



*Young Perspectives Teleconference
Update from the San Antonio Breast Cancer Symposium
January 24, 2006*

LIZ WOHL: Good evening and welcome to “Update from the 28th Annual San Antonio Breast Cancer Symposium,” a Young Perspectives Teleconference hosted by the Young Survival Coalition. My name is Liz Wohl and I am a five-year volunteer with the Young Survival Coalition, board member of the New York State Breast Cancer Support and Education Network, YSC alternate to the board of the National Breast Cancer Coalition, as well as field coordinator for the National Breast Cancer Coalition. I am also the mother of a young survivor, Jen Levinson. I will be your moderator for tonight’s call.

The San Antonio Breast Cancer Symposium is an international medical meeting that brings together scientists, clinicians, health professionals, and advocates together to hear the latest research in basic science, prevention, screening, and treatment of breast cancer. Tonight, we hope to present an overview of the latest breast cancer research as it relates to young women with various types and stages of breast cancer.

We have two panelists who have graciously taken the time to be with all of us tonight: Dr. Powell Brown and Mrs. Anna Cluxton. Let me tell you a bit about each of them. Dr. Powell Brown is an associate professor of medicine at Baylor College of Medicine. He is the leader of the Cancer Prevention Program of the Cancer Center at Baylor College of Medicine, and associate director of research at the Breast Care Center Baylor-Methodist. He is a member of the Departments of Medicine and Molecular and Cellular Biology; he’s an MD and PhD graduate of New York University, a Medical Oncologist, and a physician-scientist specializing in breast cancer treatment and prevention. Dr. Brown’s renowned laboratory and clinical efforts are focused on developing innovative and more effectively ways to treat and prevent breast

cancer.

Anna Cluxton holds an MBA in health care administration. She is the manager of the Cancer Genetics Program and interim manager of the Breast Health Program at OhioHealth hospitals in Columbus, Ohio. Anna was diagnosed with breast cancer at the age of 32, the week after her honeymoon. Her personal experience as a five-year breast cancer survivor guided her decision to focus her career in cancer and in healthcare. She is active in the patient advocacy community, currently serving on the national board of directors of the Young Survival Coalition, the affiliate taskforce, and the volunteer steering committee.

Locally, she chairs the Central Ohio chapter of the YSC and sits on the board of directors for the Breast Cancer Fund of Ohio. She's a Lifetime Television Breast Cancer Hero, recipient of an AstraZeneca Vision of Hope Award and a Project LEAD graduate. Anna has lobbied for breast cancer issues on the state and federal level and serves as an advocate grant reviewer for the California Breast Cancer Research Program. She's married to Brian Cluxton and he, too, actively volunteers with the YSC.

Before we hear from Dr. Brown, our first presenter, I would like to provide you with the logistics of tonight's call. Tonight's call is being recorded and the transcription will be made available on the YSC web site, youngsurvival.org. The format of the call is as follows: The first part of the call will be a presentation by our panel. Each presenter will impart his or her knowledge and experiences as a medical professional and cancer survivor. We will then open the call to your questions. We ask that you do not ask questions that are specific to your diagnosis or treatment. We will only have about 30 minutes to cover all your questions, so please try to keep them brief. The call is operator-assisted, so when we open the line for questions, our operator will give you instructions on how to ask your questions. If we run out of time and you still have questions for the panel, you can submit them to [info @youngsurvival.org](mailto:info@youngsurvival.org)

and we will do our best to answer them. Now I'd like to ask our first presenter, Dr. Powell Brown, to start us off. Dr. Brown?

POWELL BROWN, MD, PhD: Welcome everyone. My name is Powell Brown. As Liz said, I am a medical oncologist that specializes in treating breast cancer. I am also an academic scientist with some knowledge of basic science so that I should be able to answer some of your scientific questions as well as clinical questions. I have been asked to give an overview of the San Antonio Breast Cancer Symposium that occurred this year in December and I will do that in the next 15 or 20 minutes.

I'll give you a little outline first. I'm going to give you a bit of an introduction in a moment. I'm then going to tell you about some of the most important clinical aspects from the conference. This will range from new and exciting advances in the treatment of early breast cancer then on to interesting advances in the treatment of metastatic breast cancer. Then I'll move to screening and information that was presented there about appropriate methods for screening. Then there is a large section on prevention as well. Anna Cluxton is tasked with discussing that, so I will skip that. Then I'll move to basic science advances and briefly mention those

So moving to the introduction. This particular symposium is, in my opinion, the premiere breast cancer research symposium of the year. Basically there are two symposia that I always make sure to go to: the San Antonio Breast Cancer Symposium and the American Society of Clinical Oncology. They're about six months apart so it gives a great opportunity to hear what's most current in the last six months or year. The San Antonio Breast Cancer Symposium is well known for presenting very important clinical findings in the treatment of breast cancer, but also basic science findings that are highly relevant for breast cancer and the things in the middle that's called translational science and the advances there. And this year was

no exception, we saw a lot of advances in the basic and the translational and the clinical science that was presented.

So to start off, I'd like to talk about the treatment of early breast cancer. This is often referred to in terms of adjuvant therapy. After potentially the surgery, often one is treated with either chemotherapy or hormonal therapy and occasionally radiation therapy as well. The big news this year, I think, was the treatment of HER-2-positive breast cancer. The HER-2 gene has been previously found to be overexpressed or amplified in a proportion of breast cancers. That particular gene has now become a target of therapy and the therapy is Herceptin.

One of the discoverers of HER-2 is Dennis Slamon, and he gave a fabulous overview and presentation at the beginning of the meeting, which was absolutely outstanding. He took the whole science from the discovery of this particular gene to the realization that a subset of breast cancers overexpressed it, to then the realization that those that overexpressed it had a particularly aggressive form of breast cancer, then to the development of a therapy that targets it, that's this antibody, Herceptin, and then ultimately to showing that Herceptin is a remarkable treatment for metastatic breast cancer that is HER-2 positive.

