



Young Survival Coalition and Fertile Hope Present
Breast Cancer and Fertility:
A Teleconference for Patients and Survivors
October 11, 2004

On October 11, 2004, “Breast Cancer and Fertility: A Teleconference for Patients and Survivors” aired. Moderator Lindsay Nohr Beck, Fertile Hope’s Founder and Executive Director, was joined by three experts in the fields of oncology and fertility. Drs. Kutluk Oktay of the Cornell Institute for Reproductive Medicine, Ann Partridge of Dana-Farber Cancer Institute, and Lynn Westphal of Stanford University Medical Center presented their knowledge and expertise on the effects of breast cancer treatment on a young woman’s fertility, parenthood options and pregnancy after breast cancer.

[Fertile Hope](#) is a national non-profit organization dedicated to providing reproductive information, support and hope to cancer patients whose medical treatments present the risk of infertility.

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.

This teleconference series was made possible through the generous contributions of the [Lance Armstrong Foundation](#) and the [Susan G. Komen Breast Cancer Foundation](#).



Introduction

Young women with breast cancer face many unique issues, one of which may be concerns surrounding pregnancy and fertility after cancer and its treatment. In an effort to address these issues, Fertile Hope and the Young Survival Coalition hosted a free two-part teleconference series on breast cancer and fertility for National Breast Cancer Awareness Month in October 2004.

The goal of the series was to provide hopeful information about all of the fertility preservation and parenthood options available today. We realize that infertility in addition to a breast cancer diagnosis can be overwhelming, and hope that these transcripts provide a greater understanding of the issues and options as we understand them today.

Whether a woman is looking to preserve her fertility before treatment or investigating post-treatment parenthood options, it is important to know that there are options available at each step of the journey. We are at an exciting time in medicine – cancer survival rates are on the rise while, simultaneously, reproductive technologies are expanding at a rapid pace. New and experimental options are emerging everyday and several options exist to help survivors fulfill their parenthood dreams.

Whether you are a cancer patient, survivor, physician, social worker or otherwise, these transcripts from our teleconferences are intended to help you navigate the reproductive options available to breast cancer patients and survivors. However, as always the information presented in these transcripts is neither intended nor implied to constitute medical advice, diagnosis, or treatment. It should not be considered complete and should never be used in place of a visit, call, consultation or advice of your physician or other health care provider.

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ELLY KIRSCHNER: Good evening, and welcome to "Breast Cancer and Fertility: A Teleconference for Patients and Survivors," hosted by Fertile Hope and the Young Survival Coalition. Fertile Hope is a national, non-profit organization dedicated to providing reproductive information, support and hope to cancer patients whose medical treatments present the risk of infertility. 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.

My name is Elly Kirschner, and I am the program manager for the Young Survival Coalition. Your moderator for tonight's call is Lindsay Nohr Beck, Fertile Hope's Founder and Executive Director. Before I turn the call over to Lindsay, I'd like to provide you with the logistics of tonight's call. First, the call is being recorded and a transcript will be made available in about three weeks on the YSC website, which is www.youngsurvival.org, as well as on the Fertile Hope website, www.fertilehope.org. We will notify you as soon as it is available.

The format of the call is as follows. Part 1 will be a presentation by our panel. Each panelist will impart his or her knowledge and expertise on the effects of breast cancer treatment on a young woman's fertility, parenthood options and pregnancy after breast cancer. Some of you have submitted questions in advance of the call and we've tried to incorporate as many of these as possible into the presentations. In Part 2, after all of the panelists have spoken, we will then open the call to your questions.

At that time there will only be about 40 minutes to cover all of your questions, so please try to keep them brief. Tonight's call is operator-assisted, so when we open the line for questions our conference coordinator, Matt, will give you instructions on how to ask them. Due to the format of these calls it's difficult for us to answer questions that address specific cases or individual circumstances. So if you do have a question of a personal nature we will try to address it in more general terms as others on the call may have similar concerns. We appreciate your understanding. If we run out of time and you still have questions for the panel you can submit them to info@youngsurvival.org and we will do our best to get an answer to you. Now I will turn the call over to our moderator for the evening, Lindsay Nohr Beck.

LINDSAY NOHR BECK: Thank you, Elly. My name is Lindsay Nohr Beck and I'm the Executive Director of Fertile Hope. I will be your moderator for tonight's call. I would like to start by thanking the Susan G. Komen Breast Cancer Foundation and the Lance Armstrong Foundation for making this teleconference series possible. The mission of the Susan G. Komen Breast Cancer Foundation is to eradicate breast cancer as a life-threatening disease by advancing research, education, screening and treatment. For more information, please visit www.komen.org.

The Lance Armstrong Foundation believes that in your battle with cancer knowledge is power and attitude is everything. From the moment of diagnosis they provide the practical information and tools you need to live strong. They serve their mission through public health, advocacy, research, and education, including Live Strong, the Lance Armstrong Foundation's comprehensive resource for people living with cancer. The Lance Armstrong Foundation was founded in 1997 by cancer survivor and champion cyclist Lance Armstrong, and is located in Austin, Texas. For more information, please visit www.laf.org. We would also like to thank CancerCare, Sharsheret and FORCE for informing their constituents about tonight's call.

Young women with breast cancer face many unique issues, such as a sense of isolation, dating, managing career or school responsibilities. Foremost on many young women's minds are issues surrounding pregnancy and fertility after cancer and chemotherapy. Tonight we will try to answer some of your concerns and questions. We have a panel of experts in the field who have graciously taken the time to be here with all of us tonight: Doctors Kutluk Oktay, Ann Partridge and Lynn Westphal. We will start the call with Dr. Ann Partridge. Ann is a medical oncologist at the Dana-Farber Cancer Institute and an instructor in medicine at Harvard Medical School, specializing in breast oncology. Dr. Partridge, go ahead.

Panelist One: Ann H. Partridge, MD, MPH

Hi, thanks for having me tonight. As you said, I'm a medical oncologist, and I think one of the most important things to note as we start out this conversation tonight is the advances that have been made over the last several decades with regard to how women who are diagnosed with breast cancer will do in the future. Both from a screening, prevention and treatment standpoint, cancer survivorship has become an important issue, and we can't overlook the fact that years before this was very much not on people's radar screens.

So I'm very pleased to be someone who is able to seek out funding and do work on cancer survivorship these days both because of the realization of the importance of it and the increasing survivorship that exists, as well as the thousands of women with breast cancer who are surviving their cancer and going on to be understandably interested in having a full life - with all of the things that they want in that life, which might include future fertility and having a biological child. With that being said, I think it's important to note that there has been a lot of success when it comes to fertility preservation, first and foremost because it is not all that common in the younger women - especially very young women -- to become truly infertile.

Of course we're talking about chemotherapy when we talk about the risk of infertility from breast cancer treatment. It's important to note that radiation for breast cancer is generally only done to

the chest or to the breast-conserving surgery breast and not generally done to the ovaries, although sometimes this may be used as a separate therapy. But in general, in this country if we're going to suppress ovaries we use drugs or remove the ovaries, but if someone wanted to retain their fertility, they wouldn't choose the option of radiation to the ovaries or ovarian-suppression drugs. In general radiation is not something that if given to a woman as adjuvant therapy for breast cancer would affect her fertility since generally radiation does not go as low as the ovaries which is the way that radiation can impact fertility with other cancers, say gynecologic cancers.

