



What's New: Medical Advances for Young Women Affected by Breast Cancer ANN H. PARTRIDGE, MD, MPH

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JEAN A. SACHS, MSS, MSLP: I'm Jean Sachs, executive director of Living Beyond Breast Cancer. I want to welcome everyone to the 8th Annual Conference for Young Women Affected by Breast Cancer. (Applause) Do you like being in Florida?

AUDIENCE: Yeah! (Cheers/Whistles)

JEAN A. SACHS, MSS, MSLP: This is a good thing? Good. I want to let you know that there are 41 states represented here, in addition to Washington, D.C., Canada and 11 countries. (Applause) You have traveled far and wide to get here, and I promise that you are going to have an incredible two days. We have amazing speakers who have also traveled across the country to be here. There are so many opportunities for you to get together and talk, so please take advantage of every minute of being together.

I'm always asked by reporters, "Why do you do a conference for young women affected by breast cancer?" I'm always telling them why, and I realize I don't need to tell you guys why. You know why we do this conference. You know that you were at the beginning of your lives – in the middle of maybe raising children, going back to school, dating, meeting a new partner – and breast cancer was probably the last thing you thought you'd be facing. I'm sure in your communities it was hard to find other women who looked like you, whom you could relate to.

While this conference is really about bringing top doctors and giving you cutting-edge information, it's also about you finding each other. I always say I hope you all go home with a lot of new e-mail addresses and phone numbers and many, many new best friends to stay in touch with, because that's really why we do this.

I also want to say that this conference is a true collaboration. Living Beyond Breast Cancer and the Young Survival Coalition have been doing this together pretty much since the inception, and we really work hand in hand. This year, it is so exciting to have Susan G. Komen for the Cure as an equal partner as

YOUNG WOMEN UNITED AGAINST BREAST CANCERSM

well. I'll talk a little bit more about that. (Applause) We are so much stronger when we work together. A lot of breast cancer organizations get criticisms like, "Why are there so many groups out there, and why don't you work together?" Please hold this out as an example that we truly do do this so we can give you the best conference and not duplicate efforts.

Every year when we have a conference, there are some funny stories or amazing stories that we love to share, and so far this year the story is about traveling and how people got here. My staff, I think a few of them, sat on the runway for three hours yesterday for a quick, two-hour flight.

We had speakers who probably spent more time on the runway – like Cliff Hudis [of Memorial Sloan-Kettering Cancer Center] – than he did actually in Florida yesterday. I know of exhibitors who flew to the airport the night before because they heard there was going to be ice and they wanted to be right there.

But my best story – Roberta, I'm stealing your story – is Roberta Levy Schwartz, the immediate past president of YSC, who was in Houston with probably 25 other young women. Continental canceled their flight, and she just said, "You cannot cancel our flight." Whatever she did – and I can't believe she did this – she convinced them. There was an airplane there, but she convinced them to find a crew and fly them here. (Applause/Cheering) You have to know Roberta to know that she could actually make that happen, because I'm like, "Who did you talk to?" You go to airports these days; nobody listens to you. How did you possibly make this happen? What it really says to me is that people make incredible efforts to be here, and we so appreciate that, because the staff work so hard to make sure we put together a really quality program – but it's only helpful if you're here, so thank you so much.

I want to take a few more minutes to look at who's in the room today. I think it would be really great if those of you who have never been to the conference before would stand up so we can welcome you. (Applause/Cheering) Wow. That's wonderful. It's like a reunion for a lot of us, but it's always great to make new friends, so it's great to see you here. I also thought it would be great if the caregivers could stand, because sometimes they don't get the recognition. (Applause/Cheering) As we all know, we couldn't do this without the support of whoever your caregivers are, and it's really amazing that you'll take the time. We have a lot of sessions specifically for that group.

Then, while this is not my favorite thing to do, I would love to take a moment and think about those women who have been here at previous conferences and are, sadly, not with us today. I know we all have

someone in our thoughts. If we could just take a minute – I know all of those who aren't here would be so proud that we're continuing this legacy and we're continuing on.

Now I have the pleasure of bringing up Cindy Geoghegan, our contact at Susan G. Komen for the Cure. As I mentioned before, we've been doing this conference with the Young Survival Coalition, which has been great, and Komen was always supporting us with sponsorship, mostly, to pay for scholarships. This year, Komen approached us and said, "We really want to have a stronger partnership. We think you do such an amazing job with this conference that we don't want to duplicate efforts. We want to bring our ..." – I think Cindy says "largesse" – "... and really help you grow."

I can't tell you how incredible that is, because for us, Komen is like *the* breast cancer organization. To have them come to us and not only say they want to give financial support – they gave us \$150,000 this year (Applause) – but to also say, "We want to spread the word to our affiliates and give you the PR," that's exactly what we need. That's going to help us maybe double in size next year. Cindy was the driving force behind it, so I'm pleased to introduce you to Cindy. (Applause)

CINDY GEOGHEGAN: Thank you, Jean. I'm so gratified and inspired and excited and emotional about being here. I could tell you that as a 12-year survivor, the joke would be, "Well, you're excited to be anywhere." (Laughter) I droop on one side, I'm stupider, and I'm 35 pounds heavier than I was when I was diagnosed, but I'm still here, and I have a lot of excuses for all of my inadequacies. (Laughter) When I was diagnosed 12 years ago, I was 35. I had no family history, and I had two small kids. There wasn't a Young Survival Coalition. There wasn't a Living Beyond Breast Cancer and a conference like this.

As Jean mentioned – and the reason the YSC was founded – I didn't have anybody to talk to. I stood at the bus stop with my little kids and my hat, and I watched everybody point at me. I went to Look Good, Feel Better, and I took my mother with me, and they put all the makeup in front of her. I was in an oncology office in a very large cancer center where the tech that weighed me said to me, "You're too young to have breast cancer." So I personally understand the reason for this conference, and on behalf of Komen and our young women's advisory board and our staff, I can't tell you how honored and privileged we are to support this and to partner with you.

I'll tell you a little about the job I have. My friends call me "Helium Hand," but since I was diagnosed 12 years ago, I have volunteered for just about every breast cancer organization, advocacy effort, federal

government committee, etc., because this has become my passion. I was a Komen volunteer in Baltimore and then in New York for 12 years. I only joined the staff in June. I have my dream job. My job is to form collaborations with other organizations, to form partnerships, to bring Komen resources to people in other organizations that are doing great work and to help facilitate that.

People think of Komen as being big, bad Komen, and they fund research and they do things in our community. We're really here to work with everybody, because, as Jean also said – I keep quoting her because she's so articulate – we can't do this by ourselves. We can't do it by duplicating efforts. The world is kind of hard out there, and this is a really awful disease. Federal funding is going down, and clinical trials are being stopped. We really, really need to work together.

Komen has invested \$1 billion in breast cancer in the past 25 years. We celebrated our 25th anniversary this year. We're committed to investing another billion, actually \$2 billion, in the next decade. (Applause) In addition to these partnerships and collaborations that I'm so excited about, though, we also have a new scientific advisory board chaired by Eric Winer, whom a lot of you know, at Dana-Farber Cancer Institute. We redesigned our grants programs, because we do give a lot of money to research.

For the first time, our focus this year is actually on eliminating mortality from this disease. We're going to cure breast cancer. We're going to put all of our money – this year, you will not get funded, your research will not get funded, your outreach will not get funded unless you can demonstrate that there's a potential that the grant will greatly reduce mortality or eliminate it. We're really excited. We're in the midst of reviewing those grants. If we all work together, we'll really be able to cure this disease, which is why we're all here. (Applause)

I just wanted to thank you for this privilege, and I know Komen is in this for the long run with you all and in everything. I'd hate to say in 12 years you'll be stupid and fat, but it beats the alternative, I guess. In any case, thank you so much.

