

Cancer Therapies and Your Heart

Cancer therapies have increased the survival of cancer patients, however certain cancer treatments can damage the heart and the cardiovascular system. These side effects, including high blood pressure, abnormal heart rhythms, and heart failure, can be caused or exacerbated by chemotherapy and radiation therapy, as well as by newer forms of cancer treatment, such as targeted therapies and immunotherapies. Cardiotoxicity can occur in various forms and can include damage to the heart muscle itself, the heart arteries, or the heart valves.

Cardiological assessment before starting cancer treatment is essential and should be continued throughout, since cardiac dysfunction can occur at any time, even several years after therapy onset. High-risk individuals, in particular, should receive a detailed management plan designed in collaboration between an oncologist and a cardiology specialist.

Join us as we talk to Dr. Javid Moslehi from UCSF Helen Diller Family Comprehensive Cancer Center on nuances of what cardio-oncology care and management of patients whose cardiovascular health has been affected by cancer entails. Joining us on the panel to bring in the patient perspective are Heidi Floyd and Dr. John Antonucci.

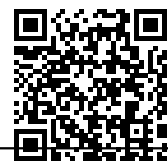
Full Transcript:

Priya Menon: Hello and welcome to CureTalks. This is Priya Menon, your host. Today, on CureTalks we are discussing the effect of cancer treatments on your heart. In other words, cardio-oncology. We have with us cardio-oncologist Dr. Javid Moslehi from UCSF Helen Diller Family Comprehensive Cancer Center. Dr. Moslehi is UCSF William Grossman Distinguished Professor in Cardiology and serves as Chief of UCSF's cardio-oncology and immunology section. He specializes in the cardiovascular health of cancer patients and cancer survivors. Joining Dr. Moslehi on the panel today is a cancer survivor and advocate Heidi Floyd and prostate cancer survivor and retired psychiatrist Dr. John Antonucci. Welcome to CureTalks, everyone.

Dr. Javid Moslehi: Thank you. It's great to be here.

Priya Menon: Dr. Moslehi, my first question is just basic so as to set the context for the rest of the discussion, what is cardio-oncology? And what does a cardio-oncologist do?

Dr. Javid Moslehi: So that's a great question. So again, I think one thing to note is this is an entirely new field and it really exploded over the last decade and the cardio-oncology really represents the intersection between the heart and cancer. As many people know, heart disease and cancer are the number one, and number two causes of death in the world, certainly in the US, but definitely in the world now. People on average, if you put all the heart disease deaths and cancer deaths together that's the majority of deaths we see. And generally, we've thought of these things, as completely different entities that if you have cancer, you're not going to have heart disease or if you have heart disease, you're not going to get cancer. And actually, we realize now, they're very intersected and in fact and I'll touch on some of these new concepts momentarily. But essentially why this field has really exploded over the last decade is the amazing advances done by many cancer colleagues of ours. Certainly, here at UCSF, at the Helen Diller Center where there are new ways of diagnosing cancers earlier, new ways of treatment for patients. And so, when patients technically survived the cancer or they beat cancer when you're talking about number one, and number two,



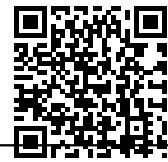
reasons for that heart disease becomes an important issue. So, but even if there was no intersection beyond that, the very fact that patients live longer with their cancer or in some cases cured of their cancer, they're going to have heart disease just by statistics. However, there are some other areas that really important, that is really been the reasons for this field exploding. We realize that both traditional and new therapies can have for cancer can have adverse effects on the heart. And we knew this for the old drugs, like doxorubicin, a drug that was made back in the 60s and 70s, and radiation that women or men can get for their cancer certainly women with breast cancer. They can have heart disease that becomes apparently so old drugs cause cardiac issues. What's been surprising is a lot of the new drugs also have a lot of cardiovascular issues that either become apparent during the treatment or during the survival period. And this latter point is especially important because right now, in the U.S. we have 18 million Americans for cancer survivors that five percent of the U.S. population and the number one cause of death, in those patients is actually heart disease not the recurrence of cancer in many cases. Certainly, that's true with prostate cancer certainly, that's true with breast cancer which we have about three to four million survivors in each type of cancer. And I think addressing these cardiovascular issues and promoting cardiovascular health in cancer survivors is a major goal of our program. There are other areas that I can expand on later, but I think that is why this field in the last 10 years has exploded. People live longer with their cancer in some cases, cure with cancer and they have heart disease in a high proportion both because heart disease is common, but also the drugs can have effects on the heart itself.

