# Newsletter

## Prostate Cancer 101, Inc.

http://prostatecancer101.org

**March, 2021**

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


Thanks for the Memories
Gene Grolle
2/13/1933-2/21/2021

For the decades of devotion in helping educate so many men who came to the meetings wondering how much time they would have in life and left with a plan, a smile and in awe of all your knowledge. We can but simply say, thank you, Gene. You will be sorely missed, not only as an important member of our core group, but as a wonderful friend. There is a big hole in our organization and in our hearts, as in many of those who counted you among their loved ones.

One of five brothers born on a farm in Manitowoc, Wisconsin who truly lived the hard farm life, you came a long way and gained so many people's respect in that journey. You joined the Coast Guard at 18 in 1951 and got to see a bit of the world, which whet your appetite for the travels you enjoyed with your brothers, Milton, Llyod, Edgar and Harlan, the only survivor. Lo the tales to be told and the wisdom you imparted that you found along the way- India, China, Paris, Greece, Russia, tall ship cruises, a safari and so much more.

You shared some of these trips with your granddaughters and helped expand their horizons and give them wonderful memories.

After leaving the service, you attended the Milwaukee School of Engineering and then was hired by IBM where you worked till your retirement in 1987 and then continued with other companies till full retirement in 1998. You never lost your thirst for knowledge, as the Reverend Stickley said in his eulogy, "Gene could talk about almost everything." And we usually learned something in that conversation.

You cherished the time with your granddaughters., Daniella, Lia and Alissa and thought the world of your son-in-law, Dino, who you knew would love and care for your daughter, Cindy and the girls.

Gene didn't just talk, he did, as long as he

could. He was a member of the Hurley Fire Company and the Hurley Reformed Church as well as the Hurley Cemetery Board, not to mention our own Prostate Cancer 101, until his big heart failed him.

I'd like to share his final words of wisdom from his memoir, which his daughter, Cindy, put together so beautifully in book form and his granddaughter, Lia, read at the service.

1 – Pay yourself first. The only thing I ever listened to from my father! If at all possible, set aside ten percent of your salary. A rainy day will come somewhere in your life.

2 – When it comes to choices in your life, don't make the easiest or most comfortable choice for you at the moment. Make the choice that will work out best for you a year down the road.

3 – Something my grandkids have heard multiple times from Grandpa – use the intellect that God gave you to the max. Likewise, use the common sense and logic ability that God gave you to the max. Facts are great, but there are times that instincts will lead you to better decisions. Science is great, but application of science will always be somewhat instinctive.

Finally – develop social skills. Be a life-long learner and you'll never be bored. Travel every chance you get. You'll learn that all people, at the gut level, are much the same. There will always be jerks but white, black, brown or yellow, the majority are trying to live by the Golden Rule. As an added bonus of travel, you'll meet many good people (I still sporadically email with some of them to this day) and your geopolitical thinking will definitely change.

Gene, you made a difference and we thank you for that contribution to our lives – friend, guru, mensch, raconteur, sharer of laughter and wisdom and times together. We'll never forget the infamous "Night of the Limoncello." You are and will continue to be missed more than we can say. You filled that dash between the years with a full life and oh those memories.

D.S.

**Our thanks to those who help us to continue our outreach.**

Stephen Altschuler
William Byrne
John Carfagno
John & Rose Gaetjen
Mike & Evelyn Graziano
Ed Hill
Tom & Mary McConnell
Don Murat
Allan Stein
Michael & Judy O'Neill
Donald Van Loan

**In Memory of Gene Groelle**

Hurley Cemetery Assn.
Kathleen McLaren
Rebecca K Masters
Deborah Smiseth
Rev. Charles & Esther Stickley
Walt & Diane Sutkowski

**In Memory of Ron Koster**

Sanford & Nancy Bernstein

**In Honor of Walt Sutkowski**

Tom Donovan

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**Prostate Cancer 101**
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We need your donations to help continue our meetings and newsletters.

# Welcome to the world of precision medicine.

That sounds futuristic, like science fiction, or a cool exhibit, something that promises great things for tomorrow, something that's not here yet.

But this is different. We have new knowledge which has given us new targets for a smarter, more scientific approach that is helping all men with prostate cancer – but particularly those who need it most, men with metastatic prostate cancer. Even a year ago, many of these men had to endure the discouraging trial-and-error process of finding drugs that work for them. We hate trial and error; it takes up valuable time and wears you down.

