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# Breaking News from the 2009 Annual Meeting of the American Society of Clinical Oncology

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Virginia Kaklamani, MD, DSc

## ELYSE CAPLAN:

Thanks to everyone for making time today to learn the latest news that was presented at the Annual Meeting of ASCO [American Society of Clinical Oncology; <http://www.asco.org>]. Today's program will educate all of you on the latest research and clinical trials that were unveiled at this year's annual ASCO meeting, the largest annual medical conference on cancer treatment in the United States.

My name is Elyse Caplan. I'm the education director at Living Beyond Breast Cancer [<http://www.lbbc.org>], and I'm pleased to serve as the moderator for today's program. Many of you know that the ASCO meeting is a time in the spring when scientists, researchers, oncologists and survivor advocates gather together to hear the latest research that affects the cancer community. A lot of information on breast cancer is presented at this annual meeting. More than 30,000 people from across the world gathered just a couple of weeks ago in Orlando, Florida, for the 2009 meeting. Some of the things that you're going to hear about [pertain to] early stage cancer, advanced, or metastatic, breast cancer and quality of life. . .

. . . I would like to tell you about our featured speaker today, Dr. Virginia Kaklamani is assistant professor of hematology/oncology and the director of translational breast cancer research at Northwestern University in Chicago [<http://www.northwestern.edu>]. She completed her fellowship in hematology/oncology and received a master's of science degree in clinical investigation at Northwestern in 2003. Dr. Kaklamani has a certification from the American Board of Medical Oncology [<http://www.abim.org>]. Her clinical interests include breast cancer and cancer genetics, and her research interests include high-risk families and the roles of exercise and diet in breast cancer. I'm very pleased to welcome Dr. Kaklamani.

## VIRGINIA KAKLAMANI, MD, DSc:

Thank you so much. We're going to focus today on what I consider the most important studies that were presented at ASCO this year. [But] I want to spend most of our time on questions, because that's where we will all understand what your main thoughts are, and we'll try to answer all of your questions.

[Let's start with] updates on surgery. [One of] the intriguing things that we've been dealing with in the past few years is lymph node metastasis in breast cancer—particularly two separate types, one of which involves isolated tumor cells in the lymph nodes, meaning that there are a few tumor cells that the pathologist can see under the microscope. If there are metastases that are very small—those are called micrometastases—in those cases, there's still a lot of debate as to what we should do as surgeons, as oncologists. Should we go in, do a full axillary node dissection and take a lot of lymph nodes out, or should we leave the axilla alone and maybe do radiation or even chemotherapy? Those questions have, for the most part, not been answered.

A couple of studies were done [in the past. Based on those.] it seems that, if there are isolated tumor cells present in the lymph nodes, then there's very little difference [in terms of outcome] between doing axillary surgery, or treating the axilla [in general], versus not doing surgery or other treatment. [In other words, in that situation] there's not a lot of benefit to doing axillary-targeted therapy, either by radiation or surgery. However, when there is micrometastatic disease, meaning there are a few more cells than just the isolated tumor cells—and the size that we usually use [to define micrometastasis] is anywhere between 0.2 to two millimeters in those axillary lymph nodes—then there seems to be an advantage to treating the axilla. [[http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst\\_detail\\_view&confID=65&abstractID=32586](http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=65&abstractID=32586)]

There has also been debate about whether [or not] to radiate the axilla in patients that have one to three positive lymph nodes. A large trial was going to be conducted in this country. It started enrollment. Unfortunately, physicians and patients had their own biases, and it was—we were unable to [go forward with] that trial. [In the near future, therefore,] we won't have a definitive answer. Instead, people are now going back and looking at how patients were treated to figure out if there is any benefit in adding radiation to the axillary region if a patient has one to three positive lymph nodes.

What seemed to be coming out of ASCO this year was that, if there is a larger tumor in the breast—over two centimeters—and there are one to three positive lymph nodes in the axilla, then there might be some benefit to treating the axilla. But if there's a smaller breast tumor—even in those one to three positive lymph nodes—the benefit of adding radiation to the axilla may be smaller.

Again, these are not definitive studies. These are studies that we're going to be hearing more about—we're going to be hearing more about the subject—in the next few years, but [the studies do offer some information] that will help us in treating our patients.

A second theme involved looking at how tamoxifen works. There's been a lot of press about, and a lot of work done to study, the metabolism of tamoxifen. Tamoxifen is not the active drug. When we ingest it, tamoxifen actually gets metabolized to a product called endoxifen; endoxifen is the one that is the active drug. This metabolism process occurs through an enzyme called CYP2D6, which is present in our liver. In some people, that enzyme works really well, and . . . they have high levels of endoxifen. [In those people,] tamoxifen works well. Then there are some people whose CYP2D6 doesn't work too well; in them, tamoxifen does not result in high levels of endoxifen. It seems, though, that a lot of drugs



can affect how [well] CYP2D6 works. Some of those drugs are antidepressants—drugs that women with breast cancer are on all the time—such as [Zoloft and other] commonly used antidepressants.

There's been a lot of debate as to whether or not women should be on these antidepressants, and there was a study [Read LBBC's story at [http://www.lbbc.org/content/news/studies-reach-different-conclusions-on-interaction-of-antidepressants-and-tamoxifen.asp?section\\_tag=G](http://www.lbbc.org/content/news/studies-reach-different-conclusions-on-interaction-of-antidepressants-and-tamoxifen.asp?section_tag=G) or the abstract at [http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst\\_detail\\_view&confID=65&abstractID=31983](http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=65&abstractID=31983)] that looked at women who were taking antidepressants while they were on tamoxifen. That study showed that there really is a difference in the levels of endoxifen [produced] depending on what kind of drugs these women are using. It showed that medications, such as Zoloft, that don't let CYP2D6 work well should be avoided, because women who are taking Zoloft and tamoxifen don't do as well as women who don't take Zoloft. But there are other antidepressants—Lexapro, for example—that really don't do much to CYP2D6. They're pretty safe; those medications are fine to use with tamoxifen.

The bottom line, in terms of these studies [Read a second study from ASCO, with a different result: [http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst\\_detail\\_view&confID=65&abstractID=32720](http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=65&abstractID=32720)] is this: if a woman decides to take an antidepressant—or is told to take an antidepressant—and she is on tamoxifen, she should definitely check with her oncologist, as to whether or not a particular antidepressant is safe to take with tamoxifen.

Moving on to some chemotherapy trials and Avastin... Avastin is a newer drug for breast cancer. It's an anti-angiogenic drug. That means that it inhibits the blood vessels from forming. In order for tumors to metastasize and grow, they form blood vessels. Avastin, which is an antibody, goes to those blood vessels and blocks them, thereby killing breast cancer cells. Avastin has already been approved for colon cancer, lung cancer, some brain tumors and, recently, breast cancer. But it was approved to be used in combination with a specific chemotherapy drug—Taxol.

A recent study [[http://www.lbbc.org/content/news/bevacizumab-plus-docetaxel-may-be-effective-first-therapy.asp?section\\_tag=G](http://www.lbbc.org/content/news/bevacizumab-plus-docetaxel-may-be-effective-first-therapy.asp?section_tag=G)]

showed that Taxotere, another taxane, is a very active drug when used with [Avastin]. But we've never really known whether or not Avastin's effectiveness is dependant upon the specific chemotherapeutic drugs that we use with it. The RIBBON-I trial [[http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst\\_detail\\_view&confID=65&abstractID=34532](http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=65&abstractID=34532)] looked not only at taxanes, but also at Xeloda, another drug that we use for metastatic breast cancer. And it looked at how efficacious Avastin was when combined with taxanes, anthracyclines and Xeloda. The trial showed that Avastin works with [all] chemotherapy [medicines]. The patients that received Avastin with Xeloda had an improvement of a couple of months in their progression-free survival. Patients that received Taxol with the Avastin also had an improvement of pretty much the same amount of time—two to three months. And patients that received anthracyclines with Avastin also had an improvement. This tells us that, as long as we use Avastin, we can pick whatever chemotherapy [medicine] we want. [Avastin] seems to be a very effective [medicine in] breast cancer patients.

