

Breast Cancer: Medical Treatment Options

Webcast

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Introduction

Andrew Schorr:

Hello and thank you for joining us once again on Patient Power, our live webcast and radio broadcast also in the suburban area of Chicago, Aurora and Naperville and around the world on the nmh.org website and also on patientpower.info. Many people listening. An important live webcast tonight, and that's the latest medical treatment options for breast cancer, whether you find yourself newly diagnosed with breast cancer, whether you're trying to avoid a recurrence, are there medicines that can help you. And if you've had a recurrence of breast cancer, if it's spread, advanced breast cancer, are there ways to make it a chronic condition and have a high quality of life and live many years.

So that's all to be discussed tonight with a leading breast cancer medical oncologist. That's Dr. William Gradishar. He is the director of breast medical oncology at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. He's also professor of medicine at Northwestern University's Feinberg School of Medicine. We've done many webcasts together. I always learn a lot.

Dr. Gradishar, thanks for being with us once again on Patient Power.

Dr. Gradishar:

It's nice to be back, Andrew. Good to talk to you.

Andrew Schorr:

Dr. Gradishar, so let's start with an overview. Your field of medical oncology and breast cancer, breast cancer in general, has been changing. You've been at it a while. How hopeful is it, because it's such a scary diagnosis for people, but I know that many, many times people are cured or if cancer has spread they can live many years. But that's what I say, but I'd rather hear what you say.

Dr. Gradishar:

Well, I think you're right. Your observation is correct. What we've realized over the last 20 years or so that I've been involved with breast cancer therapeutics is that we now look at breast cancer, number one, as a spectrum of disease--and we'll talk about different aspects of that, early stage breast cancer or patients with advanced disease--and furthermore we are now able to as opposed to what we were able to do just a few years ago is classify breast cancers based on their molecular characteristics. And it's not just an effort to try and pigeonhole breast

cancers into different slots but rather to be able to determine what the prognosis of patients is based on that and even more importantly to define better therapies based on those molecular characteristics.

So I think your comment that things have evolved is certainly true, and there is every reason I think for patients who are unfortunate enough to have this diagnosis to still feel hopeful that there are many things that are available to them, and I think as a result of that the outcomes have improved significantly over the last decade.

Screening Improvements

Andrew Schorr:

Now, of course people have been having mammograms and sometimes follow-up biopsies and ultrasounds, has the screening helped a lot? Because I know that sometimes women get to a point where they just get tired of having yearly mammograms, and I know that's been a concern.

Dr. Gradishar:

That's an area that continues to improve. The mainstay of screening remains mammography, and there are certain nuances that have been developed over time such as digital mammography, which is essentially the same sort of imaging but with computer-assisted analysis of the image so it allows in a sense a better set of eyes or a complementary set of eyes, that is the computer, to highlight things that might have been missed by the radiologist. So it's still in a sense the same technology, but it's evolved somewhat.

And mammography still has its limitations. Despite the excellence of the imaging or the expertise of the radiologist, breast cancers may still be too subtle to be identified or too small. There have been efforts to look at whether other tests complement mammography such as ultrasound or even MRI. And I think where we use these additional tests is still being investigated. It's not something that should be used for every single patient but when you used selectively these tests have shown to be helpful in identifying problems in patients.

And the net effect of all of this is that compared to the past we find breast cancers that are much smaller than they were before. So we're identifying patients that have earlier stage disease, which is critical in terms of predicting what the outcome might be.

Individualized Care

Andrew Schorr:

I've done a program with a colleague of yours at Northwestern, Dr. Julian Schink, who works in the area of ovarian cancer, and unfortunately ovarian cancer is

usually discovered late and there's less that can be done. In breast cancer now so much success, as you said, with discovering it earlier. But it's still a scary diagnosis. So a women, typically, sometimes, in rare cases a man, is told they have breast cancer. It used to be this sort of shotgun approach. You're going to do this and this and this depending on how large the tumor was or where it was. You're now talking about this biology of tumors. Help us understand that, where you are now in analyzing that particular patient's breast cancer tumor type and the biology of it and how you make decisions on what to do.

Dr. Gradishar:

So for a patient who is newly diagnosed with breast cancer the majority of such patients fortunately still have early stage breast cancer, which means the cancer has not spread beyond the breast or the lymph nodes in the immediate area such as under the arm. So that accounts for the majority of new diagnoses of breast cancer. And what's the first step in any effort to treat the disease is to first diagnose it, so we talked about imaging. Imaging certainly identifies something that looks abnormal, but ultimately you need a piece of tissue and then of course removal of the tumor.