One day, there won't be trial and error for prostate cancer drugs. Thanks to research funded by the Prostate Cancer Foundation, we have new targets – genes we now know to look for – that have led to new tests, which point us to specific drugs. Some of these drugs may not even be intended for prostate cancer, but for colon cancer or breast cancer; yet they are likely to work in your cancer if you have those same faulty genes, too.

One great thing about these drugs is that because they are gene-targeted, they don't poison your body, make you vomit, deplete your white blood cells or hurt your bone marrow.

In the past, because chemotherapy was so harsh, doctors did something that seems kind of odd now: they waited until nothing else worked before they gave it. This meant that by the time a man with metastatic prostate cancer got chemo, he was already very sick, and his cancer was very advanced. Now, because precision testing can give us a glimpse several years into the future, we know which men are likely to have their cancer come back, and we're not waiting around for that. When it comes to treating cancer cells, sooner is better than later.

It's not your father's prostate cancer anymore.

We're not done yet, not by a long shot. There's much more work to do. Already, the death rate is half of what it used to be 20 years ago. Many men who have metastatic prostate cancer are not going to die of it; with these new approaches, we are putting them into long remissions.

Our goal is cure, and we're not there yet. But we can see it; it's not just some vague hope, not wishful thinking. We're getting there, thanks to precision medicine. This is why we have raised and pushed $630 million dollars into research over the last two decades: to stop men from dying of prostate cancer.

**Precision Drugs:** If you have advanced prostate cancer and conventional hormonal therapy is no longer working, you might be helped by enzalutamide or abiraterone – but you might not. Now, instead of spending thousands of dollars and enduring months of trial and error, you can find out ahead of time if you should take one of these drugs. ***A simple blood test*** is just becoming widely available. It targets AR-V7, a particular androgen receptor variant (basically, AR-V7 allows the cancer to create an antidote to these drugs, canceling out their effects). If you are AR-V7 negative, then abiraterone or enzalutamide can put you into remission. If you are AR-V7 positive, then you will do better with another form of treatment.

I believe that every man should be asking his oncologist, "What's my AR-V7 status?" You need to help drive your treatment. This is so new, your oncologist may not know about it.

**Precision Diagnosis.** We call this clonotyping: basically, your cancer is one dot on the big data map of prostate cancer, and exactly where you are depends on the specific genes that are mutated in your cancer.

We now know that you don't just have prostate cancer: you have a very particular type of it – one of over 27 different kinds (scientists call them clones) of prostate cancer. This is not as crucial to understand if you have localized, low- or intermediate-risk disease. But it is very important to understand if you have high-risk or advanced disease. Just as we all have different fingerprints, cancer has different fingerprints, too – except these fingerprints are genetic. The genes that are mutated in your piece of the prostate cancer jigsaw puzzle are most likely different from the genes involved in the prostate cancer of the man sitting next to you in

the doctor's waiting room. Your cancer is literally programmed differently from that guy's; it's driven by slightly different software, because the DNA code is different.

This means that when it comes to advanced or high-risk prostate cancer, we know that the treatment that works on one man's cancer may not work on yours, and now we know why. So we shouldn't treat you both the same. ***We need custom-tailored treatment, and that begins with custom-tailored diagnosis.***

To show you where we're headed, it's like the difference between buying a suit off the rack and getting one crafted by an expert tailor: precision medicine is individualized. You need custom-tailored treatment, and that begins with custom-tailored diagnosis.

The old way – and by this I mean what we did even six months ago – was to treat the average. This means that if 100 men got treatment, some would benefit, and the rest would have cancer that keeps right on growing. We did our best to give patients odds, because all we could do was estimate that they might be in the group of men who are helped by a particular drug. The new way, precision medicine, means *treating the right patient with the right disease at the right time with the right amount of drug*. It's about understanding the genes. This approach works: 25 years ago, everyone who got HIV died of AIDS. Now, nobody has to die of AIDS, because we have medicines to treat it. Even the smallest genetic variant in that disease is so well-defined, we know what medicine will work best.

