



**TRIPLE-NEGATIVE BREAST CANCER:**

# Genetic Risk and Treatment Update

Rebecca Dent, MD, and Lisa Newman, MD, MPH, FACS

**OPERATOR:** Greetings, ladies and gentlemen, and welcome to the Living Beyond Breast Cancer teleconference. At this time, all participants are in a listen-only mode. A question-and-answer session will follow the formal presentation.

If anyone should require operator or technical assistance during the conference, please press "star-zero" on your telephone keypad. As a reminder, this conference is being recorded.

It is now my pleasure to introduce your host, Ms. Elyse Caplan. Thank you, Ms. Caplan. You may begin.

**ELYSE SPATZ CAPLAN, MA:** Thank you, Everett, and welcome, everyone, to the Triple-Negative Breast Cancer Genetic Risk and Treatment Update Teleconference. As Everett said, my name is Elyse Spatz Caplan, and I'm the director of programs and partnerships for Living Beyond Breast Cancer.

I'm very pleased to say that today represents the third year in a row that we've hosted this program, in collaboration with the [Triple Negative Breast Cancer Foundation](#). This partnership has been so important to all of us, to reach many more women living with or concerned about triple-negative breast cancer.

We hope that you really gain a lot from today's program. In a few minutes I will be introducing you to the chair of the board of the Triple Negative Breast Cancer Foundation, Hayley Dinerman, so she can make some opening remarks. Today's topic, as many of you know, is of great importance to so many people living [with] or concerned about breast cancer. At Living Beyond Breast Cancer, it's very important

to us to ensure the tailored information on the various subtypes of breast cancer, including the different stages of the disease, as presented throughout the year, [and] year after year, in our programming.

As I mentioned, this is the third year in a row, and we've very delighted to be able to offer this annual teleconference, so we can reach women all over the country, and ... all over the world, with information on the latest updates ... [regarding] triple-negative breast cancer.

The Triple Negative Breast Cancer Foundation has really helped us to build our attendance. And, we all know, I'm sure, that this past year triple-negative breast cancer has garnered immense attention because of some new discoveries that have been made through the research process. So, we're very excited to hear about the latest research, and what's "to come" in the future.

We have two speakers today: ... doctors Rebecca Dent and Lisa Newman. They will be touching on not only the latest research updates, but some of the risk factors for triple-negative breast cancer, and other concerns as [they] relate to genetic mutations, age, race, ethnicity, [and] ... other things.

We hope that what you hear and what you learn today will be food for thought to take back to your healthcare team, so you can ask informed questions, and get the answers you need to make the best informed decisions for your own healthcare. I'd like to just give you a couple of upcoming program notes that may be of interest to you listening today.

Living Beyond Breast Cancer's next teleconference is actually on a subject that many of you may be very interested in: it's on the subject of managing fears of breast cancer recurrence. ... [For] all of us living with a history of breast cancer — myself included, almost 19 years ago I was diagnosed — fear of recurrence has really been a number one theme that's pressing on the minds of women living with a history of breast cancer.

So, on May 19, [2010] we will have a program addressing that topic. And we hope that you'll dial-in for that. On June 11, [2010], we'll do our annual ASCO [American Society of Clinical Oncology] meeting update. Feel free to log onto [lbbc.org](http://lbbc.org) for more details about these programs, or to register.

Something else that we've done in the past year that many of you probably know, but in case you don't: In collaboration with the Triple Negative Breast Cancer Foundation, Living Beyond Breast Cancer published [a guide to] *Understanding Triple-Negative Breast Cancer*. If you don't have a copy and would like one, you can either download a copy on the [LBBC website](http://LBBC website).

Other resources I'd like you to know about that both organizations offer are toll-free help lines, as well as message boards. The Living Beyond Breast Cancer [Survivors'] Helpline number is (888) 753-LBBC (5222). And the Triple Negative Breast Cancer Foundation Helpline is in partnership with CancerCare and can be reached at (877) 880-TNBC (8622). Again, the websites for both organizations are [lbbc.org](http://lbbc.org) and [tnbcfoundation.org](http://tnbcfoundation.org).

Just a reminder that, if you can't stay with us for the full program, there will be a podcast available on our website soon after the program; and at a later date, a written transcript will also be available.

New this year is how we're obtaining our program-evaluation feedback. We hope ... [this new process is a more] streamlined way for you to tell us how we did today. We're using the SurveyMonkey online tool to help gather your feedback. So, when you get your e-mail with

the link to the evaluation, please do take a little bit of time to let us know what we did well, and what you'd like to learn about in the future — any constructive comments that can make future programs better.

Again, just to review the format for the program, I am going to introduce Hayley in a minute, and then our two speakers will do their presentations back-to-back. Then, we will move into the question-and-answer portion to conclude our program. So, without further delay I'm really pleased to welcome Hayley Dinerman, the chair of the board and director of operations for the Triple Negative Breast Cancer Foundation.

Hayley, thank you so much, to you and your team at TNBCF, for all you do on behalf of people living with triple-negative breast cancer. Welcome.

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

As Elyse mentioned before, this marks the third time that the Triple Negative Breast Cancer Foundation [has] partnered with LBBC to present a teleconference specific to this disease, and we're very excited to see part of it again. So, Elyse will — you can go right ahead and introduce our speakers, so we can get on with our program. I know everyone is excited.

**ELYSE SPATZ CAPLAN, MA:** Thank you so much, Hayley.

... I would like to tell you just a little bit about our two speakers, so you have an idea of the depth of their experience and interest in triple-negative breast cancer. Our first presenter will be Dr. Rebecca Dent, who is a nationally recognized expert in triple-negative breast cancer treatment and research.

Dr. Dent is assistant professor of medical oncology at the University of Toronto and heads up the breast cancer

clinical trials at the Sunnybrook Odette Cancer Center in Toronto. Dr. Dent also serves as chair of the locally advanced breast cancer program. In addition, she sits on the breast cancer new drug development committee for the National Cancer Institute of Canada, and has been a principal investigator for clinical trials for the treatment of advanced breast cancer, including the role of PARP inhibitors in triple-negative disease.

Dr. Lisa Newman is a professor of surgery and director of the Breast Care Center for the University of Michigan in Ann Arbor, where she serves as program director of the Breast Fellowship. Dr. Newman holds leadership positions with the Society of Surgical Oncology and the American Society of Clinical Oncology. She also serves on the breast prevention section of the National Comprehensive Cancer Network and as chief national medical advisor for Sisters Network Incorporated, a national African-American breast cancer support organization.

So, please welcome first, Dr. Rebecca Dent.

**REBECCA DENT, MD:** Great. Thank you very much, Elyse.

I want to thank the Living Beyond Breast Cancer, as well as the Triple Negative Breast Cancer Foundation. I think the work that's been done [is] extraordinary. I know that there are many women out there that are most appreciative for the support that you've provided as breast cancer ... has become quite complex, and it's quite hard to navigate through all the information that's available. So, thank you for inviting me to speak today.

