Promising News in Melanoma From ASCO 2017

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Andrew Schorr:
Hello and welcome to Patient Power. I'm Andrew Schorr on location in Chicago at the big ASCO, or American Society of Clinical Oncology, meeting, and one of the cancers that they discuss here of course is melanoma. I'm with a leading specialist from Massachusetts General Cancer Center, right?

Dr. Sullivan:
That's right. Massachusetts General Hospital Cancer Center.

Andrew Schorr:
Right. Thank you for being with us. So people with advanced melanoma, terrifying diagnosis as this has spread, and they worry about their future. Certainly there's been a lot of progress. Tell us from here what you know now and give hope to people with that illness.

Dr. Sullivan:
Absolutely. So I think the most important thing that's happened over the last decade is the identification of drugs which target specific mutations like BRAF mutations, which about half the patients with metastatic melanoma will have and identifying strategies to treat those patients with effective therapies, and then the development of really effective both single agent and combination immune therapies which really aim to target the patient's body in a way to inspire their body to kill their cancer.

Those have been the two major revolutions in the treatment of melanoma. They've been revolutions in the treatment of a number of different types of cancers. And at this meeting, we saw a few really important updates for both of those types of therapies. So in one presentation by Dr. Jeffrey Webber from NYU, he presented the long-term follow-up of the first Phase II—Phase I, Phase II trial of a combination of a BRAF inhibitor and a MEK inhibitor which blocks a protein downstream of BRAF.

That originally showed that you could give two drugs, that it was safe, that it was effective, and now we see this long-term follow-up of patients. About 10 to 15 percent of patients never needed another drug with five years of follow-up. Now, that's not everybody, but that's amazing to be one of those 10 or 15 percent of patients that enrolled on a clinical trial six or seven years ago and remain alive on effective therapy without disease progression.

And I think that was really an amazing and astounding piece of data. It wasn't a large trial. There are larger trials that are kind of creeping their way to the five-year mark as well, and we expect that that will be corroborated in these larger randomized trials that led to the approval of those drugs for patient with BRAF-mutant melanoma. But really a hopeful message is targeted therapy can—I don't know if they can cure patients, but it certainly can control disease for four, five, six, seven years, and that's pretty amazing and certainly hopeful.

The other really exciting data that was presented with regards to immune therapy is a PD-1 blocking drug. PD-1 is a protein that is on immune cells and interacts with a protein in tumor and tissue around tumor. And when that interaction happens, the T cell just can't get into the tumor, and the T cells are the things that our body uses to kill our cancer.

Andrew Schorr:
We have to wake them up.

Dr. Sullivan:
We have to wake them up, and more importantly we have to break down the walls or fill the motor whatever, analogy works, essentially get those T cells that army that's at the gates into the tumor and kill the cells.

There's a drug called pembrolizumab (Keytruda). There's a drug called nivolumab (Opdivo). Both of these drugs are approved for patients of melanoma, and we saw the follow-up data on a randomized control trial, front-line therapy of pembrolizumab versus a drug called ipilimumab (Yervoy), which is actually the first drug to show improvement in overall survival for patients with metastatic melanoma.

And in this study, we already knew that pembrolizumab was better from the last time this data was looked at, but now we're seeing three-, four-year data again, 30, 40 percent of patients alive without disease progression with these drugs, which is just astounding.

And perhaps more importantly what we learned is it's okay to stop those drugs. What every patient wants is to be cured, but what every patient also wants is to live their life and not have to be sort of lassoed to my clinic or my colleagues' clinics, coming back every two or three weeks or even four or five weeks. They'd prefer to come in every six months and get a scan that says everything's cool, go back and live your life again.

And what we're seeing is that it seems to be safe to stop these drugs if you've had a great response to therapy. And at least with about a year's worth of follow-up after stopping, the great majority of patients maintain their responses and do not have their disease grow again. And if that continues to happen, I mean that's practice-changing. That allows us to sit with our patients and say, you know, I know you've been on this for a year, and I know it's scary to think about coming off of this therapy. You're having a great response, and I now have data to say there's a pretty good chance your disease isn't coming back if we stop. And if it does, we're just going to get you started back up again. And so I think that was probably the most hopeful thing that I saw this whole—there was a great session yesterday at the oral abstract session, and I think that was the most hopeful thing I saw.

