Welcome to a series net casts brought to you by Yale University.Thank you for joining us for this edition of Yale Cancer Answers where we provide you with up-to-date information on cancer care and research. Our host, Dr. Steven Gore, is Director of Hematological Malignancies at Smilow and an expert on myelodysplastic syndromes. He interviews some of the nation's leading oncologists and cancer specialists who are on the forefront of the battle to fight cancer. If you are interested in listening to past editions of Yale Cancer Answers, all of the shows are posted on the Yale Cancer Center website at YaleCancerCenter.org. If you would like to join the conversation, you can contact the doctors directly, the address is canceranswers@yale.edu. Here is Dr. Gore.Gore Welcome back to another episode of Yale Cancer Answers. This is Dr. Steven Gore, and I am joined today by my guest Dr. Hari Deshpande. Dr. Deshpande is an Associate Professor of Medicine in Medical Oncology at Yale School of Medicine. He is here with us to discuss advances in the diagnosis and treatment of prostate cancer in recognition of the prostate cancer awareness month, known as Movember. Hari, thank you so much for joining me today.Deshpande Thank you.Gore What is Movember?Deshpande This is something that started in Australia, actually. It was designed to raise money for men's health, and they chose Movember because the idea is men would start to grow a mustache starting November 1st, take a picture of themselves with no facial hair and then they grow it throughout the month, they are not allowed to shave and then they take another picture at the end of the month or during the month to show that they have actually participated, and because of that, it brings attention to themselves when they are asked why you are doing that, they say to raise money for Movember.Gore How do they raise money? Is it donations?Deshpande Exactly. Some people will have a sign out at the front of the office to say please put some money in here for Movember, other people will do events. Here, at Yale, one of the research assistants did an auction to raise money for Movember. She was actually a woman and she wore a plastic mustache for the whole month.Gore Oh my gosh! I am going to ask what happens to those guys who do not have the robust facial hair and it looks kind of sad.2:46 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/ybmc-1787_deshpande_102516_286859_5_v1.mp3Deshpande I think you can use artificial means.Gore I see, it is really just awareness then? Has this been a very successful fundraising endeavor?Deshpande I think it could be better here at Yale. We have raised some money. Other places around the world have raised I think millions, the equivalent of millions of dollars.Gore And does it go to a specific not-for-profit? Deshpande That is a good question. I am not sure if it is not for profit, but there is a fund called the Movember Fund, which people can then apply to, to get money for research or something to do with men's health.Gore Gotcha. So, it is not exclusively for prostate cancer?Deshpande No, it is not.Gore Thanks for clarifying that. I did not know that actually. So, what is new in prostate cancer? Men have prostates and we worry about them.Deshpande That is true. I think the biggest changes over the past few years are in the early detection and screening, but there have also been some newer treatments that have come around in the last few

years as well.Gore Let us start with detection because from where I sit as an oncologist, I read a lot of conflicting blurbs, I do not go into the data too deeply and certainly I think the public is quite confused about whether people should get PSA screening or not. Deshpande I think it is very confusing and it depends on how you interpret the results of the various studies. As you know, when I was in medical school in residency, the teaching was that every man should start getting a PSA test starting at the age of 50 and continuing in some cases for the rest of their life, some places would put an age limit of about 75, but either way, it was considered the right thing to do to get a PSA test, and for people who have not heard of PSA, this is just a blood test that measures something that is produced by prostate cancer cells, and it is also produced a little bit by the normal prostate, you should not have a very high level if you do not have prostate cancer. But over the years, in the last 20 years or so, there have been many, many studies all over the world, and lots of people who got the test and then people who did not get the test, and then said, well what happened to those people? And probably the 5:52 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/ybmc-1787_deshpande_102516_286859_5_v1.mp3most recent one was just published in a very good journal called the New England Journal of Medicine, which is a premier medical journal, and they looked at 80,000 men who had been offered a PSA test. About 1600 of those who were found to have prostate cancer agreed to be randomized or split equally into 3 groups. One of the groups had just monitoring or they called it active surveillance, which meant that they did not have any treatment right but that PSAs were monitored every 3 months, and they were followed to make sure that they did not have any other signs of cancer. And the other two groups were either getting an operation right away or getting radiation right away. And what they found was that there was no difference in either the number of men who died in each group from any cause or even the number of men who died from prostate cancer. The differences were in the people who developed what we called metastatic disease. So, those whose cancer had spread to different parts of the body. They were about 3 times higher in the surveillance group than in the surgery or radiation group, but they were still small numbers, and in the article, they said it was about 6 events per thousand patient years, which is a hard thing to really imagine, but basically these are very small numbers.Gore In other words, if a thousand people were followed for a year or if a hundred people were followed for 10 years, you would have 6 people developing metastatic cancer?Deshpande Yes that is correct.Gore Well, that does not seem like a lot, but on the other hand, isn't it really bad when prostate cancer spreads to other parts of the body?Deshpande It is. And I think one of the things to remember about that particular study is those were all patients whose prostate cancer was found because of a PSA blood test, and if you look at those cancers that were found, they were all what call Gleason 6 or most of them. This is a grading score that we use for prostate cancer. Gleason 6 is the lowest grade that we usually see for prostate cancer. It goes up to 10. Gore They just happen to skip 1 through 5.Deshpande They do have 1 through 5, so the way they calculate

