



Prostate Insights

The Latest Developments in Prostate Cancer Care

Winter 2017 // Volume 20, Issue 1

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Editorial

Peter Scholz // PCRI Creative Director

Hello Researcher, welcome to a new issue of Prostate Insights, a newsletter that brings you the latest information about prostate cancer. In addition to the importance of arresting cancer growth, it is of equal—if not in some cases greater—importance to focus on quality of life issues.

Our Helpline is often asked about alternative treatments, both to fight cancer, and to cope with side effects. The featured article addresses something at the forefront of our culture's awareness: Medical marijuana. There are rumors and intimations about its anti-cancer effects, and a general mystique surrounding the subject. A recognized expert on alternative treatments, Mark Moyad, MD, author of "The Supplement Handbook: A Trusted Expert's Guide to What Works & What's Worthless for More Than 100 Conditions," analyzes the data.

A groundbreaking medical treatment called Xofigo is available. Michael Anderson, MD and Nicholas Vogelzang, MD, explain the mechanism of how Xofigo delivers radiation directly to bone metastases. They examine its proven effects on survival and its impact on cancer related bone pain. They conclude by examining areas of further research currently being conducted.

Our Helpline facilitators provide answers to the most common questions they receive in our regular monthly feature: "Helpline Corner." Don't forget, our friendly and knowledgeable Helpline staff is always available to help you find specific information about your own personal case.

Online the PCRI has a blog that is constantly updated with new prostate cancer information and other useful resources that help you understand your disease and make optimal decisions. In this issue, we have included a blog from the PCRI website to give you a taste of our online resources

I hope you find this issue to be entertaining, thought provoking, and most importantly, empowering; and that you will partner with your caregiver and medical team with confidence, armed with knowledge.

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2017 Mid-Year Update

PCRI Staff

Our 2017 Mid-Year Update is on March 25, 2017, and will be held at a new location. See this article for information about the topics, speakers, our new location, and how to register. This is an event you won't want to miss!

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Featured Article: Marijuana Cures Everything Dude?!

Mark Moyad, MD

Mark Moyad, MD, is a best-selling author and an authority on alternative treatments. In this much-requested article, Dr. Moyad analyzes clinical data and definitively answers common questions about the efficacy of Marijuana on cancer and cancer-related side effects.

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PCRI Blog Highlights

Mark Scholz, MD

The PCRI Blog is constantly updated with new information about prostate cancer. Following the PCRI Blog is the best way to stay updated with the latest information. Blogs are authored by respected doctors and researchers in the field of prostate cancer.

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Targeted Radiation Administered by Injection

Michael Anderson, MD, and Nicholas Vogelzang, MD

Radium-223 Dichloride, otherwise known as Xofigo, is the first alpha-emitting radiopharmaceutical used to treat prostate-cancer-related bone metastasis.

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Helpline Corner: Frequently Asked Questions, Answered

PCRI Helpline Staff

PCRI's free Helpline connects patients and caregivers with educated advocates and helps them understand their personal case. This article is a top ten frequently asked questions list that our Helpline receives.

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CONTACT US

+Prostate Cancer Research Institute

5777 W. Century Blvd., Suite 800

Los Angeles, CA 90045

+Phone: 310.743.2116

+Fax: 310.743.2113

+Helpline: 800.641.PCRI (7274)

+E-mail: info@pcri.org

+Website: www.pcri.org

PCRI

Is proud to announce:

2017

MOYAD + SCHOLZ
MID-YEAR UPDATE

A One-Day PCRI Conference

Saturday, March 25, 2017 // Marina del Rey Marriott
Come visit our new event location!

A unique educational experience featuring in-depth lectures about specific prostate cancer topics followed by extended Q+A with leading doctors.

This year we are proud to feature presentations by:

Robert Dreicer, MD // Cleveland Clinic // **Advanced Prostate Cancer**

Carl Rossi, MD // Scripps Proton Therapy Center // **Radiation Therapy**

Mark Scholz, MD // Prostate Oncology Specialists // **Active Surveillance**

Mark Moyad, MD // University of Michigan Medical Center // **Diet and Exercise**

Register Now!

www.pcri.org/2017-mid-year-update



Helping Men Research Their Options

Marijuana Cures Everything Dude?!

