



Triple-Negative Breast Cancer: Treatment Update and Tools for Healthy Living

April 21, 2009

Lyndsay N. Harris, MD, and Suzanne Dixon, MPH, MS, RD

OPERATOR:

Greetings, and welcome to the Living Beyond Breast Cancer and Triple Negative Breast Cancer Foundation's "Triple-Negative Breast Cancer: Treatment Update and Tools for Healthy Living" Conference Call. . . . It is now my pleasure to introduce your moderator, Ms. Elyse Spatz Caplan. Thank you, Ms. Caplan. You may now begin.

ELYSE SPATZ CAPLAN, MA:

Thank you so much, everyone, for joining us today for Living Beyond Breast Cancer's teleconference on triple-negative breast cancer. We are delighted for the second year in a row to be collaborating with the Triple Negative Breast Cancer Foundation [<http://www.tnbcfoundation.org>] on this partnership to enable us to reach many more women living with or concerned about triple-negative breast cancer.

The objective of this program is to help you understand more fully the impact of this specific diagnosis so you can be empowered with information to go back to your healthcare team and get questions answered.

In a few minutes, I will introduce the chairwoman of the board for the Triple Negative Breast Cancer Foundation so she can make some opening remarks. . . . The speakers we have today – Dr. Lyndsay Harris of the Yale Cancer Center [<http://www.yalecancercenter.org>] and Suzanne Dixon of The Health Geek – will share with us the latest medical and research updates in addition to providing some information on nutritional tips to enhance your well-being. As our operator mentioned, you will get the chance to ask some questions at the end of the program. . . .

. . . We know that after a diagnosis of breast cancer, it can be very hard to navigate through not only the medical aspects of your illness, but also the emotional, psychosocial and quality of life issues. I can certainly add that when I was

diagnosed with breast cancer 17 years ago, it was very hard to find other women, other peers to get support. As a way for many of you to connect with each other or to get some peer support, I'm happy to say that LBCC does have a toll-free Survivors' Helpline, and that number is (888) 753-LBCC (5222).

We also have interactive message boards on our Web site, and I would encourage you to start a topic on triple-negative breast cancer and talk about some of the issues of concern. In addition, the Triple Negative Breast Cancer Foundation has very active message boards, too, at its Web site [<http://forum.tnbcfoundation.org>]. . . .

. . . Without further delay, I'm very pleased to welcome Hayley Dinerman, who, as I mentioned, is chairwoman of the board for the Triple Negative Breast Cancer Foundation. We thank Hayley and also Allison Axenrod, who works very closely with Hayley, for everything they're doing connected to assisting women with triple-negative breast cancer to get through their experience and to get vital information. Please welcome Hayley.

HAYLEY DINERMAN:

Thank you so much, Elyse. On behalf of the Triple Negative Breast Cancer Foundation, I'd like to welcome you all today. I'd also like to thank Elyse and everyone at Living Beyond Breast Cancer for organizing this important program.

This marks the second time the Triple Negative Breast Cancer Foundation has partnered with LBCC to present a teleconference specific to triple-negative disease. Our organizations are also collaborating on another project that may be of interest to you. It's a publication about triple-negative breast cancer.

Those of you who are familiar with LBCC's educational materials know that they're thoroughly researched and incredibly useful. We expect that this brochure will be an excellent resource for women living with triple-negative disease, and we're

excited to be a part of it. So, thank you, Elyse, for offering us that opportunity.

Before we begin the program, I'd like to take a moment to announce that, together with Susan G. Komen for the Cure [<http://ww5.komen.org>], the Triple Negative Breast Cancer Foundation is funding the largest single research grant to date focused on triple-negative disease. You can learn more about the grant and the specific research being funded on our Web site [<http://www.tnbcfoundation.org/promisegrant.htm>].

Now, for the program. As you've heard, today we're very fortunate to have two featured speakers, Dr. Lyndsay Harris and Ms. Suzanne Dixon. Allow me to introduce them both to you.

Dr. Harris is a nationally recognized expert in breast cancer treatment and research. She's an associate professor of medicine and medical oncology at the Yale School of Medicine, and the director of the Breast Cancer Program at Yale Cancer Center. Dr. Harris also serves as co-director of the Yale-New Haven Breast Center. Her research focuses on the molecular classifications of breast cancer and the development of new strategies to evaluate and treat breast cancer. She's the principal investigator for several clinical trials for the treatment of advanced breast cancer.

Dr. Harris currently serves as associate chairwoman for breast cancer on ASCO's tumor marker guideline subcommittee and is also a member of the Cooperative Breast Cancer Tissue Resource Panel at the National Cancer Institute.

Our second speaker, Ms. Dixon, is an epidemiologist and registered dietitian. She's also an author, speaker and internationally recognized expert in nutrition, chronic disease prevention, and health and wellness. She's devoted to helping others learn about and use food and nutrients for optimal health and wellness.

Ms. Dixon is the creator of an award-winning Web site, cancernutritioninfo.com [Editor's Note:



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This site is no longer active but links to <http://www.caring4cancer.com/go/cancer/nutrition>], that was named one of *Time* magazine's 50 coolest Web sites of 2005. She has delivered over 150 lectures to health professionals, patient groups and consumer audiences, and has developed and taught medical, nursing, public health and alternative medicine coursework.

Ms. Dixon has received awards from the American Dietetic Association for innovative nutrition education programs for the public, and distinguished practice in oncology nutrition.

Now, for our first speaker, Dr. Harris.

LYNDSAY N. HARRIS, MD:

Good afternoon. It's a great pleasure to be here. What I'm going to do today is review some information about triple-negative breast cancer that may be familiar to you, but also provide an update on the latest research that tells us about the behavior of this kind of breast cancer and what researchers and physicians are doing to try to improve the outcomes of women with this subtype of breast cancer.

In 2008, it's estimated that about a million women will be diagnosed with breast cancer worldwide. Of those, 172,695 will be diagnosed with triple-negative breast cancer. What do we mean when we talk about triple-negative breast cancer? It sounds like a diagnosis of exclusion because you're talking about the absence of three things. Let me describe why that is and what we think it means from a biological perspective to have a triple-negative breast cancer.

The reason it's called triple negative is that, classically, when we've diagnosed breast cancer, we've always tested for the estrogen receptor, the progesterone receptor and, more recently, the HER2 receptor. These are proteins that live on the cancer cells, breast cancer in particular, that we think drive the growth of these tumors. When we test for that in the clinic, when the patient is diagnosed, we always look for those three receptors. So, studies that were done to look at the biology of breast cancers always put it into perspective of the ER, PR and HER2 status of the tumor.

What was discovered, though, was that when you do gene profiling of breast cancers, in fact, there is a subgroup of breast cancers that can be identified by a gene expression pattern that do not have ER, PR and HER2, but yet they cluster tightly together. What I mean by that is that they can be recognized as a separate entity in multiple

different studies. And this particular entity, the subgroup that has lack of ER, PR and HER2, appears to have a worse prognosis.