And what we do with the piece of tissue is the pathologist examines it under the microscope, confirms that it's breast cancer, and then we do some additional tests that include evaluation of the presence or absence of hormone receptors, the presence or absence of HER-2, which is a feature that is not only prognostic, meaning it helps us determine the likely course of the disease, but also these things are potentially predictive. They allow us to determine in the case of hormone receptors whether a patient might benefit from antihormonal therapy or endocrine therapy, in the case of HER-2 if present whether a patient might benefit from antiHER-2 therapies like lapatinib or trastuzumab.

And then more recently we can look at the gene profiles of tumors, whether a panel of genes are expressed or not expressed. And that information allows us to make predictions about what the patient's disease may do over a course of many years. And that kind of information allows us to tailor the therapy particularly for those patients who are going to get antihormone therapy, and the big issue is whether or not we add chemotherapy.

But stepping back one step, we make the diagnosis, we confirm it by tissue, and as a recent interview you had with Dr. Jeruss from our institution, I'm sure she highlighted the fact that then the decision for most patients is should they have surgery initially or not. In some patients we elect to give therapy that goes everywhere in the body, so-called systemic therapy, like chemotherapy before surgery, but for many patients the first step is a lumpectomy or mastectomy before making any treatment decisions that revolve around chemotherapy.

Andrew Schorr:

So you're now able to almost look at the fingerprint of a patient's breast cancer and say based on that how do we fight this particular villain, if you will.

Dr. Gradishar:

Yes. I think the key things that we take into account at that first glance, that first blush with the tumor tissue that's biopsied are those things that I mentioned, hormone receptor, HER-2 status. And then we look at the architecture of the cells, how they relate to one another, whether they look immature. And these observations, this set of findings we sort of--or constellation of findings we sort of put together, and we get a sense of what the behavior of the disease may be. And in addition that information also helps us define what the optimal therapy might be for a patient.

Andrew Schorr:

Dr. Gradishar, now in recent years in medical oncology where surgery will be a key part it used to be that chemotherapy always followed it. I mean if there were to be chemotherapy, if that were needed. Nowadays sometimes you do chemotherapy in advance of surgery. Tell us where that fits in and how you determine if that's needed and then if it does shrink the tumors what options, surgical options that opens up for the patient.

Dr. Gradishar:

What we've learned based on very large clinical trials involving thousands of patients is that for patients with early stage breast cancer, again those that have their disease restricted to the breast and with or without involvement of lymph nodes under the arm, these are patients that are generally destined to get some form of systemic chemotherapy in an effort to reduce the risk of the disease coming back. And based on clinical trials we've learned that for those patients whether you get chemotherapy prior to the surgery or the same chemotherapy following the surgery, which would be viewed as the standard approach, the outcome is identical. And the implication there of course is that for many of these patients getting the chemotherapy first and then going on to surgery certainly doesn't in any way lessen their likelihood of a good outcome.

And the other thing that we've learned from that is there are some patients who are on the cusp of operability, for instance patients who have not necessarily a large, large tumor but the tumor in relation to the size of the woman's breast makes it likely that in order to remove the tumor she'd be left with a cosmetically unacceptable appearing breast. So in those patients where they're sort of on the cusp of whether a surgeon can do breast conservation chemotherapy is often give initially prior to the surgery in an effort to shrink down the tumor. And for not an insignificant fraction of patients they become lumpectomy candidates, and again there is no compromise in the overall outcome.

And another category of patients where chemotherapy is almost universally given initially are those with much bigger, more aggressive tumors, patients with inflammatory breast cancer, patients with higher stage disease, where even though they're going to get a mastectomy in an effort to make the surgery technically more successful chemotherapy is given to shrink down the tumor and then proceeding on to a mastectomy.

Increased Risk for Breast Cancer

Andrew Schorr:

Dr. Gradishar, women must ask you all the time, Did I do anything to bring this on. Now, I've read some accounts where America's weight problem, and we do have a weight problem, but being overweight could be a factor. Tell us about that. And then we'll talk about genetics after that.

Dr. Gradishar:

Sure. The concern women have is that somehow some behavior they had or some exposure they had increased their risk of developing breast cancer so that somehow they were responsible for it. And we know that there are a number of risk factor for breast cancer including the ones that you highlighted, patients who are heavy or obese, exposure to hormones, a variety of things that have been attributed to an increased risk of breast cancer. But the key thing is we don't know for the vast majority of women, with the woman sitting in front of you, what caused their breast cancer. If you were to say is it healthier to have an ideal diet, have an ideal weight, the answer to those questions is fairly straightforward. The answer is yes. But to say that a woman who is a little bit overweight by virtue of having that extra weight that's what caused her breast cancer is a very difficult association to make.

