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THE ONCOLOGY BULLETIN

Student Oncological Advocates in Pharmacy (SOAP)
University of Georgia College of Pharmacy

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OUR MISSION

Written by Amelia Clary

The mission for SOAP has remained the same since we were founded in 2012 at the University of Georgia: to advocate for cancer patients while providing student pharmacists the opportunity to interact with this unique patient population.

Despite the extra precautions needed to protect these vulnerable patients, SOAP has remained committed to serving patients in the Athens community and working to win the fight against cancer. We held virtual events, made donations, and used social media to promote awareness about the different types of cancers and the importance of screenings.

By orchestrating invaluable opportunities to hear from experts in our field and from cancer survivors, SOAP has continued to instill a passion for patient care in our future pharmacists that will take up the torch in the fight to end cancer.

FALL 2021: A SEMESTER IN REVIEW

Despite the ongoing presence of the COVID-19 pandemic, our dedicated SOAP members were able to uphold our mission in 2021. Throughout the last year, many of our student pharmacists stepped up to the plate and volunteered their time to administer vaccines at mass clinics all throughout Georgia. In the fall, SOAP welcomed the new P1 class and reconnected with previously social distanced P2s and P3s. With an updated information board, our members educated students and faculty at UGA about the importance of vaccination against the Human Papilloma Virus and the protection against cervical cancer this vaccine offers. At the annual Pharmtoberfest event, SOAP used our famous "bra pong" board to educate passing students on the importance of regular breast exams to screen for the presence of cancer. Our Community Outreach Chair, Jessie Morris (P2), organized a drive to recruit volunteers to donate bone marrow to cancer patients through DKMS. Even with the downpour of rain, SOAP collected over 40 new donors in the effort to beat blood cancers. Because of the risk it would pose to the very population we advocate for, some of our usual of our events were switched to a virtual format or donation drives instead. However, SOAP was fortunate enough to have a hybrid panel of breast cancer survivors speak to our members. The survivors were all UGA College of Pharmacy faculty, and they shared their moving testimonies about their journey with cancer. These women also spoke about the positive impact their pharmacists had throughout their treatment, inspiring SOAP members to continue with our mission of advocating for all patients.

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VACCINE HESITANCY AMONGST IMMUNOCOMPROMISED PATIENTS

BY MERRIE BARNETT,
PHARMD CANDIDATE 2024

Immunocompromised individuals currently comprise 3% of the United States population2.
Immunocompromised is a term used to describe the body's inability to utilize it's immune system to neutralize external organisms,7 which may result in increased or prolonged infections. This may affect a wide variety of patients, and may occur transiently or chronically. A patient can be born immunocompromised or become so at some point in their lifetime, or are temporarily immune compromised.

Amongst the 3% of immunocompromised individuals, there is a current need to mitigate COVID 19 infection and COVID 19 infection severity. There are several factors when taking into account decision making regarding the COVID 19 vaccine for immunocompromised individuals. It is important to consider the incidence of COVID 19 amongst this population as well as the effects of COVID 19 in an immunocompromised patient. From case series, retrospective cohort studies, and surveys it has been observed that initial clinical symptoms are similar in non-immunocompromised as with immunocompromised patients. While the clinical symptoms are similar the outcomes vary between immunocompromised and non-immunocompromised and outcomes further vary amongst immunocompromised patients. It has been observed that cancer patients and solid organ transplant patients may be at increased risk of severe COVID 19 disease1.

The Journal of Infection has completed a systematic review to discover the potential difference in clinical outcomes and clinical presentation of COVID 19. This meta analysis also took into consideration co-morbidities associated with the immunocompromised patients. The solid organ transplant patients had higher comorbidities, higher mortality, and higher disease severity. Cancer patients also had more severe disease and adverse outcomes1.
With the negative implications amongst the immune compromised group, it is important to understand why patients in this group may or may not be getting the recommended COVID 19 vaccine. Those who are immunocompromised have been studied, specifically in a sample of patients with autoimmune and inflammatory diseases, the findings were that there were 3 clusters, with three different view points of the COVID 19 vaccine. What was seen as similar was the response to fear of COVID 19 amongst this sample. The patient sample viewed the vaccines with different levels of trust, but they all viewed COVID 19 fearfully. The main concerns patients from groups 2 and 3 had, "hesitant" and "suspicious", includes the use of new vaccine technology, lack of long term data with the vaccine in patients, and potential financial links with the pharmaceutical companies5. With this group of patients it is important to properly educate on risks vs benefits of the COVID 19 vaccine. This includes understanding the characteristics of the COVID 19 vaccines and the efficacy within this patient population.