So, researchers noted that this subgroup existed, and they looked at various features of these tumors, because it was important to understand why they all cluster together and what might be driving this worse prognosis. What they found was that these triple-negative breast cancers appear to have basal features – you may hear the terms basal-like breast cancer, basal tumor or basal breast cancer used fairly interchangeably now – and that this subtype of breast cancer is typically triple negative. Estrogen, progesterone and HER2 negative – in other words, it doesn't have those receptors.

But, it also has some positive features, meaning it has expression of certain types of proteins, and the proteins that give it the name basal-like breast cancer are proteins that are expressed on cells that are at the base of the breast cancer duct.

Let me describe what I mean by that. Think of the duct of the breast as the cylindrical tube that carries the milk out to the nipple, and it's important to realize that the vast majority of breast cancers arise from the duct of the breast. Basal breast cancers are almost all from the duct. And the location they appear to come from is not the lumen – not the center part, closest to where the milk comes – but the actual bottom of the duct.

So, if you think of the duct as a tube, the middle part closest to the empty space where the milk comes through is what we call the lumen. That's where the term luminal breast cancer comes from, because the cells that are closest to the lumen usually express the estrogen receptor and the progesterone receptor. Then, the cells that are closest to the base membrane where the duct – the tube – the outside of the tube are called the basal cells, and those cells appear to be the place where the basal-like breast cancers arise.

It turns out that may be the reason why they're estrogen and progesterone negative – because those cells are typically ER and PR negative. But, they also have specific proteins, the basal keratins, that define them and give them a certain pattern on a gene expression study.

So, these breast cancers that were recognized ... in Peru nearly ten years ago and have been called basal-like breast cancers may really arise from a separate place in the breast cancer duct. And so, they have a very specific phenotype or characteristic about them.

They also appear to have a fairly specific or predictable behavior. They're more rapidly growing compared with all of breast cancer. They're ER/PR negative compared with other breast cancers. And they appear to be more aggressive in the sense that they can spread more easily, they grow larger, and they are diagnosed at a larger size at diagnosis, typically. They can spread to lymph nodes. In some studies, there appears to be a higher rate of lymph node positivity.

The other thing that's noticed in the clinical studies of basal breast cancer is that for a given tumor size, the size of the tumor is larger compared with the number of lymph nodes that you would expect. But despite the fact that the lymph nodes are less likely to be positive for a larger tumor size, they do appear to still have a higher rate of recurrence. That means, to us in the scientific community, that they may actually spread in a different way than the lymph nodes. They may go through the bloodstream, for example.

There is evidence that that's true because many of the breast cancer studies show that they have more blood vessel infiltration, or angiogenesis, implying that it may be easier for cells to go through the bloodstream in this kind of breast cancer.

I think we all agree, though, from all the studies, that basal breast cancers, most of which are triple negative, are more aggressive. They also tend to occur in a different group of women than the average breast cancer. They're typically seen in younger women, women under [age] 50, or under 40, actually. The [cancers] tend to be later in terms of their stage [as they present] at the time [of diagnosis]. And if they do recur, they recur earlier in the average course of breast cancer follow-up; so, basal breast cancers are more likely to occur within the first three years as opposed to the average, say, luminal breast cancer that has an average recurrence rate later than [the first three years].

Now, if I can draw an analogy between this kind of situation, these breast cancers, and leukemia: We now know that there are acute leukemias that are very aggressive and very dangerous if not treated immediately; and there are more slow-growing types that can go on for many, many years. We're starting to see in the breast cancer field that the basal breast cancer is more like an acute leukemia-type of breast cancer. It's more aggressive, but it tends to recur early if it's going to recur, whereas the other types, the



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luminal types in particular, may be less aggressive but can recur late.

The good news is that if basal breast cancer is caught at an early enough stage and it's treated, it can be cured. And if it doesn't recur within that brief few years, it's extremely unlikely that it will recur. Similar to acute leukemia, we think its aggressive nature also implies that you would know fairly soon if it was going to come back again.

Now, there are many other subtleties about the diagnosis of triple-negative/basal breast cancer that I'd like to discuss with you today, some of which will need to wait until the question-and-answer session. If you look at all triple-negative breast cancers, probably 70 percent to 90 percent will be basal-like. Another 10 percent to 30 percent are non-basal triple-negative breast cancers that have a somewhat different behavior. They appear to have, in general, a better prognosis than basal breast cancers, some of which have a very favorable prognosis. So, not all triple-negative breast cancers are basal breast cancers.

The features of these other breast cancers are being very intensively studied. It's important to consider which markers may be present on a particular person's breast cancer. Let me tell you a bit more about what's recently been discovered. I know Suzanne is going to talk more about nutrition, so I'm not going to go into much detail, but there is some recent evidence that basal breast cancers and triple-negative breast cancers are, as I said, more frequent in younger women. They're also more frequent in women of color. Black women, Caribbean-American women and Hispanic women are all more likely to have triple-negative breast cancers.

Some studies suggest that having a higher BMI, or body mass index – being overweight – also carries a higher risk for triple-negative breast cancer. However, not all studies are definitive. There appears to be an association between higher BMI in premenopausal women and [triple-negative] breast cancer.

Another [finding] that was recently published is that oral contraceptive use appears to be a risk factor, particularly in triple-negative breast cancer, as opposed to luminal breast cancer. That's a bit of a surprise to us, given that [triple-negative] tumors are estrogen negative. There are complicated reasons why exposure to hormones may, in fact, induce these breast cancers, and we can talk about those if people are interested in hearing more.

It's been shown that the risk factors for basal breast cancer from the hormonal environment are slightly different than [those in] luminal breast cancer. It appears that women who start their periods early [and] have a higher number of pregnancies, or who were young at their first pregnancy, are at higher risk for triple-negative breast cancer. Shorter duration of breast feeding also appears to be a risk factor for triple-negative breast cancer.

These [risk factors] are somewhat different from [those] we typically think of as risk factors for breast cancer. We've known for a long time that starting menses at a younger age [is] a risk factor [for breast cancer]. It's been thought before that higher numbers of births or older age at first pregnancy were risk factors, but the opposite appears to be true for triple-negative breast cancer. The corollary to this [risk factor], of course, is that there may be very different hormonal risks associated with developing breast cancer, depending on the type of breast cancer that arises.

The other thing we know from the literature and our experience is that triple-negative breast cancers occur in younger women; younger women have more dense breast tissue, and increased breast density is associated with a higher risk of [developing] breast cancer. Screening modalities [for young women] may not be as effective as they could be [for] a postmenopausal woman, for example.

The studies that have looked at screening modalities in younger women have quite clearly shown that if you undergo screening, the digital mammography methodology is superior if you're premenopausal, [or] if you have dense breasts. The ability to pick up breast cancers at an earlier stage is improved with digital mammograms. So, we encourage women who are premenopausal to be screened with digital mammography, particularly if they have a family history.