Then this year the big news from the San Antonio Breast Cancer Symposium was the adjuvant trials of Herceptin. That is in early breast cancer that is HER-2-positive, after being surgically removed, the studies tested whether adding this antibody called Herceptin that targets the HER-2 protein, whether that would be beneficial if one adds it to the standard chemotherapy that these individuals get. Prior to the meeting in the fall were two large studies that were published and presented, one from an international group. It is called the HERA trial. Then a second report was from predominantly US groups, the National Surgical Adjuvant Breast and Bowel Project Group, as well as a Canadian group.

These two groups as well as the international European HERA trial demonstrated

that Herceptin medicine actually dramatically improved the disease-free survival of women who have HER-2-positive breast cancer. Said another way, when Herceptin is added to the standard therapy, the chemotherapy after surgical resection, fewer women have recurrence of their breast cancer. That was a dramatic result in that the recurrence rate was cut by 50 percent, and this is much more than one sees with the advantage of chemotherapy and is in more in line with the advantage women get who have estrogen-receptor-positive breast cancer, when they're treated with an antiestrogen like tamoxifen. So this was huge news.

Now, the other bit of news that was presented at the San Antonio meeting were details of how one treats with that Herceptin. Both of those previous large trials that I mentioned, the HERA trial and the NSABP trial, treated women with this Herceptin medicine, which is an intravenous treatment of antibody. These women received the therapy for one year after their surgical therapy of the breast cancer.

At the San Antonio meeting another trial was presented from Finland, which instead of treating for one year after breast cancer resection, they only treated for nine weeks. In that setting they saw the same reduction in risk of recurrence in breast cancer that these previous longer trials showed. That would suggest that this last year we've learned that using this Herceptin medicine for early-stage breast cancer is useful, but now from the Finnish study it suggests maybe we don't have to treat for a full year after resection of breast cancer but instead treat just for a very short time, relatively short time, of nine weeks as compared to a year.

Now these therapies are not given alone, they're given in combination with chemotherapy if it's indicated or hormonal therapy if the patient has estrogen-receptor positive breast cancer. So this was a major advance, both the knowledge that we can now use this Herceptin in the early-stage breast cancer in what's called the adjuvant setting and the additional information that may not be required that we give this therapy for a full year after resection of

breast cancer, that shorter regimens may be used. I will tell you that clinicians are now often treating for a year, but in each patient they're considering this shorter therapy as well. The other point to know is that while the large trials that have demonstrated that adjuvant Herceptin is useful, those are very large trials, so it is a very solid result.

The Finnish trial that used the shorter-term therapy was a much smaller trial and we're less confident in those results. While they're exciting and interesting and provocative, many people feel that we're not quite ready to move to the shorter therapy for everyone, and many oncologists are still falling back on the extremely strong results from those larger trials: the HERA trial and NSABP trials.

So just to summarize this part of it, within the last year we have learned that women who have early-stage breast cancer that expresses the HER-2 gene and that is HER-positive, now it is very reasonable and, in my opinion, warranted to treat with this additional therapy called Herceptin. Just to reiterate, one year of therapy treated either weekly or every three weeks is an acceptable way of treating this condition. The Finnish study suggests that it might also be feasible to treat shorter times, for nine weeks. So that was a major advance in the adjuvant setting.

A second area of discussion in early breast cancer was an update on the new test that is done on tumor specimens to predict whether one is likely to respond to chemotherapy or hormonal therapy. This is called the Oncotype DX test. Many of you listeners may have heard their physicians talk about this test. It's a test that can be used to predict the likelihood of responding to either hormonal therapy or possibly chemotherapy. At the meeting there was an update given concerning the Oncotype DX. The author suggested that the Oncotype DX test might also be useful to predict in women who have had a lumpectomy whether or not they might have recurrent disease within that breast. What was presented was that using this test a subset of

women could be identified who have a relatively high likelihood of having recurrence within the breast after lumpectomy only.

And while this is a small study and just preliminary, I don't think it would change practice yet, it suggests that the use of this test might help when they decide if they fall in the very high-risk group to add chemotherapy possibly to their lumpectomy or if they fall in the very low-risk groups, maybe to avoid chemotherapy and just use radiation therapy and/or hormonal therapy if there are estrogen-receptor-positive tumors. So that was some of the major presentations in the area of early-stage breast cancer.

Let me move to some of the advances in the metastatic setting. These are new advances discussing ways to treat metastatic breast cancer. As most of the folks on the call know, metastatic breast cancer is typically treated with either hormonal therapy if tumors are estrogen receptor-positive or chemotherapy if not or sometimes both. Now, a presentation was made discussing the medicine Avastin.

Avastin is another new targeted therapy. In this case it is another antibody that is targeted to what is called the VEGF molecule and receptor. This particular receptor is found on the blood vessels of tumors and is involved in the ability of tumors to grow blood vessels and support their blood supply. Previous studies have demonstrated that this Avastin, otherwise known as bevacizumab, is useful for the treatment of metastatic breast cancer. Dr. Miller from one of the cooperative groups presented their data from what's called the ECOG study number 2100.

In that particular study, women with metastatic breast cancer were treated with either paclitaxel chemotherapy, which is one of these taxanes, either with or without this anti-VEGF antibody called bevacizumab. In those patients who got this anti-VEGF antibody, it dramatically increased the time that women did not have progression of their breast cancer.

Now, in my opinion, this study has both a pro and a con. The pro is it's a positive study that clearly demonstrated a benefit from this new antibody, Avastin. Another benefit is this new antibody has very few side effects. The main side effect is induction of hypertension. It also can cause kidney problems. It also can cause, ironically, bleeding in some patients and potentially thromboses.

Now, while it was clearly an improvement, and the women that were treated with this medication had a prolonged time before their cancer started growing again, this was not a cure and all the patients eventually had progressive disease and eventually their metastatic breast cancer continued to grow. The other aspect is that while there was a benefit, this benefit some might consider short-lived. In this particular study, the time that the women that were treated paclitaxel chemotherapy had their disease stabilized was six months. If the women were treated with the Avastin or bevacizumab antibody, the time that their disease was stable was approximately 11 months.