There are immunocompromised patients who are both getting the COVID 19 vaccine and who are not due to hesitancy towards it. It is important to understand the current recommendations of COVID 19 vaccines for immunocompromised patients and how these patients were included/excluded in the clinical trials of the vaccines, Pfizer, Moderna, and J&J. The only patients with an immune compromising condition to be included in the trials of these vaccines are HIV infected patients. Despite the exclusion of other immune compromised individuals, there are still recommendations for getting the COVID 19 vaccine. There are several facets to the recommendations for immunocompromised individuals. The first is understanding the Moderna and Pfizer vaccines are mRNA vaccines, meaning they are safe in immunocompromised patients. The J&J vaccine is a viral vector vaccine that is also safe for use in immunocompromised patients. These vaccines are considered for not only safety within this population but also efficacy. Due to the limited nature of this population's immune system, it may be required to take into consideration timing of COVID 19 doses. An immune response is required for efficacy of these vaccines, so some immune compromised patients might need more doses for the vaccine to be effective or they might need to get the COVID 19 vaccine two weeks before starting immunosuppressive therapy3,4.

With this information, it is now recommended that immune compromised patients get a booster dose of

of either the Moderna or Pfizer COVID vaccine, whichever series they started. Currently the CDC is recommending a 3rd dose of either Moderna or Pfizer 28 days after receiving the second dose of either Moderna or Pfizer. Mixing and matching between the mRNA vaccines is not recommended unless there is no way to figure out which mRNA vaccine was previously given, then the CDC does recommend to give either Moderna or Pfizer as 3rd dose2,4.

While knowledge is important, it is useless without communicating it to patients. Pharmacists can educate patients on the safety of the COVID 19 vaccines and a patient's specific situation. Pharmacists can also tell their patients about why a 3rd dose is being recommended, and can explain the emergence of breakthrough cases with hospitalized patients who are immune compromised.

Communicating with a patient, speaking to all of their concerns, and providing accurate information are all things a pharmacists can do to inform patients6.

Overall, there is a need for quality communication with patients who are immune compromised, because some may be hesitant towards getting the COVID 19 vaccine. It is important to understand where a patient is coming from, but it is also important to understand the risks and benefits of the vaccine. The risks can include contracting COVID 19 with a pre-existing compromised immune system as well as any adverse effects of the COVID 19 vaccine. Recognizing if a patient qualifies for a 3rd dose of Moderna or Pfizer is also pertinent and should be communicated with patients.

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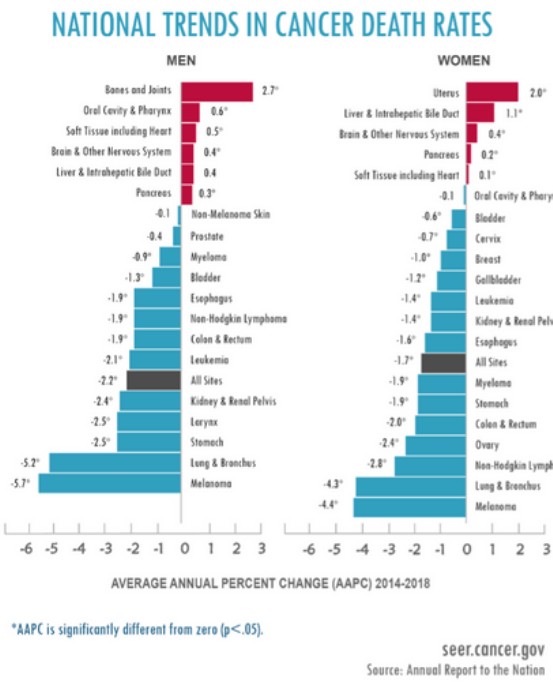
CANCER SURVIVORSHIP: A FOCUS ON FERTILITY

**BY BRIANA BELDON,
PHARMD CANDIDATE 2022**

In 2019, the American Cancer Society predicted there would be 1,762,450 new cancer cases and 606,880 cancer deaths in the United States that year.1 However, there were 599,601 cancer deaths documented in 20192, which contributed to a 27% decrease in cancer death rates in the United States from 1999 to 2019.3 Overall cancer death rates have decreased for men, women, children, adolescents, and young adults.4 There are many reasons for the declining cancer death rates which include an increase in cancer screenings, earlier diagnosis, a reduction of risk factors among the overall population, and treatment advances.3 As patient survival has prolonged, our focus has shifted to include survivorship considerations. For example, the desire and ability to have children in the future. Unfortunately, despite advancements in treatment modalities, many options still have the potential to impair reproduction. According to a survey from Armuand et al5, about one-third of surveyed survivors reported difficulty achieving pregnancy after cancer treatment. Luckily, there are options that can improve their fertility struggles.

