Prostatepedia[1]

[1]expert insight + advice

Imaging

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In this issue....

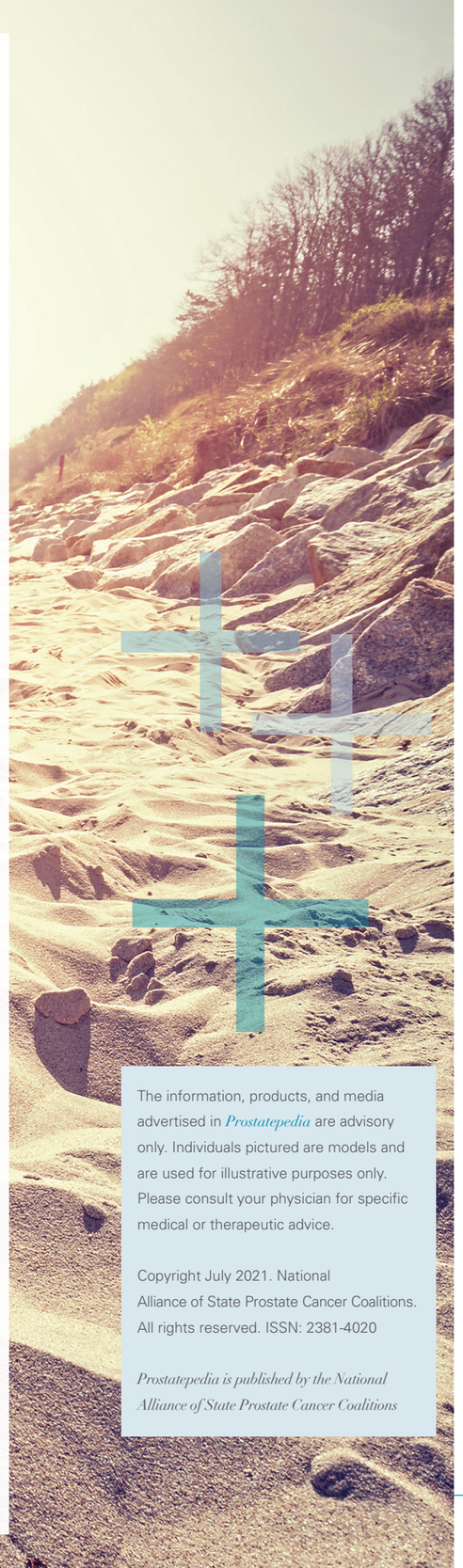
This issue is focused on the PSMA scan, which represents a major advance in prostate cancer imaging. This technique allows us to image prostate cancer metastases to bone and other sites down to 2-4 mm, far below the threshold of the commonly used CT and MRI scan.

The PSMA scan looks to improve the management of prostate cancer at several points in the natural history of this cancer. In men with newly diagnosed prostate cancer, this scan will improve our ability to identify men with early metastatic disease. These men are likely to recur after radical prostatectomy and can better be treated by approaches that take into consideration the extent of their disease.

In patients with metastatic disease, this scan is much better than the CT and bone scan in identifying the sites of metastatic disease. This will likely improve our ability to identify oligometastatic disease as well as direct radiation therapy in this setting. It is also likely to do a better job documenting response to systemic treatment as well as progression.

It is important to recognize that this scan has certain limitations. While this scan is quite sensitive, it does have a lower limit of 2-4 mm in the size of the metastases it can visualize. Additionally, there are prostate cancers that produce little or no PSMA and are thus not identified by this scan. Some metastatic lesions have been shown to have areas that are PSMA negative and areas that are positive. Thus treatment targeted at PSMA positive cancer might foster the emergence of PSMA negative cancer.

Charles E. Myers, Jr., MD Pp1



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Michael J. Morris, MD
Prostate Cancer Imaging in 2021

Dr. Michael Morris is a medical oncologist at Memorial Sloan Kettering Cancer Center In New York.

He spoke with *Prostatepedia* about imaging for prostate cancer.

What is your area of focus?

Dr. Michael Morris: I'm a medical oncologist and I'm the Prostate Cancer Section Head at Memorial Sloan Kettering Cancer Center. I generally have a research focus on new drug and biomarker development for prostate cancer, but I have a specific research interest in new ways of both imaging and treating prostate cancer patients. My research brings together medical oncology, drug development, radiology, and nuclear medicine. When you dwell in that specific place, you frequently encounter technology that can serve multiple purposes, not only new ways of imaging patients but new ways of treating them by use of that imaging.

Where does prostate cancer imaging stand today and what is on the horizon?

Dr. Morris: We're right in the middle of a major transformation in imaging and prostate cancer. Imaging has long been the acute Achilles' heel of understanding where a patient's disease is and whether a patient is responding to treatment because the imaging technologies have been so inadequate using traditional methods.

"We're right in the middle of a major transformation in imaging and prostate cancer."

Prostate cancer is a disease that generally metastasizes to bone and we really don't have any standard, good ways of imaging bone. Plus, for prostate cancer patients who have localized disease, frequently you'll know that that patient is at high risk of relapse after their initial therapy, but you don't know how to best treat them because you can't identify where their disease is at that early phase. It has usually spread to other areas before standard imaging can detect it. So you're making a lot of decisions based on probabilities, risks, or predictions, but not on actual knowledge of where the patient's disease is. That was yesterday's technology.

The technology that's coming into real practice over the next year, and which has already been adopted in other countries, is much more accurate than any imaging technology we've had to date in terms of understanding where the disease is at a given point in the patient's history. Where we couldn't see disease before, now we can identify where that disease is much earlier and with much greater accuracy and make a treatment plan based on actual accurate information. These new technologies are coming into FDA approval this year. One has already received approval specifically at the University of California, Los Angeles, and UC San Francisco. Another was just approved nationally.

What kinds of imaging are you currently using in your own practice?

Dr. Morris: We have the advantage of having a pretty large research focus at MSK in collaboration with our Molecular Imaging and Therapy Service and Radiology Department. We have a lot of novel imaging tools that are available to MSK that aren't necessarily available to every patient in the country due to our substantial multidisciplinary imaging program. But a key modality that we have is PSMA imaging, which is the cornerstone of this revolution that's happening. PSMA-based imaging is a type of molecular imaging. Traditional imaging is based on defining anatomy. Molecular imaging is based on biology – that is, detecting prostate not on the basis of changes in the structures of the body, but identifying the unique biology of the prostate cancer cell as it is different from most normal tissues. The PET tracer localizes directly to the prostate cancer cell, which has a protein called PSMA on its surface, and gives off a little bit of radiation in that area so that you can see it on a scan. So now you don't have to wait until the focus of cancer is big enough to change the anatomy of a distant site such as a bone; instead, you can see very small amounts of disease by virtue of the presence of PSMA.

Where do you think molecular imaging is going in the next few years?

Dr. Morris: It's probably going to replace most standard imaging technology because it is so much more accurate and you can identify where the disease is so much earlier. In terms of how we treat patients, we're now going to have a very different sense of the patient's distribution of disease in contexts that we never had before. For example, patients that we used to call high-risk localized disease, will be upstaged to having distant disease. We're going to have to figure out what the best treatment paradigm for those patients is, but some will be reclassified from high-risk localized to metastatic.

By the same token, for patients who had primary therapy and now have recurrent disease based on a rising PSA, we used to have to estimate where treatment should be directed. Now we'll have a sense of whether the disease has recurred

locally or in the pelvis or outside of the pelvis.

Each of these scenarios has a different treatment approach. A patient with distant disease might get systemic therapy early, while a patient who has clearly identifiable disease in the prostate bed and the surrounding pelvis might get radiation with or without hormonal therapy in that area.

The key is we wouldn't have to guess where the disease is, we would know -- we would be able to see it. Rather than decision-making based on predicted risk, we will now be able to see where the disease is.

So then the discussion will shift from where the prostate cancer actually is to how best to treat the prostate cancer that we see?

Dr. Morris: Yes. We have to figure out how to adapt our treatment paradigms to the improved knowledge of where the disease is. That will take some research. There are a lot of studies that are getting activated in which those new treatment paradigms are being explored. You're right that we're going to have to move from the novelty of the imaging to developing the best treatment patterns.

