Transcript Details
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Melanoma Treatment Breakthroughs: Improving Long-Term Survival

Announcer:
You're listening to *Clinician's Roundtable* on ReachMD. On this episode, we'll hear about the latest advances in melanoma treatment from Dr. Vernon Sondak. He's the Chair of the Department of Cutaneous Oncology at the H. Lee Moffitt Cancer Center and Research Institute in Tampa, Florida, and he spoke on this topic at the 2025 American Academy of Dermatology Annual Meeting. Let's hear from Dr. Sondak now.

Dr. Sondak:
Melanoma treatment has evolved phenomenally in the last decade or decade and a half in ways that I never thought I would see in my lifetime. Now, when we see a patient who presents with brand new metastatic melanoma with no previous treatment and shows up with lung, liver, or whatever metastatic disease, we can legitimately tell them that they have about a 50 percent chance of still being around 10 years from now based on clinical study data going back more than a decade. Before that, that person had about a 25 percent chance of living one year compared to a 50 percent chance of living 10 years, so this was a dramatic change.

Naturally, when we saw this kind of progress with advanced metastatic disease, it was the inevitable next step to say, "Can we use these drugs earlier in the process and prevent metastatic disease from developing?" "Can we use adjuvant therapy and prevent the melanoma from coming back after surgery?" And we found that, yes, we could do that with much less toxicity than what we were used to with interferon, which we used to use in the '80s, '90s, and into the 21st century. Now we've gone the full circle and said, "Okay, we're going to use those drugs right after your surgery and prevent the melanoma from recurring if we can."

Once we were comfortable with that, people started to say, "What if we actually use the drugs before surgery?" We were surprised—shocked, really—to see that just using the drugs earlier made them more effective. The outcomes were far better when we did randomized trials comparing people who got some or all of their treatment before surgery, even if it was a much shorter duration of treatment than people who got a year of treatment after surgery.

Immunotherapy has advanced. We started with a single drug—the anti-CTLA-4 ipilimumab. Then came the anti-PD1 drugs. The ones we predominantly use for melanoma are pembrolizumab and nivolumab. And then, after a while, it was natural to combine the two IPI plus NIVO, a CTLA-4, and anti-PD1. More recently, another immunotherapy combination, nivolumab plus relatlimab—or NIVO-RELA, as we refer to it—is a LAG-3 inhibitor relatlimab combined with anti-PD1, and there are several of more studies underway with these LAG-3 inhibitors. The advantage of that particular combination seems to be, at least in metastatic disease, pretty close to similar activity to the IPI-NIVO combination without as much immune-related toxicity.

We're not even close to being done with looking into new options and alternatives. We're hoping to hear whether the FDA will approve an agent called RP1. This is a intralesional therapy—an oncolytic virus, a development of the T-VEC virus that's already FDA approved—but this is a step ahead and is designed to be given with anti-PD1 immunotherapy. It's intended to reactivate the immune system. So we're looking forward to that as a possibility.

It's an exciting time, but I think we constantly recognize that we've raised the bar so high that getting over it isn't easy anymore. When you had almost nothing that worked, it was really easy to immediately say, "Wow, this is great. It's twice as good as what we had." But when you've raised the bar, you're looking for much, much smaller increments of improvement. That's harder and takes longer than when you've just got an obvious breakthrough because you had nothing to start with. In a sense, our success has made things more difficult going forward, but that's a problem that we want to have.

Announcer:
That was Dr. Vernon Sondak discussing the latest advances in melanoma management. To access this and other episodes in our series, visit *Clinician's Roundtable* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!