In both men and women, chemotherapy and radiotherapy have unique ways of inhibiting fertility. In the case of women, they are born with all of the oocytes they will have for their lifetime – called the "ovarian follicle reserve". As women age, the number of oocytes gradually decreases. Chemotherapy and radiotherapy also cause a depletion of the ovarian follicle reserve and stromal function, leading to acute ovarian failure or premature menopause.6 In contrast, men begin making sperm through germ cells during puberty, and production continues for the rest of their lifetime. The rapid division that occurs during sperm production makes sperm and germ cells targets for chemotherapy.9 This can result in a lack of viable sperm in semen "azoospermia" or low sperm counts "oligospermia". A few agents that pose the greatest risk of infertility include cyclophosphamide, ifosfamide, chloambuccil, mephalan, bendamustine, busulfan, and high-dose cisplatin.8 Additionally, radiotherapy and surgery can cause damage to structures that may be necessary for fertility in both men and women, such as areas of the brain that are involved in hormone production.8



Fortunately for our patients, there are many options that may allow them to have children after treatment. OTC involves removing a portion of one ovary before treatment and freezing it.10 After treatment, the tissue can be implanted back into the patient. In patients at risk for cancer in the tissue, including patients with leukemia, OTC is not a viable option due to the risk of re-introducing carcinogenic cells to the patient. For ovarian transposition, one or both ovaries are moved to another part of the abdomen to lessen exposure to radiation therapy. In some patients, a second procedure is necessary for conception.10 Other options currently undergoing research in women include activation of ovarian follicles, in vitro follicle culture, and artificial ovaries.7 Additionally, some studies have shown that administering gonadotropin-releasing hormone (GnRH) agonists concurrently with chemotherapy reduces the risk of developing premature ovarian failure.14 While data on GnRH agonists is still controversial, these agents may be administered as a method to preserve ovarian function and fertility, especially in patients who need to start treatment quickly.15 Men also have options for fertility preservation, including sperm banking and cryopreservation of spermatogonial stem cells (SCCs).7 Sperm banking is the first-line fertility preservation method in males, and it involves the collection and cryopreservation of sperm.

Cryopreserved sperm obtained prior to starting cancer treatment has resulted in a 13.7% live birth rate in studies.13 In prepubertal males, sperm banking is not an option due to the absence of mature sperm in the testes. Instead, these patients can undergo cryopreservation of SCCs, or testicular tissue. 7 The tissue is removed through a biopsy and, like OTC, it may not be a feasible option in patients with cancer in the tissue.

While patients are typically at the highest risk for consequences from chemotherapy, it's also important that we consider the risk to caregivers and family members who may be handling these therapies at home. Those handling oral chemotherapy agents are at risk of exposure to the medication which could result in adverse effects. Anyone touching the chemotherapy agent should wear disposable gloves to avoid direct contact with the medication.

Caregivers should wash their hands thoroughly before and after handling oral chemotherapy agents. Additionally, if pills need to be split, cut, or dissolved, the person preparing the medication should wear a facemask to avoid inhalation and an apron to protect their clothing from contamination.Cancer is a devastating disease and the treatments can also have devastating side effects including the loss of fertility. Luckily, there are many options for oncology patients who still want to conceive in the future. It's essential for all members of the healthcare team to be aware of the options that their patients have and discuss these options with the patient before therapy begins. The pharmacist on the team has a very important role in counseling the patient on the potential for fertility loss and also helping to make them aware of the reproductive options they have before beginning treatment.

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MAGROLIMAB (HU5F9-G4) IN COMBINATION WITH RITUXIMAB FOR THE TREATMENT OF RELAPSED/REFRACTORY B-CELL NON-HODGKIN'S LYMPHOMA

BY DIANA DANG, PHARMD CANDIDATE 2023

With a five-year overall survival ranging from 25-75%, non-Hodgkin lymphoma (NHL) is the fifth most common cancer in the United States.1 NHL can be considered indolent (slow-moving with few symptoms) or aggressive (fast-growing and causing symptoms). The most common types for each are follicular lymphoma (FL) and diffuse large B cell lymphoma (DLBCL), respectively. NHL can also be categorized based on where the cancer originated: B-cell lymphocytes or T-cell lymphocytes.2 Depending on the classification, treatment will vary accordingly.

