



Young Survival Coalition and Living Beyond Breast Cancer Present:

Highlights of the Fifth Annual Conference for Young Women

Affected By Breast Cancer

March 28, 2005

Introduction

ELLY KIRSCHNER: Good evening and welcome to "Highlights from the Fifth Annual Conference for Young Women Affected by Breast Cancer," a teleconference hosted by the Young Survival Coalition and Living Beyond Breast Cancer. The Young Survival Coalition is the only international non-profit organization dedicated to the critical concerns and issues unique to young women and breast cancer. The mission of Living Beyond Breast Cancer is to empower all women affected by breast cancer to live as long as possible with the best quality of life. My name is Elly Kirschner and I am the program director for the Young Survival Coalition. Your moderator for tonight's call is Elyse Caplan, Living Beyond Breast Cancer's education director.

Before we begin the teleconference I'd like to tell you how the call will work tonight. Tonight's call is being recorded and will last approximately 90 minutes. The first 30 minutes of the call will be presentations by our panel.

(Due to technical difficulties, Elyse Caplan picks up the introduction)

ELYSE S. CAPLAN, MA: Many issues were covered during the day and the conference weekend, and unfortunately we could not address all of them in a half an hour. So we are asking each of our two panelists tonight to present highlights of the workshops that they addressed which focus on treatment, research and the impact of living with a diagnosis of cancer at a young age. We want to give all of those who did attend the conference as well as those women who were not able to be there the opportunity to ask questions of our two speakers. So after their brief presentations we have allocated approximately 45 minutes or so for you to ask your own questions. Please keep in mind that we did receive a number of questions that were submitted in advance of the call, and the speakers have tried to incorporate some of these into their presentations; the rest will be taken in the Q&A.

This call will be operator-assisted, so when we open the line for questions after the presentations Jeff will give you instructions on how to answer your questions and get into the queue. Please keep in mind that due to the format of these teleconferences it is difficult to answer very personal questions, so please, if you could, address your concerns in a more general way that may apply to more women affected by breast cancer. Any questions that are of a personal nature will not be able to be addressed. If we run out of time please keep in mind that you still have time to submit more questions to either the Young Survival Coalition or Living Beyond Breast Cancer at our web sites, www.youngsurvival.org and www.lbbsc.org. We will do our very best to get back to you as soon as we can.

Also keep in mind that the transcript of tonight's program, should you need to get off the call

sooner, will be available in several weeks at the youngsurvivorsconference.org web site.

So without further ado I would like to thank you. I am Elyse Caplan. I am the education director at Living Beyond Breast Cancer and I would just like to thank everyone for taking time out of their busy days to join us this evening. For the last few years Living Beyond Breast Cancer and the Young Survival Coalition have hosted an annual conference specifically for young women affected by breast cancer.

This year on February 19th and 20th, just a few weeks ago, we had nearly 800 young women, their friends, family members and health providers participate in 23 workshops and a couple of different plenary presentations. The attendees learned about the medical and psychosocial aspects of breast cancer, and more importantly they had the opportunity to meet and network with other young women from all around the world. It was an inspiring weekend and I can say so particularly because in 1991 when I was diagnosed with breast cancer there was nothing like this available. So it really moves me beyond words to see that we have a venue to bring young women and their loved ones together with key experts to learn, to network and to support one another.

Two of our most highly evaluated workshops that were part of our conference weekend were on opposite sides of the spectrum. One was titled, "What's in the Pipeline? Emerging Treatments for Women with Advanced Breast Cancer" that was presented by Julie Gralow. The other was "Understand the Impact of Cancer on Your Life," which was presented by Dr. Ruth Oratz and Page Tolbert. We are so honored to have both Julie and Ruth with us tonight to provide us with

highlights of their presentations and to take your questions following that.

So I'm going to move right into a brief presentation of Julie and she will take it away. Julie Gralow is an associate professor of medical oncology at the University of Washington School of Medicine and the Fred Hutchinson Cancer Research Center. She is also co-chair of the Southwest Oncology Group Breast Cancer Committee. Julie's research focuses on clinical treatment trials in breast cancer and she has written and published widely on the subject. She is also a member of the American Association for Cancer Research, the American Society of Clinical Oncology, Southwest Oncology Group and the American Society of Breast Disease among many others. Julie is committed to improving quality of life for women affected by breast cancer through education, exercise and diet. She also serves as team physician and medical director for Team Survivor Northwest, which is an exercise and fitness program for female cancer survivors. Julie, we very much welcome you, and thanks for being with us tonight.

Panelist One: Julie R. Gralow, MD

Well, thank you very much, Elyse, for having me here. Having participated in Philadelphia a month ago in this wonderful conference I have to say the energy level was so high that I came back rejuvenated and convinced that I need to run a couple of more clinical trials here and there so that we can get the answers sooner. I was just very excited, and it really drives home the reason why we really need to move this field forward, and quickly. I gave both the talk in the workshop on emerging treatments for women with advanced breast cancer as well as a plenary talk on research and treatment more directed toward young women than women in general with

breast cancer. So in 15 minutes I'm just going to try to overview some of the basic ideas and concepts that I talked about. I can't go into detail with most of them, but maybe in the question and answer session if there are particular areas we can go into more detail on a few of these.

Risk Factors/Risk Reduction:

So with respect to risk factors and risk reduction, what causes breast cancer and what are some techniques for reducing our risk, especially in areas particularly related to young women? We all know that genetics plays a very important role. The younger you are at the age of diagnosis the more of a role our genes are probably playing, -- our inherited genes. In addition to BRCA1 and BRCA2, the breast cancer 1 and breast cancer 2 genes that we've known about now for several years and can test for, what's been in the news in the last year or so is a new gene that's not quite ready to be tested for more regularly, but it's called CHK2, C-H-K-2. It's a gene that looks like it might be associated with some of the families that have a moderately high risk for breast cancer but have tested negative for BRCA1 and 2. I point out this gene, and there are a couple of others that are also promising in the pipeline, to point out that we are working on discovering other genes that are related to breast cancer risk. We know that inherited genetics plays an important role in the development of breast cancer in young women. So keep your eyes and ears open for more news about CHK2 and some other genes.

With respect to what are the risk reduction strategies, well, obviously prophylactic surgery, meaning removal of your breasts, a prophylactic mastectomy; and removal of your ovaries, a prophylactic oophorectomy, can reduce your risk of developing those cancers. But they are pretty drastic procedures that only women at very very high risk would probably want to

consider. We've had an advanced question asking about what is the real reduction in risk if you have a prophylactic mastectomy and you're a known BRCA1 or 2 gene mutation carrier. The answer is it would reduce your risk of getting breast cancer or dying of breast cancer down to just a few percent. There would still be a little bit of a risk of getting breast cancer or dying of it.

But what's really important is probably figuring out first what's your true risk of getting breast cancer, what is your genetic component, what other options exist including chemoprevention, which would be taking a drug like tamoxifen to reduce your risk. And if you have your ovaries removed or kind of turned off at an early age, that can actually reduce your breast cancer risk. So there are also other options, the chemoprevention and lifestyle modifications such as getting more exercise, maintaining a good body weight, eating a healthy diet, limiting alcohol intake. In addition, screening is what we call secondary prevention. It doesn't actually prevent you from getting a breast cancer but it can prevent or reduce some of the consequences of a cancer by finding it early. So good screening is another important feature if you don't choose to undergo a prophylactic mastectomy and yet you have very high genetic risk.