When you think about this revolution in imaging coupled with the revolution in genomics, we're getting closer and closer to personalized, precision medicine.

Dr. Morris: Yes. We should also be mindful about the risks of upstaging patients with new imaging technology. Take, for example, the PSA when it was introduced in the 1980s. You had this new type of technology that could identify the presence of disease very early, much earlier than before the PSA was introduced.

And there was a period in which the prostate cancer community, both physicians and patients alike, overreacted to the PSA. It was an early declaration of disease and an early declaration of relapse. We had to learn how to use the PSA

> *"Theranostics is the logical extension of PSMA based imaging.."*

appropriately and not overreact to it. PSMA PET imaging could pose similar risks. We could overreact to information if, for example, we see a single lesion develop as a patient is on a given therapy. That doesn't mean the patient has relapsed and the therapy should be terminated. Historically, we used to stop therapy when the PSA started to rise then we realized that's an overreaction because we're stopping life-prolonging therapy at the first evidence of relapse, at the first evidence of resistance when the patient may, in totality, still be benefiting from treatment. The same risk applies to a very sensitive imaging modality.

There'll be a period where everything's in flux, right?

Dr. Morris: Yes. That was true with the introduction of CT and MRI as well. All of a sudden, clinicians could see abnormalities that they never knew was there? You had this high-resolution view of the internal structures of people's bodies. And it was hard to know which abnormalities were significant and needed to be acted on versus those that needed to be observed

serially versus those that could be ignored. We're going to have to learn how to appropriately use this new tool so that we react only to the meaningful findings.

Exactly. What about theranostics?

Dr. Morris: Theranostics is the logical extension of PSMA-based imaging. If you can see disease by virtue of radiation being carried to the cancer on a targeting molecule, you should be able to treat that disease by a therapeutic dose of radiation as a payload.

Theranostics is an approach where you use the same targeted approach to image as you then use to treat. You take an image and you see that the target is there. If it is there, you give them a treatment dose and target the disease with enough radiation to actually kill it.

The word theranostics is a combination of the words "therapy" and "diagnostics." In theranostics, the presence of the target is documented by the imaging study; and then treated with the therapeutic molecule. Both using radiation?

Dr. Morris: Yes.

Is it possible to use other kinds of therapy than those with a radiation payload?

Dr. Morris: Sure. There's a whole different category of drug called an ADC, an antibody-drug conjugate, for example, in which the antibody is doing the targeting and then carrying a payload of, let's say, chemotherapy.

What about immunotherapy? Could you use the same general practice for immunotherapy?

Dr. Morris: As long as the immunotherapy is dependent on an imageable target, then you could. More specifically, there's a class of immunotherapy in which you target the tumor based on PSMA to recruit T-cells to the cancer. So you would get a scan, establish that it's a PSMA-producing cancer, and then give them immunotherapy that targets PSMA. Bispecific antibodies can achieve this, as can CAR-T cells. These approaches are in clinical trials right now.

It sounds like the next few years are going to bring massive changes.

Dr. Morris: I think those changes are already happening.

Any final thoughts for patients about imaging?

Dr. Morris: There are some roles for which PSMA PET is not used. For example, PSMA PET still has a threshold below which disease will be undetectable. So patients with very low PSA values (such as below 0.2) should not expect PSMA to be informative. Further, there are circumstances in prostate cancer for which no PET imaging is appropriate, such as low-risk localized disease. Finally, we don't know how PSMA PET should be used to reflect the effectiveness of a response to treatment.

So just because you're reading this and it sounds interesting, doesn't necessarily mean it's right for you.

Dr. Morris: Exactly. We have data for its use in a number of contexts, and ongoing studies to expand those contexts will illuminate where PSMA PET should and shouldn't be used in routine clinical practice. Pp

Thomas Hope, MD
Prostate Cancer Imaging in 2021 and Theranostics

Dr. Thomas Hope is the Director of Molecular Therapy in the Department of Radiology and Biomedical Imaging at the University of California, San Francisco.

He is keenly interested in novel imaging agents and therapies for prostate cancer.

He spoke with *Prostatepedia* about the recent FDA-approval of Pylarify (piflufolastat F 18) and the promise of theranostics for prostate cancer.

What is the state of prostate cancer imaging in 2021?

Dr. Thomas Hope: We have two FDA-approved PSMA radiotracers. Recently, Pylarify (piflufolastat F 18) or F-18 DCFPuL was FDA-approved. This is another PSMA radiotracer, and is very similar and is in the same class as Gallium-68 PSMA 11. It is also cyclotron-produced, meaning that we can now manufacture large quantities of the radiopharmaceutical and distribute it around the country. The approval of F-18 DCF-PYL will now lead to much more wide availability of PSMA PET radiopharmaceuticals. This new approval is wonderful. Hopefully, by the end of this year we'll have much more wide availability. Although it will take a little bit of time for the different cyclotron facilities to get up and running and to figure out contracting and insurance.

"Over the next one to two years, PSMA PET will be used across large numbers of patients in the United States"

This is actually a big year for prostate cancer imaging. With the PSMA PET radiopharmaceutical approvals and wide availability, the flood gates are opened. It will be used across the country in thousands of patients a year, which will now allow us to have a better understanding of how these imaging agents should be used, when they should be used, and how the results should inform treatment paradigms for each patient.

Over the coming years there are going to be more PSMA PET radiopharmaceuticals coming down the line, but they are not going to change anything dramatically. They're going to have the same or very similar sensitivities and specificities to Gallium-68 PSMA-11 and DCFPyL. In essence, they will expand the class, rather than going from having no availability to having availability.

Are you anticipating that the next 12 to 24 months will give us a better picture of how these imaging techniques can impact treatment?

Dr. Hope: Over the next one to two years, PSMA PET will be used across large numbers of patients in the United States. Patients who were thought to have no metastatic disease before, will now have metastatic disease. This will result in what we would call a stage migration. Patients with high-risk disease that were M0 will now become M1; patients with local disease only, may be seen to have distant metastases, et cetera. All of these things will cause a re-bucketing and movement of patients based on location of disease.

At the same time, now that we know where the disease is, radiation oncologists will see it and start to irradiate it. We are going to see a lot more external beam radiation therapy targeted to oligometastatic disease that we didn't know was present before. So overall, a) patients are going to be migrating in stage based on imaging results, and then b) the imaging results are going to lead to a lot more external beam radiation therapy. All of that is going to cause a ripple effect in the landscape of prostate cancer patients.

We now have a better way to determine whether or not you have metastasis. During this two year transition phase, we are hopefully going to collect data and run clinical trials. These trials will take 3-5 years and will help us understand the best way to treat these patients.

But that is not going to happen in the next year. What is going to happen in the next year is this ground change as patients are re-bucketed. How we think about risk profiles is going to change. And then we need to reimagine how we treat these different buckets.

What is theranostics?

Dr. Hope: Theranostics is the idea that you use the same compound for both diagnosis and therapy. Although, technically it does not have to be the same compound, but we in nuclear medicine think of it that way.

For example, we have a small molecule that binds to PSMA. We can label it with radioactivity to image it, and then we can also label with radioactivity to treat it. The classic example would be Gallium-68 PSMA-11 for imaging and Lutetium-177 PSMA-617 for therapy.

But you can think about this maybe a little more broadly: we can image Gallium-68 PSMA-11, but then we can actually treat using antibodies. We can treat using car-T cells that are targeted. There are many other ways to target imageable biomarkers. Although the term originated in the radioactive therapy setting, it can be used in many other settings as well.

We are in an exciting moment. The VISION trial results will be published in two days. And those are said to be positive with positive overall survival and progression-free survival results.

In the setting of castration resistant prostate cancer, the trial data itself is maybe less exciting, as the trial in essence did not have an active comparator arm. It is not particularly shocking that lutetium-177 PSMA-617 outperforms placebo. The most significant impact of this trial, is that it will lead to FDA-approval of lutetium-177 PSMA-617. The drug will now become available to patients in the United States, hopefully by the end of this year. The theranostics revolution in the setting of prostate cancer is really close to finally happening.

