deliver pegfilgrastim the following day over a period of 45 minutes, after which the device can be discarded. The device includes a viewing window to ensure the injection is properly administered, so patients can be confident they received the full dose. Potential side effects are similar to pegfilgrastim including bone pain or pain in the extremities as well as rare but severe adverse reactions of splenic rupture, acute respiratory distress syndrome, and allergic reactions.

Neulasta Onpro\(^\circ\) is now an option to remove the need for a return clinic visit solely to receive an injection of pegfilgrastim. The elimination of at least one additional appointment provides some relief during an overwhelmingly stressful time in these patients’ lives.

Contributed by Alia Reid, Pharm. D. Candidate, 2018

Breast Cancer

Breast cancer is one of the most prevalent forms of cancer worldwide, representing 15% of all new cancer cases in the U.S. By the end of 2017, an estimated quarter of a million women will be newly diagnosed and over 40,000 will die from breast cancer. The average woman has an approximate 12% lifetime risk of developing breast cancer. The most established risk factors include: female gender, older age, family history, genetic susceptibility, dense breast tissue, Caucasian race, obesity, alcohol consumption, smoking, and past radiation or estrogen exposure. Although some risk is non-modifiable, preventative actions exist to lower the chance of developing breast cancer. Potential measures include diet modification, reducing alcohol intake, smoking cessation, avoiding drugs or treatments known to increase cancer risk, proactively stunting progression of precancerous conditions, and, in some cases, undergoing risk-reducing surgery.

One of the key preventative methods involves recognizing precancerous signs, as well as identifying notable symptoms. Diligent, regular monitoring can help uncover breast cancer early. Clinical breast exams are suggested every 3 years for women in their 20-30s and every year for women after they have reached age 40. In addition, monthly breast self-examinations can aid in early disease detection. Signs to monitor for include unusual breast swelling, irritation, pain, redness, scaliness, nipple discharge, or lumps. It is recommended to promptly report any of these symptoms to a physician so appropriate tests or imaging can be performed for diagnosis.

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Cancer Stem Cells

In 1937, when Jacob Furth and Morton Kahn demonstrated that a single leukemic cell could cause systemic leukemia when transplanted to a mouse model, the idea that cancer cells exist in a hierarchy infiltrated research as an underlying mechanism of cancer pathophysiology. Said “hierarchy” can be divided into subclasses of cells with each class manifesting a different role in the growth and development of a tumor.

At the base of this hierarchy is a small portion of cells called cancer stem cells (CSCs). According to CSC research, this class of cells is believed to be the driving force behind tumor growth and reoccurrence after treatment. In comparison to non-pathologic stem cells, CSCs possess properties of pluripotency and self-renewal. Pluripotency is defined as the capability of one cell to bring about multiple different cell types. To better conceptualize pluripotency, an example in a healthy human is the ability of stem cells in a growing fetus to differentiate into thousands of specific cell types that compromise every organ in the body. Similarly, each cell type that exists in a tumor will ultimately arise from a CSC. Self-renewal of CSCs is characterized by immortality associated with tumor growth. Stem cells’ ability to self-renew means some will separate into specialized daughter cells in order to retain a consistent stem cell population. In tumors, however, research has shown different populations of CSCs exist. Some CSCs readily proliferate, but die off early. A smaller quantity of CSCs will extensively self-renew and maintain tumor cell population long-term without differentiating into cells which make up the bulk of a tumor. Each of these characteristics emphasize the major role CSCs may play in tumor proliferation and progression. Fortunately, CSCs express phenotypic surface markers that differ from other cells expressed in a tumor. This distinction has allowed researchers to study CSC in nearly every type of human cancer.

How do CSCs change the way scientists and clinicians view and treat cancer? While radiation and chemotherapy have improved over time due to specific targeting, research has proven CSCs are generally resistant to these interventions through various mechanisms. The simplest of these mechanisms involves the relatively slow cell cycle that occurs in CSCs. In a broad sense, many chemotherapy agents are specific for malignant cells by targeting rapidly dividing cells of the body. Non-stem cancer cells are specialized, rapidly dividing cells that originate from CSCs and form the majority of a tumor. While chemotherapy may reduce tumor burden by killing off non-stem cancer cells, CSCs are not rapidly dividing and therefore not subject to the same decline in numbers. Consequently, this mechanism may correlate with why a reduction in tumor bulk is not necessarily associated with an improvement in clinical outcomes, as previously observed in practice. In addition, survival of CSC population could result in disease relapse or metastasis. Nevertheless, this mechanistic example is only one of many ways in which CSCs may enable relapse or resistance to treatment.