Surgery for breast cancer does not tend to impact on fertility in women with breast cancer because obviously the surgery is to the breast. Now, again, aside from the people who had their ovaries taken out for other reasons, either for prevention or treatment, surgery should not affect fertility with breast cancer treatment. But of course, chemotherapy can. The major things that affect whether or not chemotherapy will affect a woman's future fertility are, (1) her age at the time of treatment, and (2) the type of medication or the chemotherapy regimen chosen. We'll start with age.

In general, studies that have looked at this problem have broken women down by 30 years and under, 30 to 40 years, and over 40. Of course, this is all referring to women who are premenopausal. Unfortunately there aren't a lot of data for this, but in the few studies that have looked at common, current breast cancer therapies including AC chemotherapy and CMF chemotherapy, CMF appears to cause the risk of infertility to beyond 15 to 20 percent in women under 30.

Regarding AC, there have been three studies that have looked at the risk of amenorrhea. It's important to note that infertility does not necessarily equate to amenorrhea (or stopping having periods). Dr. Oktay, I'm sure, will talk about that more. But in terms of amenorrhea, the risk with AC is between zero to five percent in women 30 and under, which is not really that high.

So when I say it's not all that common in the very young woman, that's true. There are few studies that have looked at it, but two studies have shown zero percent. Not huge numbers, but it is still reassuring for the youngest people getting breast cancer and needing chemotherapy.

Now, of course, many more women are in their 30s when they're diagnosed with breast cancer. Of course, age is a continuum, so it's not like 31 is all that different from 30 or 29. But ages are lumped in this way for the purposes of studying and trying to make conclusions about a population, or a group of women. If you look at someone who's in their 30s, say 35, with CMF the risk of going through menopause is between 20 to 40 percent. So it goes much higher as you get older. With this age group, AC is more on the order of 15 to 20 percent.

So in this day and age where AC and CMF are considered fairly equivalent as far as the effectiveness of breast cancer treatment - if anything AC tends to be a little bit better in some studies, with a lot of caveats - any woman who is concerned about her future fertility should not take a course of CMF. I have had heard oncologists confuse that and say that CMF is less likely to cause women to go into menopause. That's just wrong: AC is less likely. So any younger woman in her 30s who is concerned about her future fertility or does not want to close off those options should choose AC if they want to try to preserve their continuing menstrual cycling.

In the 40s both numbers go up and the risks with AC are over 20 percent. With CMF, it rises to 40 to 80 percent for women in their 40s. So you can see that both regimens are different and it is incremental within the age groups. The older you are the more likely you are to enter premature menopause. One side note is that unfortunately, the studies haven't looked at what premature menopause truly is. They've looked at amenorrhea within a year after treatment. Most patients who are not cycling after a year do not resume cycling, but it is possible.

It's important to note that if you stop cycling with chemotherapy, that doesn't necessarily mean that you are postmenopausal. That has implications both in practicing safe sex and using

contraception, and for treatment. A lot of women want to use aromatase inhibitors instead of tamoxifen. Women who go into menopause or at least become amenorrheic are not necessarily in menopause. Though that's a little bit off the subject of this talk, it's something to bring up with your doctors.

Importantly, we don't have much information on the taxanes in terms of the risk of infertility or amenorrhea. There was one small study that was done and presented in San Antonio in 2000 or 2001 by someone named Stone, et al. It was an abstract and I haven't seen it published yet but I think they had approximately 30 participants. They found that using Taxol did not increase the risk of becoming amenorrheic. I find that reassuring but certainly not conclusive and more studies need to be done.

Additionally, we don't have any information on the newer ways of giving chemotherapy, such as dose-dense chemotherapy (one chemo cycle every two weeks rather than every three weeks) or using Taxotere instead of Taxol. I haven't seen any of that information. That's something that we really need to look into. Many of us are looking into studies to try and further define that for our patients so you have more information as you make your decisions.

The other important thing to think about is the difference between amenorrhea and infertility. Dr. Oktay could elaborate on this more, but as I alluded to, just stopping periods doesn't necessarily mean that you're not still cycling or that your estrogen levels are as low as someone who is postmenopausal. The other side of that coin is that just because you're having your periods, doesn't mean that you are fertile.

The one thing we do not know is whether a woman who goes through chemotherapy but continues to menstruate is as fertile at that moment when she's menstruating and going through cycles as she would have been without going through chemotherapy. For example, if a woman goes through chemotherapy at 30 and continues to menstruate at 35, we don't know that she's as

fertile as she would have been at 35 had she not gotten the chemotherapy. That's something we are studying now – we are trying to measure ovarian reserve in cancer survivors to try and answer that question. And Dr. Oktay may have some more information on that. We all think that women are not potentially as fertile but no one has any great data on that that I am aware of. That's where I'll stop and address other issues as questions come up later on, or if anything comes up in anybody else's discussion.

LINDSAY NOHR BECK: Well, great, thank you. This is Lindsay again. Our next speaker will be Dr. Oktay. He is the associate professor of Obstetrics and Gynecology at the Weill Medical College of Cornell University and the associate attending physician in OB-GYN at Presbyterian New York Hospital. Dr. Oktay?

Panelist Two: Kutluk Oktay, MD

First of all, many thanks to the YSC and Fertile Hope for organizing such a valuable event. I want to continue along the same line as Ann was speaking and make a few points about what we know about the damage caused by chemotherapy. When you look at the incidence of women losing their periods after chemotherapy, you're actually looking at the tip of the iceberg. As Ann pointed out, it's been clearly shown in experimental studies and in studies for other types of cancers, that with chemotherapy and especially the drug Cytoxan (which is included in both regimens in breast cancer), every time the drug is administered a chunk of ovarian reserve is taken away.

To explain this a little further, as we know now, women are born with all of the eggs they can have. They are born with about a million eggs or so and they use eggs from that reserve until they all run out, and that's when menopause happens. Chemotherapy accelerates this process. With each course of chemotherapy a fraction of eggs will be lost. Once the chemotherapy is finished, depending on how young the patient was at the beginning, this chemotherapy may or

may not push the woman into menopause. However, even if it doesn't push the woman into menopause, this doesn't mean that nothing happened.

For example, there's one study that looked at women undergoing IVF with a history of chemotherapy with Cytoxan versus no chemotherapy. They clearly had poor response and much lower pregnancy rates. Thus there is evidence that fertility is reduced after chemotherapy. There are also many other studies looking at long-term follow-up of children and younger adults - 10, 20, 30 years into their adulthood - and what happens many years after. They found a huge risk of early ovarian failure and infertility.

So, if you look at all of these studies that look at the incidence of menstruation and who was able to resume menstruation, it is misleading because menstruation itself is not a good marker of ovarian reserve. Two, these studies in general are short-term studies. Now, with breast cancer one problem we always encounter is that a patient may be in her 30s and once she has received chemotherapy, her ovaries have aged between six to ten years, as a wild guess. Now her ovary behaves as if she is in her 40s.

But then, many of these women won't be allowed to get pregnant for as many as five years because they are on tamoxifen. So this should factor into the decision-making about treatment and family planning, too, because by the time the ovaries start behaving like 45 that's an age where most healthy women can't conceive anyway. They should also consider how many children they are planning to have. Very young women may have time to have a child, but because their ovarian reserve is severely diminished they may not have any choice for a second.