So that's sort of a glass that's half full or half empty. The idea is the almost doubling in time that the cancer is quiescent or staying stable. On the other hand, it's only an improvement of six months. So I personally think it's up to the women with metastatic breast cancer to decide whether that six months additional quiescent disease is worth this treatment. The anti-VEGF antibody is again an IV antibody that it requires coming to the doctor's office frequently and is exceedingly expensive. Now, insurance does pay for this at this point, but I know if this is used for all women with breast cancer that the expense may become a problem.

Now, in the case of the antibody Herceptin, only patients that have the ErbB2 or HER-2-positive breast cancer can receive Herceptin. In the case of this other antibody called Avastin, all women with metastatic breast cancer are potentially eligible for Avastin, particularly if used in the early setting of the treatment of their metastatic breast cancer. So that was also an

important update from the San Antonio Breast Cancer meeting.

As a medical oncologist, I actually continue to struggle with whom to give this bevacizumab or Avastin. I take it on a case by case basis and discuss with each patient that has metastatic breast cancer, whether this improvement in keeping their disease quiet for about five or six months is worth all of the additional doctors' visits and effort to use this Avastin method. I know other physicians are, in some cases, routinely giving it. So this is a new change in the last year for our treatment of metastatic breast cancer patients. It was certainly big news at the San Antonio meeting.

Now, you might ask whether this anti-VEGF antibody is useful for the early treatment of breast cancer. We do not know the answer to that yet; but there is a clinical trial done now to test that question to use bevacizumab, this Avastin antibody, in the setting of early breast cancer after patients have had surgery to remove the breast cancer and possibly chemotherapy or hormonal therapy. This trial adds the Avastin antibody to that to see if it might benefit early breast cancer patients as well, just as the Herceptin medicine did for the HER-2-positive patients. Currently we have no results from that trial, and it may take several years to complete, so we'll await those results. So there's a lot of interest in using these antibodies or these targeted therapies for the treatment of both early breast cancer as well as metastatic breast cancer.

Let me move on to screening. There was certainly a large discussion of screening techniques and improved screening techniques at the symposia. Most of it was not at the level of clinical practice. There was an entire symposium on nanotechnology, these tiny, tiny little particles and might they be useful for screening. While it was very sort of high tech and sort of Star Wars technology, the application of nanotechnology to breast cancer screening or treatment is really far off. So it was a very exciting session but not particularly useful for clinical medicine

yet, although it was promising.

Potentially more promising were some discussions about the benefits, the pros and cons of digital mammography versus traditional film mammography. There were some authors presenting their work that was recently published in the *New England Journal of Medicine* also comparing traditional film mammography with digital mammography. I think it is generally felt that digital mammography might be better, but in fact this *New England Journal* paper and the presentation at San Antonio demonstrated in terms of screening sensitivity in women overall that basically digital mammography and film mammography were similar. It is good news for those women that get film mammography saying it is overall just as good as digital mammography, so you don't need to worry that you must get digital mammography.

On the other hand, for those that get digital mammography, if one looked at a subset of the women overall, it was discovered that digital mammography, while overall is similar to film mammography, that in some subsets digital mammography looked to be better able to identify lesions that were suspicious for breast cancer. The specific groups that looked like digital mammography might be most useful were younger women, particularly premenopausal women with dense breasts or women with very heterogeneously dense breasts, difficult breast to see masses on traditional film mammography.

Just to summarize that, the digital mammography, which is very similar to the digital camera that many of us use now, it takes a picture that is stored in a computer and the intensity of the computer image can be either made lighter or darker on the computer screen. So that's digital mammography. That is now available in many places and overall has the same sensitivity and ability to detect suspicious breast masses as film mammography. However, the digital mammography may be useful or more useful in particular subgroups, and those subgroups would be women with very dense breasts and possibly very young women who are at risk or

high risk for breast cancer. And that, I think, has a highly relevant impact for the group tonight.

There were other posters on screening techniques and efforts to improve screening, but I think my take-home message from the meeting was there were no major advances in developing new screening tests. While this is still an extremely important area of study and one that people are making huge attempts to make advances, we haven't yet made major advances over mammography.

Let me skip the prevention part that Anna Cluxton will present. Leslie Bernstein gave a fabulous talk, which Anna will tell you about. Then I will move to the basic science areas. There were several basic science things that I wanted to touch on. One is an area that many, both patients and breast cancer physicians, are concerned about, and that's called the triple-negative breast cancer. This is the worst kind of breast cancer, a highly aggressive kind of breast cancer that is negative for the estrogen receptor. It is also negative for the progesterone-receptor and it is negative for that HER-2 protein that I started off with. So the markers that we know we have targeted therapies for, this particular cancer does not express any of them.

It's a very difficult cancer to treat and the oncologists are basically forced to use chemotherapy to treat those breast cancers. There was a presentation by Dr. Chuck Perou at the University of North Carolina specifically discussing the triple-negative breast cancer. There were several presentations discussing the basic science of this, about using the new techniques of genomic profiling to look at the expression of the DNA and the RNA of these tumors. They discovered that this particular kind of breast cancer, the triple-negative breast cancer, has a particular gene signature or it's like a genetic fingerprint, which one can identify the triple negatives with.

And it's also coming out that these triple-negative breast cancers express other proteins, which might be markers and might be targets for future therapy. So actually, there is

some promise that they're not fully negative. They do express some potential target, so they'll be positive but it's just we don't have the drug for them yet. That's why this particular presentation remained at the level of basic science. However, one of the molecules that they seem to express highly is the epidermal growth factor receptor, otherwise known as EGFR. This particular receptor, there has been made antibodies to, again, some of which is the Herceptin or the Avastin that I mentioned earlier. And the antibody to the EGF receptor is called cetuximab. They all have very bizarre names and difficult to say, even for us.