The other--the question we're often asked is once diagnosed are there things that one can do that will prevent the breast cancer from coming back, which is sort of the same issue but once the diagnosis is made. And again for most women we don't tell them to make some dramatic change in their overall lifestyle. Obviously eating better, trying to exercise, decrease their weight. Obviously if they've been taking hormone replacement therapy we try to stay away from exposure to hormones particularly if a patient has a tumor that's sensitive to hormones. But I think although these things are all factors that we can say might increase the risk for a large population of patients it's not something that we can tie to an individual patient. So I think we have to be very careful when anybody is talking about these things so that a woman doesn't think that her behavior or her weight or her diet or the fact that at some point in her life she used birth control pills that particular thing is the cause of her developing breast cancer.

Andrew Schorr:

Good point. And what we're going to do is take a brief break. When we come back we're going to ask Dr. William Gradishar from Northwestern and the Robert H. Lurie Comprehensive Cancer Center at Northwestern University about genetics and the smaller of women, higher percentage among Ashkenazic Jewish women, that particular group. We'll learn more about that. Where do genetics come into play that put some people at high risk if they carry certain genes? How do you screen for it, and what actions might you take based on that? And then we'll go on and learn more about treatments, how to prevent a breast cancer recurrence, what if it does recur.

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Family History

Andrew Schorr:

Welcome back live to our webcast and radio broadcast, folks who are listening around Chicago on the radio or on the internet around the country and around the world. I'm Andrew Schorr with the programs we do every two weeks sponsored by Northwestern Memorial Hospital. I'm a cancer survivor, a leukemia survivor. Certainly I know a little bit about treatments, but I have the privilege of interviewing cancer experts regularly, and one of my favorites is Dr. William Gradishar, who is the director of breast medical oncology at the Robert H. Lurie Comprehensive Cancer Center at Northwestern University, associated with the Lynn Sage Breast Cancer Center there of course. He's the professor of medicine at Northwestern University's Feinberg School of Medicine.

We were talking just before the break, Bill, about did a woman patient do something to bring the breast cancer on. Well, pretty unlikely, but in some percentage of cases there was a gene involved that put them at higher risk. Tell us about that, what percentage of the women diagnosed with breast cancer where that's been a factor. And then we'll discuss how do you decide what to do and understand whether it's even there in you or in other family members.

Dr. Gradishar:

So one of the issues that comes up particularly when we see patients that are young or where there are multiple family members that have had breast cancer, particularly first degree relatives, meaning mothers, sisters etc., our sense of concern goes up that these might be patients who have a predisposition to breast cancer, in other words a genetic predisposition. And I think it should be emphasized because for most women we don't understand why they develop their breast cancer, so the fraction of all breast cancers that can be accounted for by some known genetic abnormality is less than 10 percent. And this is obviously an

area that is actively being researched, and there's no doubt that we'll identify other factors, genetic factors that contribute to the development of breast cancer.

Right now what most people are familiar with and acquainted with are so-called BRCA1 and BRCA2 genetic abnormalities. And, as I mentioned, these occur relatively infrequently, in fewer than 10 percent of all breast cancer patients. But the implications that if we were to identify somebody that was a carrier of one of these abnormalities if they did not have a diagnosis of breast cancer we would be concerned that they might be at a significantly elevated risk of developing breast cancer and also perhaps ovarian cancer, depending on the specific genetic abnormality. And for some of these patients, particularly those that are young, there are some obvious significant implications. You know, certainly if you identify this in somebody very young, in their 20s or even before in some cases, what are the implications. Well, if they're at elevated risk of developing breast cancer or ovarian cancer would you do bilateral mastectomies or remove their ovaries, an oophorectomy, in a woman who perhaps hasn't had an opportunity to child bear, isn't married, etc. So these are very significant implications.

But certainly if it's somebody that's older, past their childbearing years, those are the kind of ablative surgeries that are considered and have been shown to significantly reduce the risk of those carriers ever developing the disease. In patients who have a diagnosis of breast cancer and based on their history we also identify them as carriers of one of these abnormalities, we may give consideration of doing perhaps contralateral or opposite side mastectomy to reduce the risk of ever developing a second breast cancer or to remove their ovaries so if they're long-term survivors, which we hope, they don't develop an unrelated ovarian cancer.