The other question that may arise, and certainly has been discussed a lot, is whether there are other screening modalities that are better, or that should be added [to the standard]. Currently, breast ultrasound and breast MRI are both considered [appropriate] for screening, particularly [for women] in the premenopausal age range. Those modalities are recommended for women who are at higher risk [of developing disease] due to a family history of breast cancer, or a personal history of breast cancer.

I'd like to finish up the discussion and talk about the treatment of triple-negative breast cancer. We know that this kind of breast cancer is quite different from the other more common types, which are typically estrogen positive. That does not mean, however, that there aren't treatment options for women with triple-negative tumors.

In particular, we know that triple-negative breast cancers, while they appear to be more aggressive and occur, again, at a younger age, are also, in many cases, exquisitely sensitive to chemotherapy. The importance of this [finding] is that, while we don't [yet] have a drug that targets triple-negative or basal breast cancer . . . we know that chemotherapy [can] cure it. [Triple-negative] breast cancer is more sensitive to chemotherapy than estrogen positive breast cancer, and even sometimes HER2 [positive] breast cancer.

The response rates in all studies of ER negative breast cancer are always much higher [with chemotherapy] than they are in ER positive breast cancer. If caught early and given the appropriate treatment, many, many of [triple-negative] breast cancers can be cured.

When women receive chemotherapy prior to surgery and we look at the response rates, we've found basal breast cancers have the highest response rate [to chemotherapy] of all of the tumor [types]. Those women whose tumors completely shrink and disappear ultimately have the best survival.

It's really important, while we're looking for targeted agents for this group, to use the standard agents, which we know can be curative in many, many patients. Of course, targeted therapy is really the goal we aspire to, because we would like to have the "hormonal therapy" for triple-negative breast cancer, or the "HER2 therapy" – a targeted therapy [specifically for the triple-negative cancer] that goes after that specific tumor cell and spares the woman side effects as much as possible. Many, many studies have been done and published recently that look at [potential] targets in triple-negative breast cancer.

Triple-negative breast cancer is, in a way, a diagnosis of exclusion. But the more we study it, the more we realize that it isn't negative for other [characteristics]. It's simply negative for those three [traits] that [researchers have examined] – the ER, PR and HER2 [receptors]. In fact, triple-negative breast cancer has multiple tumor features, including receptors that we know are important in cancer growth.



Some of the receptors that have been shown to be present on basal breast cancers are the EGFR – that's the epidermal growth factor receptor – the MET receptor and the KIT receptor. A number of other proteins that are expressed [in triple-negative breast cancer] give us clues as to what makes those tumors tick.

Many different clinical trials are now ongoing to try to target these receptors. Typically, they're [open to] women with advanced breast cancer to see if [the treatments] are effective, and more effective, than standard therapy.

Another thing I mentioned earlier is that triple-negative breast cancers, and specifically basal breast cancers, can have a lot of angiogenic activity – in other words, a lot of blood vessels growing in the area. The large studies that were recently reported that led to approval of the drug Avastin for breast cancer showed that triple-negative breast cancers benefit from the addition of Avastin, which is a blood vessel-blocking drug, a VEGF inhibitor, that inhibits angiogenesis. Many studies are looking at adding Avastin to standard chemotherapy in the early-stage setting for triple-negative breast cancer and for other types of breast cancer. This is a strategy that people are very optimistic will be helpful in triple-negative breast cancer. [Editor's Note: A large trial of Avastin plus chemotherapy in early-stage breast cancer was stopped in September 2009 because several participants developed congestive heart failure. Avastin remains under study in other trials.]

Other areas of immense [research] activity are looking at other vulnerabilities of triple-negative breast cancer that could be used and targeted. Some of you may have heard [about] the association between the BRCA1 carrier status, or women who [have a] BRCA1 [mutation], and the development of basal breast cancer. We think most of the breast cancers that occur in BRCA1 carriers are triple negative and of the basal subtype. Recent studies suggest that those breast cancers may be more sensitive to a particular type of chemo[therapy], or [could benefit from] a targeted drug that takes advantage of the fact that these tumors are defective in DNA repair.

Two recent studies have shown triple-negative breast cancers have a very high response rate to a drug called Cisplatin. This is a chemo[therapy] drug, but it is particularly effective at inducing double-strand [DNA] breaks, and these [cancer] cells are unable to repair [the breaks] so the [cancer cells] quickly die. In addition, a small group of

women who were BRCA carriers underwent treatment with Cisplatin in Israel. This study showed that these women[s tumors] were highly sensitive [to the Cisplatin]. Their tumors – virtually nine out of ten tumors – completely disappeared with Cisplatin.

These studies are ongoing. Whether breast cancers not in BRCA carriers are equally sensitive to Cisplatin is an area of great research and is not proved, but many clinical trials are looking at Cisplatin as a chemotherapy that could potentially be used in [non-BRCA related triple-negative breast cancers].

The other targeted agent, which appears to be able to attack vulnerability in triple-negative or basal tumors, is a class [of medicines] called the PARP inhibitors. This class of drugs is able to knock out another DNA repair pathway, the idea being that the triple-negative breast cancers have a defect in one type of DNA repair pathway, and the other DNA repair pathway can be knocked out with the PARP inhibitors. This double-whammy effect leads to rapid death of [cancer cells].

There are additional targets – the HER3 receptor; the SRC protein dasatinib is an agent that targets the SRC protein. In preclinical studies, these [medicines] are shown to be more effective in triple-negative breast cancers or basal tumors [than in other tumor types] and are being [studied] in the setting of a clinical trial.

Finally – and I think Suzanne will give us a lot more information about nutrition and cancer risk – there is an emerging observation that triple-negative basal breast cancers may be more sensitive to the glycolysis pathway. [The glycolysis pathway] is the same pathway our cells use to uptake sugar and to cause cell growth [and] may be overactive in these basal tumors. So, the tumors, if you will, may become addicted to [sugars]. It's possible that drugs like Metformin and other insulin regulatory agents may be more active in [triple-negative] breast cancer [than in other types of disease].

Many, many approaches are being explored, and there's an enormous effort and an intense scrutiny of [triple-negative] breast cancer in the research field. A day doesn't go by when I don't hear about another study on triple-negative breast cancer, basal breast cancer, BRCA1-related associations with this kind of breast cancer. The breast, oncology and research communities have focused very hard on this type of breast cancer because it is aggressive and doesn't have a really satisfying treatment yet.

There is a great optimism here – because we see that, while [triple-negative] breast cancers are more aggressive, many have an excellent response to chemotherapy and can be cured. They are potentially curable by other means, such as lifestyle intervention, or are at least [potentially] preventable. Other targets are [under study in] active clinical trials.

Thank you all for listening. I'm happy to take any questions after Ms. Dixon has her opportunity to speak.

