00;00;00;02 - 00;00;31;19 WNPR (radio voice) Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital. Welcome to Yale Cancer Answers. The director of the Yale Cancer Center is Dr. Eric Winer. Yale Cancer Answers features conversations with oncologists and specialists who are on the forefront of the battle to fight cancer. Here's Dr. Winer.

Dr. Winer Tonight, we're focusing on prostate cancer in honor of Prostate Cancer Awareness Month, which is every September. 00;00;32;13 - 00;01;08;05 Prostate cancer is the second most common cancer in men. Approximately one in eight men will be diagnosed with prostate cancer this year and every year. And yet there's still plenty of confusion and confusion about who should get screened, how it's best treated, and what the latest research means for patients. Prostate cancer is also the second leading cause of cancer death in men with nearly 35,000 deaths per year, according to the American Cancer Society.

00;01;09;08 - 00;01;39;27 Dr. Winer Early detection can make a big difference, or certainly is associated with longer survival times. But the whole decision about screening versus not and how to screen is still one that's not entirely straight forward. And once the diagnosis is made, understanding the treatment options and many of the new developments in the field can definitely feel overwhelming if you're a man with prostate cancer.

00;01;41;02 - 00;02;32;28 Dr. Winer Joining us today for our discussion on prostate cancer is Dr. Daniel Petrylak, who is the chief of the Genitourinary Oncology Division at the Yale Cancer Center. And it's Smilow Cancer Hospital. He focuses on cancers of the urinary system like prostate cancer and bladder cancer in particular. Dr. Patrick is a world-renowned expert in the field. I personally have seen him multiple times on various different types of media and know that he has a great way of explaining things and he himself has not only been taking care of patients for quite a number of years, but he's been involved in truly groundbreaking research.

00;02;32;29 - 00;03;04;20 Dr. Winer So, Dan, thanks so much for being here with us tonight.

Dr. Petrylak Thank you, Eric. I appreciate the time to speak about an important women's health issue.

Dr. Winer It absolutely is. So let's just start off talking about signs and symptoms. And of course, that is prostate cancer is a very common cancer. But I think there's still confusion about what kinds of symptoms people may get.

00;03;05;20 - 00;03;32;27 Dr. Winer What are the most important symptoms and risk factors that a man should be aware of? And when should a man start worrying about these things?

Dr. Petrylak Important things to remember. Prostate cancers that it can be very not. Symptoms can be very nonspecific. Increased urinary frequency is

one that I think is pretty common. Also, sexual dysfunction is another that we see often with patients with who have a diagnosis of prostate cancer.

00;03;33;12 - 00;03;58;01 Dr. Petrylak But for the localized disease, nonspecific symptoms for metastatic disease, pain, weight loss, the types of symptoms we would normally see with any other cancer.

Dr. Winer And of all the men who are diagnosed with prostate cancer each year, how many actually present with cancer? That's outside of the prostate that has already spread to other parts of their body? It's a minority, I'm sure.

00;03;58;08 - 00;04;25;21 Dr. Petrylak It's actually changing. And the incidence of prostate cancer, this metastatic has actually increased and is kind of concerning. This has been attributed to the fact that in 2010, I believe the United States Preventative Task Force recommended against screening for prostate cancer. It originally was screening in men over the age of 75, and then they gave it a declassification, which means that you shouldn't screen at all.

00;04;26;18 - 00;04;58;12 Dr. Petrylak And we started seeing a very, very interesting trend over the last several years that the rate of metastatic disease was increasing, particularly in men between the ages of 55 and 69. So this has been attributed to the fact that there was less screening. A lot of internists not drawing PSAs as a screening test. We could talk about the advantages and disadvantages of or strengths, weaknesses of PSA, but we have been seeing an increased rate of metastatic disease, and this in some situations is as high as 30%.

00;04;59;02 - 00;05;32;03 Dr. Winer Wow. And so let's now focus then on screening and what are the ways you screen for prostate cancer?