Moving on to the effect on brain function of aromatase inhibitors versus tamoxifen... As you all know, women who are postmenopausal [and who] are on tamoxifen or aromatase inhibitors can have some cognitive function issues in terms of short-term memory. Some of it has to do with menopause. It's never really been clear whether it's the tamoxifen, the aromatase inhibitors or the menopause that's the reason for that short-term memory loss, but a lot of our patients complain about that.

One of the large adjuvant trials involving aromatase inhibitors, the BIG 1-98 trial [<http://meeting.ascopubs.org/cgi/content/abstract/27/15S/510>], looked at cognitive function in women who were on letrozole versus women who were on tamoxifen. Now, this trial—the way in which they looked at cognitive function wasn't [ideal]. They did not have a baseline on cognitive function in women. They only looked at [cognitive function] after treatment—two years after therapy—to see whether or not there was difference in women who were on tamoxifen or letrozole. They found that the women on letrozole had a better cognitive function than those who were on tamoxifen.

But, still, all of those women had worse cognitive function than women of the same age

[who were not on these medicines]. Not really sure what to make of that. You may be hearing a lot about it; some of the drug companies are going to try to push aromatase inhibitors because they know that women do complain about cognitive function. But we need more definitive studies to understand what is really going on. Is it the aromatase inhibitors? Is it the tamoxifen? What's the mechanism behind all that?

A lot of patients ask about diet, exercise and vitamin D. What do we do? What's the data? Does diet play a role in breast cancer? In women who have breast cancer, does a change in diet affect their outcome? How about exercise? And how about vitamin D? In the past couple of years, that's something that has emerged as possibly being important. There was a very nice session that summarized all the findings that we have to date [on these things], that summarized what we know and what we don't know.

Exercise: We really don't have a lot of data. We don't have many randomized trials—meaning putting half of a group of women on some exercise program and telling the other half not to exercise. We don't have that kind of data. But we have looked back to see whether or not women who exercise do better. They do—regardless of whether or not they lose weight. Exercise seems to be an independent predictor of how women are going to do, and it should be encouraged in our breast cancer patients.

In terms of diet, is there some specific diet that works better than others? Many studies have looked at that, and there doesn't seem to be a specific diet that is related to increased breast cancer recurrence. Whether it's a low-fat diet, a high-protein diet or what we call a prudent diet—meaning just a well-balanced, nutritional diet—there does not seem to be any difference. What seems to help is weight loss or, at least, weight maintenance. Women who gain weight after breast cancer diagnosis actually do worse than women who maintain their weight or lose weight. So, a woman's weight seems to be more important than the diet that woman is on.

As far as supplements go, many studies have looked at folic acid, selenium and a lot of other supplements. So far, no supplement has been found to be helpful in protecting [against] breast cancer or in helping women who have breast cancer.

There has been some issue with vitamin D. The Women's Health Initiative



[<http://www.whi.org>] did not find that vitamin D supplementation made any difference in how women with breast cancer did. But what is pretty frightening is that, when we started to measure vitamin D levels—and we only started doing that recently—we found that only 25 percent of patients are vitamin D sufficient, meaning that only 25 percent of us have adequate vitamin D levels. The rest of us, 75 percent of us, are vitamin D deficient. Women who are vitamin D deficient should be encouraged to take vitamin D and to maintain a healthy vitamin D level. Not a “higher than healthy” level—there is such a thing—but a healthy level.

Vitamin D levels can be affected by the season. In the winter, [most] women are going to have lower vitamin D levels than [they have in] the summer. Vitamin D levels can also be affected by the [geographic] area in which a woman lives. In Chicago, we really don't get too much vitamin D. I'm sure that women in Florida get a lot more vitamin D than we do. It really is very variable. And the best way to get an idea of where a woman stands is to measure her vitamin D level. A physician can measure vitamin D levels.

Finally, probably the biggest breakthrough [reported at] this year's ASCO is a new class of drugs. You guys are going to be hearing a lot about them if you haven't already. They're called PARP [poly(adenosine diphosphate [ADP]-ribose) polymerase] inhibitors. What are PARP inhibitors? PARP helps repair DNA. If we inhibit PARP, then the DNA doesn't get repaired. You'll say, “That's not good, because we thought that DNA should get repaired.” Well, in normal cells it should. But in cancer cells—if we don't repair the DNA, then the cancer cells are going to die. And it seems that, in cancers that are triple negative, meaning estrogen receptor negative, progesterone receptor negative and HER2 negative—and those are the hardest cancers to treat—there already is an issue with the repair mechanism of the cell. If, on top of that defective repair mechanism, we add a PARP inhibitor, then that cell won't be able to survive and it'll die.

So, that's the concept . . . and the same thing seems to happen in women who have mutation in the BRCA1 and BRCA2 genes. Those are genes that cause breast cancer and ovarian cancer, and they are found in very young women who are being diagnosed with breast cancer and in women who have family histories of breast or ovarian cancer. [Normal] BRCA genes repair DNA. When the

genes don't function properly, the DNA isn't repaired and we get cancer.

PARP inhibitors are being used in women who have triple-negative breast cancer and in women who are BRCA positive because, in those patient populations, there already is some kind of damage to the DNA repair system. By adding a “second damage” to the system, we kill the cells; the cells can't survive.

Two PARP inhibitors received the most press. One is called olaparib; it's an oral PARP inhibitor. A study [[http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst\\_detail\\_view&confID=65&abstractID=30774](http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=65&abstractID=30774)] looked at women who were diagnosed with breast cancer and who had BRCA mutations. That's not a huge population, but it is a population of patients. Most of them get triple-negative breast cancers, and they're very hard to treat. In the study, women were given only the PARP inhibitor—no chemotherapy; nothing else—just that PARP inhibitor. Those women had been treated previously; they'd been on chemotherapy, and most of them had been on at least three chemotherapeutic drugs. In such situations, we usually say that we're slowing running out of options. [But] 41 percent of the women who received the PARP inhibitor had a response to the PARP inhibitor. Their progression-free survival, which means the length of time between starting that PARP inhibitor and progression of the disease, was around six months. And that PARP inhibitor did not cause much toxicity. There was a little bit of fatigue and a little bit of nausea; that was it. So, it seems that this PARP inhibitor is very active—even when it's used alone, without any chemotherapy—in heavily pretreated patients. It'll be very interesting to see how well it works once we add chemotherapy to that PARP inhibitor.

The second PARP inhibitor, which ended up being [the topic of] a plenary session [that] received a lot of press, is BSI-201. It is an intravenous PARP inhibitor. A study [Read LBBC's story at [http://www.lbbs.org/content/news/medicine-shows-promise-for-triple-negative-metastatic-breast-cancer.asp?section\\_tag=G](http://www.lbbs.org/content/news/medicine-shows-promise-for-triple-negative-metastatic-breast-cancer.asp?section_tag=G) or the abstract at [http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst\\_detail\\_view&confID=65&abstractID=33185](http://www.asco.org/ASCOv2/Meetings/Abstracts?&vmview=abst_detail_view&confID=65&abstractID=33185)] looked at the use of chemotherapy with gemcitabine and carboplatin with and without that PARP inhibitor in women who had triple negative breast cancer. Again, those are the women in whom

chemotherapy by itself doesn't work that well, and there aren't a lot of options other than, maybe, Avastin. But . . . triple-negative breast cancers don't respond to Avastin [better] than other cancers do.