ELYSE SPATZ CAPLAN, MA:

Thank you so much, Dr. Harris. You gave a nice overview for our participants of some of the most common sort of markers and identity for triple-negative breast cancer. Then, moving into the research and treatment arena also helped illuminate some promise as it relates to the research process and what types of chemotherapy treatments may be most sensitive to triple-negative breast cancer and what other types of agents, like the PARP inhibitors, we need to keep our eyes open to for the future.

With that, please welcome Ms. Suzanne Dixon to our program today.

SUZANNE DIXON, MPH, MS, RD:

Thank you so much. I first want to say that I'm very pleased to participate in this program. I thoroughly enjoyed Dr. Harris' part of the presentation, as I'm sure did all of you, and learned a lot. I'm pleased to be able to offer you some information on the connection between nutrition and triple-negative breast cancer.

I'm not going to take up too much time. I'm just going to spend a few minutes going over some of the more exciting research that is going on in the arena of nutrition and breast cancer and, in particular, findings from some research on ways that nutrition can be used, hopefully, to reduce the risk of recurrence of triple-negative breast cancer.

It's important for women to be able to have ways to tackle a diagnosis like triple negative in as many ways as they can. We know, as Dr. Harris explained so well, that some of the typical standard treatments that are used with estrogen receptor-positive breast cancers, which are more common, are not effective for triple-negative breast cancer. In this sense, I feel like it's even more exciting when we can come up with some lifestyle interventions – things such as diet and exercise – that can give that extra edge to women who have [a triple-negative] diagnosis so they can take those things,



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implement them in their lives, gain a sense of control and hopefully reduce their risk of recurrence.

The first thing I want to talk about is a study that's been ongoing for a while. It's called the Women's Intervention Nutrition Study [<http://www.ncbi.nlm.nih.gov/pubmed/17179478?dopt=AbstractPlus>], or WINS, and it's a really exciting bit of research. It's a long-term study looking at a low-fat diet intervention for women with breast cancer.

When WINS was first designed, researchers didn't know exactly what to expect. Their hope was if women with breast cancer were put on a low-fat diet, it would reduce their risk of recurrence. The conventional thinking for many years has been that one of the ways a low-fat diet might help reduce risk of not only getting breast cancer the first time, but also getting breast cancer a second time, is that extra fat on the body, and possibly extra fat in the diet, seems to promote our bodies to produce a little bit of extra estrogen.

The feeling was that a low-fat diet would be great for those estrogen receptor-positive cancers. Interestingly, what was found and what's very exciting is that this type of diet intervention was more effective for women with triple-negative breast cancer.

This study looked at about 2,500 women with all different types of breast cancer and got all the information about who had what types of tumors and what types of treatments they were receiving. The women were randomized either to get a low-fat diet intervention or to eat their normal, typical diet.

After about five years, the researchers found that the diet didn't seem to be that effective at helping women with estrogen receptor-positive breast cancer to reduce their risk of recurrence, but it was incredibly effective for women with estrogen receptor-negative breast cancer.

When the researchers looked at the results as a whole, they didn't really see anything very exciting, but when they separated out the women who had ER negative breast cancer, they found that those women who followed the low-fat diet closely seemed to have a 40 [percent] to 50 percent reduced risk of recurrence.

This is pretty exciting. It points to the fact that there's a lot we don't understand about this disease, and it also points to the fact that sometimes, things we might not expect to be helpful can actually be quite helpful. This is what

the case has turned out to be from WINS, and after about five years of research, this is what [the researchers] found: The low-fat diet seemed to be most beneficial for women with estrogen receptor-negative breast cancers in terms of helping them reduce their risk of recurrence quite significantly.

I'm sure you want practical information. You say, "Okay, what exactly is a low-fat diet? How low-fat? What were these women doing? What were they eating?" One thing that's important to note is that these women had a lot of support. The ones who were assigned to the low-fat diet had a lot of support to help them achieve this type of low-fat diet, because, as we all know, in our current food climate in the United States, it's not easy to eat a healthy diet, and it's certainly not easy to eat a low-fat diet. You really have to work at it in order to achieve the type of low-fat diet that seems to be most beneficial for women with triple negative, or at least estrogen receptor-negative breast cancer.

This study made it a goal to get the dietary fat intake down to about 15 percent of calories from fat. That is very, very low fat, and it's not easy to achieve. But the researchers found that the women actually ended up eating about 23 percent of their calories from fat, compared with a typical woman who would probably eat about 35 percent of her calories from fat.

In terms of fat grams, the women on the low-fat diet seemed to eat an average of 30 to 33 grams of fat per day, while the women in the other group, the ones who did not get the diet intervention, were eating more like 50 to 60 grams of fat per day. That's quite a bit difference in the fat intake. What these numbers tell you is that it's not easy to follow a low-fat diet, but it is possible. If you want to do this, you need to get support from a doctor, a dietitian, a nutrition support group – some way to [get] the tools you need so that you can succeed.

The second thing is, if we want to get down to 20 [percent] to 25 percent of our calories from fat, we should aim lower. We should aim closer to 15 [percent] to 20 percent; that gives people a little wiggle room. If you're aiming for 15 [percent] to 20 percent of your calories from fat, it's pretty likely that you're really going to be eating 20 [percent] to 25 percent of your calories from fat. The hidden fat creeps in, and it turns out that we all eat a little more fat than we realize on a regular basis.

Tip number one is that we want to aim low in order to achieve this type of an intake. Tip number two is, if you don't actually hit that goal, that's okay, because we know the actual amount of fat in the diet was about 23 percent for the women who had this terrific response with this type of intervention.

The other thing that is important to note is that these women had a lot of support. They were given interventions with a registered dietitian, and the approach was to use behavioral, cognitive and motivational counseling techniques to help them follow this low-fat diet and [stay] excited about it, obviously wanting to achieve that [challenging] type of a goal.

These women got two counseling sessions a month with a dietitian for about four months, [for a total of] eight sessions. Then they were put on a maintenance plan from about month five of the study to about year five of the study. They saw a dietitian about once every three months. They also had some optional monthly group sessions that they could [attend].

These women also kept diet records, and they did daily fat gram counting. In other words, self-monitoring is important if you want to achieve these types of goals – also, setting some goals and working with someone who can help you when you backslide and have a little trouble meeting [your] dietary goals.

[The researchers] focused on five key behavioral points to help these women get this type of low-fat diet to work for them. One was appetite, and that is recognizing the difference between physiologic hunger, or the actual need to eat, versus wanting to eat because of all sorts of other things, such as emotion, or stress, or because you're celebrating, or because there's just food in front of you. That was a key component – helping women recognize how to cue into their appetite.

Also, addressing environmental cues – external cues that we get that trigger us to eat. Things like advertisements and billboards, and driving by a McDonald's or walking through a mall and smelling french fries – those kinds of things are external cues that can make people want to eat even when they're not hungry, so some techniques were put in place to deal with [external cues].

Dealing with high-risk situations – holidays, eating out at restaurants, special occasions, those kinds of things – you need to have a plan in place to keep your healthy eating going.