Dr. Petrylak Well, simple PSA, measuring the PSA in a patient. The cutoff is generally for, but this also means specific cut off as well. If you see an increase in the patient's PSA doubling time, you can also consider doing an MRI to confirm the findings of the PSA or the actual absolute PSA value.

00;05;32;16 - 00;05;55;01 Dr. Petrylak If there's something seen on MRI, then that can be biopsied. But this is generally the way we go about screening.

Dr. Winer And MRIs have really changed the approach to prostate cancer, haven't they?

Dr. Petrylak Absolutely. Not only with screening, but as well as monitoring patients. So, for example, there are several different types of prostate cancer based upon the Gleason score.

00;05;55;14 - 00;06;24;03 Dr. Petrylak The Gleason score is something that we use to measure the aggressiveness of the prostate cancer. Gleason six is the type of prostate cancer that you die with, not from the the seven is sort of a wild card. The free plus sign for the Gleason score is made up of two different observations that the pathologist makes is less aggressive than the four Placide

389 is in terms of the aggressive variants and those are the ones you need to worry about.

00;06;25;19 - 00;06;53;19 Dr. Petrylak But for the Gleason Sixes, those are the ones that we can watch and we can use MRI's to monitor the potential changes in the prostate. We also use PSA in that situation. So it's a diagnostic tool as well as a monitoring tool for our patients.

Dr. Winer So let's talk about PSA or prostate specific antigen. When and who should have PSA screening?

00;06;54;22 - 00;07;19;26 Dr. Petrylak We have to look at different risk groups. So there is a risk group that is involved genetically and there's a risk group that's based upon heredity. So if you're African-American, you should start should start screening at age 45. Also, if you have a family history of prostate cancer.

Dr. Winer And that's because in African-American men, prostate cancer tends to arise at younger ages.

00;07;20;21 - 00;07;46;20 Dr. Petrylak It tends to rise at younger ages and tends to be more aggressive as well. So we need to monitor that. It's interesting that that the genetics of prostate cancer has evolved over the last ten years or so. Originally, we thought that Brocha gene was just limited to breast and ovarian cancer. Will brocha gene is also seen in patients with prostate cancer and it portends a more aggressive course of disease.

00;07;47;03 - 00;08;22;10 Dr. Petrylak It's about 2 to 5% of men with localized disease. About 10% of men with metastatic disease have the Brockett Gene and especially if this is identified in the family member, this patient should be screened earlier.

Dr. Winer And these BRCA genes, which are BRCA one and two, are genes that increase dramatically the risk of a woman developing breast cancer for men who have BRCA two mutations, there's a slight increase in developing male breast cancer.

00;08;22;17 - 00;08;59;14 Dr. Winer And then they, of course, also increase ovarian cancer. But I think the association with prostate cancer for a long time was thought to be pretty weak. And now people are thinking it may be somewhat stronger.

Dr. Petrylak It was actually identified out in Utah initially. That was the first group that was seen. And I think it's important for listeners to note that the identification of BRCA in a prostate cancer patient or a patient with other types of tumors, breast cancer, ovarian cancer means this is now a family affair.

00;09;00;10 - 00;09;43;08 Dr. Petrylak The family needs to be canceled. They need to be screened as well. So if a patient comes in a prostate cancer patient as we have BRCA, then we have to think about the daughters, the sons, the

brothers and the sisters as being potential patients for or at least to identify other tumors in those patients.

Dr. Winer And just to make sure that the audience understands this and this is because an inherited BRCA mutation is passed on from mother or father to son or daughter, and there's a 50% chance at birth that if a mother or father has a mutation, that they will pass that mutation on to their child.

00;09;43;17 - 00;10;11;19 Dr. Winer Now, there are also, I believe, in prostate cancer, some somatic BRCA mutations, meaning mutations that don't affect every cell of the body aren't inherited, but develop in the prostate cancer tissue. Is that accurate?