In recent years, the advent of immunotherapy has led to improvement in long term outcomes for numerous cancers. Immunotherapies are those which augment the immune system to enhance detection and elimination of cancerous cells from the body via various mechanisms. One of the initial types of immunotherapies were monoclonal antibodies (mAbs), such as rituximab. Rituximab specially targets CD20, which is expressed on most subtypes of B-cell NHL. It remains one of the most widely used CD20-targeting mAbs in oncology.3 Unfortunately, once a patient becomes refractory to standard chemotherapy and antibody-focused regimens, prognosis decreases significantly.4 Therefore, new therapies to improve the activity of anti-CD20 antibodies is necessitated. Currently, treatment options include high-dose chemotherapy followed by autologous stem cell transplant or CAR-T cell therapy, which are limited by patient eligibility, financial ability, and significant toxicity, as well as the use of radioimmunoconjugates as palliation.5

Magrolimab is a monoclonal antibody that targets the human cell surface antigen CD47 which prevents the interaction and signaling between CD47 and its ligand signal regulatory protein alpha. This inhibition allows for the activation of macrophages and induces phagocytosis of tumor cells.6 When administered with a tumor-targeting antibody like rituximab, there is a synergistic enhancement of macrophage-mediated antibody-dependent cellular phagocytosis leading to the elimination of B-cell non-Hodgkin's lymphoma cells.4

The efficacy of magrolimab in combination with rituximab was demonstrated in a Phase 1b dose escalation cohort study involving patients with relapsed/refractory in DLBCL and FL who were rituximab-refractory. A total of 22 patients were enrolled in the study. The median age was 59 years (range, 44 to 82). The median number of previous lines of therapy was 4 (range, 2 to 10), with 21 patients (95%) of whom had disease refractory to rituximab.4 The study looked at objective and complete response rates as well as time and duration to response. Patients were treated for a median duration of 22 weeks (range, 1.7 to 70.7 and ongoing). In the intention-to-treat analysis, the objective response rate was 50% and the complete response rate was 36%. The objective response and complete response rates were 40% and 33%, respectively, for patients with DLBCL and 71% and 43%, respectively, for patients with FL. Most adverse events reported were of grade 1 and 2, with the most common treatment-related events being chills (41%), headache (41%), anemia (41%) and infusion-related reactions (36%). Adverse events occurred mostly within the first few weeks, and there were no long-term toxic effects observed.4

This initial study showed that magrolimab in combination with rituximab is safe and effective for inducing complete responses in patients with relapsed or refractory B-cell non-Hodgkin's lymphoma. Further investigation is taking place in a Phase 2 trial. 4

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MORE THAN PACKING PRESCRIPTIONS: A LOOK INTO A PHARMACIST'S ROLE IN CANCER SCREENING

BY TORI REDSHAW AND ALLISON DEAN, PHARMD CANDIDATES OF 2023 AND 2024

With almost 90% of people in the country living within five miles of a pharmacy, pharmacists are one of the most accessible healthcare providers (1). This creates an opportunity for a major impact on patient care by pharmacists as typically patients are seen more frequently in this setting than they would be by a doctor or other healthcare provider. Pharmacists go through an extensive Doctor of Pharmacy Program which includes training in disease states, medications, and how to treat patients. In the program at the University of Georgia, future pharmacists are trained on a variety of oncology-related topics such as the different types of cancer, what symptoms that cancer could potentially present as, and anti-tumor agents. With the incidence of cancer being about 442 per 100,000 men and women every year, it is imperative that these patients seek medical attention immediately to limit their cancer's spread and severity (2).

Who should be screened:

It is important to know who could be at an increased risk of developing cancer. Anyone who has a personal or family history of cancer, is exposed to carcinogens at work, has a history of tobacco use, and/or is older in age should be screened regularly (3). Additionally, anyone with common signs or symptoms should be screened. These symptoms can include fatigue or extreme tiredness that does not get better with rest, swelling or lumps anywhere in the body, pain with no known reason, and unusual bleeding or bruising for no known reason (4).

