How to Test for AML Oncogenes

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Andrew Schorr:
So, Dr. Greenberger, just for our audience. You know, people—I think the public says when you're talking about genetics, talking about do I have brown eyes or brown eyes or black hair or blond hair, whatever. Could you just help us understand where we're talking about genes here, this whole idea of oncogenes or things that have sort of gone awry, how they're different?

Dr. Greenberger:
Right. So, like Dr. Verma said, there are a number, a few number of genes that we know that are so-called drivers, and what these genes do is once they become changed, mutated—it's like picture of string of beads, and one bead on the string is changed. That will make this protein now behave aberrantly and actually drive tumor growth. So once you see that, that's sort of a red flag. So that's an oncogene, a driver.

And we're trying to understand what are the driver genes, and these genes when you see that will tell you, well, this is a good prognosis or bad prognosis. Sometimes a mutation doesn't necessarily mean a bad prognosis. It may mean, oh, that patient is going to respond. And other cases it means, no, that's a poor prognosis, and we're going to have to develop an alternative therapy or certainly be on the lookout for an alternative therapy through a clinical trial.

Beyond that, what we've discovered is every patient is different, and there may not be one mutation in a protein but there could be many mutations, and the mutations change over time. So just simply by giving the therapy you've changed the disease. So what you've started with and what you end up with are different, and we need to understand that to figure out how to tailor the therapies.

Andrew Schorr:
Okay. So, Dr. Verma, if somebody comes to Montefiore and is referred to your clinic, you're going to do certain testing both for them to get the right care and to benefit research for others as well.

But, Dr. Greenberger, I have a question for you, and that is what does the LLS tell the community of people who find themselves with AML as far as getting the testing? What should they be asking for?

Dr. Verma:
Right. Well, what we are doing, in fact we are running—we're sponsoring a trial which basically when you come in and get the initial diagnosis usually because you can look under the microscope and you see the cells and there's something aberrant, is to make sure that you actually get the genetic testing. You could have a mutation that will help a physician figure out which is the appropriate drug to be on and how to tailor the therapy.

So you want, obviously, the physician's physical assessment. You want to look under the microscope. You want to do the genetic testing. And this information can be obtained. We've done it in our clinical trial running. Really within a week you can get the information back to figure out what is the appropriate therapy.

Andrew Schorr:
Okay. So, Dr. Verma, you have patients who come from probably far and wide who finally get to you because you're a subspecialist. What—maybe people didn't get that testing somewhere else, but we have everywhere watching. What would you say? First of all, it's important to get to a specialist today based on the research that's moving forward, and what would you say to them about getting the testing?

Dr. Verma:
Well, I think in today's age it's very important and critical for every patient with MDS and AML to get this gene mutation testing done. Usually in big academic centers a lot of times the testing is done in-house where our own lab looks for these gene mutations. But now we have commercial companies, vendors that do these tests, and your oncologist or hematologist who has seen you basically has to send a tube of your blood to this company, and usually if you have MDS and AML, your insurance should cover the cost of this test. So this is not that tough to do. Once they send the tube of blood, like Dr. Greenberger said, it takes about five to seven days for your oncologist to get the results back. And then they can discuss the results with you. Some mutations are relatively straightforward. Some actually have drugs approved for them, and some the significance is not entirely clear yet.

Some mutations can actually be used to guide therapies by telling the patient, you know, how high the risk is. For example, if you have MDS, you know, a third of patients who get MDS transform to acute myeloid leukemia, so two-thirds of them do not transform to acute myeloid leukemia. And I think in terms of knowing what mutation you have, your hematologist or oncologist can determine what is the risk of you transforming to acute myeloid leukemia, and if you have AML, you know, what risk group do you belong to. Do you belong to a relatively better subgroup, or do you belong to a higher risk group where maybe in addition to just chemotherapy he may like to consolidate with a clinical trial or a transplant for example?

So it's not just drugs. The drugs, we still have relatively few of them for mutations, but the decision-making, how to tailor make the treatment for you is more instructive when you have these mutations.

Andrew Schorr:
And, Kuldip, that's exactly what you were pushing for, is you wanted the doctors to have the knowledge with you so that you could make decisions, right?

Kuldip Ahluwalia:
Correct. The challenge as a patient you run into is the institution you go to. Especially in the West Coast everyone is with an HMO or a PPO, and depending on the institution you end up in they may have set protocols and set ways of doing it. So the question is how do you get to the right physician who takes the interest in you to ask for those additional tests and then start the treatment?

Andrew Schorr:
So we're really a talking about whether it's the patient themselves or a family advocate really pushing for that, to get to somebody like Dr. Verma, who specializes in this area, right?

Kuldip Ahluwalia:
Correct. And as I mentioned in my case, when they—when I ended up in the hospital they did a biopsy. They wanted the treatment right away, to start the induction therapy right away for AML. And I insisted that we'll wait a week, make sure that we get the results and the cytogenetics, and then we start the treatment. Now, did we actually change the treatment? A little bit. But needless to say we were much better prepared as to the risks that were involved, and number two, the back-up plan, which was the bone marrow transplant for me.

Andrew Schorr:
Right. So, Dr. Verma, it's kind of complicated nowadays. In other words, Dr. Greenberger was talking about all the different variations, so it's not just one cancer anymore, is it, Dr. Verma?

Dr. Verma:
Yes, you're absolutely right. You know, physically when you look under a microscope a lot of leukemias can look similar to each other, but when you look under their mutational landscape you will figure out that it's not even, you know, five or six different types. There are probably 20 types of AML, the different sets of mutations, different combinations of mutations.

Because you may not just have one mutation. You might have a combination of two or three mutations, which might change the way they behave and how your risk is.