Melanoma Updates 2020

Combination Immunotherapy vs. Monotherapy for Metastatic Melanoma

Dr. Meredith McKean, M.D., MPH

Medical Oncologist, Investigator, Melanoma Research Program, Sarah Cannon Research Institute at Tennessee Oncology

Dr. Meredith McKean: Hi. So I'm Meredith McKean. I'm a clinical investigator in our melanoma and skin cancer research program here at Sarah Cannon based in Nashville. I'm also an investigator in our drug development unit. So I'll be discussing a few topics today. When choosing initial therapy for metastatic melanoma, there's several different options. When it comes to immune therapy, which is the only therapy available for patients with BRAF wild type melanoma there are several different options, but one way to look at this conversation is doing combination immune therapy, in general, that means with ipilimumab and nivolumab versus monotherapy with anti PD1, which is nivolumab or pembrolizumab. We have data now to demonstrate that doing combination therapy, doing both anti CTLA 4 and anti PD1. So that means both ipilimumab and nivolumab together does prolong patient's life compared to one by itself, you know, Opdivo or pembrolizumab.

So, we know it does provide a survival benefit. The challenge is we also know that it increases the number of side effects that patients have. And so whether or not to proceed with combination versus single agent is a discussion to have with your oncologist about the risk factors, the features of your melanoma that may put you at a higher risk for early progression. You know, are you having symptoms from your disease? Do you have any autoimmune conditions that might be aggravated by doing a combination approach? So there's no right or wrong answer, but I think there's a lot of good things to consider. With combination therapy, we know that the sequence is to give two drugs. Opdivo and Yervoy, also known as ipilimumab and nivolumab to give both drugs for four doses and then followed by a maintenance dose of just nivolumab. We know with increasing doses of both given together, there are more toxicities.

So, and also with your oncologist, you should generally be seen back by a provider before your next dose. So you're able to touch base and make sure are you having any side effects that need to be mitigated any reason why your treatment would be held? So that may mean shortness of breath or cough, rash, diarrhea, or irritated liver. So elevated LFTs, as we would say. Doing combination therapy is considered more aggressive, but like I said, we do know that the response rates are higher and patients in general live longer, have a higher likelihood of survival with doing combination. Moving forward with just single agent anti PD1, so Keytruda, which is pembrolizumab or Opdivo or nivolumab. We know that, you know, I say to patients, that's definitely the workhorse of the combination. We know that that agent by itself has the higher response rate versus just doing the Yervoy by itself.

So that's also a good approach. I would say that's an approach taken more likely for patients that have a less disease burden. So fewer sites of disease patients that are having any symptoms maybe patients that have a normal LDH versus an elevated LDH and definitely patients that have any concern for toxicity. So if this is a history of autoimmune conditions, such as psoriatic arthritis, rheumatoid arthritis, Crones, ulcerative colitis, and we don't have any other treatment options for patients that are BRAF wild type, then it would probably be most cautious to start with that single agent treatment by itself. Of course there's no hard and fast guidelines. And so I always would encourage any patients to have that discussion with their providers. Now I oftentimes will see patients that say, you know, I've read about that Yervoy or ipilimumab sounds really tough. I don't want to take it. Well, we still know that even though this medication has a number of side effects, the early studies by itself showed that it did help patients live longer.

And so, we do know that there's some benefit, it works differently than nivolumab and pembrolizumab. And so I wouldn't necessarily be scared of the medication. It can be a really helpful medication, but a worthwhile consideration to discuss with your doctor. The other situation to consider is for patients that do start with either nivolumab or pembrolizumab by itself, there's been more data out just even in the last year saying, well, for those patients, if you then add on the Yervoy, what are the responses? And we have a lot more information and better information, how to give that medication. And so all is not lost. If you start off your treatment with just one medication. There's good data to show that if you add the Yervoy to anti PD1 that response rates are about 30%. So we're getting more and better information about how can we maximize these medications. And even if you decide not to do both of them upfront, you can still add that in second line, but ultimately I think this is a good conversation to have with your oncologist. And they should be able to personalize that discussion and say, you know,

based on your disease, based on any other medical conditions you have, here's our suggestion and recommendation.