So because of these facts even younger patients may feel the need to resort to fertility preservation strategies. The best thing would be a medicine that would protect ovaries. Now, that brings me to the controversy about using drugs that suppress ovarian function like Zoladex and Lupron. Now, I want to say this outright here that these drugs don't work. Unfortunately

there are a few not well-designed studies, which are retrospective studies – meaning they look at a patient's record and try to make some conclusions based on what has been entered in the past rather than following a patient out after the drug was administered, or having controls that were not an active part of the study. These studies suggested some benefit, but they were comparing women who were followed maybe for a year or two or three after receiving this drug versus women who did not receive it but they were followed for ten years, 15 years. As I said, the longer you follow up somebody who received these drugs the higher the incidence would be. And there is at least one study which is designed in a better way following these patients from now into the future in a prospective design and it showed no benefit.

So, that brings us to other strategies that involve assisted reproductive technologies. Now, in breast cancer there is an advantage that in most instances between surgery and chemotherapy something like a six-week time period is allowed. This would enable us to do an ovarian stimulation, and freeze embryos for future use. Even if a patient becomes menopausal she would be able to carry those embryos in the future with the administration of a little estrogen and progesterone hormones. So once we have the embryos a pregnancy could be achieved.

The problem with this is because most breast cancer patients are sensitive to the estrogen hormone, we would not want to give them fertility drugs because they would increase estrogen levels. To get around this, there are two approaches that we designed which involve two breast cancer drugs, tamoxifen and the aromatase inhibitor letrozole. The patients can be stimulated with these drugs. In a recent study that we have completed, we showed that you can stimulate these patients with these drugs and you can obtain a reasonable number of embryos for future use. At least in the short run cancer recurrence rates are not increased compared to controls - other women, the same age and similar cancers - who didn't undergo these procedures.

Since embryo freezing is an established procedure, this should be the first thing the patients should resort to. Egg freezing is a second option, especially in women who are single and don't

want to use donor sperm to fertilize their eggs. In this technique, the egg is frozen before fertilization. However, unfertilized eggs tend to be more fragile than embryos and the success rates are relatively lower, but there has been great progress in that area as well.

A third option is the most experimental option, and that is ovarian tissue freezing. In this procedure, the ovaries or a piece of an ovary are removed by a keyhole surgery and frozen before cancer treatment that might result in infertility. In the future when the patient desires to get pregnant, this tissue is transplanted back into the patient. With this approach, embryos have been formed in patients whose ovary was transplanted after being frozen for six years. That's by our team at Cornell. Recently there was a report of a pregnancy after ovarian transplant in a lymphoma patient, even though there are some questions about the validity of that study. But nevertheless we have now either achieved or are about to achieve the first pregnancy, so it is a very experimental procedure. However, when there is no time to do ovarian stimulation this procedure may be the only option, because it doesn't require time for stimulating the patient.

Finally, a few words on in vitro maturation. This is a technique where you can collect immature eggs if you don't have enough time to stimulate the ovaries. You can collect the eggs after a short stimulation with fertility drugs, and then you can mature them outside the body instead of inside. But this is also highly experimental, because those eggs don't mature well outside the body, and the pregnancies have been limited with this technique as well.

And finally, I'll say a few things about the use of tamoxifen during pregnancy. Because tamoxifen blocks certain cells that recognize estrogen, it can have an effect on embryo development or fetal development so it should not be used during pregnancy. Even though the evidence is moderately strong in terms of its damage on fetal development, it should not be used during pregnancy. However, when it is used for ovarian stimulation and not breast cancer treatment, this drug is given before the eggs are actually collected, and embryos are not exposed to it.

Drugs like tamoxifen do not cause permanent damage to the ovaries, so they do not affect fertility permanently. However, they may cause some ovarian dysfunction while the patient is receiving it, because they bombard the ovaries and stimulate them during that treatment. In the same way, any treatment like Lupron or Zoladex that puts patients into a temporary menopause doesn't have any permanent effects. They will not alter fertility in the long run. I think I'm going to stop here, too, and maybe continue in the question and answer session.

LINDSAY NOHR BECK: Great, thank you, Dr. Oktay.

KUTLUK OKTAY, MD: You're welcome.

LINDSAY NOHR BECK: Our next speaker will be Dr. Westphal. Dr. Westphal is the assistant professor in the Division of Reproductive Endocrinology and Infertility in the Department of Gynecology and Obstetrics at Stanford University. Dr. Westphal, go ahead.

Panelist Three: Lynn Westphal, MD

Thank you for inviting me to speak tonight. This is obviously a really important topic. Continuing on the discussion from the previous speakers, patients after they've had their chemotherapy often want to know if they're still fertile. Unfortunately, there is no perfect test, and since fertility involves a number of factors there isn't one test that's going to tell someone if they're fertile. But after receiving chemotherapy, the thing that we're most concerned about is how well the ovaries are functioning. The time it takes for a cycle to resume after chemotherapy can vary - usually if cycles are going to resume they will return in about six to 12 months after the treatment.

When patients come in and want to know if they're fertile, the most common thing that physicians will do is test a hormone level called follicle stimulating hormone, or FSH. This isn't a test that gives us all of the information that we want to know about the ovary, but if the FSH

level is normal or low (low is good for these hormone levels), then as far as we can tell by this test the ovaries are functioning fairly well. If we see that the FSH level is starting to fall into abnormal ranges or is rising, then we know that there definitely has been some significant ovarian damage.

Now, there isn't an FSH level where someone can say, 'oh, you absolutely can't get pregnant.' But we do know that the higher the FSH level goes, the lower the chance of getting pregnant in the future. That's the most common test that people do when they're initially evaluating the ovarian reserve and how much damage there may have been to the ovaries. There are some other tests that people may do in association. Sometimes people will do an ultrasound to look at the size of the ovaries and at how many of these resting little follicles may be there, and that may be helpful. There are some other hormone levels that people sometimes will look at, so there may be a number of factors that are evaluated. Then depending on these results there may be various treatment options to consider. All in all, usually the best way of preserving fertility is to do something before receiving chemotherapy.

As Dr. Oktay said, chemotherapy can cause significant damage to the ovaries, and we know that when we use fertility medications in women who have received chemotherapy, we tend to find that their responses to the medications are not as good. So if someone is thinking about freezing eggs, embryos or ovarian tissue, that process is usually optimized by doing it before receiving chemotherapy. However, occasionally there are people who haven't had a chance to do that or weren't aware of those options, and then sometimes there may be this window after treatment. If this is not at a time when they can get pregnant, in those situations perhaps it may be worthwhile to consider freezing embryos if they are going to delay having children.

There's unfortunately no way to know when someone will go into menopause. We know that it is more common to go into menopause earlier after receiving chemotherapy. So depending on age and future treatment considerations, some women may consider doing these freezing

techniques that Dr. Oktay mentioned. If someone has gone through chemotherapy and their ovarian function is very poor or they have gone into menopause from the chemotherapy there are other options that women can consider. They could consider getting donor eggs from someone else.

There is sometimes the possibility of getting donor embryos. If someone is in a position where medically they shouldn't think about getting pregnant themselves, they can consider a gestational carrier, or if they froze embryos before their chemotherapy and they are not in a position to get pregnant then they may also want to use a gestational carrier. Adoption obviously is another thing that some women may want to consider.