Dr. Petrylak That's accurate. And we see that about 10% of the time there are other DNA repair mutations that we also look out for. Particularly, these are important for treatment.

00;10;12;16 - 00;10;39;10 Dr. Petrylak But there's a whole spectrum of DNA repair mutations. The most common, of course, are BRCA1 and BRCA2.

Dr. Winer So I distracted you and you were telling us about African-American men in screening at 45. What about for other individuals of other racial or ethnic backgrounds?

Dr. Petrylak Really, there's no other ethnic background that I can think of that that would have to be more alert with.

00;10;39;10 - 00;11;03;29 Dr. Petrylak I mean, family history is the most important thing.

Dr. Winer And so everyone else should be screened at what age?

Dr. Petrylak 40, for everybody else at 50.

Dr. Winer And the frequency of screening?

Dr. Petrylak So that depends upon your PSA. There are some studies that have shown that if you have a PSA of less than less than 2.5, you don't have to be screened more than every five years.

00;11;03;29 - 00;11;36;01 Dr. Petrylak Initially. But generally yearly, I think, is the right, right way to go about this at this point.

Dr. Winer And where do the concerns about screening I mean, I guess since you were talking about prostate cancers that you can just watch and wait with is one concern that you're going to overdiagnose?

Dr. Petrylak Yes. And I had the great pleasure of working with one of the godfathers of prostate cancer, Will Whittemore a number of years ago.

00;11;36;13 - 00;12;08;29 Dr. Petrylak One of his quotes was in patients who cure as necessary as possible and in those who is possible, is it necessary? So we are identifying and this is one of the problems with the use of PSA initially, we

are identifying groups of patients who would not progress. And the question is, how do we select those patients out? Because the treatments do have significant morbidity, both in terms of erectile dysfunction as well as comments and then, of course, when we start thinking about early hormone therapy, that's another issue as well.

00;12;09;00 - 00;12;36;29 Dr. Petrylak But again, we want to take a healthy patient and not make them not make them unhealthy because the treatment may not be necessary.

Dr. Winer And, you know, a lot of people will say, I'm not that interested in screening, but I am interested in trying to prevent getting prostate cancer. Is there anything that people can do to lower their risk of getting prostate cancer?

00;12;37;11 - 00;13;03;19 Dr. Petrylak Well, keeping the fats in the diet low, our heart healthy diets, is a prostate healthy diet. It does seem that the lower fat diets, the Western diet, the Western diet seems to predispose patients more towards prostate cancer. Low fat diet seems to be helpful. So that's one of the things I recommend. There have been some prevention studies. There was one of the number of years ago that looked a drug called Prosper, which shrinks the size of the prostate.

00;13;04;04 - 00;13;31;19 Dr. Petrylak And that did not conclusively showed improvement in outcome. So we generally don't have any chemoprevention trials at this point.

Dr. Winer And in men, who just as they age, have prostate hypertrophy where oftentimes they have difficulty urinating. They need to get up in the middle of the night and go frequently. Is that a risk factor for prostate cancer?

Dr. Petrylak It's a very, very nonspecific risk factor.

00;13;31;20 - 00;13;59;26 Dr. Petrylak BPH can exist independently of prostate cancer. So I think that it's nonspecific and it's independent.

Dr. Winer Okay. Well, when we come back after our break and we're going to take just a brief break at the moment. We'll get into more of the treatment issues, treatment treatments about early-stage disease and some of the newer treatments we have for men who have more advanced prostate cancer.

00;14;00;18 - 00;14;29;25 Dr. Winer I'm speaking again with Dan Petrylak, who's chief of the Division of Genitourinary Oncology at the Yale Cancer Center. And we'll be right back.

WNPR (radio voice) Funding for Yale Cancer answers comes from Smilow Cancer Hospital, where a Multispecialty team is dedicated to managing the diagnosis evaluation and treatment of prostate cancer and other urologic cancers. Learn more at Smilow Cancer Hospital dot org.