I've been asked to speak about ... triple-negative breast cancer, which I call "the new frontier in breast cancer research." ... You all have different backgrounds, but triple-negative breast cancer is called triple-negative because it is estrogen-receptor negative, progesterone-receptor negative, and HER2-negative. So, it's defined by what it doesn't have, rather than what it has.

So, just like [Hepatitis] C, before we knew what it was, we called it a non-hepatitis A, non-hepatitis B. So, it's

important to know that [medical history, to understand where we are with triple-negative breast cancer]. And I'll refer to — a little bit later — [to] what's called basal-like. Now, I'm going to go through ... new subtypes of breast cancer and why that's important, the definition in epidemiology of triple-negative, current treatment strategies that you can apply in your treatment, and some of the clinical trials out there.

So, first of all, I think it's important to know that there's increasing evidence that breast cancer is not just one disease. So, the development of therapies that ... target the steroid hormone receptors — such as tamoxifen — really led to our ability to identify that there are ER- positive and -negative breast cancers. We used to give tamoxifen and things like, that that block estrogen, to all women with breast cancer. But now we recognize it's only the women that are ER-positive that truly benefit [from that treatment]. Similarly, trastuzumab, or Herceptin, really highlighted the importance of reliably identifying tumors that amplify or overexpress HER2.

So ... this has really been an evolution in breast cancer classification. Many years ago, a pathology report ... [was] really one page: this is the line, this is how big it is, this is how many lymph nodes there are. ... This allowed us in the next phase to be able to do what's called "protein expression," and really look at — use antibodies and identify a little bit more, [the] important features of the breast cancer. This, more recently, is led through some of the work that [colleagues of] Chuck Bruhn, [CEO of Genesis Medical Center, Illini Campus], have done. [Their work] looks at gene expression profiling, and really just looks at millions of genes — how they're expressed and ... how they cluster. Why this is so important is it allows us to classify breast cancers in a totally different way [than what] ... we've done before, which hopefully will help us in our ability to [implement] better [treatments].

I like this much more simplified diagram. I know not all of you have this on your screen, but the important thing about these clusters ... is that, on the one end, we have the ones that have lots of ER gene expressions; they're

very hormone sensitive and low grade, and they do the best overall. On the other end of the spectrum, we have breast cancers that have the least amount of hormone expression, or ER gene expression, and the highest grade, and they're called the basal-leg group. They're called that really just because the researchers that discovered this decided to [name] this group based on the proteins that they express. So the proteins they express — or proteins that come for the basal-layer of the breast — [are] called "basal-like."

Now, a big portion of these are ER, PR, and HER2, so that's why we call them triple-negative. But, it's important to know that these terms aren't entirely interchangeable. Over the next couple of years, you're going to see people really trying to define, what does triple-negative mean? But, I won't get into that anymore today ... just keep [that] in mind.

... The first thing I want to focus on is that we ... used to talk about grade and ... stage, and how important stage is. But, you won't hear a lot of breast cancer doctors talking about stage anymore. Stage was based on the tumor size and the nodal status. But now, we actually look more [closely] at ... the biology, and we call this "tailored treatment." This is sort of the hot term in cancer treatment right now, but it really has fundamentally changed how doctors approach their patients.

The decision to give adjuvant chemo in early-stage breast cancer is not just based on how big it is, and how many lymph nodes are involved. ... We tailor the treatment to target specific characteristics of the tumor, ... so for hormone sensitive breast cancers, more and more we're actually just relying on our ability to block estrogen and give less chemo. For hormone negative — such as triple-negative and HER2 positive cancers — we're actually probably giving more chemo upfront.

But, why this is so important is because of our ability to identify these other two groups: ... the hormone sensitive ones, and the HER2 positive. For those of you that have this on your screen, this has allowed us to identify multiple

different treatments for these other subgroups. And what we're trying to do with triple-negative is [to] identify what the target is, to come up with just as many treatments for triple-negative as we have for these other subgroups. And I think we're making a lot of headway.

Very briefly, we know that triple-negative breast cancers, on average, are younger women, bigger tumors, and [that] ... the cells are dividing more quickly. What's really interesting is that we've also noticed, that in breast cancers that are what we call "non-basal" or "non-triple-negative," as the size of the breast cancer gets bigger, the risk of having lymph nodes gets bigger. But, in triple-negative or basal-like, it doesn't seem to have that same correlation. What that means is that maybe there's something different, or there's a path that these breast cancers take that's different, to allow them to spread. So that's what we're really trying to explore.

The other thing that's important is that the risk of recurrence is much higher in the first couple of years after diagnosis; whereas, after the first three to four years, the risk of relapse goes down quite considerably, which is very different from other subtypes of breast cancer where the risk of recurrence ... remains quite flat. ...

Now, the other thing that's different is that the places where breast cancers spread is different in triple-negative. So, in triple-negative it tends to go more to the lung and to brain and possibly liver, but is less likely to bone. And that doesn't mean it will never go to bone, it just means it's not as likely. So, what are some of the therapeutic strategies that we commonly use?

The first thing I want to highlight is that there's this myth out there that triple-negative breast cancers aren't chemo sensitive, and don't respond [well to chemotherapy]. Well, that's actually not true. So, upfront when chemotherapy is sometimes given to women before their surgery, sometimes it's because the tumors are larger, or sometimes it's just felt that the patient may benefit from chemo, what we call preoperatively, or neoadjuvantly.

Whether you define it as triple-negative or basal-like, this type of breast cancer actually has a much better response to chemotherapy. You'll see that [confirmed] for those of you on your screen. Now, what's important is that if you have ... breast cancer that's triple-negative, and you treat before surgery and ... have a really good response — meaning that when you're done with surgery there's no [cancer] left in the specimen — ... when you get the pathology report, then you're likely to do almost as well as all the other subtypes of breast cancer. So, what we're trying to do is come up with the treatments that are most likely to shrink [the cancer] down, and make nothing left there after the surgery. ...

Right now ... if you have chemo before surgery, and there's still breast cancer left after surgery, we don't have any evidence that you should get any other chemotherapy; but you would be eligible for clinical trials that are looking at new agents. Now, what are some of the standard therapies? ... To be honest, there aren't standard therapies, and that's why I've put it on your slides and brackets. So, no specific chemo regimen guidelines exist. There isn't a lot of data in which to base decisions. And there are [a] few [of] what we call "historical controls," making it challenging for people to design trials for this group; but there [are] lots and lots of trials emerging.

And so, a couple of years ago, when I used to search [online] there were about six or seven trials on ... [[The National Cancer Institute's website](#),] and now there are pages and pages of trials. So, certainly, there's been a lot of progress.

