Newsletter

Prostate Cancer 101, Inc.

http://prostatecancer101.org

December, 2019

The Prostate Cancer Information and Support Group of the Mid-Hudson

Prescribing Exercise as Cancer Treatment: A Conversation with Dr. Kathryn Schmitz Ph.D

of NCI's Division of Cancer Epidemiology and Genetics

The recommendations, as outlined in three related publications, are the products of the panel's comprehensive review of the scientific evidence on physical activity and cancer. In this conversation, Dr. Schmitz, immediate past-president of ACSM, discusses the research findings connecting physical activity with improved cancer outcomes and what these new guidelines mean for health care providers and survivors.

An expert panel has updated recommendations on exercise for people undergoing treatment for cancer and long-term survivors.

How would you describe the state of what we know about the role of exercise for people with cancer and for long-term survivors?

In the past, clinicians typically advised their cancer patients to rest and avoid physical activity. However, what we learned from early exercise research in the 1990s and 2000s contradicted that advice. In fact, the field of exercise oncology—exercise and cancer—has grown exponentially in the past decade. There On October 16, 2019, an expert panel convened by the American College of Sports Medicine (ACSM) released updated guidance and recommendations on the role of physical activity and exercise in cancer prevention and survivorship. The panel was co-chaired by Kathryn Schmitz, Ph.D., M.P.H., of the Department of Public Health Sciences at the Penn State College of Medicine, and Charles Matthews, are more than 1,000 randomized controlled trials in this field. Multiple large epidemiologic and preclinical studies have also been completed, all of which have expanded our knowledge.

We now have the evidence to tell us, with great confidence, that those living with and beyond cancer will benefit from being more physically active. We are at a point in the evolution of the field where we can dose exercise precisely, just as we do with drugs, to address several cancer-related health outcomes.

Which cancer-related health outcomes can be improved with exercise?

The ACSM panel found evidence that providing specific exercise prescriptions for a number of cancer-related health outcomes benefitted people living with or beyond cancer. As an example, we saw strong evidence that an exercise program consisting of a half hour of aerobic exercise three times weekly was sufficient to improve anxiety, depression, fatigue, quality of life, and physical function in cancer survivors.

There was also evidence of a benefit for most of those same outcomes from twice-weekly resistance exercise. However, anxiety and depression do not appear to be improved by resistance training alone, but they do improve with resistance training in combination with aerobic training. In addition, the panel concluded that there is no increased risk of lymphedema from twice-weekly resistance training.

The current evidence is still insufficient as to whether exercise can improve other health outcomes, such as peripheral neuropathy, cardiotoxicity, cognitive functioning, pain, or chemotherapy completion rate.

Can exercise improve survival for individuals with cancer?

Yes. We concluded from the evidence that exercise after a diagnosis of breast, colon, or prostate

cancer is associated with longer survival. While there is insufficient evidence to draw the same conclusion for all cancer types, there are enough benefits of physical activity, in general, that we recommend that survivors of all cancers follow the general public health recommendations for physical activity: 2 and 1/2 to 5 hours per week of moderate-intensity activity, or 1 and 1/4 to 2 and 1/2 hours per week of vigorous activity.

Of course, an exercise regimen should be tailored to fit each cancer patient's preference and functional status. To prescribe a safe and effective exercise program, the patient's age, type and stage of cancer, treatment side effects, and other health considerations should be evaluated first.

Only a minority of cancer survivors exercise regularly. What will it take to shift the general understanding about the relationship between cancer and exercise?

We need a paradigm shift here, as we have had with exercise and heart disease. If we ask the average person on the street if exercise is good for the heart, he or she will say yes. That was not always the case, but at some point there was a shift. So, we need a multipronged initiative to encourage a change in thinking. A major effort should be geared toward increasing awareness of the importance of exercise among cancer patients, as well as providers, caregivers, and the general public.

ACSM has just started a new initiative called Moving Through Cancer, which focuses on increasing awareness of the value of exercise for cancer survivors, along with educating the cancer clinician workforce to refer, coordinate, and prescribe exercise; expanding opportunities to exercise; and shifting policy so that, by 2029, exercise is standard practice for all patients living with and beyond cancer.

We believe that increasing awareness will involve reaching out to mainstream and social media, updating textbooks for exercise science undergraduates, and developing continuing education for oncology practitioners, among other efforts.

My hope is that someday, if you ask anyone walking down the street whether exercise is valuable for cancer survivors, the response will be an emphatic "Yes."