Addressing negative thinking, self-defeating thoughts – this is, I think, vitally important for anyone who wants to make significant diet changes to address their health risks. It's really easy if you're trying to do something tough, like follow a really low-fat diet, and you slip up to sort of beat yourself up. [Doing so] is not only counterproductive but also will make it even less likely that you get back on track and get yourself going again. There are creative ways to address what we all go through when we feel like we've failed to take care of ourselves as well as we should.

Social eating was the fifth component – in other words, trying to come up with some strategies for eating well when you're out in social settings, which, as we know, can be full of all sorts of tempting, not-so-good-for-us foods.

The WINS is so important. The reason I spent so much time on it is because it is one of the few randomized, controlled trials [of the role of diet in breast cancer]. It wasn't just an observational study. Women were assigned to eat a certain diet. It was long-term, and it showed great success, specifically for ER negative breast cancer. I think that's incredibly positive.

The other nice thing that comes out of this research is that . . . the research community has homed in on the effects [the low-fat diet] may have on estrogen in our bodies, but it turns out that some of these things Dr. Harris mentioned, such as insulin in the body and how our bodies respond to food and how much insulin we produce, [also] may be important, and they make really good targets for lifestyle changes.

Another thing to note about this study is that the women who were on the low-fat eating plan did lose a little bit of weight. [The impact on the risk of recurrence in triple-negative breast cancer] may have been partly [attributable to] the low-fat eating plan, and it may have been a little bit [attributable to] the weight loss. It's important to note, though, that the weight difference between the groups is about six pounds. It's not a huge amount. It's possible that that little bit of weight loss may have contributed to the ability to help lower risk of recurrence of ER negative breast cancer, but probably a big part of that reduced risk was the low-fat eating in and of itself.

The other study I want to mention is the Women's Healthy Eating and Living, or WHEL, study [<http://www.cancer.gov/clinicaltrials/results/WHEL0907>]. It didn't look specifically at ER negative or triple-negative breast cancer, but

it looked at a very intensive fruit and vegetable intervention. Again, it was like the WIN study in that women were randomized either to receive diet counseling to follow a regular diet, or to get intensive counseling so they were eating many, many servings of fruits and vegetables and trying to follow a low-fat diet [that included] a lot of fiber. We're talking on the order of ten to 12 servings of fruits and vegetables a day.

That study showed, interestingly, that this very intensive fruit-and-vegetable intervention didn't make a huge difference for reducing risk of recurrence in any type of breast cancer. [This result] may, on the surface, seem discouraging. But more research has been published since then. In 2007, a study was published in the *Journal of Clinical Oncology* [<http://jco.ascopubs.org/cgi/content/abstract/25/17/2345>] that was really encouraging for women with all types of breast cancer. While the very intensive fruit-and-vegetable intervention alone didn't seem to help, this [new] research showed that women who had a moderately high intake of fruits and vegetables – in other words, at least five servings a day of fruits and vegetables – coupled with 30 to 40 minutes of moderate-intensity activity a day, six days a week, had about a 50 percent reduced risk of recurrence.

The exciting thing about this [finding] is that the reduced risk of recurrence held across all types of weight categories. Obese women, or overweight women, [had a reduced risk of recurrence] if they ate the five servings of fruits and vegetables a day and got exercise, even if they didn't lose a pound.

In a way this [finding] is encouraging, that you don't need to "go crazy," so to speak, and focus only on eating nothing but carrots and celery. It turns out that moderate diet changes along with moderate regular physical activity seemed to be very beneficial for women with a history of breast cancer.

The takeaway message is that we need to focus on a low-fat diet, we need to focus on getting in a lot of healthy foods, but we don't need to beat ourselves up and struggle to get in 15 servings [of fruits and vegetables] a day. We also need to get regular physical activity. This is probably really important for triple-negative breast cancer because, as Dr. Harris mentioned, we're now seeing research looking at insulin as a potential, important way in which we might be able to help treat and manage this breast cancer.

It turns out that exercise and a healthy diet will reduce insulin levels in your body and help your

body process the food that you eat more effectively. You don't get the spikes in the blood sugar, you don't get the spikes in the insulin in your body, and that seems to be beneficial for this particular type of breast cancer in terms of giving your body a healthy environment in which to manage this type of breast cancer.

The last thing I want to say [before I] open it up to questions, because I know you all probably have a lot of questions, is that a lot of people ask me about dietary supplements. This is a really popular area of interest for most people with breast cancer, not just women with triple-negative breast cancer, but in all of breast cancer and other types of cancer. With the patients I've worked with over the years and the people I've talked to, and in giving a lot of lectures and classes and talks, the issue of dietary supplements comes up over and over and over again.

I'm happy to take particular questions if people have them about this arena, but one thing that is very important to keep in mind is that, by and large, research has not supported that individual nutrients that you take in the form of a dietary supplement are particularly helpful for reducing cancer risk.

There's been a lot of research in this arena, and so far, what appears to be most important is that you get your vitamins, minerals, phytochemicals – all those healthy things we find in foods – in food form. There doesn't seem to be a huge benefit to taking concentrated, isolated sources of vitamins and minerals. . . .

There is one exception, and that is vitamin D. I bring up vitamin D because it's a very important nutrient, and it is the one thing – I always say, no one will ever hear me recommending dietary supplements other than vitamin D. That's my one exception.

There was a really interesting study that looked at vitamin D at diagnosis – in other words, how much vitamin D is in the body, and how likely it is that a woman would have a breast cancer recurrence [if she had adequate levels of vitamin D in her body [http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=55&abstractID=31397]. Now, this type of study cannot prove cause and effect. It doesn't tell us that if you are low in vitamin D, that's what caused your breast cancer to recur. What it does tell us is that there is some connection between vitamin D and breast cancer, and not having enough of it in your diet and in your body may



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be detrimental in keeping your cancer at bay and not having a recurrence.

This study noted that women who were vitamin D deficient at the time of their diagnosis were about twice as likely to have a recurrence or a metastasis of their disease. Again, we can't say that the vitamin D, the low levels in the body, caused [the recurrence or metastasis], because it's quite possible that the disease itself is what caused the low vitamin D. We don't really know [the answer], but [this question] is something that's important to take a look at.

In this study, the group of women who were newly diagnosed with breast cancer were followed – and the study looked at about 500 women – only 24 percent of them had adequate vitamin D in their bodies. In other words, 76 percent of the women in this study were low in vitamin D. They were classified as either “vitamin D deficient” or “vitamin D insufficient.”

It's very easy to get a blood test for vitamin D, so I encourage all people – not just women with breast cancer – to go ahead and get that checked out, because being low in vitamin D is really common in this day and age. . . . I wouldn't ever recommend that someone go and load up on vitamin D without knowing that they needed it, but you can talk to your doctors and ask if they can check that for you. And if you need a dietary vitamin D supplement, you can add it in.

I'm going to finish up here, and I think we're ready to open it up for questions.