The first thing I want to talk about is a class of drugs called anthracyclines. ... When I talk to my patients, I say this is the A or the E drug, so Adriamycin or epirubicin. The trials for this are controversial. Some of them say that you get benefit from these drugs, and some of them say that you don't. Right now we actually don't know. There aren't good ... prospective trials looking at this. So, it is reasonable at this time to incorporate an A or an E drug, as I call it, into your chemo for early-stage breast cancer. So, the second question is: What about taxanes? So, that's pacli-

taxel or docetaxel in the early-stage treatment of breast cancer. This was the biggest study that was done, that essentially showed triple-negative and HER2 positive breast cancers — even though it had a higher chance of their breast cancer coming back — got the most benefit from adding what's called paclitaxel, or Taxol. There are, in fact, now several other studies that confirm this.

So, whether it's paclitaxel or docetaxel, all of these trials actually show that the addition of a taxane to just your standard A or E drugs — so, the FAC [fluorouracil, Adriamycin and cyclophosphamide] or the AC [Adriamycin and cyclophosphamide] triple-negative patients do better. Now, remember, these are what we call retrospective studies, but the data is mounting suggesting women do better having a taxane in the early-stage treatment for triple-negative breast cancer.

The final [treatment option I'd like to discuss]: ... What about giving the anthracyclines and taxanes together? Certainly, there are two trials giving, let's say, Taxotere, [AC], versus FAC; or giving AC-T, or A[diadriamycin] plus the paclitaxel, followed by weekly paclitaxel is better.

So, you've got lots of options. But, again, this all shows us that, even though triple-negative breast cancers had a slightly higher risk of coming back, they derived the most benefit from some of these new treatments.

So, does the schedule matter? This is a lot of the research that's been done at Memorial Sloan-Kettering looking at dose-dense therapy. But, some of my colleagues recently have pulled two of the largest trials together, and have shown us that if you're going to give paclitaxel, you give it in a dose-dense fashion: ... every two weeks instead of every three weeks [showed] ... a fairly impressive survival advantage, ...almost 30 percent reduction in the risk of relapse. Certainly there's increasing data that show that if you give paclitaxel, you should really be giving it ... either every week, so it's called weekly paclitaxel, or you should be giving it dose-dense every two weeks. Now, docetaxel, on the other hand, should be given every three weeks. It looks like [that's] how it works best and has the least amount of side effects.

Now, one of the questions I get asked all the time is, “Well, what about the role of platinum-based chemotherapy in triple-negative breast cancer?” So, platinum — what’s called the “platinum salts” are a type of chemo that have been around for actually quite a long time. Cisplatin and carboplatin are the ones that are most used in breast cancer, and they’re actually used all the time for lung cancer and testes cancer.

Now, why might we consider them for triple-negative? Well, the reason is that there is this relationship between triple-negative and what we call BRCA-related breast cancers. So, BRCA, as many of you know, is the hereditary type of breast cancer that has difficulties in repairing DNA. The BRCA basically gets inactivated through a mutation, and there are many similarities between BRCA and triple-negative; but triple-negative actually just have decreased expression of the gene. But, it means that both of these groups might be susceptible to chemos that interfere with DNA repair. And that’s what cisplatin does — it interferes with DNA repair.

So, there are several studies that have looked at this, but most of them are fairly small. Some of them are retrospective. But it does show us that there may be a hint of activity, and that’s why you’ll see a lot of studies ongoing looking at the platinum salts for both BRCA and triple-negative breast cancers.

But, the important message here is that in the early-stage treatment of breast cancer, we don’t have what we call randomized data. We haven’t compared it to our standard. And we know that, in general, these are breast cancers that are sensitive to chemo. So, right now we’re still waiting on the results of a couple of trials, like this one that Andy Tutt is doing looking at standard chemo, such as a taxane, versus a platinum salt. So, for right now, we’re not using it outside of a clinical trial in the early treatment of breast cancer.

[For] early triple-negative breast cancer, there is no specific systemic regimen. Even though triple-negative breast cancers have a higher risk of relapse, we should have a lower threshold for adjuvant chemo. But, these women have the

most to gain from adjuvant chemotherapy. Your oncologist will recommend whichever regimen [he or she] thinks is the best. And you know what? East Coast to West Coast, around the world, everybody has their “best regimen.” To be honest, I think all of these regimens are reasonable: ... dose-dense AC Taxol, AC weekly Taxol, TAC, PC [paclitaxel, cisplatin], [FEC-T, which is fluorouracil, epirubicin, cyclophosphamide, Taxotere], EC [epirubicin, cyclophosphamide] Taxol.

There may be a role for platinum salts, but right now I wouldn’t do it outside of a trial. But, always consider a clinical trial to further refine optimal chemo.

So, just a few moments about some of the strategies for what we call metastatic triple-negative breast cancer. The first thing I just want to highlight is that ... it’s really along a spectrum. Metastatic breast cancer really is not one disease. ... I’ll just move onto the next slide.

So, what are the goals? Well, the first thing is, you work together with your oncologist. What are your goals in this treatment? This is much like treating diabetes or heart disease. It’s a chronic illness. You want to prolong life. You want to control the disease. You want to improve a woman’s quality of life, get her traveling [and] doing all the things that she wants to do. You want to minimize the side effects, and make sure that you try and improve on some of the symptoms. But, most of all, you want to balance efficacy and toxicity. And you really want to look at what the patient preferences [are]: ... does the woman want IV; does [she] want oral [medicine]; how far can [she travel for] ... treatment? Things like that.

So, one of the strategies that we’re looking at now is blocking blood vessels, because some of the data suggest that triple-negative breast cancers are able to get onto a new blood supply very quickly. In fact, the tumors can grow and spread to other places earlier on in their development. So, one of the pivotal trials that’s looked at this [disease] is a blood vessel blocking drug called Avastin, which was studied first in [the] E2100 [trial], which looked at Taxol weekly versus Taxol plus Avastin. And this study showed a doubling of what we call the progression-free

survival. Essentially, what this means is that the time when they need to switch to a new treatment because the chemo's no longer working.

Now, this showed a doubling. Some of the other studies that have been done, the benefit was not quite as big. But, certainly, when you look at all the triple-negative subgroups in these trials, all of them showed a small benefit at least in the triple-negative subgroup. So, you'll see — and this was the trial that led to the FDA approval — you'll see a lot of oncologists probably incorporate weekly paclitaxel plus Avastin in [a] ... woman's treatment. This is only for breast cancers that have spread. And we do have one trial that ... is looking at Avastin in the early-stage treatment of breast cancer, but we don't have the results of that trial. That's the [BEATRICE Trial](#). And we will await those results. So, right now, outside of a trial, we would not use Avastin.

[Editor's Note: After this program, the FDA began proceedings to withdraw approval of Avastin in metastatic HER2 negative breast cancer. The withdrawal is based on the more recent studies discussed here. Get more information about the status of bevacizumab at [lbbc.org](#).]

The final area of interest, which is a huge area of interest right now, is looking at trying to interfere with the DNA repair pathway, as I alluded to earlier. And this is all the craze of talking about PARP inhibitors. PARP is an enzyme that helps us repair DNA. What normally happens is if you have a single-strand break, this is usually repaired by what's called the "basic system repair pathway." And essentially PARP is one of the central components. So, if you have a single break, usually PARP repairs it, OK? Now, if you don't have PARP, what happens is you get a single strand break, and then ... you don't have PARP, so your backup BRCA repair pathway doesn't work, so you have the double stranded break. And, as I told you, triple-negative breast cancers have decreased expression of BRCA. So, you have the backup BRCA repair pathway.