The more valuable data may be trials like the Thera-P trial, which compared lutetium-177 PSMA-617 to cabazitaxel. The Thera-P trial, which was done in academia and the Peter MacCallum Institute, will be much more relevant, because it did also show that PSMA 617 had a better biochemical progression free survival and was better tolerated than chemotherapy. That to me is much more important and really supports the use of PSMA therapy in patients with prostate cancer. Pp1

Michael Hofman, MD
Prostate Cancer Imaging: The Australian Perspective

Professor Michael Hofman, a nuclear medicine physician, is the Director of the Prostate Cancer Theranostics and Imaging Centre of Excellence (ProsTIC) at the Peter MacCallum Cancer Centre in Melbourne. He is keenly interested in radiopharmaceuticals for imaging and therapy—called theranostics—for prostate cancer.

Prostatepedia spoke with him about imaging for prostate cancer.

What is PSMA?

Dr. Michael Hofman: PSMA is prostate-specific membrane antigen, a protein that sits on the cell surface of prostate cancer cells in high amounts. In my specialty, nuclear medicine,

"Knowing the true extent of disease is critical for rational and optimal decision-making in medicine"

we use radioactive substances for both imaging and treatment. PSMA is an excellent target for imaging and also for treatment. In the last decade, there have been major advances in labeling small molecules with a radioactive probe that targets PSMA. It is evident that it's a game-changer, both on the imaging side and the therapy side.

What has been the Australian experience with PSMA? How has it changed the prostate cancer treatment landscape?

Dr. Hofman: I'll start with a little more background. We do a lot of PET scanning. PET stands for positron emission tomography. It's a widely used technique for imaging patients with cancer. It's a whole-body scan and it tells us where tumors have spread and how much tumor there is. The most commonly used radiotracer is one called FDG, which stands for fluorodeoxyglucose. It's a radioactive sugar. It's never been particularly effective in prostate cancer because prostate cancer tends to be more slow-growing; therefore, it's not using huge amounts of sugar to grow. Compared to breast cancer, lung cancer, or other cancers, PET scanning has not been used much in prostate cancer. Then PSMA came along. We did our first PSMA PET scan in our center at Peter MacCallum Cancer Centre in mid-2014. It was immediately obvious on patient number one that this is a game-changing technology. Just by way of background, the small animal data supporting PSMA PET was done by American and German groups. This technology evolved rapidly from laboratory to humans, and the first case report of PSMA PET/CT was around 2013. The first patient we imaged at Peter Mac was a man in his late 70s who was scheduled to have a prostatectomy. The PSMA PET scan showed that he had both lymph nodes in the pelvis that were involved and also bone metastasizes. His management was directed away from surgery to hormone treatment. He came for a PSMA PET scan one year later and I caught up with him. It had a huge impact because, at his age, undergoing a prostatectomy would have left him with a large number of side effects. He was going down that pathway because he wanted to cure his prostate cancer. It was obvious on the PSMA PET scan that he could not be cured because the prostate cancer had spread to other sites on his body.

Knowing the true extent of disease

"We did our first PSMA PET scan in our center at Peter MacCallum Cancer Centre in mid-2014."

is critical for rational and optimal decision-making in medicine. If you don't know what you are treating, all the things that follow from surgery to radiotherapy to drug treatments, you can be doing the wrong thing for your patients because you have an erroneous picture of the current state of disease. The images we get with PSMA PET are exquisite. We see sites of tumor as small as two to four millimeters in size that light up very brightly on the scan. Being a whole-body scan, we can look at a single image and very quickly determine where prostate cancer has spread. When we started doing this in 2014, it was a new technology. It was not funded or reimbursed, and without too much encouragement referrals started coming into the service. Word got around very quickly in the local urology community that this scan was really helping patients.

Fortunately, other sites in Melbourne, and in major cities around Australia started doing PSMA PET scans. Our regulatory framework is quite different than in the US. We don't need the equivalent of FDA approval for this technology to be adopted. It's still not reimbursed, but it is widely available. The cost is relatively cheap. A PSMA PET scan in Australia at the moment costs around 750 to 850 Australian dollars, which is approximately 500 to 550 US dollars. In Melbourne, there are around 15 to 20 centers where you can get a PSMA PET scan. We're a city of around 5 million people. In Australia, there are now more than 50 sites where you can get PSMA PET and we're a country of 25 million people. Now that FDA approval has occurred for gallium PSMA and will occur for fluorine PSMA, I think you'll see the US situation rapidly change to widespread availability, like in Australia today.

Would you be able to tell me about the proPSMA study?

Dr. Hofman: Early in 2016, we designed a randomized control trial called proPSMA. We randomized men with newly diagnosed high-risk prostate cancer, who were scheduled to have either surgery or radiation with a curative intent, to have either a PSMA PET or the current standard of care at the time, which was a CT antibody scan. We opened it at 10 sites all around Australia. It was led by myself at Peter Mac and funded by the Prostate Cancer Foundation of Australia and Movember.

At its peak, we were randomizing more than one patient every single day including Saturdays and Sundays. We recruited 300 men at these 10 sites around Australia in around 18 months. The results were published in The Lancet just over a year ago. It showed unequivocally that PSMA PET scanning was superior to CT and bone scans both in terms of accuracy, management impact, the number of equivocal findings, less radiation dose, and also being very reproducible. This is high-level evidence that governments can now use to get reimbursement of PSMA PET scanning. I understand the proPSMA study data is also being used by other countries. In Switzerland, PSMA PET scanning is now reimbursed by the government and that proPSMA study were part of the results required to achieve that.

Interesting. It sounds like this should be the gold standard going forward?

Dr. Hofman: I think it is. We will see over the next two to three years that it will be embedded in clinical practice guidelines as the gold standard. What's great about it, at least for that staging setting, is it replaces existing technology. At the moment, men have a CT scan and a bone scan. That's often two visits to the hospital, on two separate days. The PSMA PET scan is completed in 90 minutes and it's a single scan. The proPSMA study also included a health economics analysis. We had a very experienced health economist involved and they analysed the health economic aspects of a PSMA PET scan. We demonstrated that a single PSMA PET scan in Australia, using Australian real-world costings, was actually cheaper than having a CT scan and a bone scan. Those results were published earlier this year in European Urology, In the Australian context, a CT and bone scan is approximately 1350 Australian dollars and a PSMA PET scan is roughly 100 dollars cheaper.

Let's talk a little bit about PSMA as Theranostics.

Dr. Hofman: Theranostics is a word that describes both diagnostics and therapeutics. For the imaging component, we're using two main radioactive substances. One is called Gallium 68 and the other is Fluorine 18. PSMA is delivered intravenously, it travels around the body and gets

taken up into prostate cancer cells. It doesn't have any side effects. The type of radiation emitted passes out of the body. It's a low-energy radiation that's detected by the PET scanner and enables incredible, three-dimensional, whole-body images. Those radioactive substances have a very short half-life of 60 to 120 minutes, which means there is no radiation left in the body several hours later.

For Therapy we change the radioactive substance to ¬177Lutetium-PSMA617 . These radioactive molecules emit a different type of radiation called either beta or alpha radiation, rather than the gamma radiation that the imaging probes emit. These are given the same way, as an injection into the vein. They travel around the body and seek out the prostate cancer cells, binding to a PSMA receptor much in the same way as the diagnostic tracer. Once it's bound to the prostate cancer cell, the Lutetium 177 travels only 1 millimeter, emitting very high energy, a little bit like external beam radiation, but very targeted. It causes a double strand of DNA breaks to the cancer cells and results in the killing and shrinkage of tumors. It's a very effective way to deliver high doses of radiation to cancer cells, wherever they are in the body. The radioactive substance travels only 1 millimeter and gets taken up into the tumors, avoiding healthy tissue. The rest of the body doesn't see a lot of radiation. It's a very smart way to deliver a targeted treatment for prostate cancer. It is also very well tolerated with minimal side effect, compared to other standard of care treatments like chemotherapy.