Ways to recommend screening:

It may not always be clear which patients are at an increased risk, making it challenging for pharmacists to make recommendations. Due to this, pharmacists should use available educational tools to start the conversation of who should be screened. These tools include risk assessment questionnaires, pamphlets, and short videos for patients. Once patients are made aware of why cancer screening is important and who is eligible, pharmacists can then connect them with resources for a more focused screening. For example, pharmacists can provide a list of places that are free or local that perform cancer screenings (5). Overall, it is important that a conversation takes place with higher risk patients so that action, if any is necessary, can take place.

Benefits vs risks of cancer screening:

There are certain benefits and risks associated with cancer screening that should be made known to patients during discussion. Cancer identified at an earlier stage, when the disease has not yet spread throughout the body, is easier to treat and may increase the chance of survival. For instance, mammograms are x-rays used to detect lumps within breast tissue that cannot be felt from a physical exam (3). While cancer screening has been proven to save lives, issues have occurred with screening tests. Some tests may result in bleeding such as colonoscopies. Tests could show cancer when none is present (a false-positive) leading to unnecessary stress for the patient. Tests could also say no cancer is present when it actually is (a false-negative) possibly causing the patient to postpone seeking medical care (3). There is no guarantee that identifying cancer will prolong someone's life. Therefore, it is important for patients to discuss the benefits and risks of screening with a healthcare provider to make an informed decision based on their situation.

Role of pharmacists:

Along with spreading awareness on the usefulness of cancer screening, pharmacists can play a more direct role helping to reduce the risk of cancer. For example, a pharmacist can present resources on how to perform a self-breast exam and recommend yearly mammograms to women of age. Moreover, fecal occult blood tests, which screen for colon cancer, are available as home kits within pharmacies allowing a pharmacist to coach the patient through how the test works (6). When pharmacists educate patients about medications that cause photosensitivity or assist them in choosing a protective sunscreen, they are helping them decrease the risk of developing skin cancer. Likewise, pharmacists place emphasis on smoking cessation which can reduce the possibility of many cancers, including lung cancer (5). In this aspect, a pharmacist can start a conversation with a patient about their willingness to stop smoking, recommend products that would help the patient in their smoking cessation, and point them in the direction of any educational tools they might need. Overall, there are several ways in which a pharmacist can be involved in minimizing someone's risks when it comes to cancer, and no intervention is too small.

Pharmacists have the opportunity to educate patients on the importance of screening for cancer by providing information to those who are at increased risk or are experiencing symptoms. While cancer screening can be costly and does have the potential for error, it is important for the patient to discuss with their healthcare provider if they think that the benefits of being screened for cancer outweigh the risks. Ultimately, incorporating pharmacists into a role that encourages cancer screening can positively impact patient health.

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ADJUVANT OLAPARIB FOR PATIENTS WITH BRCA1- OR BRCA2-MUTATED BREAST CANCER

BY ESSILVO SULEJMANI,
PHARMD CANDIDATE OF 2023

DNA may break during cellular replication or environmental exposure causing cells to rely on DNA-repair pathways to maintain genetic integrity. However, the deregulation of these repair pathways is often associated with uncontrolled DNA damage, genetic mutation accumulation, and cancer. BRCA1 and BRCA2 are tumor-suppressor genes that encode for DNA-repair proteins involved in the repair of double-strand breaks (DSBs) in DNA via homologous recombination.1 Functional mutations in these BRCA genes hinder DNA repair, lead to irregularities in DNA synthesis, and allow an accumulation of deleterious mutations.1 Individuals with germline BRCA1 or BRCA2 mutations have shown an increased risk of certain cancers (e.g., breast, ovarian, pancreatic), likely due to these pathway failures.2

Breast cancer is the one of the most common cancers and a leading cause of cancer-related death in women worldwide.3 BRCA1 and BRCA2 mutations are the most commonly affected genes in patients with hereditary breast cancer, which accounts for 5-10% of breast cancer cases.

Treatment strategies for early-stage BRCA1 and BRCA2-mutated breast cancers, which are most commonly HER2-negative, can include surgery, radiation, and chemotherapy.2 However, newer studies and treatment strategies have unveiled a new class of targeted therapies for breast cancer, among others, centered around the inhibition of members of the PARP enzyme family.4 PARP (Poly(adenosine diphosphate [ADP]-ribose) polymerases) is an essential enzyme family for the repair of DNA single-strand breaks (SSBs). If these enzymes are inhibited, DNA SSBs accumulate due to the lack of repair, leading to replication forks and subsequent DSBs, and ending in chromosomal damage. 4 In a normal cell, these breaks are repaired via homologous recombination by proteins encoded by BRCA1 or BRCA2. PARP-inhibitors can kill tumors in BRCA1/BRCA2-defective cells via synthetic lethality: the increase in SSBs via PARP inhibition leads to DSBs that cannot be repaired by the mutated BRCA-related proteins, thus killing the cell.5