Priya Menon: So, when does a patient actually start seeing this effect on the heart? Is there a specific period or like, how much into their treatment, how much after their treatment, they actually see this?

Dr. Javid Moslehi: So, I have a little bit of perspective on this because I've started now three different programs or at least let three different programs, I was at the Brigham and Women's Hospital at Dana-Farber Cancer Center. So, the first time I started doing, this was in 2009 at Dana-Farber, 2014-15 I went to Vanderbilt and now I'm here for the last few months. The truth is when we start these clinics, the bandwidth we have is patients, who have acute toxicities from the therapies. The patient who received immunotherapy has acute toxicity and the oncologist calls me and says, well, I don't know what's going on this patient has chest pain, has some EKG changes, can you see them? So that is essentially the biggest place where we see patients, but as in other cases, where our ability sort of grew, where we had more cardiologists doing this, then we can really focus on survivors and many cases with survivors, one of the goals I have and one of the hopes I have is we can take care of these acute toxicity so we can prevent heart disease in literally many many people or survivors. So, we see them most acutely when there is this acute issue going on with the heart when they're getting chemotherapy, cancer patients. My hope is down the road we can expand this to survivors of cancer who we know are going to have heart disease. But right now, we don't know until they don't have a specific symptom and really one of the goals we have is promoting cardiovascular health in cancer survivors.

Priya Menon: Dr. Moslehi, you did mention new drugs also having an effect on your heart. So, as more and more immunotherapies are developing for cancer treatment, what are some of the specific cardiac side effects that, given your work on immunology occur during treatment with some of these agents?

Dr. Javid Moslehi: So, it's very different depending on the drug. So, old drugs like radiation and chemo, doxorubicin or anthracyclines, or Adriamycin, they go by different names would cause the pump failure. The heart doesn't pump as well. With immunotherapies, we see inflammation in the heart in a condition that we call myocarditis where there are effects on the inflammation of the heart that comes about. With some of the prostate cancer therapies we see metabolic issues, patients can have heart issues, but they can have diabetes. They can have their cholesterol change. They can have their blood pressure change. They lose muscle and they came fat with androgen deprivation therapy for the prostate. So, again, a big part of our program is promoting health in those individuals. So, it really varies across the board. And one thing that's changed in this field is we used to see patients who just come in pump failure, the heart failure, but now we have patients with immune infiltration conditions, like myocarditis. We see a lot of prostate cancer patients because of the therapies, can have cardiometabolic issues. And even where there are studies that cause arrhythmias, and then the other thing I want to kind of focus on is we talked about Cardiology, but it's really



a cardiovascular disease, right? It's not just the heart, that may be affected, it's the vessels and that's the big part of our program. Cardiologists deal with the vessels as well. And so, you can have a blockage in a vessel that provides blood to the brain, and you can have a stroke and that's a vascular problem. So, cardiovascular is a broad term. And so, we see a myriad of cardiovascular issues, especially with the new therapies. And that's a place we're really focusing on to try to make changes and promote health in patients.

Priya Menon: So, is this field of cardio-oncology dealing only with the drug toxicities or is there something more, beyond this as well?

Dr. Javid Moslehi: Yeah, so great question. So, this has actually been an incredible journey for me personally, because in 2009, I thought it was going to be about drug toxicities, and I thought it was going to be mostly about again Doxorubicin and radiation, but I learned of the new drugs. One thing we have learned over the last few years is that cancer and heart disease remember, I told you they're the number one and number two causes of death, actually have a lot of roots that go together. Common risk factors can lead to both. So, let me give you some examples. If somebody smokes, they have a higher risk of having a heart attack, but they have a higher risk of having cancer, right? But now we realize things like obesity, things like high cholesterol which we know for many years were important risk factors for cardiovascular are also important risk factors for cancer. And finally, just over the last five years, we've realized that genetics and specific gene mutations that we acquire over years in our blood cells in a condition called Clonal Hematopoiesis or CHIP is also a major risk factor for both cancer and heart disease. And one of the goals of the UCSF program is now really at the leading edge of these new frontiers in the field and really help our patients in more ways and really try to understand why these risk factors cause both. And it has some practical implications, right? We are all told we should exercise because that's good for your heart. Nobody said you should exercise because that's good for your cancer. But one thing we have realized is that many of the patients can have risk that can affect both. So, exercise addresses obesity, if you had cholesterol, it can address both cancer and heart disease. So, it has a lot of practical value for what we do for our patients as well.