Importantly, Theranostics allows clinicians to carefully determine

which patients will benefit from the treatment, not everyone is suitable. We do the PSMA PET scan first which allows us to see if there is high PSMA expression at all the sites of tumor. Around 30% of men that we screen with PSMA PET, we are able to determine they will not respond to therapy. This is important because it avoids unnecessary treatment in those men who will not benefit.

Are there any side effects? If so, what are they?

Dr. Hofman: Yes. All treatments have side effects and Lutetium PSMA definitely does have some side effects, but it is a well-tolerated treatment. The main side effects are dry mouth and dry eyes. Some of the PSMA is expressed in salivary glands, so you get some radiation delivered to your salivary glands. That causes dry mouth. Some radiation is taken up by the small bowel and that can cause some nausea. We give it as an intravenous injection so it travels around the bloodstream before finding its way to the tumors and that can therefore cause a reduction in blood counts. But in terms of very severe side effects, which we call grade three or four toxicities, they occurr at a much lower rate with Lutetium compared to chemotherapy.

Interesting. What is the VISION trial?

Dr. Hofman: VISION is an industry-sponsored trial. Novartis, a large pharmaceutical company, purchased the rights for the molecule that we used in the TheraP trial called PSMA-617, a few years ago. They conducted a big Phase III trial of over 800 men. This trial did not run in Australia. It was conducted in the US and Europe. The results will be presented at one of the world's leading Oncology conferences, called ASCO in June. By the time this is in print, those results would have been released but Novartis has already sent out a press release that's in the public domain telling us that the primary endpoint of increased survival was met. Survival was prolonged in men randomized to Lutetium-PSMA-617 compared to the other arm in the trial, which was best standard of care. These are really exciting results. Novartis will use this information to facilitate FDA approval in the US. I hope by the end of this year, this will be FDA approved and there will be an explosion in availability of Lutetium PSMA within America, Europe, and other countries where Novartis has applied for funding.

Great. That will be amazing. Do you have any trials open and enrolling now along similar lines that may be of interest to people reading this? We do have some Australian readers.

Dr. Hofman: At Peter Mac, we have been working very hard to do better because, despite the exceptional responses we see in some men, patients eventually progress. In fact, in that first trial we did in 50 men at Peter Mac, we only have 1 or 2 men still alive. There is a need to get better and longer responses with Lutetium PSMA. We believe there are a few ways to do that. One is to not use it as a treatment on its own but to combine it with other treatments. We have two trials currently open that have nearly finished recruitment investigating this, and three more in active recruitment phase. We also have a pipeline of studies about to open at the end of 2021 and in early 2022. We are bringing the use of LuPSMA forward from the last line of treatment to a first line of treatment. UpFrontPSMA is a randomized controlled trial where men with newly diagnosed metastatic disease are randomizing to either LuPSMA followed by chemotherapy or chemotherapy alone. I think that's the first trial open anywhere in the world testing LuPSMA as a first-line treatment. We have another trial called LuTectomy. where we deliver one or two cycles of LuPSMA in men prior to their prostatectomy. These are very exciting studies.

I do envisage, in the future, if the correct research is done, it is possible that Lutetium could replace external radiation as a treatment for some men or it could even replace surgery. But these are things that do need careful study. Until they have the evidence base to show this, it's not something that should just be done outside of a clinical trial.

Is there anything else you want to add for patients reading this?

Dr. Hofman: Yes. I think the challenge for many of the men reading this, particularly depending on when it is made available in different countries, PSMA PET or LuPSMA therapy is simply not yet readily available. It is a challenge to know about these new treatment options but not being able to access them. The fundamental work has now been done in imaging and the therapy so accessibility will change after US FDA approval. I think that will rapidly disseminate throughout the world and when we have our next conversation, hopefully, both the scan and the treatment are available. Pp

Bela Denes, MD
What the Pylarify Approval Means

Dr. Bela Denes is the Vice President of Global Medical Affairs at Lantheus Medical Imaging.

He spoke with *Prostatepedia* FDA-approval.

What does FDA approval of PYLARIFY® (piflufolastat F18) mean for prostate cancer patients? How will it change the prostate cancer landscape as a whole, not just prostate cancer imaging?

Dr. Bela Denes: In the last several years, there has been a tremendous amount of interest in developing positron emission tomography (PET) imaging agents to better identify prostate cancer earlier and much more accurately than the conventional imaging agents at our disposal today, which are primarily CT scans, bone scans, and MRI.

"Think of it like a Geiger counter that can detect radiation except in the case of PET, the radiation is captured by a camera and produces an image and locates exactly where the tumor is."

As most patients know, prostate cancer can at times be a straightforward disease to treat. For instance, active surveillance for low risk disease, but it also can be a very, very difficult and challenging disease to treat especially for patients with high risk features. If you look at the 10-year outcomes of men who are diagnosed with prostate cancer and undergo either surgery or radiation therapy what you find is that in 40% to 50% of those patients the cancer will recur after their initial therapy. We have to do better.

In other words, the initial therapy that's intended to cure the disease has failed and these men have a recurrence or persistence of disease. The hallmark of that is, of course, a recurrent elevated or a rising PSA. The question then is: why do 50% of men fail to be cured by surgery or radiation therapy? Is it because radiation doesn't kill cancer cells, or surgery doesn't excise them effectively? And the answer is no – those are very effective treatments in the right patients. The challenge is selecting patients properly, making sure the patients we operate on or that undergo local therapies (including radiation, surgery, cryosurgery, or high-intensity focused ultrasound therapy) have disease that's truly local and confined to the prostate and has not spread. That's been a challenge, as I mentioned, with the current imaging techniques like the CT scan, MRI, and bone scan.

These scans are good, but the problem is they're unable to locate small volumes of disease. They're not good enough. In other words, sensitive enough to detect low-volume disease that may have spread outside the prostate.

PET imaging has been and is the standard-of-care imaging in many other cancers like breast cancer, lung cancer, colon cancer, lymphoma, and Hodgkin's disease. But, till recently, agents that are sensitive enough to pick up prostate cancer have been hard to come by. A few years ago, in 2016, Axumin (fluciclovine F18) was approved for imaging prostate cancer. Axumin was the first PET agent that was widely available and useful in helping identify the location of the disease or the extent of the disease, but only in the recurrent setting after treatment.

Since Axumin (fluciclovine F18) was only approved in the recurrence

setting we could not use it upfront to identify patients who were at risk for metastasis prior to surgery or radiation therapy. And, although it is much more sensitive than CT and bone scan and those other agents, Axumin or fluciclovine F18 is not specific for prostate cancer; it's based on amino acid uptake by cells and therefore can be taken up by other cancers not just prostate cancer. Fast forward to this year and the good news is that within the last six months, two PSMA targeted agents much more specific for prostate cancer have been approved by the FDA. PSMA stands for Prostate Specific Membrane Antigen.

UCLA and UCSF received approval for Gallium-68 PSMA at their institutions at the end of December. And on May 26th, Lantheus received FDA approval for PYLARIFY, or piflufolastat F 18, previously known as 18FDCFPyL, or simply PyL, as a PSMA-targeted agent for prostate cancer in both settings, at the time of diagnosis before initial treatment with surgery or radiation and for recurrence after treatment.

The approval of PYLARIFY was based on two studies. The OSPREY trial that evaluated the sensitivity and specificity of PYLARIFY to identify metastasis prior to surgery and the CONDOR trial that looked at the ability of PYLARIFY to detect recurrent disease in men whose PSA was rising after initial treatment whose work up using the conventional imaging tools we mentioned before was negative and not informative. In the CONDOR study almost 2 out of 3 men had positive scans, scans that were able to detect and locate the site of recurrence that was not seen by conventional

Currently treatment recommendations are based on past experience and population-based predictive algorithms that have been developed by some of the top medical centers. But PSMA PET is very different in that it allows us to make individual or more personalized treatment recommendations. PSMA is a protein that's on the surface of the prostate cancer cell. And because it's on the external or outside surface of the prostate cancer cell itself, it can be imaged or targeted with a molecule that has an attached radioactive isotope on it, which then emits radiation, which can be picked up by a PET camera.