the score is, when this grading system was originally developed, the pathologist who invented it, his name is Gleason, realized that if you look at the outcome of people with prostate cancer, it does not depend on just the most aggressive area of the biopsy, which is the case for most cancer, but it is somewhere in between the most prominent area of the biopsy and the next most prominent appearance if you like at the biopsy specimen, and what he did was, he assigned a grading number of 1 to 5 where 5 was a very aggressive-looking 9:09 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/ybmc-1787_deshpande_102516_286859_5_v1.mp3area and 1 was an area that looked almost like the normal prostate. And he added the 2 numbers together and that is how we get a number of somewhere between really it is 2 and 10 I suppose. But generally, to have a diagnosis of prostate cancer and the pathologist can explain this better than I can, but the numbers start at 6. I think that is when it shows invasion into rest of the body.Gore I have never understood that thing. Thank you for explaining that to me. So, these were all pretty low grade, they all had Gleason 6, is that what you said?Deshpande Yeah. These were very low grade, the average PSA was about 4.6, which is very low. So, I think what that tells me is if you have a very low-grade prostate cancer with a low PSA, it is safe to not have surgery or radiation right away. But I think you cannot extrapolate those results to people who have higher grade disease or higher PSAs. Then, I think you have to have a more individual conversation.Gore And what is involved in this active surveillance? How often are you being seen and is it just blood tests or does it involve biopsies or MRIs or?Deshpande That has changed over the years as well. Here at Yale, for active surveillance, we have under Dr. Schulam's care, he is the head of Urology and his colleagues in Urology, they have a special MRI test which will localize an abnormal area in the prostate. MRI is a very, very good for finding prostate cancers. They are much better than ultrasounds, which is the traditional way we look at the prostate. And using the MRI, they can then guide the needle to where the likely cancer is. Now, this is important because the original way of doing a biopsy was a random biopsy, they would do 6 biopsies, often 6 from each side of the prostate or as little as 3 from each side of the prostate, 1 from the front, 1 from the middle, 1 from the back, that is sort of the minimum number on each side. The trouble with that is you might be missing the actual area, and so the MRI is a very good way of localizing where the cancer is, the trouble is you cannot do a biopsy and an MRI at the same time, so they developed this really amazing machine which will fuse the ultrasound image with the MRI, it creates a 3D computerized image and then the computer will help guide the surgeon to do the biopsies. It is like something out of a science fiction movie, but it works very well, it is called the Artemis machine.Gore It sounds very cool, but it also sounds like the procedure is maybe not so comfortable.Deshpande I would have to ask my surgical colleagues.12:12 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/ybmc-1787_deshpande_102516_286859_5_v1.mp3Gore So why wouldn't everybody want to have that malignant prostate gone? I mean, even if it is a low number of people who develop metastatic disease and even if your chance of dying is

not higher, I do not know that sounds scary, I want that thing out of there, why wouldn't I just go ahead and do that?Deshpande I think some men do. As soon as they hear the diagnosis of prostate cancer, the immediate reaction is, I want to have it removed. But you have to remember that these operations do not come without side effects, and that is the main reason that we try and tell patients what their risk is of actually getting a cancer that is going to be harmful to them or cause more problems down the line. And the main side effects are impotence, incontinence, generally uncomfortable symptoms after having an operation.Gore Yeah. And how frequent are those?Deshpande They vary in terms of the surgical sites, generally somewhere like Yale or a center which does a lot of these operations have much lower rates. I think the numbers are small, they are less than 10%, but still if you are one of the people who get these particular symptoms, then it could be problematic, especially if the disease by itself is not going to cause any problems for the rest of your life.Gore And does radiation have similar side effects?Deshpande They are similar, and they occur at different times. So, after surgery, generally everyone immediately gets side effects and then they get better overtime. With radiation, the side effects are not there right away, but they tend to occur later on and probably by about a year, the side effects are pretty similar with each type of treatment that you take.Gore I see. When I moved up to Connecticut, I decided I was going to sort of live by the values that I had been taught, which was that perhaps routine screening was not important for me since I have no family history and so on, and I went a year or two without screening, and then one of our urologic colleagues was chatting with me and told me about how his opinion that the reaction should not be to not screen, but rather to interpret the screening carefully and do not take a single value but look at how things are changing and so on, and so this year, I got screened.Deshpande I think it is very complicated, and I just turned 50, so I would be at the age later this year to think about my first screening test, and I have not got one yet.15:15 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/ybmc-1787_deshpande_102516_286859_5_v1.mp3Gore And my internist leaves it up to me, probably because I am a physician of course, but I can only imagine how it is for lay people, this is the kind of thing you would really like somebody to be direct about, you should get a flu vaccine, you need your tetanus up-to-date, you need your colonoscopy at 50, Dr. Deshpande?Deshpande Right.Gore Have you signed up yet?Deshpande Not yet. I do want to say that there are three main groups out there and they all have different screening recommendations. So, your colleague from Urology will follow the AUA or American Urology Association guidelines, and they still look towards screening as a good idea. The oncology guidelines from ASCO, which is the clinical oncology society, it is kind of in the middle. They again recommend screening to a certain extent, but the US Preventative Taskforce really recommends against it.Gore Altogether?Deshpande Yes, that is correct.Gore Wow. Well, that is a real clear message there.Deshpande Exactly.Gore Okay, so sounds like at some point if somebody is diagnosed with prostate cancer, for some people I assume get diagnosed because they are having symptoms?Deshpande