I'd like to introduce Lanita, president of the Young Survival Coalition, a group that I've had an affinity for always, because they came into this when nobody else was here. Thanks. (Applause)

LANITA MOSS: Welcome, everybody. I want to thank you and welcome you to the 8th Annual Conference for Young Women Affected by Breast Cancer. It's always an awesome sight to stand before

you, so many women who are making a journey that you didn't expect and you didn't want. But you're here. I'm glad you're all here. I also want to take this opportunity to thank the staff of LBBC and Komen for their support and commitment, because without them and the staff of the YSC, we wouldn't be here today. I want to thank you personally for that.

I am honored to be the new president of the Young Survival Coalition. I've been involved with the YSC since its inception, because I'm one of the co-founders. I continue to be in awe of how the organization has grown and how it keeps meeting the needs of young women with breast cancer. I recently celebrated my 12th anniversary for my cancer diagnosis. (Applause) One of the issues of being a long-term survivor is you have a tendency to lose perspective of what it was like when you were diagnosed, because time does heal all wounds. I find myself before all of you today, people who are perhaps just recently diagnosed or who are going through treatment or perhaps have just finished treatment, and I was really trying and struggling to find a way to reconnect with you and your journeys.

Last fall, I had the incredible and unique opportunity to participate in the Hershey's Tour de Pink, a 210-mile charity ride from Hershey, Pennsylvania, to New York City. I had never done anything like that in my life. I didn't even own a bike. I decided I was going to ride this 210 miles in three days. I bought a bike. I researched ways to train. I learned how I was supposed to eat, and I looked for what the latest fashions were in cycling for the season (Laughter), because you can never have enough opportunities to buy a new outfit. That was a lot like when I was diagnosed with cancer. I got second opinions, I did research on treatments and surgical procedures, and I mentally prepared myself for the journey that was ahead of me.

I trained all summer in the heat and in the cold. I think I put about 1,000 miles on my bike training for it, but the night before the ride started in Hershey, I voiced my concerns to my husband and to my close friends who came with me from Kansas City to do this ride, and I told them I didn't think I could do it, because I didn't think I had trained enough. I didn't think I had done enough miles. I just had this huge doubt that I didn't think I could do it. The mileage was too much. There was a category 3 mountain that I had to go over. For those of you who don't cycle, a category 3 mountain is one big hell of a honker hill. (Laughter) I was paralyzed by the thought that I was going to have to go over it.

I have a big mouth, though, and I like to talk a lot, so my concerns and my fears were overhead by some fellow riders. They rallied around me. It was like this wall of people was in my face to say, "No, Lanita,

you can do this. You will get through this. You can conquer those miles, and you can conquer those hills.” Somehow, that was like when I was diagnosed. I had friends and family rally around me and tell me, “You can do this. You’re going to be able to get through this journey.” They were there. I’m sure every single one of you has a story about how friends and family, community, have rallied around you, and how they’ve offered to take you to treatments and bring you food, and to have a shoulder so you could cry on and rest your fears.

Then the ride started. The first day, I think we did 72 miles. The second day, we rode 85 miles, and the third day was 55. Those are petty intimidating numbers, but what happens along the way is you have rest stops. I learned very quickly that all you had to do was focus on the next rest stop in front of you. It wasn’t the 85 miles you had to do; it was the 20 miles you had to do just to get to that rest stop. That’s an incredibly effective way of coping with a big issue like being diagnosed with cancer. Don’t look at the end. Only look at what treatment is in front of you or what you have to do to get through this day that you’re in until the next day.

When you do that, things become more manageable. When things are more manageable and we can control them, we feel more in control and we feel better about our journey. I started cycling during this ride by myself. I was passed occasionally by a few people, and I would talk to them. That gave me an awful lot of time to be by myself, and it was a very lonely place. It gave me too much time to think about my fear and my pain. I found a group of people who were just like me, though – and, by the way, a few of them, I think, are sitting right over there.

They had the same experience that I did. They pedaled at the same pace that I did. What turned out to be a solitary journey actually turned into a group effort, and they became my people, my peeps, my friends and my compatriots, and I was no longer alone. This conference is much like that. You all come together. You’ve walked in this very solitary journey by yourself, and now all of a sudden there are 800 other women just like you who can understand you. For some of you, it might be the first time you’ve ever had this experience.

I will not lie and tell you there weren’t bumps along the way. I rode off the road once on my bike into a ditch. I started screaming, “Oh, shit! Oh, shit! Oh, shit!” and somehow managed to keep my cool and got myself back on the road. What turned out to be potentially a really dangerous situation turned into

something that was very laughable, and we stood along the side of the road in Pennsylvania laughing about it.

I got over the category 3 mountain. I did not ride over it; I walked up it. But I got over it, and that was the point, because pushing a bike up a hill is just as hard, almost, as riding up a hill. The point is that I did get over it, and finally, after three days, I crossed the finish line surrounded by the friends I had made along the way. We had a line of us that rode across the finish line together. We were greeted by the very people who had supported me the first night, who told me I could do it and offered me encouragement every day and made sure they checked on me.

I had completed my cycling journey, and in a way I had reconnected with my cancer journey, because all of a sudden I could relate the three days that I had just gone through with the year that I had gone through when I was in diagnosis. My cancer journey was hard, and it was painful, and it was life altering, but I have to tell you, it was a journey that I would never give up for anything in the world, because it has changed the way I think. It changed the way I feel. It changed the way I conduct my life. I wish you all well on your journeys through your treatments and through your cancer experiences. There will be mountains, and there will be obstacles, but just remember that there will be experiences of a lifetime, you will make lifelong friends, and you'll have your own peeps at the end of it.

I want you all to enjoy this weekend, and I look forward to trying to meet as many of you as I possibly can. Thank you for being here and for taking the time and effort through the weather to get here. Thank you. (Applause)

I have the distinct pleasure now of getting to introduce Ann Partridge, today's keynote speaker. Ann is an assistant professor of medicine at Harvard Medical School and serves as the director of program for young women with breast cancer in the breast oncology program at Dana-Farber Cancer Institute. Her clinical research focuses on psychological, communication and survivorship issues in breast cancer, with a particular interest in the unique issues facing young women with breast cancer, including fertility concerns. Dr. Partridge serves as a member of the American Society of Clinical Oncology Survivorship Task Force, Fertility Preservation Guidelines Committee and Health Services Committee.

She is co-chairwoman of the Cancer and Leukemia Group B Committee on advocacy, research, communication and ethics. She has received awards and grants for her research, including an ASCO

Career Development Award, Tracy Starr Breast Cancer Research Fund Award and Lance Armstrong Foundation Cancer Survivorship Award. She is a member of Living Beyond Breast Cancer's Medical Advisory Board, and I'm very pleased to announce that she's one of our newest members of the YSC board of directors and the new chairwoman of our medical advisory board. Please give Ann a huge round of applause. I'm glad she's here today. (Applause)

ANN H. PARTRIDGE, MD, MPH: Thank you for such a nice introduction. I see women every day in my clinic. I run a program dedicated for young women who are newly diagnosed with breast cancer, and despite that, to see so many women who have been affected by breast cancer at such a young age all together in one room – I've been at this conference before, but today I'm struck and overwhelmed. Some of that is the sheer masses. Some of that is the recognition that you are all my heroes, in a way, getting over those mountains day by day, dose of Herceptin or dose of tamoxifen by dose of tamoxifen.

One thing that strikes me, and I'm getting very choked up right now, is how important it is – and thank you to the organizers – to bring all of you together, both for yourselves and for people like me from the research community to look and say, “Wow, we're doing the right thing by trying to move this field forward and focus on these unique issues.” Even though it's a relatively small population in breast cancer, it's such a critical population. (Applause)

The other part of me looks at this and says, “I could be you tomorrow.” I know that. Right now, I'm kind of at the end of young survival. In a couple of years I'd have to be, as Cindy refers to it, an older young breast cancer survivor. That also is one of the reasons why many of us in the medical community, many laypeople and loved ones, feel such pain, and how you all pull on our heartstrings in some ways more than the average person. It's both the, “This shouldn't happen right now, and nobody planned this; it's not fair,” – not that it's fair to anyone older – but it's also the recognition that it could be all of us. That commonality of S-H-I-T happens, and you're all dealing with it and you're going to get through it.