I think that under the area of screening, MRI, magnetic resonance imaging, is really what's most exciting to me. It's very relevant to young women who have either had breast cancer or are at high risk for breast cancer because breast MRI, in some recent studies in women at very high family risk for breast cancer, is more sensitive than mammography and is a good companion to mammography as a way of finding breast cancers at an early stage. So adding breast MRI in young women with a high genetic risk to mammography, clinical exam and self-exam is very

exciting as a way of, if you can't prevent the cancer, then finding it at its earliest possible time point.

Treatment - Surgery:

So some of that relates to some of our listeners, and some of it doesn't relate to all of our listeners, because I've talked about risk reduction and risk factors, and many of you who are listening have already been diagnosed with breast cancer. Obviously we'd like to prevent a second breast cancer but we also need to focus on treating that first breast cancer as best we can. Under the topic of treatment I've broken it up into local treatment and then systemic or total body treatment. Under the area of local therapy that would be surgical options and radiation therapy options. Again this generally applies more to women with newly diagnosed breast cancer than recurrent breast cancer.

Sentinel lymph node biopsy is an interesting way of looking at the lymph nodes that will likely reduce the long-term side effects of surgery. If you've been diagnosed with breast cancer you know that the surgical approach is focused on two things. One is removing the cancer in the breast, and the second is evaluating what's going on in the lymph nodes in the armpit or the axilla because they're a big predictor of your likelihood of recurrence in the future or not. So we need to remove the cancer in the breast, and we can do that with mastectomy or lumpectomy, and we need to evaluate the lymph nodes. And the procedure called sentinel lymph node biopsy is a newer technique where you can inject radioactive or blue dye or both around the tumor and watch where it travels to in the armpit and then just remove one or a couple of lymph nodes that seem to be draining the area of the cancer. If there isn't any cancer in that sentinel lymph node then it is highly likely that the rest of the lymph nodes will also not contain cancer and you don't

need to remove all of the remaining lymph nodes, whereas if there is cancer in that first lymph node then doing a more detailed lymph node dissection, looking at more lymph nodes, would be helpful in terms of knowing how many nodes are involved and predicting recurrence.

So in surgery we've got a general strategy now both within the breast and within the lymph nodes of actually trying to do less. We started back in the old days of breast surgery with removing not just the breast and the lymph nodes but actually part of the muscle of the chest wall. That was called a radical mastectomy, and now we've moved to modified radical mastectomies, which don't remove the muscle, and to lumpectomies, which actually retain the breast. For appropriately selected patients we have the same survival from less surgery. The same thing is happening with the lymph node surgery. We're trying to do less in appropriately selected patients where the outcome would be just as safe. And so the general strategy of surgery is that less can, in many patients, be just as good as more.

Treatment – Local:

Within radiation therapy they're kind of taking the same strategy, looking to see if they can do less and get the same or better outcomes. So a new area of research interest, and this is not entirely tested and proven and ready for prime time, involves just radiating part of the breast more intensely for a shorter period of time. We call that brachytherapy, B-R-A-C-H-Y-T-H-E-R-A-P-Y. Brachytherapy. This is a technique that instead of the six and a half weeks of breast radiation that some of you have undoubtedly gone through you can more locally radiate the area of the breast that the cancer was located in and then just do it over a shorter period, like less than a week. So that's another kind of 'can we do less, get less side effects and get just as good a result' approach we're doing both in radiation and in surgery.

Treatment – Systemic:

In the last few minutes I'll review systemic therapy. This is applicable both to early stage as well as more advanced breast cancer, because systemic therapy or total body therapy is generally treatment that gets into the bloodstream either by mouth or by injection and can target cancer cells wherever they are throughout the body. In general we have three main classes of systemic therapy: hormonal therapy, and that would be applicable to the three-quarters of patients who have hormone-receptor positive cancers. Chemotherapy is another kind of systemic therapy, and then we have the new class of biologically targeted therapies. And I'll go over just a little bit about what's exciting in each of those areas.

With respect to **hormonal therapy** we're still trying in young women to understand if there's a role for shutting down the ovaries. Will that improve survival both in the early stage setting and in the more advanced stage setting? There is a big trial going on that is both European and North American that is called the IBCSG, it stands for the International Breast Cancer Study Group, the SOFT and the TEXT trials, S-O-F-T and T-E-X-T trials. These are trials that are looking at if there is benefit on top of standard hormonal therapy to suppressing the ovaries in early stage breast cancer. I think it's a very important question. We always want to improve survival and decrease recurrences but we also know by suppressing the ovaries in very young women that there are consequences of that with respect to side effects on the heart, on the bones, etcetera.

An exciting class of hormonal therapy that's being moved into the early stage setting is the aromatase inhibitor class of therapy. In general these drugs are only given to postmenopausal women. So the question is in young women, like those of you in the audience, should we

suppress the ovaries and then add an aromatase inhibitor instead of tamoxifen and would that be better. That's also the subject of trials.

Then the third hormonal therapy category is a new class of drugs that really right now has just been tested in advanced breast cancer, but it's a pure antiestrogen. There's a drug called fulvestrant or Faslodex that is actually an intramuscular shot given once a month that is just a pure antiestrogen that appears to have good activity even in tumors that have already been exposed to other hormonal agents. So keep your eyes open for that. It is FDA-approved for advanced breast cancer.

Within **chemotherapy** I think one strategy we're looking at is should we be giving chemo before surgery in some patients or after surgery. We've made great strides in the early stage breast cancer setting with maximizing our chemo, reducing recurrences, improving survival. One group that we've made great advances in is the group of inflammatory breast cancer patients, patients who have very aggressive disease that comes on suddenly. I know there are women in the audience who have been diagnosed with this. It's scary because one day your breast seems fine and the next day it's red and it's filled with tumor. It seems scary how fast it can come on. In the past it also carried a high recurrence rate with it. But we've made great advances with respect to chemotherapy, radiation therapy, hormone therapy in this area and survival rates have gone way, way up for inflammatory patients. This is the group that we usually give chemo first and then surgery and radiation afterwards. So all of the chemotherapy advances have benefited both earlier stage breast cancer as well as our more aggressive cancers.

In the metastatic setting I'm just going to mention three chemo agents that are new kinds of drugs or new strategies of presenting old drugs. One of them is a newly FDA-approved drug just approved last month called Abraxane. It's basically Taxol but formulated in a different way. It's kind of coated so you basically are getting it over a shorter period of time and you don't have a chance to have an allergic reaction if you've ever been somebody who's been given that drug. It's probably a more specific way of delivering the drug to our cancers.

There's another common cancer agent called Adriamycin or doxorubicin. We've also got a new way of formulating this drug that might be a little less toxic to patients. So we can give the same old drugs with respect to Taxol in the setting of the new drug Abraxane and with respect to doxorubicin in a new drug called Doxil by formulating them in a different way and cutting down on their side effects. I'll just mention one more chemo agent that's not approved in breast cancer but is looking of great interest. It's approved for some other cancers. It's called Alimta, A-L-I-M-T-A or pemetrexed. We're doing some interesting studies with that in breast cancer.

I'll just briefly close by going over what's new in the area of **targeted therapy**. For the most part this applies to women with recurrent or advanced breast cancer. But we're actively working on trying to move it into the earlier stage setting. We all know that Herceptin or trastuzumab was the first biologic approved in breast cancer, and it targets the quarter of breast cancers that are HER-2 positive. So about three-quarters of you who have been diagnosed with cancer this wouldn't apply to. So we need to find other targets.