00;14;30;07 - 00;14;51;25 WNPR Genetic testing can be useful for people with certain types of cancer that seem to run in their families. Genetic counseling is

a process that includes collecting a detailed personal and family history, a risk assessment, and a discussion of genetic testing options. Only about 5 to 10% of all cancers are inherited and genetic testing is not recommended for everyone.

00;14;52;11 - 00;15;23;08 WNPR Individuals who have a personal and or family history that includes cancer at unusually early ages, multiple relatives on the same side of the family with the same cancer, more than one diagnosis of cancer in the same individual rare cancers or family history of a known altered cancer predisposing gene could be candidates for genetic testing. Resources for genetic counseling and testing are available at federally designated comprehensive cancer centers such as Yale Cancer Center.

00;15;23;08 - 00;15;51;23 WNPR Added Smilow Cancer Hospital. More information is available at Yale Cancer Center dot org. You're listening to Connecticut Public Radio.

Dr. Winer Good evening again and welcome back to your cancer answers. I'm Eric Winer. And tonight I've been speaking with Dr. Daniel Petrylak, a medical oncologist and chief of genitourinary oncology at the Yale Cancer Center. Again, this is Prostate Cancer Awareness Month.

00;15;52;19 - 00;16;20;18 Dr. Winer And we're talking about screening and treatment of prostate cancer. So in just a minute or two, we'll talk about some of the treatments for advanced prostate cancer. But I know, Dan, that even though you're a medical oncologist and you're not a urologist or a radiation oncologist, that you get asked plenty of questions about how to treat my early-stage prostate cancer.

00;16;21;13 - 00;16;53;04 Dr. Winer You've already told us that for patients who have a Gleason six prostate cancer. So these are slow growing cancers that oftentimes following patients, not doing surgery is the way to go. But for all the rest of the patients or most of them, you're usually talking about some sort of local therapy. And I'm wondering if you can comment on that, because I think for patients it gets pretty confusing.

00;16;53;13 - 00;17;26;29 Dr. Winer Should I have surgery? Should I have radiation? What are the consequences of the two?

Dr. Petrylak That's really a very important issue with our patients. And it's a complex discussion. I always am asked to be, quote unquote, “the unbiased opinions” And so neither have source or radiation oncologist. The way I look at this is that if we go back on retrospective data, we match clinical stage Gleason scores for each individual patient and look at databases with surgery and radiation oncology patients.

00;17;26;29 - 00;17;52;16 Dr. Petrylak It seems that the outcomes are very similar. So the way I broach this with the patient is given the fact that we don't have data in a randomized fashion to compare one to the other, which side effects are you willing to put up with and then what are the consequences

of doing a particular local treatment? So for surgery, the side effects are erectile dysfunction and incontinence.

00;17;53;19 - 00;18;21;18 Dr. Petrylak Usually the rectal function can return probably 6 to 12 months after the surgery. In comments varies, but it depends upon the surgeon skill as well as the patient's ability to exercise and do clitoral exercises after the surgery. One of the advantages of surgery is that if your PSA comes back and about one in three men will have a PSA rise after surgery, that you can do salvage radiation therapy after that.

00;18;22;06 - 00;18;50;26 Dr. Petrylak And that is often given along with androgen deprivation therapy, with radiation therapy irradiating the prostate, you also can have incontinence as well as impotence as side effects.

Dr. Winer Is it less frequent than with surgery?

Dr. Petrylak It's about the same frequency. But the pattern of sexual dysfunction is different. With radiation therapy, this is without hormones. You lose your potency over time because the nerves begin to fibrosis.

00;18;51;18 - 00;19;27;04 Dr. Petrylak However, in surgery you lose it and then you can regain it over time. It's sort of like a shock to the system. So different pattern. But what are the issues with radiation therapy is in certain situations you would combine it with androgen deprivation therapy. That's the deprivation of hormones, testosterone, which causes prostate cancer cells to die. Now, there have been a number of randomized trials that have shown that the combination of hormone therapy, plus radiation therapy is synergistic and leads to a better survival than radiation therapy alone.