ELYSE SPATZ CAPLAN, MA:

Well, Suzanne, thanks for running through some of the larger studies that have been done looking at diet, nutrition and breast cancer. It's a huge arena that I know we need to continue to study to get more answers. We appreciate your contribution to today's program to add to the medical research, as well as some of the lifestyle research.

Without further delay, I would like our operator to come back on and let folks know how to get into the question queue. My one reminder is we'd like to get to as many questions as possible, so please keep your question as broad as it can be. The speakers cannot manage an individual consultation, as you can imagine. Keep it broad and keep it short so we can get to as many of you as possible. Thanks so much.

OPERATOR:

Our first question comes from Hanover, New Hampshire.

CALLER:

Hi. Thank you so much. This has been very interesting. I was wondering if there are any particular foods that you would either encourage or suggest we avoid for women who've had triple-negative breast cancer. In particular, given that there's a complex relationship between hormones and triple-negative breast cancer, are soy-type products a good thing or a bad thing [to eat]?

Also, I read [that at] Johns Hopkins, they were encouraging [people to eat] BroccoSprouts, [which are] like broccoli bean sprouts. Are those something you should be having on a daily basis or not really? [Editor's note: researchers at the Johns Hopkins University of Medicine developed this product: <http://www.broccosprouts.com>]

ELYSE SPATZ CAPLAN, MA:

I'd first like Dr. Harris to answer it from the medical oncologist perspective, and then have Suzanne add her viewpoint.

LYNDSAY N. HARRIS, MD:

Okay, great. I think it's a great question, and the issue of soy in the diet comes up an awful lot in our conversations with our breast cancer patients. Remember that soy contains weak estrogens, phytoestrogens, which are naturally occurring compounds, but they bind to the estrogen receptor and have activity. The issue really is, is it safe to take soy products? Is it [dangerous] to take soy products? And does it matter if your tumor is estrogen positive or estrogen negative?

I tell my patients we do not know enough about the activity of soy and phytoestrogens against breast cancer cells to say that they are safe when taken in large quantities. I counsel my patients to use them sparingly, or use them as you would most [foods in your diet] – you know, not as a staple necessarily, but intermittently in your food intake.

That's my opinion on soy. Until we know a lot more about the activity of these natural estrogens on both ER-positive and ER-negative breast cancers, it's difficult to recommend anything specific other than moderation.

ELYSE SPATZ CAPLAN, MA:

Suzanne, do you have something to add?

SUZANNE DIXON, MPH, MS, RD:

Yeah. The question about particular foods I would encourage: One thing that is so vitally

important is that women understand that what seems to be most beneficial is the total pattern of eating. In other words, I would not put all my eggs in one basket and say, “I should definitely get soy,” or “I should definitely not get soy,” or “I should definitely eat grapes,” or “I should definitely not eat grapes.”

The key is to get as much variety and as much [nutrition] as you can from plant foods. The more you can get from fruits, vegetables, whole grains, legumes, beans, peas, lentils, all those kinds of things, the better.

People say, “Well, what about reading nutrition labels and these sorts of things?” I always say you don't need a nutrition label to tell you that an apple is good for you, and you don't need a nutrition label to tell you that broccoli is good for you. If it's a food that has a label, you probably shouldn't eat that much of it anyway. I think basing our diet around whole plant foods is key for health.

I encourage cruciferous vegetables. They're incredibly healthy foods. They [take] a lot of actions in the body. One area of research that has been of interest to a lot of food scientists is this question of how [cruciferous vegetables] affect estrogen metabolism, and they seem to affect it very favorably. They seem to push the body to make the natural estrogens that we produce – there are lots of different varieties of estrogens, and some are stronger and some are weaker. And it seems that when you eat cruciferous vegetables, it pushes your body to produce more of the weaker, what I call “softer” estrogens, which don't have a strong activity in the body. Eating cruciferous vegetables pushes your body to produce a better ratio of [“softer”] estrogens, so they're positive in that way.

A lot of people say, “Well, what about for estrogen receptor-negative tumors?” But there are so many activities about these foods that have nothing whatsoever to do with estrogen. For example, cruciferous vegetables help the body detoxify. When your body comes across something that is a toxin, say, from cigarette smoke or something you've breathed or eaten, or anything you might encounter in your daily life, your body will package that up and get it ready to excrete in your urine or your stool. You can turn up the speed and the efficiency of how your body packages up those little toxins that we're all exposed to every day, all day long, and get them out of your body.

Cruciferous vegetables [are] great for detoxifying. A lot of people are interested in this concept of detoxing ... There isn't any evidence



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that any fancy detox diet is going to do anything for you, but there's plenty of evidence that eating a lot of healthy cruciferous vegetables – broccoli, cauliflower, chard, kale, bok choy, all those green, leafy things – will help your body detox and take better care of itself. So, I encourage [eating them]. But, by and large, focus on plant foods, focus on variety.

In terms of soy, which, as Dr. Harris mentioned, comes up over, and over, and over again, I strongly discourage people from taking any concentrated soy dietary supplement – soy powder, soy pills, isolated isoflavones. That's the type of phytoestrogen that's found in soy. I do not think we know enough to say that [concentrated soy supplements are] safe or helpful.

Soy foods are perfectly fine and healthy if you eat them in moderation. The American Cancer Society [<http://www.cancer.org>], which tends to be on the conservative side, has come out with a statement saying that the amounts of soy that are typical in an Asian diet, which is where this whole idea came from – so, a serving or two a day – are safe and okay for women with a history of breast cancer to eat. I adhere to not going toward the supplements or the pills, or the soy protein powders, anything like that. Also, there's no reason to eat a lot of processed soy foods – soy chips, and fake soy meats and all those things. They tend to have more fat, more sodium.

I encourage women, if they want to include soy, to go for those traditional soy foods that we know have been eaten for thousands of years in the typical Asian diet – so, tofu, tempeh and standard foods that we know people have eaten for many, many years with –.

ELYSE SPATZ CAPLAN, MA:

Suzanne, I think between you and Dr. Harris, we have a lot of information. Soy is a huge topic for everyone concerned about breast cancer. And due to timing –.

SUZANNE DIXON, MPH, MS, RD:

Sure –

ELYSE SPATZ CAPLAN, MA:

– I would like to move on to our next question and hope that everyone who listens to the answers just keeps in mind, as we always say here, that it's an individual conversation with your healthcare team, your oncologists, etc., as to what may be safe or effective. This is certainly an area for a lot of ongoing research, and we're glad to see that we're looking at some of the kinds of clinical research

that is needed so we can answer this question much more clearly in the future. Thanks to both of you. Can we move to the next person?

OPERATOR:

Yes. Our next question comes from Chicago, Illinois.

CALLER:

Thank you very much. I just want to thank Dr. Harris and Suzanne for their information. As an employee of Breast Cancer Network of Strength [<http://www.networkofstrength.org>], I am here professionally, but also personally, being a triple-negative breast cancer survivor myself. At the age of 34, I was diagnosed. I'm currently 38, four years cancer-free.

