



Melanoma Updates 2021

Treatment Options for Metastatic Melanoma

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Dr. Douglas Johnson: So, hi, my name's Doug Johnson. I lead the melanoma program at Vanderbilt University Medical Center and Vanderbilt Cancer Center. And today I'll talk to you a little bit about how we treat melanoma when it's become metastatic or when the melanoma is spread to different organs. Now, this used to be a really grim situation, certainly still a very serious situation, or even 10 years ago, we really almost had no effective treatment options. Basically there was a few things we could occasionally try like chemotherapy or a really powerful immune drug called hydros interleukin two. But really those very rarely worked. And unfortunately, patients had an average survival of well under a year in most cases. So, things have changed quite a bit though in the last 10 years, which is really good news, certainly for our patients. And so, we actually have a wide variety of treatment options.

And so, I'll go through those just a little bit. So, there's really two major ways we treat melanoma. So, the first is with immune therapies. So immune therapies or treatments that they're given, like chemotherapies that are given through the vein as an infusion, and they stimulate the immune system to attack the cancer. And so, the hope is that the tumors we can see and any cells that might be floating around as well, that the immune system will be stimulated. And will target and hone in and destroy any of those cells wherever they may be. And so, there's a couple of different ways we do this. So, the first way is with a single drug. So, it can be two different drugs, but given one at a time, so one's called Opdivo or nivolumab and the other one's called Keytruda or pembrolizumab. And so those treatments, they're given every somewhere between two and six weeks, depending on the regimen.

But they're given again, like I said, I have through the vein and then a scan is done after about three months on treatment and to see whether somebody is responding to treatment. And so, with those drugs, they have a success rate of about 40 to 45%. So, in other words when, if you compare the scan before treatment versus the scan after treatment, you see a significant shrinkage in 40 to 45% of people. And the good news is



when those treatments work, they have oftentimes a long-term response. So, in other words people don't respond just for a few weeks or a few months, but patients in many cases respond for years and years, maybe even indefinitely. And so actually when those treatments are given about 40% of people are alive and well, five years later, so many of these people are probably cured with treatment about one out of five people will have a more significant immune system side effect, which we'll talk about another video.

If you're interested in that, feel free to check out that video. But in general, these treatments are very well tolerated. Now we can also use immune therapy drugs in combination. So, we're often using these treatments, the drug Opdivo or nivolumab is combined, and at the same time with another immunotherapy drug called ipilimumab or Yurvoy. And so, these treatments are given basically one after another. They're given every three weeks for four treatments. So, you basically get the treatment at week zero week three, week six, week nine. And then the scans gotten in week 12 to see whether somebody is responding to treatment. And these two drugs together actually increase the odds of success. So, like I said, with a single drug, you only have about, you have about a 40 to 45% success rate with the two drugs together. You have somewhere between a 55 and 60% success rate. And again, like I said, I define success by a dramatic tumor shrinkage of the scan.

And like I said, many patients who responded to have these very long-lasting responses, which may even amount to a cure. And with a combination about 50% of people are alive and well, five years later after getting this treatment. So again, going from a situation where you have, you know, almost a 0%, five-year survival now to about 50% is quite an improvement. Not where we want to be, but it's certainly an improvement over historical numbers. The other treatment that we sometimes will get, well before I moved to the other treatment class, sometimes we give those two treatments in sequence. So sometimes we might start with a single drug and then if the single drug doesn't work, then we add the second drug on, the Yurvoy. And so you can give, you know, start with a single drug and then move to the combination.

And you can oftentimes get just as much mileage with that kind of approach as well. So that's another option for many people. Now, the other way we often treat patients with advanced melanoma is with targeted therapy and so targeted therapies an options for the 50%, about half of melanoma patients have a mutation in a gene called B RAF. Now, that sounds like a bunch of Greek there. So I'll try to break that down a little bit. So every cancer is more or less a genetic disease. The cancer cells have mutations, so they're not assuming mutations in the rest of you. So it's not necessarily something that you got from your parents or passed down, but the cancer cells themselves have a particular mutation in this gene called B RAF. And so this mutation kind of is you can think of it kind of like as an engine that causes the cancer cell to grow and divide.



And so, if you can block that engine or turn it off with some medications, you can cause the cancer to shrink and hopefully go away. And so about, like I said, about half of melanomas have this B RAs mutation. And so we can give a couple of different pills. There's three different FDA approved combinations. We can give basically a pill to block the B RAF gene and the pill to block the next link of the chain after that. And those pills can be quite effective. In fact, when they're given to people, people often will feel better and have improvement pain and things like that, any kind of symptoms that the cancer's causing. Even after a few hours, it's quite remarkable how fast these treatments work. They work on average for about a year to a year and a half before the cancer sort of figures out a way around them in most patients. And so some people do have long-term responses to treatment, but unfortunately most of the time, they work in almost everybody, but then the cancer figures out a way around them eventually.

But they can certainly be very powerful treatments as well. So those are the current standard of care for the first line treatment of people with melanoma. And it's also you know, to take another step back when people have that B RAF mutation, you can certainly start with one, one treatment and then move to the other. So you could start with immune therapy and then go to the targeted therapy to start with the targeted therapy, go to the new therapy. We honestly don't know what's the best order. There's some clinical trials ongoing to study that right now. There's a number of other treatments, hopefully in development. So hopefully a future video a few years from now, we'll have a number of other treatments to tell you about as well, but those are currently the main treatment options that we have for a metastatic melanoma. So thanks for your time.