00;19;27;17 - 00;19;57;09 Dr. Petrylak So, of course, we want to select those patients that you want to do combination therapy with. However, side effects of hormone therapy and routine depravation therapy or hot flashes, weight gain, loss of muscle mass fatigue, loss of libido and loss of sexual function. For the most part, about 65% of men will regain their testosterone levels. Maybe not to baseline, but they'll become non castrate after the hormones are stopped.

00;19;57;22 - 00;20;23;08 Dr. Petrylak So you have another element that goes on in terms of side effects. So if a patient comes in with high risk disease and they say, well, why should I have radiation therapy and hormones over surgery, it's sort of a bit of a gamble for the patient. You know, you can go with the surgery and then potentially not have to do further treatment afterwards, not be exposed to hormone therapy.

00;20;23;08 - 00;20;59;24 Dr. Petrylak With radiation therapy, You probably for most cases, you have at least a short course, sometimes 18 months of hormone therapy as well. So all of those have different implicate actions. And that's why it's important to individualize your treatment. Forgive a patient.

Dr. Winer And is there any reason to think about age as one way that you're individualizing? So, for example, if you're talking to a 60 year old man, are you

going to tend to emphasize one treatment or another in a different way than you would for an 80 year old man?

00;21;00;23 - 00;21;26;05 Dr. Petrylak Great question. So in the past, we've often said that 74 is the cutoff for radical prostatectomy. But I look at the physiologic age rather than the chronological age. Certainly I've had sixty year olds who have multiple medical problems who it's not appropriate for that patient to undergo surgery. Similarly, I've had patients 75 and 80 years old that have done very well.

00;21;26;05 - 00;21;52;25 Dr. Petrylak Now, I'll give you a specific example without naming the individual, a comedian who lived to the age of 100 had a radical prostatectomy at 80 for high grade disease, and he lived another 20 years. So this is why it's very important to select the patient in this particular situation and see what their performance status is, see what their co-morbidities are.

00;21;52;25 - 00;22;24;17 Dr. Winer Got it. Now I want to move on and talk about advanced prostate cancer, and this is when prostate cancer has spread, oftentimes most frequently to the bones, but potentially to other organs as well, and to lymph nodes. What are the initial treatment options you think about there?

Dr. Petrylak So the initial treatment option is, Anderson, deprivation therapy, which means depriving the patient of testosterone. 00;22;25;05 - 00;22;54;26 This causes the prostate cancer cells to die. And that's done with either an injection or a pill that will basically interfere with the signal from the brain to the testicles to make testosterone.

Dr. Winer And this is this is because most prostate cancer cells, if not all, at least initially, are dependent on testosterone to grow. It's like a fuel for them.

00;22;55;11 - 00;23;21;00 Dr. Petrylak It's a fuel. And testosterone comes from a number of different sources, comes from the testicles, it comes from the adrenal glands. It also comes from the prostate cancer cells themselves when they become resistant. So now the trend is to add a second drug to the initial drug that that interferes with the pathway I mentioned before. And these drugs will block the binding of testosterone to its target.

00;23;21;27 - 00;23;50;29 Unknown And this these types of drugs, they're called anti-androgen. These types of drugs will basically improve survival over what we see with just simply the blocker alone. So this should now be considered to be standard as first line therapy and fortunately, only about 40 to 50% of patients in this country are offered that treatment, adding anti-androgen. And this is an important issue in terms of education of our patients.

00;23;51;20 - 00;24;27;05 Unknown There's really very little reason not to receive an anti androgen upfront, along with what's called an RH agonist or antagonist.

Dr. Winer Got it. And in the best of situations, let's say you take care of a

man who has prostate cancer that has spread to his bones. How long can these initial treatments work?