Can Exercise Help Treatment-Related Side Effects?

In addition to demonstrating a number of exercise-related benefits for cancer survivors, the ACSM reports also highlight several emerging areas of research, including whether exercise can ameliorate treatment-related side effects (e.g., cardiotoxicities, peripheral neuropathy) or facilitate treatment tolerance and effectiveness.

According to Frank Perna, Ed.D., Ph.D., program director in NCI's Division of Cancer Control and Population Sciences (DCCPS), the evidence for exercise's impact on many of these outcomes is promising but still insufficient. However, he explained, DCCPS is supporting studies that will help to strengthen the evidence base and address these questions and others related to the impact of exercise on cancer.

What is the most important take-home message for providers in these updated guidelines?

Since many cancer survivors are sedentary, the first and most important message providers can give their patients is that they don't need to become marathoners to reap the benefits of exercise. Going from no exercise to some exercise will be useful for their health.

The ACSM's recommendation to providers is simple: Ask cancer patients about their physical activity. If their activity is inadequate, providers should advise their patients to do more.

Even if that is all providers have time to do, it demonstrates to patients that physical activity is an important part of managing their health and lays out the expectation that being physically active is healthier than being sedentary. This is true even for patients with advanced disease and those experiencing limitations, although those cancer patients will need a medically supervised program.

Are clinicians prepared for these discussions?

Adding yet another task to a clinician's to-do list for patient encounters is a challenge. But providers who routinely ask their patients about physical activity and provide referrals to exercise programs told us their patients both enjoy and feel empowered by the exercise program. This, in turn, can become a bright spot in the clinical encounter and encourage the practice of discussing exercise.

The primary reason that providers do not have these discussions with cancer patients is lack of time. However, some have expressed concern that they don't have the training needed to answer questions about exercise or that they may feel uncertain about the safety of exercise for a particular patient—and frankly, most people, and particularly health care providers, don't like being faced with questions they cannot answer.
This is what the Moving Through Cancer initiative is eager to address. The website helps providers refer patients to places where their questions can be answered and high-quality exercise programs

can be provided. Since most exercise programs require physician approval before patient participation, physicians are key to recommending such programs to their patients.

What sorts of behavioral and infrastructure changes are needed to incorporate exercise into standard cancer care?

In addition to raising awareness, we need to find ways to make exercise oncology a standard part of cancer care. This would include professional development for cancer care providers that incorporates training in how to have brief, informative, and effective conversations about physical activity with patients. It would also include professional development for rehabilitation practitioners, such as physiatrists, occupational, and physical therapists; and exercise science students and fitness professionals.

There is a need to develop instruction that can be dropped directly into curricula so that these practitioners are armed with knowledge about how best to help cancer patients become physically active, including how to design exercise prescriptions that deliver the right amount of exercise to meet the specific needs and abilities of their patients.

Sufficient resources must be allocated by insurers and communities so that high-quality exercise programs are widely available and accessible. The Moving Through Cancer initiative has a growing registry that we hope will become a trusted resource for oncology professionals to use for referrals to appropriate programs, as well as a resource to help patients and families find programs near them.

We also urge investigators to help advance the science in this area. There is a rich evidence base on exercise and cancer, so we're encouraging researchers to conduct implementation science and health care delivery research to better understand how to encourage the adaptations needed so that all people living with and beyond cancer can be as active as possible.

Is there a role for survivors in helping to advance progress in this area?

There are multiple examples of patients being the catalyst to shift cancer care. Survivors and patient advocates can help create change in clinical cancer care by demanding that practitioners assess, advise, and refer patients to appropriate exercise programs.

The ACSM expert panel—which included NCI researchers Charles Matthews, Ph.D., Frank Perna, Ed.D., Ph.D., and Steven Moore, Ph.D., M.P.H.—reported its findings and associated guidelines in three recently published papers:

Exercise Is Medicine in Oncology: Engaging Clinicians to Help Patients Move Through CancerExit Disclaimer

American College of Sports Medicine Roundtable Report on Physical Activity, Sedentary Behavior, and Cancer Prevention and ControlExit Disclaimer

Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary RoundtableExit Disclaimer

Source URL: https://www.cancer.gov/news-events/cancer-currents-blog/2019/cancer-survivors-exercise-guidelines-schmitz?cid=eb_govdel

Contributions

Our thanks to those who help us continue our outreach

Robert & Agnes Dietrich
Lewis & Helen Gardner
Robert & Mary Gauverau
Manfred & Birgit Kastner
Bob Miggins

In Memory of Ron Koster
Walter & Susan Libenson

In Memory of Ward Miller
Walt & Diane Sutkowski

In Memory of Keith Ogden
Barbara Ogden

Prostate Cancer 101 is a 501 (c) (3) IRS approved non-profit organization. Your ***tax deductible*** donations should be mailed to:

Prostate Cancer 101
c/o Diane Sutkowski, Treasurer
8 Alcazar Avenue
Kingston NY 12401-4302

We need your donations to help continue our outreach. Remember – we are all Volunteers.