With respect to relatives of Herceptin we have two new drugs, neither of which are approved,

both of which are in studies that look quite exciting and might be approved in the next year or two. One of them is called pertuzumab or Omnitarg, and it targets HER-2, but it might also work in patients whose tumors are not HER-2 overexpressing. And another drug called lapatinib, which targets HER-1, which is epidermal growth factor receptor, and HER-2, that's looking very interesting. We're targeting the blood vessels associated with cancer growth, and that's called antiangiogenic therapy. When a cancer cell tries to recur and grow again it needs to bring nutrients in and bring blood vessels in. So antiangiogenic agents and therapies are recently approved in colon cancer, and we're looking for some studies to come out pretty soon in breast cancer. They're looking very promising as a treatment for advanced breast cancer. We're going to investigate them in earlier stage disease.

Then last on my list of things to mention before concluding is a class of drugs called bisphosphonates. Drugs in this class would include maybe Fosamax that you might take for osteoporosis or Actonel or, if you have recurrent breast cancer and it's in the bones, then Zometa and Aredia are two drugs that are in this class. We can use this class of drugs that basically shut down bone breakdown not necessarily to treat cancer cells directly but potentially to treat them indirectly. You know that breast cancer recurs commonly in the bone, and some of you listening probably have bone metastases and you're probably on one of these drugs. These drugs will slow down the rate of progression in the bones by slowing down bone breakdown. So they don't directly impact the cancer cell; they prevent the cancer cell from being able to break down bone.

Now, if bisphosphonates can be used to slow down the growth of cancer cells once we know that they're in the bone, we're investigating whether they can prevent the cancer cells from being able

to establish themselves in the bone in the first place. So we're about to start a huge, 6,000-person trial that will be open to both early, young breast cancer patients as well as older breast cancer patients, and it will test three different drugs in this class, three different bisphosphonates, to see if in early stage breast cancer, before it's recurred, if we can actually give these drugs for a couple of years and prevent bone metastases and improve survival from breast cancer through pretty non-toxic drugs that at different doses we use to treat osteoporosis all the time.

So I've gone over a whole lot and I've gone over my time, so I think it's Dr. Oratz's turn to speak. But I hope I've answered some of your questions already in this brief outline and we'll have some time to address some of these things in more detail during the question and answer.

Discussion

CAPLAN: Thank you, Dr. Gralow. You covered so much in about 15 minutes' time. My head is spinning. I think you covered many of the medical aspects and some of the biologic or targeted treatments that are ongoing and that are on the horizon for women to hear about. You gave us the names of some of the new agents so that women can take these questions back to their own health care team. You've discussed some of the quote "old drugs" that are reformulated such as Abraxane and Doxil that have these nice little packaging reformulations that make the side effects minimized. You've discussed aromatase inhibitors, which of course are of interest to premenopausal women because we hear that that's not something that premenopausal women could take, however with ovarian suppression maybe we could. And you've really given a lot of food for thought and I know a springboard for many of the questions that will follow the next presentation. So thank you so much for all of that in a short time.

I'd like to move into introducing Dr. Ruth Oratz who is a medical oncologist with us tonight who presented a stirring workshop at Sunday's program about the impact of cancer on your life. Dr. Oratz practices at the Rocky Mountain Cancer Center Rose Medical Center in Denver, Colorado and is associate professor of clinical medicine at New York University School of Medicine. Dr. Oratz's practice focuses on breast diseases, breast cancer treatment and women at high risk for developing breast cancer. She is active in clinical research and has been published widely. Ruth is a fellow of the American College of Physicians and holds many memberships including the American Society of Clinical Oncology, American Association for Cancer Research among others. She is a medical consultant for CancerCare and serves on the advisory boards of Sharsheret and Cancer and Careers. Ruth, we welcome you to this evening's program.

Panelist Two: Ruth Oratz, MD

Well, thanks very much. It's fun sort of reliving what we did in Philadelphia a few weeks ago. I really have to mirror Julie's comments. It was my first time participating in that conference, and I really was extraordinarily energized by the strength, the courage and the beauty of all of the women who I met in Philadelphia. We talked about so many things in our session on Sunday, really a whole range of topics. My assignment, I guess, with Page was to talk about the long-term impact of cancer on the life of a young woman.

There are so many issues that come into play that when I started to think about it the first thing I came up with was, well, what do I worry about? What does the doctor worry about? And then I thought about, well, what is it that the patient worries about? And where do those things

intersect? And where do they collide? So in terms of the things that I worry about as a doctor, and of course I share this with my patients, our number one concern is recurrence. Is this cancer going to come back?

Follow-up by medical team:

So in that regard, close follow-up, a good relationship with your team, and that's for young women often going to be a team of medical oncologists, maybe follow-up with your surgeon or radiation oncologist, and continued surveillance, also GYN, whether that's a general gynecologist or a GYN oncologist who's following you, it's very very important that you have a good, strong and continuous relationship with a good health care team. I have recently relocated. I'm sure you heard in my biography. How does that work? She's on the faculty at NYU, which is in New York City, but she's practicing in Denver. So I know that we move around in our lives and we can maintain these affiliations. So even if you relocate geographically you can stay in touch with your original team of doctors and maybe get another team in your new location to kind of tide you over in that transition until you feel comfortable that you have the right team to collaborate with.

I really want to emphasize that this is a collaboration between the patient and her team of health care providers. So follow-up is very very important, follow-up for recurrence, and we do that mostly by seeing one another. So taking a history, hearing what's going on and physical examination, that's the most important component of follow-up. Sometimes we do blood tests, and that may include tumor markers like CEA or CA 27.29. Sometimes we do scans. I think that the details of what the appropriate follow-up is for any given individual patient is a program

that she has to work out with her doctor and her team, because it may vary a little bit depending on your original stage at presentation, what kind of treatment you had and so on and so forth. So follow-up and surveillance is very important.

The other thing that I worry about as a doctor after recurrence is whether or not a second malignancy could occur, a new cancer. Now, in a woman, a young woman who's already had a history of breast cancer, whether or not she has a defined genetic mutation, that is, whether or not she has a BRCA1 or 2 or even a CHK gene mutation, she might be at risk for a second breast cancer, that is a new primary breast cancer in the same or the opposite breast. So we watch very carefully for that. We also know that there are other malignancies that cluster with breast cancer. If a woman has already had one tumor she is at slightly increased risk for getting another form of cancer.

As Dr. Galow mentioned, if a patient has a BRCA mutation we know that there is an increased risk of ovarian cancer and perhaps pancreatic cancer if it's a BRCA2 mutation. So we watch carefully for that. There are other genetic syndromes and then sort of clustering syndromes where we watch out for colon cancer and uterine cancer. Those tend to occur a little bit later on at an older age and I think are pretty easily screened for by doing colonoscopy and pap smears and good GYN exams on a regular basis. So that's something I watch out for with my patients. I don't think we need to get overly alarmed about those second malignancies, but it's something to keep kind of in the back of our minds.

There is a very very rare but real possibility that chemotherapy and radiation therapy can cause second malignancies. Those are treatment-related cancers, and those could be either leukemias or less commonly sarcomas. Again as a doctor that's something I keep my eyes open for, but it's rare and I would say occurs really in a very very very small number of patients. Those are the sorts of cancer problems that I worry about.