Yes. That is true, and I think we are going to see more of that these days. So, in the screening era, most people diagnosed because they had a high PSA. So, they really did not generally have any symptoms. But now, I think we are beginning to see more people who come in because they have symptoms. It is usually of a large prostate. So, that is difficulty going to the bathroom, passing urine or dribbling, having a poor stream and sometimes bleeding in the urine as well.Gore And those symptoms, from what I hear, are common in people as they get older, as men would get older, right?17:42 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/ybmc-1787_deshpande_102516_286859_5_v1.mp3Deshpande That is absolutely true and in fact a large prostate is much, much more common than a prostate cancer. So, we see about I say 200,000 cases of prostate cancer a year, but the incidence of having a large prostate as you get older is much, much more common than that.Gore Well, I mean if all these guys who have large prostates are having the dribbling problems and other sort of late-middle age problems, which of them should be getting further diagnostic testing?Deshpande I do not think anyone has really come out with a good way of telling who should get the tests and who should not, but generally I think if you have someone, especially a younger person who is developing symptoms like that, then I would be more likely to get a PSA test and do imaging tests.Gore Gotcha. So, anyways, here we got this guy who has got prostate cancer one way or the other, and then he has got this big decision to make about how it is being managed, and who helps them with that? Is that the surgical urologist, do they get involved with medical oncology.Deshpande Here at Yale, I think we have a great system, so we have a meeting which I know you have in hematology as well called the tumor board meeting where we meet with all of our colleagues, so that is medical oncology, surgeons and radiation doctors as well as the people actually looking at the MRIs and ultrasounds, the radiologists, and the pathologists, who look at the biopsy, and we all come together to look at the case as a whole and say well, what is the best option for this particular patient and then whoever has seen the patient will go back and explain what we decided.Gore And do you do that with every new patient?Deshpande We do it with as many of the new patients as we can. Some of the new patients have either already made up their mind and it does not help to discuss their case, so there are some of those we do as well, but generally we try and do every new patient.Gore Wow. And is there usually a unanimous or a consensus decision or is it sometimes a bit contentious? Deshpande I would say sometimes there are differing opinions around the room, and I actually run that particular tumor board, so I have to come up with a message from the board, so it 19:55 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/ybmc-1787_deshpande_102516_286859_5_v1.mp3difficult sometimes, but generally if there is a difference, I will let them know that most of the room decided on one option, but some people had another option and this was their reason for it.Gore Having worked with you on a number of committees, I am sure you are the most politie person about making sure that everybody's voice has been heard and that everyone is reasonably accepting of the outcome.Deshpande