In Memoriam
Ward Miller – 1927-2019

We are saddened to report of the passing of our good

friend, faithful donor and longtime assistant keeper of the mailing list, Ward Miller. Until about a year ago Ward was my double check for the member and mailing lists and would print out the labels to mail to me for the newsletter. He was a wonderful balance in keeping things straight and keeping me in equilibrium, for which I am grateful.

Ward was a man of amazing abilities and accomplishments. He majored in physics at the University of Chattanooga, spent 14 years in the Army Air Corps during WWII and the Korean Conflict rising from Master Sergeant to Second Lieutenant. He later served as an aide to the Assistant Secretary of the Army, commanded the 24th Signal Battalion in Korea and later the 99th Strategic Signal Support Company at Ft. Dix, NJ. He retired as a Major in 1958 with eleven medals and ribbons.

He had a career with IBM starting in Endicott retiring as a Senior Programmer in 1987, which gave him a chance to pursue so many additional avenues in a busy fulfilling life. While in Endicott he was lucky enough to meet his heart's desire, his wife, Nina, whom he married in December, 1952. Nina passed away in September, 2018 just a year plus a few weeks prior to Ward after 66 years of a loving relationship. He missed her more than we can say.

Ward won awards as a freelance photographer, became a licensed pilot, taught antique clock repair and helped with many newsletters for various clubs. He was a life Member volunteer firefighter, EMT with LaGrange and a weather observer for the National Weather Service. The list of his memberships and accomplishments could go on for pages. He was a man to be admired and respected.

Let it be known, that here was a truly good man, who loved his wife, his children, his country and most everyone he met. It was indeed my honor to work alongside him at PCa101 for all these years. Well done, my dear friend. I will miss and treasure the time we shared and am privileged to have gotten to know you.

D.S.

Hyperthermia in Cancer Treatment

What is hyperthermia?

Hyperthermia (also called thermal therapy or thermotherapy) is a type of cancer treatment in which body tissue is exposed to high temperatures (up to 113°F). Research has shown that high temperatures can damage and kill cancer cells, usually with minimal injury to normal tissues (1). By killing cancer cells and damaging proteins and structures within cells (2), hyperthermia may shrink tumors.

Hyperthermia is under study in clinical trials (research studies with people) and is not widely available.

How is hyperthermia used to treat cancer?

Hyperthermia is almost always used with other forms of cancer therapy, such as radiation therapy and chemotherapy (1, 3). Hyperthermia may make some cancer cells more sensitive to radiation or harm other cancer cells that radiation cannot damage. When hyperthermia and radiation therapy are combined, they are often given within an hour of each other. Hyperthermia can also enhance the effects of certain anticancer drugs.

Numerous clinical trials have studied hyperthermia in combination with radiation therapy and/or chemotherapy. These studies have focused on the treatment of many types of cancer, including sarcoma, melanoma, and cancers of the head and neck, brain, lung, esophagus, breast, bladder, rectum, liver, appendix, cervix, and peritoneal lining (mesothelioma) (1, 3–7). Many of these studies, but not all, have shown a significant reduction in tumor size when hyperthermia is combined with other treatments (1, 3, 6, 7). However, not all of these studies have shown increased survival in patients receiving the combined treatments (3, 5, 7).

What are the different methods of hyperthermia?

Several methods of hyperthermia are currently under study, including local, regional, and whole-body hyperthermia (1, 3–9).

In local hyperthermia, heat is applied to a small area, such as a tumor, using various techniques that deliver energy to heat the tumor. Different types of energy may be used to apply heat, including microwave, radiofrequency, and ultrasound. Depending on the tumor location, there are several approaches to local hyperthermia:

- **External** approaches are used to treat tumors that are in or just below the skin. External applicators are positioned around or near the appropriate region, and energy is focused on the tumor to raise its temperature.
- **Intraluminal** or **endocavitary** methods may be used to treat tumors within or near body cavities, such as the esophagus or rectum. Probes are placed inside the cavity and inserted into the tumor to deliver energy and heat the area directly.
- **Interstitial** techniques are used to treat tumors deep within the body, such as brain tumors. This technique allows the tumor to be heated to higher temperatures than external techniques. Under anesthesia, probes or needles are inserted into the tumor. Imaging techniques, such as ultrasound, may be used to make sure the probe is properly positioned within the tumor. The heat source is then inserted into the probe. Radiofrequency ablation (RFA) is a type of interstitial hyperthermia that uses radio waves to heat and kill cancer cells.