Essentially what you get is selective death of those cancer cells that don't have this BRCA to repair it. And what's

really neat is only the cancer cells lack BRCA. So, there seems to be little effect on the normal tissues, and that's really what we're after. So, what we call this is tumor-specific lethality. We want to spare our normal tissues, and ... just kill off those cancer cells.

... One of the best known of these trials is the BSI study. So, BSI-201 is a PARP inhibitor that's given [by] IV. This study that was presented last year by Joyce O'Shaughnessy, compared what's called gemcitabine and [carboplatin], which are two chemos, versus the same chemo plus the PARP inhibitor. This was a very exciting study presented first at ASCO last year, and then updated more recently at [the] [San Antonio](#) [Breast Cancer Symposium.] Basically what it showed was a response rate of 16 percent, which increased to almost 50 percent. This means tumor shrinkage when you gave the drugs, so it's quite a significant increase, and then, a similar increase in survival from about 5.7 months to 9.2.

Then, the data was updated again, as I mentioned, where it increased by about five months, from 7.7 to 12.2 months. And that's by giving the addition to chemo of this IV PARP inhibitor.

Now, there is a Phase III trial that just closed. And I understand that the company will have "compassionate [use] of PARP inhibitors] at the sites that have this trial open, and we'll await those results in the next little while.

[Editor's Note: In late January 2011, the manufacturer of BSI-201, now called iniparib, announced that the phase III trial discussed in this transcript had not met its primary goals of increasing overall survival or progression-free survival. The study involved women with triple-negative breast cancer who received iniparib as their first treatment for metastatic disease; a subgroup of women who took it as a second or third treatment for metastatic triple-negative breast cancer had some improvement in overall survival and progression-free survival. The researchers who conducted this trial will report on the findings at an upcoming medical meeting; check [lbbc.org](#) for updates.]

Now, the other PARP inhibitor is olaparib, which is made by AstraZeneca. This was a trial presented by Andy Tutt. Now, this was a really interesting trial, because this is an oral pill that's given ... twice a day. And in this study, it was just for BRCA carriers, but they'd had multiple previous treatments: so anthracycline, taxane, Xeloda, sometimes platinums. And despite all this, there was a response rate with the slightly higher dose of 400 twice a day of 41 percent. So, almost half the patients had shrinkage despite the fact that they'd had all these other treatments before. And when you look at this plot, what you can tell is that almost all patients in that particular study had some kind of shrinkage with this medication, the olaparib. And what's nice is it had very little side effects and ... it's a pill, so you're not having to [travel to] chemo[therapy treatments], and have an IV. This was just the pill ... on its own, not with chemo.

So, I urge you to look out for some [of the] trials that we'll be reporting soon. This is a study by Karen Gelmon, who's an oncologist in Canada, who did a study looking at triple-negative and ovarian cancer and BRCA carriers. And this will be presented at ASCO. Similarly, in Canada ... along with our colleagues in Australia and Europe, we look to giving weekly Taxol plus the olaparib. We did have some trouble with low blood count. So, we're waiting on the second part of this trial right now. But, this will be presented, as I said, at ASCO. Then, these are sort of two interesting trials that have recently emerged. One of the questions I often ask is, "OK, if I get pre-op chemo, and I have lots of cancer left after my surgery, what should I do?" And I say, there is nothing to do.

These two trials are actually ongoing [and] are really exciting. So, one of them is ... by Kathy Miller ... is looking at cisplatin on its own, versus cisplatin plus ... another PARP inhibitor, which is made by Pfizer. And this is a [study](#) that's recently opened.

There's another trial that's ongoing, which is looking at if you had adjuvant chemo for triple-negative breast cancer, state one to three. There's a [vaccine therapy](#) for triple-negative breast cancer. And this is just one

single — we call it a single-armed trial where patients are getting this adjuvant vaccine and trying to boost immunity to MUC1. So, we don't know a lot about this yet, but certainly if people are interested, this is one option after you've finished your treatment.

So, these are some of the new strategies for triple-negative breast cancer, and ... there are many, many more. But, just to show you — so, we're looking at targeting DNA repair, blocking blood vessels, looking at blocking something called EGFR, and multiple other interesting pathways. ...

The take-home messages really are the following. In early triple-negative breast cancer, the myth is that all ... triple-negative breast cancers don't do well. But, if [women] get chemotherapy, the absolute benefits for chemo are greater, and a woman can actually do extremely well. But, I think we do need to be aggressive with adjuvant chemotherapy. For patients that have cancer that has spread, what we call metastatic, there are a number of different chemotherapy options. But, there really is a balance between response and side effects. And finally, always consider a clinical trial. There are a number of new drugs that are being explored, both in the early setting and for breast cancer that has spread.

The important thing is that there's actually some recent data, and actually several years ago there was some data as well — and this was presented at ASCO last year — that showed the impact of study participation on survival of early-stage breast cancer patients. Basically what this showed — and there were some issues with the study — but what it showed was that overall survival for women involved with the study was better than women that were not involved in the study. ... That is likely the case [because] ... it used to be that trials were sort of a sugar pill versus an active drug. .... This was 40 years ago. And women felt ... like they were being guinea pigs. But, all the studies that we do in breast cancer now are either comparing the standard treatment, versus the standard treatment plus something potentially better; or they're looking at potentially another new drug.

So, what I always say to patients is —... they laugh, but I have this sort of magic trick of different treatments. And if I can add something else into that bag of the number of different treatments ... I think that's a good idea. And you always have the option of getting off of a study if you [realize after signing up that you are] not interested in it. But, certainly, there are a number of different options. A lot of them are listed on the Triple Negative Breast Cancer Foundation website. And I have to say, it's probably more updated than a lot of websites out there that we even use as trial lists.

So, what I hope to do is to make triple-negative breast cancer sort of the new HER2, and the non-ER, non-HER2 breast cancer. By doing that, we will hopefully identify numerous therapies for this type of breast cancer, like we have for these other breast cancers over the last ten to 20 years.

With that I'd just like to say thank you, again, and thank you to all the patients [who] ... —are going through studies, considering enrolling in studies, and [who] continue to inspire oncologists like myself to continue with our ongoing research. So, thank you.

**ELYSE SPATZ CAPLAN, MA:** Well, thank you so much Dr. Dent. You went through an immense amount of information that is really getting us quite current. I would like to move into introducing and welcoming Dr. Lisa Newman for her presentation.

**LISA NEWMAN, MD, MPH, FACS:** Good afternoon, everybody. So, I would like to start out by adding my appreciation to that expressed by Dr. Dent to the Living Beyond Breast Cancer and Triple Negative Breast Cancer Foundation for putting this program together. It's, indeed, an honor to be able to join all of you today and to talk about triple-negative breast cancer.

