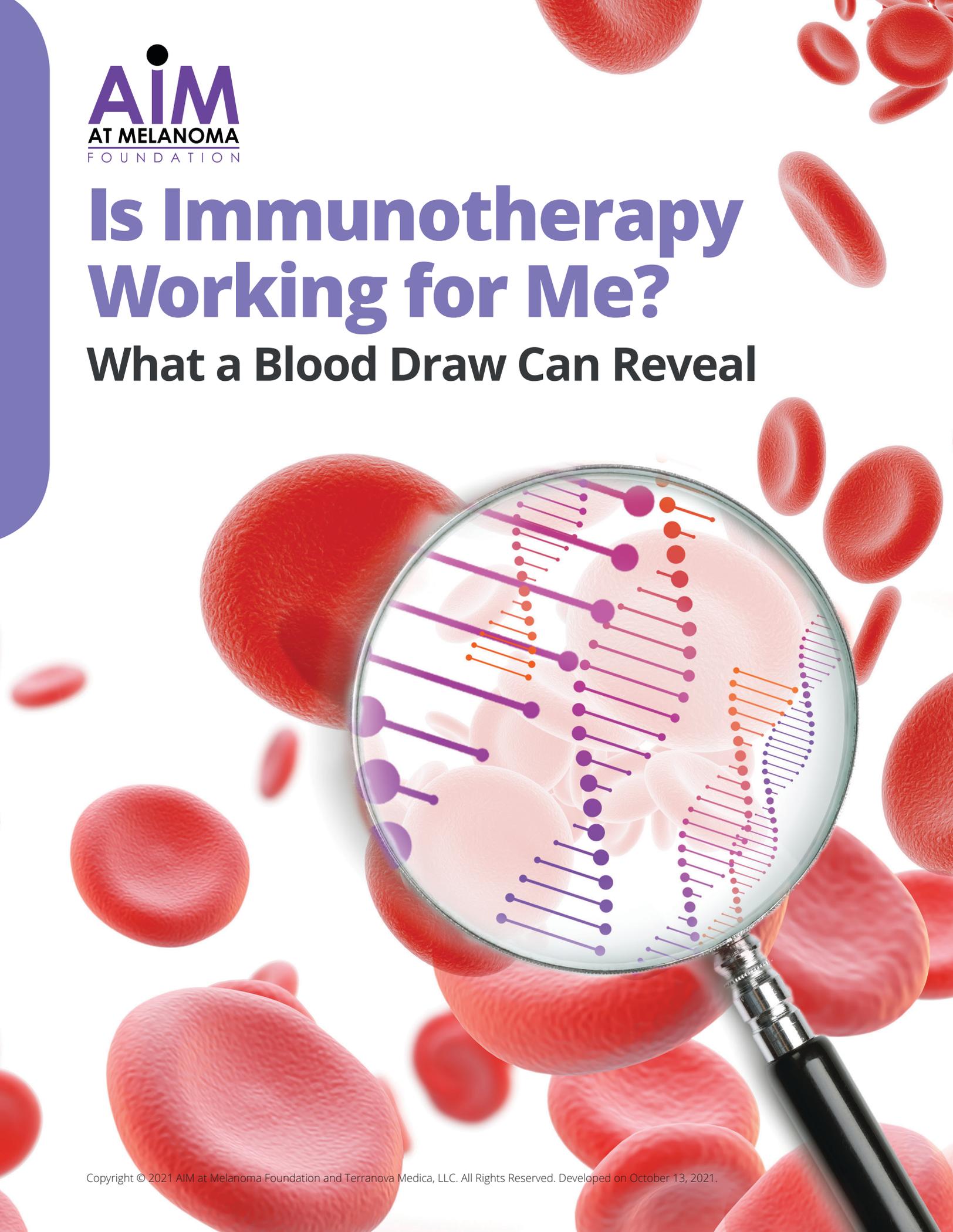


Is Immunotherapy Working for Me?

What a Blood Draw Can Reveal



THE PROMISE AND CHALLENGE OF IMMUNOTHERAPY

Developments in immunotherapy have made a real difference to patients with advanced cancers that are hard to treat or cure. These developments have been made possible by drugs that “take the brakes off” the immune system (checkpoint inhibitors). However, at most, only one in five patients (20%) who receive immunotherapy will have a response that lasts.