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Breast Cancer (Continued From Page 2)

In addition to self-monitoring, women ages 50-74 are recommended to receive biennial mammograms for further breast cancer screening. Women ages 40-49 may also elect to be screened in this manner, depending on their risk factors and history. Another helpful screening measure involves testing for mutations in BRCA1 and BRCA2. These genes are responsible for producing tumor-suppressing proteins; therefore, mutations can increase a patient’s risk of developing breast cancer. Women with a family history of breast or ovarian cancer, BRCA1 or BRCA2-related cancers, or breast cancer diagnosed prior to age 50 should consider obtaining testing for mutations in these genes. Positive test results for BRCA1/2 mutations are the most common justification for prophylactic, risk-reducing surgeries, including lumpectomies and mastectomies. However, these procedures are typically only utilized when benefits outweigh risks. The National Cancer Institute has a breast cancer risk assessment tool available for women to calculate their own risk at [https://www.cancer.gov/bcrisktool/](https://www.cancer.gov/bcrisktool/).

Once breast cancer is diagnosed, treatment is precisely chosen based on a patient’s hormone receptor status, genetic risk, and disease stage. Treatment is widely variable and includes options such as chemotherapy, targeted hormonal therapies, monoclonal antibodies, radiation, and surgery. Breast cancer treatment is unique in that each patient is treated on a case-by-case basis, and further drug development promises to improve individualized outcomes even further.


Contributed by Catherine Rothery, Pharm.D. Candidate, 2020

Disparities in BRCA Gene Counseling and Testing Recommendations in African American Women

Breast cancer is one of the top two causes of cancer-related deaths in women. Approximately 5-10% of breast cancer are hereditary, and almost half of these cases are due to BRCA1 and BRCA2 (BRCA1/2) mutations. The National Comprehensive Cancer Network (NCCN) guidelines recommend practitioners refer women for genetic counseling and testing who have early-onset breast cancer diagnosis (before age 50), bilateral and multiple breast cancer presence, family history of breast cancer, and/or ovarian cancer diagnosis (at any age). BRCA1/2 genetic testing is used to identify women at higher risk for developing breast and cervical cancer and to reduce risk of complications for those with breast cancer. Test results aid patients in selecting prevention strategies such as initiating mammogram screenings earlier and more frequently, providing for risk assessments on close relatives of patients with positive results (so they can benefit from increased prevention and screening measures), and allowing for treatment guidance (deciding on pharmacological therapies or surgical procedures) in patients with breast cancer.

Although genetic testing among women has increased in the twenty years since its inception, high-risk African American women are almost two times less likely to undergo BRCA1/2 counseling or testing than high-risk Caucasian women, suggesting the presence of racial disparities within cancer genetic counseling and testing. Although African American and Caucasian women are at similar risk for breast cancer diagnoses, African American women tend to be diagnosed with breast cancers that are more aggressive, advanced, and have an earlier onset, which increases African American women’s breast cancer-related mortality, making this inequity issue even more pressing.

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As an exciting new area of cancer research, the role of CSCs and theory of an existing cell hierarchy continues to evolve as supportive evidence steadily grows among cancer types. As our understanding of CSCs grow, novel interventions in treating and, perhaps, curing cancer are possible.


Contributed by Behren Bass, Pharm.D. Candidate, 2020

Immune Checkpoint Inhibitors

As the understanding of cancer pathophysiology and biologic targets advance, oncology treatments have the potential to become more individualized and specific. Immunotherapy is one innovative treatment born from advances in our understanding of how cancerous cells and the immune system interact. Immune checkpoint inhibitors (ICIs) are a type of immunotherapy that target checkpoints in the body’s immune system. Cancer cells often have the ability to evade these checkpoints. By targeting this aspect of the immune system, ICIs enhance the body’s recognition of cancer cells and the ability to signal for their cell death. Ipilimumab is a CTLA-4 inhibitor that has shown improved survival in patients with metastatic melanoma. PD-1/PD-L1 inhibitors, such as nivolumab and pembrolizumab, are indicated in the treatment of various solid tumors to improve clinical outcomes. While these immunotherapy agents carry a lower risk for certain chemotherapy toxicities such as myelosuppression, there is a higher risk for immune mediated adverse events (imAEs) such as: arthritis, colitis, diarrhea, fatigue, hypophysitis, myalgia, pneumonitis, skin rash, neuropathy, and hepatotoxicity. Severe imAEs may warrant cessation of ICI treatment while mild to moderate may require treatment interventions including hospitalization. Therefore, any intervention which may increase risk for imAE is clinically relevant and warrants further investigation.

