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WTIC Newstalk 1080

Treatment Advances in
Melanoma

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Healthline with Yale Cancer Center is a weekly broadcast on WTIC Newstalk 1080

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This is Healthline. A joint venture of WTIC NewsTalk 1080 and Yale Cancer Center. Yale Cancer Center is a resource for cancer programs throughout Connecticut developing new advances in prevention, screening, diagnosis and treatment. On Healthline, you will hear from some of the leading doctors in the country. Healthline is not intended to provide medical advice. Yale Cancer Center urges you to consult with a qualified physician in your community for diagnosis and for answers to your medical questions, and now, our co-hosts, oncologists, Ken Miller and Ed Chu.

Miller Good morning and welcome to Healthline. My name is Dr. Ken Miller, and I am the Director of the Survivorship program at the Yale Cancer Center in New Haven. I am here in the WTIC studios with my colleague and co-host, Dr. Ed Chu, who is the Chief Adult Oncologist at the Yale Cancer Center. Good morning Ed.

Chu Good morning Ken. Healthline with the Yale Cancer Center is our way of providing you with the most up-to-date information on cancer care every Sunday at 8:30 a.m. on station WTIC Newstalk 1080. Our Healthline program features some of the nation's leading oncologists and cancer specialists who are in the forefront of the battle to fight cancer right here in our State of Connecticut.

Miller Each week, Ed and I will be joined by different experts from the Yale Cancer Center. Together we will discuss the myths about cancer, the latest treatments available to people with cancer, and advances in clinical research. Our goal is to give you help and hope by providing information and answering your questions. If you would like to submit a question about cancer to Healthline, please email us at Healthline@yale.edu. We will try to answer your questions on a future broadcast.

Chu Today our program focuses on treatment advances in melanoma, and our special guest experts today are Dr. David Leffell, Professor of Dermatology and Surgery, and Chief of the Section of Dermatologic Surgery and Cutaneous Oncology at the Yale School of Medicine. He is also author of the well known book called "Total Skin." Our other guest is Dr. Mario Sznol, Associate Professor and Vice Chief of Medical Oncology, and an internationally known expert in the field of melanoma and drug treatment.

David, Mario, thanks so much for being with us today on Healthline.

Miller Let's start with a quick overview. David, what is melanoma?

Leffell Malignant melanoma is a cancer of the pigment cells of the skin. The top layer of the skin or epidermis contains pigment cells that can turn malignant, can turn cancerous.

Chu So David, typically we think of melanoma and skin cancer as being the same thing, but there are other types of skin cancers, aren't there?

Leffell There are indeed. The most common forms of skin cancer are basal cell carcinoma and squamous cell carcinoma, but melanoma, the third type, is the most concerning because it really has the potential to be quite serious.

Chu What are the risk factors in individuals who are perhaps at highest risk for developing melanoma?

Leffell The best established risk factors for skin cancer in general and melanoma in particular are individuals with blond or red hair, fair skin, blue, green or gray eyes. These are individuals who are especially susceptible to the harmful effects of the sun and are therefore at increased risk for melanoma.

Miller Along those lines, in terms of the sun, how does the sun cause melanoma? Can you tell us something about the process?

Leffell It is well known now that [ultraviolet radiation](#) from the sun causes mutations in the skin cells, and it is felt that these mutations, if they occur in certain genes that control cancer development, can actually lead to the development of skin cancer.

Miller So, is this genetic? Is there a genetic predisposition?

Leffell Melanoma is a type of skin cancer that is caused both by the sun in many cases we believe, but there also are individuals who develop melanoma as the result of an inherited tendency.

Miller And how common is melanoma?

Leffell Melanoma is increasing in incidence. It is actually the most common cancer in women ages 25-29. In 2005 alone, there were 60,000 new cases of malignant melanoma diagnosed.

Miller Which actually is a huge number. We all think about breast cancer as being very, very common, but melanoma really is a much larger number than I knew myself.