**We shouldn't be treating prostate cancer; we should be treating you.** Precision medicine also means that *your prostate cancer may have more in common with colon cancer, or breast cancer, than with some other man's prostate cancer, because you may share the same genetic mutations.*

**Precision testing.** There is a new blood test called the Cascade Genetic Test that could change your life. Your doctor may not know about it; it's that new. But if you have metastatic prostate cancer, or your father had it, you should know about it; so should your sons and daughters, and your grandchildren. The "cascade" part of the test is the domino effect to the next generations; that's the part that will save lives and stop the cycle of lethal cancer from bad genes. A patient recently asked, "Why didn't my urologist tell me?" Because it's very new.

This test, developed by PCF-funded research, tells you if you have a mutation in one of 16 genes called "DNA damage-repair" genes. These genes are little mechanics; their job is to fix problems in the DNA. When they break down, errors don't get fixed, and over time, this can lead to cancer. Some of these genes are pretty famous: BRCA1 and BRCA2 are well-known causes of breast and ovarian cancer.

Another is a gene called WNT. It's mutated in 100 percent of colon cancers and a target in more than 25 percent of ovarian cancers that are chemotherapy-resistant. If you have a faulty WNT gene, then what makes most sense is a drug that has WNT as its bullseye.

Still another gene is called PTEN, and it is mutated in more than 40 percent of all lethal breast cancers, more than 60 percent of lethal ovarian and uterine cancers, and 40 percent of brain tumors. PTEN is like the emergency brake on a car; if it doesn't work, you're in trouble. Now, imagine that car is parked on a hill: just as the car rolls downhill and picks up speed, so does cancer start growing unchecked without this gene.

So what we need – and are actively working on – are PTEN-targeting drugs that act like a *caltrop*. This is an ancient, highly effective weapon, used by the Romans to deter chariots and still used today in the form of spike strips that puncture your tires if you go the wrong way. If the brake is off and the car is rolling, this will slow it down and eventually stop it. *When* – not if – these drugs become available, they will not only help men with prostate cancer, but many men and women with different cancers, as well.

Now, a PTEN-targeting drug is not going to help a man with a faulty BRCA1 gene; but a drug like olaparib or rucaparib – both of which target BRCA1 – could help that man get his cancer into remission.

Have you heard of an "orphan disease?" That's what we're dealing with here. Orphan diseases affect just a few people compared to heavy-hitters, diseases like lung cancer or diabetes that affect millions. They tend to languish when it comes to funding for research and treatment. But if those

orphan diseases could be combined somehow, the numbers of people affected would really go up, and the pharmaceutical industry would have a lot more incentive to develop drugs to treat them.

*We now know that advanced prostate cancer is a bunch of orphan diseases.*

Here's another example: 3 percent of men with metastatic prostate cancer have a mutated MMR gene. A young PCF-funded investigator named Julie Graff has had amazing results in some men with metastatic prostate cancer using a drug called pembrolizumab, which is in a new class of drugs called checkpoint inhibitors. These drugs help the immune system recognize cancer as the enemy, and use the body's own powerful T cells to kill the cancer. Specifically, pembrolizumab is a "PD-1" inhibitor, and is approved by the FDA to treat melanoma. Melanoma is not prostate cancer, but some people in both categories have precisely the same MMR mutation, and for them, pembrolizumab produces results that have been called miraculous. In some men, the cancer that lit up their scans when the study started either shrank significantly or disappeared entirely just a few months later. Their PSA dropped dramatically – from more than 2,000 down to 0. They stopped taking pain medication.

Graff's protocol is laid out. If you have the right genetic mutation for this study, you should be able to get this drug, and you shouldn't have to fly to Oregon, where she is, to get it. It's not chemo. No one has ever seen metastases in the liver disappear like this – yet they really do, and you can see the images for yourself here. Over the next few months, as soon as it's available, we will have information on hospitals that are offering these drugs in clinical trials. This is precision oncology.

**Precision family genetics.** Another PCF-funded investigator, Dr. Heather Cheng, has started a program at the Fred Hutchinson Cancer Research Center in Seattle, Washington that is the first of its kind in the country. She is offering treatment based on the genetics of your cancer. If it involves a gene (like the ones we talked about above) that might be carried by your sons and daughters, she offers them genetic counseling – so your daughter can get high-risk screening for breast and ovarian cancer if she needs it. Every man treated for prostate cancer there will have custom-tailored treatment based on an understanding of the genes that need to be targeted to make him better. Reach out to Seattle Cancer Care Alliance (URL: seattlecca.org/contact/feedback) to inquire. We hope to see similar programs starting at centers of excellence around the country.

