Mayo Clinic Q & A_ Dr. Matthew Goetz - Systemic therapies fo...

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SPEAKERS

Dr. Halena Gazelka, Dr. Matthew Goetz, Narrator

N **Narrator** 00:01

Coming up on Mayo Clinic Q&A,

D **Dr. Matthew Goetz** 00:03

And the goal of that systemic therapy is simply to either inhibit the growth of cancer cells or to kill them and to eradicate them from the body.

N **Narrator** 00:12

Systemic therapy refers to any type of cancer treatment that targets the entire body. Often this treatment is used for women with breast cancer. But today, there are also several types of therapies that best suit the needs of each individual patient.

D **Dr. Matthew Goetz** 00:27

The good news is that we have a variety of medications, a variety of drugs, such that if a woman is unable to tolerate one medication, we can try another medication. And that's one of the really wonderful things that happens through the process of drug development is that we know that one drug does not fit all. And so, having a number of different options is very important for our patients.

D **Dr. Halena Gazelka** 00:47

Welcome, everyone to Mayo Clinic Q&A. I'm Dr. Halena Gazelka. It's October again, which means it's time to raise awareness for breast cancer. A particularly important topic since one in eight women will be diagnosed with breast cancer during their lifetime. Today, however, we're going to explore systemic therapies for breast cancer. That means

things like drugs that are either taken by mouth or IV, and they can target breast cancer almost anywhere in the body. Types of systemic therapies include chemotherapy, hormone therapy, targeted drug therapy, and immunotherapies. It's an alphabet soup. But here to help us decipher it today is Dr. Matthew Goetz. Dr. Goetz is a medical oncologist at Mayo Clinic. He's also the Co-leader of the Mayo Clinic Cancer Center Women's Cancer Program, and principal investigator for the Mayo Clinic Breast Cancer SPORE Grant. I think that everyone is familiar with the concept of breast cancer and even thinks they have some understanding of how it might be treated. But today, we're talking specifically about what we call systemic therapies. And I'm wondering if for our listeners you could help us to define that a bit.

D Dr. Matthew Goetz 02:01

So, a systemic therapy is simply a medication that's delivered, it could be by mouth, or it could be delivered, for example, through a vein. And the goal of that systemic therapy is simply to either inhibit the growth of cancer cells or to kill them and to eradicate them from the body.

D Dr. Halena Gazelka 02:20

And tell me about some of the types of systemic therapy, Matt.

D Dr. Matthew Goetz 02:24

So, there are actually quite a variety of different systemic therapies. Classically, the one we think about most commonly would be chemotherapy, a medication that's delivered most of the time by vein with some of the side-effects that people have we commonly think about with chemotherapy, which is hair loss, perhaps some nausea or vomiting, fatigue, and even some effects on the blood counts such as, for example, the hemoglobin, the white blood cells, or the platelets. The goal of chemotherapy is simply to kill cancer cells. And depending on the type of cancer, depending on the situation, chemotherapy can be very effective at either eradicating or substantially reducing the total volume of cancer cells in the body.

D Dr. Halena Gazelka 03:13

So Matt, I know there are multiple other types of systemic therapies. There's hormone therapy, targeted drug therapy, and immunotherapy that I have on my list, and I'm sure you have many more that you could describe for us. How do you as an oncologist decide what kind of therapy a woman should receive for her breast cancer, or a man?

D Dr. Matthew Goetz 03:33

So, great question. In fact, for breast cancer, the most common type of breast cancer that accounts for about 70% of breast cancers are the estrogen receptor positive, or hormone receptor positive type of breast cancer. And very simply, in this situation if you were to think of a cancer cell being present in the body that's estrogen receptor positive, we know that those cancer cells can respond to estrogen or hormones. And that can be used almost by the cancer cell as a way to grow or proliferate. And so, when we use hormonal therapy, most commonly for breast cancer we're using drugs simply to either block the estrogen receptor, or to remove, or substantially down regulate the estrogen receptor or even estrogen. And so, those treatments have been shown to be very effective, and quite honestly, they're the mainstay of what we do. And using medications that target the estrogen receptor have been a

huge success in breast cancer. These medications have been shown to reduce the risk for breast cancer recurrence, as well as to prolong survival, and therefore are again widely used and really have made substantial reductions in breast cancer mortality as we think about the past few decades.