Leffell It's a substantial number, and in reality, it's responsible for 7-8,000 deaths a year. Many people think of skin cancer as something that is not very serious. You develop something on your skin, you go to the dermatologist and take it off. We are trying to educate the public about the importance of being suspicious of lesions that could be melanoma, because melanoma can kill if it is not diagnosed promptly.

Chu So, what can you tell our listening audience about the type of lesions or skin conditions that they need to watch out for that might put them at increased risk for developing melanoma?

Leffell That's such an important question because our ability to prep people for what they have to look for can be lifesaving. We talk about the ABCDs of melanoma. If you have a

particular growth that's asymmetric when you look at it, in other words, if you imagine your mind's eye folding it over and the two sides don't match, that's an asymmetric lesion. That's concerning. If the borders are irregular, if the color includes brown and black, or red or white, irregular pigmentation is very concerning. If the diameter is greater than say 7mm or the size of a pencil eraser, that's important. And I actually add another criterion. And that is suspicion. I have been amazed over the years about how patients know their own bodies best. They might not be able to describe it, but I am amazed at how often patients come in and say, "Doc, I just don't like this thing." I'll look at it and I won't be especially concerned. But it comes off because in the end when it comes to melanoma, the customer is always right.

Chu And typically, if one were to notice any of these abnormal skin conditions, who should they seek help from?

Leffell Very often the primary care doctor should be able to identify a lesion that is of concern, and some of the other factors you look at are a lesion that itches or bleeds, or crusts. These are all abnormal changes, and should draw the attention of the examining physician.

Miller I have heard people talk about [atypical moles](#), and obviously there are some people that just have a ton of moles. So can you say something about atypical moles? Does that cause melanoma? Is that a predecessor?

Leffell Atypical moles are normal moles that have become atypical or abnormal. They have gone sour, so to speak, and some people actually believe that these are growths that are precursors to or lead to melanoma. It's a controversial area, but we do know that people who have a lot of atypical moles (which by the way used to be called [dysplastic nevi](#) – listeners might have heard that term), really should be followed closely because they may well be at an increased risk of developing melanoma.

Chu So how does a diagnosis of melanoma get made?

Leffell Initially, on physical examination, when you look at the lesion, if there is concern that there is melanoma, a biopsy has to be done. There is no way to diagnose melanoma without a biopsy. There is no machine; there is no device other than looking at the specimen under the microscope. And a biopsy is really a pretty straightforward procedure. It is done in the office with a little bit of local anesthetic, the kind that the dentist might use, and the specimen is taken off and then submitted for analysis in the laboratory.

Miller Can you say a little bit about a skin survey? I have heard that term used before. Who should have that done, who should be doing it, and what do they look for?

Leffell We recommend that individuals who are in high risk groups, people who have had a family history of melanoma, have a lot of atypical moles as you mentioned earlier, or any of the other risk factors that I mentioned, should have a full body skin examination. And

what I mean by that is an examination from the head to the toes, and between the toes, and the soles of the feet. Melanoma, although we believe that the sun plays an important role, can in fact occur where the sun doesn't shine. So a full body skin examination is critical if you are going to identify things at their earliest treatable stage.

Chu We have an email from Barbara in Glastonbury which I think addresses a very important issue.

I have heard that people with darker skin tone have a decreased risk of developing skin cancer and melanoma. Is this true?

Leffell Well it is. It's actually the counterpoint to the risk factor, namely people with Type I and Type II skin, or fair skin. The [pigment](#) that people with darker skin tones have protects the skin to some degree from the damaging effects of ultraviolet radiation, and what's kind of neat is, under the microscope you can actually see those pigment granules form a skullcap over the nucleus of the cell where the DNA is kept, so we know that the pigment is intended to protect the skin cells. But even people with darker skin tones need to protect themselves against the damaging effects of the sun.

