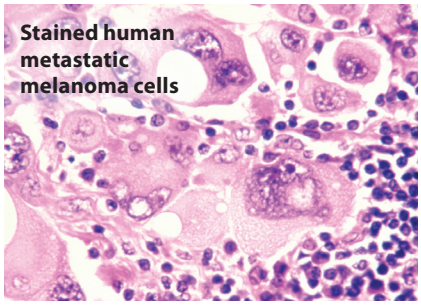
Stained human metastatic melanoma cells

New monoclonal antibody is a "source of hope" for patients with metastatic melanoma

Bette Weinstein Kaplan

Metastatic melanoma rarely comes up in discussions about cancer survivorship, and when it does, the context is usually negative. In fact, unresectable metastic melanoma has always been a dramatically frightening diagnosis. The situation has recently changed, however, thanks to two new drugs developed in collaboration with research oncologists at Memorial Sloan-Kettering Cancer Center in New York, New York. As one researcher, Jedd Wolchok, MD, PhD, said (oral communication, June 2011), "What we have now, at least for the first time in my memory, is sources of hope. We now have treatments that actually benefit people."

LIFE-PROLONGING DRUGS

The new medicines that have a real ability to prolong life for people with metastatic melanoma are ipilimumab (Yervoy), a monoclonal antibody, and vemurafenib, an experimental BRAF inhibitor that is taken orally. According to Paul Chapman, MD, one of the developers of vemurafenib, the actions and side effects of these drugs are different than those seen with standard chemotherapy agents.

Wolchok, a principal investigator of ipilimumab said, "There are some people who have had long-term responses lasting 4 or 5 years and more with ipilimumab. Now the conversations that we have with patients start with, 'There are things that we can offer you that actually do help.' We didn't have evidence of that before for any other treatments. What we stress now is that the clinical trials that we've spent so long working on have shown that there are several ways to treat melanoma that actually are providing benefits."

NO RIGHT AND WRONG ANSWERS

Do patients believe such encouraging news about a disease with such a deadly reputation? Wolchok answered, "They do. Because really, what's the alternative? What they read on the Web is usually pretty starkly negative. And what they hear from their friends is that chemo doesn't work for melanoma—which I think is an exaggeration because there are some people who [achieve] very meaningful benefits from standard chemotherapy. What I tell people is that there are really no right and wrong answers with melanoma." The difference now is that science is actually leading us toward treatments that prolong lives. For some people, it may be only a couple of months; however, Wolchok has patients who were facing very grim prognoses 5 years ago who are now alive and well. "The response can be quite variable from person to person," he explains.

The researchers are aware that the majority of people with melanoma are not going to be cured with just one medicine. Wolchok reported, "As we seek to benefit not 20% or 30% of patients but many more, ipilimumab is going to be combined with other medicines, such as the BRAF inhibitors like vemurafenib." BRAF inhibitors cause dramatic regressions in 50% to 60% of people with melanoma who have a BRAF mutation. However, the responses do not last more than several months for most people. Ipilimumab can produce long-term disease control; therefore, "combining ipilimumab and BRAF inhibitors is something that we are all very eager to do. And it cannot come soon enough," Wolchok said.

IS ADMINISTRATION DIFFICULT?

Wolchok was confident. "It's not a difficult drug to administer." A local oncologist can do it. It is an antibody, needs a 90-minute infusion, and does not require any premedications. But knowing how to manage the side effects that can occur requires a bit of education. "I think oncologists may need to rethink how they handle some symptoms that they believe they know how to handle: for example, diarrhea. Oncologists are very good at treating the diarrhea that occurs from chemotherapy, but the diarrhea that occurs with ipilumumab has to be handled in a completely different way," Wolchok explained. Ipilimumab-related diarrhea

should be treated like ulcerative colitis or Crohn disease, which is to prescribe corticosteroids.

