



Melanoma Updates 2021

The Role of Neoadjuvant Treatment in Melanoma Care

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Dr. Meredith McKean: Neoadjuvant treatment has been an area of great interest in melanoma really over the last five years or so. Neoadjuvant treatment, what this means is that this is using medications before patients head to surgery. This has been a successful approach and tumors like breast cancer and rectal cancer. And this has really helped push the envelope in melanoma. So now that we've seen success in both the metastatic and adjuvant setting with immune therapy and targeted therapy, there's been a lot of interest to try to move this even earlier and to say for patients with locally advanced stage three or stage four melanoma would applying immune therapy or targeted therapy at that time point before going to surgery, could this be helpful and how might this be helpful? Well, we've seen in other tumor types that this can make the tumors potentially smaller and therefore easier for surgical resection.

And we've also seen that this can be helpful to understand the biology of that patient's tumor and understand how you know, how is that tumor responding to different types of treatment? What might be some of the potential disadvantages and why it's still being explored in research? Well, this is because we know that patients heading to surgery that we know the outcomes there. We can then administer adjuvant treatment, but what's unknown is, is there a risk of patients progressing on systemic therapy prior to going to surgery? And so that's why it's been an exciting area of research, but it's still under clinical trial investigation trying to determine is this beneficial for patients with melanoma. Now there's been a number of different clinical trials using targeted therapy. And so, this is looking at targeting B RAF, MEK inhibition, and also in a different immune therapy clinical trial.

There's been a number of different combinations evaluated with immune therapy, looking at both the combination of anti PD1 and anti CTLA4 anti PD1 just by itself, or looking at novel combinations that have yet to be approved in the metastatic setting.



What we've learned from these early clinical trials has been overall exciting. So what we've seen is that patients that undergo treatment with either targeted therapy or immune therapy and the clinical trials have investigated different periods of time, whether that is two treatments or 12 weeks of treatment, and then going to surgery, what the studies have demonstrated is that the response when that tumor has been removed whether that's the primary tumor lymph nodes, when that disease has been removed and then evaluated by a pathologist, looking at that response to treatment can be predictive of a patient's overall long-term outcome.

And so, it looks like the amount of tumor death in that resected specimen correlates with relapse free survival and overall survival. This has been particularly the case in immune therapy. There is a recent study out from the collaborative group, looking at Neoadjuvant studies, demonstrating that patients that had a path CR meaning all of the tumor was gone at the time that that tumor was removed, that patients at two years, 96% of patients remained without any relapse of melanoma. This was still relatively true for targeted therapy, but that percentage was not as high. So, at this point it's still under investigation, but definitely a very exciting opportunity in melanoma. It's not uncommon for us to see patients that are considered stage three, but have a number of tumors and wanting to be able to get medication started right away, as opposed to waiting for that patient to go through surgery and then start adjuvant therapy.

Many of these trials also include a period of adjuvant therapy after surgery to correlate with what we know has been successful in helping relapse free survival for immune therapy, overall survival with targeted therapy in the stage three setting, meaning that on these clinical trials, patients are treated with a time period of medication before going to surgery, and then additional medication to complete a full year of treatment. The timing is just getting some of that treatment prior to going through surgery. So, I think this is a very exciting area of research in melanoma. I think this is an opportunity for patients for us to be able to receive treatment earlier. And it's also an opportunity for us to get an early look by evaluating newer immune therapies, newer treatments in melanoma, and being able to see very early on what's happening with the tumor. So, I think there's definitely more to come in an exciting area of research.