But most of our young patients are, in fact, going to be fine and they're going to be cured of their original breast cancer. So at a certain point although I am concerned about second malignancies I really have to think a lot about what is the general health of this young woman who's going to live for a really really long time after her breast cancer diagnosis and treatment. So general health means we keep track of things like are you eating well, are you exercising appropriately, not smoking, moderate alcohol intake, watching your general blood tests to make sure you're not developing diabetes, keeping track of your blood pressure and so on. So all the stuff that I call "well baby care," you know, the stuff you bring the babies to the pediatrician for is what you should be getting as part of your follow-up from your oncologist and your health care team.

A very important issue for women with a history of breast cancer who have undergone treatment either with chemotherapy or ongoing with hormonal agents is bone health. So all of us are going to get osteoporosis. That's just a fact of life. After menopause all women will lose bone density and, in fact, men will lose bone density, too, as they age. But chemotherapy, early onset menopause and some of the hormonal agents that we use can speed up that process, and we can see accelerated loss of bone density. So that's something we need to pay a lot of attention to and make sure that we jump in early with preventive agents.

Dr. Gralow mentioned that bisphosphonates, which have an important role in treating low bone density and osteoporosis, and we have some evidence now that these agents may or may not be helpful in preventing bone metastases. So that's an interesting class of drugs to think about in terms of bone health. There are some new drugs that are being looked at in clinical trials that have a different biologic mechanism of action to maintain the sort of metabolic activity of bones. That's something that we should pay attention to, as well as calcium and weight-bearing exercise. Remember, your upper extremities have to bear weight, as do your lower extremities. So osteoporosis and bone health is very important.

Another, I think, medically important general subject is cardiovascular health. Again, as women get older the risk of heart attack and stroke increases and some of our treatments may impact on our cardiovascular health. Tamoxifen, for example, has a favorable impact in terms of lowering the total cholesterol and having a good kind of effect on the lipid profile. The aromatase inhibitors don't seem to give us that protective benefit with respect to cholesterol. So again, depending on what treatment an individual patient is on I think we should pay attention to what's going on with her lipid profile and other cardiovascular risk factors. There's lots that we can do there that we know is preventive in terms of maintaining good health. Again, not smoking, maintaining an ideal body weight with a healthy diet that's low in fat and high intake of fruits and vegetables and good exercise. So those things are really important for our general health, bones, and our cardiovascular health.

Those are the things that I focus on in the medical follow-up of the patient, but there is so much more to remaining healthy, especially after a diagnosis of cancer at a young age and I think especially after the treatments that we impose on you for that cancer. Those treatments are surgical, chemotherapy, hormonal treatments, the new biologic therapies and radiation treatment.

Psychosocial impact of cancer:

So what is it that you, the young patient, worry about going forward? Well, of course the number one thing is you want to be healthy and you want to live a long time. Let's take that as a given. If we say that those are the things I'm going to worry about what are all of the other things we have to think about? Well, we really need to think about not only your physical well-being but your emotional and your social well-being. And that's a really big factor. There's a lot that goes into being emotionally and socially healthy, and that's true for all of us, but I think particularly after a cancer diagnosis and a cancer treatment there are very special challenges that come up.

One of the big issues, of course, is fertility. And for a young woman, whether she's had children or not had children, the question of future fertility is really really really a big question. We know that many of our chemotherapy regimens will reduce fertility anywhere between 30 percent and 70 or 80 percent depending on which drugs and which schedule. A very important factor is the age at which you have received those chemotherapy drugs, and we know that younger patients at the time of diagnosis and treatment have a higher likelihood of retaining their fertility, of being able to become pregnant after treatment, than older patients. So the older you are when you're exposed to chemotherapy the more likely it is that you will no longer be able to conceive

naturally after chemotherapy.

There's a lot of research into this area right now and a number of specialists who are looking at options for preserving fertility. There are some programs that are looking at ways to get eggs out quickly and freeze them and have them be viable. That's not quite yet ready for prime time but is technology that we're certainly working on. In the way that we have young male patients give a sperm donation and then freeze that before chemotherapy we'd love to be able to do that for our female patients before we give them chemotherapy. So we're certainly working on that.

There is also some research using the LHRH analog drugs like Zoladex and Lupron, which turn off the ovaries and try to quiet them down, shut them down during chemotherapy. There's now a large intergroup study going on to see if treatment with Zoladex, starting about ten days before chemotherapy and then continuing during the chemotherapy treatment, will help to prevent what we call ovarian failure, help to prevent the ovaries from being damaged by the chemotherapy. The endpoint in this study is to see if women will resume their normal menstrual cycles after the chemo is completed and then also to measure the sort of chemical hormone levels if they've gone into menopause or not.

One thing that's important to keep in mind is that a lot of women will have either irregular periods or will actually stop menstruating because of chemotherapy. But again depending on the age at which you get the chemotherapy your periods may resume six months or even a year later. So even if you've had this temporary irregularity or complete stopping of your periods, what we call amenorrhea, that doesn't mean that they'll never come back. That's again something that's

variable from one individual to the next. So there are lots of concerns about fertility and lots of issues around research going on there. It's a very very active and busy area right now in research for young women.

I think second after fertility for a lot of my young patients is their concern about relationships, and that has to do with no matter how old they are or what their relationship status is when they start out, some women are single, some people are in a marriage, some people are in a relationship with an important other and some people are kind of in between all of those things. So what happens to your sex life, what happens to your personal life after you've gone through this treatment? Again I think we all come into this experience of breast cancer with who we were when we started out. But our sexuality, our sense of self-image, intimacy and libido are all dramatically affected by the treatments that we use for breast cancer.

Surgery can leave you with completely normal looking breasts if you've had breast-conserving therapy and a small surgery for lumpectomy, and some women have had really major surgery with bilateral mastectomies. That can have a whole range of impact on your sense of self-image and quite frankly even on the sensations that you feel in your breasts. Just because someone has had more or less surgery doesn't mean that she's had more or less of an impact on her own self-image or on her own sort of sense of her sexuality. So it's not necessarily that more surgery means you feel worse and less surgery means you feel better. Sometimes just having had surgery is enough for someone to feel that that has an impact on her sense of self.

Chemotherapy certainly has lots of effects on how we feel. I think a lot of women are very fatigued during chemotherapy and experience a real decrease in libido, and that can persist for some time after treatment; as well, the hormonal treatments that we use that either compete with estrogen, drugs like tamoxifen, or turning off estrogen production can result in vaginal dryness and discomfort during sexual activity. Sometimes there are things we can do about that. Then the whole question of libido and sexuality I think is really very very individualized. I think the most important thing is to be open about it with your doctor. If you can start talking to your doctor about how you're feeling and what your questions are -- we can't fix everything but there are certainly some areas where we might be able to help. So I think that the doctors and the patients have to all be more open to these questions of body image, of sexuality and of some of the just truly physical aspects of surgery and the treatments that we give for breast cancer.

In terms of relationships, I mean, sex is a big part of it but it's not the only part of it. There's so much more that fills in our relationships with our loved ones and our family members, our spouses, our partners, our children, our parents, our siblings, the people we work with. You heard that I'm on the board of a group called Cancer and Careers, and Cancer and Careers is a web-based support system that has lots of information about how do you keep working through and after a cancer diagnosis, lots of specific questions. What if you need to cut back on your work? What if you want to work part-time? What are your benefits? What are your legal rights? How do you interact with your co-workers? How do you interact with your boss? What about the people who report to you? What information are you required to share? What information can you keep private?

So I think that work is a very very important part of our lives, and how we integrate work and career and maybe reprioritize work after a cancer diagnosis is one that deserves a lot of attention, and I would certainly refer you all to *cancerandcareers.org*. It's a great web site, and I think we try very hard to provide information that's meaningful to help you integrate work and career into surviving and living beyond breast cancer.