In **regional hyperthermia**, various approaches may be used to heat large areas of tissue, such as a body cavity, organ, or limb.

Deep tissue approaches may be used to treat cancers within the body, such as cervical or bladder cancer. External applicators are positioned around the body cavity or organ to be treated, and microwave or radiofrequency energy is focused on the area to raise its temperature.

Regional perfusion techniques can be used to treat cancers in the arms and legs, such as melanoma, or cancer in some organs,

such as the liver or lung. In this procedure, some of the patient's blood is removed, heated, and then pumped (perfused) back into the limb or organ. Anticancer drugs are commonly given during this treatment.

Continuous hyperthermic peritoneal perfusion (CHPP) is a technique used to treat cancers within the peritoneal cavity (the space within the abdomen that contains the intestines, stomach, and liver), including primary peritoneal mesothelioma and stomach cancer. During surgery, heated anticancer drugs flow from a warming device through the peritoneal cavity. The peritoneal cavity temperature reaches 106-108°F.

Whole-body hyperthermia is used to treat metastatic cancer that has spread throughout the body. This can be accomplished by several techniques that raise the body temperature to 107-108°F, including the use of thermal chambers (similar to large incubators) or hot water blankets.

The effectiveness of hyperthermia treatment is related to the temperature achieved during the treatment, as well as the length of treatment and cell and tissue characteristics (1, 2). To ensure that the desired temperature is reached, but not exceeded, the temperature of the tumor and surrounding tissue is monitored throughout hyperthermia treatment (3, 5, 7). Using local anesthesia, the doctor inserts small needles or tubes with tiny thermometers into the treatment area to monitor the temperature. Imaging techniques, such as CT (computed tomography), may be used to make sure the probes are properly positioned (5).

Does hyperthermia have any complications or side effects?

Most normal tissues are not damaged during hyperthermia if the temperature remains under 111°F. However, due to regional differences in tissue characteristics, higher temperatures may occur in various spots. This can result in burns, blisters, discomfort, or pain (1, 5, 7). Perfusion techniques can cause tissue swelling, blood clots, bleeding, and other damage to the normal tissues in the perfused area; however, most of these side effects are temporary. Whole-body hyperthermia can cause more serious side effects, including cardiac and vascular disorders, but these effects are uncommon (1, 3, 7). Diarrhea, nausea, and vomiting are commonly observed after whole-body hyperthermia (7).

What does the future hold for hyperthermia?

A number of challenges must be overcome before hyperthermia can be considered a standard treatment for cancer (1, 3, 6, 7). Many clinical trials are being conducted to evaluate the effectiveness of hyperthermia. Some trials continue to research hyperthermia in combination with other therapies for the treatment of different cancers. Other studies focus on improving hyperthermia techniques.

To learn more about clinical trials, call NCI's Cancer Information Service at 1–800–4–CANCER (1–800–422–6237) or visit Clinical Trials Information for Patients and Caregivers.

Selected References

1.van der Zee J. Heating the patient: a promising approach? Annals of Oncology 2002; 13 (8):1173–1184. [PubMed Abstract]

2.Hildebrandt B, Wust P, Ahlers O, et al. The cellular and molecular basis of hyperthermia. Critical Reviews in Oncology/ Hematology 2002; 43(1):33–56. [PubMed Abstract]

3.Wust P, Hildebrandt B, Sreenivasa G, et al. Hyperthermia in combined treatment of cancer. The Lancet Oncology 2002; 3 (8):487–497. [PubMed Abstract]

4.Alexander HR. Isolation perfusion. In: DeVita VT Jr., Hellman S, Rosenberg SA, editors. Cancer: Principles and Practice of Oncology. Vol. 1 and 2. 6th ed. Philadelphia: Lippincott Williams and Wilkins, 2001.