Think of it like a Geiger counter that can detect radiation except in the case of PET, the radiation is captured by a camera and produces an image and locates exactly where the tumor is. And because it's on the prostate cancer cell itself, it doesn't matter if that cell is in the lymph nodes, if it's in the area of the prostate or the prostate bed, or if it's in bones, which is a common site of metastasis or spread of prostate cancer. So, unlike a bone scan which only looks at bones, PSMA PET scan will allow us to evaluate all the tissues in the body with a single scan.

There's a huge advantage to this agent because it specifically targets the prostate cancer cell. What your readers may not be aware of is that PSMA-targeted PET scanning or PSMA PET/CT is new in the US, but it has been widely used outside the United States, especially in Europe and Australia where it is now the standard of care. We've been a little bit late to the game in the US, but we're catching up, and we now have two FDA-approved PSMA agents in the marketplace.

There are some differences between the two. The gallium PSMA is only available at UCLA and UCSF because it has what's called an institutional approval. PYLARIFY (piflufolastat F 18), the product that Lantheus had approved, is going to be widely commercially available. And it is the first and only commercially available PSMA agent in the US currently.

With the FDA approval, PYLARIFY (piflufolastat F 18) is going to be widely available to a lot of patients over the next year. What impact do you think that is going to have on how we approach prostate cancer care?

Dr. Denes: If you talk to the experts in prostate cancer, they will all agree that PSMA imaging of prostate cancer, whether in the initial setting, where you're trying to determine whether the disease is localized to the prostate, or in the recurrence or progressive setting is going to be a major game-changer

"It is the first and only commercially available PSMA agent in the US currently."

for men with prostate cancer because it will give us visibility to the disease that we have not had previously. We have data as I mentioned from the CONDOR trial, which was one of the two trials that were submitted to the FDA and formed part of the basis of the approval. In the CONDOR trial, the median PSA for the 200 plus men was 0.8. What that means is half the men in that trial had a PSA less than 0.8, where CAT scans, bone scans, and MRIs are not helpful. In these men, including men with what we consider low or very low PSA levels, PYLARIFY (piflufolastat F 18) was able to detect the site of recurrence in almost 70% of the patients.

Interesting. It'll be interesting to see what happens over the next two or three years, as we will understand a lot more about prostate cancer as it plays out over the population.

Dr. Denes: I think we're going to learn much about prostate cancer in the next two to five years. More than we have in the last 10 or 15. If you look at some of these images, there are patients who have relatively low PSAs where we used to think that you're not likely to have distant metastasis to the bone unless your PSA is over 20 or your PSA is over 30. But we're seeing patients with low PSAs now in the single digits that have metastases outside the prostate to lymph glands or to the bone. We're going to learn a lot just because of the visibility that this agent affords us.

It's like turning on a light in a dark room.

Dr. Denes: Correct.

Is there anything else readers should know?

Dr. Denes: PYLARIFY (piflufolastat F 18), like all F18-labeled agents are made in cyclotrons. Cyclotrons have the capacity to produce large batches of PYLARIFY to be able to image dozens of patients. The goal is to make sure that men with prostate cancer in the US will be within one or two-hour drive from a center that offers PYLARIFY imaging. It takes a little bit of time for those cyclotrons to come online and get approved by the FDA to manufacture PYLARIFY (piflufolastat F 18). We are starting with a handful but expect to have all online by the end of the year. We are contracted with three different manufacturers, all of which have cyclotrons, and will have about 30 manufacturing sites throughout the US. So, between now and the end of the year, we expect to have a manufacturing capability to provide PYLARIFY (piflufolastat F 18) to 90+% of the men with prostate cancer in the US.

Any final thoughts?

Dr. Denes: In the last five years, we've had a number of new drugs approved for the treatment of advanced prostate cancer by the FDA, but we lacked better, more sensitive imaging to help guide the use of those agents. And now we're catching up with approval of PSMA targeting agents that can actually tell us where the disease is so we can better match the disease to treatment options for these men. It is a huge leap toward precision medicine, personalized medicine.

Do you think it's possible to understate how important this approval is for prostate cancer imaging?

Dr. Denes: It's a game-changer for prostate cancer management because if you think about it, you can't hit or treat what you can't see. Right?

Right.

Dr. Denes: From that standpoint, it's a huge advantage, and it will make a tremendous difference in the way patients are selected for various therapies and will personalize treatment for the majority of those patients. And hopefully, will translate into better long-term outcomes. Pp[1]

John Dowling
Brexit + PSMA-PET Scans

John Dowling, Vice-Chairman of Europa Uomo, talks about the Irish experience with PSMA-PET scans.

Being a smallish island situated off the coast of a bigger island has impacted Ireland politically, historically, and culturally. The recent departure of the United Kingdom (UK) from the European Union (EU) is impacting men in the early stages of metastatic prostate cancer medically.

The population of the Republic of Ireland is 5 million; the UK has more than 12 times that number. Since joining the EU, citizens of smaller countries, such as Ireland, benefited from reimbursement mechanisms for rarer specialized treatments and testing, such as PSMA-PET scans, that are more readily available in larger and richer European population centers.

The basic procedure to receive a PSMA-PET scan under the EU agreement is the patient's specialist treating physician makes a declaration stating that his or her patient requires a PSMA-PET scan. Irish patients who obtained the scans in other EU countries had the costs reimbursed to the treating country by the Irish Government. There were, of course, additional bureaucratic hoops to be jumped, but that was the basic procedure. Irish citizens could access specialized treatments unavailable in Ireland in the neighboring UK, where many Irish people live and work. In addition to the UK, Irish people could travel further afield, to Sweden, Germany, Italy, etc. With the prospect of the UK leaving the EU in 2020, the Irish Health Service Executive decided to fund a single PSMA-PET scan unit in Ireland—this was not as positive a move as it might first seem.

Many prostate cancer patients read of the PSMA-PET scan with interest for years before a single unit was finally opened in Ireland almost three years ago. PSMA-PET scans were seen by many newly metastatic prostate cancer patients as the "magic scan" that could reach the parts other scans could not. "Jim," the former secretary of the Irish prostate cancer support group Men Against Cancer (MAC), actively sought access to a PSMA-PET scan. His prostate cancer was aggressive with a biopsy Gleason score of 4+5. He reckoned he needed the scan urgently.

It was clear to Jim that his cancer was progressing, but the scans then available in Ireland could not show the location of the tumor or tumors. Jim was sure such information would guide possible treatments and greatly reassure him and his family that they had a proper handle on the situation.

For a considerable period, Jim was very matter-of-fact about his aggressive cancer. We were the same age, born just before the end of World War II. Both of us were Dublin lads, originally from the same part of the city. Our paths crossed in later life—at one time I was Jim's trade union representative before either of us ever knew the other had prostate cancer. We eventually met again in MAC. We compared notes—my PSA was a bit lower than his; Jim's Gleason score was considerably higher than mine. Following his diagnosis of prostate cancer, the trajectory of his PSA was rapidly upwards, whereas mine was almost static.

Jim was a semi-retired public servant with many interests. He was a high-profile volunteer board officer of one of the biggest Irish charities. Jim was also a pilot. He had been excluded from his cockpit following his cancer diagnosis. Most of all, Jim wanted to get back in the air. He was certain that the PSMA-PET scan was his way back to flying again.

Jim knew he had a tumor that was not being picked up with the scans then available in Dublin. He was resourceful and persuasive. His oncologist certified that he was an appropriate candidate for a PSMA-PET scan, so it became a question of where to go for it.

Jim decided on Heidelberg, Germany, and was excited about his pending trip to this beautiful city. His colleagues in MAC awaited developments, perhaps with just a little anxiety, but also with the kindly expectation that they would be hearing good news soon from Germany.

"Irishmen who previously had a multiplicity of choice for PSMA-PET scans, no longer had access to the nearest English-speaking locations."