I have found, and I'm sure that a lot of you have found, that there are surprises. People who you think are there for you all of the sudden disappear. They go and hide in the closet once you get the cancer diagnosis. Then there are other people who you never really knew cared so much about you who all of the sudden come out of the woodwork and there they are, really there to support you in a very meaningful way. Embrace those surprises; accept them. Understand that if there are people who are running away maybe it's out of their own feeling of insecurity. Maybe they care about you so much that it just scares them a lot and it's hard for them to deal with it, and it doesn't mean they don't love you. Or maybe there are other issues in those individuals' lives that just make it difficult for them to be there for you.

By the same token I would say embrace and allow the people who are there for you and who love you and can support you to be part of that important support network. Pick and choose. You don't have to let everybody in all the way. But I would say open the door and let some of those people in at least some of the way. So support and community, whether that's from family, from friends, in the workplace or from other community sources, whether that's a church group or a social organization that you belong to or your book group or your daughter's Girl Scout troop, wherever you can find that I think that that's also very very helpful.

Patient/Doctor Communication:

What are the tools we can use so that the doctor's concerns and the patient's concerns don't collide but actually come together? I think the most important thing is that we share our information and our concerns, that we set priorities that are clear so that when you go in to meet with your doctor you really know what your questions are and that your doctor is prepared to give you that information and have a conversation with you. Sometimes you find that you get into the office and you're slotted into some little 15-minute check-up spot there and you have this huge list of things you need to go over. Speak up. You may not be able to address everything on that visit. Then you should say to your doctor, "You know what? I'd really like to come back in a few weeks. Let's set aside 30 minutes or 60 minutes so we can really have a conversation about these things that are on my mind."

And that's okay. You don't have to finish everything in your little 'once every three or four month' check-up. If you feel you need more time, schedule that time with your doctor. If you need referral to a specialist for assistance in another area make sure that you get it. So I would say the most important thing is that we communicate clearly with one another and that we are respectful of each other's needs, the doctors and the patients. I think that by keeping those channels open and trying to address all of these concerns, not just the physical ones but emotional and psychological as well, that you will find that you can really move forward and have a very long and healthy life after a breast cancer diagnosis.

Discussion:

CAPLAN: Ruth, you just, similar to Julie, gave a thumbnail sketch of so many different topics. Before we move to the Q&A session I'd like to sort of summarize and say some of the things that I felt that you addressed that are of utmost importance to younger women with breast cancer –

Distinguishing that it doesn't matter what surgical treatment a young woman has, whether it's lumpectomy or mastectomy, that there's profound impact on one's life, and that there may be a perception out there that women who have not had a mastectomy must be doing differently or better than women who've had a lumpectomy because they've had less breast tissue removed. We all know that women who have had any kind of breast surgery may be left with different sorts of feelings, sensations, and etcetera, related to their breast cancer.

You both raised the issue in different ways about ***irregular menstrual periods***, and I would like to echo that birth control is really important and finding a safe and effective method of birth control is something that you really need to be discussing with your oncologists and gynecologists because we don't know for how long one's menstrual period may stop, and the age of a young woman when her breast cancer is diagnosed may impact her menstrual cycle and her menopausal status.

You talked about ***fertility***, of course a pressing interest to women on this call. I think what maybe one of both of you can talk about in the Q&A is how do medical oncologists work with reproductive endocrinologists. We know some of the pretreatment concerns, but I know some women talk about how hard it is to get one doctor to talk to the other and how does that work

well.

The last two things I'd like to comment on are: you both talked about being proactive about your *bone health*. As premenopausal women we know that some of the chemotherapy treatments may impact our bone health, and that's something that we need be aware of ahead of time because there are good treatments to prevent bone loss or to treat it as well.

And one of the last things you spoke about, Ruth, was *support and how to get support*. One of the things that rung true in my head as you were talking about how younger women affected by breast cancer are often in the position to be giving care to people, whether it's children, whether it's a partner, etcetera, and how hard it is for some women that when breast cancer is diagnosed early in life to be on the receiving end of needing support and needing care, and how awkward and uncomfortable that may be but how necessary it is. So that's sort of my thumbnail sketch of both of your overviews, and I thank you so much for your expertise. If Jeff could come back on the line he could give instructions to the participants on how to get into the question queue so that we can get some questions answered. Again one reminder to try to keep your questions more broad so that they aren't too personalized and appeal to more women. Thank you.

Question and Answer Session

JEFF: Our first question comes from New Jersey. Go ahead please.

QUESTION 1: *Yes, thank you. As a dentist I've seen lots of patients who are on bisphosphonates for either osteoporosis or after having breast treatment, as myself. So it's a concern because the bone loss is arrested. However, because the osteoclastic activity is decreased, if those patients need to have surgery on their jaws for different reasons, whether it is that they would like to have impact fixtures placed or they actually have some type of pathology in the bone that needs to be removed by the oral surgeon, the oral surgeons are coming back and saying that there is dead bone there essentially. It's not reacting the same as normal, healthy viable bone. This is posing a problem for us in the dental community. Can you respond to that?*

GRALOW: So the entity that the caller is talking about is a side effect or an associated symptom that can happen. Osteonecrosis of the jaw is something that's been seen in cancer patients that are on long-term, high-dose intravenous bisphosphonates, in general not the doses that are given orally and used for treatment of osteoporosis. We actually didn't know that this was a side effect at all, because it's so rare and uncommon, until about a year and a half ago when a couple of reports came actually from oral surgeons that some cancer patients had this poor healing of the bone. It's basically exposed bone that doesn't heal well that seems to be associated with cancer treatment and also getting these very high dose bisphosphonates to treat bone metastases.

There was just a hearing that was held by the Oncology Drug Review Group through the FDA, just a hearing within the last month looking at all of the cases worldwide of osteonecrosis of the jaw that have been reported. Basically the end result was that this is a real entity that is being found now. It is incredibly rare. There are several hundred patients now reported throughout the world who have had this poor bone healing related to bisphosphonates, and there are hundreds of thousands of patients treated with these high doses.

So the long and the short of it is if you go on a high-dose, intravenous, monthly bisphosphonate and if you stay on it for many years you have a higher risk of having poor bone healing if you need to have your tooth pulled or if you need to have some work that involves the bone of the jaw. And you should talk with your dentist about the fact that you're on a bisphosphonate. It doesn't mean you can't have procedures. It means we need to think of things differently. If you are on osteoporosis doses of bisphosphonates I really don't think that there is any concern. This is being followed very closely, and we really haven't seen this.

As I told you we're going to be studying whether or not these high doses of bisphosphonates, the doses used to treat bone metastases, not to prevent osteoporosis, if they can prevent the occurrence of bone mets. In those studies we will carefully be making recommendations with respect to dental procedures, and we will also be carefully following what the true incidence of this is. So it's something that we're following. I don't think it's something that has a high enough incidence that it would prevent me from ordering it in a patient. It just means that we need to be talking about it, and it gets to the issue of communication between multiple providers as well as the patient.

JEFF Our next question comes from Oak Park, Illinois. Go ahead, please.