Miller When people hear the word "melanoma" sometimes it is very frightening, but it is my understanding that most people are diagnosed with the very early stage melanoma. How is that treated?

Leffell You are quite right. The vast majority of melanomas that are diagnosed are at the very early, highly curable stage. And the treatment that is required, and Dr. Sznol I'm sure will talk more about it, is relatively straightforward. A simple [excision](#) with margins of normal tissue is sufficient to achieve the type of high cure rate that we are talking about, and that procedure is typically done in the office or in one day surgery, and it really is nothing that listeners need to be frightened of. In fact, it is a straightforward procedure and doesn't necessarily have to be very complicated when you are treating the early stages of melanoma.

Chu And again, who is the best person to be doing that surgical procedure? Is it a primary care provider, a dermatologist, or someone like you, David, who is really trained in expertise in dermatologic surgery?

Leffell I think that the best person is the one who understands melanoma and treats a lot of it. I think treatment at the earliest possible stage can be performed by a general surgeon, a plastic surgeon, or a dermatologic surgeon. Regardless of who performs the procedure, you want to make sure that you take advantage of an organization that has experts who span the areas of expertise for melanoma.

Miller Can you say more about that? Who is on that team?

Leffell I think the best opportunity for getting comprehensive advice about the management of melanoma comes from a multidisciplinary melanoma panel like we have at the Yale

Cancer Center, and they include people like Dr. Sznol, who is a medical oncologist. Mario, would you like to comment more about the panel?

Sznol In fact we include in our melanoma unit, dermatologists, pathologists, radiologists, plastic surgeons, all of these people provide input into the optimum management of melanoma at all stages of the disease.

Miller I would like to remind our listening audience that we would love to hear from you, and you can email your questions to us at Healthline@yale.edu. We are going to take a short break, and then we will be back to hear more from Dr. David Leffell and Dr. Mario Sznol from the Yale Cancer Center.

This is a medical minute brought to you as a public service by the Yale Cancer Center. Cancer patients become patient survivors the first day they are diagnosed. There are over 10,000,000 cancer survivors in the United States, and the numbers keep growing. However there are long-term side effects of cancer including heart problems, osteoporosis, fertility issues, impaired growth and an increased risk of second cancers. Ending cancer treatment can be both exciting and scary. Most people are relieved to be finished with the demands of treatment, but many also feel concerned about whether the cancer will come back, and what they can do to prevent a relapse. Cancer survivors require long-term specialized care and support. For more information, log onto to www.YaleCancerCenter.org. That address once again is www.YaleCancerCenter.org.

Chu Welcome back to Healthline. This is Dr. Ed Chu and I'm in the WTIC studios this morning with my co-host, Dr. Ken Miller, and our special guest experts, Dr. David Leffell and Dr. Mario Sznol, two of the leaders of the melanoma disease unit here at the Yale Cancer Center. David maybe we could pick up where we left off at the break. Once a melanoma skin lesion is removed, is there anything further that needs to be done?

Leffell There is definitely in terms of monitoring the patient. In terms of other procedures, treatments and the nature of the monitoring, it really depends on how thick the melanoma is, and this goes back to something we were saying before the break. The thickness of the melanoma determines its seriousness. So very early melanoma that can be diagnosed as a stage when it is highly curable requires different kind of monitoring than melanoma that is more advanced. One of the things that we deal with all the time are individuals who have melanomas that are somewhat more advanced, and I think that perhaps Mario can talk about the types of things that are done after that.

Miller Let me ask you a question along those lines, Mario. For a patient who has a melanoma that is thick or where there has been some spread of cells to the lymph nodes, what are the strategies that are being used to try to prevent recurrence?

Sznol There is one drug, [Interferon alpha](#), that's been proven to prolong the time between initial resection and later recurrence. Patients with high risk melanoma who have very deep melanomas, who have melanomas that have spread to the regional lymph nodes, the

lymph nodes that are closest to the primary lesion that was resected, we offer those patients a year of treatment with Interferon alpha.