Come on Moyad man,
what is the truth here?

Over the past several years, as I traveled, I always knew that at least one person in the audience would ask THE QUESTION. And, if I gave a lecture in Colorado I would get THE QUESTION many, many times! THE Question is whether or not "Marijuana is beneficial or is a treatment for _____" and in the blank fill in every possible disease that has impacted humankind since the beginning of time! So, excuse me for using the words "dude" or "man" a lot in this column but, since we are talking about marijuana, I thought it was appropriate.



Mark Moyad, MD

University of Michigan

Jenkins/Pokempner Director of
Preventive & Alternative Medicine

BOTTOM LINE

One of the best reviews and meta-analysis of marijuana (aka "cannabinoids"-some of its active ingredients) for medicinal use concluding with the following after examining 79 clinical trials (with over 6450 participants) [1]:

"There was moderate-quality evidence to support the use of cannabinoids for the treatment of chronic pain and spasticity. There was low-quality evidence suggesting that cannabinoids were associated with improvements in nausea and vomiting due to chemotherapy, weight gain in HIV infection, sleep disorders, and Tourette syndrome. Cannabinoids were associated with an increased risk of short-term adverse events (AE's, aka side effects)"

The AE's that were more common in these clinical trials were the following: Dizziness, dry mouth, nausea, fatigue, sleepiness, sedation, euphoria, vomiting, disorientation, drowsiness, confusion, loss of balance, and hallucination. OUCH!!! It sounds like a pharmaceutical TV commercial where the person comes on and lists all the potential side effects really fast like they are studying for a career in auctioneering.

Next, an expert from HAAAARVARD (I love to say that) looked at 28 randomized trials and stated the following [2]: "Use of marijuana for chronic pain, neuropathic pain, and spasticity due to multiple sclerosis is supported-by high-quality-evidence." YEAH!!

However, this author expressed some of the side effects or concerns with marijuana use such as: "addiction and worsening of psychiatric illnesses such as some anxiety disorders, mood disorders, psychotic disorders, and substance use disorders..." OUCH!

Also [2]: "Regular marijuana use results in physical problems as well. It is associated with increased incidence of symptoms of chronic bronchitis and increased rates of respiratory tract infections and pneumonia. Preliminary research points to an association between marijuana use and myocardial infarction, stroke, and peripheral vascular disease." OUCH! OUCH!

Then, in one of the most recent respiratory reviews of marijuana, the following concerns were expressed after looking at 48 articles [3]: "The research indicates that there is a risk of lung cancer from inhalational marijuana, as well as an as-

sociation between inhalational marijuana and spontaneous pneumothorax, bullous emphysema, or COPD. A variety of symptoms have been reported by inhalational marijuana smokers, including wheezing, shortness of breath, altered pulmonary function tests, cough, phlegm production, bronchodilation, and other symptoms." OUCH x 3!

Look, I am excited about marijuana and some of its medically active ingredients (aka "cannabinoids") to help patients with a variety of conditions, including cancer pain, to reduce nausea and vomiting, to perhaps improve appetite, and for kids and adults with seizures that do not respond to other options. It is interesting. HOWEVER, it is also overhyped in some areas of medicine ("fights cancer"?). And can it come with numerous concerning side effects and high costs for some patients? OH YEAH BABY! Medical marijuana has now become a massive area of profit for many state governments and owners of those groovy medical marijuana facilities, so always seeking the real truth, apart from the hype and cash flow, will be critical! So, please read on ladies and germs! ►

PLEASE TELL ME MORE DUDE MAN!