Priya Menon: Dr. Moslehi you mentioned CHIP, so what is CHIP? Is this another emerging area in cardio-oncology, can you talk a little bit about this?

Dr. Javid Moslehi: Yeah. So, CHIP is very new terminology. We didn't actually know much about it five six years ago, but we've just learned about this some over the last few years. So, turns out as we get all get older, the blood cells in our body that come from the bone marrow can acquire mutations and there is a group of cells that can grow, okay, when we look at a five-year-olds blood cells, they're all pretty even but we look at the 75-year-olds there are more cells that are one type of clone. So, our oncology colleagues knew this years ago and they called it, they didn't know what it means so they called this Clonal Hematopoiesis. Meaning these mutations occur, you get a bunch of cells that are exactly identical, but they didn't know what it meant. So, they called the Clonal Hematopoiesis of Indeterminate Potential or CHIP, okay? So, that was 20 years ago. We learned about 10 years ago that these mutations can increase the risk of you having blood cancers and possibly other types of cancer, but when they looked at a lot of the population of patients with CHIP, it turns out these patients have significant heart disease. And in fact, many places like Memorial Sloan-Kettering, like Dana-Farber have started CHIP clinics where again it's another way of preventing both cancers that we knew about 10 years ago, but the cardiovascular disease and there's a lot of interest in terms of determining what we can do for these patients. Do they just get a good old cardiac disease like checking your cholesterol stat, giving you a statin or there are new drugs we want to think about with these patients, as it's a different crowd that we have to think about? So, there is considerable interest in this area and one of the hopes of the cardio-oncology clinic is we can have the best and the first CHIP clinic in the west coast and that's one of the areas will be focusing on.

Priya Menon: Thank you. Thank you, Dr. Moslehi. So, I'm just going to get the panelist on for their questions now and as I get back with some of my own at the end. So, we have Heidi Floyd who is a breast cancer survivor, with over 10 years of experience in health care. Heidi, please ask your questions.



Heidi Floyd: Hi, thank you very, very much.

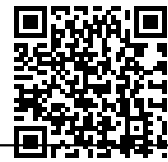
Dr. Javid Moslehi: Hi, great to meet you.

Heidi Floyd: Great to meet you too. Thank you for this incredible conversation. I really appreciate it. I have a couple of questions that I'm not speaking on behalf of myself as a cancer patient, but also for my entire community, if you will. There's a lot of possibility of having identical question. My first one is does accepting the risk of the treatment knowing that you're going to go in for treatment for your cancer that might lead to cardiovascular disease means that we cancer patients will have limited ability for things like exercise once we've completed our course of treatment. Does that mean more limited for the rest of our lives in exercise?

Dr. Javid Moslehi: Well, so first of all, I was involved in survivorship in breast cancer specifically in 2013. Back then a major study came out where women who had radiation as part of their breast cancer treatment, turns out women who get radiation have seven percent increased risk of heart attacks, strokes, and sudden heart death for gray of radiation than yet. This was a very huge study, came out in New England Journal of Medicine 2013 and I wrote the editorial for it. And I think one of the number one things and I don't know if I want to clarify something before I specifically answer your question is, the people came out and said, well, nobody should get radiation for breast cancer. That's not what we're saying at all. It's just recognizing that you have a high risk of heart disease and finding ways of preventing it. Your question specifically about exercise touches on something and it really touches on the dogma that we used to think about. So, we used to think, if you have cancer, you shouldn't be moving around. Certainly, we use to think 50 years ago, if you have heart disease, you should be sitting around, not do anything. Well, I have news for you for both of the patients, exercise can be a big tool to promoting health with them as long as there are no acute cardiac issues as long as they get cleared by a doctor, as long as they don't have a major blockage in a major artery not using a cardiac example for their setup for a heart attack. But if they get cleared, we think exercise can be very, very helpful in fact. So, in terms of what we can do for our patients, one of the things that I was fortunate to be involved with is the NCCN, which is a National Cancer Center Network. About 2014, I got called to serve on this group and I happened to be the single only cardiologist in this big group that's all entirely on oncologists. So, they're all oncologists. I'm the only cardiologist and one of the goals was to develop ways for our patients, we can promote cardiovascular health in patients, breast cancer survivors, prostate cancer survivors, and so forth. And one of the things we came up with was the so-called ABCDE checklist. That's now part of the NCCN guidelines for all cancer patients in terms of promoting cardiovascular health. This included among other things we can go through the ABCDE in another moment, but the E was really exercise, but it also represented other things like EKG and Echo that some patients may need to get. But it was really exercised and again, the pro goal is to promote cardiovascular health, and this is a simple checklist that's now part of the NCCN guidelines which is a guideline that every oncologist needs to follow. So, to answer your question, exercise, as long as cleared by your doctor, very good for you. That's how we used to think in 2000-2005. Now, it's 2022, we have a new appreciation of how good exercise is both for your heart, but also potentially for cancer.