So the antibody cetuximab is used to treat EGFR-positive tumors, and Dr. Perou described the clinical trial that is being done at the University of North Carolina in Chapel Hill, in which women with triple-negative breast cancer are treated with either this cetuximab antibody alone or with a cetuximab antibody with traditional chemotherapy, specifically with carboplatin therapy. That trial is ongoing. We have no results from it, but it represents a translation of the basic science studies of the triple-negative breast cancer into at least a clinical trial.

Now I'll just end with one more basic science find, which is there was a lot of discussion about the particular breast cell that becomes the breast cancer. What is the earliest, earliest cell that would evolve into a breast cancer? The scientists debate this a lot. There was heated discussion on this topic, but there's now the feeling that cancers have a stem cell. Just like embryos have a stem cell that grows into a full embryo, there might be a cancer stem cell as well. And actually there was presented at this meeting a lot of data to suggest that that is true, that there is a cancer stem cell that may provide basically the continuing production of cancer cells.

The theory proposed is that one of the reasons we often are unable to cure metastatic cancers is because our chemotherapies kill the more differentiated or the more

developed cancer cells, but that these chemotherapy do not kill the stem cell, the one cell that can then propagate more cancer cells. Until we get a therapy that kills that stem cell, the theory is that maybe we will not be able to cure metastatic cancer. Therefore there is a huge effort to both identify and discover what this stem cell is and then to target drugs to the stem cell to kill it. The people that are following this theory would suggest if we had a good therapy for these cancer stem cells that we could cure metastatic breast cancer much more easily than we can now.

So I think that is an overview of some of the advances in the San Antonio Cancer Symposium and I look forward to additional questions. Maybe we can go into any of those areas in little more detail. With that, I think I'll turn it over to Anna.

LIZ WOHL: Thank you, Dr. Brown, for that very interesting presentation. That was just fascinating. Now, Anna?

ANNA CLUXTON: Thanks, Liz. So, as Dr. Brown said, I'm going to be touching on Leslie Bernstein's talk about risk reduction, which was a very elegant presentation and very well received. But I wanted to talk about why I felt that would be appropriate for the YSC constituency, and part of it has to do with my job during the day managing a cancer genetics program and a cancer risk program.

So risk reduction is obviously a big area of interest to me for work, but outside of work, being a breast cancer survivor I'm always wondering if a risk reduction strategy could be applied to survivors, sort of the flip of tamoxifen being used as a risk reduction strategy for women at high risk and that was part of the STAR trial which should be throwing its results out to us soon. But that came from being used as a treatment for breast cancer and could it be used as a preventative method for breast cancer, so I kind of flip in my head, the things around that are used as a risk reduction for non-affected individual, could those of us who have survived breast cancer or living with breast cancer use some of these same strategies to increase our disease-free

survivability or overall survivability.

I also thought I would talk about a couple interesting presentations, one which was very particular to young women and actually involved one of our constituents from the San Francisco area, and then also a session that was done in the general session that was about using radiation therapy, as opposed to doing an axillary dissection. So those were two interesting ones.

So first let me talk about a poster that was done. One of the key investigators in this poster was Lucy Berlin. Lucy Berlin is a YSC member from the San Francisco Bay Area and she's involved with a group called Bay Area Young Moms with Breast Cancer. She did this in collaboration with Stanford University and University of California at San Francisco. The poster that they did was a retrospective survey on neoadjuvant chemotherapy versus adjuvant chemotherapy and talking with young women who were treated with neoadjuvant chemotherapy and comparing their experiences and attitudes as they went through treatment.

So I just again, wanted to comment that I think it's really great that the San Antonio Conference is so wonderful and unique that it gives us as advocates the opportunity to work directly with scientists. And in the past, the YSC has had the pleasure of working with Dana Farber and a lot of other really great institutions. And if you go to our web site, you'll actually find current studies that we're working on in sort of collaboration with other institutions.

So this was a pretty small study, but I think it was really great. They interviewed 24 patients, seven of whom received neoadjuvant treatment, 17 received standard adjuvant treatment, and the difference between those being neoadjuvant before definitive surgery and then adjuvant treatment being given after definitive surgery. So the biggest observation that came out was that most women who did not receive neoadjuvant felt that they were not given enough information to have made their decision about whether or not they should get neoadjuvant. Every woman who was offered neoadjuvant chemotherapy agreed to undertake it. One of the

things this poster did not address was if there are any benefits to neoadjuvant, and certainly Dr. Brown can speak to that and sort of the science of doing neoadjuvant or not. But this poster again was really looking at the psychological needs and the attitudes around doing neoadjuvant.

The women who did not receive neoadjuvant typically had had an excisional biopsy so they were not really candidates for neoadjuvant. Their medical oncologist didn't mention it or offer it to them or the surgeon might have advised against neoadjuvant, sort of saying that they needed a definitive surgery beforehand. Some of the perceived benefits by the patient, regardless of whether or not there are actual clinical benefits, the perceived benefits by the patient were this ability to monitor your response. So if you're taking chemotherapy and you actually see some reduction in the size of your tumor, then you have this perceived benefit that the chemo drug must be working.

Another benefit is the ability to start your treatment quickly. Those of us who have gone through surgery and chemotherapy know that there can sometimes be a wait between the time that you're diagnosed and the time that you have your surgery and that wait can seem like a really long time. The ability to start chemotherapy and feel like you're doing something right off the bat can have a real impact on reducing someone's anxiety. Some of the concerns that came out of it by those that were interviewed is that even if their tumor was not showing any response, that there wouldn't be a change to their regimen. Probably for most of them that would be true. So that's a genuine fear although, you know, when it plays out, you have certain standard courses of therapy that you're taking, so we know what the ultimate outcomes are, but as you're going through it, it can have a different feeling.

Then there's some misinformation that can be spread through the nature of just going through this therapy, worried about metastatic spread because you're having things course through your blood or just a variety of misinformation. So I thought that was a really interesting

and well-done study and wonderful again that it would involved an advocate who really spearheaded this study and really congratulations to her for getting a poster at San Antonio. I think there maybe some other stuff that comes out of that. So that was really interesting.