So these are long discussions. We often engage the group within our center that are the genetics people who not only do the testing but also go through all the discussion related to what the implications are, not only for the individual who is the carrier but it's much broader than that, other family members, children of the individual who is known to be a carrier. So it's a very long, it's a very involved discussion. But I think it's very critical for those individuals that are carriers, but it's also important to realize for the audience that this still accounts from the minority of all breast cancers that are diagnosed.

Andrew Schorr:

And I mentioned Jews of Eastern European or Ashkenazic descent, there's a little higher likelihood there if I'm right.

Dr. Gradishar:

Right. That's one group. Some of the original work was done on relatively isolated populations like Icelandic people, the Mormons, and certainly the Ashkenazi Jews where the prevalence of these abnormalities seem to be higher. So for instance if

you are evaluating a patient who is an Eastern European Ashkenazi Jew your suspicion about these things might be a little bit higher.

And the other implication of course is that in some families the size of the family is quite small, so when you start asking for a family history and rather than finding that there are five sisters and two aunts with breast cancer you basically end up with maybe one or none, it doesn't eliminate the possibility that there could be a genetic abnormality, particularly if the patient is young because it can in a sense be masked by smaller number of people in the family so it doesn't have an opportunity to show itself. So I think when you're dealing with a particular population where you know the prevalence might be much higher than the average population, Ashkenazi Jews, then you would be much more suspicious of that as a possibility for why the patient developed the disease.

Treatment

Andrew Schorr:

Let's resume our discussion of treatment. So someone is diagnosed. You do these kind of assays to understand what treatments might be right. Where are we now in improvements to the treatment, someone being treated for the first time for breast cancer? And I know we're looking at different breast cancer types so different drugs come into play. So first of all, have we gotten--not just more specific, but have we gotten it better because obviously people worry about the side effects of treatment, losing their hair, tired, nausea, various things that you hear from the lady down the street who had breast cancer years ago. Where are we now with making the range of aggressive treatment, specific cancer-killing, hope for a cure and just being easier to take?

Dr. Gradishar:

For patients with early stage breast cancer, as we were discussing earlier, we take into account the size of the tumor, the lymph node involvement and all the markers or genetic assays that may be helpful in defining prognosis and possibly influencing the treatment decisions. For patients who are hormone receptor positive they are going to get antihormone therapy.

And often a point of confusion is we will hear often in the lay press or in the media that hormones and breast cancer, they shouldn't go together. Hormones are bad. So when we're talking about hormone therapy I think it's very important that what we're really talking about is antihormone therapy. So to be precise we're trying to interfere with hormones. So for any patient that has a tumor that expresses what we refer to estrogen and/or progesterone receptors, those are patients that will receive some form of antihormone therapy. Drugs like tamoxifen, or drugs like aromatase inhibitors if they're postmenopausal. And what these drugs are meant to do is interfere with the effect of hormones and how they might influence the

growth of individual tumor cells that might be around. So that's a very clear recommendation that's shown to reduce the risk of disease coming back and improve survival.

And above and beyond that certainly if patients have bigger tumors, involve lymph nodes, then the discussion also revolves around whether or not they'd benefit from chemotherapy. And the other distinction that has to be made is that chemotherapy for one type of cancer is not the same for another type of cancer. So oftentimes, understandably, patients talk to their friends, they talk to their neighbors, the lady down the street, and sometimes there are bad stories, sometimes there are good stories, but you can't confuse one patient's predicament or their disease and the therapies they've received or been recommended to necessarily apply to what's recommended for a patient with breast cancer.

So what we've evolved to in terms of using chemotherapy is that we've tried to be more selective in identifying those that really need it. And part of the thing that is a true advance, I think, is being able to look at the genetic profile of patients. And in those that have tumors that are sensitive to the effects of hormones, knowing that they're going to get an antihormone therapy we can use those assays to predict whether or not there would be additional benefit from chemotherapy.

You spoke or mentioned, are patients going to have problems with fatigue and throwing up and a variety of other things. These are all side effects that can be associated with chemotherapy. It certainly depends on the disease. I think what we've seen over the last decade, not only in breast cancer but in a variety of other malignancies, is that when we use chemotherapy we're better able to manage their side effects. And certainly as relates to breast cancer therapy most women, as a general statement I tell patients that they should be able to maintain their level of activity related to their family, to work, to their responsibilities. They might feel a little bit more fatigued, but this is something that is tolerable. We have treatments that if not eliminating nausea completely certainly decrease it, help with blood counts so fatigue is less. So many of the things that patients were most concerned about and perhaps experienced more commonly a decade ago are far less frequent today.