The Centers for Disease Control and Prevention currently recommends the annual influenza vaccination for all people 6 months or older, including patients with cancer unless contraindicated. Contraindications would include if the patient had received a bone marrow transplant in the past 6 months or if the patient had received intensive chemotherapy or anti-B cell antibodies within 6 months. However at this time, a lack of evidence is available for the safety of concurrent vaccination in patients with cancer who are receiving immunotherapies.

The University of Georgia College of Pharmacy PGY2 Oncology Resident, Morgan Gwynn, is conducting research to fill this gap in literature and provide basis for further studies. The goal of her research is to determine if there is an increase in imAEs following inactivated influenza vaccination (IIV) in cancer patients receiving ICIs and to evaluate for any potential correlation between increased cytokine levels and incidence of imAEs. In a prior small study, the incidence of imAEs following influenza vaccination in patients receiving certain ICIs, nivolumab or pembrolizumab, was 52%, which was reportedly higher than historical controls. Dr Gwynn’s current study expands upon the prior report by including all ICIs, CTLA-4 inhibitors and PD-1/PD-L1 inhibitors, as well as a combination of CTLA-4 and PD-1/PD-L1 inhibitor treatment. Furthermore, her study includes sub-group analyses of patients with various malignancies, lengths of immunotherapy treatment prior to IIV, and previous history of imAEs.
Disparities in BRCA Gene Counseling and Testing Recommendations in African American Women (Continued From Page 3)

One of the main predictors of patient adherence to genetic counseling and testing is healthcare provider recommendation and referral. Physicians are less likely to refer African American patients to genetic counseling and testing. Explanations for this pattern in physician recommendation have not yet been clearly defined; however, several studies have suggested different reasons for this disparity. African Americans were less likely to report on extended family medical histories either due to less knowledge of cancer diagnoses in those family members or due to physicians not asking about second-degree family history. Other studies suggest physicians were concerned about financial challenges including insufficient insurance coverage (or lack thereof) and the expensive cost of genetic testing.

Although some studies have found differences in the demographics of physicians who treat predominantly black populations compared to those treating fewer black patients, no difference in quality of care issues have been found. Therefore, this is an unlikely explanation for the racial disparity in genetic testing. However, there is still significant racial segregation within the care of breast cancer patients that needs to be explored.

In another study, medical care for black patients was heavily distributed among a relatively small number of providers who were more likely to work in medical settings with lower outcomes and quality of care for breast cancer patients. A national survey also identified that providers caring mainly for minorities had a decreased chance of ordering genetic testing for risk assessment, which may be due to hospital administration and logistics, making it more difficult for physicians to order the supplies needed to care for their patients.

Fortunately, pharmacists can help counter the health inequities African Americans face. Community and ambulatory pharmacists play a vital role in promoting breast cancer screenings and recommending genetic testing to high risk populations. Pharmacists can use screening algorithms to assist in referring patients for genetic testing and address benefits and perceived barriers for those with any reservations.

Increased efforts are needed to improved testing for inherited mutations, such as BRCA1/2, in high risk African American breast cancer patients. Advantages of genetic testing include personalized medicine and prevention leading to more successful health outcomes with higher qualities of life. Due to pharmacists' earned respect, trust, and ease of accessibility, pharmacists can reach diverse and underserved communities to address the racial disparities in BRCA 1/2 genetic testing and counseling among African Americans.