The next study that I thought was really interesting that was presented, this is a prospective study and it was presented on Friday and it is entitled, “Prospective study of axillary radiation without axillary dissection for breast cancer patients with a positive sentinel node.” This study is still being done at Mass General, Brigham and Women’s and Dana Farber. I’m not sure if I understood whether or not the actual accrual was closed or not. I’m thinking that it is and at this point they’re in the following phase.

So what they did with these patients is that patients who were clinically a tumor size of a one or two and clinically node negative, and what that means is that they didn’t have any flow in lymph nodes to make the surgeon or the medical oncologist suspect that there is already advanced cancer in the axillary area, that they would have their breast-conserving surgery, meaning a lumpectomy, and they would have a sentinel node biopsy during the surgery. If that was positive, the standard step that happens in most cases, that if you have a positive sentinel node biopsy, you go on to have an axillary node dissection and that helps determine the type of chemotherapy that you’ll receive and radiation therapy, etcetera.

So with these patients, if they had a positive sentinel node, they stop there. They did not go on to complete the axillary node dissection. Instead when the patients received radiation treatment, they actually had their axillary area radiated. Thus far, they’re at a median follow-up of 32 months with about 73 patients that are enrolled thus far, and the early follow-up is showing extremely ... well, let me just recap, the benefit to all of this would be decreased numbness. So for any of you that have had axillary dissections you certainly can attest to the numbness that you have through your whole arm and underarm area. A better range of motion,

less time out of work, because you don't have this limited range of motion and, seemingly and possibly, a decreased risk for lymphedema.

So the early follow-up on this study is showing that all of their thought is holding true, that if they radiate the axillary area instead of removing what could be a lot of positive nodes that you maybe able to afford treatment to that area. So that's an interesting study and one to kind of keep an eye out for of what could happen in the future.

Then lastly, just to speak to Leslie Bernstein's talk about risk reduction ... and Dr. Brown is actually being pretty modest because he was also part of the official satellite symposium. What happens is every night at San Antonio you have all these different pharmaceutical companies and other organizations that sponsor little dinner symposiums and it may be to talk about one thing or another, but there's an official dinner symposium and that's held on Saturday night. That had a wonderful panel of four speakers, of which Dr. Brown was one of them and that also was on risk reduction. So that was a really wonderful talk too.

But in Leslie Bernstein's particular talk, she did a great job of giving an overview of everything that has been done in the area of risk reduction. She started off by dividing risk reduction into two areas, those that are not modifiable and those that are. So the things that we can't change: being women, our age, as those of us that are survivors are all too familiar. We know that your risk for breast cancer increases as you get older because we've all heard some things contrary to that. Your gender, obviously, if you're a woman that's your biggest risk for developing breast cancer. Your race or ethnicity. Any proliferative breast disease or benign breast disease, if you've had biopsies with atypical ductal hyperplasia or things of that nature. Your family history, the age at which you started having periods and the age at which you go into menopause. So the things you can't really change, although she did talk about some things that are being looked at to change those.

Then the things that you can change or the things that we do have limited control over would be our pregnancy history, the status of our ovaries, meaning do we have them or don't we, do we breast feed or do we not. If we have had radiation treatment at a younger age, for say lymphoma. And then this is where it was really interesting with some of these lifestyle things that we can change. The biggest one that I thought was really interesting was in the area of physical activity and adult weight gain obesity and our alcohol intake. Then also she talked about green tea and soy.

So just looking quickly at this area of your age at which you have your periods starting and how that can change or not change, it's sort of interestingly related to exercise. So first of all, in several different studies in the past year that have come out and some of you may have seen kind of hit the headlines, is that overall, women who exercise what I consider a high amount in my limited time to exercise, but four to five hours per week, so that's about an average of 45 minutes a day, have a greatly reduced risk of developing breast cancer. Some studies were even showing up to 50 percent risk reduction. That's pretty incredible and impacting. There have been other studies showing lesser amounts but still enough to make you sit up and take notice about exercise in general and what it can do.

How that could actually impact even younger women and how I think this is relevant to our constituency is again going back to this as survivors what can we do to reduce our risk of developing further breast cancer, but also to our sisters and our mothers and our daughters and what kind of information can we give to them because they are certainly at a higher risk by the nature of us being survivors. But exercise in women of reproductive age, especially younger women and teenagers, seems to have a higher effect on this occurrence of cancer.

And they think that that could be women that are really strong athletes and especially in their teen years tend to disrupt their period cycle and that could have some impact.

Your overall lifetime physical activity at a higher level seems to lower your risk of breast cancer. So that was just really, to me sort of this light bulb moment and just a really impacting thing that I've been telling to everybody I can even get a chance to talk to about.

She also talked about green tea. So I came away from San Antonio thinking, all right. I'm going to exercise four to five hours a week and I'm going to drink a cup of green tea a day. That was because of a couple interesting studies that looked at green tea. One in particular was the University of Southern California, from which actually Leslie Bernstein is from, and they interviewed women who were Asian. So they live in the Los Angeles area and they were Chinese, Japanese, or Filipino.

They interviewed women who had developed breast cancer and also women who never had breast cancer and they asked them a lot of questions but they asked them about their tea intake, green tea and black tea, and they also asked them about their soy intake, how much they ate daily and also just general questions about their diet. They also noted the women's reproductive history and any other factors that could be looked at. Then they compared the answers of the women who had been diagnosed with breast cancer versus those who had not.

What they found was that drinking black tea was not associated with any increased risk or any change in risk whatsoever. Women who drink at least three-quarters of a cup of green tea a day seem to have about half the risk of breast cancer as to women who drink no green tea. And women who ate soy more than once a week also had about half of the breast cancer risk of those who didn't.