Let's just review a few facts about marijuana [1-3]

- Marijuana has many; names: "Pot," "weed," "grass," "ganja," "joint," "reefer," "dope," "Scholz" (okay, I made that last one up).
- Before the Marijuana Tax Act of 1937, cannabis was actually used medicinally, and in 1970, it was officially classified as a Schedule 1 drug because of its potential for abuse, lack of safety, and other reasons. Other schedule 1 drugs include ecstasy, heroin, and LSD.
- Over half of the states in the U.S. currently have laws legalizing marijuana in some form! Wow! Wow spelled backwards! Marijuana itself is not FDA approved to treat any medical condition (ahhhhh, the irony).
- Marijuana=Cannabis=from the Cannabis sativa plant. And, over 60+ cannabinoids and 400 compounds have been found in marijuana. Cannabinoids are some of the active ingredients in marijuana that could treat some diseases.
- The most well-known cannabinoid is THC (tetrahydrocannabinol), which is the primary ingredient thought to cause the "high" or "buzz" (this is what I am told-I have no experience with it, except in college when someone FORCED me to smoke and inhale it, or else they would not let me leave the fraternity house).
- Interestingly, two cannabinoid (THC-like) drugs known as "dronabinol" (THC in sesame seed oil) and "nabilone" (another THC copycat) have been available in the U.S. for some time as FDA-approved oral prescription drugs! These drugs were approved for nausea and vomiting caused by cancer chemotherapy and also for appetite stimulation in medical situations that could cause unhealthy, excessive weight loss ("wasting" or "cachexia"). Some "experts" think these drugs should be tried first before moving on to the other options mentioned in this article.
- Another cannabinoid that is getting a lot of interest is Cannabidiol (CBD), WHICH DOES NOT CAUSE INTOXICATION or the HIGH of THC. And, this CBD is being tested now in many medical situations, including as a topical oil to rub on the skin of an area impacted by cancer pain or because of other types of pain (arthritis, etc). In fact, I have known many patients in the past 5 years that tell me they get good relief from their pain when using this topical CBD oil and apply it directly on the site of their pain. I have parents tell me that CBD, when ingested, might impact the number of seizures their child is experiencing. Of course, this is not definitive proof, but it is interesting based on what we know from some studies. The future of research for cancer and the treatment of side effects will be the impact of CBD in many clinical trials.

Medical Form	Comments from Mark "The Dude" Moyad
Hashish	Concentrated resin cake which is ingested or smoked
Hashish Oil	Cannabis oil plant extraction which is usually smoked or inhaled
Infusion	Plant material mixed with a medium that is not volatile, such as a cooking oil or butter, and ingested
Marijuana	Dried plant consists of flowers, leaves, and stems and usually smoked or vaporized
Tincture	Liquid extract of cannabinoids and is consumed sublingually (under tongue)

Table 1

HEY MOYAD DUDE MAN TELL ME EVEN MORE!

Cannabis comes in all shapes, sizes, and delivery systems or ways to get some of the active ingredients. The table below lists some of the most common [1-3].

Let's just face the facts as they exist right now: Human evidence currently suggests that marijuana could be a treatment for chronic pain, nerve (aka "neuropathic") pain, and muscle spasms due to multiple sclerosis or from other neurologic issues. There is also some evidence that it could help with seizures, post-traumatic stress disorder, and questionable or limited evidence on glaucoma. In fact, in 2014 the American Academy of Ophthalmology once again stated that marijuana is NOT a proven treatment for glaucoma [4,5].

So, where can I look to learn even more about oral (or topical) CBD for example? In my opinion, you need to look at some of the clinical trials that have just been completed in other areas of medicine to get some idea of what might happen to you when you ingest CBD. For example, it is interesting that recently published data from the first large-scale prospective study using CBD in patients with treatment-resistant epilepsy was promising [6]. A total of 162 children and young adults aged 1 to 30 years were given a 99% purified oil-based form of an oral (although some received it through a gastric tube) cannabidiol ("Epidiolex" from GW Pharmaceuticals, London, UK) as an additional treatment to their current anti-seizure drugs. Mild to moderate side effects were common and included sleepiness in 25%, reduced appetite in 19%, diarrhea in 19%, fatigue in 13% and convulsion in 11%, but only 3% stopped treatment because of a side effect. The study was 12 weeks, but it shows a fairly good short-term safety record for a drug. It also shows that there are notable side effects just like a drug. Concerning effectiveness, there was a median reduction in monthly motor seizures of 36.5%, which is similar to the impact of some commonly used antiepileptic drugs in this popula-

tion. What is also interesting is that in these kinds of studies (and others) the potential for a major placebo effect is strong. For example, data from Colorado shows that patients of families who moved to this state to help treat their loved ones were two times as likely to have a larger than 50% seizure reduction (47% responder rate) compared with the patients who already had been living in Colorado (22% response) [7]. Regardless, this CBD (Epidiolex) study showed enough success to remain optimistic.