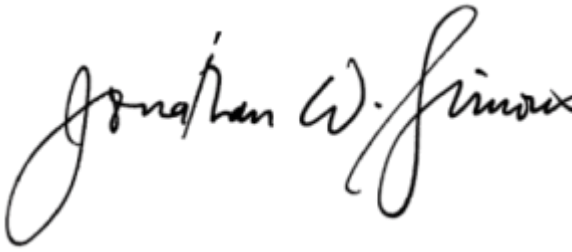
**Precision biopsy.** Pathologists can't get this kind of genetic information just from looking at prostate biopsy tissue under a microscope and determining the Gleason grade. So just as it's not your father's prostate cancer treatment anymore, it's not his biopsy, either. Pathologists today look at the DNA of prostate cancer cells. We are also working toward what we call a "liquid biopsy," where pathologists can isolate some prostate cancer cells that are circulating in the blood and look at that DNA, as well.

**Precision patients as partners.** Everything I'm talking about right now is not going to become widespread without men and their families *driving the standard of care*. There is a frontier, a leading edge of medicine, and that's what you need to be seeking. Ask your doctor for the AR-V7 test. Ask your doctor for the Cascade Genetic test. Ask your doctor if you are eligible for a clinical trial of a checkpoint inhibitor. This is all so new. But we have turned a corner on prostate cancer, and there's no going back. We've seen it with HIV. We are seeing amazing results in metastatic prostate cancer, and in other metastatic cancers. We have momentum.

You are an essential part of this. It is crucial that we have men with prostate cancer willing to help other men with prostate cancer: sharing your stories, sharing the latest news about treatments and research – so they can ask their doctors whether it will be right for them.

What kind of prostate cancer do you have? Let's figure it out and go from there.

Welcome to precision medicine.



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# Medical Detection Dogs

MILTON KEYNES, England and LOS ANGELES, Feb. 17, 2021 /PRNewswire

MILTON KEYNES, England and LOS ANGELES, Feb. 17, 2021 /PRNewswire/ -

- New research from a multinational, cross-disciplinary team of scientists from Medical Detection Dogs (MDD) in the UK, the Prostate Cancer Foundation (PCF), Massachusetts Institute of Technology (MIT), Johns Hopkins University – and a friendly pair of specially trained cancer-sniffing dogs at MDD – has scientifically validated that a dog's nose may hold the key to prostate cancer detection: a more accurate, non-invasive early diagnostic tool able to differentiate between potentially lethal high Gleason Grade cancers and low-grade, less dangerous cancers.

Observations dating back to the mid-2000s have shown that dogs can accurately sniff out early prostate and other cancers with impressive accuracy, but researchers have not known exactly *what elements of scent* the dogs were detecting and how they were processing the information. In a new paper published today in PLOS ONE, for the first time researchers combined three approaches – canine olfaction detection, artificial intelligence (AI)-assisted chemical analysis of the volatile organic compounds (VOCs) in urine samples, and microbial analysis of the same urine samples of men who underwent biopsy for suspected prostate cancer.

A four-year-old Labrador and a seven-year-old Vizsla were trained to detect the odor of prostate cancer in urine samples collected from patients with the disease, including Gleason 9 prostate cancer – the most lethal tumors that would benefit the most from early detection.

Results showed the dogs' olfaction system was 71 percent sensitive – the rate at which the dogs correctly identified positive samples – and 70-76% specific – the rate at which the dogs correctly ignored negative samples including those with other diseases – when detecting Gleason 9 prostate cancer from blinded samples. The dogs also correctly identified when 73% of blinded patient samples did not have the disease. This compares favorably to the most commonly used prostate cancer test, the PSA blood test, and demonstrates how a new screening tool based on the dog's nose could support the PSA test and improve early diagnosis, leading to better health outcomes and saving lives.