**≤1 IN 5
(20%)**

**OF PATIENTS
TREATED WITH
IMMUNOTHERAPY
HAVE A
LONG-LASTING
RESPONSE**

- Cancer can figure out ways to avoid being detected by your immune system, even when you are receiving immunotherapy
- Researchers have been looking for new drugs (used alone or together) to help your immune system better detect and fight cancer in the body
- For this reason, it’s important to be able to tell (as early as possible) if immunotherapy treatments are working or not working for you, so that other approaches can be taken, if necessary
- So you and your cancer team can make the best decision for your health, you will want to know the answers to the following questions:

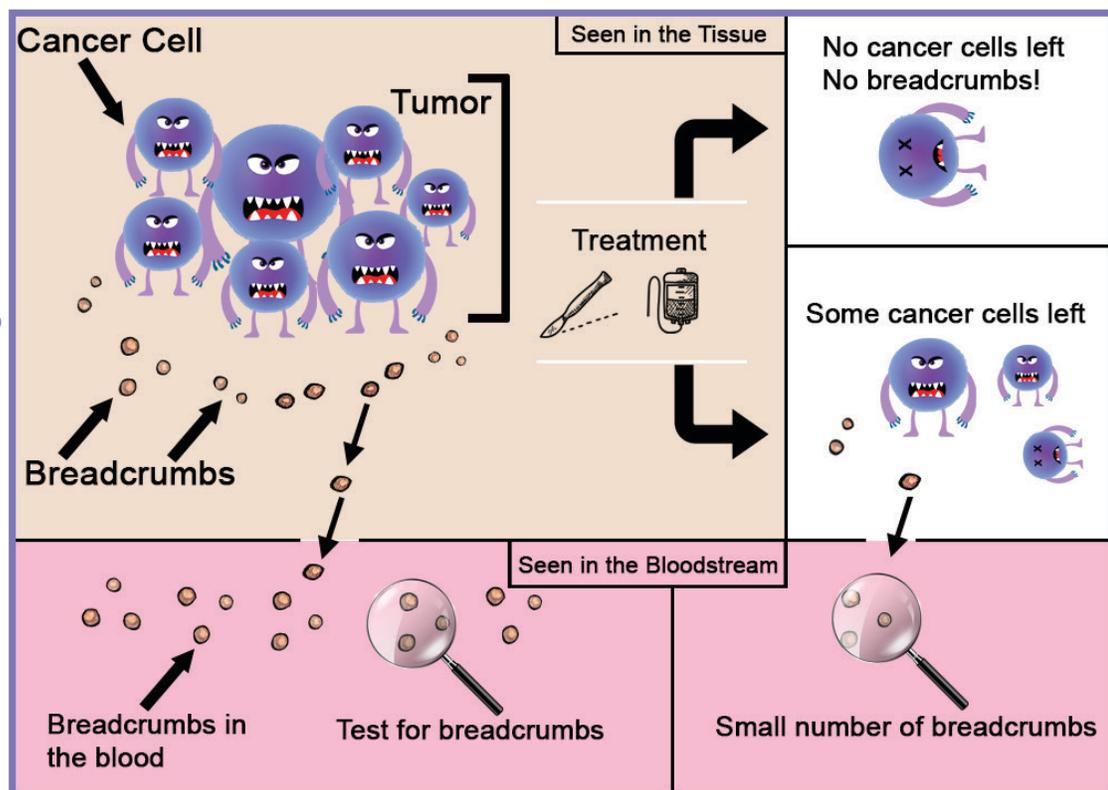


A NEW BLOOD TEST CAN HELP GUIDE DECISIONS ABOUT YOUR TREATMENT

Imaging scans are often used to see if treatment is working and shrinking your cancer, but it takes time for these changes to show up on scans. A test that can be used even earlier than a scan would be very helpful to tell if your treatment is working. Cancer cells can shed tiny pieces of DNA. Think of them like little breadcrumbs, as shown in the figure below. Studies have shown that as tumors grow, they release more “breadcrumbs.” Of course, these breadcrumbs are tiny and couldn’t even be seen on a scan. But your cancer doctor can detect them by using a new blood test.