QUESTION 2: *Hi, thank you for having this conference. I will give a brief synopsis of my history, but I have two general questions that are applicable to advanced breast cancer. I'm 29 years old and was diagnosed last year with infiltrating ductal cancer presenting with inflammatory breast cancer characteristics with metastasis to the liver and the bones. And this year, exactly a year later, I was diagnosed with breast cancer in my other breast while I've been on chemotherapy through the whole year and now have possible lung metastasis. My first question is how common is it to have bilateral breast cancer in young women? I have been tested for BRCA1 and 2, which is negative. In what way, if any, does the inflammatory component change prognosis in women like me? Number two, with respect to a specific hormone receptor issue in the sense that I am estrogen-receptor positive and I have been on Zoladex for treatment and a question of whether Zoladex is equally as effective as oophorectomy in advanced breast cancer. Thank you.*

GRALOW: Ruth, do you want to take that one?

ORATZ: Well, as we said at the beginning of this conference we really can't do a sort of consultation over the telephone with respect to an individual's treatment. But just a few specific comments. I think that once breast cancer has metastasized we really focus our treatment on trying to control the distant disease, that is, the metastatic disease. And treatment is targeted at that metastatic disease. So whether the tumor was inflammatory at its primary diagnosis or not

doesn't have that much of an impact on what treatments we would choose once the cancer has spread. So looking at the molecular characteristics of that cancer, if it's estrogen-receptor positive we would think of having a component of hormonal therapy in there. Chemotherapy I think still is the mainstay of treatment for metastatic disease. And as Julie said we're really, I think, aggressively looking at a lot of the new biologic targeted therapies using monoclonal antibodies and small molecules and antiangiogenic kinds of treatments. So I would actively explore clinical trials for advanced disease.

In terms of having a second primary breast cancer, this is something that we see in young patients, and you said that you had genetic testing, which is appropriate that you were referred for that. The fact that they didn't find a genetic abnormality may or may not mean that there was no familial susceptibility to breast cancer. Again, we always have our antenna up in very young women that there could be a genetic component to this even if we haven't yet identified the gene that's responsible for that individual case. In that situation the second primary breast cancer is treated sort of independently. It's a new, independent event. Now, in the context of metastatic disease we would, of course, try to integrate treatment so that we're treating that second cancer with intent to make sure that we eradicate it and at the same time use therapy that may be appropriate in the setting of metastatic disease.

I think also when we're treating recurrent or metastatic disease there's a lot that goes into that treatment as well. Certainly the most important component is the choice of the medical regimen to try and control or eradicate the cancer. But we really need to pay a lot of attention to the other kinds of therapies that we use, again, protecting bones, making sure that your blood counts don't

drop to a dangerous level, using growth factors when that's appropriate so you don't have low white blood cell counts and infections or you're not getting too anemic and getting fatigued, making sure that you're not having too much weight loss or weight gain during treatment and so on. So the management of side effects to maintain quality of life during treatment is really really important and you should be sure to be addressing those things with your physician. So I know that's a kind of general broad-brush stroke answer but it's difficult to give personal one-on-one kind of consultation in this setting.

JEFF: Our next question comes from Newbury, Ohio. Go ahead, please.

QUESTION 3: *Thank you. I have two relatively quick questions, I think. One is have there been any studies as far as organic foods, what types of the meat, what types of diets are best? I have inflammatory breast cancer, stage IV, mets to the spine. Then another study that I've been following and I wasn't sure if you had any information on is at Temple University, a PLK-1 gene. It's a medication that interferes with it and I guess the tumors die. I was just wondering if you had any information on that.*

ORATZ: Why don't I take the diet question, and I'll let ... Julie, I don't know if you know about that PLK gene. In terms of diet I think what most of us would recommend is a well-balanced, healthy diet. So that means lots of fresh fruits and vegetables, and I think that's the best way to get your vitamins and minerals. Probably to limit fat. In terms of carbohydrates I try to emphasize whole grains and the carbohydrates that are not too complex. So not too much starch, if possible. But it's perfectly all right once in a while to have a cookie or a piece of bread. That's

okay.

In terms of the protein in the diet I think that the current recommendations are that you need an adequate amount of protein. It's okay to get your protein from animal sources. We don't really have any data that links whether the protein comes from organic food or not organically raised animals, but there is some perhaps anecdotal concern about whether poultry products and beef products have excess additives, hormones, and growth factors in that food. I'm not sure that if we ingest, by eating, the meat from an animal that was treated with a hormone or a growth factor that that means that we as human beings are actually being exposed to an increased amount of that hormone or not. I haven't seen any studies that look at those measurements. I don't think there's any harm in eating organic food, but I'm not sure that it's been proven that that is actually a risk factor one way or the other. But I do think that it's important to maintain a good body weight and not to gain too much weight, to limit the amount of fat and to try to maximize the amount of fresh fruits and vegetables in terms of vitamins and so on.

I kind of go by the old Hippocratic method, which says everything in moderation, nothing in excess. I think that's true of our vitamins and supplements also. Again we don't have any data that says that taking very large amounts of these supplements is good for us, and, in fact, it may even be not so good in some circumstances. On the other hand we don't want to be deficient in vitamins and minerals. So it's find that happy balance that's difficult. It's hard for us as physicians and scientists to get a handle on this. It's hard to do clinical trials that document exactly what we should be eating and how we should be doing it. So I would say everything in moderation, nothing in excess and go for balance.

GRALOW: I would totally support everything that Ruth has just said. There is really no data that it's healthier for us or it will impact our cancer risk to eat organic foods, but I can support it because actually it's the right thing for the environment and everything else. So it's not a bad thing for us, and it may be good for us and it's a responsible thing with respect to sustaining our environment and cleaning it up.

So with respect to the second question, which was the PLK-1 study that's going on at Temple University, this is a very early study and I'm not sure yet what my level of enthusiasm for drugs targeting this gene is because I could look out there and probably find several dozen other very interesting studies that looked great in tissue culture and they looked great in animal models and that they're just about to start testing in humans, which is where this study is.

I think that as opposed to playing up this one study, which is a good example of smart, biologically targeted therapy, I'd just like to use this as an in to discussing the whole idea about how a better understanding of the gene changes that lead to cancer is going to lead to a whole new era of targeting drugs that are directed to what's abnormal about the cancer cell. That should in theory be more specific because it's something that's abnormal about the cancer cell and it shouldn't cause as much toxicity to normal cells if this gene or protein isn't abnormal in the normal cells.

So PLK-1 is a gene that is associated with cancer cells being able to survive and divide, and when you block it you prevent that from happening. So that is an example of understanding that

this is important in at least some cancers,(and we're not sure which ones and we're not quite sure how to test it in humans yet), then targeting a therapy to turn off the activity of a gene that shouldn't be turned on and is part of the whole cancer process. So that was the way Herceptin was developed for HER-2, and we've got some other genes that we're targeting with some new therapies, none of which are approved yet.

But it's just a general approach toward being smart about what's causing the cancer cell to survive and live and spread and then making a drug that shuts that off. And it's a very exciting new era, and it's going to help a lot of women like the caller who's dealing with her stage IV bone metastases. Hopefully if you have bone metastases and you're on good therapy you'll live to the point where some of these drugs, and I'm not sure if it will be the PLK-1 inhibitor or what, some of these drugs will be developed that will really benefit you. And I think there's a high probability that that will happen, that we'll have some exciting, new, targeted drugs and we'll understand more about your cancer and we'll understand more about these drugs in the near future.

JEFF: Our next question comes from Philadelphia. Go ahead, please.