With that, I'm going to start. One of the important caveats – I don't mean this as an apology. ... One of the things I hate is going into a room of people who are experts in their disease and telling you what your disease is about. I'm going to give generalities, and I'm not going to give a whole lot of stats, but I'm going to give a whole lot of kind of, “Here's what's around, here's what's new,” as I've been requested to do.

I think each of you needs to understand, however, that each of you is the expert in your own disease, in your experience. While there are generalizations and averages, both in this talk and when you're talking to your doctors and other people with whom you make decisions as well as your family and loved ones, you need to remember that. While averages and stats are important and helpful to a degree, you're not a stat; you're an individual. You know that. Your experience is your own, and unfortunately you do have to own it. Embrace it and know that you're the expert in your own disease. I strongly recommend doing that as you move forward through all of this, wherever you are in the course of your survivorship.

What I'm going to do is give you an overview of the biology of breast cancer in young women, what we know and what we're not so sure about. Then we're going to focus on some of the issues that are more unique to younger women, and specifically on some of the newer findings. As Lanita said, I do research in a lot of the psychosocial issues and fertility issues in young women. I'm not going to spend a lot of time on that during this talk, because it's not relevant for everybody and it's kind of a niche of a niche. I'm happy to answer questions about that, and we do have time for questions at the end of this. There is some new stuff there, but I'm going to talk more about the big new stuff that probably is more relevant to more people in the room, and I'm happy to answer questions about those issues later or anything else that comes up.

This is just to give some perspective on why you are a unique group. You can see these are the age-specific probabilities of developing breast cancer. We all hear the 1-in-8 statistic. By age 30, though, it's 1 in 1,800 or so. If you think about your average high school – which probably has 600 people in a class or 200 people, depending on how big your school is; some big high schools have 2,000 people – about one woman in that high school class will get breast cancer before she's 30, in the big classes. Then it goes up by age. The vast majority of young survivors are in their 30s, their later 30s, just because of the demographics going up over time.

Just to give you some perspective, that's why conventionally, when studies have been done on premenopausal women versus postmenopausal women, focusing on their unique issues, anything about very young women tends to get swamped by the majority of women, even in premenopausal groups, who are in their 40s, because you can see that by age 50 it's one in 70. While young women do participate in clinical research, and you all do so well and strongly, the numbers just aren't there for many of the large studies to make good generalizations, but we are working on that, and we're also designing more studies focusing on very young patients. I'll talk about that later.

What does this amount to? These are the statistics from last year, the newest ones, which include women up to 45 from the American Cancer Society, which is good and bad. It makes things look kind of like, “More people; we need to dedicate more resources,” and I think that’s why they might have done it. On the flip side, though, when you include ages 40 to 45, you wash out the really young because the numbers just get so great. Including women up to 40 – and of course young is in the [age] of the beholder; it’s not to exclude anybody, but I think some of the issues are very different for a 23-year-old than for a 42-year-old. Some things may be the same, but some things are very different.

More than 12,000 women are [age] 40 or younger at diagnosis, and about 2,000 also will develop DCIS, noninvasive breast cancer, which translates to about 14,000 women in the U.S. alone, and there are thousands and thousands more women worldwide. I’ll show you data later from Korea, where they had several thousand young women in a database, and we work very closely with groups in Europe – for instance, the International Breast Cancer Study Group, where they have a dedicated kind of maven for young women, a gentleman named Aaron Goldhirsch, who’s very prominent in the field of breast cancer and also is very dedicated to young women’s issues. You have fans and supporters and people who are proactive across the Pond; but there are thousands of other women across the world, so the numbers get bigger.

What is the problem with breast cancer in young women, beyond just having it and having to go through it? Young women with breast cancer tend to present with more advanced-stage disease. There is no reliable screening for young women. Breast cancers are often more difficult to detect in younger women versus older women clinically, and the extreme example of this is women who are having babies. A pregnant breast or a lactating breast – many people are diagnosed during pregnancy or shortly after pregnancy, and it’s very difficult. These are the situations where a woman had something going on, but even with the most vigilant doctors, it’s hard to discriminate a breast mass that’s completely benign in a milk duct, or an infection or inflammation or something that’s more concerning.

Then, the delay-in-diagnosis issue – the “You’re too young to get breast cancer” response. I think sometimes we say that emotionally because we just feel like, “What the hell? This shouldn’t happen.” Saying that and acting like this couldn’t be breast cancer, which has happened all too often in the past with healthcare providers and patients, everybody saying, “That can’t be,” burying your head in the sand and providing reassurance that you can’t provide – that’s where things have changed, in my perspective,

even over the past five years. We're studying this, but I think anecdotally we're seeing a lot more providers recognizing that breast cancer does happen in young women – gynecologists, primary care docs – and being quicker on the trigger to say, “Let's get you in for that ultrasound. Let's go through a menstrual cycle, but you're going to see me next month and we're going to make sure this doesn't go away.”

I think that's due, in large part, to groups like the Young Survival Coalition and Living Beyond Breast Cancer and Komen getting the word out there. There has been a lot of media coverage recently, over the past five years, pushing by the advocacy groups, which I think is fabulous, to get the word out there. The vast majority of lumps in a young breast won't be breast cancer, but we need to have an awareness that it can be, and what are the proper amounts of time one can wait. We're studying this to a degree, but the awareness is definitely improving, in my experience. I'm hearing fewer and fewer of those, “It took me so long to get into you because the doctor said it was nothing, go away.”

The other problem about breast cancer in young women, as if just having it isn't enough, is that younger women tend to get a more aggressive type of breast cancer. Now, young women can also get old lady breast cancer, meaning very benign-looking – it's cancer, but it's very wimpy. I call it wimpy in terms of low grade, hormone receptor positive, HER2/neu negative. You can get that, but younger women are more likely to get triple-negative disease, as you heard about yesterday from Cliff Hudis, or high-grade disease. Younger women are also more likely to present, again, at more advanced stages, which may be related to the issues of the more aggressive biology and may also be related to the lack of screening, as I mentioned.

It's clear that there are more ER-negative tumors in younger women. It's clear that PR negativity is more common in younger women, and that markers of higher grade are more common in younger women. What wasn't clear, and what I thought for several years, was that HER2/neu was also more common in younger women. I actually just wrote a chapter on this, and I reviewed all the literature on this, and that doesn't appear to be the case necessarily. I think we have more work to do in that way, and some larger studies are ongoing that will help us with that, but it does not appear that HER2/neu positivity is much more common or more common at all in younger women. The data are mixed, so I would say I'm not sure about that. Certainly young women do get HER2-positive disease, though, and that's about 25 percent, 27 percent.

This is just to show you some recent data pertaining to the biologic differences. They looked in a large data set of Korean women, and they had 14,000 Korean women who were diagnosed under age 35. That's a large group of women diagnosed under 35 in a population-based study. They compared them to older premenopausal women, over 8,000 women ages 35 to 50. What they found was, not surprisingly, hormone receptor positivity was more common in the older group. Greater T stage and N stage – that is, size of tumor and number of lymph nodes – was more common in the younger group. The HER2/neu status did not differ by group. That is just a little evidence to show you that more biologically aggressive disease, in general, is more likely to occur in young women. But that doesn't mean biologically less aggressive disease can't occur in young women, because it does.