This is the first truly controlled study – both human researchers and dogs were double-blinded on which samples were from cancer patients versus otherwise healthy patients. The findings demonstrate that canines can be trained to detect the most aggressive and lethal form of prostate cancer from the VOCs. While previous studies using analytical techniques such as Gas Chromatography-Mass Spectrometry (GC-MS) to identify individual molecules performed well under tightly controlled laboratory conditions, this new work takes into account the dynamically changing background odor environment of the real world. Identification of the molecules in the odor could lead to the development of an artificial dog nose that detects prostate cancer in urine in much the same way biosensing machines known as machine olfactors are beginning to learn from the way trained dogs sniff out drugs and explosives, which also have unique molecular odorant signatures.

Dr. Claire Guest, Co-Founder and Chief Scientific Officer of Medical Detection Dogs and lead study author, said, "This study showed that a dog's nose could hold the key to an urgently needed, more accurate, and non-invasive method of early prostate cancer diagnosis. Specialist-trained cancer detection dogs, Florin and Midas, detected extremely aggressive prostate cancers quickly and accurately from urine samples, even discriminating these against urine from patients that had other diseases of the prostate. This additional information could support the PSA and would provide earlier, non-invasive, sensitive detection of clinically aggressive prostate cancers that would most benefit from early diagnosis, simply from a urine sample. This has enormous potential and in time the ability of the dogs' nose could be translated to an electronic device."

"One of the main points of this work is that the dogs aren't just detecting prostate cancer, they are detecting the most lethal prostate cancers – those that would benefit the most from early detection. Results could now lead to the future development of a more sensitive and specific prostate cancer diagnostic beyond the current PSA test," said Jonathan W. Simons, MD, PCF president and CEO, and study co-author. "With compelling evidence of this approach, we are planning larger-scale studies using canine olfaction, urinary VOCs and urinary microbiota profiling to develop a machine olfaction diagnostic tool, a 'robotic nose' if you will, that may ultimately take the form of a smartphone app of the future."

"Imagine a day when smartphones can send an alert for potentially being at risk for highly aggressive prostate cancer, years before a doctor notices a rise in PSA levels. The incredible work of these dogs is critical as we advance this program to develop an improved method of early prostate cancer diagnosis. Equally important is that men can be citizen scientists and contribute to the bio bank that will help us eventually solve this problem that is urgently needed. Once we have built the machine nose for prostate cancer, it will be completely scalable to other diseases," added Dr. Andreas Mershin, physicist and research scientist, The Center for Bits and Atoms, Massachusetts Institute of Technology, and study co-author.

Other study contributors included: Department of Pathology and Department of Urology, James Buchanan Brady Urological Institute, The Johns Hopkins University School of Medicine, Baltimore MD; Cambridge Polymer Group, Cambridge, MA; Department of Chemistry and Biochemistry, University of Texas at El Paso, El Paso, TX; Imagination Engines, St. Charles, MO; and, Department of Psychiatry, Harvard Medical School and Massachusetts General Hospital, Boston, MA. To access the published study, please visit

https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0245530.

This work was supported by a Prostate Cancer Foundation research sponsorship to the MIT Label Free Research Group at the CBA, Johns Hopkins University School of Medicine, and to Medical Detection Dogs and by National Cancer Institute of the National Institutes of Health Award SCICA245675.

**About Medical Detection Dogs**
**Medical Detection Dogs** is the world-leading organization for research into canine olfactory diagnostics. We train dogs to detect the odour of disease with the aim of developing faster, more efficient and less invasive diagnostics that lead to better patient outcomes. Our Bio Detection research includes cancer, neurological disease and bacterial infections and has the potential to benefit millions. We already apply what we know about the science of canine olfaction to benefit people by training Medical Alert Assistance Dogs, which help individuals manage complex, life-threatening medical conditions.

www.medicaldetectiondogs.org.uk

**About the Prostate Cancer Foundation**

The Prostate Cancer Foundation (PCF) is the world's leading philanthropic organization dedicated to funding life-saving prostate cancer research. Founded in 1993 by Mike Milken, PCF has raised more than $865 million in support of cutting-edge research by more than 2,085 research projects at 244 leading cancer centers and universities in 22 countries around the world. Thanks in part to PCF's commitment to ending death and suffering from prostate cancer, the death rate is down by 52% and countless more men are alive today as a result. PCF research now impacts more than 70 forms of human cancer by focusing on immunotherapy, the microbiome, and food as medicine.

Learn more at www.pcf.org.