Dr. Petrylak I think it's important at the onset to emphasize to the patient that this disease is controllable but not curable. 00;24;27;20 - 00;24;48;16 So I can keep patients going. For 5 to 7 years, I've had patients who've exceeded ten years. So there are you know, it is possible for a long term survival with this, but on average it's about 5 to 7 years.

Dr. Winer And of course, you know, the truth is we don't know what's going to be available in three years, four years, five years.

00;24;48;16 - 00;25;17;24 Dr. Winer So if you're talking about allowing someone to live a reasonably healthy life for another 5 to 7 years, it could be much longer given the pace of discovery.

Dr. Petrylak Well, the pace of discovery has really been almost frenetic recently, and it causes clinicians a lot of difficulty, I guess, or angst in selecting what's the right treatment to give in a given situation, because we don't really have the molecular markers that are seen, for example, in breast cancer and lung cancer.

00;25;17;24 - 00;25;44;12 Dr. Petrylak We're developing those. And that's, I think, an exciting area. But, you know, the first chemotherapy to improve survival was identified 21 years ago. That was docetaxel based upon some of our work. And now we have multiple agents, other hormones. Theranostic approaches, the PARP inhibitors which target the BRCA positive patients. And the question is what's the right sequence to treat these patients?

00;25;44;25 - 00;26;15;16 Dr. Petrylak We've gone from a situation where patients, when they become resistance to their primary treatment's only lived about a year and now we've pretty much got that to about 30 to 36 months. So we've really made some market improvements. The question is what's the future going to hold.

Dr. Winer And you've been very involved in a class of drugs that are called PROTACS, and maybe you could tell us a little bit about PROTACS, and what their impact has been on prostate cancer.

00;26;15;29 - 00;26;42;16 Dr. Petrylak So this is one of the most exciting things that happened with my move to Yale 12 years ago. There was a seminar that happened that occurred on Wednesday afternoons with the chemistry department. Craig Cruz, who is a very well known chemist and has developed several drugs for cancers. I was at that seminar and I was giving this lecture on prostate and came up to me and said, 'Would you have interest in the drug, a new drug for prostate cancer'?

00;26;42;23 - 00;27;15;21 Dr. Petrylak And of course I said, of course I do. And so he had a group of people from his company down to my office later that week and this drug that Craig has developed is something called a PROTAC. And what that drug does is it targets proteins and uses the body's natural mechanism

of degrading proteins. We turn our proteins over pretty regularly such that the androgen receptor, which is the target of testosterone, is degraded and it causes the prostate cancer cells to die.

00;27;16;09 - 00;27;51;09 Dr. Petrylak We've identified specific mutations that these protects will target, and we've seen that about half of patients have significant declines in PSA with this particular drug. So it's very, very exciting. The other exciting part about this is something I didn't really expect to see, but it's been found that these protects or actually upregulate a target on the prostate cancer cell corpsmen and the one that we're working with called RV seven, six, six is one of the most potent ones that's out there in upregulation.

00;27;51;28 - 00;28;21;29 Dr. Petrylak So we're targeting PSA with drugs such as Mutation 177 SMA, which is a radio isotope that's linked to a a molecule that targets the specific target on the surface, the prostate cancer cell. And we're going to sequence the RV seven, six, six, along with the Latisha and PSA with the thought that this will actually make this drug work effective or the two drugs more effective together.

00;28;22;09 - 00;28;54;04 Dr. Petrylak So we're very, very excited about this study that's coming up.

WNPR (radio voice) Dr. Daniel Petrylak is chief of genitourinary oncology at Yale Cancer Center and Smilow Cancer Hospital. If you have questions, the email address is cancer answers at Yale Dot edu and past editions of the program are available in audio and written form at Yale Cancer Center dot org. We hope you'll join us next time to learn more about the fight against cancer. Funding for Yale Cancer Answers is provided by Smilow Cancer Hospital.