This is really cutting-edge. I think we need more work here, and we need to fund more researchers – thank you, Cindy – to look at the pathways and the actual biology of breast cancer in young women. One of my colleagues down at Duke has recently looked at a bunch of tumor samples and found that the pathways – the growth signals that cancers get and grow based on – may be different in younger women versus older women in general. That doesn't mean they're all different. It just means that you're maybe more likely to have a certain deregulated pathway if you're younger than older, and that young women's cancers, least some of them, may represent a distinct biologic entity with unique patterns.

There is also evidence – and we've known this clinically for some time, and we've seen it but now there are very good data – that young age not only predicts certain biologic features of the cancer, but it can vary by a function of race and age. In particular, young African-American women have long been seen – and now we have data to back it up – to be more likely to get triple-negative tumors. As many of you know, those can be more aggressive. The good news is that they also tend to get the most benefit from the treatments, like chemotherapy, and get the most risk reduction from our better, state-of-the-art chemotherapeutic regimens, and there tends to be less hormone receptor-positive, wimpy breast cancer in that population.

If breast cancer is a different mix of diseases in younger women versus older women, should treatments be different? That raises that question. The first and obvious question, and one we're hopefully going to answer at some point in the next decade, is whether hormonal therapy should be different for younger women than for older women. In particular because of the obvious differences in ovarian function, should we suppress ovaries for women with hormone receptor-positive disease? Does that add to our current treatments? Should there be different chemotherapy or targeted therapy for younger versus older women?

In the year 2000, the National Cancer Institute put out a statement after a consensus conference. The bottom line was that combining ovarian ablation with chemotherapy when tamoxifen is involved has not been shown to provide additional benefit, but that ovarian ablation adds about the same benefit to chemotherapy. It's about the same benefit. Some women who cannot or don't want to receive chemotherapy could get ovarian ablation alone. Ablation means suppression. You can do that with medications, too. That sounds so harsh, "ablation." You can suppress ovaries with medication. We don't use it a lot in the U.S. We're much more likely to use chemotherapy because of both patient preference and doctor preference, but I think that's something to bring home to your doctors to discuss, because it's certainly an alternative for some women who have lower-risk disease and really want to avoid chemo.

The other issue is for women who have higher-risk disease and really want additional therapy, and I'll talk about this more in a second. The 2001 St. Gallen Conference – this comes from Europe and that colleague, Aaron Goldhirsch, I mentioned. They have a more proactive, "We probably should suppress people more frequently and have been doing it for a longer time," approach. Their statement was that endocrine therapy, including ovarian suppression with medication and tamoxifen, is at least equal to conventional chemotherapy – which we knew – for premenopausal women. They were more proactive, saying you should do this if you want to, whereas the U.S. is more like, "You can do it, but we're not sure it's as good." Both are true.

What do we know? Ovarian suppression is better than nothing for hormone receptor-positive disease. We also know that ovarian suppression plus tamoxifen is way better than nothing. It makes a huge difference. There was a big study just done in Asia where the conventional therapy is nothing except surgery, and they're not screened. Thank goodness for modern medicine over here. The bottom line is that for hormone receptor-positive disease, it made a huge difference in survival to get these endocrine therapies compared with the women who got nothing. Hopefully the standard is going to change and has changed in Asian countries, at least in China and some of the other more developing Asian countries.

Ovarian suppression is ineffective in hormone receptor-negative disease. We know that. So is tamoxifen. Ovarian suppression is comparable to CMF-type therapy. That's the other caveat. A lot of the comparisons of chemotherapy to ovarian suppression use older regimens. Many of you in the room have probably never heard of CMF [cyclophosphamide, methotrexate and fluorouracil] chemotherapy. I've given it twice in my career, because I started doing this in the late 1990s, when we all moved to

anthracyclines, like Adriamycin or epirubicin-type chemotherapies. A lot of the older studies, and in Europe, they used a lot of CMF. Not sure that it's quite as good as the anthracycline-based chemotherapy.

Tamoxifen wasn't used at that time, either. A lot of the studies didn't include tamoxifen, and we know from big studies that chemo plus tamoxifen is better than chemo alone. Nobody is willing to give up tamoxifen. You could argue that in some patients you might forego chemotherapy to get ovarian suppression, but there are caveats there; it may not be as good. This is the actual caveat: Is ovarian suppression plus tamoxifen better, worse, the same compared with chemo plus tamoxifen? That's an open question. Is ovarian suppression equal to an anthracycline-based regimen, not the older CMF regimens? Does ovarian suppression add to chemo plus tamoxifen for women who have higher-risk disease who want to do everything they can?

I was talking to a patient of mine about this recently, and she said to me, "I don't care if my bones fall apart at 60. I need to be here for my children in the next five years or ten years." A lot of us feel that way and understand that and would be willing to make tradeoffs – not that they're so simple – to buy time now if it were going to buy time. The problem is that we don't know.

The other open questions are what about ovarian suppression and aromatase inhibitors? Should ovarian suppression be considered after chemotherapy in women who continue to menstruate? We don't have a great handle but have concerns about the toxicities, particularly long term, of ovarian suppression. We know the short-term toxicities. It can be horrible for some women; it can be a walk in the park for some women. The long-term toxicities worry us: cardiovascular health, bone health and even mental health. There is a concern that very premature menopause – which many people will get with chemo also – can have detrimental effects down the line.

What's going on to answer these questions? The good news is that there is a large study. Many of you may know about this or may be on this study. Thank you if you're on it, because I think it's going to answer one of the major questions here. It's the SOFT trial, which is randomizing women, which means a computer picks what treatment you get. You and your doctor or providers decide: All of these treatments are reasonable, I understand the uncertainty in the field, and I'm willing to enter this trial. That's the strata. Whether or not you got chemo, you're going to get randomized to ovarian suppression plus tamoxifen; or ovarian suppression plus exemestane, an aromatase inhibitor also known as Aromasin.

By the way, I will say the trade names and the generics as much as I can, recognizing that I'm not paid by any of them to be here. I don't have any conflicts in the way you worry about. I have done some consulting for one of the companies that makes an aromatase inhibitor. But I'm going to tell you not to take them off-study, so I'm not being paid to say anything they want to hear.

That's the randomization for women going on SOFT. This trial is still open. It is halfway accruing. It's a critical question. If you're someone who is a candidate for this study – either you're menstruating and didn't get chemo, or you're menstruating after chemo, which the vast majority of young women do, and have a hormone receptor-positive disease – and the study is open in a place where it would be reasonable for you to get your care, I strongly recommend thinking about it. We don't know the answer, and if we don't know the answer, you have to go with your preferences and your values. Some people are comfortable with allowing fate to give you the answer in terms of what you should take, but that's an individual or personal decision.

It's over halfway there in terms of accrual, and I'm really optimistic it will get there because it's clipping away. It's open throughout the world, and it's run by that International Breast Cancer Study Group that Aaron Goldhirsch chairs. TEXT is the sister study to this study. This is for the believers. This is for the people who say, I think ovarian suppression is going to add. I want to give it to my patients, or my patient wants it. So I only want to randomize them to tamoxifen plus ovarian suppression or that aromatase inhibitor, exemestane, plus ovarian suppression. I don't want to give someone the tam[oxifen]-alone arm.

This study, because it kind of appeals to our more-versus-less approach, particularly for younger women – and all of these women are premenopausal – has accrued. We filled the docket there. They've hit the sample size, and we should have an answer to this over the next five to seven years, is my hope. It could even come sooner. It won't answer the fundamental question of ovarian suppression adding to tam[oxifen], but it will add the aromatase inhibitor question versus tamoxifen question in the setting of an ovarian suppression drug.

Finally, there was a study that looked at whether you really need chemo. Women were randomized to ovarian suppression or chemo – I'm sorry, I take that back. Everybody got ovarian suppression. Everybody got hormonal therapy with tamoxifen or exemestane. They were randomized to chemo or no chemo. That is a critical question. Wouldn't it be nice to get away from chemo for people with hormone receptor-positive disease? The problem is that the study didn't accrue. They had to close it, which speaks

to the fact that nobody was willing to take that chance. We know we can get women through chemo. We know people can get through that mountain.

