Recent Updates & Advances in the Field of Ovarian Cancer
With Dr. Lauren Carcas, Miami Cancer Institute

National Webinar Transcript

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Presented by:

SHARSHERET
The Jewish Breast & Ovarian Cancer Community

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Disclaimer: THE RECORDING OF THIS PROGRAM HAD A DELAYED START. THESE ARE THE OPENING REMARKS. INDICATION OF WHERE THE RECORDING BEGINS IS ON PAGE 3.

Melissa Rosen:

I want to thank everyone for joining Sharsheret this evening, for a timely and important conversation about recent updates and advances in the field of ovarian cancer. As most of you are aware, September is Ovarian Cancer Awareness Month. Each fall, we have become accustomed to seeing pink everywhere, as the world raises awareness about breast cancer. This month, we promote teal! Ovarian cancer is sometimes known as a silent disease. With symptoms that mimic many common conditions, it is often not diagnosed until the cancer is advanced. So in September let's work together to raise awareness about the signs and the symptoms and about being proactive about risk reduction when it comes to ovarian cancer.

Melissa Rosen:

Before we begin, I do have a few housekeeping items to share.
First, I would like to thank our sponsors for today's ovarian cancer webinar.

- The Basser Center for BRCA
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- and the Miami Cancer Institute

And actually, this evening's program is happening in collaboration with the annual Sharsheret Summit. I will share additional information about the Summit later this evening.

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And I want to thank our program partners for collaborating with Sharsheret to enhance support and education for all those impacted ovarian cancer.

- The Amy Krouse Rosenthal Foundation
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Melissa Rosen:

The webinar is being recorded and will be posted on Sharsheret's website along with a transcript. Participant faces and names will NOT be in the recording.

We received some great questions through the registration process…

(RECORDING BEGINS HERE)

Melissa Rosen:

...the registration process. [inaudible 00:00:03] the registration process, that I am sure that questions will arise during tonight's presentation. Please use the chat box and we will address them during the Q&A session at the end of the webinar. As a reminder, Sharsheret has been providing telehealth services to breast and ovarian cancer communities for over 20 years because cancer is so much more than a physical experience. In addition to our many formal programs to help women and their families navigate different aspects of the cancer experience, I want to remind you that our clinic or social workers are available for one on one support. They can answer questions, connect you to appropriate resources, allow you to vent on a difficult day and so much more. And as always our support services are 100% confidential and 100% free. As we move into the webinar itself, I also want to remind you that Sharsheret is a national, not for profit cancer support and education organization, and does not provide any medical advice or perform any medical procedures.

The information provided tonight by Sharsheret and by our guest doctor, they're not substitutes. It's not a substitute for medical advice or treatment for a specific medical condition. You should not use tonight's information to diagnose or treat your health issues. Always seek the advice of your physician or qualified healthcare provider with any questions regarding your specific medical condition. Before we get started with tonight's expert, we are so lucky to have our Sharsheret caller with us to share her experience. Lynette is from South Dakota, joining us from South Dakota tonight. And I wanted to say before we have you, thank you so much for being willing to share your story.

Lynette Melby:

Hi, I'm Lynette Melby. My journey started a little over 10 months ago, so I'll tell you my diagnosis story. But if I can leave you with any concept this evening, it's the importance of advocating for yourself. It possibly, and probably saved my life. I'm a practicing nurse practitioner, so I'm in the system. And boy, have I learned how difficult it is not only to advocate for yourself, but to get your provider to listen and believe sometimes. Mine started early on a Friday morning, last October, I went to the ED with some abdominal pain. The lovely PA there did labs, EKG, vitals. And she said, "No, Nope, you're good." And she said, "We've had a lot of gastritis going around." So I looked at her and said, "Ashley, we're in a small town." I said, "I haven't been in this ED in 15 years, I'm not a hypochondriac." And she said, "I can do a scan if you want me to." And I said, "Yes, let's do that." So she did.

By Monday, I was in front of an oncologist and on Wednesday had surgery and they took out a football sized tumor. I have stage three A clear cell ovarian cancer. My life was possibly saved because I got that scan. She's a neighbor, she grew up with my daughter, they were in each other's weddings. I know that's why I got that scan. And it shouldn't be that way, but that's how it worked for me. When I look back, I see that I had about six years of various diagnoses that, of course all turned out to be the ovarian cancer. My PCP, when I told her that I just couldn't eat very much, my stomach was full, diagnosed me

with gastroparesis, which means your stomach isn't emptying and treated for that. Then they found a hiatal hernia, sent me to a gastroenterologist who did scopes and yep, over half of my stomach is up above my diaphragm.