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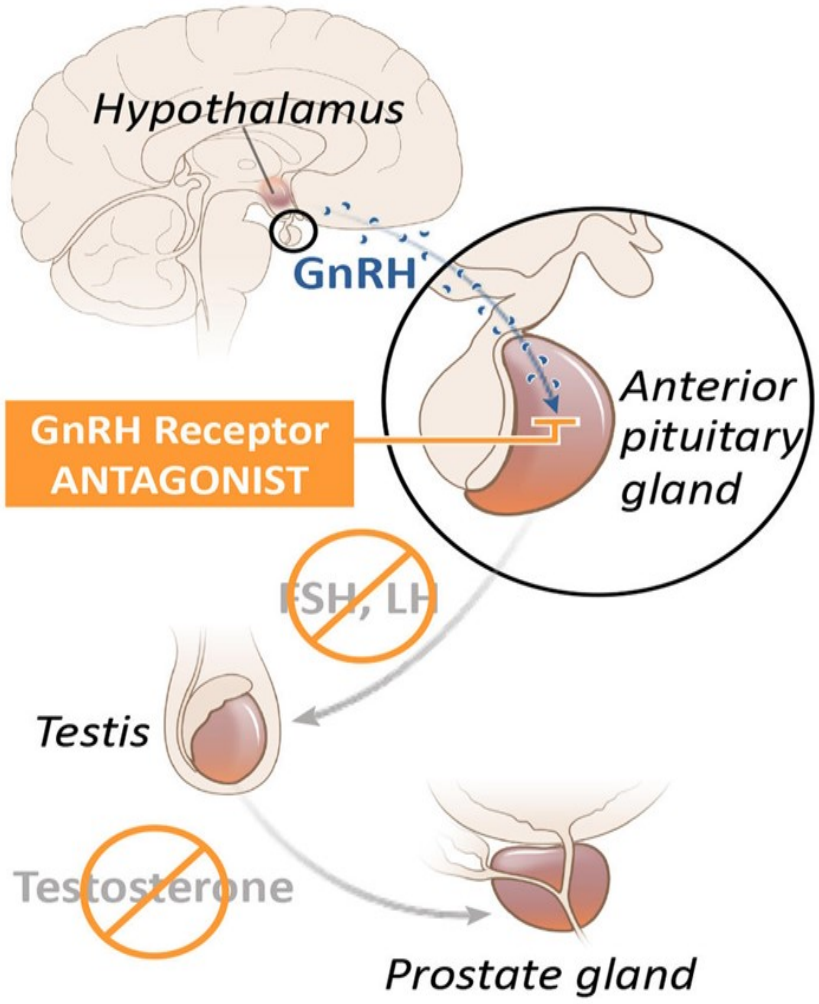
# Relugolix Approval Expected to Alter Treatment for Advanced Prostate Cancer




Credit: Courtesy of Dr. Neal Shore

A new drug approved by the Food and Drug Administration (FDA) is expected to immediately affect the treatment of some men with prostate cancer. In a large clinical trial, the drug, relugolix (Orgovyx), was shown to be more effective at reducing testosterone levels in men with advanced prostate cancer than another commonly used treatment, leuprolide (Lupron).

Treatments that block the production of the hormone testosterone by the testes have been the cornerstone of advanced prostate cancer treatment for several decades. Known as androgen deprivation therapy (ADT), these treatments are akin to putting a stopper in a car's gas tank: robbing prostate tumors of the fuel they need to grow and spread.

In the clinical trial, relugolix was also much less likely than leuprolide to cause serious heart issues, said Neal Shore, M.D., of the Carolina Urologic Research Center, who led the clinical trial on which the approval was based, called HERO. That's important, Dr. Shore said, because leuprolide and other ADT drugs have been linked with an increased risk of cardiac events, including heart attacks and heart failure.

"For me, this [approval] is significant," Dr. Shore said. "Many of the patients we start on testosterone suppression are at risk of having a cardiac complication."

Given its superior ability to reduce testosterone and safety with regard to heart-related effects, Dr. Shore said, "it's perfectly arguable" that relugolix should be the preferred choice for ADT in men with advanced prostate cancer.

Alicia Morgans, M.D., who specializes in treating prostate cancer at the Robert H. Lurie Cancer Center of Northwestern University, generally agreed.

"I believe this is a new standard of care for men with [advanced] prostate cancer," Dr. Morgans said. "It meaningfully and effectively lowered testosterone levels, which is what we manipulate to try to control prostate cancer."

