PATIENT POWER

UCSF Medical Center

The Latest Approaches For Melanoma Treatment

Webcast

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What is Melanoma?

Andrew Schorr:
Melanoma can be found anywhere in the body and is often more aggressive than other types of skin cancer. Coming up, Dr. Susana Ortiz from UCSF Medical Center in San Francisco will discuss clinical trials that study genes to tailor treatment for melanoma and other advances being made in melanoma treatment. It's all next on Patient Power.

Hello and welcome to Patient Power sponsored by UCSF Medical Center. I'm Andrew Schorr.

When you think about skin cancer, and skin cancer is quite common, there are several types. The scariest of all, quite frankly, is melanoma because melanoma can spread through the lymph system to many places in the body, and unfortunately when it spreads then it can be difficult to treat and can lead to death. So obviously you want to be avoiding melanoma if you can, catching it early and having it surgically removed.

But the other part that we're learning now is there are different subtypes of melanoma, and fortunately there are medications being developed to target different subtypes and have more effective treatment. So that's good news if melanoma has advanced.

Explaining all that to us is a melanoma specialist from one of the nation's leading research centers, of course, UCSF. That's Dr. Susana Ortiz, a dermatologist. She's an M.D., Ph.D. there. Dr. Ortiz, just to review, what is melanoma exactly?

Dr. Ortiz:
Melanoma is, as you mentioned before, the deadliest type of skin cancer and arises from transformed melanocytes. These are long-lived pigment-producing cells that reside within the skin. Melanocytes, as you mentioned before, are around the entire body, and melanoma could get started anywhere in the body.

Andrew Schorr:
I understand sometimes it will show up as a mole or a spot, but it can be of unusual shape, have different colors. And while we think of it often in people who are fair skinned, red haired, with freckles, etc., it could be anybody, right?

Dr. Ortiz:
Melanoma can arise any place in the body. The progenitors arise from the neural crest, which is a part, a very important part during embryonic development, and migrate into the epidermis all over the body, not only the skin but also mucosal sites, for example oral mucosa or ob-gyn-related mucosal areas. Also for example the retina, this is the pigment that we have on the posterior aspect of our eyes.

Andrew Schorr:
Wow. Well, of course, at least as far as the skin that many of us can look at ourselves, it's so important, I know, for people to get a check with a dermatologist pretty regularly as you get older because obviously you want to eradicate this, treat this, as early as possible. And in melanoma that's particularly important, isn't it, Doctor, that if it can be just one little spot that you can remove surgically and it hasn't spread deeper, that's a good thing.

Dr. Ortiz:
Yes. I totally agree with you. It is very important that everybody goes to a dermatologist at least once a year. We are very lucky in the sense that melanoma is--evolves on the skin. We are going to be able to see it. We have in the clinic very important tools, not only our experienced eyes. We have also special lights called dermatoscopes that allow us to see the pigmentary pattern of moles that are evolving to what we call a dysplastic nevus and then what would be the beginning of a melanoma. By going to a the dermatologist regularly as you would go to the dentist or to the ophthalmologist, melanomas can be seen and discovered and treated earlier.

Andrew Schorr:
So important. Now, unfortunately, it may not be observed. Someone may not have gotten a checkup, it just wasn't caught, it was in one of those unusual places, and now it's spread. And I mentioned about the cells getting in the lymph system and going somewhere else. Where might they go? I think of the liver. Are there other places as well?

Dr. Ortiz:
Yes. Liver is a common organ that is a target of melanoma cells. Also brain, lungs, a GI tract. To be honest, once it's in the lymph system melanoma cells could go anywhere.

Andrew Schorr:
All right. And then it's more difficult. Then we start to talk about systemic therapy. So you've had different powerful drugs over the years that try to fire big guns, if you will, at the melanoma cells wherever they've gone, and I know it's been difficult. So where are we now with what you'd call targeted therapies and also understanding subtypes, genetic subtypes of melanoma, and how do you handle that at UCSF?

Dr. Ortiz:
Well, it's very important that we understand nowadays that there are different kinds of melanoma. As you mentioned before, there are subtypes. These subtypes are defined based on the status of key melanoma genes and pathways or their combination. To explain this better, each subtype is defined by one key oncogene. An oncogene is like a driver that would tell the cell to divide with no restriction. How we handle these at UCSF, the first thing we do is to try to analyze every melanoma by a genetic analysis. So we do what we call sequencing. We try to find, first of all, which is the oncogene driving the melanoma.