I'm a proponent of that study. Dana-Farber was the only center in North America that opened that study. It's a critical question, but everybody else said, "My patients won't go in it. I won't put my patients on it." Even in Europe, where they tend to be a little less interventionist and a little more pro-endocrine therapy, they were not able to accrue. I think we'll still learn a lot from the other studies.

For some women, the right thing as an individual is to not get chemo. That's an individual decision with your doctors, recognizing the pros and cons and what we do know in the absence of data like this – randomized, controlled strata data. In the meantime, before we have these studies, what should we do?

As I said earlier, if you're a candidate, and SOFT, that trial with the three arms, is something that you're willing to do, and it's the right thing for you personally and, might I add, location-wise – I hate when people drive 400 miles to see me for something. I'm happy to give an opinion, but I hate it for them when they say, "I'll get my care here." I say, let's think about your quality of life here. If you really need to be cared for here, I will take care of you. But that's a long drive, and you have little kids at home, or you're working. You all have to think about that, too. You need your lives to go on, too.

In the meantime, if you're not going to go on study, tamoxifen remains the standard of care for women with hormone receptor-positive disease. Ovarian suppression is a consideration in addition. It's not a free lunch, and I'll get to that. But it's a reasonable alternative in some patients with hormone receptor-positive disease, particularly those with lower risk, as an alternative to chemotherapy. If you either can't receive it or really don't want to – not that anybody wants to – then the optimal way ultimately may be for very young patients with very aggressive hormone receptor-positive disease that someday we should be giving everybody everything to eke out every bit of benefit. We'll learn that from SOFT, or at least we should.

I think, as an aside, that at this time aromatase inhibitors have not been appropriately studied in premenopausal women. I would argue that they really don't have a role, except when you can't tolerate the other treatments, because there are other risks. I would not recommend taking aromatase inhibitors outside of a trial. I have people on them sometimes because they couldn't tolerate tamoxifen and we

really wanted to give them something, but we don't know it's as good. We certainly worry about the toxicities in a different way, because it's a lot less known, even in postmenopausal women.

As an aside, the quality-of-life considerations are not nothing. The potential side effects for a given individual from ovarian suppression are substantial. I have had women who are miserable. I'm not saying everybody. People go on it, and the majority of people do okay, just like the majority of people on tamoxifen. But we know tamoxifen works, so I'm more willing to make people a bit more miserable on something like tamoxifen, because I know they're going to get statistically a benefit, than to lump on ovarian suppression when I don't know it works. The minute someone starts to show me signs of intolerance or misery, I say, maybe this isn't the right thing, even though we thought it was the right thing for you. That's obviously a personal decision and kind of a try-it-and-see-how-you-feel if you're going to go that route, but have a low threshold for discontinuing it when you don't know it's going to help you and it's clearly compromising your quality of life.

I think there are other questions: Do bones get better after suppressing ovaries, because we know suppressing ovaries thins bones? It's doubtful. I've done a lot of work in this area. We don't have long-term studies, but the way these drugs work, the ovary ticks away. Over time and age, ovaries become less active and less fertile. Ovarian suppression is not toxic to the ovaries, so we don't think it interferes with fertility, except for the fact that during the time you're on it, you can't and shouldn't get pregnant – some people can, but you shouldn't – and that is time where your ovaries are aging.

There are also studies that have looked at women's preferences. In an interesting Australian study, women who were surveyed said they needed a lot more benefit to justify ovarian suppression than chemotherapy. On the flip side, a more recent study done by a woman who's the maven of quality of life, particularly with hormonal therapies, found that over 75 percent of women, if given the choice, would take ovarian suppression over CMF-type chemotherapy. Mind you, these were healthy women without a history of breast cancer, so they had never truly faced the diagnosis. I suspect that if I asked for a show of hands in here, it might be very different, depending on your own personal experience with any of the drugs as well as your concerns and where you are. Take these with a grain, but I think it's interesting that people are looking at these things in terms of trying to inform people about decision-making and which way to take studies.

Switching gears from hormonal therapy – and forgive me to people who have hormone receptor-negative disease – should the chemotherapy or targeted therapies be different for younger women? The short answer to that is probably not different for younger women at the current time based on the state of the knowledge, but certainly targeted and tailored to the kind of cancer that they have. The good news is that the incremental benefits of the newer regimens – cytotoxic drugs, targeted therapies – are present across age groups. ...

[Missing Material]

ANN H. PARTRIDGE, MD, MPH: ... taking a bisphosphonate may prevent that bone decrement. So stay tuned. If it's the right thing for you, enter into trials that look at that so we can learn more about you and others. The other couple things: cardiovascular health. We need longer-term data on a lot of these things and we're trying to do that. Another big thing for younger women is the implications of second breast cancers. You have a lot longer to live with that breast, and genetic issues in particular may change how you feel about having more drastic surgery. I'm not saying everybody should do that – being young certainly doesn't preclude having breast conservation. In fact, the majority of my young patients are able to have breast preservation, and I support that for a lot of reasons. The genetic issues are important. Anybody under [age] 35, in particular, should be talking to their doctor about getting genetic counseling and considering getting tested. The risks are so much higher in younger women, because that's the way genetic breast cancer tends to present.

The other issue is if women were tested more than a couple of years ago for a genetic mutation, for a BRCA1 or BRCA2 mutation, the testing has changed. Some newer testing called BART testing looks at larger changes that weren't captured before. The previous test looked at the trees but might have missed the forest. The BART testing is looking at the forest, too. Anybody who is newly diagnosed and getting tested will get that, most likely. I think they have some algorithm for doing it. People who were tested in the past didn't have that BART testing part, so some centers are contacting people. Some people are no longer in touch with their center.

If you're someone who got genetic testing and it's more than two or three years ago, you might want to talk to your doctor about BART testing. In particular, it gets approved by insurance and by Myriad [Genetics, the manufacturer of the BART test] for people with strong family histories. If you had all of the other things that fit – like your mother had breast cancer or your aunt had breast cancer or your

father's mother had breast cancer – you might want to talk to your doctor and have that BART testing, because it might help inform your future health decisions and those of your relatives. There are numerous other potential concerns, which I'm sure you all can share with me more than I could today in the interest of time.

The final thing: What's new on the forefront? A big *New England Journal* article last year looked at MRI in patients who have had breast cancer for the contralateral breast. This is a really critical issue and really pertinent for younger patients. Many of you in the room are probably going to tell me mammograms were useless. For most of my patients, mammograms do very, very little. (Applause) I'm not saying we shouldn't use them, but you can't rely on them as much. You can't rely on them for anybody. They're not perfect tests, but they're way more imperfect in younger patients.

This study looked at MRI screening in women newly diagnosed. Their mammogram had been normal on the other side. The side where they had the breast cancer, that was dealt with. The other side, the mammogram was normal, the breast exam was normal. What they did was take almost 1,000 women, and they did an MRI on the other breast within a year of diagnosis. It might have been right upfront; it might have been within a year. They found 30 additional breast cancers in the other breast out of nearly 1,000 women, which translates to about 3 percent of women having something going on in the other breast. This did not vary dramatically by age in this study, although the study is small, relatively – if it were 1,000 women, you would expect only 60 of them to be young women, so it would be very hard.