5.Falk MH, Issels RD. Hyperthermia in oncology. International Journal of Hyperthermia 2001; 17 (1):1–18. [PubMed Abstract]

6.Dewhirst MW, Gibbs FA Jr, Roemer RB, Samulski TV. Hyperthermia. In: Gunderson LL, Tepper JE, editors. Clinical Radiation Oncology. 1st ed. New York, NY: Churchill Livingstone, 2000.

7.Kapp DS, Hahn GM, Carlson RW. Principles of Hyperthermia. In: Bast RC Jr., Kufe DW, Pollock RE, et al., editors. Cancer Medicine e.5. 5th ed. Hamilton, Ontario: B.C. Decker Inc., 2000.
8.Feldman AL, Libutti SK, Pingpank JF, et al. Analysis of factors associated with outcome in patients with malignant peritoneal mesothelioma undergoing surgical debulking and intraperitoneal chemotherapy. Journal of Clinical Oncology 2003; 21(24):4560–4567. [PubMed Abstract]

9.Chang E, Alexander HR, Libutti SK, et al. Laparoscopic continuous hyperthermic peritoneal perfusion. Journal of the American College of Surgeons 2001; 193(2):225–229. [PubMed Abstract]

Related Resources

Chemotherapy and You: Support for People With Cancer
Radiation Therapy and You: Support for People With Cancer

Radiation Therapy to Treat Cancer

Taking Part in Cancer Treatment Research Studies

Reviewed: August 31, 2011

Source URL: https://www.cancer.gov/about-cancer/treatment/types/surgery/hyperthermia-fact-sheet

Altering Diet Enhances Response to Cancer Treatments in Mice

September 3, 2019, by NCI Staff

A diet low in methionine, a nutrient cells need to repair DNA damage, may make therapies like chemotherapy more effective.

People must eat to survive. And the cells that make up the body eat too. Or more accurately, cells break down and rebuild food into the individual molecules they need to stay alive and grow. This complex network of processes is called cellular metabolism.

Cancer cells can alter their metabolism to survive, so targeting cancer cell metabolism has become of great interest to researchers. Questions being asked include: Is it possible to attack a tumor's nutritional needs as part of cancer treatment? And could this be done by tweaking a cancer patient's diet?

A new NCI-supported study suggests that the latter may be possible. In the study, researchers showed that feeding mice a diet very low in the nutrient methionine improved the ability of chemotherapy and radiation therapy to shrink tumors.

When the researchers tested a low methionine diet in six healthy adults, methionine levels in their bodies fell and they experienced metabolic changes similar to those seen in the mouse studies. However, the study was not designed to test the effect of methionine restriction on cancer treatment in humans.

The concept of using specific dietary changes to enhance cancer treatment "is really at the very early stages," said Jason Locasale, Ph.D., of Duke University, who led the new study. "And there's not going to be one be-all, end-all diet for [treating] cancer. But these aspects of diet seem to have all kinds of really interesting effects on cancer outcomes, and we have to take them seriously."

A Dietary Vulnerability

Methionine is an essential amino acid that plays an important role in cellular metabolism. The body cannot produce methionine from scratch, so it must come from food. Methionine is most prevalent in animal products, such as lean meat and eggs, but also can be found in lower quantities in plant sources.

Normal cells can also recycle methionine that has already been taken into the body, explained Michael Espey, Ph.D., of NCI's Division of Cancer Biology, who was not involved in the study. But some cancer cells lose this ability when they mutate, he added. This means that they become completely reliant on the diet for their methionine requirements.

Methionine is needed by cells to repair damaged DNA and reduce oxidative stress, Dr. Espey explained. So depleting methionine from cancer cells targeted by DNA-damaging therapies, such as chemotherapy or radiation therapy, "may enhance the ability of these treatments to kill the cancer cells," he said.

"Cancer researchers recognized this feature and surmised that methionine could be a potential weakness,

because anything that a cancer cell has become reliant on is a good target, as long as you have some sort of treatment to attack that vulnerability," said Dr. Espey.

In their study, Dr. Locasale and his colleagues first measured whether cutting the amount of methionine in the diet of mice could quickly reduce the amount of methionine available to cells in the body. They found that switching mice to a diet about seven times lower in methionine than normal reduced the levels in cells after 2 days.
They then fed the low methionine diet to mice carrying tumors derived from either of two types of human cancer cells. Methionine restriction alone greatly slowed the growth of tumors derived from one of the cell lines, and slowed it somewhat in tumors derived from the other cell line.