Genetic Mutations

Andrew Schorr:
What are some of the names of these, by the way. People may have heard of it. What are some of the names of these driver genes in melanoma?

Dr. Ortiz:
Oh, for example, BRAF, cKIT, NRAS, CDKN2A. Also, as we stride towards the genetic discovery of these mutations we finally have realized that melanoma has shared oncogenes with other cancers as well. So we are not alone. We have a lot of background knowledge from other cancers that also share these mutations and these oncogenes.

Andrew Schorr:
All right. Does that mean then that you're developing drugs or there may even be existing drugs that will work against that genetic mutation?

Dr. Ortiz:
Yes, exactly. That's what I want to mention. There are many drugs in the market that are working for other types of cancers that are currently also used in melanoma.

Andrew Schorr:
All right. So the way to think of it then, and the way you think of it at UCSF is, yes, it's a melanoma, but we want to understand its genetic subtype. Do we have a medicine that's on the market that we know works against that genetic oncogene, if you will, that cancer driving mutation? Or is there one we have in clinical trials, and can that give us more effective therapy for that patient? Did I get it right?

Dr. Ortiz:
Yes, exactly.

Andrew Schorr:
All right. Now, so when someone comes to UCSF or other major centers now where they're studying melanoma is this typically what's happening now, there's this genetic sequencing that's going on to see what is their subtype?

Dr. Ortiz:

Yes. I mean, not every program has the capability to sequence every single melanoma because we are in a moment where obviously not all the insurances are going to be able to pay for these costs and not all the programs are going to have the economical power to afford all these costs, so it's not done all over, in every center in the United States and certainly not in every center in the rest of the world. All the centers are riding towards that. We are all trying to get mutation analysis right.

What we do at UCSF is we try to sequence every single melanoma. And when I say we try to is that sometimes we might sequence but not find the mutation or oncogene. But what we currently do is if a patient comes to us, the first thing we get biopsy material that is sent to pathology to first get how deep, how bad is this melanoma. Second, the DNA of this material is extracted and sent to our labs where we run a panel with the most common mutated oncogenes in melanoma. If using this panel we don't get to find a mutation we have other tools in the lab that we use in order to discover the mutation. These are the very first steps.

And then once we know the mutation we have a multidisciplinary meeting with our oncologists and pathologists and decide, first of all, what kind of surgery needs the patient and in which trial the patient belongs given the mutation that has been discovered.

Andrew Schorr:
I want to just make a couple of points for our listeners.

Dr. Ortiz:
Yes.

Research at UCSF

Andrew Schorr:
So, as you described, you're really on the leading edge of melanoma detective work, if you will, but also noting that with some of these oncogenes there are medicines that are aimed fairly effectively at them. And so if you're a patient you want that analysis to go on, and you want to have the targeted therapy. The buzzwords now are personalized medicine. Sometimes it's called precision medicine, so you want that.

Now, let's take that a step further, Doctor. In research at UCSF you take an approach and you use medicines and there are different ways you analyze how are you doing. Is it effective? Is it killing the cancer? Is it shrinking the tumors? Where are we headed in trying to follow the patient on their journey to make sure that you can do course corrections, if you will, make changes if you see that you may be killing some of the cancer cells but not all and you want to do better?

Dr. Ortiz:
Okay. So in research what we do is we follow very carefully the evolution of the patient and the patient tumors. As I want to make clear, when melanoma spreads

usually it doesn't spread to one site. It might be spread in different sites of the body. During the therapy we monitor via imaging first, how the metastases are evolving and how the metastases are responding to therapy. Then when a patient is responding obviously the patient continues to be in the trial. When we see that the metastases are not responding research-wise we analyze this material.

And I want to explain to our patients something very important. There are cellular events that occur very rapidly, very rapidly after therapy, okay? These are called phosphorylation events. These are events that occur in the cell, okay? These events are going to tell us which drug to use or how at the very first moment the cell is responding to therapy. But then there are events that occur later in the cell, and this is called expression, protein expression, and these events are going to institute or are going to determine, better said, if the tumor will respond to therapy or not.