D Dr. Halena Gazelka 05:00

Matt, I had seen a lecture here the other day that sometimes these therapies are even being used to prevent breast cancer in women who are very high risk it sounds like.

D Dr. Matthew Goetz 05:09

That's right. And if you think about breast cancer being first of all common, but also mostly being estrogen receptor positive, it might make sense then to actually potentially use a medication like tamoxifen, or like an aromatase inhibitor with the goal of again targeting the estrogen receptor, and potentially then reducing the risk of developing breast cancer. And so, these medications like tamoxifen, like the aromatase inhibitors have been used in patients that are at high risk for developing breast cancer, and then have been shown to be quite effective in that setting.

D Dr. Halena Gazelka 05:47

Matt, when you talk about estrogen receptors, how do you get that information? Do you take a blood test from the patient? Or do you have to have a piece of the tumor itself?

D Dr. Matthew Goetz 05:57

Yes, very good question. So, we measure the estrogen receptor through a particular immunohistochemical assay. And so, this is an antibody test where we take a piece of that tumor tissue, and in the laboratory they measure using this antibody, the amount of the estrogen receptor that's present. As you can imagine, knowing that these medications like tamoxifen, like the aromatase inhibitors, they have such a profound effect to reduce the risk of developing breast cancer recurrence. It's very important that our assays, that is our tests to assess for the presence of the estrogen receptor, they have to be above board. And in fact, there's a lot of work that's been happening over the last 20 years to make sure that these assays are reliable, that they're repeatable when we get the study it means we get the same results when we test it one day and the next day, and that way clinicians can use that information to reliably tell a patient Yes, you will get benefit from, in this case a drug like tamoxifen, or the aromatase inhibitors,

D Dr. Halena Gazelka 07:07

You mentioned that there are multiple types of systemic therapies which makes me think there would be one for everyone. But are there some individuals who are not candidates to have systemic therapy?

D Dr. Matthew Goetz 07:17

It's a great question. So, systemic therapy is really given for a number of reasons. If you can imagine a patient who is diagnosed with breast cancer and those cancer cells have spread to other parts of the body, such as the liver, or the bone, or the lung, we refer to this as stage 4 breast cancer. For those patients, systemic therapy really is the

predominant therapy that we would use to slow down, eradicate, eliminate those cancer cells. And we know that in that situation that even though breast cancer in most cases is not curable, that those systemic therapies can substantially prolong a woman's life. When a woman is first diagnosed with breast cancer, and she does not have any obvious evidence for cancer that has spread, let's say throughout the body, we know that for a woman who is diagnosed with early-stage breast cancer, there is certainly a chance that there may be cancer cells that are occult. That is that we simply can't see even with our best assays. And using a drug like tamoxifen, for example, or an aromatase inhibitor can actually work to prevent those occult seeds that we can't see from ever germinating. And that's one of the beauties of the systemic therapy, if you will, is to do that in such a way that you reduce the risk for recurrence. Now, there are some women that may not be able to tolerate. You said there may be some women that are not candidates for these medications. And certainly we do encounter that. The good news is that we have a variety of medications, a variety of drugs, such that if a woman is unable to tolerate one medication, we can try another medication. And that's one of the really wonderful things that happens through the process of drug development is that we know that one drug does not fit all. And so, having a number of different options is very important for our patients.

D Dr. Halena Gazelka 09:14

Matt, tell us a little bit about the Mayo Clinic approach to systemic therapy for breast cancer. And also what kind of research is ongoing in this area? I would imagine because this affects such a large amount of the population that there must be a lot of research you conduct?

D Dr. Matthew Goetz 09:28

There is and from a standpoint of the group here at Mayo Clinic, we're one of six centers in the country that has a specialized program of research excellence, which means that we have a cadre, a large group of individuals that are doing research in this area, research in the area of drug development, for example, research in the area of prevention. We have a group that's developing new vaccines to actually prevent breast cancer, a very exciting approach. And we have multiple different studies ongoing where we're developing new drugs. And what's really exciting about this research is these drugs that are being developed are actually being discovered here in our own shop by our own scientists. So, of course, it's one thing and we're always excited to take a drug from a drug company and bring it here to Mayo Clinic for our patients. But I can tell you it's a whole new level of excitement when we see a drug discovery, a new target that's identified in the laboratory by our own scientists, and we move that into the clinic. And we've done that multiple times. So, getting back to your first point, and that is well, how do we manage patients who have let's say, cancer that spread? The first thing, of course, is to look for the presence of these important receptors. We've talked about the estrogen receptor, very, very important. One of the receptors we haven't talked about is the HER2, and HER2 is a protein that's present on about 20% of breast cancers. And this has been an amazing success story over the past, really 20 years. When I first started my training here, we had patients who had HER2 positive breast cancer that was incurable. And over the past 20 years, there have been multiple new drugs that have developed that I think we're getting to the point where we have taken that risk for recurrence in patients with HER2 positive breast cancer, and we've probably reduced it by 70 to 80% with the use of these new drugs.