The benefit for the women who drink green tea was mainly seen in women who also had small amounts of soy in their diets, which is interesting for us I know because I am sure what gets brought up in a lot of women's minds is well, soy or tofu, it's a phytoestrogen, should I be eating that, should I not? So this all plays into that. But I think really the take-home

message of that shows certainly that adding exercise to your lifestyle and serious consideration of drinking green tea, it seems as if they could have some impact overall in risk reduction

Then of course, there is the sort of more well-known areas of risk reduction, such as taking tamoxifen if it's a high-risk population, whether you're a breast cancer survivor who is hormonally positive or if you were just high risk, so say, again, our sisters or our mothers, that they can actually take tamoxifen as a risk reducer. But one of the things that Leslie really touched on is how there's such a noncompliance issue, meaning that the side effects from taking the tamoxifen seem to overshadow a woman's willingness to take it. Certainly again those of us who take it because we were prescribed it as part of our post-breast cancer therapy who have had side effects can imagine that somebody who sort of lacks the motivation of having had breast cancer might be a little less inclined to take it every day like they're supposed to.

I think that's actually about all I wanted to cover on this unless there was something else Dr. Brown or Liz that you think I should touch on.

LIZ WOHL: Anna that was very fascinating. It looks like we have to dust off our gym clothes.

ANNA CLUXTON: Exactly.

LIZ WOHL: Thank you so much. I think now we're going to open the call to questions. Please remember to keep your questions brief and general.

OPERATOR: Our first question comes from Natalie.

NATALIE: I wanted to know where I could find more information on the triple-negative study? I didn't catch the doctor's name -- Chuck Perou?

POWELL BROWN, MD, PhD: The doctor that presented that is Charles Perou at the University of North Carolina in Chapel Hill. I think he has a web site that you could go and see what he's doing. Now his work that he presented at the San Antonio meeting is not

published, so you cannot easily find that, although the San Antonio Breast Cancer Symposia presentations I believe they're still on the web site for that meeting. On the other hand, the earlier data classifying or sub-classifying the different kinds of breast cancer and one of the groups being the triple negative is found on Dr. Perou's web site as one of his publications. So I would take a look there to start with.

NATALIE: Thank you.

ANNA CLUXTON: If I could jump in and add something to that. You are right. You can actually access, if you are so inclined and willing to use a dictionary at the same time, you can go to the San Antonio web site, which is www.sabcs.org, and you can access the abstracts to the presentations. You can abstract posters, you can see the agendas and after a while, I think it will take maybe another four or five weeks to get up there but you can actually see streaming video of the presentations. But again it can be a little cumbersome. You might have to look some things up because it's obviously given at the very high level of all of the clinicians. But for those of you that are interested and so inclined it can be a very interesting web site.

OPERATOR: Our next question comes from Sara. Go ahead, please.

SARA: Yes. I apologize; I missed Dr. Brown's first probably ten minutes of his review and I'm not sure if anything new was covered on breast conservation surgery. I'm in my fifth month of chemotherapy. I've done neoadjuvant therapy and have been very pleased with that choice, have seen tremendous shrinkage in my tumors. I had two tumors in my left breast, one which was five centimeters, the other was three centimeters, as well as two lymph nodes affected. Unfortunately my breast cancer was not detected very early. But I've had great success with my chemotherapy. I have three treatments left and I'm now looking at surgical options. I've been reading and pulling up information. Is any there information out there on the

advantages of younger women going ahead and having a mastectomy versus just doing the lumpectomy?

POWELL BROWN, MD, PhD: I think there are several questions in your comments. The first one is were there any discussions of breast conservation therapy. Typically to the oncologist that means is there a comparison between lumpectomy versus mastectomy. I don't remember any major discussions on that topic, although there was a presentation that discussed whether there was any delay on therapy by doing either lumpectomies versus mastectomies. The discussion was if you do a lumpectomy sometimes you don't get all of the tumor and they have to go back in to do a re-excision and were there any sort of a long-term consequences of that. The conclusion of this small presentation was no, there are no negative problems with having that re-excision and having it slightly delayed because of that.

Now the other question it sounded like you were talking about was the topic of neoadjuvant therapy, where you get your chemotherapy before you get your surgery. And the chemotherapy is designed to shrink both tumor and then surgery can come back later. And one of the reasons to the neoadjuvant could be that lumpectomy is planned as opposed to mastectomy. I think as Anna Cluxton mentioned, more and more doctors are using this neoadjuvant therapy with the chemotherapy preceding the surgery.

SARA: Right. And that's what I've done.

POWELL BROWN, MD, PhD: Correct. That's what I understood. And in fact that has several benefits. One: you can often shrink a cancer and make the surgery more minimal. But two: it tells the doctors what chemotherapy is really working. Because if you have the chemotherapy after the surgery you don't really know if it's shrinking the cancer. So there are some advantages to that. Certainly for the larger tumors, pretty routinely we've used the neoadjuvant chemotherapy. So I think yes, that's a frequently done plan. In terms of are

there data to say that lumpectomy versus mastectomy after neoadjuvant therapy, I don't think there are the huge trials that have been done to compare lumpectomies versus mastectomies that had previously been done without the additional chemotherapy. But the impression is that the older data would apply to this setting as well. I think the bottom line is many people are using neoadjuvant therapy and it'll often allow lumpectomies.

ANNA CLUXTON: In general, Dr. Brown, the original data in the studies that were done comparing mastectomy to lumpectomy with radiation, and NSABP is the name of the group that did that, and forgive me for not knowing which like B1 or B2 or something like that that clarifies as to which study it is, but that has had about a 20 year or maybe longer look at data to see that they are equivalent, as far as overall survivability. But I do think you can pull out a little bit of premenopausal women in that and note a slightly increased risk for local recurrence. So if you had the lumpectomy with radiation you might be more likely to have a recurrence in that breast and have to go back in and either have a mastectomy or have resection later on, but the overall survivability rates are the same.

POWELL BROWN, MD, PhD: Absolutely, and I might just jump in and make another comment that I didn't have a chance to address earlier. Many questions previously have pertained to the aromatase inhibitor medicines that are often used in postmenopausal women. These medicines are typically not used in premenopausal women. This is often a question by premenopausal women: Why can't we use the aromatase inhibitors in premenopausal women?