My question is [whether there are] any statistics showing how effective radiation has been for [treating] triple-negative breast cancer. Also, with how high the statistics are for the BRCA1 gene showing in triple-negative breast cancer patients, why aren't more patients being encouraged to participate in genetic testing [for BRCA mutations]?

I'm just a little concerned, with triple-negative breast cancers [that are] BRCA1[-related], that [these cancers] can go on and affect not just our daughters but also our sons. Why isn't there more of a push toward genetic testing for these triple-negative breast cancer patients in addition to the radiation component? Thank you.

ELYSE SPATZ CAPLAN, MA:

Dr. Harris?

LYNDSAY N. HARRIS, MD:

Yes. Those are really great questions –

SUZANNE DIXON, MPH, MS, RD:

Uh-huh.

LYNDSAY N. HARRIS, MD:

Thank you for asking them. To take the first question, Dr. Bruce Haffty's group published that women with triple-negative breast cancer had just as much benefit from radiation – with lumpectomy and radiation, breast conservation – as women [who have other types of breast cancer; <http://jco.ascopubs.org/cgi/reprint/24/36/5652.pdf>]. The observation is that triple-negative breast cancers can be safely treated with radiation – with lumpectomy and radiation.

It's true that younger women do appear to have a higher risk of local recurrence, but it's a complicated question because we know that, as you mentioned, the genetic predisposition in

younger women is more likely. How much of that is related to genetic predisposition and how much is related to radiation not working has been a bit of a controversy. The evidence now is fairly comfortably in favor of breast radiation for women who want to undergo breast conservation, provided there's no other reason why they're unable to.

The second part of the question is the BRCA1 carrier/triple-negative breast cancer relationship, and why genetic testing isn't being encouraged. I think it is being encouraged, [but] it depends, of course, on the institution. Judy Garber's group from Dana-Farber Cancer Institute recently published that roughly 10 percent of women with a diagnosis of triple-negative breast cancer have a BRCA mutation – between 9 and 10 percent. That's not, obviously, 100 percent, but [the rate of BRCA mutation] is higher than you would expect for all women coming in with a [breast cancer] diagnosis.

In our practice, and I think in many practices in the country, when we see someone with a triple-negative breast cancer, particularly a woman younger than [age] 50, we refer her for genetic counseling. That is an important point to make. As you say, it affects not only the woman herself, regarding what kind of prophylactic treatment she may wish to undertake, but also her daughters and her sons, because we know that the BRCA gene is an autosomal gene. [The BRCA gene is] not on the sex chromosomes. It's on chromosome 17, so [if a woman has a BRCA mutation, it is] just as likely her daughter or her son could inherit it.

While the risk is still quite low – we know that less than 10 percent of patients with a diagnosis of breast cancer will have a strong dominant genetic predisposition – we think the triple-negative breast cancers do enrich for a group of women who are more likely to carry the BRCA gene mutation.

ELYSE SPATZ CAPLAN, MA:

Okay. Thank you for that excellent question. We're going to move to the next question, please.

OPERATOR:

Our next question comes from . . . California.

CALLER:

Hi. I want to ask Dr. Harris a question about the Avastin, the blood vessel blocking agent. Is that something that's used now for treatment, and when did they start using that?



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LYNDSAY N. HARRIS, MD:

Right. Avastin is now approved by the FDA for women with advanced breast cancer, meaning it's gone beyond the breast into other places in the body. We frequently use Avastin in combination with paclitaxel, or Taxol – that's how it's approved by the FDA – for women with recurrent breast cancer. That, of course, includes women with estrogen negative and estrogen positive breast cancer. It has been shown in the clinical trials that led to the approval of that drug that [women with] triple-negative breast cancers benefit just as much as women with estrogen positive breast cancer, for example, so we do believe it's a good treatment option for women with advanced breast cancer.

In the early stages of breast cancer, Avastin is being looked at in clinical trials. At least ten trials that I'm aware of are incorporating Avastin to either preoperative, or adjuvant, therapy – in the setting of a clinical trial, with the whole idea being that this may be a good approach to take in addition to the standard agents to improve outcome. [Editor's Note: To find clinical trials, visit clinicaltrials.gov]

I have to say, though, we don't know the answer to [the question of using Avastin in early-stage triple-negative breast cancer], and while we are very optimistic that it will [offer] an added advantage to women with triple-negative breast cancer, we need the clinical trial data to prove it, because it doesn't always follow that what we see in metastatic breast cancer occurs in early stage. [Avastin also] has toxicity. There are complications with bleeding and clotting that occur on Avastin, [and it is also an expensive medicine]. . . .

ELYSE SPATZ CAPLAN, MA:

Okay, thank you.

OPERATOR:

Our next question comes from Las Vegas, Nevada.

CALLER:

Hi. I want to ask a question for people [with cancers] like [mine], slightly estrogen positive. It's been, I know, very controversial, to use Femara, or one of the [aromatase inhibitors, for cancers like mine.] I wanted to get your opinion regarding that.

Also, if you could address possibly [it], I've read some research regarding BRCA "down regulation," [that] even if [the cancer] turned out to be negative on both [BRCA1 and BRCA2], it changes with the basal.

LYNDSAY N. HARRIS, MD:

I can take that if you like, Suzanne.

SUZANNE DIXON, MPH, MS, RD:

Oh, yes. Please do.

LYNDSAY N. HARRIS, MD:

Okay. The first question, I think, is a little easier – there are certainly enough studies that say if you have any estrogen positive cells, you may benefit from hormonal therapy. Typically, we would recommend it – an adjuvant treatment with an antiestrogen, either an aromatase inhibitor, such as Femara, or tamoxifen, depending on your menopausal status and other features.

It may be that lower levels of estrogen receptor are associated with less benefit from hormonal therapy, but it's been hard to show that there's no benefit whatsoever, or [that there's no benefit with people who have] low levels. It's also very difficult to know what the cutoff should be [for estrogen positivity]. At the moment, we tend to treat "ER poor" or "ER low," but not ER negative, breast cancer with hormonal therapy. The actual decision [should be made based on] your risk of recurrence, though, and [taking into account] the risk/benefit ratio for you. That's a discussion to have with your physician.

The second question I [am] a little bit less clear on. Down regulation of BRCA1 can occur without mutation in the gene... Unfortunately, we don't have good tests that help us understand which breast cancers have down regulation of the gene but don't have a mutation. The tests themselves are not that reliable yet, and the genetic testing, other than sequencing and looking for a mutation, has not been [FDA] approved because it isn't reliable. A lot of [research] is being done in that area.

We hope to know better in the future if there are patients who are predisposed to breast cancer because they have something in their genes that makes the level of BRCA lower, but they don't actually have a mutation. Those tests are not yet available clinically, but people are working hard on those.

ELYSE SPATZ CAPLAN, MA:

Okay. Thank you for that, Dr. Harris.

OPERATOR:

Our next question comes from Havertown, Pennsylvania.