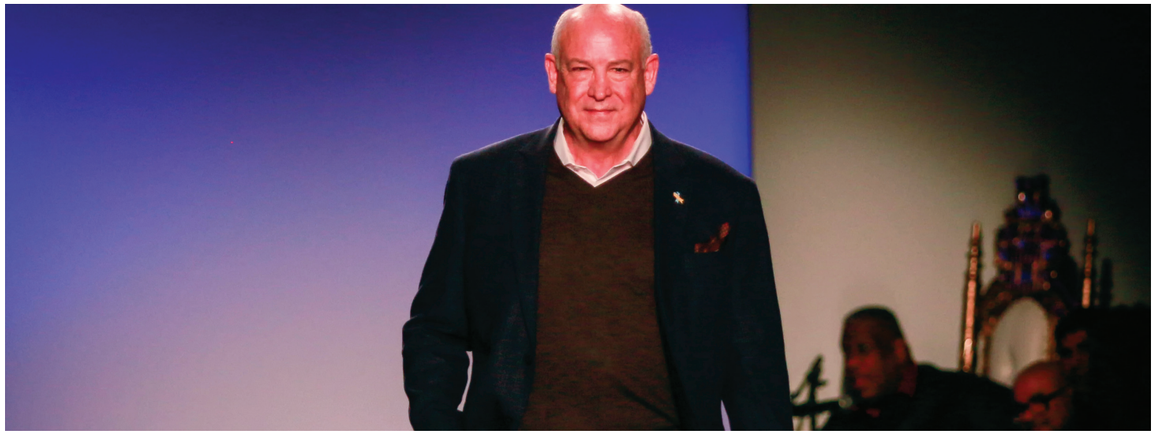
The PSMA-PET scan certainly lived up to its reputation for finding aggressive tumors. Jim wanted to know if the location of any tumor would prove to be operable and/or treatable. The result, however, was not quite what Jim was expecting. The scan found a tumor. Indeed, the scan revealed a total of 21 tumors. They were everywhere: spine, hip, visceral organs, and brain. Jim returned to Dublin a shaken man. He appeared, at times to be almost in denial. Those of us in MAC knew it was now only a matter of time and it appeared that his family knew this also. His beloved plane would have to remain on the ground as a different journey beckoned.

Jim died a few months after his return from the PSMA-PET scan. We still miss him. It would be glib to say that good secretaries are hard to find, but his remit permeated so many organizations, all of which drew on Jim's boundless compassion, his articulate delivery, and his indefatigable energy, which was evident up to a late stage in his illness.

In Ireland, meanwhile, the story moved on. The Irish Health Service Executive provided funding for a single PSMA-PET scan unit. Paradoxically, this reduced the availability of the scan to Irish patients. As one bitter radiation oncologist complained: Irishmen who previously had a multiplicity of choice for PSMA-PET scans, no longer had access to the nearest English-speaking locations. In Britain, because of Brexit, they were now further limited to one unit, in one hospital for the whole state. Yeah, sure, there were "plans" for additional units, but this is always contingent on equipment funding, and even more crucially, on the provision for ongoing staffing costs.

In the meantime, the wait time for men with suspected metastatic prostate cancer grew and grew. It appears that if an EU country has even one unit for PSMA-PET scans, the door is closed for access to another country's facilities for that treatment using the EU reimbursement system. A case of one step forward and three steps backward? Pp!

Patients Speak
Mike Crosby: My Story



Mike Crosby talked to *Prostatepedia* about his prostate cancer journey and experiences with imaging.

Tell me about your prostate cancer journey.

Mike Crosby: After a long career in the Navy, I was diagnosed with prostate cancer in 2015 at the Phoenix VA Medical Center. It was during the middle of that whole public mess about scheduling and delays. So, I was right in the middle of that because of my affiliation with Phoenix. At the VA, I was diagnosed. Well, I was actually told that I most likely had cancer, but they told me to come back in six months and they would do another PSA and my only option was surgery. I stepped out of the VA at that time and had a biopsy the next day through a referral from a family member.

The biopsy came back as a Gleason 7, 4 + 3. I had been talking to a family member by marriage who is a radiation oncologist at Swedish Health Services in Seattle. We immediately decided something had to be done and SBRT Radiation treatment was probably the best course. I went to Seattle and had my first CyberKnife in 2015. New Year's Eve 2015 was my last dose. I had five fractions and my PSA looked great. Over the next few months, it went down to below one, I think it was about a 0.7. While recovering we moved to Oklahoma City for work. We moved the job, opening another office there.

In October 2018, I went in for my annual physical and the normal checkups, and my PSA had started to rise again. After finding a urologist active in the VA CHOICE Program he ordered my first imaging which was an Axumin scan. It identified very clearly involvement of one lymph node. It was a presacral lymph node and was not able to be operated on or surgically removed. They referred me back to where I originally had my first CyberKnife treatment. I went back to Seattle and had another CyberKnife treatment on that one lymph node. And, sure enough, the PSA went down again, responded properly, no side effects, no toxicities or anything. After about another year, my PSA started rising again.

Upon this rise, I was referred to West Los Angeles VA where a clinical trial is taking place with 18F-DCFPyL PSMA imaging. It's the only place in the US that's doing that, in conjunction with Progenics, now Lantheus. You have to be a vet to get into the clinical trial. It's free and open to all vets at any stage of the disease. They did the imaging and a biopsy of tissue in my previously treated prostate that was showing an uptake on the PSMA. It also showed another involvement from two more lymph nodes, very slight. I mean, it wouldn't have been seen on the CT or an MRI, you could hardly see the lymph nodes, and there were no real irregularities with them or anything, but it showed up just like it's supposed to on the PSMA, which is huge value to patients. I can attest that it has changed the management of my disease. I mean, just the ability to find where the disease is using this PSMA screening and imaging is unique and it's great. I believe that it's going to change the way we manage the disease in the future.

How did you find this clinical trial? Was it something your doctor pointed you toward or was this through your own research?

Mike Crosby: I'm kind of a loudmouth advocate for VA patients and I have my own prostate cancer advocacy organization called Veterans Prostate Cancer Awareness. I had been asked to speak at the American Urological Association advocacy conference in Washington, DC. I was on a panel with one of the physicians from West LA, one from Houston, and Florida Congressman Neal Dunn. At a break, we began talking about my case and issues with some of the VA bureaucracy. Dr. Shelton, the physician out of West LA said, "You need to come out to the VA in Los Angeles and we will do the imaging for you."

> *"It's one of these tools that's going to allow us to more accurately stage cancer upon diagnosis and it's also going to allow us to check up on and make sure that the treatments are actually working, correctly."*

What was the physical process of the imaging like?

Mike Crosby: It's nothing more than almost a normal PET scan, PET/CT, or an MRI. You essentially just are injected with the nuclear medication or the nuclear imaging PSMA and you wait for about an hour as it travels through your body and gets soaked up by all any membranes that are floating around. Then you go and do a PET scan and that's it. There's nothing special, there are no side effects really. It's just like going in and having any kind of imaging done.

Did you then take the results back to your team in Phoenix?

Mike Crosby: No, I'd moved out of Phoenix. One of the beauties about the VA is you can get care almost anywhere, right? It is truly the largest integrated healthcare system on the planet. It's extremely easy to move from one VA to the next. All your electronic healthcare records can be seen. It's very seamless from that perspective. I still get all my healthcare from the VA and my wife is angry because she can't get into the VA. I do love the care, I love what the people are doing, and the physicians are some of the best in the world. My oncologist is Dr. Matt Rettig who is also the head of prostate cancer at UCLA and he is also the head oncologist at the West LA VA.

I've got an interventional radiologist, Dr. Reza Berenji running the imaging trial for the PyL substance, and a Radiation Oncologist Dr. Nick Nichols. They are just great people. These are some of the leaders in the industry and they pick the VA because they just like it. They work in the VA three-eighths of their time and they're just some of the best doctors on the planet.

They detected the second recurrence and I went through a battery of tests. It was decided jointly that I would start on a process that was extremely aggressive. I was placed on androgen deprivation therapy (ADT) plus—Lupron (leuprolide) and Xtandi (enzalutamide). They found this bit of recurrence in my tissue that had already been radiated before and so they couldn't take it out. I mean, it was too small but it was a Gleason 8. The urologist who did the next biopsy said she wouldn't operate because it was too close to my sphincter and urethra. It was too delicate for anyone to operate on.