PARP inhibitors are currently utilized in many types of cancer, including metastatic breast cancer. The OlympiAD trial was a phase III trial of olaparib in metastatic breast cancer patients with HER2-negative BRCA pathogenic variants, comparing olaparib to conventional chemotherapy.6 OlympiAD showed olaparib had better progression-free survival than conventional chemotherapy and paved the way for olaparib to be approved by the Food and Drug Administration (FDA) for HER2-negative metastatic germline BRCA-mutated breast cancer.

Conversely, the clinical benefit of PARP inhibitors in the adjuvant setting for early-stage breast cancer has yet to be determined. Adjuvant therapies for HER2-negative breast cancers remain scarce as Capecitabine is the only adjuvant therapy currently recommended by the National Comprehensive Cancer Network (NCCN) following systemic therapy for triple negative breast cancer (TNBC).7 As a response to the paucity of treatment options in the adjuvant setting, OlympiA was designed to test the clinical effectiveness of Olaparib as an adjuvant therapy for HER2-negative, BRCA-mutated patients following the completion of standard adjuvant or neoadjuvant chemotherapy and local therapy.

OlympiA was a prospective, multicenter, multinational, double-blind clinical trial with eligible patients assigned to receive either olaparib 300mg or placebo orally twice daily for 52 weeks. Inclusion criteria included the following: 18 years of age or older, germline BRCA1 or BRCA2 pathogenic or likely pathogenic variant, and high-risk HER2-negative primary breast cancer following neoadjuvant or adjuvant chemotherapy. Exclusion criteria included non-detrimental BRCA1 and/or BRCA2 mutations, evidence of cancer metastasis, exposure to an investigational agent within the previous 30 days prior to randomization, received chemotherapy within 3 weeks or radiotherapy within 2 weeks of randomization, concomitant use of medications that may interact with olaparib, or a secondary cancer. Patients were also excluded if they were pregnant or breast-feeding.

The primary efficacy outcome for OlympiA was the time from randomization until the date of the first occurrence of ipsilateral invasive breast tumor, locoregional invasive disease, distant recurrence, contralateral invasive breast cancer, second primary invasive cancer, and death from any cause. Secondary endpoints included distant disease-free survival, overall survival, and safety.

OlympiA randomized patients from June 2014 to May 2019 with 1836 patients randomly assigned to either olaparib or placebo. At the 3-year mark, the percentage of patients alive and free of invasive disease was 85.9% in the olaparib treatment arm compared to 77.1% in the placebo arm (difference, 8.8 percent; 95% CI, 4.5 to 13). Invasive disease-free survival was also found to be longer in the olaparib treatment arm compared to the placebo, with olaparib providing a 42% lower risk of death compared to the placebo treatment (hazard ratio 0.58; 99.5% CI, 0.41 to 0.82). The olaparib treatment arm also saw a higher distant disease-free survival at the 3 year mark (87.5% vs. 80.4%; difference, 7.1%; 95% CI, 3 to 11.1).

OlympiA demonstrated that olaparib treatment given for 52 weeks as oral adjuvant therapy following neoadjuvant or adjuvant chemotherapy results in significantly longer survival free of invasive or distant disease when compared to placebo in HER2-negative, BRCA-mutated patients. At the start of the OlympiA trial, there were no approved targeted adjuvant therapies for HER2-negative disease. Prior to the closure of OlympiA data collection, the Create-X trial indicated the clinical effectiveness of capecitabine in the adjuvant treatment of TNBC,8 Seeing that OlympiA did not directly compare olaparib to capecitabine, it is impossible to prove superiority of one agent over the other at the present time. However, following the publication of OlympiA, the American Society of Clinical Oncology (ASCO) and NCCN issued an update to their guideline recommendations to include one year of adjuvant olaparib for eligible patients.9

In summary, OlympiA demonstrated that olaparib given as adjuvant therapy following neoadjuvant or adjuvant chemotherapy in patients with high-risk, HER2-negative early-stage breast cancer with a germline BRCA mutation can increase survival at the 3-year mark, free of invasive or distant disease when compared to placebo. While olaparib is not commonly preferred due to its adverse event profile,10 further studies will need to be done to determine the clinical effectiveness of olaparib vs. capecitabine.

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