One concern in future studies is the potential for drug interactions because cannabidiol can block liver enzymes of metabolism and could increase the concentration of some drugs to dangerous levels [8]. All of the drugs it clinically impacts are not known as of yet, so, if using it for cancer side effects, just keep this in mind and check with the doctor or medical team you trust for the latest information on this and other issues. Still, do not use CBD or marijuana until you have read the dramatic final part of this column!

THE MOYAD OVERALL HIP & GROOVY SUMMARY- BUCKLE UP FOR 12 GNARLY THINGS!

So, let's review what I have learned thus far about marijuana or some of its derivatives from my 25+ years of experience and reviewing much of the literature:

1. Personally, if you are healthy, I think the risks of marijuana outweigh the benefits unless, of course, you win the lottery and just want to try it one time to celebrate the fact that you no longer have to ever listen to your boss or some of your annoying coworkers ever again. Marijuana is NOT proven to be heart healthy and in fact could be heart unhealthy, and the smoke does not make the lung tissue happy even though you could feel temporarily happy. Both cigarette smoke and marijuana can contain cancer-causing compounds such as "nitrosamines," "phenol," "polycyclic aromatic hydrocarbons," "vinyl chlorides," blah blah blah.

Thus, both types of smoke can contain particulate matter and carcinogens.

2. The two 1985 FDA-approved THC-like drugs (dronabinol aka Marinol, and nabilone aka Cesamet-both mostly THC copycats) should be discussed more often as an option for nausea and vomiting prevention in cancer chemotherapy treatment, and to help encourage weight gain and appetite stimulation in

Human evidence currently suggests that marijuana could be a treatment for chronic pain, nerve (aka "neuropathic") pain, and muscle spasms due to multiple sclerosis or from other neurologic issues.

cancer patients. Interestingly, there is even some evidence of dronabinol improving "dysgeusia" the taste of food and appetite in one small study (see the last reference-number 12). Interestingly, zinc supplements (50 mg 3 times a day) are arguably first line evidence for dysgeusia (see reference 12) and have their potential for side effects (that is a different Moyad article dudes and dudettes). Taste changes are not uncommon with chemotherapy and other drugs.

3. A variety of forms of medical marijuana should also be considered for nausea and vomiting and to stimulate appetite and weight gain in some cancer patients.

4. A variety of forms of medical marijuana (from topical, edible, and inhalable) should also be considered for different types of cancer pain because they may have less toxicity than using narcotics and could be just as effective in some cases. There are also certain kinds of pain that simply do not respond to major medications, and in these cases medical marijuana should be discussed or investigated. ►

5. A variety of forms of medical marijuana make a lot of people (including state governments) a lot of moola-it has become a major cash cow (get it..."moola"). Graze on that joke for a second. I know I milked that joke for all its worth! So, the sheer profitability of marijuana now causes many people to highlight all the potential benefits and fail to mention the reality or evidence. This is also known as a conflict of interest!

6. Marijuana is "natural" so should I get excited about it? Just because it is natural is not the reason I get excited about diddly squat (aka anything)...I mean, poison ivy and arsenic are natural folks, but I usually do not recommend those things, except to my big brother when he pushed my face in the snow when we were kids. I get excited when patients have more and more effective options and the benefit outweighs the risk, and this is why I am currently excited (and because Oreo cookies have a new limited-time-only strawberry and chocolate flavor out and it is also exciting. And this could be useful to know if you try any of the things discussed and get hungry...).