Enhancing Treatment Effects

The researchers next tested whether adding dietary methionine restriction to cancer treatments in mice could magnify the effects of those treatments.
In mice bearing tumors derived from human colorectal cancer, low doses of the DNA-damaging chemotherapy drug 5-fluorouracil (5-FU) failed to shrink the tumors. But when the mice were fed the methionine-restricted diet during 5-FU treatment, their tumors shrank. Analyses of metabolism showed that the production of molecules needed to repair DNA, which requires methionine, had been altered as expected.

The researchers also tested the combination of methionine restriction and radiation therapy in mice engineered to grow aggressive soft tissue sarcomas. The combination of the methionine-restricted diet plus radiation therapy slowed tumor growth by about 50% compared with the combination of a normal diet plus radiation.

More Knowledge Needed
In a proof-of-concept follow-up experiment, six healthy middle-aged adults were recruited to eat a low methionine diet for 3 weeks. The diet contained about 80% less methionine than an average normal diet. Protein was mainly supplied through a methionine-free dietary supplement. The diet also included fruits, vegetables, and refined grains, which are naturally low in methionine.
In the human study, the low methionine diet quickly reduced the amount of the amino acid available to participants' cells and altered the cells' metabolism, similar to what the researchers had observed in mice fed a methionine-restricted diet.

Methionine restriction "is a potential strategy" to treat cancer, Dr. Espey said. "But more research is needed into the correct dose and timing, and the amount of restriction that's necessary to balance the positive effects on enhancing cancer therapy versus the negative effects on the body's normal physiology."

Among other things, methionine is needed to maintain nerve cells and muscle mass, he added. "So there could potentially be side effects of restricting methionine in the diet [in the long term]."

"We can speculate that there's going to be all kinds of interesting nutritional interventions that could influence cancer, but we're nowhere near the point of really being able to prescribe these dietary interventions," added Dr. Locasale.
For other diseases where metabolism is known to play an important role—such as cardiovascular disease and diabetes—dietary interventions are an important part of treatment, Dr. Locasale said.

"Over the last 10-15 years, we've come to understand that cancer also has a huge metabolic component to it," he continued. "Cancer cells have different nutrient requirements and different metabolic demands than normal tissue. But we have almost no knowledge of how nutrition might influence demands. We're just starting [to learn] right now."

Source URL: https://www.cancer.gov/news-events/cancer-currents-blog/2019/targeting-cancer-metabolism-low-methionine-diet?cid=eb_govdel

FDA Approves Bayer's Nubeqa® (darolutamide), a New Treatment for Men with Non-Metastatic Castration-Resistant Prostate Cancer

July 30, 2019

WHIPPANY, N.J., July 30, 2019 /PRNewswire/ — The U.S. Food and Drug Administration (FDA) today approved Nubeqa® (darolutamide), an androgen receptor inhibitor (ARi), for the treatment of patients with non-metastatic castration-resistant prostate cancer (nmCRPC). The FDA approval is based on the Phase III ARAMIS trial evaluating Nubeqa plus androgen deprivation therapy (ADT), which demonstrated a highly significant improvement in the primary efficacy endpoint of metastasis-free survival (MFS), with a median of 40.4 months versus 18.4 months for placebo plus ADT ($p<0.0001$). MFS is defined as the time from randomization to the time of first evidence of blinded independent central review (BICR)-confirmed distant metastasis or death from any cause within 33 weeks after the last evaluable scan, whichever occurred first. Nubeqa was approved under the FDA's Priority Review designation, which is reserved for medicines that may provide significant improvements in the safety or effectiveness of the treatment for serious conditions.

"Patients at this stage of prostate cancer typically don't have symptoms of the disease. The overarching goals of treatment in this setting are to delay the spread of prostate cancer and limit the burdensome side effects of therapy," said Matthew Smith, M.D., Ph.D., Director of the Genitourinary Malignancies Program, Massachusetts General Hospital Cancer Center. "This approval marks an important new option for the prostate cancer community."

In the U.S., over 73,000 men are estimated to be diagnosed with castration-resistant prostate cancer (CRPC) in 2019. About 40 percent of these patients have prostate cancer that has not spread to other parts of the body and is also associated with a rising prostate-specific antigen (PSA) level, despite a castrate testosterone level, which is known as nmCRPC. This is important because about one-third of men with nmCRPC go on to develop metastases within two years. PSA monitoring is important to identify patients and help offset undertreatment in men before the disease spreads.