The study showed that, by adding the PARP inhibitor to the chemotherapy, the women's response rate increased from 16 percent to 48 percent. That's a huge increase in response rate, and this again shows us that chemotherapy only produces a 16-percent response rate, which is pretty minimum. That was increased to 48 percent with the use of the PARP inhibitor. Progression-free survival increased from 3.3 months to 6.9 months. That's a pretty big increase in progression-free survival; that is significant. And women lived longer. There was an improvement in overall survival, from 5.7 months to 9.2 months. That's a significant improvement in overall survival—in a patient population that, up until now, hasn't had any other options—just as a result of the use of a PARP inhibitor combined with chemotherapy.

This to me, is the biggest breakthrough [that was reported at ASCO]. We're going to be hearing a lot more about these PARP inhibitors. And not just about these two; other companies are producing their own PARP inhibitors, and we'll be hearing about [them, as well]. I'm really looking forward to seeing these studies in the future—especially studies involving the triple-negative and BRCA positive patient populations.

[That's] my update on ASCO. I'm very glad to take questions.

#### ELYSE CAPLAN:

Dr. Kaklamani, thank you so much for highlighting a variety of topics. I think our listeners probably appreciated hearing about the chemotherapy and PARP inhibitor updates, since [that news] was very much in the press, and also about the quality-of-life studies in terms of diet and exercise, [as well as about] the RIBBON-I trial and the anti-angiogenesis update. All the things that you covered are really great springboards for questions from our audience.

#### OPERATOR:

Our first question comes from Long Grove, Illinois.

#### CALLER:

I'm a 51-year-old BRCA negative breast cancer survivor. I'm ER positive and I have a fairly strong family history of breast cancer. About two years ago I had a mastectomy and a full axillary dissection. Twenty-eight lymph nodes were



removed; eight had cancer. I completed chemotherapy, the TAC treatment in October 2007 and radiation therapy in December 2007. All other pre-op scanning reflected no metastatic disease. I took tamoxifen for 15 months. I am now postmenopausal, and I started Arimidex in April of this year. I have osteopenia.

I'm hoping you can speak about the benefit of IV Zometa, whether or not anything was presented at ASCO relative to past and current clinical trials, the impact on the potential reduction in the risk of recurrence versus side effects and, specifically, if there's anything related to postmenopausal women who have already completed treatment.

**VIRGINIA KAKLAMANI, MD, DSc:**

That's a question I get asked all the time. Unfortunately, we don't have a lot of data. The Austrian trial that was presented last year at ASCO [<http://www.ncbi.nlm.nih.gov/pubmed/18718815>] was actually recently published in *The New England Journal of Medicine* [[http://www.ncbi.nlm.nih.gov/pubmed/19213681?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\\_ResultsPanel.Pubmed\\_DiscoveryPanel.Pubmed\\_Discovery\\_RA&linkpos=2&log\\$=relatedarticles&logdbfrom=pubmed](http://www.ncbi.nlm.nih.gov/pubmed/19213681?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DiscoveryPanel.Pubmed_Discovery_RA&linkpos=2&log$=relatedarticles&logdbfrom=pubmed)] It showed that adding the bisphosphonate Zometa to the adjuvant treatment of women with breast cancer improves their outcome. Those women do better.

The problem, as you all know, is that most insurance companies don't pay for IV Zometa because it hasn't been approved. And this is really the only trial that we're going to have that looks at women who took Zometa versus women who didn't. Many trials that are happening in this country are looking at Zometa versus oral bisphosphonates, but no trial is looking at bisphosphonate versus no bisphosphonate.

I'm hoping that, at some point, they ask for approval for Zometa, because I think it's a great medication. Right now, [patients] with osteopenia may be able to have it covered once a year instead of twice a year. And that is what we usually recommend for our patients.

The women in the study were premenopausal, but they were given Zoladex, so they were made postmenopausal. So, I think bisphosphonates and Zometa work regardless of the menopause status of a woman.

**CALLER:**

So, related to reduced risk of recurrence?

**VIRGINIA KAKLAMANI, MD, DSc:**

Exactly.

**CALLER:**

Even when it's given up to a year and a half after treatment was completed?

**VIRGINIA KAKLAMANI, MD, DSc:**

Well, we don't know that. The study was done with women who did not even receive chemotherapy; they were just started on tamoxifen or an aromatase inhibitor and Zoladex with or without Zometa. So, that's what we know. But I do give it to my patients if they're—especially if they have a higher risk of recurrence, even if it's been a while after treatment.

**CALLER:**

For the bone health or for the potential reduction in risk?

**VIRGINIA KAKLAMANI, MD, DSc:**

For both. Bone health—the potential reduction in risk—unfortunately, we don't have that indication. I do it with that data in the back of my mind, thinking that I'm probably helping those patients as well.

**CALLER:**

In terms of the side effects—the necrosis of the jaw and the renal dysfunction—are you concerned about that at all?

**VIRGINIA KAKLAMANI, MD, DSc:**

Not too much. We check for renal dysfunction every single time a woman gets Zometa, so I'm not concerned about that at all. As far as osteonecrosis of the jaw is concerned, I think there's a lot of press about it, and dentists are kind of going nuts over it. We're not seeing a lot of cases, especially with Zometa being given twice a year. The data that showed some osteonecrosis of the jaw involved Zometa that was given monthly. But we always recommended that a woman has a dental exam twice a year, which is the [standard] recommended time period.

**CALLER:**

I was wondering, are the PARP inhibitors—I know that you said they're being used for triple-negative cancer or that they're in research right now. Can women who are estrogen/progesterone positive and HER2 negative benefit from this?

**VIRGINIA KAKLAMANI, MD, DSc:**

We don't know. We don't think so. PARP inhibitors work in cells that already have deficient mechanisms in terms of DNA repair. And those

cancers tend to be those triple-negative breast cancers. I think that, in the future, we're going to have tests for DNA repair genes and we're going to find that some of these ER positive tumors may have deficiencies in the DNA repair mechanism, which might make them eligible for PARP inhibitors. But, so far, all the clinical trials are targeting either BRCA positive women or triple-negative women.

**CALLER:**

I'm 50 years old and I'm five years out from having had ER positive [cancer]. I was premenopausal prior to taking Adriamycin and Cytoxan and [having] radiation, and I was given several Zoladex injections to put me in that postmenopausal state. They tried to give me Arimidex and Aromasin, but I did not tolerate [them], so I was put on the tamoxifen. I've recently been having issues with fatigue and constipation, and the gums in my mouth [are] covering some of my teeth and are beginning to bleed. My doctor said that they might keep me on tamoxifen for more than five years. I was wondering if any studies have proved that that would be a good thing. You also mentioned that you could test your blood to see if, in fact, it's an effective drug for you.

**VIRGINIA KAKLAMANI, MD, DSc:**

The one study that was completed in this country that looked at tamoxifen for five years or more showed that five years was actually more beneficial than ten years of tamoxifen. Women who took tamoxifen for ten years did a little bit worse. They almost had a decreased survival benefit. It was almost significant.

However, two much larger European studies are being done right now. We have some preliminary data from those studies that show that—it seems that, by around 2012, we will have that definitive data that tamoxifen given for ten years may actually be better than tamoxifen given for five. We don't know. Honestly, in practice, most of us just use five years of tamoxifen. We try to push aromatase inhibitors after that because there is data that shows that giving an aromatase inhibitor after five years of tamoxifen is beneficial.