7. Do I think marijuana or one of its compounds can fight cancer or encourage the growth of cancer? Yes! Since we do not know at the moment and some laboratory studies suggest both possibilities, we have to be honest. We have no idea except it could reduce some symptoms/side effects of cancer and the treatment of cancer. It is really irresponsible to use a laboratory study as definitive proof that marijuana fights cancer? For example, there was a drug that impacts one cannabinoid receptor in the brain that so many "experts" were convinced would be a great weight loss drug. It was marketed in Europe briefly (known as Acomplia-google that bad boy) but was removed from the market because of serious side effects such as

anxiety, suicidal ideation, nausea, and some new cases of multiple sclerosis that may have been drug-related [9]. The gluteus maximus/bottom line is for every cannabidiol study that suggests it fights cancer in the laboratory, other studies suggest the opposite, or simply the potential for toxicity of normal cells [10,11]. Interestingly, the expression of cannabinoid receptors on a tumor could actually be there for improved survival and could be a correlation of tumor grade. For example, THC has been shown to promote tumor growth in some immunocompetent animals. So, when or if receiving immune stimulating drugs, this could be an issue [12]. Look, if you are a mouse or a rat we can cure you of almost anything today, but until we get more human studies we have no idea if it fights, accelerates, or does nothing to the growth of cancer.

8. Hemp milk does not contain THC but in some cases is fortified with 450-500 mg of calcium per cup, so you could drink one cup a day instead of taking a calcium supplement. Hemp seeds are also a groovy source of protein.

9. I believe President Clinton did inhale the marijuana he tried. And, I think other presidents also smoked and fully inhaled marijuana at least once. I have no proof but anyone going into politics today has got to be somewhat "high" to get involved in this reality TV show cage match!

10. Stress, anxiety, depression, pain, nausea and vomiting, and appetite stimulation are some of the areas where affected cancer patients in a desperate situation could theoretically (what a politically correct word for "just go ahead and look into it") determine if it is an option. Always remember that there are also many other good options in these situations that should ALSO ALWAYS get some attention. For example, megestrol is a drug used in prostate cancer to reduce hot flashes, and it also can stimulate ap-

petite at a different dosage if needed. In other words, researching all of the side effect treatment options, and not just the impact of marijuana, is critical.

11. I find it embarrassing and ridiculous that in some cases of advanced cancer or other situations where a person needs to feel comfortable, they are not offered the option of marijuana, CBD, or another alternative option to at least try, and instead have to "live with it" or get hooked on narcotics (and some of the ugly nasty side effects that come with these approved drugs). Objectively speaking, a discussion of the positives and negatives of marijuana to prevent or treat some side effects should be given to cancer patients just like any other conventional or alternative option.

12. There is a potentially bright future for some types of marijuana delivery drugs for patients dealing with cancer and other issues. For example, nerve pain or nerve issues from chemotherapy are an ugly side effect and "Nabiximols" (trade name="Sativex" from GW pharmaceuticals, which also has the drug "Epidiolex," which is a CBD product for epilepsy mentioned earlier) is an oromucosal spray containing cannabinoids (THC and CBD in a 1:1 ratio-wow dual threat!) that has shown some promise for pain in small clinical trials [13,14]. Epidiolex has a good chance of FDA approval for certain seizures and, since it does not make you "high," it and other CBD products will continue to get research for cancer side effects and other medical conditions [15].

13. Oh, and by the way, Darth Vader was Luke's father and when in doubt in any murder mystery you should be suspicious of the butler. And I do believe that BigFoot is alive and well in the Upper Peninsula of Michigan, and goes bowling with Elvis and Jimmy Hoffa every Friday night. Later Dudes & Dudettes! ▲

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PCRI
BLOG

PROSTATE CANCER INFORMATION AVAILABLE ONLINE

The PCRI Blog contains past Insights articles and posts from leading experts in the medical field. It is the best way to gain a foundational understanding of the world of prostate cancer and how to understand your specific prostate cancer case. It is updated regularly with new information.

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Prostate Size Matters

BY MARK SCHOLZ, MD

There are many factors that one must take into account when choosing a treatment for prostate cancer, from PSA, Gleason score, percent core's positive, etc. One factor that deserves a closer look is prostate size. The following is a post from our blog, visit the blog to see more posts like this one.

Having a large prostate is generally considered to be a bad thing because it is associated with urinary malfunction—slow urination, getting up frequently at night and, in the worst case scenario, total urinary blockage—an emergency condition that requires insertion of a catheter.

Treating urinary problems such as these is a big business. A variety of herbal extracts containing ingredients such as saw palmetto, as well as medications such as Flomax and Proscar, are commonly prescribed and used with varying success. When a total blockage occurs the urologist swings into action with lasers, microwave treatments, or a good old-fashioned TURP (transurethral resection of the prostate), sometimes referred to by laymen as the “rotorooter job.”