"We know that men with nmCRPC are still in the prime of their lives and are at a critical point in their disease when action needs to be taken," said Howard R. Soule, Ph.D., Executive Vice President and Chief Science Officer, Prostate Cancer Foundation (PCF). "For 26 years, PCF has been focused on research aimed at improving patient outcomes and we welcome the addition of new treatment options that provide men with more choices when working with their doctor to select what's right for them."

"With the approval of Nubeqa, we now have a new therapy that extends MFS and allows physicians greater flexibility to treat men living with nmCRPC," said Robert LaCaze, Member of the Executive Committee of Bayer's Pharmaceuticals Division and Head of the Oncology Strategic Business Unit at Bayer. "Bayer is proud to take this latest step forward in the nmCRPC treatment landscape. Nubeqa is the newest addition to our prostate cancer portfolio and reflects Bayer's commitment to finding treatments for men at different stages along the prostate cancer continuum."

In the ARAMIS trial, both arms showed a 9 percent discontinuation rate due to adverse reactions.1 The most frequent adverse reactions requiring discontinuation in patients who received Nubeqa included cardiac failure (0.4 percent), and death (0.4 percent). Adverse reactions occurring more frequently in the Nubeqa arm (≥2 percent over placebo) were fatigue (16 percent versus 11 percent), pain in extremity (6 percent versus 3 percent) and rash (3 percent versus 1 percent). Nubeqa was not studied in women and there is a warning and precaution for embryo-fetal toxicity.

Overall survival (OS) and time to pain progression were additional secondary efficacy endpoints.1 OS data were not yet mature at the time of final MFS analysis. The MFS result was supported by a delay in time to pain progression, defined as at least a 2-point worsening from baseline of the pain score on Brief Pain Inventory-Short Form or initiation of opioids, in patients treated with Nubeqa as compared to placebo. Pain progression was reported in 28 percent of all patients on study.
Bayer has filed for approval of Nubeqa in the European Union (EU), Japan, and with other health authorities. Nubeqa is developed jointly by Bayer and Orion Corporation, a globally operating Finnish pharmaceutical company.

Nubeqa will be available in oral tablets for adults. For more information, visit www.NUBEQA.com. For additional information, please visit Bayer Website.

Source URL: https://www.pcf.org/news/fda-approves-bayers-nubeqa-darolutamide-a-new-treatment-for-men-with-non-metastatic-castration-resistant-prostate-cancer/

Cancer Mutations and Immunotherapy Drugs

July 23, 2019 | By JANET FARRAR WORTHINGTON

Picture, if you will, a laundromat. One of the washing machines is messed up; it stops in mid-wash cycle, and leaves your clothes all wet and soapy. Which one is it? From the outside, they all look the same. If nobody tells the repair guy which one is broken, how's he going to know which one to fix?

The immune system's great warrior cells, called T cells, face a similar predicament with some types of cancer, including prostate cancer – because the cancerous cells don't look that different from normal cells. If the T cells could speak, they might say, "What am I, psychic? How am I supposed to know which ones I'm supposed to kill?" Hard to believe, but many cancer cells aren't considerate enough to advertise their presence to the immune cells that would gladly kill them! From cancer's standpoint, this is a win.

But some cancers, to the immune system, stick out like the proverbial sore thumb. They look sketchy. This makes it a lot easier for the T cells to notice them. **Why do some cancers look like the enemy invaders they are? Genetic mutations.** Our cells copy DNA constantly, to make new cells. Sometimes, our little genetic copiers make mistakes. They make typos, and sometimes, despite our genetic army of very good spell-checkers and quality-control experts, these typos don't get caught.

When one of these spell-checker genes, called a DNA mismatch repair gene, is defective, these mistakes start to add up over time. With each mutation, the cancer cell looks just a little bit different. The rate of these mutations can be estimated by looking at their results: **microsatellite alterations. These are genetic error messages, short bits of repeated DNA.**
Cancer cells that have a lot of mutations – as estimated by the number of altered microsatellites — are much easier for the immune system to see. These pieces of DNA are biomarkers, and a pathologist looking at the cancer under the microscope, would say these multi-mutated cancer cells are **"microsatellite instability-high," or MSI-H.**

In colon cancer, for example, the presence of MSI-H is so important, and so common, that knowing this biomarker status is the key to determining treatment: in MSI-H patients with several forms of cancer, certain immunotherapy drugs are much more likely to work than they are in other patients.