Then I had an instance of incontinence that I'd never had before. And if I hear one more thing that says, well, at your age, I would urge all providers not to start out with, well, at your age. I'd never had incontinence before. I went to a urogynecologist and she said it was a mystery, then I got acne. So I'm sitting in front of my dermatologist and I said, "I'm 71 years old, I've never had acne." And so she treats me for acne. And my PCP had also made an appointment for me to see a surgeon for the big lump above my belly button that she was sure was a hernia. Well, of course, that was all that football size tumor. It was pressing down on the bladder, pressing on the stomach, pushing my stomach up, causing most of this.

So I had six rounds of chemo that went great, that I started an oral chemo that I have to be honest is more difficult than the infusion chemo. Because I know how to research, did my own research and knew that the medication I was going on, that you should have labs once a week for the first month. And my oncologist said, "I'll see in a month." then I said, "Well, don't we need to do these labs?" And he said, "Your numbers are strong. They've always been strong, you're okay." Well, by day 10, I had a pretty severe side effect of some bleeding, some spontaneous bleeding. But day 10 was on a weekend and I'm in the system, so I work in the system so I didn't call in on a weekend. Called in on day 12, later found out that the message was never relayed to my oncologist. I was told that this was to be expected on this drug, so I waited my month.

And by the time I came back in one month, they almost hospitalized me. My blood work was so bad. So I've had success advocating for myself and then not success. But I guess what I'd leave you with is maybe a little bit on how to advocate. I would encourage you not to be that patient who is always complaining many and most side effects will ease after a couple of days. If something's intolerable or whatever, then of course you have to call in. But otherwise I'd say give it a chance. Many people feel that the squeaky wheel gets the grease. And in these situations, a lot of times the squeaky wheel just isn't heard any longer, yet they're always complaining. It's okay to do your own research. I do a lot of mine, but don't depend on Dr. Google and don't depend on commercial sites. Make sure you're doing Mayo clinic, Johns Hopkins, national institutes of health, Cleveland clinic.

And then if you do have a question, providers and people in the offices are... Most people will help you if you ask for help. And a good way to do it rather than challenging the person is to say, "Could you help me? I'm trying to understand this." And let them explain to you. They don't know your questions if you don't tell them your questions. And then the other things would be that, just remember that we're all human, be kind. These medical offices are so understaffed and so overworked and those folks have bad days too. And I would say, and let me apologize to our doctor here, I would say that just remember most of that patient care is done by your nurses, your techs, your aids, your front office, people, et cetera. And just be cognizant of that and be kind to them. That's what I have to say.

Melissa Rosen:

Thank you so much. Thank you. And you know what struck me is all of the smaller diagnoses you had leading up. We talk about how ovarian cancer frustratingly, the symptoms are similar to so many symptoms we, as women have anyway. Our stomachs are bothering us, whatever it is. So that's something definitely to keep in mind. Thank you so much for sharing your story. We are so very fortunate to have our doctor here with us today. Dr. Lauren Carcas is a medical oncologist who serves as a patient's primary cancer care physician. Diagnosing and staging the disease as well as treating it using

chemotherapy, hormonal therapy, biological therapy, and targeted therapies. She monitors the patient's progress, provides supportive care and coordinates treatments provided by other specialists. Dr. Carcas has conducted numerous clinical trials to improve care and outcomes for cancer patients. And she's published her clinical results in medical journals and presented at symposia. She is a member of several professional societies, including the American society for clinical oncology, sometimes known as ASCO, the American Society of Hematology and the American College of Physicians. Dr. Carcas the floor is yours.

Dr. Lauren Carcas:

Thank you. And I am just going to share my screen and that should do it. That should be showing everybody. And I just want to thank you again for the opportunity to be here and to speak with you. I will tell you that I don't disagree with what Lynette said. I would not be half of the caregiver I am for my patients without my team. It requires a team, but I also look at my job a little bit differently from some other doctors. I choose to see less patients so that I can spend more time with my patients. And I think that if you look around for the doctor that fits you, you should be able to find that doctor as long as you're not in a tiny, small town somewhere where there's only one, but you should be able to find that doctor.

I just want to start first by letting you know that I think that one of the best features of a physician is to be a good teacher. Because if you can teach a patient, if you can take the time to teach a patient, what they have, they're much more likely to be adherent with the therapy that's recommended because they're going to understand why it's being recommended. It took me years. I trained for four years of medical school, I did three years of internal medicine, I did a chief resident year, I did three more years of hematology oncology to be able to do what I do and to be able to recommend what I recommend. And it would be really absurd to think that a patient from the time they're diagnosed, from the time that they see me, which might be a week, might be two weeks, might be a month even, can gather all of that information and synthesize the information.

So I think that it's really important that we also, as physicians have patience with our patients. That when they come in with a spiral notebook with four pages of questions, it's because they want to be educated on their disease. So as they've said, I am a medical oncologist. I am not a surgical oncologist. I do not do the surgeries to debulk. In certain areas of the country and is becoming more and more this way, gynecologic oncologists are now doing the surgery and medical oncologists are doing the medical therapy because that medical therapy is changing and it's changing rapidly, which is a really good option for patients. I specialize in breast cancer and gynecologic malignancies, but because I have had a handful of patients with gene mutations, I have a large number of patients in my practice that are young and have hereditary predispositions.

