



BRAF in Melanoma

Answering Questions, Addressing Misconceptions



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.

About *BRAF*



“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 tumour). 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 tumour. Still, having said that, the *BRAF* mutation can be present in other tumour types, including lung cancer and colorectal cancer. But, typically, that's because the mutation occurred spontaneously in those other tumours, so having a *BRAF*-positive melanoma does not mean you are any more likely to have a *BRAF*-positive tumour 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 tumour, 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 tumour, 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.



***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 tumour. 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. Either targeted therapy or IO treatments can be prescribed. You should discuss how each is administered (tablets versus IV) and the side effects associated with each with your medical team.

“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.





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Selected Reading

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