It may not "necessarily replace every [ADT] option for every patient, but it's definitely a new standard that appears safe and effective," she continued, especially for men concerned about any potential heart-related risks.

**Going After Testosterone**

Prostate cancer that is confined to the prostate is typically treated with surgery or radiation therapy. Once it advances beyond the prostate, either to nearby tissues or to other parts of the body (e.g., bones, liver), ADT is typically used.

Although several drugs for ADT are available, in the United States leuprolide is the most commonly used option. Known as an LHRH agonist (also called a GnRH agonist), leuprolide acts on the pituitary

gland—a tiny organ within the brain that is responsible for producing a hormone that eventually decreases the production of testosterone by the testicles. It is given to patients as an injection into muscle, typically every few months.

Reducing the production of testosterone to very low levels with drugs is often called medical (or chemical) castration, because it achieves the same results as surgical removal of the testes.

Relugolix is known as a GnRH (or LHRH) antagonist. It also acts on the pituitary gland, but in a way that more directly and rapidly blocks testosterone production in the testes. In addition, it is a pill that patients take every day.

**Testosterone's Trail**

Testosterone's production in the prostate begins with the release of a hormone called GnRH by the hypothalamus in the brain. The GnRH then binds to the pituitary gland, via a special receptor, causing the pituitary to produce two other hormones, LH and FSH. In men, these hormones cause the testicles to make testosterone, and in women they cause the ovaries to make estrogen and progesterone.

ADT "wasn't necessarily something we thought would be improved upon, because … we've had good strategies to lower testosterone with good medications for decades," Dr. Morgans said. The development of drugs like relugolix is important, she added, because it "took something we've been doing forever and tried to make it better."

**Improved Testosterone Suppression, Lower Cardiac Risks**

More than 900 men with advanced prostate cancer whose tumors still relied on testosterone (known as hormone-sensitive prostate cancer) were enrolled in the HERO trial, which was funded by Myovant Sciences, the manufacturer of relugolix.

Participants were assigned at random to take relugolix daily for 48 weeks or to receive leuprolide injections every 3 months for the same length of time.

Approximately 97% of men treated with relugolix reached and maintained very low testosterone levels through 48 weeks, compared with 89% of men who received leuprolide. In addition, men in the relugolix group also did substantially better on several other measures, including being able to return to normal testosterone levels within a few months of stopping therapy.

The latter finding is "very important," Dr. Shore said. Suppressing testosterone for long periods can lead to significant side effects, he explained, including fatigue, hot flashes, and bone problems. And in clinical practice, ADT might only be used for short periods, such as when it's being given along with radiation therapy.

"So if your testosterone level returns to normal values faster after stopping ADT, that to me is a real positive," he said.

Side effects were generally similar in both treatment groups, although diarrhea was more common in men treated with relugolix. The biggest difference, though, was the effect on the heart: Twice as many men in the leuprolide group than in the relugolix group (6.2% versus 2.9%) had a "major adverse cardiovascular event," which included nonfatal heart attack or a stroke.

When the HERO trial investigators looked specifically at men who had a history of heart problems, the difference in the frequency of these cardiac side effects was even more stark: 17.8% in the leuprolide group versus 3.6% in the relugolix group.

The potential heart risks associated with long-term ADT with LHRH agonists such as leuprolide have come into sharper focus over the past decade, Dr. Shore said. In discussions with colleagues who specialize in studying and treating the cardiac effects of cancer treatments, he continued, "they've told me that the likelihood of a typical man undergoing ADT having a major cardiac event is upwards of 30% to 40%."

**Impact on Everyday Care**

Fatima Karzai, M.D., of the Genitourinary Malignancies Branch in NCI's Center for Cancer Research, called relugolix "an exciting option" for men with advanced prostate cancer. Its most obvious role will be in men with advanced prostate cancer who also have cardiovascular disease, Dr. Karzai said.

Although trial participants who received relugolix had a more than 50% lower risk of serious cardiac events, she said it's unclear exactly why it poses less of a threat to the heart. Some studies have suggested, she noted, that the difference in how the two drugs work may also influence how they affect plaque deposits in the cardiovascular system.