Chu I think one of the great developments that have taken place over the years is this issue of [sentinel lymph node](#) sampling. Perhaps Mario or David, you could comment on that?

Sznol I am happy to comment. If the melanoma is deep, usually those patients are referred to a plastic surgeon. We are very fortunate to have two very experienced plastic surgeons at Yale who have done many of these procedures. They do a wide excision, and if the lesion is more than a mm thick, they will do a procedure called the sentinel node procedure in which they inject dye near the initial melanoma, trace the dye to the closest lymph nodes, then drain that primary melanoma, and then do a resection of that initial lymph node. If that lymph node has melanoma, it portends poor prognosis. Those patients are at high risk for having later recurrence.

Miller I will ask both of you. We received an email from Kate who lives in Middletown and she says:

I was diagnosed in 2004 with Stage II melanoma that was removed with surgery, and I did not require additional treatments. Are there any things that I should be watchful for in case the disease returns?

Leffell I think that there are a couple of things. First, anyone who has had a melanoma diagnosed needs to have regular examinations by their dermatologist, and I recommend full body skin examination twice a year at least. You know you go to the dentist twice a year. The least you can do is get checked out for recurrent melanoma or other problems related to the melanoma. The recurrent melanoma that develops at the surgical site and metastatic melanoma is melanoma that develops, as Dr. Sznol was saying, at a region distant from the site where it was removed either in the lymph node or in the skin itself.

Chu Are there any blood tests or diagnostic imaging tests that one can use to help determine whether or not the melanoma has come back?

Sznol There are blood tests. The [liver function test](#) could determine whether the melanoma has gone to the liver. We do other blood tests that are not specific but can help to determine if melanoma has spread. We generally follow patients with chest x-rays, and in some patients over time we may do more sophisticated procedures such as CT scans to determine whether the melanoma has recurred.

Miller We have another email that I want to share with you. This is a fellow named Bill from Wallingford. He said:

I was recently diagnosed with melanoma. How can I tell how serious it is?

He is also asking too in the second part of his question, is there anything he can do for himself in terms of diet or exercise, or any kinds of positive things that people with melanoma can do? ?

Sznol We don't know that there is any relationship between diet and exercise in recurrence of melanoma. Obviously people should eat moderately and stay out of the sun. In terms of risk of recurrence, there are three things that we look at. How deep the melanoma is. There are certain things we look for under the microscope that gives us determination as to whether it might recur, and also whether the lymph nodes were involved. The more of those risk factors that one has, the more likely the melanoma is to recur. And when it recurs, it's likely to recur not just on the skin but perhaps in other organs, like the lung, the liver, the brain. When it recurs in those organs, it is serious and difficult to treat and can lead to death. So it's important to follow people. We usually follow people every three months with x-rays and blood work to determine whether their melanoma has recurred, but the people we follow so closely are those who have the poor prognostic signs of the high risk features.

Leffell Mario touches on a very important thing. When we see patients at the Yale Cancer Center who are referred to us because they want a second opinion regarding melanoma, one of the first things that we ask for is the pathology report and the actual original biopsy slides. Because it is so important to have a dermatopathologist who is an expert in interpreting melanoma evaluate the specimen, because that really does decide whether the patient is seen by someone like Mario, or someone like Dr. Stephen Ariyan, or Deepak Narayan, or oncologic surgeons, or someone like myself.

Miller We are going to take a break for a survivor story. And then we are going to be back and talk about what's available now, and the latest breakthroughs for treatment of patients who have advanced melanoma. Again we would like to encourage you to email us your questions at Healthline@yale.edu. Now we are going to take a break for a survivor's story.

A few years ago the diagnosis of cancer was a death sentence for many patients, but today, thanks to advances in clinical research, we are turning the corner in the battle against cancer. There are over 10,000,000 cancer survivors now living in the United States. They are the true heroes in the war against cancer. Here's the story of a hero from Hamden.