The critical piece here, too, is the biopsy – so, the MRI was done, and only 3 percent of women had a cancer, but 12 percent of women ended up with a biopsy. For every four women who got biopsied, only one got diagnosed with a cancer. You may hear that and say, “Okay, I want an MRI.” Many of my patients hear that and do. Many people, particularly after you're through the throes of diagnosis and treatment and you're just getting back to your new normal – I feel like that's such a cliché – you're getting done and you know that a lot of these interventions have a price. I think people say, “Oh, I want to do everything.” Then, after a while you're like, “Okay, everything sucks.” (Laughter)

These are not things you should just decide in a rash, emotional moment and really think through when there aren't clear benefits. There is no clear evidence that those 3 percent of cancers detected by an MRI wouldn't ultimately have been detected in another way, that detecting it early is going to improve how people do. I'm showing you these data, because I talk to all of my patients about it now. I don't think I

short-sell it. I give them the data. I say my concerns. I would say it's about 50/50. About 50 percent of people say, "I want it," and about 50 percent of people say, "Let's just get my mammogram. I feel pretty good right now. Let's talk about it next year." That, again, is an individual decision. But it's worth talking about.

Insurance may not pay for it, but it does help that the American Cancer Society put out some guidelines. You can see, basically, there was insufficient evidence to recommend for or against MRI screening. The arrow points to women with a personal history of breast cancer, including invasive or non-invasive disease. Women who have a known predisposition, a hereditary mutation, BRCA1 or 2, or a history of Hodgkin's disease and radiation, where the risks are so much higher – for the average woman with breast cancer, even young women, the risk of getting another breast cancer in the other breast over the next five years is about half a percent to 1 percent per year. That gets cut in half by people taking hormonal therapy.

That's not that high, whereas for a person with a gene mutation, it's about 20 percent over the next five years. For a person with Hodgkin's disease, it's also much higher. In that setting, for those people, we typically recommend doing it because their risks are so much higher. The probability of having a false positive on MRI also is much higher. Take this one home, think about it, mull it over if you haven't already thought about it. Talk to your doctors. I'm not telling you to get MRI; neither is the ACS. What I'm saying is think about it, know that it's out there and figure out whether it's the right thing for you.

Finally – and this is what I focus on for my research to a degree – young women face substantial psychological issues. We know this from a lot of data. You know it because you know it. Young women are at an increased risk of psychosocial distress when compared with older women. Why? It's obvious. Young women are more likely to be diagnosed when a lot of things matter more than they do when you're older – things like role functioning. I'm not saying things don't matter to older women; don't get me wrong. But things like role functioning work – you're at the part of your career where you're going like this, and "poom," you get hit with a breast cancer. You're taking care of small children, you're out-of-pocket to begin with, and you get hit with breast cancer. Beauty and attractiveness, particularly for women who are single and dating – this is tough stuff. We know this.

Sexual functioning studies have shown it tends to be harder on the younger patients, patients going through premature menopause. Patients who are more sexually active are going to take a harder hit

compared with their peers. Of course, fertility and family planning: It can be a devastating experience for a young breast cancer patient, as I'm sure many of you know, to have to deal with, "I want to have my life, but I also want to bring new life into this world. How can I have my cake and eat it, too, and get everything I've always wanted?" It's a lot of hard decisions, managing of expectations and rethinking a lot of things, which is not fun. We know this. All of these things can be interrupted by breast cancer. Even the threat of it can be distressing. You may not be infertile after your breast cancer treatment, but even the thought of it makes you freak out, and that's understandable. These things are all compounded by the relative lack of information about many of these issues for younger patients – because we've only been focusing on this in the past couple of years to a great degree – as well as the relative lack of a peer support group. I have many patients, even in my waiting room, who tell me that the older ladies come in and say, "I don't care about my stuff. I felt so bad for that young woman sitting next to me." Or the younger women come in and they're like, "I'm the only one under 50 here." No offense to our mothers and sisters and everyone else; it's just that there's a lack of peer support in our communities.

We're working on this. You guys are all together. You're working very hard on this. You have to bring this back to your communities and support. You're already doing that. Supporting groups like the YSC. Supporting getting women involved. Outreaching to the medical clinics and to your doctors and saying, "Hey, you need to have this pamphlet or this website and give it to your patients when you think of it. We realize you're busy, but just put it out in your waiting room; give it to your nurse." Groups like Fertile Hope for women who are interested in fertility.

There are a lot of resources out there that don't get tapped: Living Beyond Breast Cancer, Komen. All of these groups don't get tapped as much as they should, especially in the women in the throes of diagnosis. More awareness of these things on your part – I know I'm preaching to the converted, but spread awareness and recognition; talk to your doctors and bring some pamphlets in when you go in and say, "Can you put this in the waiting room, because I know you don't see a lot of young women? But for all of the young women, just put it in the waiting room." Things like that are making a difference and can make more of a difference.

In conclusion, young women, as you know, are more likely to have more aggressive breast cancer and suffer from breast cancer both psychologically and physically. I do believe, though, that increasing recognition and the development of more interventions to treat breast cancer, in young women specifically, and to deal with the fallout are improving outcomes. We're going to hopefully show that in

the near future from some data that we all got. Future research should help tease out the biology effects of newer risk markers and things like ovarian suppression in younger patients, and hopefully at the same time – of course, if you're doing well, your quality of life is much better in general, so improving quality of life for younger patients with breast cancer.

It's really important – and I'll end with this one: Things are going on in the right direction. This is a slide that shows the mortality rates of women both in the United States and the United Kingdom. You can see around the mid- to early 1990s, things took a deep dive. It really is going in that direction. It's very exciting to be someone who's here today to talk to you guys, to be a part of this wonderful movement to improve things for your group. Thank you. (Applause)

JEAN A. SACHS, MSS, MSLP: Thank you, Dr. Partridge. That was wonderful. If you have a question, raise your hand. I know you're all going to have a lot of questions. We'll try to do as many as we can.

WOMAN: Hi. I had a total hysterectomy, and I've been on tamoxifen for five months. My doctor wanted to switch me to an AI, but I'm feeling like I like the idea of being on the tamoxifen for the full five years and then doing the AI for the next five years. Is that something they've studied or something you'd recommend?

ANN H. PARTRIDGE, MD, MPH: I like your thinking. The short answer is that you can do it, because technically – and I'm trying to generalize things – if a young woman is definitively postmenopausal, and there's not much more definitive than taking the ovaries out, then you can be treated as a postmenopausal woman. Period.

That being said, we don't have long-term outcomes, nor do we even have short-term outcomes on the ramifications of an aromatase inhibitor upfront in a woman who has undergone surgical menopause. That's kind of a one-two punch to the estrogen. The ovaries go, and they go quickly with surgery or with chemo where you have an abrupt transition to menopause. Then suppressing the estrogen even further with an aromatase inhibitor, which is what an aromatase inhibitor does – your concerns about that are very legitimate. Many of us are worried about that. That is why the TEXT trial – suppression of the ovaries with tamoxifen versus suppression of the ovaries with exemestane – is being done.

The answer to your question specifically is going to be answered. In the meantime, it depends on how you feel about it, and one of the critical things you're alluding to is that breast cancer – especially hormone receptor-positive breast cancer, we know – is something that has a kind of long horizon where women remain at some risk. Risk goes down over time, which is great. The five-year mark is a good one to hit. Every year that you go out, every day you go out and the breast cancer hasn't come back, we should be happy. But breast cancer can come back at year six, five, four – any of those times. Again, the highest risk is in the first couple of years for both hormone receptor-positive and -negative disease. So, the idea of a strategy where the one-two punch is in sequencing tamoxifen followed by an aromatase inhibitor is something that many of us believe might be the right choice.

There is a study going on among postmenopausal women – you are functionally at this point, and many of you may also be – that is going to answer that question. It's called the BIG [Breast International Group] 1-98 trial. It also started in Europe. They are taking women who are postmenopausal – not sure how they got there – and randomizing them to receive aromatase inhibitor first, or tamoxifen followed by an aromatase inhibitor, between two and three years. That's the major question that you want answered.

