Do you have questions about BRAF?

The AIM at Melanoma Foundation is pleased to answer questions and address misconceptions raised by patients regarding BRAF. This commentary is provided by Lisa Kottschade, APRN, MSN, CNP, Associate Professor of Oncology at the Mayo Clinic in Rochester, Minnesota, and an expert faculty member of the Melanoma Nursing Initiative.
“What is BRAF?”

BRAF is a gene that tells your cells how to grow. A BRAF mutation is a change in a BRAF gene. That change in the gene can lead to an alteration in a protein that regulates cell growth that could allow the melanoma to grow more aggressively. Approximately half of melanomas carry this mutation and are referred to as mutated, or BRAF positive. Melanomas that do not carry the mutation are referred to as wild-type or BRAF-negative melanomas.

“So, BRAF is inherited? If my parents have the mutation, I will inherit it.”

No, BRAF mutations are not inherited. They are acquired—or somatic—mutations and occur within a body cell (in this case, the tumor). In contrast, genetic—or germline—mutations affect the sperm or eggs and therefore can be inherited from our parents. BRAF is not like BRCA, which you may have heard about in relation to breast cancer and familial susceptibility. With BRCA, there is a genetic risk factor that gets passed on. This does not happen with BRAF. Therefore, you shouldn't be concerned about passing the mutation on to your children.

“If I have a BRAF mutation, does that mean I need to be screened for other cancers?”

No, the BRAF mutation is not inherited. This is a mutation limited to your melanoma tumor. Still, having said that, the BRAF mutation can be present in other tumor types, including lung cancer and colorectal cancer. But, typically, that's because the mutation occurred spontaneously in those other tumors, so having a BRAF-positive melanoma does not mean you are any more likely to have a BRAF-positive tumor elsewhere.
What Your BRAF Status Means

“I am young, so it makes sense that I would be BRAF positive.”

Yes. BRAF mutations, amongst melanoma patients, are more common in younger patients. However, this does not mean older patients cannot have BRAF mutations. They should still be screened for the BRAF mutation if they are diagnosed with melanoma.

“I am BRAF positive. That's bad—it means my cancer will come back.”

No, that's not true. Even though BRAF-positive melanomas can be more aggressive, many factors can affect the risk of your melanoma coming back. These include the characteristics of your original tumor, such as how deep it was, whether it was ulcerated, whether any lymph nodes were involved, and whether your melanoma had spread to other sites. Your BRAF status is only one piece of the puzzle in assessing the risk of your melanoma coming back.

“I am BRAF negative. That means I am going to be OK.”

No, unfortunately, that's a myth. BRAF status is only one part of a much more complex melanoma picture. Other factors that play a part in the outcome of your case include the depth of the original tumor, the presence of ulceration, the number of lymph nodes involved, and the extent (if any) of spread to other sites in your body.

“You need to know your BRAF status because it will tell you how you developed melanoma and what you need to avoid so you don't develop another one.”

Your BRAF status does not tell you anything about how you developed your melanoma, so caution in the sun is important for all patients with a melanoma diagnosis. Practicing sun safety and regularly checking for any new melanomas are two ways of monitoring your skin status. Some studies suggest that BRAF mutations tend to occur on patients without chronically sun damaged skin, but you still need to be sun safe! Although the BRAF test won’t tell you whether you will develop another melanoma, it is important to know your BRAF status. It will let you know what treatment options are appropriate.
BRAF Testing

“I am a Stage II melanoma patient. They don’t test for BRAF in Stage II.”

This is not entirely true: Testing is appropriate if you are participating in a clinical trial. So if you have Stage II melanoma, consider seeing a medical oncologist, who can discuss how likely your melanoma is to come back and what you can do to lower that risk.

“Who should be tested for BRAF?”

BRAF testing is recommended for all patients with Stage III and IV melanoma. In addition, some Stage II melanoma patients, in the context of a clinical trial, should also undergo BRAF testing.

“How is the BRAF test performed?”

BRAF testing requires tumor tissue. Your oncologist’s office will see what tumor tissue is available to test. DNA will be extracted from the tissue to look for the mutation. To ensure an adequately sized sample, additional biopsies may be necessary. If you are a Stage III or IV melanoma patient and the test has not been ordered, you should ask your oncologist to order it.

“How long does the BRAF test take to perform?”

Anywhere from 1 to 3 weeks may be needed to perform the BRAF test. While it can be frustrating to have to wait for this test, it’s important to remember that BRAF testing is a key part of the puzzle in determining the treatment plan for your melanoma.

“Is the BRAF test reimbursed?”

Generally, yes, the BRAF test is reimbursed for all patients with Stage III and IV melanoma. However, you may be required to pay a copay, depending on your insurance plan. For testing as part of a clinical trial in Stage II disease, the test is usually paid for through the clinical trial.
BRAF Status: Consideration in Treatment Decision-Making

“If I'm BRAF positive, it means I'm being treated with regular chemotherapy.”

That's a myth. There is targeted therapy specifically for patients who have the BRAF mutation. It is not chemotherapy: It's designed to address your specific type of tumor. Traditional chemotherapy does not work very well in melanoma. Targeted therapy, on the other hand, is more “specific” and has much better outcomes than those seen with chemotherapy. Targeted therapy has side effects that differ from those of chemotherapy. You won’t see the traditional side effects such as hair loss, nausea, and vomiting that you see with chemotherapy. Targeted therapy has a different set of side effects.

“If I find out that I'm BRAF positive, then I'll have to take the 'BRAF drug' before they allow me to take the really good medicine, immunotherapy.”

That's not true. First, both targeted therapy and immunotherapy are really good medicines. Secondly, since patients with BRAF mutations are eligible for either targeted therapy or immunotherapy, you and your team will decide what's best for you in terms of which type of agent to start Stage IV treatment with. There is no set order for how these drugs are to be given. In the Stage III setting, after surgery to remove the melanoma, you will work with your provider to determine which therapy is best for you.

“If I am BRAF negative, I won't be able to get an effective therapy.”

That's not true. You will be eligible for immunotherapy and potentially therapies being studied in clinical trials.
We thank Novartis Pharmaceuticals for an unrestricted educational grant in support of this important educational initiative.

### Selected Reading

AIM at Melanoma Foundation. The Melanoma Learning Center. Frisco, Tex.: AIM at Melanoma Foundation; 2014. Available at: aimatmelanoma.org/the-melanoma-learning-center/


Know Your Test Program (genetic mutation testing at no cost, offered by Novartis and Quest Diagnostics). Available at: https://www.knownowbraf.com/ Accessed November 13, 2019.