Andrew Schorr:

That's all good news. Now, as far as beating the cancer, so we talked about targeted therapies. You use the profiling and other understanding to pick which treatment is right. Now, you mentioned along the way HER-2/neu. It used to be that women who had tumors that expressed HER-2/neu, that would be a more aggressive breast cancer and maybe a less positive diagnosis, if you will. But then a targeted therapy was developed to go after that type of tumor. Tell us about that as a development in breast cancer. I know it's a certain percentage of women in breast cancer, but it sounds like it gave them an advantage of having a very targeted therapy for their specific biology.

Dr. Gradishar:

What we knew for some time, for the past 20 years, is that if you looked at all patients and looked at the tumors that developed in patients with breast cancer about, say, 20 to 25 percent of them were patients who developed tumors with HER-2 positivity, H-E-R 2. And if you looked at nothing else and just sort of looked at that factor we knew that women who overexpressed that factor in their breast cancer compared to women who did not, all other things being equal, size of the tumor, nodal status, etc., that women with this HER-2 factor had a worse outcome. The disease tended to be more aggressive. So it had a bad behavior. So when you heard that it tended to make you worry that this was a patient that may have a more aggressive tumor is as a result the clinical course might be a little more rocky than the typical patient.

In the last decade we developed the drug called trastuzumab, or Herceptin as it's commercially known, and that was an antibody that was directly targeting tumors that had this HER-2 feature. You could swim in it, if you didn't have that HER-2 feature it wouldn't do anything beneficial for you. But for the patients who had that HER-2 factor present on their tumor cells, whether they had advanced disease, meaning metastatic, or whether they had early stage cancer where there was no evidence of the disease if you took x-rays, in addition to their chemotherapy if they had Herceptin or trastuzumab added there was a dramatic increase in the likelihood of having an antitumor response if they had metastatic disease, an improvement in survival. And even in the patients with early stage disease where there was no evidence of the tumor being present but we had a concern that they were at risk, when trastuzumab or Herceptin was added to chemotherapy it dramatically reduced the risk of the disease ever coming back. So this was a clear indication that looking at particular factors in a breast cancer and developing therapies that target that offer an opportunity to really significantly improve the outcome of patients.

And since then the newest drug that's been approved in addition to trastuzumab, or Herceptin, for that subset of patients that are HER-2 positive is called lapatinib or Tykerb. Herceptin is something that is given IV, lapatinib is something that is given orally as a pill, and it's approved for the patients with metastatic disease who've progressed after receiving Herceptin. So although Herceptin is very good as a treatment for metastatic breast cancer, for most patients despite the improvement it's not curative. But we've now developed therapies that can potentially work even after Herceptin has stopped working.

So I think this is a perfect analogy of how we look at things that happen in the lab, how experiments that are conducted in petri dishes, moving on to animals and then ultimately developing drugs that can target those things have resulted in a better outcome for patients.

Andrew Schorr:

That's certainly a great story, and as we know we hope to look at characteristics of other breast cancer types and develop targeted therapies for them. And there's a lot of work going on related to that. We're going to take another short break. When we come back we're going to answer questions related to, well, if you've been treated for breast cancer the last thing you want is to have a recurrence. Where are we now with the medical approaches to limit your risk of recurrence of breast cancer. And then, as we round out our show, we'll say, well, what if it has recurred. What will you do then. Can you live with breast cancer as a chronic condition, if you will, and then still go on and have a pretty good quality of life and hopefully many years. All that coming up as we continue our live broadcast. I'm Andrew Schorr. We'll be right back.

Recurrence

Andrew Schorr:

Welcome back and thank you for joining us this evening for our live broadcast on ihealth at nmh.org, the Northwestern Memorial website. We're also going out on the radio in suburban Chicago and Aurora and Naperville and around the world on the various websites, including ours, patientpower.info. And then the replay will be in the ihealth section of nmh.org. Folks may also find it on the new Microsoft health search engine, health.live.com.

We're visiting with Dr. William Gradishar, who is the director of medical oncology at the Robert H. Lurie Comprehensive Cancer Center at Northwestern University, right down there at the Prentiss Women's Hospital, right downtown in Chicago. Beautiful new place.

Dr. Gradishar, so most often the treatment is successful and women say, okay, I hope I'm cured, but I'm going to go on about my life, but there's always the worry of recurrence. What are the approaches you use now to help women lower their risk of recurrence?