Heidi Floyd: Very good. Thank you. If someone's about to go into treatment as a cancer patient, are there any sort of warning signs that they should look out for in reporting to their oncologists whether their nurse or anybody regarding cardiovascular issues?

Dr. Javid Moslehi: Absolutely. So, there are risks, their cardiac signs that we always warn our patients, the things like chest pain, things like shortness of breath, especially when you're exerting yourself. But there are also ABCD also aligns with risk factors that are absolutely critical. So, the A represents Awareness of cardiac signs actually. So that's one of the things, A stands for, A also stands for Aspirin and some people could benefit from Aspirin, B stands for Blood pressure and measuring the blood pressure. So, you may not have heart disease, but guess what if your blood pressure is 180 over 100, you're going to have heart disease in 10 years and that's something that needs to be checked and addressed. C stands for both Cholesterol that we need to check in every patient but also Cigarette smoking. D stands for Diets. It stands for Diabetes that everybody needs to get checked. And also, D stands for Dose of chemotherapy. So, the A, in this case, stands, for Awareness of cardiovascular disease, is about the patient's doing what the cardiac signs are, but



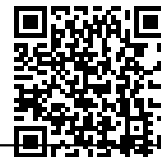
the other things in the ABCDE, really pertain more to cardiac risk factors. Things we know for many years can lead to heart disease and if we prevent those, this is why there's so much focus to get the blood pressure down, let's get the cholesterol down, let's get the sugars down. It's all to prevent heart disease and recognizing it in cancer survivors is probably one of the number one goals for the ABCDE checklist.

Heidi Floyd: Okay. Very good. Thank you. Kind of going along your conversation earlier about how there was a discussion about radiation and then immediately following that we shouldn't do radiation and in your response was no, we absolutely should. Along that same vein you discussed Dr. Robison and the cancer patient when I was first diagnosed, I happen to be pregnant at the time and I had a wonderful oncologist who treated me with that medicine during my pregnancy. So rather than kind of demonizing it I acknowledge it as one of the medicines that kept me alive. So, can you please explain how this medicine, in particular, it's not just for moms who are trying to get rid of cancer but also, everybody living inside of us all the babies?

Dr. Javid Moslehi: Absolutely. And this is an area in that we have an active investigation. I run a basic science lab and one of the things we just had a meeting with our colleagues here in radiology with Dr. Rubison on is how we can access cardiac function as patients are getting the therapies actually. As you know probably you got probably four doses of AC or Doxorubicin. You didn't give it all at once. One thing we learned about 30 years ago is you don't give it all at once because that can have dramatic effects on the heart. So now we space it out that's the whole reason we space it out. We give four doses usually for breast cancer smaller amounts each time. And for lymphoma, we give six doses again in smaller amounts, but you get that. So, one of the things is you sort of get that and I think one of the points is to monitor the heart and really understand why it is some people have heart problems not everybody does. The other important issue is we used to give a ton of doxorubicin but primarily because of a heart issue, you only get a certain amount of doxorubicin. So, in your case, in breast cancer, usually get about 240 milligrams, with lymphoma, you get 300 mg. We used to give 700-800 milligrams of doxorubicin before and so that's been one of the ways to decrease the risk that comes with doxorubicin. Although I will just be if I can just add one more point. In fact, one of the main areas of cardio-oncology is it exists is because of breast cancer because it's not just doxorubicin, people get a percentage of patients get a drug called Herceptin. And that requires monitoring the heart during the course of getting the treatment. People get radiation. Now, people are getting immunotherapies. And when you combine all these different drugs, you can have a whole different profile of toxicities. And again, part of our goal here is both monitoring and identifying who can have heart problems. So, for example, we may decrease the dose, we may initiate cardioprotective drugs in those patients earlier, we may try to get their risk factors down. So, it's all things we can do and if I can add one more piece to it with radiation. Again, it's not to give radiation but because of this realization, a lot of the radiation oncologists now have had interventions to promote heart. So, one of the things they do in some places, they have you go supine getting the treatment, other times they have you breathe in, taking the heart out of the picture. And so those are all small yet effective strategies, we can all have to decrease the cardiac risk for patients. So, I think awareness is absolutely critical not just for the patient but also for the oncologist and physicians.

