



Patient Education for Melanoma Skin Cancer

Neoadjuvant Therapy in Melanoma

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TRANSCRIPT

So, what I'm going to suggest is, the better way to do this when it's possible is to flip the script, turn things around: give drugs first, operate second. When the tumor is still there, before surgery removes it, give the treatment. This is called neoadjuvant therapy. And here's why we do it.

There are a lot of potential advantages of what we call neoadjuvant therapy. It's a long list, but I'm going to focus on two of them. When the tumor is still there on the day we start treatment, we have the ability to assess the response of that treatment. We can see if the tumor is growing or shrinking. If we wait and do surgery first and give drug treatment after for a year, we don't have a single day where we know whether that treatment was working or not. We don't know if the patient was already cured. We don't if the treatment was a complete failure. We only know they're coming back to the clinic and getting treatment.

Another benefit — it's not as big of a benefit, it's kind of the booby prize — is there are times we're giving these drugs and they're totally failures, not working at all, and the patient is getting surgery and drug treatment and neither of them is helping. If we use the drugs first and they are clearly not working, we may be able to avoid surgery, switch to a different treatment, and get just as good an outcome with a lot fewer side effects.

So, why hasn't everybody been doing this neoadjuvant therapy all along? Well, there were a lot of concerns, a lot of worries that maybe there would be problems if we did this. And those problems were progression and enlargement of the tumor, leading the tumors that we can take out today to be unresectable a month or two from now. Turns out, that concern was over-emphasized; it doesn't turn out to be that big of a concern.

But what does turn out to be a big concern is that side effects of the treatment could come in and delay or even prevent the surgery. So, this isn't for everybody, and it always has to be done very carefully. But if we do this, then we have a huge advantage because the tumor is there, the treatment has been given, and at the time of surgery, we can assess exactly how well the treatment has worked.



Now, most of the time in the past, we assessed the treatment by doing a CAT scan: is it a little smaller, a little bigger? Is it exactly the same? And we thought, based on that, that we knew what was happening in the tumor. It turns out, we didn't know what we didn't know. We didn't even realize how little we understood about tumor response. Until you take that tumor out and look at it under the microscope, you don't realize just how much of a response you've had.

So, with neoadjuvant therapy, we're turning from an x-ray, a scan response to a microscope assessment of the response. Are the cancer cells actually dead? We call that the pathologic response. And this pathologic response has huge implications. Pathologic response rates make a big difference and are much more significant to predicting the long-term outcome than even any of the responses we were seeing with a CAT scan.

I want you to see what that actually means in this graph. These different lines represent all patients, they all got neoadjuvant immunotherapy anywhere from one to a few weeks, sometimes a couple of months, and then had surgery. And in every case, this tumor was looked at under the microscope, the pathologist made an assessment of the response. And that could be a pathologic complete response meant no living cancer. Just one or two doses of drugs, yet no living cancer. Still a big lump, but no living cancer.

Among those patients, 96% lived couple of years after their surgery. 96% of patients who started with a big tumor in their lymph nodes reduced to nothing, living in a couple of doses, and that's still affecting that patient positively for two years. But every last cancer cell didn't have to be removed. This line near pCR is 90% dead and this line in green is 50% to 90% dead. We now think that maybe the 50% to 90% isn't quite as good as it looked in this particular study. But all three of them look a lot better than the patients whose tumor continued to survive and lived through those doses of immune therapy without much effect at all.

So, you see the predictive power, I can give you just two or three doses of drugs and know what's going to happen for years ahead if I do surgery and remove the tumor and look under the microscope at what happened. But I can do more than that, more than just predict the future: I can change what I do for you.