QUESTION 4: *Hi, yes, I'm interested in learning about things that are alternative kind of ... not remedies, but ways to make chemotherapy and radiation therapy more effective and less stressful on your body. Specifically I'm interested in immune building and just keeping up a quality of life that I have now prior to ... a week prior to chemo.*

ORATZ: I think that the first thing to think about being starting chemotherapy, let's say for a newly diagnosed patient or someone with advanced disease who's starting on a new regimen, is to maximum your well-being before you begin. So the healthier you are coming into treatment the better it's going to be for you to be able to maintain that level of wellness. You're absolutely right to ask this question, because I think there's lots that you can do to help ameliorate or counter-balance some of the very strong side effects of particularly chemotherapy treatment in young women.

It's very important to stay well hydrated. If you're well hydrated that helps your body flush out the toxins and the drugs and the metabolites that you don't need to have hanging around. So we want the drugs to get in there and do what they have to do, and then we want them to get out. So hydration is very very important and a good thing that you can do. Don't overdo it. Remember, everything in moderation, nothing in excess. But stay well hydrated. That goes for diet as well. So again focus on that healthy diet that's going to bring all of the good nutrients in. If there are days when you don't really feel like eating a whole lot, that's okay. Drink your fluids. Maybe try to get some nutritional value through juices or soups or other fluids if you don't feel like a lot of solid food. If nausea becomes a real problem and you're not eating well make sure you address that with your physician. There are definitely things we can do to overcome nausea and help you have an appetite so you can have good food intake.

I think exercise, and I know Julie is going to agree with this ... I think exercise is critically important. Chemotherapy really slows you down and causes fatigue. If you're someone who already has a good exercise regime do your best to maintain it. You may have to modify it.

You've had surgery. You're going to be going through treatment. But the more active you can stay ... and I like fresh air, so the more that you can do outdoors I think the better you're going to feel. But you're not in training for the marathon during chemotherapy treatment. At least you shouldn't be. So don't push yourself to the point of utter exhaustion or challenge yourself to do your personal best during your third cycle of chemotherapy. The goal is to maintain a good, active level that enhances your sense of well-being, not that makes you feel frustrated, exhausted and wiped out. So those are the sort of simple things that you can have lots of control over.

Oh, and I would also add sleep. Sleep is very important. But if you're not sleeping for 12 hours through the night it's okay. Lots of people have sleep disturbance during treatment. This is emotionally a really really difficult time. There's been a lot of upheaval all of the sudden. You get this cancer diagnosis; you have surgery; you have anesthesia; you get pain medicine. Then we give you all this really difficult chemotherapy with drugs that make you drowsy and then drugs that make you hyper if you get some steroids along with it, and your sleep cycle may be very disturbed. The less that you do in terms of taking drugs I think the better off you're going to be.

Sleep when you're tired; try to get sleep through the night. But if you wake up during the night or you don't get a full night's sleep, don't freak out. It's okay. Rest during the day if you need to take a nap or if you need to just slow down, that's okay. We don't want you to be a couch potato. Remember, if you stay active that will also help get you back into a normal sleep cycle. So that's to be expected and that can be a little bit difficult sometimes to get through. But make sure you get your rest even if it's not in consecutive hours. Break it up during the day if you can.

In terms of other things I think that there are a lot of other modalities out there that can help. Some people find that acupuncture is very helpful, particularly for nausea or for pain control. If you have access to a trained, certified acupuncturist that's something you may think about. There are a lot of, I think, herbal remedies that are helpful for nausea if you find you don't want to use a lot of the medicine. Sometimes eating ginger or mint can be very helpful with nausea, and some of my patients here have found that instead of taking drugs they'd rather drink mint tea or eat some fresh ginger and that that helps. There are some practitioners who are very expert in herbal and naturopathic remedies. I think again in that area I would say talk to your doctor, find out who in your locale is really well-trained and who understands what your chemotherapy regimen is going to be and make sure that you're not doing something that's going to interfere with it. But you need to talk to people who are really expert in that. Julie, do you want to add anything to that?

GRALOW: I would just say with respect to the complementary therapies and the supplements and all, I don't feel that I'm an expert in this so I use several naturopaths in our area who specialize in cancer to help me because that's what they specialize in. My general comment is I am very willing to work with the patient and with a complementary provider like a naturopath on trying to get the best out of everything. I do know that too much of anything is probably bad for you, and we know that very high doses of antioxidants during chemotherapy and radiation therapy can actually sometimes help the cancer cell repair itself or at least in theory could do that.

So different recommendations would be made with respect to supplements and vitamins and all depending on what kind of treatment you're getting and where you are. That's why I find it important to have help from a complementary provider who's truly trained in this and knows what all of these different things are. A lot of my patients come in with a bottle that they've found on the shelf that claims to be a miracle cure and then when we look at what's actually in it ... one time I had a patient taking something that said it was supposed to help with alertness. And the patient was feeling quite fatigued, but then all of the sudden the nausea got out of control. We realized that this naturopathic product that was over-the-counter had very high doses of caffeine in it. So the more she took it to help with the fatigue of chemotherapy the more caffeine she got and then she got nauseated in exchange. And it took a while for us to sort out what was even in that compound. So that's why I like to do this in combination with a provider who understands some of these combinations, some of these remedies a bit better.

And I agree that there are things ... if we manage the nausea, the GI upset, the pain, the sleep disturbances, the anxiety, the depression and all through kind of stress reduction, imagery and massage, acupuncture, all of those things can be wonderful. I think a healthy, common sense kind of diet, a well-balanced diet with lots of fruits and vegetables is really important and we can get our vitamins and minerals in a natural way like that. I absolutely agree with Ruth that getting at least some degree of physical activity and exercise during chemo even though sometimes you have to push yourself a little bit is a good way to prevent debilitating loss of muscle and can help you with your energy a bit.

CAPLAN: This is Elyse just chiming in with all of the good information that both of you just offered that the women on the call really need to remember that any herbal supplement or remedy that they feel is good to take -- it is very important to tell their medical oncologist and other providers just to make sure that there are no reasons not to take it during treatment or to wait until after treatment because of an interaction that may happen. I know we get those kinds of questions at Living Beyond Breast Cancer and I think the Young Survival Coalition also gets that. Some things that may be good for you may be good for you at a specific point in time in your treatment plan. I think we have time for another question, Jeff.

JEFF: Our next question comes from Garden City, New York. Go ahead, please.

QUESTION 5: *Hi, I've got actually two questions. Just looking at the tracking of the incidence of young women with breast cancer, what has been done in the last, say, five, ten or 15 years? Has there been an increase in the number of women, young women, with breast cancer? Are we tracking better? Did we not track years ago? What are the numbers showing?*

GRALOW: Elyse, you may have the most detailed information. I generally follow the reporting annually of the American Cancer Society that lists cancer statistics and incidence, and it does it by sex and by geographic location and by age and all. Although the average age of diagnosis of breast cancer has dropped slightly over the past decade it's not a major drop. But Elyse you may have more information about exact numbers.

CAPLAN: I don't have it at my fingertips, but it's certainly something that we can look up and follow up on.

GRALOW: I read this report every year and haven't seen major trends that the very young women under 40 has been increasing out of proportion to the rates that it's been climbing up in all ages. Clearly because this is such a common disease if only a small percentage of women are diagnosed in their 20s and 30s it's still in absolute terms a large number and a big problem, as has been evidenced by all of the women who have been participated in Living Beyond Breast Cancer and the Young Survival Coalition.

CAPLAN: Was that an answer to your question?