We hopefully will have results from that in the near future. The fact that we don't have results yet and the study has been going on for a long time implies that there probably aren't huge differences, because studies get stopped earlier when there are enormous differences that come out early. There probably aren't huge differences early, so no matter what you do, you're probably doing something fine as long as you're getting hormonal therapy in the first couple of years. We'll get the information.

I would say there is evidence that switching between years two and three for postmenopausal women from tamoxifen to an AI is better than tam[oxifen] alone for five years. There is very clear evidence for that. I would recommend a middle-ground approach – not switching right now, but switching at years two to three, because I think there is enough data to support that. Your doctor's recommendation is also fine if you wanted it, if you're postmenopausal.

The choices for the average postmenopausal woman, when she's diagnosed, is tam[oxifen] for two to three years and then switching, or five years of an AI. But we don't know when to stop, and the duration issue and coverage beyond that is something that is concerning for women, so many women do like the tam[oxifen] followed by the AI.

The other issue here that probably speaks to many of you in the room is whether you are postmenopausal. Are you premenopausal? We often can't tell. It's a matter of watch and wait. Will I bleed tomorrow? Will I bleed again? I see this all the time. People come to me. This is what I study, too. We know that younger women especially are very likely to have periods stay through chemo – to be irregular but stay – or to have them go away temporarily and come back. I've had many people who we really thought were probably postmenopausal. They've gone a year out, and they haven't had a period. They're on tamoxifen, though. When we switch them – I actually don't switch them – they often will eventually have their periods come back during that time. Or I check their hormones, and even though they're not having periods, they're in the premenopausal range.

Even for older women whom you expect to go into more permanent menopause, when they switch – we've all tried to switch between two and three years; we want to try for people to get more risk reductions – we've seen a lot of patients who, within that year of switching, you check the hormones. They haven't had a period for two or three years. They got their chemo at 45, they're 47 or 48 now.

I had this happen to me this fall. I'm not switching people anymore, I decided, after this. I'm joking, but I go through this with people. This fall, a woman called me. We switched her in early winter. I said we need to check your hormones again when you've been on it for a couple of months. In June, she didn't feel like getting her blood drawn. We said fine, get it at your primary care in the next month or so, whenever you can. She didn't. She's busy. She has kids. She's running around.

She calls me in December; her periods are back. Her OB-GYN checked her hormones, and lo and behold, she had premenopausal estradiol levels. And she's on an aromatase inhibitor. It doesn't work. You don't expect any benefit in that setting. She came in, and I felt bad. I said, "You didn't get your blood drawn, and we asked you to do that." She said, "Well, you know, da da da." I wasn't blaming her, but just kind of figuring out what happened. I felt bad, because maybe we shouldn't have switched her. She said, "Yeah, about the midsummer, all of my hot flashes went away. My vaginal dryness went away. I felt like a teenager again." (Laughter)

I said, "That's probably when the hormones came back." This was November/December. I said, you haven't been uncovered for that long then. I'm close with this patient. I understand; she didn't want to call me. Why would she want to not feel like a teenager again? (Laughter)

I think this is a moving target in terms of ovarian dysfunction and menopause, particularly for you guys, for the youngest patients with chemo. Unless you've had something like surgery, you have to be super careful. I will tell you that a group at University of Michigan is writing a study. I'm going to help run it. We're going to try to develop an algorithm for how to safely switch women who have been on tamoxifen for a couple of years who want to switch, but we're not sure they're in menopause. We're going to develop an algorithm for how to follow them by studying it and allowing the people who want to switch to do it carefully, checking hormones at a specific time. We'll have more information on that.

In the meantime, I would argue that if you're not sure, especially if you're very young – how often can you check hormones? Are you going to come in every day and check them? – you just can't do it. I'm erring, even in my 40-somethings, on the side of caution and giving people four to five years of tamoxifen, unless they're intolerant. I want to watch them very closely based on that experience.

We've published a paper on this. Others have, too. We have to be very careful. But I recognize that for many of you, that's a tough place to be in terms of what do you expect, whether you want babies or not, things like that. It's very tough. There are some things that can be looked at to know in the here and now where you are, but that may change.

WOMAN: My question is related to the BRCA1 or 2, the PARP inhibitor [Editor's note: these are new medicines under study that target cancers caused by BRCA mutations] you talked about. Is that only for triple negative?

ANN H. PARTRIDGE, MD, MPH: I think so. I can find out. I think so, though. That was my impression. The patient I put on it was triple negative. Do you know more than I do?

WOMAN: Oh, absolutely not. This is my first time hearing about it, so I was interested.

ANN H. PARTRIDGE, MD, MPH: I can find out for you. I'm pretty sure it's only for triple negative, but I can find out. What you're alluding to is that BRCA2 mutation carriers are more likely to have hormone receptor-positive disease than triple-negative disease. BRCA1 mutation carriers are more likely to have triple-negative disease, although they can still have hormone receptor-positive disease. I'm not 100 percent sure, now that you're pushing me on that. I know that it's triple negative for sure. It was

under the group under triple negative. I know the bigger thing is BRCA1 or 2 associated, so if it's not BRCA1 or 2 associated triple negative, you can't get on it. I don't know the contra...

WOMAN: Thank you. Were you ever at University Hospitals of Cleveland?

ANN H. PARTRIDGE, MD, MPH: No.

WOMAN: Thank you for your presentation. We definitely got a lot of information. The BART genetic testing that you referred to: I was genetically tested and found to be BRCA1 positive. Would I still need ...

ANN H. PARTRIDGE, MD, MPH: No.

WOMAN: Is that finding a different gene?

ANN H. PARTRIDGE, MD, MPH: No. It's the same. It's looking for forest rearrangements in the same gene. If you've already spotted it, then you're all set. That's a good question. You're looking for a child lost in the woods. It's a big woods – the genome, even the gene – so if you focus on individual trees, you may miss the kid. It's a good way of looking, but you may miss the kid. If you step back a little, though, and you can look at bigger sections of forest, sometimes you see something that looks abnormal; it stands out. It's like a higher view.

WOMAN: My question is about the pathology report. When I was diagnosed, it was recommended that I have a bilateral mastectomy. I had high-grade DCIS, invasive. But when my report came back, my surgeon called and said, "You have some strange lymphoma marker." What does that mean? Have you heard of that? He said he had never heard of that. He said, "I can tell you, you don't have lymphoma. But we don't know what this means." Then, subsequently, 16 months later, I had a recurrence. My mind keeps coming back to whether that lymphoma marker has something to do with it.

ANN H. PARTRIDGE, MD, MPH: I can't speak specifically to that without looking at the pathology and things like that, but in general – and I think what will be relevant – when young women are diagnosed with breast cancer in particular, in any breast cancer, you really need good, critical pathology review. Not all centers are alike in that way. Not all pathologists are alike in that way. One thing I often recommend to

people is that they get a second opinion at the mecca, if you have one near you, at least to get your pathology reviewed. Not everybody needs that. Some things are bread and butter. You can even ask your doctor, “How good is your pathology? Do I trust all of these things?” Ask specifically about the markers. Does it all make sense?

If a person has a low-grade, HER2/neu positive cancer, when they’re conventionally high grade, you’d say, “Hmm, that doesn’t make sense.” You hope your oncologist would know enough to say, “We need to get this reviewed somewhere else.” We do it all the time, even at Farber. Our pathologists will kind of tell us, “This didn’t make sense. So we re-tested blah, blah, blah, and we sent this out to blah, blah, blah.”

A good pathologist and a good pathology review is critical. If it were me, I would have it sent to one of the meccas where they have pathologists who dedicate their lives to looking at breast pathology. You’re not going to offend anybody. In fact, often the oncologists are going to want to do that, particularly in situations that don’t quite make sense.

There are medical mysteries. There are things out there where the head of breast pathology looks at it and says, “This doesn’t really make sense.” We see this sometimes, and she’ll look up all of the reports, meaning all of the literature, and she’ll say, “There were two cases, and ba, ba, ba.” And she gets everything for us, and we say, okay, weird things happen.