Now, in terms of deciding when to get pregnant, this is something that the woman needs to discuss with her oncologist in terms of her particular situation and when it may be safe for her to conceive. How long to wait after treatment is open to debate. In general, most women are told to wait between two to five years. Again, that depends on the type of treatment that they're undergoing, the stage of their disease, and individual factors.

In general, it doesn't seem that pregnancy is associated with an increased risk of recurrence in women who have had breast cancer. A number of people have looked at the risk of recurrence. In general women who get pregnant after they've been treated for breast cancer seem to do as well as women who haven't gotten pregnant. In terms of the children that are born after treatment for breast cancer, there has been no increased risk of birth defects. The children seem to be just as healthy as any other child that is born.

In women who have one of the genes that increases the risk of breast cancer, obviously if there is a genetic basis for their cancer this could be passed on. There are people who have done pre-implantation genetic diagnosis for genes that increase different types of cancer risk. There are a

number of ethical issues involved with PGD. There are some people who have in various situations done testing for certain genes that can increase different types of cancer risk.

Women who have been treated for breast cancer, if they do get pregnant and deliver, can usually breastfeed. Usually the unaffected breast will produce sufficient milk, and it is safe for the infant to breastfeed.

One last question, as Dr. Oktay talked about a little, is that taking tamoxifen or Zoladex should not change future fertility. Obviously fertility will not be normal and you shouldn't be getting pregnant while you're on them, but it shouldn't affect the chance of getting pregnant in the future. If you are taking tamoxifen you should use some other form of contraception. There are some women who do use tamoxifen after their treatment as a fertility drug. It can be used to increase fertility when it's given, usually for a short period of time after treatment. Anyway, I will turn it back over to Lindsay and questions.

LINDSAY NOHR BECK: Great, thank you, Dr. Westphal, and thank you to all of you for your great presentations. We've heard a lot of information, and I'm sure our callers are anxious to ask their questions, so we will now open the lines to questions. The operator, Matt, will instruct you on how to indicate that you have a question.

Question and Answer Session

QUESTION 1: *Yes, I'm currently on Lupron, and I heard one of the speakers say that it doesn't work. My doctor put me on it to help preserve my ovaries. And I was just wondering, do you know why he said it would work and this speaker is saying that it does not work?*

KUTLUK OKTAY, MD: There are two reasons, well, let me give you the reason why your doctor said that. As I mentioned in my remarks there were a couple of studies which were not carefully designed. Let's say that the extent of available data was in a way comparing apples and oranges, and that gave the impression that it was helping. In other words, if you look at one woman who did receive this treatment and you follow her for just one year and do not know what happened five years down the line, and compare her to a woman who didn't get the treatment but she was followed for ten years, just because you didn't observe the first group enough you could find a difference. And on the other hand, there was one study before these studies which randomly allocated treatment between two groups, both men and women, and did not find a difference.

The second reason why we say that is because the eggs we're trying to protect with these treatments are called primordial eggs. These are not growing eggs and they are not sensitive to any kind of hormonal manipulation. What Lupron or Zoladex does is shut down your follicle-stimulating hormone. It is follicle stimulating, but it only stimulates those eggs that have already started growth. So biologically there's a lack of plausibility that it should work.

Now, there is an argument that 'what is the harm? Why can't we just give that?' Now, we shouldn't confuse that with the use of Zoladex or Lupron for the medical treatment of your breast cancer maybe Dr. Partridge can comment on that. That's a different reason why they're used. I want to touch on what the harm may be because there is also evidence that, especially with breast cancer, if you shut down the estrogen hormone during chemotherapy you can actually make breast cancer cells less sensitive to chemo drugs. So just because we think a treatment is without harm, doesn't necessarily mean that. We have to be careful about that. I'll stop right here.

ANN H. PARTRIDGE, MD, MPH: I can just follow up on that. In general for a hormone receptor positive cancer, using Lupron or suppression of the ovaries is a very reasonable

additional treatment for hormone receptor positive cancer. There are several studies ongoing in this country trying to address the actual amount of benefit that they add in various situations, and whether they add anything or how much they add relative to chemo plus tamoxifen. I suspect that they will, but currently it's just not clear what the risk/benefit ratio will be in that setting. There are several studies available.

Using Lupron during treatment in an effort to suppress the ovaries and to preserve fertility, there is an ongoing debate, with all due respect. There is currently an open, randomized trial for women whose tumors are hormone receptor negative, which kind of takes the treatment aspect out of it. It's an intergroup study that suppresses ovaries during the period of chemotherapy and tries to address the exact question that we're talking about.

So the bottom line is we don't know the answer in any kind of clear fashion. There have been some studies that have been done. As Dr. Oktay pointed out, they've been poorly done, and they've been misinterpreted. And some people say, 'what's the harm?' Dr. Oktay is right, we don't know if there is any harm, especially in people who are hormone receptor positive. There is concern that slowing down hormone receptor positive cancer cells may make them less sensitive to chemotherapy.

We don't have great data for that with the use of Lupron, but we know that we don't like to give tamoxifen at the same time as chemotherapy because of a study that showed that administering them together is not quite as good as administering them sequentially. I don't think we know the true answer, and there is a randomized trial to address this question.

Although I take Dr. Oktay's information and his experience in this to heart in that I don't know if it's going to be effective. We all hope it's going to work but, from the biologic plausibility standpoint, it might not and there is harm. The other part of the potential harm is the symptoms.

As you're going through chemotherapy you probably know better than we do it's not pleasant to also be going through premature menopause, even if only temporary. I'll stop there.

KUTLUK OKTAY, MD: Let me add one thing, too. The other harm could be that if we think that this is reliable and don't do anything else to preserve fertility then eventually there could be an indirect harm, too. So if you're considering this there should also be a possibility of entertaining other approaches as well.

QUESTION 2: *I have a couple of different questions related to these topics. First of all, I had my ovarian reserve checked, and as I think it was Dr. Westphal who talked about the FSH levels. I was told that you would like to see the number be ten or less. My number was 15 after going through the chemotherapy Adriamycin and Taxotere two years ago for my breast cancer. How fast does that number rise or do we know? And what does a 15 really mean? Does it just mean that it's diminished ovarian reserve and that it will just be more difficult for me to get pregnant without other drugs? And between the tamoxifen and the letrozole that was mentioned by Dr. Oktay, what data or what information do you have as far as dosing to help produce more eggs in order to get pregnant?*

LYNN WESTPHAL, MD: How old did you say you were?

QUESTION 2, continued: *I was 30, so I didn't do any cryopreservation or freezing of eggs or tissue or any of that. I was aware of it but was told that because I was 30 the chance of getting my fertility back or gaining my cycles back, which I didn't realize that just menstruating ... I thought that that was enough. But now as I listen to this call obviously that's not the case. So now I'm 32. But at the time I was 30. I purposely did not take the Cytosan, because I had read that it was the most harmful to the ovaries. So I chose to go Adriamycin and Taxotere.*

LYNN WESTPHAL, MD: Well, the fact that your FSH is elevated does mean that there definitely are some changes in your ovaries and your ovaries are acting a little bit older than you. In terms of response to medication, we tend to see that when your FSH level is rising your response to medication is not going to be as good. But occasionally there are people with elevated FSH levels who respond much better than we expect. So your pregnancy rates are going to be lower than expected for your age, so I think you just have to work with the reproductive endocrinologist and see how your ovaries actually function when they're stimulated.