My comments are going to focus on ... the epidemiology of triple-negative breast cancer, what we know versus what we don't know about risk factors for this disease. Unfortunately, I will say right off the bat that we really do not know a whole lot about what causes triple-negative

breast cancers. We are really just now beginning to generate an understanding of the true heterogeneity of breast cancer as consisting of several different types of disease. And while it is exciting, as you just heard from Dr. Dent, to explore some of the novel therapeutic strategies that may become a big part of the future in treating these biologically aggressive triple-negative breast cancers, at this point in time we really don't know, with a lot of confidence, how to accurately predict which women are more likely to develop triple-negative breast cancers, compared to the much more common non-triple-negative breast cancers.

So, for those of you who have access to the website, the first slide that I am showing here summarizes some of the major features that are most prominent among women with triple-negative breast cancers. And there are basically four features that show up pretty consistently in the various epidemiologic studies that have been published, three of which I am showing on this slide.

Number one is the fact that triple-negative breast cancer patients tend to be younger, compared to women that have non-triple-negative breast cancers. And I have a few different ... sources for this information listed on this slide, and I will not belabor the point. But, in general, we tend to see triple-negative breast cancers significantly more commonly in the younger aged to premenopausal population of women.

Number two, triple-negative breast cancers tend to be larger at the time of diagnosis. And there are a few references listed here as well, including the reference that Dr. Dent already presented to you guys, where Dr. Dent demonstrated that the average tumor size for triple-negative breast cancers at time of diagnosis is approximately three centimeters, compared to just two centimeters at time of diagnosis for the non-triple-negative breast cancers. Also, as Dr. Dent demonstrated, the triple-negative breast cancers are more likely to be diagnosed with no axillary lymph node metastases, compared to the non-triple-negative breast cancers.

We have also demonstrated the higher frequency, or predisposition, for the ... triple-negative breast cancers to be associated with hereditary susceptibility. And women with BRCA1 mutation associated breast cancers are, indeed, more likely to have triple-negative cancers compared to women in the general population, who are diagnosed with what we call sporadic breast cancer.

... One [study](#) published by Bruce Haffty and colleagues, they saw among women who were being managed by breast conserving surgery for their breast cancers, that approximately a quarter of these women with triple-negative tumors were positive for a mutation in the BRCA1 gene, compared to only 1.7 percent of those women with other patterns of breast cancer. The fourth feature that I will talk about in the latter half of my presentation is related to the fairly consistent finding that triple-negative breast cancers are also more common among women with African ancestry.

So, what have we learned about the epidemiology of triple-negative breast cancers compared to non-triple-negative breast cancers? Well, since triple-negative breast cancers do account for the minority of breast cancers that we diagnose in women — within the United States, North America, and around the globe — the majority of the epidemiologic risk factors that we have identified [for breast cancer in general] are, in fact, risk factors that identify women more likely to be diagnosed with estrogen-receptor positive tumors, and therefore, by definition, tumors that are not going to be triple-negative.

The risk factors that we most commonly look at [generally in breast cancer] are related to parity [the number of times a woman has carried a pregnancy to term and delivered a baby], and number of pregnancies that a woman has had, body mass index, and exogenous [outside] hormone exposure. And, in general, the risk factors that we're all familiar with are [associated with hormone-positive breast cancer]: women who have multiple pregnancies, because of the multiple interruptions of their estrogen cycles ... are less likely to be diagnosed with breast cancer. Women who start their child bearing at younger ages are less likely to develop breast cancer, again, because of the interruption

of their hormonal cycles. And women who have exogenous hormone exposure in the form of hormone replacement therapy following the menopause are more likely to develop a breast cancer, because of the additional hormone exposure to the breast tissue.

Women who are postmenopausal and who are obese have higher circulating estrogen levels, because of the metabolism through fatty tissue. And this can increase the rate of having breast cancer in the postmenopausal ages. But, again, the vast majority of these factors identify women who are at risk for developing non-triple-negative breast cancers.

And in looking at the epidemiology of triple-negative tumors, what we have come to surmise is that there may actually be a whole host of different hereditary, reproductive, and environmental exposures that drive the likelihood of women developing the triple-negative tumors.

Usually, when we are trying to identify risk factors for particular diseases, in particular breast cancer, what we do is to perform [case] control studies. [In those studies,] we look at large populations of women who have breast cancer, and compare features in those women to similar features in women that do not have a diagnosis of breast cancer. [Then we] try to figure out which of the features or which of the risk factors are associated with being diagnosed with the disease. And so, these types of case control studies are now being applied specifically to identify risk factors for triple-negative tumors.

In one study, the Women's CARE Study, investigators found that mammographic density is, indeed, associated with a higher likelihood of developing triple-negative breast cancer, as it has also been found to be a risk factor for being diagnosed with non-triple-negative breast cancer.

The [Carolina Breast Cancer Study](#) found that having multiple — two — multiple pregnancies, starting child bearing at younger age, that these were risk factors for developing triple-negative breast cancer, which is actually contrary to what we typically think of as being risk factors for the majority of breast cancers that are diagnosed in

the general population of women. The Carolina Breast Cancer Study investigators also found that having an elevated waist-to-hip ratio was associated with an increased risk of having triple-negative breast cancer.

In the [Cancer Surveillance System](#) from the state of Washington, they actually found that there was no significant difference in having the risk of a triple-negative breast cancer compared to the risk of having a non-triple-negative breast cancer when you looked at parity, number of pregnancies, and the age at having your first child. So, in general, unfortunately, while we are developing an appreciation that the risk factors for triple-negative breast cancer may be different compared to the risk factors for having a non-triple-negative breast cancer. We are not, I'm afraid, identifying any consistent patterns. So, we are not, at this point, able to reliably identify women at risk for having these triple-negative tumors.

Now, part of the problem leading to all of this variation, consistency, and results is related to what Dr. Dent very eloquently described in the beginning of her presentation. When we look at the triple-negative tumors, all we can really say is what particular markers at this point in time are not expressed by these tumors. We have very limited information about which molecular markers are expressed by these tumors. And it's quite possible that we need to identify markers that are reliably and consistently expressed in the triple-negative breast cancers, in order to identify reproductive factors, environmental factors, hereditary factors [and] other types of exposures, in order to identify which of these features will cause these cancers to develop.

Dr. Dent also mentioned that the triple-negative breast cancer pattern is really not a perfect surrogate for the basal breast cancer subtype. And it's quite likely that both the triple-negative tumors and the basal breast subtypes are a very heterogeneous population of tumors, and it may be that there will be a variety of risk factors that predicts the likelihood of developing different subsets within these populations of triple-negative and basal breast tumors. But, again, one feature that has been pretty consistently demonstrated in several different studies is the association between African ancestry, and

the likelihood of developing a triple-negative tumor. This is where I will focus most of my remaining comments, because it is entirely possible — and it's a very exciting and provocative hypothesis to presume — that we might be able to identify heritable risk factors for being diagnosed with a triple-negative breast cancer by studying particular populations of women based upon their geographically defined ancestry: by looking at African-American women compared to women who live in contemporary African populations.