Sometimes, if you have a cancerous tumor removed by surgery or even if treatments have successfully shrunk the tumor to the point that it doesn’t show up on a scan, a few cancer cells might be left that are too small to see with imaging, as shown on the right side of the figure below. But if there are cancer cells left, they will shed “breadcrumbs,” and your cancer doctor can use this blood test to detect them.

This blood test identifies the “breadcrumbs” specific to your tumor. It can be used to monitor how your treatment is working or detect if the cancer has come back. Studies have shown that this blood test can be used to tell if there is cancer left in your body during and after treatment. However, even though this test works well in various types of tumors (including melanoma), it is not helpful in detecting cancer that develops in the brain or in monitoring the response to therapy there.



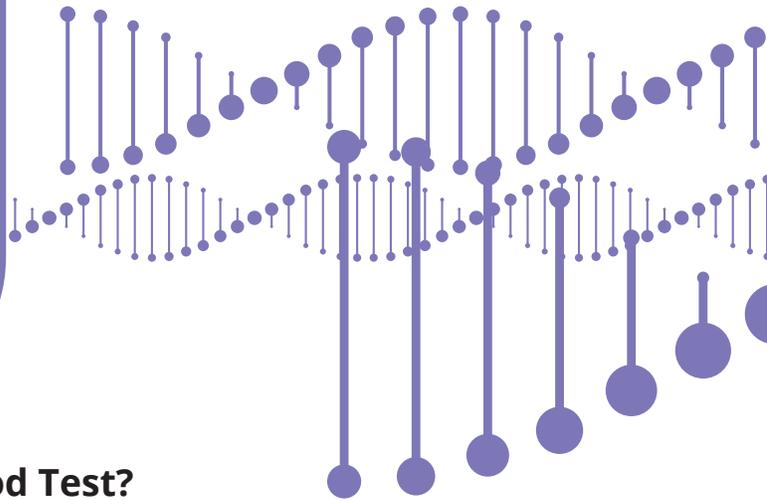


Why Additional Ways Are Needed to Assess Your Response to Treatment

Doctors typically use imaging scans or your cancer symptoms (worsening or getting better) to guide decisions about your therapy. As mentioned, it takes a while to see these changes, and it may still be unclear what to do.

For example, it takes time to use the immune system to fight cancer. Sometimes, new tumors may form early on, when the immune system is revving up. As the immune system starts attacking the tumor, the tumor might start to swell up or expand. This could mean the treatment is working. But on a scan, the tumor will look bigger. Therefore, it can be hard to tell if the treatment is working or not working just by looking at scans. If there's no sign of cancer on your scans, your doctor may wonder if it's safe to stop treatment.

A test that provides a clear, early answer would be most helpful!



What Should I Know About This Blood Test?

- The test requires drawing blood as well as collecting a small piece of the tumor that was already removed during your biopsy or surgery
- The tissue part of the test (using tissue already removed during your biopsy or surgery) looks for characteristics specific to your tumor. It will take about 3 weeks to get this important information and personalize the test for you
- Once the specific characteristics of your tumor are known, your cancer doctor can use the blood test at different times during and after the treatment to gain information needed to help you and your cancer team make the best decisions for your health
- The blood may be drawn at your doctor's office or another lab. It may even be possible to have a lab person come to you to draw it. Your doctor will talk with you about these options
- When using the blood test during and after treatment, your cancer doctor will get results from the test in about 1-2 weeks

Do I Really Need to Do This Extra Blood Test?

- It's important to have timely information about whether your treatment is working or if the cancer has come back. **Remember, your cancer doctor can follow the breadcrumbs to clue your cancer team in on what to do!**
- Your cancer team may use the test to help make decisions, as shown in the table below:

Decision Being Considered	If the Test Shows	Potential Next Step
Switch to a different therapy?	The level of "breadcrumbs" doesn't drop or disappear over time during your treatment	You and your cancer team may need to try something different
Use more than one drug together instead of using one drug alone?	The level of "breadcrumbs" rises during treatment with only one drug	You and your cancer team might decide to add a second drug to see if the combination works better
Continue using your current treatment?	The "breadcrumb" levels are dropping	Your cancer team can have more confidence that the treatment is working. You and your cancer team may keep your current treatment going
Imaging scans show no evidence of cancer. Stop treatment?	The blood test shows no "breadcrumbs" left	You and your cancer team may decide to stop your treatment and monitor you with the blood test

A PATIENT'S PERSPECTIVE:

"The test was a very useful tool. It gave us the information we needed to make a decision about future treatment. Knowledge is power. I am really glad this test was available to me."