D Dr. Halena Gazelka 11:25

Wow, that's amazing.

D Dr. Matthew Goetz 11:26

Yeah. And so, HER2 positive breast cancer once feared in many ways for some patients now is something where we say well, this is a good thing, because we have very active drugs that that can work. Probably the area that is, I would say, still an area of intense research is so-called triple negative breast cancer. And you say, Well, what is that? Well, that's really tumors that have the absence of the estrogen receptor, and the absence of the HER2 receptor. And triple negative breast cancer is first of all, an aggressive disease. Second, we see quite a bit of differences in the incidence of this triple negative breast cancer according to ethnicity. This is seen at much higher rates in African American women than in Caucasian women. And so, when a woman has a diagnosis of triple negative breast cancer, traditionally all we've used, and it's worked by the way, is chemotherapy or classic chemotherapy like we talked about at the beginning. But one of the real success stories that's moving forward in triple negative breast cancer right now is the use of immunotherapy. And breast cancer has kind of lagged behind because some of the other tumors such as melanoma and lung cancer, they've been using immunotherapy for a while, but it's taken us a while in breast cancer to understand that immunotherapy does work, but it seems to work predominantly in triple negative breast cancers. And predominantly as well, by the way, it also seems to work in HER2 positive tumors. So, we just recently had the FDA approval in the last year or two for drugs that actually are working to activate the immune system against cancer. And that's a really exciting development for breast cancer.

D Dr. Halena Gazelka 13:14

That is really exciting. I'm fascinated by what you said about vaccines, because I feel like the whole world is obsessed with vaccines right now, and how quickly vaccines were developed for COVID, for instance. But how amazing to be able to prevent cancer with vaccines.

D Dr. Matthew Goetz 13:31

Right. And I think that one of the, if you will, the Holy Grail, or the real question for cancer is what are the antigens that we should be targeting when we're developing a vaccine? For COVID it's quite clear, you've got the proteins related to the virus, and vaccines that have been developed against this are highly successful. When you're developing a vaccine to treat something like breast cancer, one of the things you really have to be very careful about is knowing what are the antigens. The antigens, of course, are proteins that are present on many different normal cells in our body that can't be targeted with these vaccines. But we also want to do it in such a way that's safe. And so, there have been a number of vaccines that have been developed with varying degrees of success. One of the vaccines that is quite advanced here at Mayo Clinic that comes out of the laboratory of Dr. Keith Knutson in Florida, is a vaccine against the folate receptor. And that study is ongoing in patients with triple negative breast cancer. And we're very excited to hear about the results of that study. It's been ongoing for some time. There are also vaccines that have been targeted against HER2. And so, these are other studies that are ongoing, focusing on that HER2 protein. But in the primary prevention setting in patients that do not have breast cancer, but are simply at risk for developing cancer, we need better approaches, and the whole idea of a vaccine is incredibly appealing, because these vaccines, of course, we know to treat infectious disease have been very safe. But we also know that vaccine approaches to treat something such as HPV have been highly successful in reducing the risk of developing cervical cancer. So, this of course is what we want. And there's a fair amount of research that's ongoing right now in this space.

D Dr. Halena Gazelka 15:27

Well, if you have piqued the interest of our listeners, Matt, is there a way that they can learn more about what kind of clinical trials might be occurring at Mayo Clinic for breast cancer?

