



Melanoma Updates 2021

Adjuvant Treatment Options for Melanoma

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Dr. Roman Groisberg: I'm Dr. Roman Groisberg from the Rutgers Cancer Institute of New Jersey. I'm a medical oncologist in the department of melanoma and sarcoma, medical oncology, and I specialize in treating melanomas. So today I'm going to talk to you about two very important topics in the management of melanoma. One of them is something called adjuvant therapy and this is another fancy speak for just saying this is treatment in addition to surgery for lower stage disease. And the way I want to sort of approach this is by having you think about melanoma as this disease who is risk of upcoming back or doing something bad to you as increasing with increased stage. And most people are familiar with cancers that are stage four or stage three, or stage two or stage one, right. Where stage four disease is kind of usually the very worst where the disease has metastasized or spread to other places in the body.

Whereas something, stage one in melanoma is like a very, very small thing that's just cut out. And usually, you don't hear from again. And Stage two and three are sort of in between where stage two are basically melanomas that are just a little bit on the bigger side more deeper. In stage three disease usually involves melanoma that has spread from the primary site on the skin, into a lymph node that's kind of regional to it. So, it's kind of on its way, traveling. There are some exceptions to this, but we'll kind of keep it at that basically. And what we know is that the higher the stage, one, two, three, the more likely the melanoma is to come back again and to be heard from. And we actually subdivide this into A, B, and C as well. And just to kind of give you a little bit of a frame of reference stage one melanomas are mostly cured by small procedures, either at the dermatologist or with a melanoma surgeon.

And that's pretty much the end of that. Most stage two melanomas do very well with surgery as well, and we kind of leave them alone. But it's really the stage three melanomas, the ones that have left that primary site and moved along on their way to escape, that are the ones we worry about the most. Because depending on how advanced that is, how far it's moved along, how many lymph nodes are involved, those



sorts of things, the higher, the chance that the melanoma will come back. And so historically we really didn't have anything to help that along because we didn't really have any good therapies. So, we just did the surgery and then we hoped and prayed. Well thankfully times have changed in melanoma and we have a quite a collection of very effective therapies now that are approved and highly effective for preventing the relapse or the disease coming back.

And so, I'm just going to spend a little bit of time talking about these, and because there's really two classes of drugs that are approved in this setting to prevent disease from coming back. One is the immunotherapies, which I'm sure you hear about other parts of this program and the other one is called targeted therapy which you probably also will hear about in this program. And so as far as immunotherapies go, there are currently three drugs that are approved and, on the market, one is an older drug called ipilumab. It was the first drug to be approved for this adjuvant setting meaning after surgery. And it had fairly modest results and quite a high rate of toxicity. And so, I mentioned this really now is a historical reference more than anything else because in sort of the modern era in 2021, while it's not impossible to use that drug, but it is not common. And the other immunotherapies are two drugs. One is called Nivolumab and the other one is called pembrolizumab.

You may have seen commercials for these on television but they are what's called anti PD1 checkpoint inhibitors, but basically what they do is they allow your immune system to see the tumor or see any floating melanoma cells that have left the station and shows your immune system how to kill them. Right. And hopefully the idea is to kill every last floating melanoma cell that has left the station that wasn't removed by the surgeons and these drugs have two advantages, one is that they are for the most part, very well tolerated and treatment is usually prescribed for a year. And depending on which drug you choose, you may be coming back for treatment every two, three, four, even six weeks, depending on which drug and which schedule you choose. But therapy is given for a year. And most patients do very, very well with that. And they really reduce the risk of this melanoma coming back by a fairly sizable, absolute percentage.

So, you can sort of, and I'm going to kind of generalize a little bit with these numbers, but you can sort of imagine a patient whose risk after surgery of a melanoma coming back is 40% based on their stage. Well, by doing this additional therapy, you're reducing that chance. And now it's only maybe a 20 or 30%. So, it's actually quite meaningful in absolute terms. And so that's kind of the first option for adjuvant therapy. The other option is this targeted therapy is and they are available to only patients who have what's called a B RAF mutation, B R A F. Which is about 50 or 60% of melanomas. And these drugs have a couple of advantages. One is that they're oral. So, it's sometimes



more convenient. The other nice thing about them is that for the most part if somebody develops a side effect of the drugs, actually the side effects go away very quickly.

As soon as you stop the drug, they are I'm going to kind of in quotes, say equivalent to the immunotherapies. And I say that because the individual clinical trials that showed these drugs to be effective kind of numerically, they are very similar which is kind of not to say that these drugs have ever been compared to each other, because they haven't. Which kind of makes it a little bit of a discussion with your medical oncologist on which to use, considering that there is no actual data to suggest that one is better than the other. So, a lot of it comes down to personal preference. That, and there's the presence of this B RAF mutation.