Heidi Floyd: Great. Thank you. You said that the reason that we have Vector was in this because of breast cancer patients. I think you said that and that I find that fascinating and I told Priya that when we were emailing back and forth, I want to discuss this with someone for quite some time. Doxorubicin is one of the chemotherapies, one of the handfults that has their origins in an utterly fascinating and not often discussed part of research amongst the patient population anyway. These are soil-based microbes and I find it to be wildly innovative. Can you share with me how crucial things like that are, new innovation, creating new medicines that are hopefully less harmful to organs like our heart? How important is that kind of R&D to people like yourself or others out there trying to save all of us?

Dr. Javid Moslehi: So, this is actually just picking up this that you mentioned. It was actually identified in Italy, the Southern south of Rome from the soil is near the Adriatic Sea which is where Adriamycin comes from. So, the Adriamycin name comes from the Adriatic Sea, and it was always red, which is work doxorubicin came. It was a big fight between the French and the Italians and so the name doxorubicin or Daunorubicin recognized both the French and the Italian origin of it. But this was back in the 1950s and 60s



absolutely, the whole reason, this whole field of cardiology exists is the enormous number of new therapies that have come through the door. 20 years ago, or 30 years ago now, in breast cancer was trastuzumab or Herceptin, in the last couple of years with breast cancer has been immunotherapies, immune checkpoint inhibitors, PD-1 Inhibitors. The most common type of cancer in the last few years has been CDK4/6 Inhibitors, which we have a unique cardiac profile that we see with them. And many drugs that are affecting the PI3 kinase system are being advocated or being tested in breast cancer and those all have metabolic issues. In fact, it's expected that your glucose goes up when you're getting these therapies and how we kind of combined and think about these all in parallel, when it's that the patient can be getting multiple therapies, is really one of the goals of the program in terms of how to give these drugs safely to patients and how to prevent having heart problems that we don't have to trade one disease for another business a few years later.

Heidi Floyd: Thank you. Thank you so much for your information.

Priya Menon: Thank you, Heidi. Next on the patient panel is Dr. John Antonucci. Dr. Antonucci, has metastatic prostate cancer and cardiovascular disease. He is part of AnCan an advocacy organization that's devoted to the support and navigation of patients with cancer. John, please ask the questions.

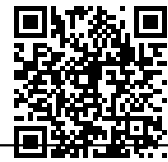
Dr. John Antonucci: Hi, nice to meet you.

Dr. Javid Moslehi:.... Great to meet you, John.

Dr. John Antonucci: You too. CHIP brought my attention when you were talking just now. Will everybody get it eventually, if we live long enough, it sounds like maybe it's a...?

Dr. Javid Moslehi: Really great question. It's one of those things we knew very little about but not everybody including at least a number of New York Times articles that is on this topic because it's just so interesting and they're literally biotechs popping up. In fact, there is a new company South of San Francisco, that's all focused on CHIP inpatient. So, one thing we know is CHIP, the recurrence of mutations in this condition is called CHIP. But again, we don't know what CHIP means. We know it increases the risk of heart problems and slightly increases your chance of lymphoma, leukemia, other blood cancers, and possibly other cancers slightly increases, doesn't mean everybody gets it just means there is a slight risk. But if you actually look at the patients as we get older, we recruit, it's just a matter of age. And initially people thought well of course, it just means people are older and older people are the ones who get cancer and certainly older people have heart disease and it has nothing to do with, it's just a matter of, it's just a sign of people getting older and that's what we are checking. Some seminal papers came out in the last few years that suggest CHIP mutations by themselves increase the risk of cardiac disease, forget about the age. So even though its more common as we get older, the field now feels that CHIP mutations by themselves increase the risk of heart disease itself. And that's something that we need to understand better. There's been a lot of interest in things like inflammation. is it causing inflammation in the body that then leads to heart disease? There're also other interests where other diseases could be affected, which may increase the risk of other diseases like emphysema in the heart and that's also an area of intense research. So, five years ago, the idea was maybe it's only patients who are getting older but now the field feels the mutations themselves can promote heart disease and it's something we and others are trying to understand. And by literally having the first CHIP clinic that at least I'm aware of in the West Coast, we join other groups like Sloan Kettering Memorial Sloan-Kettering in New York, Dana Farber of trying to understand this process better and really see the patients to see how best we can help them.