D Dr. Matthew Goetz 15:36

Absolutely. So, you certainly can go to mayoclinic.org, and you will eventually get to the space which relates to the clinical trials, and there's a link there. And so, that'll tell you a little bit about the clinical trials that are ongoing. We have clinical trials that are, as I mentioned, that are going here at Mayo, in breast cancer focused on some of our own discoveries as well as some of the most cutting-edge drugs and treatments that are really making a difference in the lives of patients. And one of our goals when we develop our breast cancer clinical trial portfolio is to have a balance of those clinical trials that are coming from our own discoveries, as well as some of the most promising drugs that are being developed elsewhere, not only here in the U.S., but of course across the world. And so, that's of course something that is incredibly, incredibly gratifying to be able to take a new drug to a patient who otherwise has run out of options, and to really see that drug make a difference in a patient's life.

D Dr. Halena Gazelka 16:41

That has got to be really amazing to do that kind of work. Thank you for sharing that.

D Dr. Matthew Goetz 16:46

You're welcome.

D Dr. Halena Gazelka 16:47

Say Matt, earlier you mentioned something that sort of piqued my interest, that there are effects of ethnicity perhaps on the types of breast cancer that women might be prone to develop? Are there other health disparities that are related to breast cancer? And how is Mayo Clinic going about trying to equalize and provide good care to everyone?

D Dr. Matthew Goetz 17:12

Yeah, that's a great question. And it's really a passion of ours, especially as it relates to our Spore. We have a researcher whose name is Dr. Fergus Couch, and Dr. Fergus Couch recently just was awarded the Mayo Investigator of the Year award. And he's done a lot of work as it relates to the identification of genes that are associated with the risk of developing breast cancer. And one of the things that Dr. Couch has done is he's collaborated with groups across the country to develop these very, very large cohorts, maybe up in that range of 30 to 40,000 women who have a diagnosis of breast cancer, and he's matched them to controls to those who don't, and through this work he's identified a number of genes where the risk of developing for example, triple negative breast cancer appears to be much higher in African Americans than in Caucasians. And so, it's this type of work I think that's critically important. The other thing that we're quite interested in doing is understanding, for example, for a given drug, and I'll give you the example of the drug anastrozole, which was developed years ago and has been a powerful drug, a drug that has made a huge difference in the lives of women. This is an aromatase inhibitor, but when it was developed, it was developed with a one dose fits all, one milligram a day. And one of the questions that comes up, of course, is does that particular dose work for all patients?

D Dr. Halena Gazelka 18:40

Right.

D Dr. Matthew Goetz 18:41

And so, we have research that's been ongoing in our group, led by Dr. Liewei Wang and Dr. James Ingle, that has actually found that there's a substantial proportion of patients, perhaps upwards of 15%, who take that one milligram per day dose of anastrozole and don't adequately reduce their estrogen levels. And in another analysis of a large clinical trial, it seems that that group of patients may not be getting as much benefit from the drug and may have a higher risk of breast cancer recurrence. So, one of the areas of focus, getting back to ethnicity, we're very focused right now, is that dose of anastrozole, one milligram a day, is that the best dose for African American females, is that the best dose for Hispanic, and this really hasn't been looked at. And this is an area of intense research focus right now.

D Dr. Halena Gazelka 19:32

And so, obviously very important that our clinical trials are available to all to participate in.

D Dr. Matthew Goetz 19:38

Absolutely, and this is something that Mayo Clinic in the community of health engagement has been really focused on. And as many people do know, Mayo Clinic recently recruited Dr. Cheryl Willman as our new Cancer Center Director, and Dr. Willman has a passion for addressing issues of diversity. And this issue of seeing variable responses as we go across and we look across different ethnicities, Dr. Willman, has had a track record of identifying genes or gene variants that have differential effects as we look across different populations. And that's where we have to be. We have to be at a point where we say, listen, our goal is to develop new drugs, but not only new drugs is to learn how best to use the drugs that we have in our armamentarium. And we know already that there is substantial variation as we look across these different drugs and to be able to individualize, and as Dr. Weinshilboum, one of my mentors, says the right drug, at the right dose, for the right patient. And that's what we need to be focused on.

D Dr. Halena Gazelka 20:49

That's great. That's a great saying and I'm very pleased to report the Dr. Willman will be joining us on Q&A coming up. So, listeners should watch for that. Thank you, Matt. I learned so much today.

D Dr. Matthew Goetz 21:00

Thank you.

D Dr. Halena Gazelka 21:02

Our thanks to Dr. Matthew Goetz, oncologist at Mayo Clinic for being here today to discuss with us systemic therapies for breast cancer. I hope that you learned something, I know that I did. We wish each of you a very wonderful day.

N Narrator 21:15

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