So, let's very basically now review the features that describe the breast cancer burden of African-American women. Over a lifetime, African-American women are actually less likely to be diagnosed with a breast cancer, but they're more likely to die from breast cancer. African-American women are more likely to be diagnosed with tumors at larger stages, the larger sized tumors, and the tumors that are node positive at diagnosis.

African-American women also have a younger age distribution for the disease. And so, even though the lifetime incidence of breast cancer is lower for African-American women, if you look at American women younger than age 45, the population-based incidence rates of breast cancer are higher for the African-Americans compared to white American women.

We also see this increased frequency of adverse prognostic tumor features where African-American women are more likely to be diagnosed with the high grade aneuploid tumors, the estrogen receptor negative tumors, and as we've mentioned already, the triple-negative breast cancers.

Also, a feature that we do not discuss very commonly, but which is very poorly understood, is the fact that the African-American community has a higher population-based incidence of male breast cancer. Male breast cancer, obviously, accounts for a very small proportion of breast cancers overall, but this proportion is two- to three-fold higher when you look at African-Americans compared to non-African-American communities. This higher frequency, this higher likelihood of being diagnosed with an estrogen-receptor negative tumor in African-Americans, is seen in

African-American women compared to white American women regardless of the age category at which the woman is diagnosed, regardless of the stage at diagnosis, and regardless of her income level.

So for those of you who have access to the Internet, the table that is demonstrated on this slide demonstrates data from the National Cancer Database where we are looking at proportions of African-American compared to white American women being diagnosed with ER-negative tumors, after categorizing the women by age: less than 45, 46 to 60, and 61 to 80 years of age. [They were also categorized] by stages I, II, III and IV at diagnosis; [as well as] by income level, less than \$30,000 a year, \$30,000 to \$45,000 per year, and more than \$46,000 income per year.

In all of these different strata, the African-American women [have] roughly twofold higher [likelihood of being] diagnosed with the ER-negative tumors compared to the white American women. If you also look at actual population-based statistics on breast cancer incidence rates, generated by the Surveillance Epidemiology and End Results [SEER] program in this country, we again see that, regardless of stage and type of breast cancer, the population-based incidence rates of estrogen-receptor negative tumors is higher at all deciles of life for the African-American women compared to white American women. And the incidence curves that are demonstrated on these graphs are from senior data, looking at women that have inflammatory breast cancer compared to women with locally advanced breast cancer, compared to women with non-locally advanced breast cancer, again, showing incidence rates that —the ER-negative tumors that are higher within each of these types of cancers for the African-American women compared to the white American women.

It's also valuable, I think, to look at international data when we try to disentangle the effect of racial ethnic identity from likelihood of it being diagnosed with ER-negative and triple-negative tumors. Because within the United States [there is] ... very strong association between African-American ethnicity and poverty, and lack of access

to the healthcare system, [so] it's very difficult to disentangle those confounding effects from the pattern of breast cancer that's being diagnosed. So, it's interesting to look at international data where you will still have differences in income level and socioeconomic status, but you do not tend to have as much racial-ethnic diversity compounding the socioeconomic indicators, as we see within the United States.

In international studies, such as studies from Scotland, studies from Sweden, and studies from England, you actually do not see any association between poverty rates and likelihood of being diagnosed with an estrogen-receptor negative or a triple-negative breast cancer. So, this suggests to us that racial-ethnic identity may be the more important determinant of women at risk for having an estrogen receptor negative or a triple-negative breast cancer, over and above the income level or socioeconomic status of that patient.

Lisa Carey, [MD], and colleagues with the Carolina Breast Cancer Study Group went one step further beyond looking at estrogen receptor status expressions for African-American women, and actually looking at the frequency of the triple-negative breast cancers in African-American women compared to women of other racial ethnic backgrounds. And they demonstrated, in what has now become a landmark study, that African-American women, especially if they are in the premenopausal age range, have an approximately twofold higher likelihood of being diagnosed with triple-negative tumors of the breast.

The findings from Lisa Carey and colleagues have now been replicated in many other data sets: data sets looking at single institutions [and] patient populations, as well as data sets looking at surveillance epidemiology, and then results-findings, which is the ... population-based data set for the United States.

Here I think it is worthwhile to start looking at African ancestry, and what we might learn about African ancestry as a means of identifying the pathogenesis, the drivers of triple-negative breast cancers. Now, because of the slave

trade from four centuries ago, we suspect that women in Western Sub-Saharan Africa — because that was the location for many of the slave colonies — that women in this part of the continent of Africa will have at least some shared ancestry with African-American women.

And, indeed, there are very interesting features when we look at parallels between the breast cancer burden of African-American women, with the breast cancer burden of women that have true hereditary breast cancer. [And those parallels] ... lead us to suspect that there might be something related to African ancestry, in and of itself, that increases the risk for having these types of tumors.

We see the same younger age distribution for breast cancer in African-American women that we see in women with hereditary susceptibility for disease. We see the same frequency of the ER-negative and aneuploid tumors, and we see the same higher frequency of male breast cancer for populations of women that have African ancestry, whether you're talking about African-American women or African women. And you see these same patterns in women that have known hereditary susceptibility for the disease in the form of a mutation in the BRCA1 gene.

And so, again, I think this is where it's very exciting to look at the breast cancer burden of contemporary African populations as a strategy for trying to learn more about the pathogenesis of triple-negative breast cancer. The bar graphs that are demonstrated on this slide — for those of you who have access to the Internet — indicate some very provocative patterns when we look at the breast cancer burden of three different populations: African-American women, women from Western Sub-Saharan Africa, and white American women. For age, average age of diagnosis, the average age is the youngest for African women at only 45 years; it's the oldest for white America, women at 62 years; and intermediate at [age] 57 for African-American women.

Frequency of male breast cancer is about 4 percent in Africans, one-half to 1 percent for white Americans, and, again, intermediate at 2 percent for African-Americans. The portion of women with ER-negative tumors [has] similar stepwise patterns, [with the] highest frequency

at 75 percent in African women, [the] lowest frequency at approximately 20 percent for white American women, and intermediate at about 40 percent for African-American women.

These consistent stepwise patterns suggest that there may be something associated with extent of African ancestry that predicts risk for having certain types of breast cancer: male breast cancer, young breast cancer, and ER-negative tumors. [For] ... African-American women, [there is] a lot of admixture — related to the last four centuries of genetic admixture — you'd expect all of these features to be intermediate in expression in African-Americans. But, since Africa is obviously the founder population for all of mankind, whatever [predictions] for risk of having these types of tumors is something that we will see in women around the globe.

This is where we have been very excited about our studies at the University of Michigan in exploring patterns of breast cancer for African-American women, white American women, and women from Ghana, with Ghana being the population representing Western Sub-Saharan Africa. The cancer-treating facility that we have been partnering with is the [Komfo Anokye Teaching Hospital](#) located in Kumasi, Ghana. And we have been comparing the patterns of breast cancer in the three different populations that I mentioned earlier, by looking not only at our University of Michigan and Ghana population, but also by looking at breast cancer patients from the Henry Ford Hospital in Detroit, Michigan.