The answer to that question is that those medicines do not sufficiently lower the body's estrogen level as they do in postmenopausal women. The premenopausal women's production of estrogen is so strong that the aromatase inhibitors, which lower the body's estrogen level, just don't work in premenopausal women. So that's the answer to a frequently asked question.

OPERATOR: Thank you. We do have a question from the site of Bobbi. Go ahead, please.

BOBBI: Yes, hi. You mentioned Avastin for treatment for metastatic breast cancer. Is there like a specific kind of metastasis that Avastin would be good for? Because I have bone metastasis.

POWELL BROWN, MD, PhD: Avastin was used for all types of metastatic breast cancer, including patients with bone metastasis. So there's not a discrepancy of one type or another. That particular presentation didn't break it up in terms of subsets, for example, bone versus visceral metastasis versus skin. So at this point it is considered for any woman with metastatic breast cancer.

BOBBI: Okay. Is that in addition to what you're having right now? Because like with my case I'm having Aredia or the bisphosphonate as a treatment every four weeks and I have Femara for my hormonal treatment. Now is that in addition to what I have now or is it a replacement for bisphosphonate or how do you go about this?

POWELL BROWN, MD, PhD: It is used in addition to the other therapy, not as a replacement. It was demonstrated to work best in people that had newly diagnosed metastatic breast cancer. So one of the questions is: If you've had metastatic breast cancer for a while and you're on various treatments or you've gone through three or four different treatments, would it add a benefit at that point? This particular study did not address that. So we are considering it for newly or recently diagnosed metastatic breast cancer patients who have not had lots of other therapy. But it can be used in addition and often is either used with hormonal therapy or after you progressed on hormonal therapy with the first chemotherapy.

BOBBI: Well, I was just diagnosed in June of last year, so I guess I could be considered as a recent ...

POWELL BROWN, MD, PhD: It would be reasonable to discuss that with your physician.

BOBBI: Okay, great. Thank you.

ANNA CLUXTON: Liz, while we're waiting, I thought maybe you could talk about the great advocacy scholarship program that there is for San Antonio and just their whole program and how great the Alamo Breast Cancer Foundation has that program set up.

LIZ WOHL: That's a wonderful idea. Each year the Alamo Breast Cancer Symposium offers scholarships to advocates. One of the requirements is that you have completed the NBCC project LEAD program. They put together a session with mentors every night. Dr. Brown of course was a mentor at one of the mentor sessions. Advocates go to the conference and then they meet each night to hear health professionals, doctors, and scientists, discuss what was most interesting at the conference. It's a wonderful way to get a first chance to attend this type of meeting.

ANNA CLUXTON: It is such a really great meeting for advocates because you really have equal access to all the sessions and depending on your confidence level, you can certainly walk up to any researcher and ask them a question about current or horizon research and it's just such a wonderful and empowering experience. But as you mentioned it's required that you have attended Project LEAD and that's another wonderful experience, too.

LIZ WOHL: To get information about Project LEAD, I think we have some of that on YSC web site. We certainly encourage all YSC members to do that.

ANNA CLUXTON: Yes, definitely. It opens up a lot of opportunities for you when you're at the point post-treatment or at a point in time where you're ready to understand more about breast cancer and what you can do to impact young women and how we are researched and treated in general.

LIZ WOHL: Anna, you're the perfect example of someone who's gone on to sit on peer review research panels with scientists. You do the California Breast Cancer Research Program. Do you want to talk a little bit about that?

ANNA CLUXTON: Sure. California has a really great program where they use cigarette tax and also now I think individual donations on your state tax forms. And it funds breast cancer research just within the state of California. So every year they take research grant applications and the panels that review the grants and sort of confer this is worth studying and this is not are made up of people who have to be from outside of California, so that gives all of the other 49 states the opportunity to come and sit on these research panels.

It's really what the Department of Defense breast cancer research process was modeled after. But it's a great opportunity and I'm very thankful for it, not the least of which is the great opportunity to travel out to San Francisco and sit at a table and be on the same level really to know that your opinion means just as much as the researcher next to you who's commenting on this grants application. Your input really carries the same amount of weight and again you're helping to sort of influence the scope and impact of research and it's a great learning experience.

OPERATOR: Thank you. At this time, we do have a follow-up question from Natalie L. Go ahead, please.

NATALIE: Hi, thanks. I might as well take this chance. There is never usually an opportunity. And it may be a random question, but I'm someone who has finished treatment back in May. I always toy with whether it makes sense to keep attending these things and learning about all these great new treatment options, which I can probably not take advantage of. So my question is: Are there ever cases of where someone who had cancer and has finished treatment, a year or two later something comes out that they could then take in an

adjuvant setting again?

POWELL BROWN, MD, PhD: That's an excellent question and many patients are faced with it because actually the advances and the changes in therapies go so rapidly. In general, typically we will offer these newer therapies to women that have had breast cancer within the last year. If you're more than a year out often the benefit of that additional therapy is unknown to somebody that's already done well for a year. So I don't know that there's any data to say it's best to do this.

But I think there's a general consensus that past a year out, we generally don't offer these newer therapies to people that have previously gone through their therapy. Now if you were 13 months that's debatable. This has occurred this year frequently in my practice with patients who had early-stage breast cancer who were treated and who were HER-2-positive. Prior to this year we never gave them Herceptin. Now all of a sudden we are giving people Herceptin. So I have gone back to patients who had HER-2-positive disease over the last year and offered them Herceptin, but somebody two or three years out, I have not.

NATALIE: Yeah. Avastin sounds intriguing but it doesn't sound like we'll be in a place to offer that to someone like me any time soon.

POWELL BROWN, MD, PhD: I would say at this point we have no idea if Avastin helps people in the adjuvant setting. So I wouldn't be upset that you're not getting that.

NATALIE: Thanks.