QUESTION 2, continued: *So the tamoxifen ... because I had already tried Clomid but then got the vision side effects, I cannot continue to take that. So I'm wondering about the tamoxifen and the letrozole that was mentioned for helping fertility for short-term use.*

LYNN WESTPHAL, MD: I think you could try either one of them. Did you respond to the Clomid?

QUESTION 2, continued: *I don't know because after two days of taking it I had the side effects and I had to stop.*

LYNN WESTPHAL, MD: Oh, you just stopped it. So I think hopefully you would do better on either the tamoxifen or the letrozole, and I think you just need to see how your ovaries respond when you take the medication. And obviously you've had everything else evaluated to make sure that your tubes are open? ...

QUESTION 2, continued: *Yes. Everything. Yes, that was fine.*

KUTLUK OKTAY, MD: Can I take a stab as well? Now, you said that your level was 15. That was two years after completion of chemotherapy? And we have to also know the exchange rates when you're talking about your FSH levels, because in certain labs the upper limits are

higher. So you actually know that this test that you had done was at a commercial laboratory and the level that you had was told to be high?

QUESTION 2, continued: *Yes.*

KUTLUK OKTAY, MD: In general if your FSH level is significantly over the upper limit the pregnancy success rates, regardless of the treatment, is pretty low. However, if you have to undergo stimulation, what we found is that letrozole in your situation might be better. In terms of having side effects, clomid and tamoxifen are very similar. So letrozole might be a better choice. But if your FSH ... and you have repeated those levels and they remain the same, is that correct?

QUESTION 2, continued: *I had it done only once, and they called it the Clomid challenge test.*

KUTLUK OKTAY, MD: I see. You may want to repeat that to make sure there wasn't a lab error, but if that's the case the odds may still be low. But at the same time I'm a little surprised that you had this outcome without Cytosan, and I wonder if you have any family history of early menopause. It could be beyond that as well because you didn't use Cytosan.

QUESTION 2, continued: *Yeah, that was surprising. As far as the number 15, though, how high is that? I mean, obviously less than ten. But I was told that someone in menopause would be at like 100.*

KUTLUK OKTAY, MD: Well, the assays vary but usually it's about 30. And the number people in general use around 12 or so. If it's above that that means your reserve is diminished and that your likelihood of pregnancy is very low. So you're not in menopause but your reserve is severely diminished, that's what it means. Thank you.

QUESTION 3: *I'm a two-year survivor of an estrogen positive breast cancer. My husband and I are wondering ... we would like to have another child. And we are debating because some of our oncologists say that if you have those increased levels of estrogen it could cause a recurrence, but from what I hear you guys saying you're saying in general that you haven't seen a difference. Is that the case or what ... do I need to do more research?*

ANN H. PARTRIDGE, MD, MPH: As a medical oncologist, obviously this is a choice but in terms of treatment we typically recommend the best breast cancer care based on trials that have shown efficacy. Some of this depends on how risky your disease was and whether or not the benefits are worth it, but we generally recommend that people get their full course of adjuvant hormonal therapy and often that...

QUESTION 3, continued: *I did not go through chemo; I did not go through radiation. And they felt that we caught it so early, I had a three-millimeter invasive. It was very small, so I didn't have to go through any therapy. That almost scares me more that I didn't go through chemo or something to get all of the cancer.*

ANN H. PARTRIDGE, MD, MPH: So in general, just for everybody else listening, we generally recommend that you finish your adjuvant therapy, including hormonal therapy, which as you know lasts between two to five years, as Dr. Westphal said. We try to negotiate, realizing that you want to have what you want in life, and as all of the reproductive endocrinologists are saying, your fertility is diminishing with age and then we've piled all these treatments onto you. Especially if you haven't done anything beforehand, to find that balance for some women it means coming off tamoxifen early and saying, 'well, it's not really worth that extra benefit, because I really want to try and have a child.'

Trying to figure out how fertile a person is after treatment is important. Because if you're going to come off a treatment that may help you, you want to know that it's probably going to be likely

that you can get pregnant. That being said, we generally recommend for anybody who's had a breast cancer, even someone with a tiny breast cancer that didn't need much adjuvant therapy or any adjuvant therapy, that you wait at least two to three years, because that's the period of time during which you have the highest risk of recurrence.

The vast majority of cancers, if they're going to recur, recur within the first five years. But the most aggressive ones tend to recur within the first two to three years. So at a minimum we want people to wait two to three years. That being said, all of the studies that have ever looked at it, as Dr. Westphal alluded to, have never shown a decrement in terms of risk of recurrence for women who go on to get pregnant versus those who don't.

QUESTION 3, continued: *Even with an estrogen positive?*

ANN H. PARTRIDGE, MD, MPH: Even with estrogen positive. Even when stacking the deck. One of the ones that was done through the IBCSG, the International Breast Cancer Study Group, and published a couple of years ago in JCO, that even stacked that deck and took more favorable cancers in women who had not had a pregnancy and compared them to less favorable cancers in terms of stage, grade. If anything they stacked the deck to make pregnancy after breast cancer look bad. And in the end it looked like there was no effect on survival in any kind of negative way. In fact, it showed actually a benefit. There were fewer recurrences in the people that had pregnancies.

Now, I don't go around telling people, 'go get pregnant, you'll do better from the breast cancer standpoint.' But that is a fact from that study and several other studies, and I think something that's not talked about much, but it has definitely been seen in several studies. There is a big important caveat here. There is something called the healthy mother bias, that women who are able to survive to go on to have a pregnancy are healthier. Obviously they're alive and able to

get pregnant. And that may be something that we just don't understand also about the biology of those women. But if anything the data of women who go on to get pregnant look a little better.

QUESTION 4: *So my question is about the five years being on tamoxifen. I'm 37 years old and I'm currently going through chemotherapy. And at the end of surgery and radiation I am supposed to go onto tamoxifen for five years. So at 37, five years of tamoxifen puts me into my 40s, and I'm wondering what your recommendation is about the idea of fewer years on tamoxifen.*

ANN H. PARTRIDGE, MD, MPH: From my standpoint as a medical oncologist that's something I would discuss with your doctors. If you're someone who has high enough risk that they're recommending chemotherapy, then I would think very hard about not coming off it early. But that's really a personal decision, a medical decision, and I would have to know all of the intricacies of your tumor, your risk and things like that. But in general, I think if you have high enough risk of the cancer recurring to have warranted chemotherapy, I would think hard and discuss it with your doctors. Maybe see where you are in a couple of years. See how you tolerate it rather than making plans right now for three years from now or two years from now. What does anybody else think?

KUTLUK OKTAY, MD: We're just reproductive endocrinologists here. (Laughter)

LYNN WESTPHAL, MD: Well, those are always hard decisions to make. And obviously that's a personal decision that you do need to make with your oncologist. There are women who are willing to maybe do the trade-off of not knowing and possibly having a slightly higher risk of a recurrence if they stop earlier, but if having a pregnancy is more important to them and they're willing to take that risk, I have seen patients who have decided that in their situation that was the right thing for them. But again, everyone looks at this decision in a different way.