What about prostate cancer? Only an estimated 3 to 4 percent of men with prostate cancer have **MSI-H, mismatch repair-deficient (dMMR)** cancer. But for those men, knowing that they are in this **subgroup of patients** could make a **huge difference in their treatment and prognosis.**

"We used to put everyone with advanced prostate cancer in the same category," says PCF Young Investigator Wassim Abida, M.D., Ph.D., medical oncologist at Memorial Sloan Kettering Cancer Center. The thinking was, "if it's cancer that is sensitive to hormones, then everyone gets the same androgen deprivation therapy (ADT). Then, if that doesn't work, everyone gets the same chemo. But now we're starting to understand the biology of the disease, the mutations in DNA that can drive the prostate cancer to grow. And based on that, we can develop selected treatments for different groups of patients, depending on what the biology of their particular cancer is. Now we need to know: how is person A's disease different from person B's disease, and how can we use that knowledge to treat them differently?"

There are several important points of interest about these subgroups, or phenotypes of cancer: One is

that, in terms of treatment**, the particular gene may matter more than the organ it happens to affect.** For example, a man with prostate cancer who has the same mutated gene as a person with colon cancer, or melanoma, or breast cancer, or another type of cancer, may have more in common with that person than with another man who has prostate cancer, but who has a different genetic mutation.

Also, "even though we can identify patients with MSI-H cancer, **not all of them respond to immunotherapy,**" says Abida. "And some who *do* respond eventually have progression and growth of their disease, and we don't know why," although he and colleagues are working hard to find answers. Another key point: MSI can develop as the cancer evolves, which means that it may not be present in a man's initial needle biopsy for prostate cancer – but it could be found in a biopsy of a metastatic tumor. One day, it might be found by looking at circulating tumor cells in the blood, but that technology is not quite ready yet.

Abida recently was lead author of a large study published in *JAMA Oncology*, looking at the prevalence of MSI in prostate cancer and its response to pembrolizumab, an immunotherapy drug called a "checkpoint inhibitor." In the study, Memorial Sloan Kettering investigators did "molecular profiling" on biopsied tumors from more than a thousand patients with prostate cancer. Of 1,033 patients, just slightly over 3 percent (32) had "MSI-H/dMMR" prostate cancer. Eleven of these men, who had castration-resistant prostate cancer, received pembrolizumab; of these, six had a greater than 50 percent drop in their PSA levels, and four men had radiographic responses – on images, their cancer appeared significantly smaller. "Five of these six responders were still on therapy for as long as 89 weeks," when the study was written.

So, although just about 3 percent of men were in this MSI-H/dMMR subgroup, some of them responded to a checkpoint-inhibitor, and some of them responded exceptionally well. "This is our future," says medical oncologist and molecular biologist Jonathan Simons, M.D., CEO of the Prostate Cancer Foundation. "Precision diagnosis and precision treatment. One single form of treatment may not ever work for all men with metastatic prostate cancer. But if we can't help 100 percent of men with one treatment, we can find multiple treatments that each work for smaller groups of patients. These exceptional responders are the key to helping us understand how."

https://www.pcf.org/c/cancer-mutations-and-immunotherapy-drugs/

About Janet Farrar Worthington

Janet Farrar Worthington is an award-winning science writer and has written and edited numerous health publications and contributed to several other medical books. In addition to writing on medicine, Janet also writes about her family, her former life on a farm in Virginia, her desire to own more chickens, and whichever dog is eyeing the dinner dish.

Source URL: https://www.pcf.org/c/cancer-mutations-and-immunotherapy-drugs/?utm_source=NewsPulse&utm_medium=email&utm_campaign=JULY19NP

Prostate Cancer 101, Inc.
8 Alcazar Avenue
Kingston, NY 12401-4302

1st Tuesday

4:30 p.m. monthly

SEMINAR
For
Newly Diagnosed

Hurley Reformed Church Hall, Hurley, NY

Membership and Administration

If you have *moved*, have a *new email* or *phone* or *no longer wish to receive the newsletter*, please let us know.

It's up to you to keep us informed so we can keep you informed.

Diane Sutkowski
845-331-7241
dsutkowski@hvc.rr.com

PCa 101 Seminar
First Tuesday of every month

Gene Groelle 845-419-5128
Gro226@aol.com

Arlene Ryan 338-9229
ryanarlene918@gmail.com

Walt Sutkowski 331-7241
wsutkowski@hvc.rr.com

Diane Sutkowski 331-7241
dsutkowski@hvc.rr.com

Website & Newsletters

http://prostatecancer101.org

Walt Sutkowski
845-331-7241
wsutkowski@hvc.rr.com

Prostate Cancer 101 is a 501(c) (3) IRS approved non-profit organization