Relugolix is not the first GnRH antagonist to be approved by FDA to treat men with advanced prostate cancer. Degarelix (Firmagon) was approved more than a decade ago. However, degarelix is given as a monthly injection, and the injections can cause intense pain at the injection site, greatly limiting its use.

Dr. Karzai noted that there are still questions about using relugolix in patient care. For example, there might be problems with men's ability to take a pill every day, as opposed to only having to get an injection of leuprolide or related drugs every few months.

Dr. Morgans agreed that this could be a concern but noted that men with more advanced forms of prostate cancer also receive other drugs that are taken as pills and have been generally good about using them as prescribed.

The ability to take a pill at home rather than having to travel to the doctor's office for an injection definitely offers an upside, Dr. Morgans said. "It's nice for patients to have that control."

Source URL: https://www.cancer.gov/news-events/cancer-currents-blog/2021/fda-relugolix-prostate-cancer-androgen-deprivation-therapy?cid=eb_govdel_cancerinfo

## New Age Peak: Advanced Prostate Cancer Increasingly Common in Men Under 40

Although prostate cancer is considered a disease of older men, some recent research suggested an increase of cases in younger men.

While research is still exploring the issue of younger men with prostate cancer, incidence rates are increasing.

A new global study found that the incidence of prostate cancer in men ages 15-40 increased approximately 2% per year since 1990. Also, in the U.S., men in this age group were six times more likely than older men to have metastatic prostate cancer when they were diagnosed.

For men in the U.S., the 5-year relative survival rate for men diagnosed with prostate cancer when they were 40-80 years old was between 95% and 100%. But for men who were diagnosed when they were 15-24 years old, the 5-year relative survival rate was only 30%; the rate was 50% for men 20-29 years old and 80% for men 25-34 years old when they were diagnosed.

Further research is needed to determine the cause of these trends and how the biology of cancer in younger men differs from that in older men.

Dr.Catalono's response

For the usual "garden -variety" prostate cancer, called adenocarcinoma (cancer arising from the tiny glands within the prostate organ), the rule is that it rarely is diagnosed in men under 40. The garden-variety prostate cancer tends to be diagnosed in a localized stage and behaves less aggressively in men under 65. However, in men over 65, the incidence rate, tumor stage, and disease aggressiveness increases progressively with increasing age.

This article above calls attention to the fact that advanced, aggressive prostate malignancies also occur in men under 40, and this is being observed more often in recent years.

As is the case with garden- variety prostate cancers, these tumors in young men are more common among African-American men and less common among Asian men than among white men. Also, compared to older men, most young men with garden-variety prostate cancer have localized disease at diagnosis and a lower proportion of high-grade tumors.

However, the prostate cancers diag-

nosed in men under 45 are more likely than those diagnosed in older men to have metastatic disease.

Some caveats should be considered concerning this study. First, the authors report that the average annual percent change in incidence is greatest in men aged 30- 45. Since the incidence was a very small number, to begin with, a relatively small increase in numbers would be magnified as a disproportionately greater increase in the percent change (i.e., small changes in very small numbers translate into large changes in percentages).

Secondly, screening for localized prostate cancer is infrequent in men aged 30-40 so slowly-growing tumors may go undetected for many years. However, advanced-stage tumors are less likely to go undiagnosed for long.

Thirdly, the authors measure patient survival as the 5-year relative survival, which is the survival of a man diagnosed with cancer compared to the survival of a man not diagnosed with cancer. The relative 5-year survival of younger men with or without cancer tends to be greater than that of older men, because younger men have a longer life expectancy.

Lastly, the features in the tumors diagnosed in the younger men were different: they were usually poorly differentiated, metastasize early, had lytic rather than sclerotic bone metastases, and responded poorly to hormonal therapies. This suggests that these tumors may have different biology from the garden-variety prostate cancers. Although the authors discuss possible factors that could contribute to the increasing rate of prostate malignancies diagnosed in younger men, the cause is unknown.

**Thus, the "bottom line" is that that there are now two age peaks associated with advanced prostate cancer: one in men aged 25-40 years and the other in men aged 70 years and older.**

Cancer. 2020 Jan 1;126(1):46-57. doi: 10.1002/cncr.32498. Epub 2019 Sep

***Source URL: https://drcatalona.com/quest/a-new-age-peak-advanced-prostate-cancer-increasingly-common-in-men-under-40/***

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