QUESTION 5: *I heard you speak, and another caller had alluded to this, too, about regaining your periods and having that not necessarily be an indication that your fertility has resumed. I just was wondering if you could elaborate on that.*

LYNN WESTPHAL, MD: Well, we know that fertility declines as we get older. And there are women who are 50 years old who are having regular cycles, but it doesn't mean that they're fertile. So just because you're having regular cycles doesn't mean that your eggs are good quality or that they're good enough to produce a healthy pregnancy. So there's a spectrum between going into menopause and infertility. So infertility may just be the beginning of the spectrum. Unfortunately just having cycles does not mean that your ovaries are producing normal eggs.

QUESTION 6: *The first caller had the exact same question as I said, but I'm going to rephrase mine a little bit. I have also been recommended Lupron. I am estrogen negative, 33, desperately want to have kids some day in the future. But I just had a concern about my health more than anything else. Even though I'm estrogen negative is it okay for me to just put my ovaries in a frenzy, basically to overstimulate me for a few weeks right before I start chemo and then potentially ... now I'm going to have huge second thoughts about doing Lupron. But the concern from my oncologist was if I'm doing Lupron, which then shuts my ovaries down after it's been super hyperstimulated, if any of that would cause any physiologic problems for me or lessen the effect of chemo, because I would start chemo basically right after the egg retrieval process.*

ANN H. PARTRIDGE, MD, MPH: So you're having eggs retrieved?

QUESTION 6, continued: *No. Well, embryos. Eggs retrieved for freezing of embryos.*

ANN H. PARTRIDGE, MD, MPH: So you guys could comment on the need for that and stimulating the ovaries. I think you need that. But if you're ER negative I'm not worried about

the hormones doing anything in terms of your breast cancer. I'm not worried about there being any decrement in terms of how you do because your cancer is not at this point driven by estrogen. So I wouldn't worry about it from that standpoint. From a physiological standpoint we know that long-term deprivation of estrogen prematurely puts you at risk for bone mineral density loss and a collection of other things ... like we know heart disease ... way down the line. And there are other things that people are concerned about. And, I think less data. Maybe the reproductive endocrinologists could comment on it. But from a breast cancer standpoint I'm not worried about it. It sounds like if you're trying to preserve your fertility then I think it's probably the best way to do it.

KUTLUK OKTAY, MD: This is this issue that ... I was always concerned. Now, with what we call estrogen receptor negative patients we're talking about a percentage of cells. If they have less than a certain percentage we call them negative. Maybe that's not significant with the normal levels of estrogen, but our concern has been if you do stimulation and the levels are now ten times higher, would now those low levels of receptors be significant?

ANN H. PARTRIDGE, MD, MPH: Well, I think that what you call negative ... we only call something negative if it truly doesn't have hormone receptors on it. And zero to ten percent we call low positive. And ten percent or greater we call positive. So I think if you truly have no hormone receptors on your tumor, which many people do that are ER negative, we consider that ER negative. I agree that if someone is low positive or positive I think that does raise concerns.

QUESTION 6, continued: *I actually don't know that distinction. It might be on my pathology report, but I do know that my oncologist was a little bit concerned, like the doctor was saying. Because even though I'm negative I think he might be thinking what the doctor is thinking, that there is still a chance. He wasn't thrilled about it but he was okay with me doing the drugs.*

ANN H. PARTRIDGE, MD, MPH: I tell all of my patients not to go back on birth control pills, even though some of them are hormone receptor negatives. We know that estrogen may have had something to do with their original cancer. We know that taking out ovaries in women with BRCA1 mutations, the breast cancer predisposing genes, that those women are much more likely to get hormone receptor negative cancers. But go figure. Taking out ovaries seems to prevent their cancers. So we know estrogen probably has an effect even on ER negative cancers when they're being formed at some point along the way. But we also know in people with truly ER negative cancers, treatments like tamoxifen or other hormonal treatments don't help them. So it doesn't appear that the estrogen drives those cancers anymore. Does that make sense?

KUTLUK OKTAY, MD: Yeah, it makes sense. But there's one point I want to make, though. When you have the cancer, you perhaps have a larger mass of eggs that can be subjected to treatment versus after undergoing chemotherapy and surgery. You can tell us if I'm wrong here ... when a woman is receiving tamoxifen and is receptor negative the effect may not be apparent. But I wonder if the patient still has the disease, and if we do this would the amount of negligible risk become more significant? If the patients come to us with receptor negative cancer, in most of these we see that there is always a percentage point of receptors in these reports. So, we recommend stimulation using either tamoxifen or letrozole. With letrozole stimulation, we can shut down the estrogen levels to almost normal levels. So I personally prefer to do stimulation with one of these drugs in any breast cancer patient.

ANN H. PARTRIDGE, MD, MPH: I think there's no harm in doing it. I'm just telling you that I don't think there's great harm if you weren't using that in the hormone receptor negatives. There may be some harm in some individuals but I doubt there is much in a truly ER negative patient. But I don't think there's harm in using it as long as it works, right? It still works as well for you, doesn't it?

KUTLUK OKTAY, MD: Yes. I mean, with the letrozole we find results that are quite similar to those with standard stimulation protocols.

QUESTION 6, continued: *So is letrozole an alternative to Lupron for shutting down the ovarian reserve during chemo?*

LYNN WESTPHAL, MD: No.

QUESTION 6, continued: *What is letrozole?*

KUTLUK OKTAY, MD: It depends on what you're talking about. If you're talking about whether you would use letrozole to shut down your ovaries to protect against chemo, no. The answer is no. And the answer to your medical treatment, Ann can comment on that.

ANN H. PARTRIDGE, MD, MPH: In general, the aromatase inhibitors have not been tested enough in pre-menopausal women. There are currently available studies looking at whether or not they are better than tamoxifen. But when you give an aromatase inhibitor to a younger woman, you have to also shut the ovaries down with either medication, radiation or oophorectomy, because the purpose in treatment with the aromatase inhibitors is to suppress estrogen. In premenopausal women you don't suppress enough when you're treating. You need to also suppress the ovaries because that's where the bulk of the estrogen is coming from in a premenopausal woman.

KUTLUK OKTAY, MD: I think you also asked what an aromatase inhibitor is. Aromatase is an enzyme, the factory that makes estrogen. And so you shut down that factory and the body cannot make estrogen. And the main source of that factory in non-menopausal women is the ovary. Most of that estrogen factory is in the ovary. You can shut it down by up to 90 percent. However, you can't shut it down enough to have no estrogen. But for our purposes, when we do

stimulation we want to get ten eggs. Ten eggs mean ten times the amount of estrogen. If we can shut down the estrogen we will get ten eggs but hormone levels will be consistent with getting one egg, which is like the natural cycle. That's the idea behind using letrozole as an ovarian stimulant.