We have found similar stepwise patterns that I described previously in terms of the Ghanaian women being the youngest age at diagnosis, compared to African-American women and white American women. And we have found the same patterns that I mentioned previously when we look at frequency of ER-negative tumors and triple-negative tumors, with both types being most common in Ghanaian women, intermediate in frequency for African-American women, and lowest in frequency for the white American women.

These features continue when you ... specifically look at the locally advanced and high grade tumors. These types of patterns are also being seen by investigators looking at breast cancer patients from other parts of Africa, such as Nigeria and Senegal, and also from East Africa, looking at Kenya. We are also looking at some of the novel markers that might be useful in the future, for identifying treatment strategies for the triple-negative breast cancers. Specifically, we are looking at the EZH2 marker, and we are also looking at markers of memory stem cells, such as ALDH1, and thus far finding some very provocative patterns, which in the interest of time I will not belabor. ... But, for those of you who have access to the Internet, I have presented some of those patterns in tabulated form.

The last thing that I want to comment upon is the issue of mammography screening for breast cancer, and how some of the recent controversy that has been generated by the United States Preventive Services Task Force updated screening recommendations for mammography; how some of these updated screening recommendations might have some unintended adverse consequences, when it comes to looking at populations of women that are at higher risk for having triple-negative breast cancers, and the populations of women at risk for having early onset disease.

As most of you are probably already aware, the traditional conventional screening recommendations, that most societies have advocated, recommend annual mammography starting at age 40 for women at average risk, sometimes even younger for women with hereditary predisposition and strong family histories. But, in November of 2009, the U.S. Preventive Services Task Force issued an updated guideline recommending against routine screening mammography for women in their 40s. And there has indeed been some inconsistency in the randomized controlled trials looking at the potential value of mammography for decreasing breast cancer mortality in the younger aged women. However, those randomized at clinical trials looking at mammography have a lot of ... reasons why we can't assume that those findings can be perfectly brought into the contemporary mammography screening discussion.

There were a lot of women in the convention — in the traditional mammography screening trials — who did not have a mammogram even though they were assigned to have mammography, or they had a mammogram even though they were randomized to not receive mammography. The mammography technology was not nearly as sophisticated in those historic trials as it is today.

So we have many reasons to suspect that the benefit from mammography may actually be substantially greater for both younger aged women, as well as for older age women, compared to what was actually documented in those older studies. So, what the U.S. Preventive Services Taskforce did was to commission a meta-analysis, and a large reevaluation of the historic randomized clinical trial data looking at mammography screening. And they came up with two different ways of looking at mammography benefit. One method was to look at number needed to invite to screen, in order to save one life. Another strategy was to look at life-years gained when screening 1,000 women.

And what the taskforce received in the evaluation of these different strategies was the following comment:

If the goal of a national screening program is to reduce mortality in the most efficient manner, then programs that screen biannually from age 50 and older are among the most efficient. But, if the goal of a screening program is to efficiently maximize the number of life-years gained, then the preferred strategy would be to screen starting at age 40.

What the taskforce, however, opted to issue was this guideline that they recommended screening to begin at age 50. But, women should be aware of the caveat that the statisticians who did the actual studies did actually see a benefit in terms of life-years gained for screening younger aged women.

Also, we have to understand that [for] women who are at high risk for developing breast cancer at younger ages — such as African-American women and women with hereditary susceptibility — it's even more important to be aggressive in screening. Because these women are

going to be at the highest risk for being diagnosed with advanced stage tumors at younger ages.

And we do have ample data looking at the benefits of mammography for triple-negative breast cancer demonstrating that mammography is, in fact, valuable in ... [detecting] triple-negative breast cancers. There are also some exciting emerging studies showing that magnetic resonance imaging [MRI] may have some added value in the early detection of triple-negative breast cancer. And I will stop there. ... Dr. Dent and I, I'm sure, are both looking forward to whatever questions you and the audience might have.

**ELYSE SPATZ CAPLAN, MA:** Well, thanks again so much, Dr. Newman, for your very thorough presentation, [which brought] a lot more perspective to it. I know we only have about ten minutes left on today's program, so for right now I'd like Everett, our operator, to give instructions on how people can ask questions.

**OPERATOR:** Thank you. Ladies and gentlemen, at this time we'll be conducting a question-and-answer session. To ask a question by Web you may click on the "Ask a Question" button on the left-hand side of your screen, and type your question. To ask a question by phone, please press "star-one" on your telephone keypad at this time. A confirmation tone will indicate your line's in the question queue.

You may press "star-two" if you would like to remove your question from the queue. For participants using speaker equipment, it may be necessary to pick up your handset before pressing the star keys.

One moment, please, while we poll for questions.

**ELYSE SPATZ CAPLAN, MA:** And Everett, while you're polling, I'm going to start with a question that came in through the website. ... There are several questions for the doctors to address about follow-up testing, after treatment is completed for early-stage, triple-negative breast cancer.

Can both of you, or either of you, make comments about blood work, PET [and] CAT scans, MRIs of the breast?

**REBECCA DENT, MD:** Sure. Maybe I can start and then Dr. Newman can afterwards. So, from a systemic standpoint, from a whole body standpoint from breast cancer as a medical oncologist, we don't do any other blood tests or CT scans or PET scans after a woman's finished chemotherapy. There were studies looking at doing CTs and bone scans on a regular basis. And then, unfortunately, people didn't do better if they had scans. We didn't pick anything up sooner, to make a difference, and certainly a clinic visit [is important] ... however often your doctor deems necessary.

I usually do four to six months for the first couple of years, and then after year-three, it usually goes to about a year: ... [an annual] follow-up with a physical exam.

Now, it doesn't mean we never do scans, it just means we do them when there's a reason to do [them]. So, if I'm examining a patient, or if there's something I'm concerned about, then I would order a scan that's appropriate to how the patient feels, because certainly by doing tests you can expose the patient to more radiation than they need. [And] you can undergo tests that aren't needed, that in themselves can actually cause problems. So, we just do a clinic visit, along with the breast imaging that's deemed necessary by the surgeon.

**ELYSE SPATZ CAPLAN, MA:** Dr. Newman, do you have anything to add?

**LISA NEWMAN, MD, MPH, FACS:** No, I wouldn't add anything to that.

**ELYSE SPATZ CAPLAN, MA:** OK. The next question I'd like to ask is also related to risk for recurrence. Could you both — and maybe we'll start with Dr. Newman — comment on the risk for recurrence. ... In the first couple of years after adjuvant treatment is completed, what the risk may be and for mid-term or longer-term survivors of triple-negative breast cancer; how that is affected?

**LISA NEWMAN, MD, MPH, FACS:** Thanks. ... I'll let Dr. Dent talk about the distant organ recurrence from triple-negative breast cancer. But, as you heard from her, we tend to see most of the recurrences from triple-negative breast cancer within the first five years after diagnosis and treatment.