Contributed by Diane Ayuninjam, Pharm.D. Candidate, 2020
Intraperitoneal Chemotherapy in the Treatment of Ovarian Cancer

Intraperitoneal (IP) chemotherapy is used in the treatment of certain abdominal cancers, such as ovarian, appendiceal, and gastric1. IP effectively administers high doses of chemotherapy directly into the site where the cancerous cells are located. Two methods for IP chemotherapy administration are currently available. The first standard type includes an implanted subcutaneous port, which is attached to the ribs within the peritoneal space. This method allows for administration of chemotherapy to be performed at an outpatient facility at regular intervals. The second type, called Hyperthermic Intraperitoneal Chemotherapy (HIPEC), is administered as a warmed chemotherapy into the peritoneal cavity in an operating room following cytoreduction surgery1.

Administration of chemotherapy directly into peritoneal region may be advantageous in minimizing systemic adverse effects; however, side effects are often more severe than with regular chemotherapy. Patients may experience more abdominal pain, nausea, vomiting than individuals on IV chemotherapy. These adverse effects caused some patients in a study of women with advanced ovarian cancer to stop their treatment prematurely. However, even though some patients who received IP chemotherapy did not finish the prescribed treatment course those who received IP chemotherapy lived longer than the women who only received IV chemotherapy2.

IP chemotherapy for the treatment of ovarian cancer allows for an elevated drug concentration to be sustained within the abdominal cavity, which has been found to improve outcomes1. The high drug concentration within the abdominal cavity is advantageous for patients with epithelial ovarian cancer that is restricted to this region at the time of initial diagnosis3. A prospective cohort study reported an improved 3-year overall survival in patients with stage IIIA ovarian cancer who had ≤ 1 cm tumor deposits after surgery, where the tumors had spread to the uterus, colon, and the surface of the peritoneum, with the treatment of both IP and intravenous (IV) chemotherapy compared with IV chemotherapy alone4. The 3-year overall survival (hazard ratio = 0.68±0.26, a=0.05) was 81% in 201 women treated with IP/IV chemotherapy as compared to 71% in 201 of women treated with only IV chemotherapy4. In addition, no differences were found in infections (p=0.62) or nausea/vomiting (p=0.44) between these groups4. Therefore, the addition of IP chemotherapy is instrumental in increasing efficiency in the treatment of ovarian cancer.

Immune Checkpoint Inhibitors (Continued From Page 4)

The primary outcome is evaluating the incidence of imAEs. The incidence of imAEs will be determined through patient questionnaires, laboratory results, and physician assessment. Patient medical records 60 days prior and 60 days following IIV administration will be evaluated. The degree of severity of imAEs is then graded in severity according to the Common Toxicity Criteria for Adverse Events (CTCAE) v4.03. The incidence of imAEs following IIV administration will then be evaluated in comparison to historical incidence5.

In addition to incidence of imAEs, 30 types of cytokines will be evaluated. Secondary/exploratory endpoint of this study will be to report change in cytokine levels in all patients from baseline (pre-vaccination day 0) to day +14/+21 and day +28/+42 after vaccination6. Furthermore, correlation of cytokine level changes and incidence of imAEs will be assessed1,3.

This study will assist physicians in determining the risk versus benefit of IIV in patients receiving ICI therapies. Dr Gwynn will present her results at the 2018 HOPA Annual Meeting.


Contributed by Brooke Cottle, Pharm.D. Candidate, 2021
Intraperitoneal Chemotherapy in the Treatment of Ovarian Cancer (Continued From Page 6)

Despite the findings of clinical trials, which confirmed a survival benefit with the integration of IP chemotherapy in the treatment of ovarian cancer⁴, a prospective cohort study found its use in clinical practice is not extensive⁴. The use of IP chemotherapy in eligible patients varied significantly from 4% to 67% at the six National Comprehensive Cancer Network centers included in this study⁴. Therefore, data suggests IP chemotherapy is underutilized in clinical practice despite known benefits to patients with advanced ovarian cancer.

In addition to treating ovarian cancer, IP chemotherapy may be utilized in the management of peritoneal surface malignancies in addition to the treatment of malignant peritoneal mesothelioma, malignant ascites, and peritoneal carcinomatosis from gastrointestinal cancers⁵. As medication experts, oncology pharmacists can offer valuable drug information necessary in optimizing IP chemotherapy through assisting in proper selection of patients eligible for IP chemotherapy as well as verification of proper doses, dilution, preparation, and administration⁵. Pharmacists can also provide crucial education on the risks and benefits of IP chemotherapy to providers and patients to enhance to successful utilization where appropriate.


Contributed by Anjali Jarrett, Pharm.D. Candidate, 2020
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