QUESTION 7: *I'm thirty-six years old, diagnosed with a hormone receptive breast cancer. And I've never been pregnant before. So before chemo my husband and I opted to have embryo cryopreservation. Now, I may have to go on a five-year tamoxifen regimen, but that will mean waiting until I'm 40 to be pregnant the first time. Is it an alternative to have my ovaries removed after my chemo and radiation and to the transfer right after? Instead of waiting for five years and having to go through tamoxifen regimen.*

ANN H. PARTRIDGE, MD, MPH: So in terms of your treatment? The short answer is no. The long answer is that right now ... this is complicated. But in general the treatment for breast cancer beyond chemotherapy in women with hormone receptor positive cancers is tamoxifen. And ovarian suppression has never been shown to be equivalent to tamoxifen. We know that ovarian suppression is equivalent to chemotherapy in some studies. But we don't know that it's equivalent to tamoxifen or that it can replace tamoxifen, plus you would want to ... it's the duration also.

So the studies that have shown a benefit to ovarian suppression or have looked at ... actually there is no evidence of ovarian suppression being as good as tamoxifen. That's the bottom line. There are ongoing studies right now that are looking at whether ovarian suppression adds to tamoxifen. But tamoxifen, at least in this country, is the standard of care. Since we know that chemotherapy is equivalent to ovarian suppression in patients with hormone receptor positive cancers, and we know that tamoxifen is better than chemotherapy in terms of the absolute risk reduction, meaning you get more bang from your buck with tamoxifen, people have been reluctant to do replace tamoxifen. It's generally such an important risk reduction drug. That

being said I think again it's something you should really talk to your doctors about, and everybody is different. And when you hear about the risks and the benefits pertinent to your particular situation you can kind of figure out what works for you.

QUESTION 8: *I was diagnosed two years ago with a HER-2 positive tumor of two centimeters and one lymph node positive. And nobody ever really speaks about HER-2 positivity and pregnancy. And perhaps that's because we're sort of a smaller population. But I'm wondering if any of you can speak to that particular population that I belong to.*

ANN H. PARTRIDGE, MD, MPH: I don't think we know anything about HER-2 positivity and pregnancy, except that we know that it's not a very common thing to have ... when women who get breast cancer while they're pregnant who are diagnosed while pregnant they don't tend to have HER-2 positive tumors. But I don't think it's ever really been looked at. HER-2 neu is such a new marker on cancers in the last five to seven years. And the data on pregnancies is so much older and takes so long to mature that I think it will be several years if not decades before we have information on HER-2 positive cancers and risks of recurrence and things like that. So I'm sorry but I've never even seen anything written about that, except that I think it's less frequent in women diagnosed during pregnancy.

QUESTION 8, continued: *I was diagnosed right after pregnancy. I had one child.*

ANN H. PARTRIDGE, MD, MPH: I think it's less common from what I've seen, although I have a number of patients like you.

QUESTION 9: *My question is similar to a question that was already asked about pregnancy, the increased risk for recurrence. I was actually diagnosed while I was pregnant. Do you think that there is an increased risk for recurrence due to the fact that I was diagnosed while*

pregnant? If I got pregnant again would there be a higher risk of recurrence or anything like that?

ANN H. PARTRIDGE, MD, MPH: I think that there's no evidence that there is an increased risk, despite trying to look.

QUESTION 9, continued: *Would you say that it's the same as the answer you gave before pretty much?*

ANN H. PARTRIDGE, MD, MPH: Right. But I think while there's no evidence we're all a little wary and cautious. I might worry a little bit more about someone who was diagnosed during pregnancy for emotional reasons more than science. But that being said you have to kind of take all that with a grain of salt. I would really want someone diagnosed during pregnancy to get the full five years of tamoxifen or to wait several years to get pregnant if they had a hormone receptor positive cancer,

QUESTION 9, continued: *I actually needed to stop tamoxifen at three and a half years because it caused a lot of cysts on my ovaries that they were worried about.*

ANN H. PARTRIDGE, MD, MPH: So I think again it's just something to talk about with your doctor. Despite looking, there is no evidence of any kind of decrement to having another baby, although there is not enough evidence out there. There are some ongoing studies looking at it but they are not available for us right now.

QUESTION 9, continued: *I don't want to come back to the whole letrozole thing again, but if I'm understanding correctly, is it something that stimulates the ovary so that you would be able to get pregnant on your own? In other words, I had that FSH test that you talked about. My test came like as a 45. But I've actually had my period for six months since then. So you*

gave me some new information as far as the fact that I'm getting my period but my FSH is really high. So would there be danger in me doing something to stimulate my ovaries so that I could get pregnant again? Is that another thing that ... I did have the hormone receptor positive breast cancer. So would that cause a problem doing something like that? And is letrozole the thing? Because I'm still a little confused. I don't mean to bring it back to that conversation again, but...

KUTLUK OKTAY, MD: What letrozole does is that it shuts down the factory in your body that makes estrogen. Your brain senses this and then starts sending signals to your ovaries in the form of follicle stimulating hormone, forcing your ovary to make extra eggs, thinking that there is not enough estrogen, because eggs are the source of estrogen or the cells that harbor those eggs. As a result it causes the ovary to work harder and produces extra eggs. But that's only if the ovary has those reserve eggs.

Now, if your ovary is now past the point that it doesn't have enough eggs, which is signaled by high FSH levels, then regardless of what kind of treatment you receive it's not going to have much effect. As a matter of fact your body is already trying hard to send signals to your ovaries, that's why your FSH is high; 45 is twice, maybe three times higher than the level we would get if we were to give you fertility drugs. So your body is already working hard. Unfortunately these treatments are not going to help if a certain threshold is passed.

And in terms of ... I just want to add to Dr. Partridge's comment. I think there was a study that initially said that if you're diagnosed with breast cancer during pregnancy, those tumors are more aggressive. But then when they compared the prognosis to women with similar stages who were diagnosed without the pregnancy, they found that and in general the explanation was that because breast cancer during pregnancy is often overlooked, these cancers are found at a later stage. So as Dr. Partridge said, there's no evidence that pregnancy itself makes the cancer worse.

QUESTION 10: *I think Dr. Oktay just addressed part of it, but I'm still a little confused. If my cycle doesn't return within six to 12 months is there something that I should be trying sooner rather than later? In other words, would you consider using either tamoxifen or letrozole and is there an ideal window of opportunity that if you don't use it within a certain time you miss it?*

KUTLUK OKTAY, MD: Well, I suppose you addressed that question to me. First of all, are you under any other treatment after your breast cancer?

QUESTION 10, continued: *Yes. Chemo. And the chemo was finished.*

KUTLUK OKTAY, MD: It was finished but were you estrogen receptor positive?

QUESTION 10, continued: *No, estrogen negative.*

KUTLUK OKTAY, MD: I see. I think the first thing that you will have to discuss with your oncologist is whether they would agree with you undergoing ovarian stimulation to get pregnant if you have resumed your menstruation and have normal reserve, or to at least freeze embryos or oocytes for future use before aging takes its effect. Having said that, we don't want to stimulate anybody until at least six months have passed since chemotherapy, because there may be damaged eggs sitting around. Now, the risk of having a genetically abnormal child is not increased in women who receive chemotherapy. However, there are some laboratory studies in animals that suggest that if you do get pregnant immediately afterwards, because there are those eggs that have been damaged genetically by chemotherapy, and the body has yet to clear them, then there may be an increase in genetic abnormalities. So we recommend waiting at least six months. But your medical doctor's recommendation may be longer than that. But at least they may give you an option to undergo stimulation with letrozole or tamoxifen at least to preserve eggs or embryos.