[Regarding your second question]—yes, there is a genetic test. [It] tests CYP2D6 and how well it works in different women, and it can tell us whether or not tamoxifen will be an effective drug. We don't do it at Northwestern—most places don't do it—but it's a pretty easy test to do. Mayo Clinic [<http://www.mayoclinic.com>] does it, and they have most of the data on that test. But there



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are some studies that did not confirm the initial study's findings that, by doing this test, we will definitely know whether or not tamoxifen works. We're pretty skeptical about it.

The bottom line is this: Tamoxifen is a good drug. Aromatase inhibitors seem to be a little bit better. If we can put a patient on an aromatase inhibitor, that's what we do. But if we can't, and if we don't have any other option, we'd rather have a patient stay on tamoxifen than not.

**CALLER:**

My doctor is looking at—this is the last year that I should technically be on the tamoxifen. And you said the results aren't going to be out until 2012. So I'm not sure what I should be doing. I've already tried Arimidex and Aromasin, and I didn't tolerate [them].

**VIRGINIA KAKLAMANI, MD, DSc:**

I would try to see whether or not there was some way to put you on an aromatase inhibitor.

**ELYSE CAPLAN:**

It's great that you're asking questions, and who knows what we'll learn over the next year. I guess that, when you get to that point a year from now—when you're sort of at that point of considering a discontinuation of therapy—your oncologist and you can re-engage in a dialogue about the benefits of continuation of treatment versus switching to something else.

It's so hard, as Dr. Kaklamani said—there's a lot of research that's been reported. Some of it is preliminary. Some of it is definitive and some of it is not yet definitive, but we've got to keep our eye on the studies. And I just want to—as I'm speaking about this, I'm thinking about the importance of women—and men, for that matter—participating in clinical research trials. I think this is a really good opportunity to underscore the importance of people asking their physicians about whether or not they are eligible for a clinical trial; that is how we will get answers to these really pressing questions. If more people participate sooner rather than later, it won't take quite as long for the research to be reported. Would you agree, Dr. Kaklamani?

**VIRGINIA KAKLAMANI, MD, DSc:**

Absolutely. That's a great point. I talked earlier about this Austrian trial. Austria has nine million people. The United States has over 300 million people. And Austria has more breast cancer patients on clinical trials than the United States

does. This means, to me, that it can be done. I'm not going to look at it in any negative way, but [I'm focusing instead on] the positive messages that we get from this. If a small country like Austria can do a large trial and show us how bisphosphonates and Zometa work, then we should be able to do it, and we should be encouraging our patients [to get involved]. And our patients should be encouraging us [as clinicians] to participate in clinical trials.

**CALLER:**

Just for clarification, then—there's not a blood test you can take while you're taking tamoxifen to see if it's being effective in your system?

**VIRGINIA KAKLAMANI, MD, DSc:**

Yes, there is. It is a blood test that looks at our DNA and at how CYP2D6 works. It is a test that we can order. We send it out to Mayo. We rarely do it because it doesn't necessarily change what we do with our patients, but it is available, absolutely.

**CALLER:**

You talked about tamoxifen. I'm a seven-year survivor and well past menopause. I took tamoxifen for about two years with no side effects, and then my oncologist felt that the Aromasin would be better. I will be finishing up my fifth year in July. Have they come up with anything regarding continuation of the aromatase inhibitors for more than the five years?

**VIRGINIA KAKLAMANI, MD, DSc:**

That's a great question. The answer is no, and we all struggle about what to do, exactly, with somebody like you. The data so far [indicate that] five years of the aromatase inhibitor [is the way to go]. There is a Canadian trial that's looking at ten years. It has not been completed yet. And oncologists are all over the board in terms of urging patients to continue past five years or not. But there is no data.

**CALLER:**

So, my security blanket is leaving me, huh? But I guess I'm grateful for what I have. Thanks for your answer. I hope that they'll come up with something new soon, or maybe there'll be a trial I can get into.

**VIRGINIA KAKLAMANI, MD, DSc:**

Absolutely.

**CALLER:**

I had invasive DCIS [ductal carcinoma in situ]. It was in my lymph nodes in my arms seven years ago. I was ER/PR positive and I do have the

BRCA1 mutation. I've had recurrences in my lymph nodes two times now. But the PARP inhibitors—they would not do anything for a person who is not triple negative?

**VIRGINIA KAKLAMANI, MD, DSc:**

But you are BRCA positive?

**CALLER:**

Yes.

**VIRGINIA KAKLAMANI, MD, DSc:**

Then you would be eligible for a PARP inhibitor trial, absolutely.

**CALLER:**

Okay. And what are the two that are out there now?

**VIRGINIA KAKLAMANI, MD, DSc:**

Well, none of the PARP inhibitors have been approved by the FDA. They haven't even been submitted for approval by the FDA. There is an AstraZeneca PARP inhibitor. There's a BSI PARP inhibitor. There's an ASI PARP inhibitor. Pretty much every company has its own PARP inhibitor.

Two major PARP inhibitors were presented that ASCO. One of them is olaparib, from AstraZeneca, and that study involved BRCA positive patients. The other one is the BSI PARP inhibitor, and that study looked at triple-negative breast cancers. There are differences between the PARP inhibitors, and there are PARP1 and PARP2. There may be differences [in how each reacts to a specific PARP inhibitor]. And it's extremely early to know which is to be the best one; [I don't know when] we will ever answer that question. But they seem to be effective drugs. Now, just a correction, for clarification: DCIS means noninvasive breast cancer. When breast cancer either invades the breast tissue or goes to the lymph nodes, we call that invasive breast cancer—ductal carcinoma or lobular carcinoma; whatever it is. We don't call it "in situ" because that can be a little confusing.

**CALLER:**

That was my original diagnosis. Then, after they got in there, they changed it to invasive ductal carcinoma. Right now they're kind of guiding me by my tumor markers because they seem to be a good indication of what's going on. I started out with this recurrence. The [tumor marker was] in, like, the 120s, and now [it's] down to 38, and I'm taking carboplatin, Avastin and Abraxane. Is the PARP inhibitor something I should save for the future, when these aren't working, or is it something that I should include now?



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**VIRGINIA KAKLAMANI, MD, DSc:**

I would not change something that seems to be working. If you have scans—we generally like to look at are scans—if your scans are getting better—

**CALLER:**

Yeah, my scans have gotten so much better, but they're just looking at my tumor markers now.

**VIRGINIA KAKLAMANI, MD, DSc:**

That's all you need. If these drugs stop working at some point, the next thing would be to look at PARP inhibitor clinical trials.

**CALLER:**

You said that tamoxifen and Zolofit should not be taken together. Does that also pertain to aromatase inhibitors and all SSRIs? I don't know if Lexapro is an SSRI. What is the difference between Lexapro and Zolofit?

**VIRGINIA KAKLAMANI, MD, DSc:**

There is a big difference between Lexapro and Zolofit. They're both SSRIs; they're just different. All this data does not [pertain to] aromatase inhibitors at all. It just affects CYP2D6, which is involved in tamoxifen metabolism, not aromatase inhibitor metabolism. It is safe to take Zoladex and aromatase inhibitors.

**CALLER:**

Okay. And the lady just mentioned tumor markers. My oncologist, who's the senior scientist at this large medical center, does not believe in tumor markers, and it worries me.