I was referred to another group that is a sponsor of our non-profit called HALO Diagnostics who are doing a focal laser ablation technique, and it's an incredibly accurate

technique. It's a long procedure, about three hours, but they go in and essentially ablate the tissue that's involved. You're kind of in this weird position for three hours. They only did 25 MRIs to map out where the tissue is. They take this device, the laser basically, and they insert it and they ablate in a very, very accurate, I mean, down to sub-millimeter accuracy, the dense tissue that's cancerous.

After that, I was prescribed another 35 rounds of radiation, 25 in the pelvic bed, plus five and five on each one of the lymph nodes, stereotactic body radiation therapy (SBRT) on the two lymph nodes they had found with the PSMA imaging. Then I waited for a couple of months doing the ADT and now we are in a period of Active Surveillance. I'm on a sort of chemical holiday right now and I'm due for another PSMA in about two months. I'm the only person in the trial because I agreed to aggressively attack this random recurrence in my prostate tissue and lymph nodes. Its been a bit of a journey as all of this was accomplished within a timeframe of about four months.

And so they did a PSMA afterward to see if it had worked, to see if anything happened, if there was a change, and there was a change. There was no cancer found.

That must have been a relief.

Mike Crosby: Yes. My PSA has been undetectable for the last few months, mostly, I think, because of the ADT suppression, but I've been off of it since January. That imaging was done about a month ago and it showed no trace of cancers where all of that treatment had gone on at all the lymph nodes. Now we're waiting for either a rise in PSA and another PSMA imaging. We'll do

another PSMA in about two months to see what's happened. And, as I said, it's one of these tools that's going to allow us to more accurately stage cancer upon diagnosis and it's also going to allow us to check up on and make sure that the treatments are actually working.

This is one of the key advantages of this new technology PSMA imaging. Once you kill the cancer or you treat it one way or the other, we need to see at a microscopic level how you're responding to that treatment. Before, we were always given images like bone scans and MRIs along with the standard PSA blood test. I've had all those too and what we're finding is those are just not as accurate as they probably could be. That's just the limit of technology. This is allowing us to see and to identify the cancer in your body, which I think is allowing the physicians to treat it more accurately. We're getting into more and more precision between this identification of the cancer tissue, along with all of the DNA sequencing and treating, taking your exact cancer treatment and customizing it to your body: understanding how is it going to react; what's the best treatment; what are the best drugs; and what's the best-optimized outcome?

Would you highly recommend other men with prostate cancer seek out this particular kind of test?

Mike Crosby: I would absolutely. And we're actually promoting that right now for any veteran at any stage of prostate cancer. Any stage. It doesn't matter, if you've got it and you've been diagnosed, you can go to West LA VA and have the scan done.

What about people in other parts of the country? Do you have any similar programs, or would you help someone in another part of the country find one?

Mike Crosby: If they can get themselves to West LA or we've worked with a couple of guys to get them there. I'm working with a couple of airlines to try to get them to give us some tickets and that sort of thing as a donation to help veterans get to this technology.

It's just a one-day scan, right? Can they fly in for a few days, get it done, and then fly home?

Mike Crosby: Not even one day. You fly in, it takes about one to two hours, and you're done. You get the injection with the nuclear medicine and they have to time it fairly precisely. They'd probably want you to come in the day before, spend one night, go in, and then you can leave because they have to spin up the stuff in a cyclotron, which is offsite. It only stays active for a couple of hours. It has a very short lifespan. So, they have to move it to the hospital while you're there and then inject you with it, do the scan, and then it all goes away. The logistics have been very easy. We've had guys from Florida, Virginia, Kansas, and Illinois. They fly in the day before, take them up for the scan, takes about two hours, and they'd get on a flight that evening and go home.

How can any veterans reading this reach you?

Mike Crosby: Contact Information mike.crosby@veteransprostatecancer.org T: 571-215-2715

Patients Speak
Greg Shay: My Story

Greg Shay spoke with *Prostatepedia* about his prostate cancer journey and experiences with imaging.

Tell me about your diagnosis and experience with imaging.

Greg Shay: I had an annual physical, DRE, and a PSA. I had not had a PSA for two years. My primary care doctor retired suddenly, so I got a handful of my records and went to a new doctor. For some reason, we did not do a PSA during the first visit. We did a PSA on my second annual visit, which came back on March 2, 2020, with a PSA of 14. He said, "Something's going on. I want you to go see a urologist." I went to see a local urologist that he got me into. (This was before everything was locked down with COVID.) The urologist said, "I want to do a 12-core biopsy."

A friend of mine runs the Informed Prostate Cancer Support Group, which has a thousand members down here in San Diego. I wasn't a member then, but he said, "Get him to order a multiparametric MRI."

The urologist said, "No. Your insurance won't approve it until we get the biopsies done." And I said, "Order it and let's see. I'll pay for the MRI if need be." Medicare approved it, so I got a multiparametric MRI, which showed a lesion on the right side of my prostate.

"If you're newly diagnosed, take control of your diagnosis."

I exited from that urologist because I didn't like my first experience and I went with Dr. Richard Lam in Marina Del Rey at Prostate Oncology Specialists, a three-doctor group recommended by my friend who runs that nonprofit, Informed Prostate Cancer Support Group. Dr. Lam said, "Here's what I want. I see your imaging. I want a soft tissue." Not an MRI, but, a bone scan and a soft tissue scan. (I can't remember exactly what the soft tissue scan was.) He said, "We are going to eventually do a biopsy, but I want to get those two imagings back and you can get those in San Diego, right at the same place you got the multiparametric MRI."

When they came back negative, he did a punch biopsy with three punches and said, "I'm not going to do the shotgun punch. I'm going to punch where the lesion is using ultrasound. And so I'm going to target exactly the tumor or the lesion." Did that. Came back cancerous and he said, "Okay. I see your bone scan and your soft tissue scan came back negative. That's good. But with this lesion, I want you to get a PSMA PET scan." And he says, "You'd have to pay for that yourself. It's not FDA approved." This was June 2020.

How much did it cost you?

Greg: I went to UCLA and it cost me $2,250. I paid for it out of pocket. The radiation oncologist was Dr. Amar Kishan up there at UCLA. The PSMA PET scan came back and showed my lesion, obviously. It also showed that I had two lymph nodes that were cancerous. So all the previous scans would have shown no spread. The results changed all the focus of treatment recommendations. From there on, I went to 39 photon radiation treatments. That was last year, July, August, and part of September. Lived through that. Don't want to go through it again. And I started on three-month Lupron (leuprolide) injection and Xtandi (enzalutamide) pills daily, four pills once a day. I'm headed into 11 months of that treatment. He wants me to go until the first of September with the Xtandi (enzalutamide). My last Lupron (leuprolide) shot is on the first of July.

You got the PSMA earlier than you might have if you had followed recommendations and it has definitely changed the course of your treatment.

Greg: Yeah. The PSMA was not recommended by anyone until I got the biopsy and the biopsy results back and then my oncologist, Dr. Lam, recommended the PSMA PET scan at UCLA. It wasn't approved then. It's approved now.

I would have gotten treated with negative soft tissue and negative bone scan. I would have gotten treated a certain way, I'm assuming. When the PSMA PET scan came back with a spread, that changed the course of my treatment for sure.

Do you have thoughts for other men who are reading this about the PSMA? Obviously, it's changed your journey.

Greg: Yes. I have been told that it is the standard of care in Europe or Great Britain, right.

And in Australia, I believe.

Greg: So it should be the standard of care here and so should the multiparametric MRI before a 12-punch biopsy, but I know we're not talking about that, but yeah. I'm 100% a believer. My question down the road is: Do I get another one?

At what point has your oncologist suggested that would be in order?

Greg: He has said, "Let's just wait and see. Let's get through your treatments." My PSA has gone to 0.02 for nine months. That's a good reading and his goal is to wait until my drug treatments are done to see if I hold under a PSA of one.

What would be the reasoning behind a second PSMA? Is the idea to see if the treatment worked and it has eliminated the cancer that it found initially?

