



# **Melanoma Updates 2020**

## **Adjuvant Therapy of Melanoma**

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Dr. Sanjiv Agarwala: My name is Dr. Sanjiv Agarwala. I'm a professor of medicine and oncology at Temple University. And I'm going to talk to you today about Adjuvant therapy for melanoma. So I'll start by introducing the topic of what is adjuvant therapy. And then we'll talk about what the options are and how I approach this in the clinic. So adjuvant therapy, as you may know, is a treatment given post surgery. So the surgical treatment has been done. Hopefully the patient is cured, but we do know that in some instances, unfortunately, because the tumor, the melanoma removed was what we call high risk for recurrence. It may come back. So adjuvant therapy is given by a medical oncologist usually to try to lower that risk. And this involves the administration of drugs given over a period of time which have been shown in clinical trials to reduce that risk.

So, let's start by first defining what is high risk melanoma. This is done by surgical staging. So when a melanoma is diagnosed there's a certain step-by-step procedure that's followed, including identifying the need for what is called a lymph node mapping to find out if the melanoma has spread from the skin to a nearby lymph node. And if it has spread to that lymph node, which is determined, as I said, by surgical staging that is considered high risk, that's an example of high risk. So once a patient has been diagnosed with high risk melanoma, based upon that kind of a procedure, a decision is made whether to give Adjuvant therapy and if so what it should be. Mostly when a patient has involvement of lymph node nearby adjuvant therapy is administered. However, sometimes when there is a very little amount of melanoma in that lymph node, it's sometimes even just one cell, for example they're might be a discussion with the doctor regarding whether adjuvant therapy is worth it or not.



Having said that, once the decision to give adjuvant therapy has been made, then almost always there is a test performed, which may have already been done called a BRAF or BRAF mutation testing on the tumor. This is simply done to find out if the tumor has that mutation, which allows there to be another choice of what frequent to use. So once this testing is done, we would divide patients up into those who are B R A F or BRAF positive, or B R A F negative. Also known as BRAF. Wild-Type, let's start with if a patient is BRAF Wild-Type. If you are BRAF Wild Type and adjuvant therapy is recommended, then usually it is done with immunotherapy. And it is usually done with what's called a checkpoint inhibitor that affects the PD1 pathway. So they are called PD1 inhibitors, and there are two approved by the FDA pembrolizumab and nivolumab.

They're both very similar, they're quite safe and quite effective. There have been clinical trials, done with both agents that have shown they both work better than either not doing a treatment or doing something else. And I'm not going to talk about that something else because we no longer do those anymore. These treatments are given intravenously. These are immunotherapy antibodies. And as I said, they're very safe, but they need to be monitored by your doctor to make sure that things are going okay. And the treatments usually go for about a year. On the other hand, if there is a BRAF mutation present that you or the patient is BRAF positive, then there is another choice in the mix, which is agents that target the BRAF pathway, the FDA approved agents, in that setting are two oral drugs. Dabrafenib and trametinib, they inhibit the BRAF pathway together, and they are quite effective. And as I mentioned, they're pills, they're not given intravenously.

And that is also a choice and of course, the next logical question is if you'll BRAF positive, can I also get immunotherapy? And the answer is absolutely yes, the same anti PD1 agents that work in someone who does not have the mutation also work if you have the mutation equally well. So it really is a choice. And of course, then you'll ask which one should we choose? And the answer is, we don't know, it is a personal preference of between really, what is oral drugs pills versus intravenous treatment, which sounds like pills are a logical choice. But the pills are every day and more than once a day. Whereas the intravenous treatment can be once every three, four or even six weeks, depending upon the drug picked. And the toxicities or side effects are different as well. So this does take a, a good discussion with your doctor regarding what you know, the preferences might be. And it often was down to a personal preference.

Clinical trials are ongoing to find out which is better, but we don't know that yet. Right now we would say they're both equally effective. So it's good news for patients that we have effective Adjuvant therapies. I must say, in the past, we did not. And there's lots of



research ongoing to see if we can learn more about defining what is a high risk patient, who should get it, which treatment should be given, and so on. But right now that is the state of the art of this treatment. And more than likely you will have a detailed discussion with your healthcare team regarding what the correct options are. Thank you.