QUESTION 10, continued: *And is there a difference between using letrozole or tamoxifen?*

KUTLUK OKTAY, MD: Well, we just did that study and what we found was that you tend to get a little bit of higher number of embryos and eggs if you use letrozole instead of tamoxifen. But in terms of cancer recurrence there doesn't seem to be any difference. This is the short-term follow-up. So we tend to favor letrozole over tamoxifen currently.

QUESTION 11: *Hi. I was diagnosed at 35. The tumor was 2.2, just a trace in the sentinel lymph node. I went through Adriamycin, Cytoxan as well as Taxol. I've been on Arimidex/Zoladex for one year. And you haven't talked a whole lot about aromatase inhibitors. I've written down as much I could. You call it an enzyme shutdown, the production of the enzyme. And could you just elaborate a little bit on aromatase inhibitors? And I know I'm probably an odd duck out there. But it seems like I think that Arimidex and Zoladex are kind of a new thing. How long has it been out there? Give me some history.*

ANN H. PARTRIDGE, MD, MPH: That's something that we're actually studying right now. And I'm not sure why your doctor didn't put you on tamoxifen rather than...

QUESTION 11, continued: *Oh, I was on tamoxifen for two months. I'm ER/PR positive. And they found out that after one year tamoxifen probably wouldn't give me much benefit. And I wasn't tolerating it well. I mean, I was (Overlap).*

ANN H. PARTRIDGE, MD, MPH: It didn't give you benefit ... how do you know?

QUESTION 11, continued: *It was after a year. It just came out, I think, in January of last year.*

ANN H. PARTRIDGE, MD, MPH: You're talking about a study that came out that changed ... So I think you have to be really careful about interpreting the literature. I think that we're seeing a lot of this in the country. At the present time the use of aromatase inhibitors in younger women, in premenopausal women, has really not been studied very well. It's being studied right now. And so we do it sometimes, of course with Lupron, as we've talked about, unless someone is made postmenopausal in another way like surgery or radiation.

We do it when we don't have another choice. In general the choice, the standard of care is tamoxifen. But sometimes people don't tolerate it so we switch. But from a benefit/risk standpoint I wouldn't personally recommend an aromatase inhibitor for a younger woman outside of a clinical trial right now if I had tamoxifen as a choice. Because there is at the present time no evidence, let alone evidence of improved benefit, for younger women.

QUESTION 12: *I'm 37 with an ER negative tumor and eight months post-chemo. We did freeze embryos and saved six before my chemo started. What is the success rate that you see with post-chemo women? Is it any different from women who haven't had chemo in terms of implantation? And would it be any different with a surrogate?*

KUTLUK OKTAY, MD: Studies have shown that chemotherapy does not affect the functionality of the uterus, but radiation does. As Dr. Partridge pointed out, you don't generally get radiation to your ovaries with breast cancer, even if you had local radiation. And so there is no reason to think that you should do better by having a surrogate just because of that.

LYNN WESTPHAL, MD: Yeah, the only situation where I think there is a benefit or people may consider using a gestational carrier is if their oncologist wants them to wait five years to get pregnant but they want to have a child sooner. They may use a gestational carrier in order to have their child sooner, or if for some reason they have some uterine abnormality or if there's something about their disease where their oncologist is worried about them getting pregnant.

QUESTION 12, continued: *Is the success of the implantation related to the age of the eggs or the age of the person at the time of implantation?*

LYNN WESTPHAL, MD: It's related to the age of the eggs. Unless something has happened with your uterus, your age is much less significant.

QUESTION 12, continued: *And one more follow-up. I've been told I should have my ovaries out for various reasons, and I've been told that I could implant without ovaries.*

LYNN WESTPHAL, MD: Yes, that's absolutely true. You could have your ovaries removed. There are women who don't have ovaries for various reasons who get pregnant using egg donors. So you do not need to have ovaries in order to get pregnant.

LINDSAY NOHR BECK: We have time for one more question.

QUESTION 13: *I am nine years out of chemo and I was ER negative. I've had two kids since without any kind of medications or drugs. I got blessed. I'm going through some weird menstrual things, and I don't know if they're all ... am I getting menopause early? I don't know what is going on and it's kind of a little scary. And my OB-GYN doesn't know what's going on either.*

LYNN WESTPHAL, MD: What's going on with your ...

QUESTION 13, continued: *Well, I'm not ... my period comes whenever it wants to. Whereas it didn't do that before. It lasts anywhere from three days to 15 days. And sometimes it's heavy and sometimes it's light. And it's just ... there's no rhyme or reason to any of it.*

LYNN WESTPHAL, MD: Well, it's possible that you are perimenopausal, because you can see some bleeding abnormalities. But you probably should have some other evaluation depending on your situation. Sometimes people will recommend doing a biopsy of your endometrium. You may want to have an ultrasound to see if there's something else that could be causing your bleeding to last longer, to be so abnormal. Sometimes there are other things in the uterus that can cause abnormal bleeding. So there probably are a few other things that your gynecologist could check. And they could check also to see what your FSH level is ... if your FSH level is high then you probably are in this perimenopausal state.

QUESTION 13, continued: *Last October, October two years ago, it was really crazy. And we went in and she took out one of my fallopian tubes and one of my ovaries. And she said she just didn't like the look of them. And then ever since them my periods are just kind of really crazy. And I don't know if that has anything to do with it or not.*

LYNN WESTPHAL, MD: Why did she take out your ovary?

QUESTION 13, continued: *She didn't like the way it looked.*

LYNN WESTPHAL, MD: But she did the surgery because you were having abnormal bleeding? So it was abnormal before the surgery and then became more abnormal.

QUESTION 13, continued: *Yeah, and I did Cytoxan, Adriamycin and 5-FU. And I have not been on any kind of hormone replacement, anything at all.*

LYNN WESTPHAL, MD: Well, I mean, I think there probably are a few other tests to think about doing, and checking your FSH level, also checking your thyroid and prolactin to see if there are any other explanations for this abnormal bleeding.

LINDSAY NOHR BECK: That was our last question. I would like to thank everyone for their enthusiasm and questions that have contributed to make this teleconference a great success. We hope you found it helpful and that your questions were answered. Again, if you have more questions or if you were not able to ask your question tonight please send them to the Young Survival Coalition at the e-mail address info@youngsurvival.org and we will try to have them answered. Fertile Hope and the Young Survival Coalition are here to provide you with the information you need as young women with breast cancer and to serve as a point of contact for you. If you're already on our mailing lists you will continue to receive information about upcoming programs or newsletters and announcements that affect you as a young woman. If you are not on our mailing lists please visit the Young Survival Coalition's web site at www.youngsurvival.org or the Fertile Hope web site at www.fertilehope.org to register.

That concludes our program for this evening. Again, I would like to thank our presenters, Doctors Kutluk Oktay, Ann Partridge and Lynn Westphal for joining us and offering their knowledge, time and experience. We couldn't have had this teleconference without the help of the Susan G. Komen Breast Cancer Foundation and the Lance Armstrong Foundation. And a thank you to CancerCare, Sharsheret and FORCE to help you all know that this call existed tonight. I would also like to thank our operator, Matt. A transcript of this call will be available in three weeks and will be posted on the Young Survival Coalition's web site as well as the Fertile Hope web site. Finally, thanks to all of you! We hope that you will join the YSC and Fertile Hope for future programming. Good night and be well.

(END OF TRANSCRIPT)