Greg: To see if it spreads somewhere else. I'm assuming PSMA PET scan can see other places that have potential cancer in them, right?

Yes.

Greg: I'm not that versed on PSMA PET scan, but if it targeted my cancer in that one area, I would assume that it will show other areas of cancer spread. But, like I said, I'm not that versed in it, but yes, I want to get another one down the line somewhere.

Do you now talk about your experiences at support groups that you attend?

Greg: My friend has asked me if I would. There used to be a monthly meeting. There isn't anymore.

Not even through Zoom?

Greg: No. No. There are a thousand members and they have doctors who present and they have patients who tell their story and it's a pretty neat group: the Informed Prostate Cancer Support Group. It's free to join and I like reading their monthly newsletter. Some of the doctors, my doctor, my radiologist, and someone from UCLA have been presenters. I can't remember the doctor's name. It's a cool group. They've asked me if I would share my story and normally, in a live meeting, you stand up and you share your story, but they haven't

started that back again, due to COVID. I'm happy that I had great advice, found a super oncological team who directed me to good imaging, PSMA PET scan, and several choices for radiation. Going through all this, my whole thing was, "Gosh. If I would've just gone with this urologist who will remain nameless, I would have been on another path and possibly had my prostate removed." That wouldn't have cured my problem because my cancer had spread. The PSMA PET scan identified that it spread and sent me on a different treatment path. A more, I guess, intense treatment path. Thirty-nine radiation treatments is no walk in the park.

No. How are you dealing with the side effects?

Greg: Side effects from radiation are gone. Side effects from Lupron (leuprolide) and the pills, excuse me, suck. Hot flashes, my hands are swollen and I feel like I've got arthritis in my hands. They're terrible side effects. I had side effects from radiation, but the radiation stopped September 15, 2020. It took me about two months to pretty much get over the side effects from radiation. It was photon radiation. I guess that's more directed than general radiation. There's a photon therapy center here in San Diego. I had a great team working on me that tailored my treatments. I went through 39 of them. Thank goodness it wasn't 40 because I was about at the end.

Yeah. You were ready for it to be over, right?

Greg: Oh boy! And because it's cumulative, it took a couple of weeks until those real main side effects started to level out and subside. Yeah. I was right at the end of my

ability to cope.

But I'm dealing pretty well. I'm in good shape in general. I'm taking some stuff to minimize the hot flashes and some stuff to alleviate the hand pain. I'm hoping all this goes away. I'm an athlete and I stay in great shape. I'm a swimmer. I like to walk with

"Be your own patient advocate."

my dogs.

Is there anything else you want to say to the men reading this? Either about PSMA, imaging in general, or just any thoughts for men who may be newly diagnosed?

Greg: If you're newly diagnosed, take control of your diagnosis. Don't listen to the first someone who wants to do something. Do a lot of reading, a lot of checking. Thank goodness I had great advice. For example, my brother was a day away from surgery to remove his prostate in New York when they closed New York due to COVID. I talked him into having a Zoom call with my Dr. Lam and sent him on a different course through Sloan Kettering in New York with radiation and no prostate removal. And it was because he got some new advice and did some more reading. I was going through this ahead of him, although he was diagnosed ahead of me, and I got on a good train. Just take control, ask questions.

I got a support group of five other treated individuals, professionals that I know now that I can call and say, "Hey. How was your treatment? How did this go?" One of them went through a five intense radiation treatment at UCLA. I didn't choose that path. My brother is one of my support group. The guy who got me into my prostate oncologist and this support group is now 86 years old and was diagnosed in 1998. He says, "Greg, don't consider this a death sentence. Yes, you have a serious cancer, but now that you have a plan and a process, go through it, and keep on your process." Get a support group. Ask questions. Don't take the first advice. Be your own patient advocate.

Excellent advice. And not just applicable to prostate cancer, but to any kind of disease that you face.

Greg: You've got that right. In the medical profession, they read the chart and give you 15 minutes. I have a list of questions, but now I've been on the phone for 15 minutes and think of 15 more questions when I get off the phone. Then you have to try and figure out where those questions can get answered. Support group, online, do your own research, and be your own patient advocate. Pp

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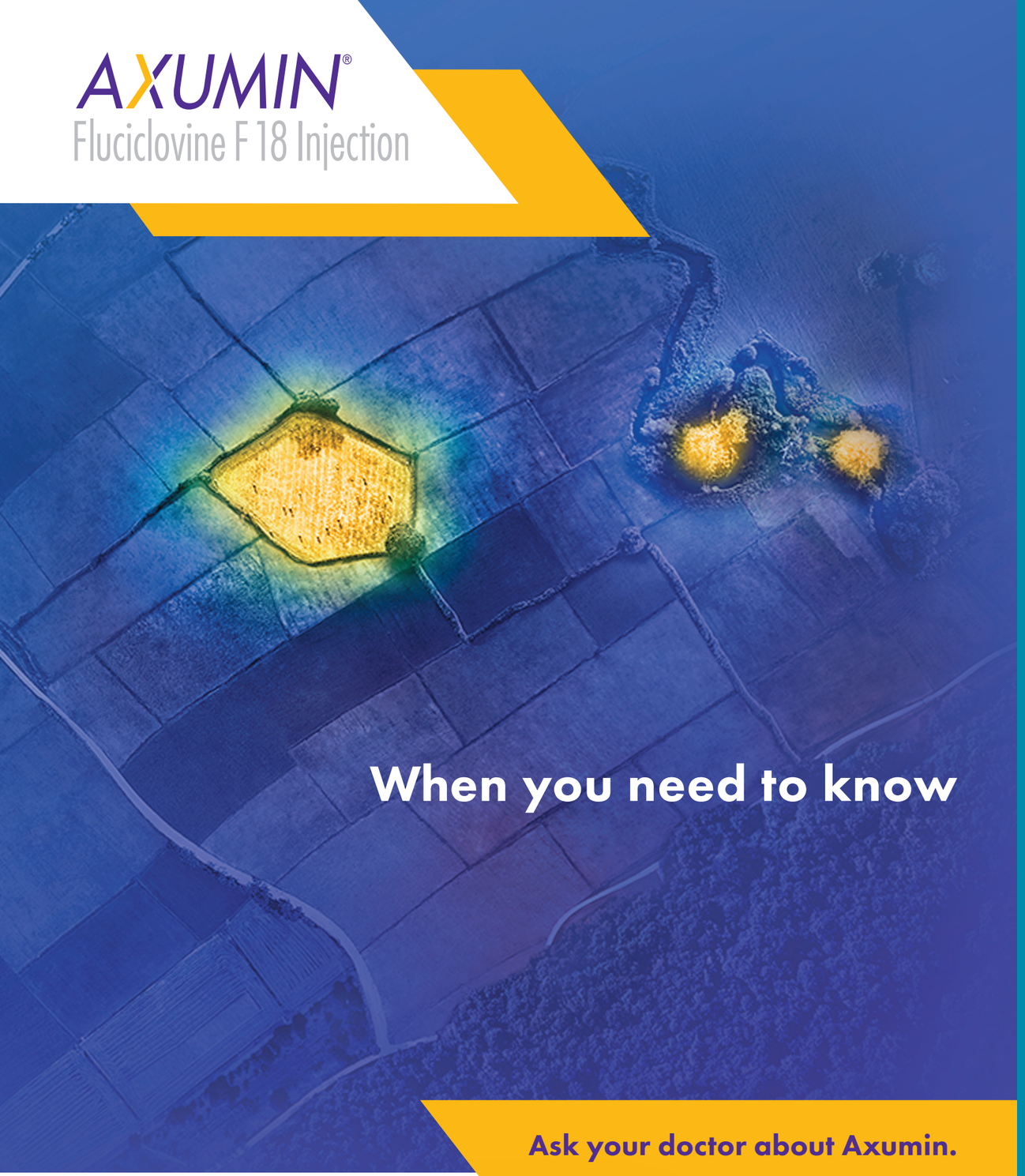

When you need to know

Ask your doctor about Axumin.

BLUE EARTH DIAGNOSTICS
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