CALLER:

Yes. Hi, Dr. Harris and Suzanne. I appreciate all of your help. My question has to do with the blood test CA 27.29. I was diagnosed in October with triple negative. I had stage II and had the lumpectomy. I did the four rounds of chemo. [The cancer] was in two of my lymph nodes, and now I'm doing radiation.

My doctor told me when I started [treatment] – before I started chemo – that [my] blood test was 218, and when we finished, it was 228. All of my tests have been negative, and everything I'm reading about this blood test [says] that it's not very efficient and there are a lot of false positives. I wanted to know what your thoughts are on this test.

My doctor has said he will repeat this test as much as we can, but what are your thoughts on this test? He's thinking maybe there's still something going on in my body.

LYNDSAY N. HARRIS, MD:

I need to ask for a clarification. . . : Are you a BRCA carrier? Is that right?

CALLER:

I'm not a BRCA carrier. . . . I went through the [genetic] counseling, and since there's no family history, I'm the family history. They said I don't qualify through my insurance to have the test, and they thought I was at a very low risk to have [a mutation in] the BRCA gene.

LYNDSAY N. HARRIS, MD:

Okay. And you're doing the CA-125?

CALLER:

No, the blood test that he said he drew that's still high is CA 27.29.

LYNDSAY N. HARRIS, MD:

Uh-huh. Uh-huh.

CALLER:

And that was at the end of my chemo.

LYNDSAY N. HARRIS, MD:

Okay. The CA 27.29 is a blood tumor marker. It's a protein that is made by some cancer cells and shed into the body. We sometimes measure [the CA 27.29 level] in early-stage breast cancer, [but] it's typically not recommended [in this setting]. The reason – and we just published the ASCO [American Society of Clinical Oncology] guidelines on this about a year and a half ago – is that while [the test is helpful for] prognosis, it doesn't appear to be useful for making treatment



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decisions. [<http://www.asco.org/ASCOv2/Practice+%26+Guidelines/Quality+Care/Practice+Guidelines/Clinical+Practice+Guidelines/Assays+and+Predictive+Markers/American+Society+of+Clinical+Oncology+2007+Update+of+Recommendations+for+the+Use+of+Tumor+Markers+in+Breast+Cancer>]

Provided that you've completed the course of therapy that we would typically recommend for known [lymph node] positive breast cancer, which it sounds like you have, following people with these tumor markers has never been shown to be useful. So, the question arises, what's the purpose of following [the marker] other than creating anxiety? The current recommendations of the ASCO tumor marker guidelines, and my recommendations, are not to follow CA 27.29 or I5.3 or CEA in early-stage breast cancer patients because there's no evidence that they improve outcome or help you make a treatment decision.

ELYSE SPATZ CAPLAN, MA:

Okay, I think that's really helpful. I know that tumor marker tests are definitely a question that comes up because different doctors follow different practices, and it always gives rise to questions that women have moving forward at the completion of treatment. We have time for one last question.

OPERATOR:

Our last question comes from Southside, Alabama.

CALLER:

Thank you. This question is for Dr. Harris. Recently, I was diagnosed with a second primary breast cancer that is triple negative with a metastatic lesion to the lung. I've had a wedge resection of the lung and am taking Avastin as well as Ixemptra. I didn't really hear you speak about Ixemptra, and I wanted to know what you thought about this drug and its effectiveness.

LYNDSAY N. HARRIS, MD:

Ixemptra is ixabepilone. It's a new class of chemotherapy drugs that is approved for breast cancer. It's definitely active, meaning it's good at shrinking breast cancer. The question we are all struggling with at the moment is where it should be placed in terms of the armamentarium, if you will, of treatment options. Because I'm not as familiar with your [specific case], I don't know the answer to why this [regimen] was chosen over paclitaxel, which would be the standard [treatment]. I can tell you from what we know about the behavior of breast cancer that both Avastin and ixabepilone are active agents.

We typically use paclitaxel and Avastin. Other agents have been looked at in combination with Avastin. But the only randomized data that exist currently are with paclitaxel and Avastin, and with docetaxel, or Taxotere, and Avastin. And both of those show an advantage to adding the Avastin to a taxane.

What makes us a little concerned about adding Avastin to different drugs is that there are now two studies that looked at using Zeloda with Avastin that were not particularly encouraging. In fact, one was completely negative, showing no benefit of adding Avastin to Zeloda, and the other was not very encouraging, although it wasn't randomized.

In general, both of those drugs are active. If there's a reason you can't get a taxane, [the Avastin and Ixemptra] is an understandable choice.

CALLER:

Would it be because I had Taxol with my first cancer? I had an estrogen negative, progesterone negative but HER2 positive breast cancer, [for] my first primary. So, I had the AC [Adriamycin, Cytoxan] and the T [Taxol] – and Herceptin.

LYNDSAY N. HARRIS, MD:

How long ago was that?

CALLER:

I was diagnosed in June 2006, and then was diagnosed in February 2009 with this new cancer.

LYNDSAY N. HARRIS, MD:

Right. That may be the reason your oncologist chose to use [a different regimen]. I would just mention to the audience that the clinical trial that led to the approval of Avastin with paclitaxel was both for women who have had Taxol before and also for women who hadn't.

Women who had previously [taken] paclitaxel in the adjuvant setting also benefitted from the addition of Avastin to the paclitaxel. [<http://content.nejm.org/cgi/content/full/357/26/2666>]

ELYSE SPATZ CAPLAN, MA:

Dr. Harris, you raise a very important point as it relates to clinical trials, which is probably a good note for us to tie things up on. And that is, participation in clinical research is vitally important for us to get answers to improve treatments for all breast cancers, obviously, including triple negative, and that what you just highlighted, Dr. Harris, is something that's really important, in that the Avastin/Taxol study was using Taxol in women who previously got it.

What I'd like participants to take away is, again, our programs are designed to help you get information so you can formulate questions to take back to your oncology team and find out what applies best to you. I think hopefully some of what you learned from Dr. Harris' response, and others who are on the call who may have similar questions have learned from this answer, is to keep your questions going, and sometimes using drugs previously may be introduced again in certain specific settings.

With that, typically, I would like to ask speakers for any closing remarks, but I think we're out of time. I very much would like to thank Dr. Harris and Ms. Suzanne Dixon for their time and expertise in today's program. You really covered a lot of information, and I hope our participants have a lot of good news to take forward with them and provide hope for the future.

Again, thank the Triple Negative Breast Cancer Foundation so much for the generous collaboration and spreading the word. And we continue to look forward to the development of our *Guide to Understanding Triple Negative Breast Cancer* brochure that Hayley mentioned we're working on in 2009.

Again, fill out your evaluations, and please stay in touch with us at [lbbc.org](http://www.lbbc.org) [<http://www.lbbc.org>] and tnbcfoundation.org [<http://tnbcfoundation.org/index.html>]. Thank you, everyone, and I hope you have a good rest of your day.

[END OF TRANSCRIPT]