When it comes to local control of the disease, there have been some studies demonstrating that women with triple-negative breast cancer have slightly higher rates of local recurrence, following lumpectomy and radiation for the tumors. But, in general, we do not see triple-negative breast cancer as being a contraindication to breast conservation surgery for the disease.

**ELYSE SPATZ CAPLAN, MA:** Dr. Dent, anything to add?

**REBECCA DENT, MD:** No, I ... just think that — keep in mind that a lot of the data we have is using older treatments. So, even in our own study patients, for the most part, [they] had just received CMF, sometimes AC [Adriamycin and cyclophosphamide]. But, it'll be interesting to look at ... the BEATRICE Trial, [which is] looking at giving more modern treatment, such as the addition of taxanes, [and] being a bit more aggressive with chemo.

You may see some of the statistics change so that the relapse rate, I suspect, will not be as high. And that's what we're all hoping for.

**ELYSE SPATZ CAPLAN, MA:** OK. Thanks to both of you for that. I think I'd like to move to, um, taking a couple questions by telephone. Everett?

**OPERATOR:** Certainly. Our first question on the line today comes from [a woman] in Vacaville, California. Please proceed with your question.

**WOMAN:** Uh, yeah. I have a couple of quick questions. How often do you see somebody get ER/PR positive cancer and then get a recurrence, or another cancer on the other side, of the regular triple-negative cancer?

**LISA NEWMAN, MD, MPH, FACS:** Most studies are now demonstrating that women who have a second breast cancer, a new contralateral breast cancer on the other side, usually the features of those cancers are going to be similar to the features identified in the first cancer, diagnosed in the first index breast. So, it tends to be unusual to have a different ... pattern for a second, new-primary breast cancer.

**WOMAN:** Have you seen it? Because that's happened to me? I was wondering if you'd ... actually ... seen it. ...

**LISA NEWMAN, MD, MPH, FACS:** Absolutely. It's — ... but it's not the most common. But, it definitely happens. And that points to the importance of looking at markers all over again ... when there is a recurrence or change in the pattern of the disease.

**WOMAN:** OK. The other thing, real quick, on the chemo treatment for triple-negative, the TAC [Taxotere, Adriamycin, cyclophosphamide] treatment: Is it better than — to get the — did you — did I understand you to mean that it's [that the] dose-dense every two weeks is better treatment than the [every] three weeks?

**REBECCA DENT, MD:** No. To be honest, I think we are giving Taxotere — the best [treatment is] to give that drug is every three weeks. If you're going to give Taxol, it should be given every two weeks, or every week.

So, if you're getting Taxotere, and you're getting TAC, then TAC is perfectly good.

**WOMAN:** OK. So, they're as effective whether it's two or three weeks apart.

**REBECCA DENT, MD:** Yeah. So, the bottom line is Taxotere — there were studies looking at Taxotere every week, ... every three weeks, ... and then Taxol every week, or every three weeks. And the winners in that study were Taxol given every week, and Taxotere given every three weeks. ... That's why I said any one of those — you'll just have differences — I call it the apple pie phenomenon.

Wherever you worked and you developed that drug, you like the way that that regimen works. But, if you're getting TAC, that's perfectly good treatment for a triple-negative breast cancer.

**WOMAN:** OK, thank you very much.

**OPERATOR:** Thank you. Our next question comes from [a woman] in Winthrop, Washington. Please proceed with your question.

**WOMAN:** Hi. I was just questioning the — it was my understanding that breast cancer really was not noticed in Africa until the '60s. I was curious how the genesis of that concept kind of works together. It would occur to me that there's something more to the story. Thank you very much.

**LISA NEWMAN, MD, MPH, FACS:** ... Your question is quite appropriate. Breast cancer has not been studied aggressively in African populations. A lot of other diseases, especially infectious diseases, have been studied much more aggressively in Africa. Overall, the breast cancer incidence rates in the contemporary African populations [are] substantially lower, compared to the incidence rates of breast cancer in other parts of the world. And this is going to be related to a whole host of factors related to reproductive patterns, diet, a lot of different things.

Nonetheless, we do see substantially higher risk of having certain types of breast cancer in the African populations. And this points to the potential value of research opportunities to learn more about the inherited basis, or the heritable factors for triple-negative breast cancer. It may be that the features we identify in African populations will be features that can be used for either prevention or for treatment of the tumor, which will obviously be useful to women around the world, regardless of racial ethnic background.

**WOMAN:** Thank you.

**OPERATOR:** Thank you. Our next question comes from the [a woman] in Colorado Springs, Colorado. Please proceed with your question.

**WOMAN:** Yeah, I was wondering, at what age do you recommend that African-American women should be screened by mammogram or clinical breast exam?

**LISA NEWMAN, MD, MPH, FACS:** I would say, still, that starting at age 40 is appropriate for African-American women. For women that have a strong family history of early onset disease, a breast cancer diagnosed in relatives in their early 40s or 30s or even younger, that those women should start to have their screening at younger ages. And the rule of thumb that we use: ... a woman should start her mammographic screening five to ten years younger than the youngest age of breast cancer diagnosis in her family.

**WOMAN:** Thank you.

**ELYSE SPATZ CAPLAN, MA:** And with that, I'm afraid to say that we're coming toward the close of our program. Again, I want to thank Dr. Rebecca Dent and Dr. Lisa Newman for their expertise and their time. There was so much information shared.

I know we could not address all the subjects that we had hoped to today, [such as] some of the lifestyle modifications you might be able to make to reduce risk for recurrence, but that [subject] ... was covered on last year's triple-negative breast cancer teleconference. And that transcript is on [lbbc.org](http://lbbc.org).

So, if you're interested in that particular subtopic, I encourage you to read the transcript from last year's program, and stay in touch with us. ...

Again, I express great gratitude to the Triple Negative Breast Cancer Foundation for the work that they're doing, extending the partnership through the annual program and the brochure that we've published together.

[I'd also like to] ... remind folks on the line of ... peer resources. You've got Living Beyond Breast Cancer's Survivors Helpline at (888) 753-LBBC (5222), and the Triple Negative Breast Cancer Foundation's Helpline, in partnership with CancerCare, and that number is (877) 880-TNBC (8622).

Again, message boards on both websites are a great place for you to post your [thoughts]. And Living Beyond Breast Cancer also has a blog. And I encourage you to check out our [blog](#). I'm sure we'll have a lot more to add about Triple Negative Breast Cancer Foundation.

So, please, everyone, have a wonderful day. Best wishes in your journeys. And please [visit] ... [lbbc.org](#) and [tnbcfoundation.org](#) for continued educational support. Again, doctors, thank you very much.

**LISA NEWMAN, MD, MPH, FACS:** Thank you.

**OPERATOR:** Ladies and gentlemen, this does conclude today's teleconference. You may disconnect your lines at this time, and thank you for your participation.

[END OF TRANSCRIPT]