It should be made clear that many large prostate glands cause no urinary symptoms whatsoever. Also, urinary problems like those described above can occur in men with normal sized glands.

Therefore, you need to be aware that the connection between prostate size and urinary symptoms is a loose one.

A normal, healthy prostate gland is a walnut-sized organ that weighs approximately 15 grams in young men and around 30 grams (about an ounce) in men age 50 or older. The prostate gland is the only organ in the body that keeps growing as you age. Enlarged prostates can weigh as much as 100 grams or more (the size of a small orange), and are more likely to lead to urinary problems.

However, as it turns out, having a large prostate can actually be a good thing, at least as far as prostate cancer is concerned. Several studies show that men with large prostate glands tend to have lower Gleason scores. When men with big prostates are treated with radical prostatectomy, studies also show that they are less likely to have cancers that have spread through the capsule or into the seminal vesicles.

No one knows for sure why big (where cancer is concerned) is often better. One theory is that men with bigger prostate

glands get biopsied more frequently and at a younger age because their PSA levels run higher. Therefore, the cancer is being caught at an earlier stage and monitored.

Another theory is that bigger prostate glands result from hormonal changes within the gland, and that these hormonal changes somehow have an inhibitory effect on cancer growth. The particulars of these purported hormonal changes are never specifically elucidated.

Regardless of the cause, men with smaller glands—say with prostate volumes less than 40 grams—should be aware that, all other things being equal, their risk of harboring a higher Gleason score or a type of cancer that invades through the capsule is somewhat greater than it is for the men who have larger glands.

Prostate size is an additional factor besides Gleason score, PSA, and the percentage of core biopsies involved with cancer, that needs to be considered when going through the treatment selection process. ▲

Originally posted on verywell.com

Targeted Radiation Administered by Injection

**Michael Anderson, MD +
Nicholas Vogelzang, MD**
Comprehensive Cancer Centers of Nevada

Radium-223, marketed as Xofigo, is a novel pharmaceutical with a unique mechanism of treatment that is proven to increase survival in men with advanced prostate cancer. It is an important tool in the modern arsenal of treatments for advanced disease.

OVERVIEW

Radium-223 Dichloride, otherwise known as Xofigo, is an injectable radiopharmaceutical used to treat prostate cancer. The FDA approved Xofigo in May of 2013. The clinical trial that led to the FDA approval was called the ALSYMPCA trial. Eligible patients were randomized in a 2:1 fashion to either receive six monthly intravenous injections of radium-223 or best standard of care, such as antiandrogen hormonal therapy, local external beam radiation, corticosteroids, estramustine, or ketoconazole. The men who received radium-223 had improved survival and a reduction of bone pain. The patients who were not initially treated with Xofigo were later allowed to cross over into the radium-223 arm, once the researchers realized the capacity for Xofigo to increase survival. Radium-223 was also shown to lower the risk of symptomatic skeletal events, such as the need for palliative external beam radiation or surgery to treat bone pain and bone fractures.

Radium-223 is an alpha particle emitting radioactive isotope. Traditionally, the radioactive isotopes used to treat bone metastasis from prostate cancer have been beta emitting. Strontium-89 and Samarium-153 were the two approved radioisotopes used most commonly in

the treatment of metastatic prostate carcinoma to bone, before the approval of radium-223 dichloride. Strontium-89 and Samarium-153 reduced bone pain but did not improve overall survival. Unfortunately, the side effects of treatment, most notably depression of blood counts and anemia, were greater with Samarium-153 and Strontium-89. Beta emitting radioisotopes result in more radiation to the bone marrow than alpha emitters. Radium-223 deposits energy along a shorter pathway and results in a much lower amount of radiation to the central bone marrow component of the bone. Thus, patients experience less bone marrow suppression and are potential candidates to receive additional treatments along with radium-223, making it a more attractive treatment option. Radium-223 is administered in microcurie doses, whereas the activity administered for most therapeutic radioactive isotopes are in millicuries. Millicuries are a thousand times bigger than microcuries. So, radium-223 is more effective than older radiopharmaceuticals but at the same time accomplishes these effects much more efficiently, using much less radiation. This occurs because radium localizes the radiation much more accurately near the tumor. ►



Author Biography

Nicholas Vogelzang, MD

Dr. Vogelzang is a renowned medical oncologist and cancer researcher with 35 years of internal medicine and medical oncology experience, with special areas of expertise in genitourinary cancer. His CV on Pubmed lists four publications (26 in 2013) in addition to numerous book chapters and abstracts. He has given hundreds of lectures and presentations to his peers.