Dr. John Antonucci: How interesting it's going to be really interesting to follow. Well, breast cancer and prostate cancer have some real interesting contrast as regards the heart. Now, when heart cancers get radiated, it doesn't radiate the heart and you use a lot of immunotherapies in breast cancer and very, very few of us with prostate cancer get immunotherapies. We have a few people getting Pembroluzumab. But mostly it's what you talked about at the beginning that we get cardiometabolic risk factors and stressors. And not only do we apparently get them from our treatments, right? But we come in with a lot of them. Don't



we? So are we really...

Dr. Javid Moslehi: Absolutely.

Dr. John Antonucci: Are we really pretty convinced then that are LHRH drugs are quite a significant cardiac risk factor?

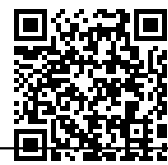
Dr. Javid Moslehi: So, that's been a point of great discussion back when I was at the Dana-Farber working with some outstanding colleagues. So, my friend, Paul Lewin and Tony D'Amico who are kind of radiation oncology experts, and Phil Kantoff who then went to Sloan-Kettering, this was always a discussion we had, and the controversy was what we know for a fact they if you're on androgen deprivation therapy or these hormonal agents, they're going to increase your blood pressure, they're going to increase your cholesterol, they're going to increase your sugar's. That's not debatable whatsoever. We also know unequivocally that if you have more sugars, if you have worst cholesterol, if you have worst blood pressure, you're going to have a higher risk of heart disease and there was considerable controversy as to whether the drugs themselves can have heart problems and that turns out to be the case. So, number one, some of the studies we did when I was at Vanderbilt looked at the risk of arrhythmias in patients getting androgen deprivation therapy. We've got several papers published that showed that there is this risk of arrhythmias independent of risk factors. We definitely now recognize that patients with more cardiac risk factors, turn out to be the most common majority of our patients. They are the ones who unequivocally have a high risk of heart disease, but there are some nice studies by Phil Kantoff and Tony D'Amico, that's suggesting trials. If you take the 45-year-old with no heart problems whatsoever and the one who exercises and runs marathons, they probably don't have as much of a risk when they go on androgen deprivation therapy. But definitely, the majority of our patients with risk factors can have heart problems from the therapies. And then one thing that's changed now, we used to give one drug Lupron, everybody got Lupron went home. Now, there are combining therapies. Now, we're combining abiraterone, which works a different pathway with Lupron. We're using enzalutamide in combination with Lupron. And so really, what's changed now is not if you're not just using one drug, we're using a combination of drugs, which is really where the field is going. And there's actually some very interesting data that came out last year, was respectfully with respect to how you target this pathway. There are these GnRH agonists which are drugs like Lupron and there are Antagonists and there are a number of drugs that have been developed, and they did a trial showing which one is more effective with lowering the testosterone. It turns out the antagonist, the newer drugs were more effective in lowering your testosterone. You may say that's a big deal, we're not looking at cancer and point, but the real difference between the study was a difference in cardiac outcomes. The patients on antagonists think of much less events than the ones on the traditional Lupron. This is also a new area, and this is an area we and others are trying to investigate. So going back to your question, no question, the risk factors are affected, but in many majorities of the patients not all patients, beyond the risk factors that are changed that affect heart disease risk, the drugs themselves can have heart problems and we think that is true with cardiac patients. And then the last one I want to bring up is a sort of synergy thing, okay. You can have a drug that increases your risk of having a heart problem by 5%, not a big deal. But if you combine therapies, it can now become a 60 percent increase, there is a synergistic effect with a risk factor have with the drugs now the second drug. Right now, we're looking at a real risk for those patients.

Dr. John Antonucci: That's very helpful. So, it's not all just mediated by the elevated blood sugar or the elevated triglycerides, right? It's also got its own independent risk.

Dr. Javid Moslehi: Yes.

Dr. John Antonucci: And what arrhythmias did you mean?