LIZ WOHL: Dr. Brown, I think I'm going to ask you another question. You were talking about tamoxifen for young women and how the aromatase inhibitors aren't generally used. I'm just wondering because I know that now we're giving the aromatase inhibitors after five years of tamoxifen for postmenopausal women, are you seeing instances of younger women on tamoxifen for five years who when they're done with tamoxifen for whatever

reason become postmenopausal and go on to the AIs?

POWELL BROWN, MD, PhD: Another superb question. The use of aromatase inhibitors in association with tamoxifen remains a bit difficult for the oncologist and for the patients. You mentioned one setting where people take five years of tamoxifen followed by aromatase inhibitors. There are two other settings which oncologists use in the postmenopausal setting, which is either starting with the aromatase inhibitor straight away or treating only for two or three years of tamoxifen and then switching to the aromatase inhibitor.

So those three different sorts of schedules all are being used now. Now for the premenopausal women, as you stated, tamoxifen is really the only game in town for treatment of estrogen-receptor-positive breast cancer. But would it be reasonable to treat that for five years with tamoxifen and during that time if they became postmenopausal, treat with an aromatase inhibitor? We do not have any clinical trials to guide us there. So I guess the honest answer to your question would be I don't know.

Now there are two points I want to make to this, though. First is, many women who go on tamoxifen might have either interference with their periods or begin to go through perimenopause. That does not necessarily mean that they have absolutely reached menopause. So that the aromatase inhibitors in some women that are perimenopausal and they get treated can stimulate the resumption of menstrual periods.

In fact, these aromatase inhibitors have in the past been used as fertility drugs to stimulate ovulation, so that I'd be very careful about using aromatase inhibitors in women that are perimenopausal. That's the first point. The second point is there are now clinical trials asking whether it might be useful to use aromatase inhibitors in premenopausal women in which we have shut down ovarian function with other medications. These are the GnRH agonists; one of them is Zoladex. That medicine can absolutely stop ovarian function, stop your menstrual

periods and stop your ovulation in a premenopausal woman, in a sense medically putting you into menopause.

And one can do that; we know that that medicine can be used in premenopausal women with metastatic breast cancer as a treatment of breast cancer. And now there's a clinical trial called the SOFT trial that is being conducted internationally asking whether or not using the medicine to shutdown ovarian function either in combination with tamoxifen or in combination with an aromatase inhibitor. And the aromatase inhibitor that's being used is called exemestane or Aromasin, and that is being compared to just using tamoxifen in the premenopausal setting. That trial is ongoing, is open both in the United States and in Europe, and is an excellent trial to address this question whether there is a way to use aromatase inhibitors in premenopausal women.

So while they can never be used in a premenopausal woman that has continuous menstrual cycling, theoretically it's possible to shut off a premenopausal woman's cycling medically with these GnRH agonists and then potentially use the aromatase inhibitor. I don't know the results of that trial. That trial is continuing, but within the next few years we should have an answer to whether there might be a way for premenopausal women to gain the benefits of the aromatase inhibitors.

LIZ WOHL: That's very interesting. Do we know what happens when a woman stops taking that GnRH agonist? Does she resume her period or is that just something we don't know?

POWELL BROWN, MD, PhD: It kind of depends on how long you've taken it and whether your ovaries have reached a point where they would go through menopausal naturally. But in general if it's done at a very young age and they're only for a transient time, one would have resumption of menstrual cycling. On the other hand, in breast cancer setting, the

only time we use that medicine are ... that's not quite true. Most of the time we use that medicine is in the metastatic setting and we would not want ovarian function to return, so we rarely stop the medicine to see.

The one exception to that might be using these things in an adjuvant setting. There are physicians that might take a perimenopausal woman and use this ovarian suppression to convert that woman to menopause, so that they could then be treated as a menopausal woman. That's not really standard clinical practice and it would be much unheard to enroll such women in the SOFT clinical trial.

LIZ WOHL: Very interesting. I think we have time for one more question. Do we have one?

ANNA CLUXTON: Liz, while we're waiting real quick, I thought I'd throw in about actually to speak to the woman's comment about if I'm so much past treatment, what is my benefit to these teleconferences and sort of paying attention to this type of information. So if you're in that boat where you're kind of like, "This stuff doesn't really mean a lot to me right now," there's a really great place for you to go and that would be the conference that we do every year.

And we're coming up on the sixth one, February 24 through 26, and that's an in-person conference in Denver, Colorado. And the web site where you can get information is youngsurvivorsconference.org or you can jump off of our web site, there's links to it, but there's travel scholarships available, so it's a very wonderful conference to go, no matter what your stage is post-treatment. And it's also great for your supporters, your spouse or your partner to attend as well.

LIZ WOHL: Yes. And I have to say as well, to be in a room with so many other young women and to just make acquaintance of all these other people is just quite an amazing

experience. I'd like to thank you all so much for your enthusiasm and questions that have contributed to making this teleconference such a great success. We hope that you found it helpful and that we answered your questions. And if you do have more questions or if you think of something that you didn't ask but would like to ask, you can email them to info@youngsurvival.org and we will do our best to answer them.

The YSC is here to provide you with the information you need as a young woman with breast cancer and to serve as a point of contact for you. If you're registered on the YSC web site, and I assume most of you are, you will continue to receive information about upcoming programs, newsletters, and announcements that affect you as a young woman. If you're not on our mailing list, please visit youngsurvival.org to register.

This concludes our program for the evening. Again, I'd like to thank our presenters, Dr. Powell Brown and Mrs. Anna Cluxton for joining us and offering their knowledge, time, and experience. Of course I'd like to thank our operator for helping so much this evening. In about three weeks a transcript of this call will be available and posted on the YSC web site at youngsurvival.org. Again thanks to all of you. We hope you'll join us for our future programming including our February 1 teleconference entitled, "Issues of Diversity in Young Women with Breast Cancer." Of course as Anna said, we hope to see you in Denver for our sixth annual conference from February 24 to 26. Youngsurvivorsconference.org is where you'll get all that information. And thank you all for participating in this call and good night.

[END OF TRANSCRIPT]