Michael Anderson, MD

Dr. Anderson received his undergraduate degree in Biochemistry from the State University of New York in Stony Brook, New York in 1990. He earned his medical degree in 1995 from the State University of New York, Upstate Medical Center in Syracuse, New York.



Above: Dr. Vogelzang answering questions from Mark Moyad, MD, the PCRI Conference Moderator, after his keynote presentation at the 2016 Prostate Cancer Conference

The special physical properties of alpha emitting radioisotopes, as well as the lower amount of activity needed to obtain a clinical benefit, make the administration much easier, and shielding requirements are much more convenient.

After intravenous injection, radium-223 is distributed primarily in the bone and intestine. The major route of elimination of any excess radiation that is not targeting the tumor is through the intestines. Therefore the side effects, if any occur, are related to the GI tract. Nausea, vomiting, and diarrhea can occur. If too much of the bone marrow is exposed to radium-223, lowering of the white blood count or platelets can occur. As a precaution, prior to each monthly injection of Xofigo, a check of the complete blood count (CBC) is necessary.

IN USE

Radium-223 dichloride is the first FDA-approved agent that extends overall survival in castrate-resistant prostate carcinoma by exerting an antitumor effect on bone metastasis. Because of its mechanism of action and favorable side effect profile, radium-223 is an attractive agent to consider using in combination with other agents. Radium-223 can be used

with other FDA approved agents such as abiraterone (Zytiga) and enzalutamide (Xtandi). These agents act on the androgen pathway. While it is not currently routinely recommended to administer chemotherapy with radium-223 dichloride because of the potential added effects on the bone marrow, small studies have shown the feasibility of this approach. In our clinic, we routinely use radium-223 dichloride in combination with agents such as abiraterone and enzalutamide. The side effect profile of these hormonal agents in combination with Xofigo is favorable, with no real added bone marrow or GI toxicity. Whether using these combinations will have a synergistic or additive effect on overall survival is currently an area of investigation. We have also administered radium-223 in combination with chemotherapy in select patients. We observed greater bone marrow side effects in these patients with no increased GI toxicity. Some patients treated in this fashion, especially those with very advanced disease, may require more frequent blood transfusions. In my clinic, we prefer to use radium-223 in patients with less advanced disease. We have found that men with lower burden of skeletal metastasis, and fewer areas of uptake on bone scan, will often have better responses.

THE FUTURE

Future and current research with radium-223 is looking at combining radium-223 with other novel agents such as atezolizumab, a new type of immune treatment (the PDL-1 antibody), looking at combining it with chemotherapy, and examining the use of repeat treatment with radium-223 six months or greater after completing the first 6-month course of treatment. This important study will answer a burning question about whether or not using radium-223 dichloride early on in this disease is optimal. Many physicians are very selective about starting radium-223 because insurance will only pay for six injections in the patient's lifetime. The doctors may want to hold Xofigo "in reserve" until the patient's need is severe. Questions like this don't come up with other agents such as

abiraterone and enzalutamide because they can be given indefinitely, until the patient's disease progresses, as there is no time limit on the insurance coverage for these agents.

Radium-223 should be administered by a committed team of healthcare professionals that should include a medical oncologist and radiation oncologist, or nuclear medicine physician who is licensed to handle radioactive materials. This team needs to understand how to manage advanced metastatic prostate carcinoma to deliver this unique agent to the appropriate patient at the appropriate time. ▲

NOTE:

Currently the FDA has approved radium-223 for a single 6 month treatment schedule due to the structure of the ALSYMPCA trial. Further trials are underway that will investigate alternate treatment schedules.