Ten years ago when I was diagnosed with aplastic anemia, there was no cure. After teaching math for 35 years, I was forced to retire. Then I met Dr. Tom Duffy at the Yale Cancer Center. He told me about a new procedure called a mini-stem cell transplant. He encouraged me to put my life in the hands of Dr. Stuart Seropian, one of the few doctors in the country doing this procedure. On January 17, 2004, I had a stem cell transplant at the Yale Cancer Center. At age 70 I feel like a new man. I owe a great debt of gratitude to the terrific staff at Yale Cancer Center. They literally saved my life.

This survivor's story has been brought to you by Yale Cancer Center.

Miller Welcome back to Healthline. This is Dr. Ken Miller, and I am in the WTIC studios with my co-host, Dr. Ed Chu and our guest Dr. David Leffell and Dr. Mario Sznol who are two experts in the field of the treatment of melanoma at the Yale Cancer Center.

Chu So Mario, let's get down to how we treat patients with advanced melanoma. What are some of the treatment options available for patients?

Sznol First let me clarify. Patient's with advanced melanoma are those patients who have melanoma that has spread to other organs, the lungs, the liver, and in some cases the brain. They are at high risk for death from their disease. This is a serious disease and it behaves very much like lung cancer or breast cancer that is advanced. The standard treatments for melanoma involve chemotherapy, which does not work very well actually, and biologic agents like [Interleukin 2](#) and [Interferon alpha](#). Of those, the one that has the best activity is the Interleukin 2. It can, in a small number of patients, cause very durable complete remissions and possibly cures.

Miller I want to ask you more about that. It is a fascinating thought that our immune system can help battle cancer. How does that work? Can you tell us more about it?

Sznol Strangely enough, melanoma is one of the most responsive tumors to immunotherapy, and the Interleukin 2, we believe, activates a specific kind of cell in the body, a lymphocyte that then attacks the tumors specifically. That lymphocyte actually recognizes melanoma specifically and does not recognize other normal tissues for example.

Miller Using that same idea, is there a way to turn on the immune system to prevent melanoma for people who are at high risk?

Sznol There are many, many clinical trials ongoing and many efforts to do that. We call those cancer vaccines. They are different from infectious disease vaccines, which prevent the development of the disease. Here you already have melanoma and you receive a vaccine to try and prevent its recurrence. But unfortunately, at least at this point in time, none of the vaccines that have been tested have actually had a beneficial effect.

Chu So Mario, just getting back to Interleukin, when you were at the NCI you played obviously a very important role in helping to develop Interleukin 2 as a therapy for melanoma, and here at Yale you have been modifying the dosing and scheduling of Interleukin 2. Perhaps you could just tell our listening audience what you have been doing to try to maintain the efficacy but reduce toxicity.

Sznol That's a good point. Interleukin 2 is now given 3 times a day, often in intensive care units or in monitored settings. It has many acute toxicities, although people get through it, they find it is a difficult time in the hospital. We have tried to develop a slightly modified regimen with less toxicity. We have now treated a fair number of patients over the past year with the modified regimen. We believe that we can do this safely on an

inpatient floor. The patients seem to tolerate it well, and some patients have had very good responses to the treatment.

Chu And are you adding any other treatment approaches to the Interleukin 2 therapy?

Sznol At the moment, we have plans to do so. We haven't yet started those clinical trials, but we plan to add the transfer of [lymphocytes](#) to patients very similar to a program that's being piloted at the surgery branch at the National Cancer Institute.

Miller Can you say a little more about that? What are lymphocytes and how do you anticipate doing this kind of research?

Sznol Lymphocytes are a specific type of blood cell that recognize abnormal tissues in the body and can kill them. So we can generate these lymphocytes outside of the body by taking them from melanoma tumors. We reset the melanoma tumors and can grow the lymphocytes outside of the body to very large numbers, and then we can give the lymphocytes back to patients in combination with Interleukin 2. The Interleukin 2 and the combination of lymphocytes form a uniform attack on the tumor, a highly coordinated attack on the tumor that causes tumor regression.