Dr. Gradishar:

The thing that we try to do is to offer patients the most effective adjuvant therapy that reduces their risk. So that involves, as we've been discussing, if appropriate, antihormone therapy, if appropriate, chemotherapy, plus or minus the addition of targeted therapies like Herceptin. And the hope is that that eliminates any microscopic disease that may develop. And we're now evaluating a variety of new drugs in clinical trials including Avastin, which is an antiangiogenesis therapy proven to be helpful in patients with advanced disease. The typical evolution of any new treatment is that you show that it's effective in patients with more advanced disease, and if so then you try to determine whether it can further reduce the risk of the disease ever coming back. So drugs like Avastin or drugs like lapatinib or

Tykerb, which is the newer anti HER-2 therapy, are all in clinical trials in patients with early stage breast cancer to see whether they incrementally improve outcome of those patients.

One of the things that patients often concern themselves with once diagnosed, once completing therapy is the issue of what should be done in an effort to monitor or identify the disease if it were to recur. And I think it should be emphasized that based on a lot of data from clinical trials that there is not a lot of compelling data that tells us that you should do lots of things to people who otherwise feel well. So one of the common questions is, When am I getting my blood tests, my CAT scans, my PET scans, my MRIs, etc.

And for patients with early stage disease the most effective thing that we have is talking to patients, examining patients, and in a sense pulling the trigger on doing additional tests, only if there's a complaint that suggests that there's a problem. And although this can be in some cases very discomfoting to patients that they're not being, quote/unquote, aggressive about looking for the disease, there's absolutely no evidence whatsoever that doing lots of tests to people who otherwise feel well really changes the course of their disease in any meaningful way.

And one of the consequences of doing lots of things to patients who otherwise feel well is that occasionally you'll find something slightly abnormal on a test that only leads to additional tests, potentially biopsies, more tests, and almost never does it really help us help the patient in any meaningful way. So the typical monitoring for the patients is to see them back at frequent intervals of every three or four months for the first couple of years and thereafter every six months. And should they have complaints of course they're addressed and the appropriate tests are ordered, but specifically we don't do a lot of testing. National guidelines suggest that not a lot of testing be done for the very reason that we're not trying to make patients more anxious, particularly if the testing isn't going to help us help them.

Andrew Schorr:

Now, we've talked about this before. Let's go down this road again. So coming right out of Northwestern, actually, we had the development tamoxifen, and that's been around for years. And now this class of medicines, aromatase inhibitors that postmenopausal women would take to limit if their tumors were fueled by estrogen to keep that at bay and lower their risk. Where are we now with recommendations of women taking that, postmenopausal women? And how long can you take them? And also maybe you could comment on any side effects that come up and how those could be managed.

Dr. Gradishar:

As a result of clinical trials done over the last 15 years we know that antihormone therapy is very effective, and that was based on trials that were done even longer ago than that. And the drug that you every referred to, tamoxifen, has been

around now for over 30 years and is still probably the most widely used anticancer therapy around the world, certainly with regards to breast cancer. But tamoxifen has been in a sense supplanted at least to some degree by newer drugs like aromatase inhibitors. And the distinction between the two drugs in a very simplistic way is that for patients who have these hormone receptors present on their tumor we know that using an antihormone therapy of some kind reduces their risk. Tamoxifen interferes with the receptor. It actually sits on the receptor, and it blocks estrogen from stimulating a tumor cell. And what the newer drugs, the aromatase inhibitors do is actually prevent the body or decrease the body's ability to make estrogen. So they actually act in different ways. And a key distinction in addition to that is that tamoxifen can be used in both pre and postmenopausal women, whereas the aromatase inhibitors are only useful in postmenopausal women.

To your question of benefit, we know that incrementally the aromatase inhibitors appear to be somewhat better than tamoxifen, not dramatically better but incrementally better. They are generally recommended, be it tamoxifen or aromatase inhibitor, for no less than five years of therapy. And we're now looking at even longer durations of therapy, either with a single agent, meaning an aromatase inhibitor alone, or in sequence, tamoxifen followed by an aromatase inhibitor, and looking at durations of therapy that go out to ten years, and trials are even looking at durations of treatment beyond that. And the whole idea is that if you can demonstrate that a certain number of years of therapy reduces your risk of recurrence, what might the addition of, say, an additional five years do.

You're also correct that with any therapy you give--whether it's chemotherapy, whether it's Herceptin, we're talking about antihormone therapy--the good is also associated on the other side of the coin with the potential for side effects. And the flip side of the good is that with the drugs like tamoxifen as an example we've known for many years that there's an increased risk of blood clot--it's low but nevertheless real--an increased risk of uterine cancer that's small but nevertheless real and it's higher than the average woman.