-Rebecca, Stage IV melanoma patient

RESEARCH OPPORTUNITY

You may be able to participate in a research study that looks at how measuring the “breadcrumb” levels with the blood test might improve how patients and their cancer teams make decisions about treatment. The test will also help researchers learn more about your cancer. You may want to talk with your cancer team about clinical trial options. To learn more, you can go to www.clinicaltrials.gov or ask our AIM at Melanoma expert here [<https://www.aimatmelanoma.org/support-resources/talk-to-a-medical-expert/>]

REIMBURSEMENT DETAILS

- Medicare: Covered
- Commercial insurance: The maker of the blood test will work with the patient and the insurance company for reimbursement
- Discounted rate for cash payment

FREQUENTLY ASKED QUESTIONS

Will my insurance company pay for this blood test?

Yes. Although the blood test has not yet been fully approved by the FDA, it has been given “breakthrough” status, which means it provides more effective testing for an important condition than currently available options. This breakthrough status allows the people who developed the test to work with the FDA to speed up the approval process. As a result, the test is paid for by insurance companies, and it can be performed by an approved laboratory.

How do I get the test if I decide that I want it?

After you have a discussion with your cancer team, your doctor can complete a form requesting the test. Once your blood samples are received by the lab, they will contact the hospital where you underwent your biopsy or surgery to get the tissue sample needed to complete the testing.

What if my tumor tissue was previously removed?

Once your cancer doctor orders the test, the lab will work with the hospital where your biopsy or surgery was done and let them know what they need to complete the testing.

What if there is not enough tissue available?

Unfortunately, if there is not enough tissue available (the lab and hospital will determine this), the test cannot be performed. Your oncology team may be able to explore other options if no tissue is available.

FREQUENTLY ASKED QUESTIONS CONTINUED

Do I need to go to my cancer doctor for blood draws?

No. You can have your blood drawn at various labs. You can also request that a lab professional come to draw your blood for the test at your home or a location of your choice at no additional cost. Contact your doctor's office to make arrangements if you prefer to have your blood drawn at home or at another approved lab.

What will my out-of-pocket expense be?

This varies from patient to patient; however, there are financial assistance programs available. Your doctor's office can answer questions based on your insurance and assist you in connecting with the available financial assistance programs.

Further Reading/Resources

Bratman SV, Yang SYC, Iafolla MAJ, et al. Personalized circulating tumor DNA analysis as a predictive biomarker in solid tumor patients treated with pembrolizumab. *Nat Cancer*. 2020;1:873-881.

Lee JH, Menzies AM, Carlino MS, et al. Longitudinal monitoring of ctDNA in patients with melanoma and brain metastases treated with immune checkpoint inhibitors. *Clin Cancer Res*. 2020;26:4064-4071.

McDowell S. Liquid biopsies: past, present, and future. American Cancer Society. February 12, 2018. <https://www.cancer.org/latest-news/liquid-biopsies-past-present-future.html>

Natera, Inc. BESPOKE Study of ctDNA Guided Immunotherapy. <https://www.clinicaltrials.gov/ct2/show/NCT04761783>

Robert C. A decade of immune-checkpoint inhibitors in cancer therapy. *Nat Commun*. 2020;11:3801. <https://doi.org/10.1038/s41467-020-17670-y>

Seremet T, Jansen Y, Planken S, et al. Undetectable circulating tumor DNA (ctDNA) levels correlate with favorable outcome in metastatic melanoma patients treated with anti-PD1 therapy. *J Transl Med*. 2019;17(1):303. doi: 10.1186/s12967-019-2051-8

Reimbursement questions: <https://www.natera.com/oncology/billing/>

Compassionate Care program for uninsured patients or those concerned about their ability to pay: Contact signaterapc@natera.com