So at the UCSF we analyze the proximal events and we analyze the protein expression events that are going to determine if the patient responds or not. These analyses are giving us insight towards what's going on in a metastasis when it stops responding to a given inhibitor.

Andrew Schorr:
Right. I think that's so important for patients to understand. So based on the initial analysis there will be a treatment plan, but then you have to monitor that treatment plan, and here in a very scientific way, to see how is the plan doing because the cells are sending messages, in a way, that can be observed and adjustments can be made. And the goal of course is to keep refining therapy so that it continues to be on target for that patient, correct?

Dr. Ortiz:
Correct.

Andrew Schorr:
All right. Well, it's a very exciting area. So let's talk about melanoma. It's been so hard when it spreads. Are you encouraged with these experimental medicines you're using, with the subtypes, with new uses for medicines you have? Are you encouraged? You see patients every day.

Dr. Ortiz:
Yes. Yes, I am. We are very encouraged. I think the treatment for melanoma is evolving in a very positive way. We are better off today as we were 10 years ago, and we see publications constantly where we know more and more about the information and the pathways that melanoma cells are using to divide and to spread.

Clinical Trials

Andrew Schorr:
Well, what I would say to our listeners is if you were diagnosed with melanoma this is--all cancers are serious. This is a major league cancer, if you will. Certainly if there's a concern that it can't all be eradicated with very straightforward surgery, where there's a concern that it's spread in your body, then that's where you want to get to a research center such as UCSF where you can hear from Dr. Ortiz the level of study that's going on, the targeting that's going on.

And also the important message here is clinical trials. So if you're diagnosed with something where it's evolving, clinical trials--and it did for me, with my leukemia--may give you the opportunity, the access to, if you will, tomorrow's medicine today. We don't always know, but it's something certainly to discuss.

And Doctor, am I right that if someone is on a clinical trial and you find that that approach is not working for them you may well have another clinical trial that they could switch to?

Dr. Ortiz:
Yes, certainly. This is happening every day in our clinic.

Andrew Schorr:
All right.

Dr. Ortiz:
Some clinical trials are more permissive than others, but nowadays, especially in melanoma, clinical trials are being very flexible in order to get the patient the best therapy that the patient deserves.

Andrew Schorr:
The other point I'd make for our listeners is with melanoma it's one of those illnesses where you don't--I would say I you don't want to see a generalist, you want to see a specialist, and that is what Dr. Ortiz and her team--that's what they do at UCSF is you want to have--and you talked about this multidisciplinary team. So they're all focused with an understanding on melanoma pathology. You're in dermatology. I'm sure you have other surgeons that get involved and other radiation specialists as well all together, and you discuss the cases together to come up with the best recommendation, right?

Dr. Ortiz:
Yes. This is a very important point that you are making. It is not only a multidisciplinary team of melanoma. It's that in these sessions we also see other oncologists from other cancers, like, for example, breast cancer, or leukemia, as you have experienced, and since, as I mentioned, cancers share mutations and oncogenes and pathways we get information from other specialists as well in terms of which therapy to use or which trial to put a patient on.

Andrew Schorr:
Right. That's a very good point. As a matter of fact the drug that I was--one of the drugs that I was treated with for leukemia had been approved for lymphoma, and I was part of the information gathering, if you will, of would it work for a particular leukemia. But they knew there was a similarity, and by being in a clinical trial it proved it, so that certainly can be true in melanoma.

Dr. Susana Ortiz at UCSF, I want to thank you for being with us, helping us with a window into where melanoma treatment and research is headed. And for our patients who are listening, again my recommendation, you want to connect with a specialist such as Dr. Ortiz and a team that works with her, not just in melanoma but bringing that knowledge from other cancers as well so that you get the treatment that's best for you.

And for all of us, I know, Doctor, I'm going to my dermatologist every year religiously so hopefully I never get to the point of needing these therapies and that if something is spotted it can be dealt with at the earliest stage. That's the best medicine, right?

Dr. Ortiz:
Yes, that is in fact.

Andrew Schorr:
Okay. Thank you so much for being with us. This is what we do on Patient Power time after time is connect you with leading experts from UCSF Medical Center, and you could hear the level of science that's going on there, and you want that benefit for you.

I'm Andrew Schorr. Thanks to joining us. Remember, knowledge can be the best medicine of all.