Dr. Javid Moslehi: So, this study that we had their one of the things we look at in all cancer patients and everybody getting a new drug is called QT prolongation, which is how the heart repolarizes. What we found out a few years ago from when I was at Vanderbilt, and we could send you a number of papers are that men and women it turns out have different levels of these QT prolongations. So, boys and girls have the same



exact amount or when they hit puberty, women are at increased risk of these types of arrhythmias compared to men. And we think that's testosterone lowering that otherwise, we get older, they get closer together on all of this of course gets the worse stage. But one thing we found is when you basically have these hormonal treatments, you increase the risk in men in terms of having these arrhythmias, and these arrhythmias are called Ventricular Tachycardia. And there's a French name for the type of ventricular arrhythmia called Torsades de pointes, which is how the EKG looks when you have these arrhythmias. So, that's another area we've been investigating over the last few years and one that we're going to pursue here at Vanderbilt. I'm sorry here at UCSF. We did this Vanderbilt now it is UCSF.

Dr. John Antonucci: You tell us a little bit about who should go on aspirin these days?

Dr. Javid Moslehi: Yeah, we used to think aspirin was the best drug to put everybody on. So, let's just be very clear. If you've had a heart event. If you had a heart attack, no question you should be on aspirin. That's when we call secondary prevention. What has changed now is our perception of the relative benefits of aspirin in primary prevention, patients would never have heart disease. The truth is much of the early studies done, were done on patients, were on no other therapies. So, when he's got the aspirin, there was a big benefit, but now the drug that we think most people should be on is a Statin actually. And the question really comes, how much more benefits are you getting on aspirin? Which is one of the reasons why the primary prevention, it's sort of locks this luster. I think I can speak for most cardiologists, who would argue statins should be your number one drug you should be on. If there's one drug you're going to be on, it's not Aspirin because once you're in a Statin, the relative decreased risk, that's when you add aspirin is much smaller than if you are on no other treatments. And there have been a number of nice papers written by some of my colleagues, you're probably well aware of this. Because this has been a number of New England Journal of Medicine editorials, and actual papers with it. So, this is why when we develop the ABCDE guidelines, we specifically specified that it should be a discussion with your doctor, that it should be for certain patients. And so that I'll leave it at that.

Dr. John Antonucci: Great point.

Dr. Javid Moslehi: And a great question though.

Dr. John Antonucci: None of those changes for those of us who are on ADT, right?

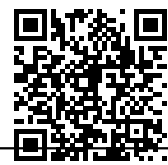
Dr. Javid Moslehi: Well, it should not primarily because you don't have heart problems. But again, one of the things that we do at Vanderbilt, and we're going to do at UCSF monitor the patient's risk factors when they go in ADT. To be honest with you, at least my experience at Vanderbilt was, it's the urologist, the surgeon, the radiation oncologist that puts you on ADT 90% of the time at Vanderbilt. And they're just a busy Clinic. They probably don't know most about cholesterol. Well, if you check cholesterol, it comes back this, what do I do now? And so, this is the kind of place where primary care doctors and cardiologists can partner up with. And again, I wish I would have the bandwidth to help every one of these patients. We're starting a new practice, a new clinical program, there are three of us seeing patients. So a lot of times that becomes not as much of a focus just because but it is an important area and I think especially with prostate cancer patients. It's decreasing the risk of events that can occur later. That's literally as important probably as important as anything else.

Dr. John Antonucci: Priya, could I ask a couple more?

Priya Menon: Yes, John five minutes.

Dr. John Antonucci: Okay, I've had both patients and friends say I've only got a year to live. Why the heck should I stop smoking? Why can't I smoke all I want? What do you say?

Dr. Javid Moslehi: Yes. That's a really good question. So, a couple of points I want to bring up, first of all, the number one thing I've learned from my oncology colleagues is cancers that we used to call effectively