**VIRGINIA KAKLAMANI, MD, DSc:**

I don't believe in tumor markers, either. You're in a great place. I know the oncologist there. We sometimes order tumor markers, not to look at whether a breast cancer comes back or not—the recommendations definitely recommend against that—but, in women with disease that has spread outside the breast—metastatic disease—sometimes they can be helpful in terms of following patients. Scans are really the best way to look at things. But sometimes, if we have only disease [in the bone], the bone scans may not show us a very accurate picture; in those cases, a combination of the bone scan and the tumor marker may help us; it may help guide us to know whether or not the treatment is working. But, in general, we do not do tumor markers for women who don't have metastatic disease just to follow them or to see whether or not their cancer's come back.

**CALLER:**

I had metastatic disease twice.

**VIRGINIA KAKLAMANI, MD, DSc:**

Still—in most patients, I do not follow tumor markers.

**CALLER:**

I was wondering if anything was said about sarcomas of the breast during that conference.

**VIRGINIA KAKLAMANI, MD, DSc:**

I did not attend the sarcoma sessions, so I'm not sure. In the breast cancer sessions, there really wasn't anything much talked about in terms of sarcomas. It depends on what kind of sarcoma it is. A lot of these breast sarcomas don't seem to be too aggressive, and we just treat them with surgery. So far, chemotherapy has not been shown to be beneficial. But I'm generalizing.

**CALLER:**

Mine's come back twice, and I did have my breasts removed. I've been treated with chemotherapy for a year.

**VIRGINIA KAKLAMANI, MD, DSc:**

There doesn't seem to be a new option, as far as chemotherapy goes, for sarcomas. Sarcomas are very hard to treat.

**CALLER:**

My oncologist worked where you work. He used to work in the office that you're working in. And I'm just amazed that—why did I go through a year of chemotherapy?

**VIRGINIA KAKLAMANI, MD, DSc:**

Well, sometimes chemotherapy's better than nothing, but chemotherapy works better in some diseases than in others. In general, chemotherapy doesn't work as well in sarcomas as it works in other diseases. It doesn't mean that it doesn't work. And, in a lot of patients, we see sarcomas being cured with chemotherapy.

**ELYSE CAPLAN:**

The take-home message is that everybody's situation is very individualized. And, obviously, our speaker is giving the broader viewpoint—

**CALLER:**

I would just like her opinion. Do you think it'll reoccur?

**VIRGINIA KAKLAMANI, MD, DSc:**

I have no idea.

**CALLER:**

Do you think my—would you give me a percentage? Would you tell me what you honestly think, in terms of a percentage?

**VIRGINIA KAKLAMANI, MD, DSc:**

It depends on what kind of sarcoma it is. It depends on where it recurred. It depends on—

**CALLER:**

Breast.

**VIRGINIA KAKLAMANI, MD, DSc:**

—it depends on how it [responded] to chemotherapy. There are so many different factors that go into this that there's no way we could look at percentages in general. There are no general percentages.

**ELYSE CAPLAN:**

—If this is an important question to you, we encourage you to go back to your oncologist.

**CALLER:**

Yeah, I did.

**ELYSE CAPLAN:**

And, you know what? If you're not satisfied and you feel that you need a second opinion, it would be perfectly appropriate if you—

**CALLER:**

Well, if you live in Sandpoint, Idaho, [a town of] 5,000 people—come on.

**ELYSE CAPLAN:**

Well, we appreciate your concerns and questions, and we hope that you'll get all your questions answered that'll help you make the best decisions for your health care. Take the best care.

**OPERATOR:**

Thank you. Our next question comes from San Francisco, California.

**CALLER:**

I'm running off to my exercise class, so I'm in the car, but I wanted to get this question answered. What is the recommended vitamin D level in terms of supplementation? And, related to that—[different people recommend different blood levels of vitamin D]. Do you have a recommendation as to what the vitamin D blood level should be?

**VIRGINIA KAKLAMANI, MD, DSc:**

First of all, I'm glad you're going to your exercise class. Second, oral vitamin D uptake doesn't necessarily correlate with intravenous vitamin D levels [in terms of] the levels that we measure. It seems that 36 to 40—I think it's nanograms per



liter; I forget the actual value—is what we usually shoot for. But every lab has its own assays and uses its own points. As long as it's in this medium range—not low and not high—that's what we usually shoot for. And we may need a lot of vitamin D—thousands and thousands of units of vitamin D—to achieve that level.

**CALLER:**

Is there too high a level?

**VIRGINIA KAKLAMANI, MD, DSc:**

There is too high a level, yes.

**CALLER:**

Really? Okay. Thank you.

**VIRGINIA KAKLAMANI, MD, DSc:**

You're welcome.

**CALLER:**

I'm seven years out. My tumor markers are always slightly elevated. I know that some doctors use [tumor markers] and some don't, but, when they rise a little bit, then occasionally I do PET scans or CAT scans. Now I'm going to go back in for a CAT scan and kidney work—you know, the kidney blood test. What else can you use when you're a few years out from having had surgery, chemo, radiation and Arimidex, to know? How else do you check?

**VIRGINIA KAKLAMANI, MD, DSc:**

We don't check. All the guidelines recommend against checking. The reason is very simple. Scans that we do—or, tumor markers that we do—are not accurate in detecting metastatic disease, and you are pretty much the poster child, based on how you're describing your case. [Say] you have a tumor marker that's going up. You do a PET scan, and guess what? The PET scans are fine. And you've been going through that cycle, and I'm sure you're a nervous wreck during the month or so in which this whole thing is happening.

**CALLER:**

Right.

**VIRGINIA KAKLAMANI, MD, DSc:**

And then you're waiting for your other tumor marker, which takes place a couple months later. And, basically, your seven years [consist of] more downs than ups for no reason whatsoever because your disease hasn't come back. That's the main reason we're not checking. Also, we actually did studies to see whether or not, if we check and actually find metastatic disease earlier, that's going to help our patients, because that's a main concern

for us. And the answer, again, is no; it doesn't help our patients.

Whether we find metastatic disease now or six months from now or nine months from now, our patient is going to do exactly the same thing when she has symptoms. The only difference is that, until that time, she's going to be a nervous wreck because we're going to be checking all these markers and all these scans. So we recommend against all of these.

**CALLER:**

I have some lumps that we're following, so do I just do the breast MRI, then?

**VIRGINIA KAKLAMANI, MD, DSc:**

Breast imaging is always done because [that gives us information that we can actually use to] cure our patients. If we find local recurrence, [meaning] recurrence in the breast, then we can still go in—do surgery; do radiation; even do some more chemotherapy, if needed—and patients can get cured. If the disease spreads outside the breast, we can still treat it—and treat it pretty effectively—but, unfortunately, we can't cure it, which is why we don't go nuts looking for it. Again, it doesn't change anything.

I would suggest—I know you're now going to go for your scans, and I'm sure you've gotten them throughout the whole process—is to stop checking these markers from now on. Still do breast MRIs or breast mammograms, whatever the radiologist is recommending, but just do local imaging.

**CALLER:**

Do you think maybe a breast MRI, because mammograms don't work, and then a CT scan occasionally to see if these lumps have changed?

**VIRGINIA KAKLAMANI, MD, DSc:**

Not a CT scan. A CT scan doesn't really catch much in the breast. Ultrasounds may help. MRIs may help, absolutely.

**CALLER:**

Now they're looking at pelvic; abdomen; lung—

**VIRGINIA KAKLAMANI, MD, DSc:**

Those we recommend against doing.

**CALLER:**

—or a CAT scan.

**VIRGINIA KAKLAMANI, MD, DSc:**

We recommend against all of those.