I try to.Gore You are very talented at that. Okay, so the patient gets a recommendation and they have had their primary treatment. We have already sort of discussed what happens if they decide not to have active therapy, in terms of surgery or radiation, but let us take the people who have had surgery or radiation treatments, are they good to go, do they need follow-up?Deshpande They still need follow-up. So, for instance, in the people who have had an operation, we expect their PSA to be undetectable after surgery. So, if they have a PSA that is even a little bit detectable, so greater than 0.2, which is a very, very low PSA, then we often would recommend they see a radiation doctor as well because the chances are, there is just a little bit of cancer left and there is a good chance that with radiation they can have a very long period where they would not see the cancer again. But generally, after either surgery or radiation, they will be followed for the first year maybe a little more frequently and then after that less frequently with just PSA checks to make sure that there is no evidence that the cancer is coming back. It is hard to tell people that even after a big operation or a very intense radiation, there is still a chance that the cancer can come back, one cell could have escaped and started growing somewhere else.Gore And would I be correct in assuming that in those patients who need additional radiation on top of their surgery, the chance of side effects becomes worse.Deshpande Yes, that is correct, and I think that is something that radiation doctor will discuss with those patients individually.Gore Well, it is no wonder people worry about prostate cancer. It is not a straightforward pathway and it seems like even with the best treatments, it can be difficult.Deshpande Yes.22:26 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/ybmc-1787_deshpande_102516_286859_5_v1.mp3Gore And so then, what happens if the PSA starts to come back after they have had their primary treatment, that must be very scary for patients?Deshpande It is, and that scenario where I think there is a lot of research right now, so generally if the PSA starts to come up but it is rising very slowly, in other words, it is doubling in a time period that is greater than 6 months, then most oncologists feel that it is safe to just keep watching those patients as long as they do scans, usually a bone scan and a CAT scan and there is no evidence of any cancer on those scans. The PSA test is very, very sensitive. The CAT scans and the bone scans will only pick up a cancer if it is more than about 1 cm in size or may be a little smaller than that. So, if the PSA is rising much more rapidly or if the scans show that there is cancer somewhere, then the first line of treatment usually or historically has been to reduce the level of testosterone using various methods and that started in the 1940s. Back then, we only had orchiectomies to achieve that.Gore That is removing the testis.Deshpande That is correct. And obviously that is a very traumatic operation for any man to have. Now, we have medications that can do the same thing but in just a form of a shot every few months. And then, a couple of years ago, people looking at men with quite advanced cancer who were just diagnosed, who had not had prior hormonal therapies, but who now have cancer that was in the bone or in other organs and they randomized them to get either the standard treatment, which was just reducing the hormones

or adding chemotherapy to the hormones, and for the first time, we saw a significant survival difference in men who had what we call extensive metastatic disease at presentation who were treated with 6 rounds of chemo upfront and then continued their hormone treatments versus those who just had hormone treatments alone.Gore I am 10 years out of date. Okay, what is coming up, what is new, what should we be looking forward to?Deshpande Daniel Petrylak, who is the head of the Medical Oncology/Urology section, has brought in a lot of new clinical trials over the past few years. So, since about 2010 now, we have had 7 or 8 new treatments for prostate cancer. Generally, these are either new ways of effecting testosterone, production or the effect on the cancers, or ways of providing better supportive care, so if the cancer spreads into the bone, we now have medications that can strengthen the bone. We have been using those for women with osteoporosis for a while, but now they have also been shown to be useful in not just prostate cancer but almost any cancer that spreads to the bone, and we are looking at some newer treatments. There is an interesting treatment called Provenge, and it is actually the first vaccine that was ever produced for cancer. It is a way of taking the 26:33 into mp3 file https://ysm-websites-live-prod.azureedge.net/cancer/ybmc-1787_deshpande_102516_286859_5_v1.mp3patient's immune cells out of their body and then in a lab, they are combined with an antigen or a protein that is commonly found on prostate cancer cells and then inject it back into that patient, and in the initial studies, it did not affect the PSA, so people were a little bit disappointed. When they followed those patients, they actually lived longer, and they repeated the study and again it did not affect the PSA, but the patients lived longer and some of the experts such as Dr. Petrylak feel that even though the PSA levels are not dropping, they are rising at a slower level after these treatments are given and so patients actually get some benefit out of it. It takes longer for the disease to reach a point where it causes problems.Gore Are the cells injected into the prostate or just into the blood stream?Deshpande Into the blood stream.Gore That sounds better. I know there are a lot of these new drugs that we hear about that are activating the immune system, is anybody combining this kind of vaccine approach with some of these immune drugs?Deshpande That is a good question. I am not sure about if there are any combination trials going on. I know that some of these new immune treatments that you would have seen on the commercials on TV and heard about which are really very, very effective in diseases like melanoma or lung cancer or in your case Hodgkin's lymphoma, they are I would say disappointing in prostate cancer. They really have not shown as much benefit as we would have thought they would.Gore Got it. I noticed Dr. Deshpande that you are not growing a beard. It is not November 1st yet.Deshpande No, it is not November 1st. Gore I would like to see because I think that you look like you can grow a rather robust beard. Thank you so much for joining me on Yale Cancer Answers. This has been a really enjoyable and informative discussion on prostate cancer, and perhaps I am a little less anxious than I had been, although I was not really terribly anxious as you can tell. This is Dr. Steven Gore wishing everybody in our audience a happy and

healthy tomorrow.This has been another edition of Yale Cancer Answers. We hope that you have learned something new and meaningful. If you have questions, go to YaleCancerCenter.org. for more information about cancer and the resources available to you. We hope that you will join us again for another discussion on the progress being made here and around the world in the fight against cancer.