So if you look at the newer drugs, the aromatase inhibitors, which are incrementally perhaps better than tamoxifen in reducing the risk of breast cancer from coming back, we've found that those drugs are not necessarily associated with blood clots or uterine cancer, but what they are associated with is the potential for bone loss. So postmenopausal women in the absence of a diagnosis of cancer are at risk for osteopenia, osteoporosis, a thinning of the bone over time, and that's largely due to the absence of estrogen as a woman goes through menopause. So if you think about that women and then add a drug that further reduces her level of estrogen, the aromatase inhibitor, although it may be doing good things for the breast cancer it also has a potential effect on thinning of the bones. So that's one of the side effects we watch for. In addition, some women can have musculoskeletal

complaints or arthralgias, just joint discomfort with the aromatase inhibitors. So we are aware of that and we monitor that and we question patients about that who are on these therapies for an extended period of time.

Andrew Schorr:

Sleep problems sometimes, other things like that you can help with?

Dr. Gradishar:

Well, for instance, tamoxifen is a drug that has been associated with hot flashes. Of course women undergoing menopause, again in the absence of a diagnosis of breast cancer, in the absence of tamoxifen can have hot flashes. If you treat a woman with tamoxifen they can also have hot flashes. Sometimes it's difficult to tease out is it a woman going through menopause or is it the tamoxifen or is it sort of an additive effect? Hot flashes, as many women know, can be distressing. Fortunately for most of them they're not extreme, but for some of them they can be. It can disrupt sleep, wake them up. And for women who have had them during the middle of the day when they're at work and they feel flushed and sweaty it's very a uncomfortable and sometimes embarrassing feeling. But for most women--again there are exceptions, for most women the frequency, the intensity of hot flashes dissipate over time.

We've tried a variety of different therapies to treat hot flashes, and among those the thing we know that works the best is the one thing we're not going to give patients, which is estrogen. So we've tried a variety of things over the years. Most of those things have not uniformly eradicated hot flashes, but there are certain medications that we try. And in a fraction of patients they're successful so that they decrease the frequency and the intensity, basically taking the edge off hot flashes, and as a result women are better able to cope.

Andrew Schorr:

We're going to take another short break, and when we come back we'll discuss what if breast cancer comes back, how do you treat it then. We've mentioned some of these drugs, Avastin, lapatinib, Tykerb, that have been used there and are being used also earlier. But I know there are many options we have now to help keep that cancer at bay even when it's advanced. We'll hear more about that from Dr. William Gradishar from the Robert H. Lurie Comprehensive Cancer Center of Northwestern University when we come back with more of our live broadcast. Patient Power sponsored by Northwestern Memorial Hospital.

Treating Recurrence

Andrew Schorr:

We're back for our final segment on Patient Power as we discuss medical options for the treatment of breast cancer. And as we continue our discussion with Dr. William Gradishar, who is the director of breast medical oncology at Northwestern, we

wanted to talk about what if cancer comes back.

Dr. Gradishar, I've been at town meetings with you and other experts from Northwestern and around the country where we've been in rooms full of women who have been living many years with advanced breast cancer when for the women newly diagnosed that's their worst fear, that it comes back, and they think, well, then it's all over. But really that's changed greatly, hasn't it?

Dr. Gradishar:

I think that's correct, Andrew. And what we try to convey to women who are in this circumstance is that breast cancer that comes back, although we'd love to say and make the claim that we can cure the disease, we infrequently do that but it's highly treatable. And we try to draw the distinction that many of our therapies today are very well tolerated, as we were talking about earlier, and no one wants to have this problem. We accept that as sort of a baseline thing that is true of every single patient that's diagnosed with this. So we're not trying to say it's a silver lining that you have breast cancer, but the key point is I think the one you made, and that is with the advances in therapies, for many patients, although we can't use cure as the goal, we can treat it successfully for many, many years.

And I think what's different today than it had been in the past is for many women despite the inconvenience, and of course there are some side effects with therapy, most women can go about their business even while undergoing treatment for advanced disease. And we have one of the good things I suppose about breast cancer therapeutics is the list of options we have for patients is rather extensive. So even when one therapy has been successful for a period of time or even if we choose something that fails to really impact on the tumor, we have another set of options that are available and we can go from one to the next to the next.

And the key strategy in treating breast cancer is to try and exploit the characteristics of the tumor that we know are present. So if it's somebody that has hormone receptor positive breast cancer to use antihormone therapy. HER-2 positive breast cancer, to try and use drugs like trastuzumab or lapatinib with or without chemotherapy. And then of course chemotherapy remains integral. And we try to use any therapy that seems to be working for as long as it's able to have an antitumor effect and where it remains tolerable to the patient. We use the adage that we never want to make the therapy worse than the disease. So as patients go through therapy they may remain on something for an extensive period of time, and we carefully monitor the side effects that they're experiencing hopefully so we're not impacting in any major way on their quality of life, at least as it relates to the therapy they're receiving.