The other thing that we saw that really I think will help us do define how we use all these drugs either together or in sequence, there's been a lot of developments with combining PD-1 drugs and ipilimumab. And there's combination nivolumab and ipilimumab, and it leads to responses in the great majority of patients, but it's highly toxic. And really what we need to do is figure out who should we expose people to that toxicity and who don't we need to expose people to that toxicity, because again our patients want to be alive, they want to have complete responses if possible, and they want to enjoy their lives and not have a lot of toxicity.

And so there were two really important trials looking at patients with brain metastases. I mean, a patient gets diagnosed with melanoma, and it's crushing. A patient then has a brain MRI that shows brain metastases, and it's almost like we sort of sucked out all the hope out of them when we tell the results. And now there's nivolumab plus ipilimumab in patients with active brain metastases, a population that's almost always been excluded from our clinical trials showing not just activity but amazing activity, 50, 60 percent response rates with these combinations in the front-line setting showing remarkable benefit in a population that never had remarkable benefit before.

And, importantly, one of those trials is randomized to a single agent of nivolumab, and the combination looked better. And I think now we have a strategy to approach to say, you know what, we do know how to use this drug and in whom. At least in patients with brain metastases, we should really strongly consider using this combination. And, truthfully, I've never been a great proponent of giving the combination to everyon, but now I'm probably going to be a proponent of giving the combination to patients with brain metastases, because the data was that good.

Andrew Schorr:
Wow. What a hopeful report. So I have a question, just two clarifications. At the beginning, you mentioned about the BRAF mutation, but you said it was not all the patients. So if somebody is watching this, they don't have BRAF, do you have strategies for them?

Dr. Sullivan:
Everything I said after BRAF…

Andrew Schorr:
Applies.

Dr. Sullivan:
…applies. All of the immunotherapy strategies apply to all patients with melanoma that arose on the skin and likely will also apply to patients who have melanoma that arises on their mucosal surfaces or their eye.

Andrew Schorr:
Okay. And where does testing come in so that the doctor and the patient know what are we dealing with in their case?

Dr. Sullivan:
Yeah. So it's been now routine. For every patient that comes in we do BRAF testing. There are a few other mutations, and we do some testing as well, and now most patients and actually most providers really want as much information as we can get that's potentially usable. So we send off a panel of 50, 60, 70, 80 genes looking for all kind of potential mutations that are actionable. The majority of these are BRAF, about half our patients will have that, occasionally find these other mutations that we can, if the immunotherapy doesn't work, have other potential options.

Andrew Schorr:
So it sounds to me for patients wherever they may be now is to first they and their doctor know what are we dealing with, and it sounds to me like there's a whole new area of medicine that's there to help them long term, even when it's spread to their brain.

Dr. Sullivan:
Exactly. And I think what's critical about this is sort of all these developments have happened when these drugs were already approved or just about to be approved. And I think it sort of speaks to the fact that if we can identify important questions that can be answered in a clinical trial that's still worth thinking about a clinical trial as your first option as a patient, because, you know, we're not going to give placebos studies where somebody gets the good stuff, and you don't get anything. We're way beyond that. We're forever randomizing patients. We're randomizing to something really pretty good against something that we hope is going to be better, and more and more we're trying to sort out who are the right patients to treat, when should we—when can we cut back on therapy and reduce side effects? How can we reduce side effects, potential other agents? There's just so much, so many important questions that we can now build, or ask through clinical trials and build upon all the wonderful work that's been happening over the last decade or more.

Andrew Schorr:
Wow. Thank you so much for being with us. What a great, great report. So I think people with even the most advanced melanoma, this is really very hopeful news and important to know what you're dealing with, have a specialist like this who can plug you into the latest science, whether it's all these approved therapies or, as he said, clinical trials.

On location in Chicago, I'm Andrew Schorr. Remember, knowledge can be the best medicine of all.