**CALLER:**

So, just to clarify—if a woman has symptoms, Dr. Kaklamani, then that would be the appropriate time for imagining studies or other studies to be ordered? To investigate the cause of the potential symptoms?

**VIRGINIA KAKLAMANI, MD, DSc:**

Absolutely. But, without symptoms, there's no need to be checking on them.

**CALLER:**

But are my lumps my symptoms?

**VIRGINIA KAKLAMANI, MD, DSc:**

Well, your lumps are enough of a symptom [to warrant an] MRI, but they're not [enough to warrant] a CT scan of your pelvis.

**CALLER:**

I want to ask a question about diet and breast cancer. Isn't it true that there isn't much data, and that there are simply not a whole lot of trials in that area, because the pharmaceutical companies are not really interested in searching in that direction?

**VIRGINIA KAKLAMANI, MD, DSc:**

There have been large trials that have looked at diet and breast cancer, and many trials have looked at low-fat diets and different types of diets in breast cancer. Those trials have all been pretty much negative, especially when you control for weight loss. Obviously, a diet that caused weight loss may have worked a little bit better than a diet that did not cause weight loss. But, if we control for weight loss, [we've seen that] the specifics of the actual diet itself don't seem to do much.

As far as supplements go—again, there have been a lot of studies done with supplements. There haven't been studies of every single supplement that's out there. Supplements are so unregulated—they can't be regulated by the FDA—that it's extremely hard to do studies. So I'm not going to blame the pharmaceutical companies. Women have participated in several dietary studies, and we just have not found anything that can guide our patients as to what diet to use.

**CALLER:**

I had cancer and treatment with chemo and radiation and tamoxifen and Aromasin, each for two and a half years. I'm two years out of treatment now. Last year I had mass tongue cancer and surgery for that. When they did the lymph node surgery, they found thyroid cancer in one lymph node. Now I'm wondering if my immune



system was affected by the breast cancer treatment and, if so, if there's something I can do to boost my immune system.

**VIRGINIA KAKLAMANI, MD, DSc:**

In general, breast cancer therapy, especially chemotherapy, does not seem to affect the immune system in the long run. While a patient is on chemotherapy, obviously, his or her immune system is a little down. But it doesn't seem that occurrence of secondary cancers is increased after breast cancer therapy. So I don't think that that's the case, at least in general. Obviously, we're not going to know in specific cases.

There are not a lot of things to do for your immune system. Exercise really strengthens the immune system, as does a well-balanced diet. But no medications have been shown to strengthen the immune system.

**CALLER:**

I'm a vegetarian and I was estrogen receptor positive. I know there are questions about soy. Have they ever reached any conclusion?

**VIRGINIA KAKLAMANI, MD, DSc:**

The soy story is pretty complicated. There seems to be good soy and bad soy, and that's where the story's complicated. It seems that, in women who don't have breast cancer, soy may even be protective. That's one of the theories as to why Asian women have a lower incidence of breast cancer compared to women in the Western world. At the same time, soy can be mildly estrogenic, so it may be not the best thing for women who already have breast cancer. But that's really all we know. Studies have been done that looked at prevention and different types of soy. I just usually tell my patients to not overdo it on soy. If you want to go out and have sushi and have a little bit of soy, that's okay. But I would not switch all of my protein intake to soy.

**CALLER:**

I have cut it down considerably, but I had been eating it for three years before my breast cancer showed up. I had been a vegetarian. I wasn't sure if that had anything to do with [my cancer] or not.

**VIRGINIA KAKLAMANI, MD, DSc:**

It should not.

**CALLER:**

So the mouth and the thyroid wouldn't be related? The radiation therapy I had was rather high up because my tumor was right at the top of

my left breast. And it was the left side of my tongue that had the cancer in it. You don't think that was related to the radiation?

**VIRGINIA KAKLAMANI, MD, DSc:**

Usually cancers that occur [as a result of] radiation therapy arise around ten years after radiation. It takes a little while. Again, that's in most cases. Now, there is a genetic syndrome that links thyroid cancer to breast cancer. If you have other people in the family with breast or thyroid issues, I would suggest that you talk to your oncologist about that. But, as far as tongue cancer goes, there doesn't seem to be any relation. It really depends on how much radiation your head and neck area received. Usually, regardless of how high up the breast cancer is, they're pretty good at shielding these other structures.

**ELYSE CAPLAN:**

We really appreciate your call, and we hope that you [continue to have] your questions answered as you move forward with your care.

**CALLER:**

I have stage IV breast cancer that has metastasized. If you addressed that, I missed it. Was there any new information that's come out regarding that?

**VIRGINIA KAKLAMANI, MD, DSc:**

There are a lot of drugs that we're now using in clinical trials. And, obviously, we're testing them in metastatic breast cancer first. Depending on the type of cancer—there was a large Avastin trial, a RIBBON-I trial, that showed that Avastin is a great option for women, regardless of the type of chemotherapy they use [[http://www.asco.org/ASCOv2/Meetings/Abstracts?vmview=abst\\_detail\\_view&confID=658&abstractID=34532](http://www.asco.org/ASCOv2/Meetings/Abstracts?vmview=abst_detail_view&confID=658&abstractID=34532)]. Also, there are other tyrosine kinase inhibitors that seem to work by focusing on EGF receptor; focusing on HER2 receptor; focusing on angiogenesis; [focusing on] other molecules, such as RAD001. There a lot of new agents.

**CALLER:**

Well, I'm estrogen negative, and I've been on Xeloda for about a year. Right now they're saying that I'm stable, but I've heard a lot about Avastin and some other drugs, and I guess I'm just not sure.

**VIRGINIA KAKLAMANI, MD, DSc:**

Are you HER2 negative as well [inaudible]?

**CALLER:**

I'm negative for that.

**VIRGINIA KAKLAMANI, MD, DSc:**

The PARP inhibitors would be the best option for you, as far as new drugs go. If what you're doing right now is working, keep doing that. But if, at some point, that stops working, then start to look at other drugs. Those PARP inhibitors seem to be the most promising agents right now.

**CALLER:**

Okay. And, as far as you know, there are clinical trials going on?

**VIRGINIA KAKLAMANI, MD, DSc:**

Absolutely.

**CALLER:**

You actually have responded pretty much to the question that I had formulated. I just have a little addendum. I'm 65. I was diagnosed in 2002, so it's been seven years. I have been on an aromatase inhibitor—Aromasin—for five years. When patients go off the aromatase inhibitor after five years, do you ever advise them to then go on to tamoxifen—kind of the reverse of what you had described earlier?

**VIRGINIA KAKLAMANI, MD, DSc:**

That is a great question. Unfortunately, we don't have a lot of data [on that]. We have one study that, in a weird sort of way, answers that. It was a BIG I-98 trial that looked at tamoxifen followed by an aromatase inhibitor, an aromatase inhibitor [alone] and an aromatase inhibitor followed by tamoxifen—all of those for five years. It seems that all of these arms were identical [in terms of results]. Therefore, we don't know whether or not we will get a benefit from adding tamoxifen after five years of an aromatase inhibitor. We really don't. When we decide to do something, most of us decide to continue the aromatase inhibitor.

**CALLER:**

I, too, have a question about diet. I know that different types of diets have been studied. I seem to be—I've had breast cancer for less than one year. I was diagnosed in July, and I made some very positive changes to my diet. One of the things that I seem to read a lot about is that sugar feeds cancer. On the one hand, we hear that we shouldn't have any type of sugar at all; on the other hand, we hear that there are no studies that prove that. Where is this information about sugar coming from? Can you please address the issue?