DISCUSSION POINTS / FURTHER STUDY

Some ideas to discuss with your doctor or your support group

- **WHAT ARE YOUR EXPERIENCES WITH XOFIGO?**
- **WHAT WAS ITS EFFECT ON BONE PAIN?**
- **HOW DID YOU HEAR ABOUT IT? REFERRED BY A FRIEND? PERSONAL RESEARCH? DOCTOR RECOMMENDED?**
- **WHEN IS THE BEST TIME TO USE XOFIGO? HOW WILL IT WORK WITH MY CURRENT TREATMENT PLAN?**
- **HOW ARE THE SIDE EFFECTS, DID YOU HAVE TO TAKE ANY ADDITIONAL MEDICATIONS?**

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Helpline Corner: Frequently Asked Questions

PCRI Helpline Staff

Has anyone ever beaten this disease? What are my chances of beating this disease?

If you are going to "get" cancer, prostate cancer is the best cancer to "get". It "typically" is a slow growing cancer; allowing you plenty of time to research how to best "beat" this disease. However, there are aggressive cancers, and that is why you need to discern which you have. This is where paying attention to PSA is important. Yes, "beating" prostate cancer is possible.

I just want to get it out!

We need to change this mindset of "just get it out." This way of thinking almost always leads to prostatectomy - which more times than not, is not the best treatment. There is not a guarantee that you will "get it out." So coming to terms and educating yourself about your cancer is imperative to having a healthy, happy, "relaxed" mindset and life!

What is the best treatment for prostate cancer?

As is almost always the case in any treatment selection, you need to ascertain what type of prostate cancer you have. Then, and only then, can you choose the best treatment. Many questions need to be asked and pertinent information must be obtained in order for you to have the best answer to this question! The good news is that both can be achieved!

Does testosterone give you cancer?

A bit of a complicated question, see short answer below. Read Jeffrey Turner, MD's complete article in November 2015 Insights. There is no concrete evidence whatsoever that testosterone causes prostate cancer, though it is clear that testosterone can stimulate existing prostate cancer cells to grow. The take home message, therefore, is that men who appear to have been cured of prostate cancer can indeed consider taking testosterone without concern that it will induce new tumors. This is a very different scenario from patients who have existing cancers, especially those who have aggressive, widespread, and castrate-resistant disease. Potentially, such individuals with existing cancers could be harmed by taking testosterone.

Why does my doctor want to put me on Lupron and Casodex before doing radiation?

As a man ages, his prostate size increases. Therefore, if he has a "larger" prostate, it is advisable to "shrink" the prostate. Lupron (hormone therapy) achieves reduction of the prostate size. This is desirable so that the radiation area can be reduced and beams better focused. When taking a hormone drug (Lupron), there is a possibility of a "PSA Flare". Casodex is used to block this Lupron flare.

After being diagnosed with prostate cancer, how do you know if you are a good candidate for "active surveillance"?

First, you need to understand your biopsy report. Within the report, there is something called a "Gleason Score". If your Gleason score is 6, you typically would be a good candidate for Active Surveillance. When your score is a 7 or higher, more "components" need to be assessed.

After initial PC treatment, when/how soon should secondary treatment be started if there is a PSA rise?

A prostate cancer relapse is signaled by a PSA rise after treatment. The term "biochemical failure" which means you are "relapsed". The use of Nadir (lowest PSA score after treatment) plus 2 (+2ng/ml) is typically used and is a determinant of patient outcomes, and therefore, it is used to decide when treatment should be started. (Phoenix Definition) The rate that the PSA doubles typically dictates "which" treatments can be used.

How long can someone be on Lupron before "resistance" sets in?

The time period varies among men. In some patients, hormone therapy may slow disease progression for more than a decade; in others, it may keep cancer in check only for a few months. Eventually, prostate cancer cells begin to resist the treatment. A new oral medication called ARAMIS is being evaluated in men who have rising PSA levels on Lupron and whose bone scans remain clear. For more information, visit: <https://clinicaltrials.gov/show/NCT02200614>



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The Prostate Cancer Research Institute is a 501 (c)(3) charitable not-for-profit organization located in Los Angeles, California. Our mission is to help men research their options. We assist them with their research by disseminating information that educates and empowers. Our programs help them understand their type of prostate cancer and the best way to treat and manage it.



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