When the FDA approved ipilimumab, a Risk Evaluation and Mitigation Strategy (REMS) program, which is sort of an educational tool kit for oncologists, was required.[1] Wolchok and his colleagues worked with the manufacturer, Bristol-Myers Squibb, to develop the book's treatment algorithms. The REMS delineates techniques for treating the side effects of ipilimumab and is written clearly, with flow charts and illustrations. According to Wolchok, "Any oncologist could master this drug; it's not difficult to master."

NURSES HAVE AN IMPORTANT ROLE

Nursing is critical for success with ipilimumab because the nurse has most of the primary contact with outpatients when they call from home about symptoms. The nurse does symptom triage, and those who have experience with ipilimumab are able to do this independently. "They know what the treatment algorithms are and they are able to formulate a plan," said Wolchok. "I think there's really quite a nice interplay between physician and nurse in this management plan."

RuthAnn Roman, RN, BSN, Clinical Research Nurse III in Melanoma/Sarcoma Oncology at Memorial Sloan-Kettering Cancer Center, agrees (oral communication, June 2011). "We work very diligently on educating the patient about the importance of reporting symptoms," she explained. Patient education is key in treating patients receiving ipilimumab. Nurses have to educate patients about how the drug works to help them understand why it is important to report symptoms quickly. If GI symptoms are reported early, we can treat the symptoms without medication to keep things calm and can continue to dose patients.

Although a lot of patients will end up on corticosteroids for the diarrhea regardless, sometimes things can be kept at bay for a little while by altering the patient's diet. Many patients feel that if they report symptoms, they are not going to get any more treatments. But if the symptoms escalate it becomes harder to treat them, and that could prevent patients from ever getting dosed again in their lifetime. If one dose is skipped, it is not the end of the world. There have been no correlations between having side effects and responding to treatment.

INFUSIONS ARE EDUCATIONAL OPPORTUNITIES

"Infusing ipilimumab is one of the easiest things you can do," said Roman. "It's giving straight drug." The infusion nurses have very few issues during that time except to reinforce to patients that they must report symptoms. Because this is a fully human antibody and there is a very low risk of allergic reactions, there is no need for supportive care while you're infusing. No premeds. No after monitoring. The drug does not have to go through a mediport; it is very easy to infuse. Nurses are going to be sitting with a patient who will tell them that she is not feeling better. Roman teaches nurses that their job is to reassure the patient and remind her that most patients respond late with ipilimumab. Teaching the patient the mechanism of action is very important. The drug has an indirect effect and that takes time. This is not chemotherapy.

Roman tells patients, "Forget everything you know about chemotherapy. It does not apply here. This is immunotherapy and it works differently. The drug is going to work on your T-cells, and your T-cells are going to work on the melanoma, and that takes time. It takes time for [your] immune system to learn the lesson."

She added, "I just want nurses to learn how the drug works, teach that to their patients, and reinforce to the patients that they must report symptoms." No symptom is too small. Everything should be reported. Remind the patients that they should ask questions and be involved with their own care. "I tell patients what I believe. There's a lot of hope. Clinical trials are working. Have patience. Be mindful that we're doing everything we can. It's not an easy road. And that's the same thing I tell myself," Roman said.

THE IMPORTANCE OF CLINICAL TRIALS

The research team stresses how important clinical trials are. Wolchok said, "Nurses and doctors should talk to patients about clinical trial participation because that's what is going to give people access to the next generation of even better therapies, and that's what is going to help us make progress even faster. It is just so important that we have things to build on that we really didn't have before." Therefore, patients should be encouraged to visit clinicaltrials.gov. Because this is not the end of melanoma—this is the beginning of the end. ■

Bette Kaplan is a medical writer based in Tenafly, New Jersey.

REFERENCE

1. Yervoy (ipilimumab): serious and fatal immune-mediated adverse reactions. http://www.yervoy.com/hcp/rems.aspx Accessed July 14, 2011.

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