**VIRGINIA KAKLAMANI, MD, DSc:**

Thank you so much for giving me the opportunity to answer that question; I get it all the time. Sugar feeds every cell in our body, including those in our brain. If we don't have sugar, we die. We do need sugar. [But that] doesn't mean we should be going on a sugar rush and . . . eating a lot of sugar. [The goal is to maintain] a well-balanced diet. There's a thought that cancer cells that are metabolically more active than other cells consume more sugar. Some physicians even gave insulin to patients to decrease their [blood] sugar [levels]. Then, instead of giving them regular doses of chemotherapy, they gave them lower doses of chemotherapy, thinking that, if the cells are deprived of sugar, then not that much chemotherapy is needed. Unfortunately, all these—they weren't even studies—all these case theories failed miserably.

Just don't overdo it with sugar. That's where a lot of the studies come [into play]. Many involve PET scans, for example . . . we inject radioactive sugar, and it gets eaten up by the cancer, because [the cancer is] where most of the sugar [travels]. But [our bodies] need sugar [as part of] a well-balanced diet that includes carbohydrates, proteins and lipids.

**CALLER:**

I have stage IV breast cancer. When I first got diagnosed with the metastasis to the bones I was on tamoxifen, and my doctor said that it didn't work. He took me off it—that was, maybe, eight months after I was diagnosed. Now, [after having had an] ovariectomy and so on, I'm wondering—is [Aromasin] the same thing as tamoxifen? Doesn't it work in the same way? And should I be taking those AIs?

**VIRGINIA KAKLAMANI, MD, DSc:**

Aromatase inhibitors work differently than tamoxifen. Aromatase inhibitors can be used in women who have estrogen receptor-positive breast cancers. I'm wondering if, for some reason, your physician thought that you had estrogen receptor-negative breast cancer, in which case, neither tamoxifen nor aromatase inhibitors would work.

**CALLER:**

No. I am ER/PR positive. And I asked him, later on, before getting my ovariectomy, whether or not I should go back on that. He says I shouldn't because it didn't take away the pain. That was his thought.

**VIRGINIA KAKLAMANI, MD, DSc:**

There are other endocrine therapies. You should probably ask about those because you might be eligible for them.

**CALLER:**

Okay. So the AIs might be the way to go, though.

**VIRGINIA KAKLAMANI, MD, DSc:**

The AIs might be an option. There's another drug, called Faslodex, that we also use. Megace is an older drug, but it's still a good drug for ER positive breast cancer.

**CALLER:**

I read something a few months ago that said there may be some newer ways to scan the breast other than via an MRI. I was wondering if there's been any further research on whether [inaudible] to mammograms and MRIs, particularly for postmenopausal women who have dense breasts—if there is any other device that can be used.

**VIRGINIA KAKLAMANI, MD, DSc:**

There are several experimental tests but, in the clinic right now, we use ultrasounds, MRIs and mammograms. The digital mammograms tend to do a little bit better when the breast density is an issue. But we are still, you know, "stuck" with these three tests.

**CALLER:**

I'm 42-years old [and I've been a] breast cancer survivor for less than one year. I do have triple-negative [breast cancer]. My BRCA gene test was negative. I had a lumpectomy; the lymph nodes were negative. I had six chemo treatments and 29 radiation treatments. I just finished all that in February. Would I be a candidate for the PARP inhibitor clinical trials, since I have finished all of my treatments?

**VIRGINIA KAKLAMANI, MD, DSc:**

No. There are no trials that look at PARP inhibitors as maintenance therapy right now. Right now you're considered cancer free, so there's no other therapy that we would be recommending.

**CALLER:**

Okay. My other question is this: I didn't know that I had triple-negative [breast cancer] until after I'd had my surgery, when I went to the oncologist. Now I'm kind of second-guessing the decision to have had a lumpectomy instead of a mastectomy. Do you think there's any—because of the type that I have—

**VIRGINIA KAKLAMANI, MD, DSc:**

Not at all. The type of surgery that's performed really has to do with how big the tumor is and what the surgeon feels the cosmetic result would be. A mastectomy gives pretty much the same results as a lumpectomy with radiation. A triple-negative tumor does not change that.

**CALLER:**

Okay. The stage was low—like, stage I—but my grade was high. How does that factor in?

**VIRGINIA KAKLAMANI, MD, DSc:**

Triple-negative breast cancers are usually grade 3, so that would not surprise me. It does not mean much.

**CALLER:**

So the grade isn't any more a factor than the stage? Or is one more important than the other?

**VIRGINIA KAKLAMANI, MD, DSc:**

Stage is more important than grade.

**CALLER:**

It was stage one, so that's better than it being—

**VIRGINIA KAKLAMANI, MD, DSc:**

Absolutely.

**CALLER:**

So, then, you don't recommend having any type of PET scans or—

**VIRGINIA KAKLAMANI, MD, DSc:**

I would not.

**CALLER:**

It's been a year since I found it. I've had one mammogram and they've done one tumor marker, and that's all they've done. So—

**VIRGINIA KAKLAMANI, MD, DSc:**

We would just be doing mammograms. We would not be doing anything else.

**ELYSE CAPLAN:**

Again, just to highlight something that came up earlier in our program—follow-up testing is really limited today. The guidelines that have been established have not shown benefit to it. And, in fact, there's—we know that, in many cases, psychological or emotional upset is caused by doing follow-up tests in the absence of symptoms.

**CALLER:**

Okay.

**ELYSE CAPLAN:**

We certainly appreciate that you're at that point in your post-treatment recovery. That may



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feel scary. And it's great that you're asking questions and seek support from people who can help you through this. It is not an easy time when you finish your cancer treatment and you move into sort of recovery mode.

**CALLER:**

Yeah. This seems to be harder than having all the treatments. And I didn't even think about that until after I'd finished them.

**ELYSE CAPLAN:**

Absolutely. At Living Beyond Breast Cancer, we've definitely recognized that. And it's your job to sort of educate those around you who can be your supporters—to make them aware that you still have needs; that they're just different now. Take the best care, and stay in touch if there's any way we can help you.

Just riding on this comment—I would like to let the audience know that Living Beyond Breast Cancer has a toll-free Survivors' Helpline that can help women who are concerned about moving forward with their lives after active treatment is done and they're in follow-up care. The toll-free number is (888) 753-5222. Please feel free to call. We've got wonderful, trained volunteers who give peer-to-peer emotional support and who really can resonate with [and help you with] your concerns.

**CALLER:**

I have a question concerning the indication for use of aromatase inhibitors. The patient is postmenopausal and she was taking estrogen. She was diagnosed with early stage DCIS in February. She had a lumpectomy; she was sentinel node negative; she had radiation treatment. The tumor was estrogen positive. Her younger sister had breast cancer, but both of them are BRCA1 and BRCA2 negative. She's not interested in taking tamoxifen because of all the side effects. Could this person benefit from using an aromatase inhibitor?

**VIRGINIA KAKLAMANI, MD, DSc:**

Aromatase inhibitors have not been studied in DCIS. There's a clinical trial, which has finished accrual, that looks at tamoxifen versus aromatase inhibitors for DCIS, but we really don't have any data. Tamoxifen really is the one systemic option we have right now.

**CALLER:**

My question is similar to the one that was asked earlier. I can't take tamoxifen due to blood clot history. I didn't know if there was anything else I

could take. I'm premenopausal and I just finished radiation in March.

**VIRGINIA KAKLAMANI, MD, DSc:**

If you're premenopausal, aromatase inhibitors do not work. It really is going to come down to having a discussion with your physician about what the reason for blood clots may be, whether or not you think tamoxifen will significantly change that and how high the risk of the breast cancer is, and then deciding whether to go with tamoxifen anyway or to try to make you postmenopausal and then give you an aromatase inhibitor.