death sentences are now cancers that you can live with for many years. The example, I want to bring up to everybody was what happened with melanoma and immunotherapy, right? Melanoma was a death sentence for all intensive metastatic melanoma right. Now, I don't want to be dramatic, but that's what it was. Point five percent of people could have some response, point five percent but with immunotherapies and especially when you combine immunotherapies, I just looked at the recent data is greater than 50% of the patients. We went from point five to fifty percent. The one example I want to bring up is former President, Jimmy Carter, right? President Jimmy Carter at the age of 90 had metastatic melanoma that went to his brain and his liver. Any other era would have been a death sentence certainly to a 90-year-old. He is about to turn 97 now and I kind of check this usually and he's been cancer-free for the last few years. So, what we used to think is sort of you have no shot. This is a case where a 90-year-old gets melanoma, which went to his brain can live. So first of all, our ideas of how long you have to live can programmatically be different, true for every type of cancer. So that's one thing to bring up, I think the second is also the idea that I brought up earlier, which is these risk factors. So why check your cholesterol in somebody who has only advanced cancer, is this potential that can decrease the risk of cancer? If you treat the cholesterol, you could be a treatment regimen, if you will, and people are testing that idea now for cancer. I'll just use an example of the prostate, I just got off the phone yesterday with one of my colleagues at the University of Colorado where they're testing, metformin, a diabetes drug for prostate cancer treatment. Multiple trials like that are ongoing now. And so, I will say this, first of all, and my answer to the person would be first of all when we used to think, could be a month to live, it could be years. It could be you're one of the people who survived cancer and again much of the data we have on cancer comes from five years ago. Nothing gets updated takes five years to update the numbers. And then the second issue is that these common risk factors play a role. I think it can really help cancer itself, too.

Dr. John Antonucci: What do you watch out for after a cardio-oncology patient has recovered from acute covid?

Dr. Javid Moslehi: Yeah, so we wrote a paper back in 2020 when covid came out and the issue there was actually the growing number of patients who get immunotherapies and specifically immune checkpoint inhibitors. So, at least how we think of it is causing a lot of issues is this activation of the immune system. And so, do we even give patients immunotherapies, which would further activate the immune system? And to be honest. The reason this was promoted was this patient came, this is early in 2020, had lung cancer, got immune checkpoint inhibitors. Had this lung problem that we thought was pneumonitis and then March and February, March came, and it turns out the patient had covid. And so now with getting the immunotherapy, I would argue their immune systems is probably more active. And so, this becomes a real dilemma for us, for the oncologist primarily with immunotherapy specifically. Again, another area where we are very interested in is one thing that's opened our doors with this cardio-oncology is our appreciation that immunotherapies can have these effects on the heart, nobody appreciates this five years ago. And we also recognize these issues can have problems for overtime and I would argue, that we wrote a paper on this with Alan Beck who is a new faculty member here at UCSF. I was at Vanderbilt at the time, but it was a circulation research paper. Where we actually argue, if you look at the cardi oncology population. If you see how I mean or therapy affects the heart, it could be a doorway. It could be a kind of give you some perspective on covid where we think the same process occurs with heart issues. Just let's not forget, heart issues are a big part of covid, and we think it's because there's an activation or activation of the immune system. That's what's driving the ship. That's what many people think happens. But if we study the cardio-oncology patients, we can learn about how to best take care of covid. I will also say one last point is if you look at the data that came from initial trials, with covid, it was the same therapies people were giving for patients with immunotherapies, cancer patients getting immunotherapies, with side effects and cardiac side effects. Drugs, like Polatuzumab, which is a six inhibitor, something that was being tested for covid.

Priya Menon: Thank you, John. Thank you, Dr. Moslehi. I just have one more question before we wrap up for the day. I was just wondering like the treatment agents that you use, is it the same for people with cancer and without the heart treatment?

Dr. Javid Moslehi: Treatment for heart disease?



Priya Menon: Yeah.

Dr. Javid Moslehi: So, we think, yes and no. So, in general, the most common reason for heart disease is coronary heart disease. So, we generally don't have other drugs to use, we use statins, we use in patients who have had an event aspirin. So, with the drugs that we have that we use in general just because we not only better as this field as evolved, but we are also actually interested in we have had to deal with new therapies. So, for example, myocarditis, a checkpoint inhibitor, associated myocarditis, we came up with a drug called the _____. It's actually a drug that was made before and we had a case report in New England Journal of Medicine. We have now 50 patients including at UCSF treated successfully. We think it's an effective therapy, but it's for this type of myocarditis. We don't know if it's true with other forms of myocarditis. And then there is this whole interest of things like CHIP, for people with CHIP, we talked about CHIP earlier are they just going to have a little heart attack and move on or is it a different type of heart attack which is why there is a lot of interest in terms of defining, whether this is a different type of heart attack. It may be a different drug that's needed. And so that's an area we and others are promoting and really trying to understand at a deep and mechanistic level.

Priya Menon: Dr. Moslehi, thank you very much. I think it has been a very informative session. Heidi, John thanks for joining and asking those great questions. As we are wrapping up for the day. And we also thank UCSF Helen Diller Family Comprehensive Cancer Center. This talk will be available on curetalks.com. Thank you, everyone, and have a great evening.

Thank you very much

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