I don’t know what that means. It’s not ringing a bell with me enough to say, “Oh, it must be blah, blah, blah.” You do need critical pathologic review, though. If you have not had a second pathological opinion, then that’s the situation where you definitely should have it.

CINDY GEOGHEGAN: Can you define what a mecca is?

ANN H. PARTRIDGE, MD, MPH: What a what is?

CINDY GEOGHEGAN: A mecca – for us stupid people.

ANN H. PARTRIDGE, MD, MPH: That’s a good question. A National Cancer Institute, or NCI-designated cancer center – they’re all over the country. They’re not everywhere, but they’re all over the country. Most of you should have one within a day trip. It might have to be on a plane. The mail can go

without you. Often the pathology goes with the treatment obviously. If you don't feel like you physically need to be seen, but your pathology is weird or you want a second pathology review, your pathologist can send it themselves, and you don't have to physically go.

It's an NCI-designated cancer center. Again, they're all over the country. They have specialists who focus on particular cancers. You don't want to come to me or see my breast pathologist for your colon cancer or for your routine appendicitis. We can do it, but you really don't want that. We're focused on one particular problem. It's the jack-of-all-trades versus the master of none. I don't mean that to be pejorative. We need people on the forefront. You can't be that focused. I don't think I could go out and become a regular oncologist right now. I'm joking. I probably could, but I'm so super subspecialized.

These cancer centers have individuals who are paid to do one thing and focus and move the field forward. That's true from the clinicians to the radiologists to the pathologists. That's a situation, especially if you have weird pathology – “weird” meaning something that doesn't quite make sense, isn't garden variety – where I definitely want to have it reviewed.

WOMAN: I have four questions, all related. One: Are there any differences in performances between surgical versus chemical ovarian suppression? Two: Is there a length of time that people can take the chemical suppression method? Three: Is there a safe practice or standard practice for taking AI? Like five years for tamoxifen; what's the number of years for AI? And four: Are there patients who have terrible experiences with AI, tell the doctors that – I've taken tamoxifen before. Now I am taking a break. Can I go back to tamoxifen?

ANN H. PARTRIDGE, MD, MPH: Good questions, and they're all related. The first was the chemical ablation or suppression versus surgical ablation. Surgical is definitive – you can't get them back – whereas chemical is suppressed with a GnRH [gonadotropin releasing hormone] analogue, basically a medication that interferes with the endocrine loop and suppresses ovaries. The endocrine suppression can be limited. I strongly recommend if someone is going that route, particularly in younger patients, that they get suppressed monthly, they get the shot monthly, because there is more evidence for breakthrough – that is, ovaries still functioning despite the suppression in the every-three-month shot. Monthly is what I recommended. People can still break through that. I haven't seen the data recently, but it's very low. It may be good enough, breaking through a tiny bit.

Ovarian removal is much more definitive, and you don't have to get a shot, but you have to weigh the fact that it is not reversible and it's invasive. Duration-wise, which was your very good question, we typically, from most of the studies done in Europe, treat with ovarian suppression, if we're going to do it, from two or three up to five years, because that's the optimal – at least to date – tamoxifen length. That is the optimal, in postmenopausal women, aromatase inhibitor length.

The question of whether to keep going on ovarian suppression, we don't know the answer. If your ovaries are gone, you have no choice. If your ovaries are still there and you can stop the medication, you may feel like you're a teenager again, and there may be some symptoms that go away, which may be really good for your quality of life and may not affect your breast cancer outcomes.

Until we have more data, we tend not to do things that are drastic and irreversible, and that we can do with medicines, unless a person really wants to. I do have people who really want to, but most of my patients hear all that and say, "All right, let me see where I am, if I can do it temporarily, because that's so permanent, and you're telling me I don't have to." Every now and then, I'll check someone. They'll ask me. They'll say, "I felt like my vaginal dryness is better," and I'll check their hormones. They're still usually suppressed. I've never had a person break through the monthly. I have had people break through the every-three-month, and I know there is a good literature on that.

I answered one, two and three. What was the last one?

WOMAN: Tamoxifen – do people go back on it?

ANN H. PARTRIDGE, MD, MPH: I do that all the time. Aromatase inhibitors are not a free lunch. They're a good drug. They're slightly better upfront than tamoxifen in postmenopausal women, again, with the caveats that a few years of tam[oxifen] followed by an AI may be better than an AI alone. Clearly we want to incorporate them for people who are definitively postmenopausal, but a large minority of patients can't tolerate them or become miserable, particularly due to the arthralgias – aches and pains – that women can experience. I switch a woman to another AI or back to tamoxifen at least – and I don't have that huge of a practice, but it's a good size – every three months.

The answer to your question is yes. There is some literature to support delaying tamoxifen and then going back to it. There is a French study for women who never got tamoxifen – I don't know why they never got it – where they actually added it later, and then some women didn't get it. They did a randomized

study. The women who got it added on later, a couple of years out – and I think they were up to ten years out – were less likely to have their cancers come back than the women who didn't ever get the tamoxifen, even when it wasn't added for several years; were less likely to have future breast cancer events.

Tamoxifen prevents breast cancer, too. We know that. Women who have had breast cancer are at higher risk of breast cancer – meaning new primaries, a new breast cancer, not the old one coming back, but we know it prevents that, too. If someone, for instance, decided for whatever reason that they didn't want to take tamoxifen for a year or two – not that I would recommend that in most situations – then they may change their MO about that and they can still go on it. Probably not with as much benefit as previously, and you'd have to weigh the pros and cons of that, but you can do switches. You can go back on it.

Generally, five years is the standard recommendation for tamoxifen right now, although recently at San Antonio, a large meta-analysis of many studies where they're looking at ten versus five suggested that a little more may be better. It's so preliminary that I wouldn't do it yet. They didn't present anything about the toxicities, and we know that the toxicities, like blood clots and cancer of the uterus, increase dramatically when you get beyond five years, so I wouldn't do it yet. But it's something to think about.

CINDY GEOGHEGAN: We have one last question. I apologize that we didn't get to everybody, but there will be another Q&A after Dr. Block speaks, with Ann and Dr. Block.

WOMAN: Thank you. I was diagnosed when I was 38. I went through a three-month diagnosis because they couldn't figure out whether or not it was what it was. I had a couple of mammograms and a couple of ultrasounds. A couple of weeks ago in Houston, I went to the Rose [nonprofit organization; <http://www.the-rose.org>], and they were unveiling their new SomoVu ultrasound, which is a whole-breast ultrasound that is supposed to be more effective in helping to diagnose young women because of the denseness and all of the other issues that we as young women face in trying to get diagnosed. Have you heard about SomoVu and how that is working toward helping to get us diagnosed more quickly?

ANN H. PARTRIDGE, MD, MPH: That's a very good question. I have not heard of that particular technology. I know that ultrasound is getting better and better. Mammograms are getting better and better, even for younger women with digital mammography. You should be having mammograms. They're not perfect, but they get better over time. The breasts become less dense over time, generally. Then, with all

treatments, tamoxifen makes mammograms less dense over time; ovarian suppression, the hormonal milieu changing, makes mammograms better. Then, of course, there are MRIs to tie in.

Ultrasounds are generally very good for discriminating whether something is concerning or whether it is not. We tend to err on the side of, if we're not sure, there's nothing like tissue – there's nothing like a biopsy. Then you can be much more definitive. You may get something strange under the biopsy, particularly in a person where you're not sure, but the only definitive screening test for cancer is getting a biopsy.

We say in oncology, "Tissue is the issue." Sometimes you just need to go there. I'm not saying biopsies are pleasant experiences, but I would say that all of the technologies in the world, until you figure out a way to biopsy people without cutting them, they're all limited.

CINDY GEOGHEGAN: Thank you, Ann. (Applause)