Chu What are some of the other clinical trials that you have been developing here at the Yale Cancer Center?

Sznol We have been very fortunate to work with some other novel immune therapies that come from industry. We are very excited about one drug. We were the first to administer this agent to humans. It activates T lymphocytes in a different way than Interleukin 2. We have been working with others, they are called [monoclonal antibodies](#), that also activate lymphocytes to attack the tumor. We have several protocols that involve choking off the blood vessels that feed the tumor, a strategy that has been successful in other cancers such as lung cancer, colon cancer and breast cancer. Based on some work by one of the molecular biologists at Yale, Ruth Halaban, we have been looking at ways to turn on genes in cancer cells that turn the cancer cells off.

Chu I understand that you just recently received word from the National Cancer Institute that your melanoma team was awarded a Center of Excellence for melanoma, and in fact it was rated the top melanoma center in the country. Perhaps you can tell our listening audience what that means, and what that means with respect to the types of novel therapies that patients could be offered here.

Sznol We believe that we have received funding for several novel translational programs. This will give us an opportunity to develop new types of approaches for melanoma. This funds not only lab research work that generates new agents, but also funds clinical trials to test those agents in patients.

Chu Again, not to overstate the issue, but I think that is one of the real benefits of being a designated comprehensive cancer center, the ability to take terrific basic science ideas

and bring them into the clinical setting where we can really advance therapies for patients.

Leffell I think you are exactly right. In my experience, the patients who come to us with melanoma have really two questions: 1) am I going to be OK? and 2) where do I go to get the most advanced treatment, the most advanced approach as to treating my problem? I am biased of course, but by definition the advanced work is going on at University centers and I am very fortunate personally and professionally to be part of the Yale Comprehensive Cancer Center where people like Dr. Sznol and others are developing novel treatments for our patients.

Miller We are coming to an end of this segment. Again, I want to thank Dr. David Leffell and Dr. Mario Sznol for joining us, and we are going to ask them for a summary and for the most important points that we want to share with our listeners. We want to encourage you also to go to our website which is www.YaleCancerCenter.org for more information about cancer, about melanoma, and about resources that are available to you and to our listening audience here in the State of Connecticut.

Before we sign off, Mario and David. In your opinion, what are the key points that we really want to share with the listening audience today?

Leffell From my point of view, one of the most important points is that melanoma, when diagnosed early, is highly curable. So when in doubt, check it out. If you have a lesion you are concerned about, don't procrastinate. Procrastination is normal, but in this case it can be dangerous. If you have a lesion that you are concerned about, have it checked out promptly.

Miller Mario, what do you want to share in terms of treatment of patients with advanced melanoma?

Sznol From my point of view, I think the key point is that standard treatment for melanoma does not offer major benefits for patients, and the standard of care really is clinical trials, and I would advise patients to seek centers that have high quality clinical trials.

Miller It was exciting today to hear about some of those trials that are really turning on the immune system. Hopefully that is going to offer a lot of promise.

I would like to thank Dr. David Leffell and Dr. Mario Sznol from the Yale Cancer Center for joining us today on Healthline.

Chu I also would like to thank David and Mario for a really terrific session. And remember to tune in to WTIC Newstalk 1080 every Sunday at 8:30 a.m. for Healthline with the Yale Cancer Center. Our next program will focus on the treatment of ovarian cancer, and our special guest will be Dr. Peter Schwartz, who is the John Slade Ely Professor of Obstetrics, Gynecology and Reproductive Sciences at the Yale School of Medicine and

one of the nation's leading experts in the treatment of ovarian cancer. Until then, this is
Dr. Ed Chu

Miller and Dr. Ken Miller

Chu from the Yale Cancer Center wishing you a safe and healthy week.