Again, tamoxifen is the only thing that's been approved for DCIS. But I do have patients that have had a history of blood clots; I've checked with our hematologist, and we have decided that it's reasonably safe to put them on tamoxifen. And they've done well. But it's a very careful selection process.

**CALLER:**

My veins were damaged severely from a previous blood clot. I think that that's why they're not putting me on it. So you're saying that it's better not to be on anything?

**VIRGINIA KAKLAMANI, MD, DSc:**

It depends on the type of breast cancer that you have. It may be worth talking about making you postmenopausal and putting you on an aromatase inhibitor. It depends on the risk of breast cancer.

**CALLER:**

When do you think that the PARP therapies will be available?

**VIRGINIA KAKLAMANI, MD, DSc:**

I'm hoping [they'll be available] very soon. I think the two companies will probably start programs in which they will be offering those because they seem to be extremely active drugs in breast cancers for which we don't have a lot of other options. Unfortunately, we still have to go through randomized clinical trials; larger trials. But I'm hoping that we'll soon be able to at least offer them to our patients. But you're going to be seeing a lot of clinical trials on them, and there are ongoing clinical trials.

**CALLER:**

As far as local recurrence with triple-negative disease goes, am I correct in thinking that recurrence in triple negative [is usually not to the area where the cancer first appeared]? It's usually to other parts of the body?

**VIRGINIA KAKLAMANI, MD, DSc:**

That is correct. And it's correct with every cancer, actually, not just triple negative. The highest incidence of recurrence is in other organs, such as the bone, the liver or the lungs, depending on the type of breast cancer.

**OPERATOR:**

Thank you. Our next question comes from Holland, Pennsylvania.

**CALLER:**

I'm a lot more confused now. I know you said that you don't use tumor markers, and that some doctors do and some doctors don't. You use more scans than you do tumor markers. But my understanding is that it's not a good idea to have a whole lot of scans, if you don't need them, because of all the radiation and everything that you get from scans. I am metastatic.

**VIRGINIA KAKLAMANI, MD, DSc:**

We don't think that the radiation received from scans affects much, especially in women who are not in puberty, as far as risk of cancer goes. We consider those scans pretty safe. At the same time, the general recommendation is that we do scans every three months or so. That can change. If a woman has what seems to be stable disease or is doing well and she has a tumor that's responding to treatment, we can go six months without scans. But we don't, as a rule, use tumor markers instead of scans because they could be misleading.

**CALLER:**

I actually went for more than a year—probably closer to two years—without having scans because I was doing quite well on the hormone inhibitor. And the tumor marker was stable. When it went up, we immediately did the scans. But I had not been getting scans every three months or six months or—I didn't seem to need them.

**VIRGINIA KAKLAMANI, MD, DSc:**

Every case is a little different, but, as a rule—we can be unpleasantly surprised by tumor markers, so we try to use scans as a way to predict therapy. We do have patients that can go up to nine months or a year without scans. But we scan most of our patients every three to six months.

**CALLER:**

I'm on tamoxifen. I'm postmenopausal, but tamoxifen is all I can afford. I was very interested in your comment on Zolof and other SSRIs interfering with tamoxifen. I'm not currently on any of those, but it's good to know. The one thing



I am wondering about is grapefruit. Grapefruit and grapefruit juice can interfere with SSRIs. Can grapefruit or grapefruit juice interfere with tamoxifen, aromatase inhibitors or any of the other cancer drugs?

**VIRGINIA KAKLAMANI, MD, DSc:**

To the best of my knowledge, we don't tell our patients that are on tamoxifen or aromatase inhibitors not to eat grapefruit or drink grapefruit juice. But grapefruit and grapefruit juice should not be taken in if patients are on some other drugs—such as Tykerb, which is an oral tyrosine kinase inhibitor, for example. Grapefruit does change the body's absorption of certain drugs—you're absolutely correct—but tamoxifen and aromatase inhibitors don't seem to be two of those drugs.

**CALLER:**

Is Tykerb a cancer drug?

**VIRGINIA KAKLAMANI, MD, DSc:**

It is a cancer drug. It's [used to treat] HER2 positive tumors.

**ELYSE CAPLAN:**

And, at this time, it's used in women with metastatic breast cancer. Is that right, Dr. Kaklamani?

**VIRGINIA KAKLAMANI, MD, DSc:**

That is correct. We're doing some studies [of its use] in the adjuvant [setting], but they're still just studies.

**CALLER:**

I have a question about preventive care. Is there anything that actually works for the prevention of the mouth sores that you can get from different types of chemo—not something that's used after you've got them, but something that keeps them from coming? Also—the question about Zometa. Is there any additional data on long-term use if it's used in the metastatic cancer setting for—to the bone?

**VIRGINIA KAKLAMANI, MD, DSc:**

Frequent use of salt-and-soda washes [and other] mouthwashes throughout the day can help prevent mouth sores. There's an ingredient in certain toothpastes that seems to also help, but that is—our transplant colleagues are studying that, and I'm not sure how successful that can be. Using a mouthwash of Colgate toothpaste mixed with a little bit of water may actually help. That's pretty much it; there's not much more [information on the prevention of] mouth sores.

As far as long-term effects of Zometa are concerned—we've been using Zometa for metastatic breast cancer, metastatic prostate cancer and lung cancer for a long time. And our metastatic breast cancer and prostate cancer patients live for a long, long time. We know what it does. We know that we have to be careful with the kidneys and we know that it can cause osteonecrosis of the jaw. Otherwise, it seems to be a pretty safe drug, and we're all very comfortable about using it.

**CALLER:**

But how often do you typically use it?

**VIRGINIA KAKLAMANI, MD, DSc:**

Well, we should be using it once a month. But, because a lot of chemotherapies are given every three weeks, many of the patients who are on Zometa end up getting it every six weeks; I do that as well. The company that produces Zometa has been trying to do a trial in which women would be randomized to receive Zometa once a month versus receiving Zometa once every three months. That trial has not been able to accrue patients—it's not an easy trial to accrue, unfortunately—so I have a feeling we're never going to know if we can use it every three months instead of every month.

**CALLER:**

My doctor said that there are a lot of questions about how often Zometa should be used, and for how long.

**VIRGINIA KAKLAMANI, MD, DSc:**

Based on the way in which the drug gets metabolized in the body, it looks like we should be using it as often as every three weeks—that's when the metabolism goes down. But studies have shown that once-a-month dosing is pretty safe, and, knowing that this is a chronic injection, we've been pushing it a little bit—up to every six weeks or so. But there is no—

**CALLER:**

Even in patients who use it for years?

**VIRGINIA KAKLAMANI, MD, DSc:**

Correct.

**ELYSE CAPLAN:**

With that, I would like to thank Dr. Kaklamani for all her time and the expertise she's shared with us today . . . Dr. Kaklamani, do you have a closing remark you'd like to make?

**VIRGINIA KAKLAMANI, MD, DSc:**

I want to thank everybody for all their questions; they were all wonderful, and they helped this discussion. And I just want to share with you how enthused we are about the next few years. There are so many targeted drugs coming out, and so many pathways being targeted, that the treatment of breast cancer is going to be extremely different in the next five or ten years compared to what it is now. And this is due to all your help and the help of the patients that have participated in these clinical trials.

**ELYSE CAPLAN:**

And I think that's a very hopeful and positive note to end on . . . I thank everybody for their time today . . . And thanks, again, to Dr. Kaklamani. We wish you all the best.

[END OF TRANSCRIPT]