Clinical Trials

Andrew Schorr:

Dr. Gradishar, let's talk about clinical trials for a minute. So you are at an academic medical center, and many of the new drugs end up coming out of research from Northwestern and places like that, university research centers. When a woman has advanced breast cancer is that part of the discussion, Is there a clinical trial that might be right for you that possibly might give you tomorrow's medicine today. After all, you mentioned Avastin as an example or Herceptin, drugs that have been proven to be effective that are now approved in different areas of breast cancer came out of research and women participating in trials. So how does that discussion go now? And how much do you have to offer as part of the clinical trial discussion if someone comes for care at your center?

Dr. Gradishar:

Well, certainly at centers like ours and other centers that are similarly positioned, large places, tertiary care centers, but also I might add even in the community clinical trials are very important. And I think you highlighted the key point, and that is that for patients when we discuss a therapy, whether it's for patients with early stage disease or for patients with advanced disease, we like to have two basic forks in the road. One is we discuss the standard therapies that are available and then we discuss clinical trials that are exploring either new therapeutic options that are new drugs or new ways of even giving older drugs.

And I think a key point that you made is that when we talk about the standard therapies those are the outcome of clinical trials that were done in the not-so-distant past. So when we talk about Herceptin as a standard therapy if you're HER-2 positive, the only reason that that drug became approved and that we understood that it really had a dramatic impact on patients' outcome was for those patients courageous enough to participate in clinical trials that asked whether or not standard chemotherapy with or without Herceptin made a difference. We didn't know at that time not so long ago, just a few years ago, that Herceptin added anything to chemotherapy. So patients were willing to be randomized to standard therapy, which was chemotherapy alone, or Herceptin plus chemotherapy.

Oftentimes patients use the phrase, Well, I don't want to be guinea pig or I don't want to just be experimented on, but I think the important point to make about clinical trials is that they're all done in such a way that the standard the care, certainly with respect to large randomized trials, that the patient at minimum gets what's viewed as standard of care, and the question is often Can we do better than that. The unknown of course is whether the new permutation or the new drug added to standard therapy will incrementally improve outcome. We don't know the answer to that, and that's frequently why we have to recruit literally thousands of patients to a clinical trial to determine whether that maneuver has resulted in a better outcome.

Even when we're doing clinical trials that are a new drug all by itself the trials are set up in such a way that they don't compromise a patient's outcome because the eligibility are frequently defined in such a way that in order to go on a clinical trial a patient must have exhausted what we view as standard therapy. So the alternatives at that point are not viewed as that favorable, and as a result something that looks promising that's early on in its development is viewed as the equivalent of what is standard, equally safe based on what we know. And I can't say it enough, and it's what we say every day to multiple patients, that clinical trials really afford you an opportunity hopefully to participate in a therapy that's going to ultimately improve the outcome hopefully of you but also other patients as well.

Andrew Schorr:

Thank you for that. And I'll just put in my plug for clinical trials. So I'm a leukemia patient who decided to be in a phase II clinical trial that was just at one medical center, and it worked. And the treatment that I had is what most people get now for that version of leukemia, and I hope it works for a long time. The leukemia seems to be at bay now. So I would certainly recommend people consider it.

Dr. Gradishar, just in summing up, just in the brief time we have, you've been at this, as you say, 20 years or so. How encouraged are you for people, whatever version of breast cancer they're given--and I know it varies greatly--but generally how encouraged are you as far as the progress we've made?

Dr. Gradishar:

Well, we always wish things moved even more rapidly than they do, but if you take the long view and have a little bit of perspective, meaning over 10 or 20 years, in the field of breast cancer you can see the advances made on all fronts, not only in patients with advanced disease but improvement in outcome in patients with early stage disease, prevention, something we didn't talk about, and even the diagnostics we use, the imaging studies that are available, the genetic assays that help us look at breast cancer, all of this has made a significant improvement in outcome.

Andrew Schorr:

Very encouraging. Well, I'm delighted to hear you say that. We've been visiting with Dr. William Gradishar, who is the director of breast medical oncology at the Robert H. Lurie Comprehensive Cancer Center at Northwestern University. Bill, thank you for being with us once again.

Dr. Gradishar:

My pleasure.

Andrew Schorr:

This is what we do on Patient Power. We're delighted it's sponsored by Northwestern Memorial Hospital. We'll be back in two weeks with our discussion with a leading breast cancer surgeon. As always, knowledge can be the best medicine of all. I'm Andrew Schorr. Have a good night.

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