QUESTION 5, continued: *Yeah, that's fine. I guess what I was looking at, which may be more of a separate question, was a follow-up study. First are we tracking younger women or how long have we been tracking younger women and then in terms of any follow-up study of young women with breast cancer. What's the longest follow-up study with women with breast cancer, young women?*

ORATZ: I don't know that we have specific studies that track young women, let's say under age 40, with a diagnosis. We certainly have studies of very long-term follow-up. The studies that compare mastectomy to lumpectomy have almost a 20-year median follow-up, which means half of the women were followed for longer than that. But that was women of all ages, of course. So

it's only recently that we've been doing these kinds of clinical trials. In our clinical trials, although we collect information about the age of the patient, there are very few studies that specify very young age, again, because that's a small percentage of the breast cancer population. We do have pretty long-term follow-up that includes young patients in those cohorts.

GRALOW: But I think with respect to a study that might have a very high proportion of young women, some of our early studies looking at ovarian suppression, for example, and its impact on breast cancer recurrence and survival, those would have been restricted at least to premenopausal woman. And we have some follow-up on some of those studies that's out 15 to 20 years. So because the incidence of breast cancer, the average age is 62 or so in this country, most of our studies include some young women but it's a small percentage. It's tough to break them out and see if they're doing differently than the older women.

There is a group here in Seattle where I'm based at the Fred Hutchinson Cancer Research Center that has focused a lot of research effort not in following patients from one specific study, but they've collected women who were diagnosed with breast cancer at a young age, for example, under the age of 40, and then seen what has happened to them and looking for different factors that predict for recurrence and predict for a second breast cancer and predict for survival, and are there things that are unique about young women versus older women. So Dr. Janet Daling, D-A-L-I-N-G and Kathi Malone, M-A-L-O-N-E, are two researchers at the Fred Hutchinson who have focused a lot of their career on looking from an epidemiologic standpoint at women diagnosed at a young age with breast cancer.

CAPLAN: I think that's great information. I have one question to put out to both of you before we wrap up, because I know we only have a few minutes left. I know we get a lot of questions from women who are estrogen receptor negative, because more women with breast cancer have ER positive disease, and with the advent of many hormonal therapy choices many women with ER negative disease are feeling as though what's here for me, what's new for me. I think if each of you could just make a very brief statement about the value and impact of chemotherapy for women with ER negative breast cancer and sort of what's on the horizon that will probably be helpful to some women on the line.

GRALOW: Well, we know that although about three-quarters of breast cancer is estrogen receptor positive, when you talk about very young women with breast cancer that's a lot lower. So there are a lot more young women who have estrogen receptor negative breast cancer, so this is a very relevant issue for the women on the call. What we saw at a recent meeting in San Antonio in December with respect to impact of chemotherapy in the early stage breast cancer setting was a nice breakdown of three large national trials that have been done over the last decade and a half or so.

In those trials it was broken down -- the estrogen receptor negative patients and the estrogen receptor positive. In all three of those trials we saw an advance made in the adjuvant or early stage treatment of breast cancer. In one of them we looked at three different doses of giving Adriamycin. In another we looked at adding Taxol, and in the third we looked at giving chemotherapy in a standard, every three-week way or a newer, dose-dense way. In each of those protocols there was a clear winner that led to our current chemotherapy regimens.

When you broke it down by ER positive and ER negative we saw that a good portion of the benefit of each of these advances was in the ER negative women. The ER positive women had a small advantage to giving a little higher Adriamycin and adding Taxol and doing the new dose-dense approach to chemo. But the ER negative women had major improvement in survival with each of these steps along the way. So although it's frustrating to be ER negative and not have hormonal therapy as an option, you need to know that when you get your chemotherapy you are getting a far greater advantage than if the tumor was ER positive.

I think that's part of what Elyse wanted me to get at. And since we talked about finding targets and then designing drugs for them, technically estrogen receptor was the first target that we had a drug to treat in breast cancer, and that was tamoxifen or actually ovarian suppression, targeting the estrogen receptor. But those approaches to treatment came about before we understood anything about the estrogen receptor. So it is a biologically targeted approach, although the drugs weren't designed because we knew about estrogen receptor, although subsequently we've learned about them.

So estrogen receptor is important. So is HER-2, and half of ER negative patients are HER-2 positive. Maybe epidermal growth factor receptor, or HER-1, is important, maybe RAS and some of these other genes we talked a little bit about, the PLK-1. A whole bunch more genes are on the horizon and although we understand estrogen receptor and HER-2 better than any other proteins and genes associated with them we're going to understand a lot more and we're already on the road to understanding them and designing drugs to target them.

CAPLAN: Ruth, do you have anything to add?

ORATZ: Oh, I think Julie gave a terrific and really complete answer. A lot of those drugs now are already going into clinical trial. Some of the antiangiogenic factors are being tested, the antiepidermal growth factor receptor agents. The tyrosine kinase inhibitors are being looked at in breast cancer. So I think that this is a very fertile ground for research and I think that investigators are recognizing and acknowledging the very important need for defining these biologic factors. So we're going to see chemotherapy certainly as a mainstay of treatment for ER negative and some ER positive patients, of course. But I think this whole new 21st century of genomics and proteomics and understanding the molecular biology of the tumor cell, and the stroma, the environment that the cancer cell lives in and how the cancer cell interacts with the sort of surrounding tissue is going to help us understand where to go with our treatment.

CAPLAN: Thanks to both of you. I know that it's like the new frontier -- that down the road women will be given many different treatments for their breast cancer because it will be very tailored and very specific depending on the antibodies and the proteins, etcetera, that are found. Thanks to both of you for really covering so much information in the past 90 minutes. I would also like to thank the callers who have stayed on the line who have submitted great questions and those that were able to ask their own questions personally. You gave a lot of character to the program and enabled our speakers to address some of your own personal concerns that are of concern to others. We hope you found it helpful.

If those of you who weren't able to ask your questions still have them at the end of the program feel free to send them to info@youngsurvival.org and we'll do our best to get answers back to you. Please keep in mind that at the Young Survival Coalition and Living Beyond Breast Cancer, we are here to help provide you with the most up-to-date information and support for young women affected by breast cancer. We want you to know that we are point of contact for all of you. If you're not currently on our mailing lists please feel free to visit the web sites of both organizations at www.youngsurvival.org and lbcc.org. You will need to register on each individual web site because we don't share our mailing list to protect your privacy. So thanks to all of you. I would like to turn the program over to Elly for a few housekeeping notes

KIRSCHNER: Thanks, Elyse. You were a great moderator and especially thank you for saving me and jumping in earlier when I lost my phone connection. Just two more things I want to talk about. A command performance recording of tonight's call will be available for the next two weeks. You, as well as your friends, your family members, your colleagues, can listen to this recording at any time day or night by calling 800-934-3033. It's a toll-free call. In addition a transcript of the call will be available in about three weeks and will be posted on the conference web site at www.youngsurvivorsconference.org as well as on the web sites of LBBC and the YSC.

Also in the next couple of days we will be sending everyone on the call an evaluation form via e-mail. Your feedback is much appreciated, so please take a few minutes to share your thoughts about this program, as your comments will help both the YSC and LBBC to create programs that best meet your needs as young women affected by breast cancer. So this concludes our program

for this evening. Again, I'd like to thank our presenters, Dr. Julie Gralow and Dr. Ruth Oratz, for joining us and sharing their knowledge, their time and experience. Thank you, Jeff, for facilitating this call as our operator. We'd also like to thank Aventis for underwriting tonight's teleconference. Finally, thanks to all of you on this call tonight. We hope you will join us for future programming. Good night and be well.

(END OF TRANSCRIPT)