Dr. Lauren Carcas:

So let's just start first with what is cancer? I think that this is just such a fundamental, a lot of people don't know. So every cell in our body has a job to do. And that little tiny cell goes, and it does its job and then it replicates itself and then it's programmed to die. But if for some reason that specific tiny cell loses its signal to die or becomes resistant to its signal to die, maybe it's a toxic insult, maybe it's a history of radiation. Maybe it's a hereditary gene mutation that leads to its resistance. To be able to receive that signal, that cancer cell or that cell then becomes immortal. And one immortal cell makes

two and two make four and four make eight. And as those cells continue to grow, it actually creates the tumor, which then over time is able to invade towards the lymphatics and spread to distance sites.

This is a schematic of that. What you can see is there is the cell mutation, the one cell that has some mutation that makes it resistant. It begins to overpopulate and multiply that's hyperplasia. But in doing so, the factory loses a little bit of its quality control. So now it's creating more dysfunctional cells and those dysfunctional cells turn into a cancer, but that cancer still is encapsulated, but eventually it's able to invade through that membrane of where those cells are allowed to be and hop into the lymphatics or hop into the blood flow to be able to spread to distance sites.

Ovarian cancer is a little bit different. When you think of breast cancer, breast cancer tends to spread very predictively. It goes from the breast to the lymph nodes of the armpit. Ovarian cancer also spreads through the lymphatics and through the blood system. But it also, I always tell my patients, it spreads through the abdomen like seeds of a dandelion. When you blow the dandelion and those seeds kind of get stuck all around the abdominal wall. It has a different type of seeding, not just that typical spread. But what exactly is ovarian cancer? It really is an umbrella term. It is diagnosing or categorizing a spectrum of disease that includes serious epithelial ovarian cancer, it includes fallopian tube cancer and primary peritoneal.

So the peritoneum is basically the lining of the entire abdominal cavity. And then you've got your fallopian tubes and your ovaries, which are self explanatory, but you can see the other names down below. Mucinous, low grade, endometrioid, clear cell, which we just heard about undifferentiated. That means that we don't really know what kind it is, but it's definitely of the ovary or it's from one of the sex organs. Borderline tumors, or those tumors that have low malignant potential, sarcomas, carcinoid, and metastatic tumors. So it is really that umbrella term for all of those. For ease, I'm going to say ovarian cancer, but it really refers to any of those. So let's keep looking at what ovarian cancer actually is. It's the second, most common gynecologic malignancy in the United States. But it is the most lethal gynecologic malignancy. 70% of patients present already with advanced disease. We consider advanced disease to be at least stage three and stage four. It could also be potentially those patients that are right at the border of stage two. But it's unusual and usually an incidental finding to find those early stage one patients.

Dr. Lauren Carcas:

So looking at the most recent statistics, this is the estimated new cases of ovarian cancer that will be diagnosed this year. It's just shy of 20,000. And unfortunately this next side is the estimated deaths from ovarian cancer this year, which is 12,800, just shy of 13,000. This next slide shows exactly those same two numbers, but it also shows you the incidence rate. The incidence rate is still, even though this is the most up to date data that you can get, it's still from 2014 to 18, it's about 10.7 women per 100,000. Death rates are 6.5 women per 100,000. So when you look at it that way, we know that 20,000 is a huge number. There are towns with less people. But when you're looking at it per 100,000, you're seeing that it's a less common tumor. So let's look at the ovarian cancer risk factors.

Remember this is knowledge is power. Age, we know that the risk for ovarian cancer increases with age. Half of ovarian cancers are diagnosed at ages greater than 63. Overweight, we know that if you're overweight, there is not necessarily a predisposition to developing ovarian cancer, but if you do get ovarian cancer, it does have a negative impact on survival. We have a hard time understanding why that is, but we know that it does exist. Late pregnancy or no pregnancy. Family history of ovarian cancer or other cancers. And having a family cancer syndrome. This is important, and we'll focus on this in a little bit more detail in future slides, but having a family cancer syndrome is a really important thing when

we're talking about ovarian cancer. Up to about 25% of ovarian cancers and this is probably at least 25% are hereditary. And I just listed a few of the genes that are associated with ovarian cancer.

We know it's BRCA1 and BRCA2. We also know that the genes that are associated with Lynch syndrome, which are MLH1, MSH2, MSH6, PMS2 and EPCAM are also higher risk genes that may have an increased association with ovarian. They also have increased risk for colon cancer and endometrial cancer and other malignancies. But since this discussion is really focusing on ovarian, I wanted to bring that to your attention. The MUTYH gene, which is also another polyposis gene or a colon cancer gene can have an association with increased risk for ovarian cancer, ATM, BRIP1, RAD51C, RAD51D and PALB2. And then finally, a history of breast cancer. We know that people who have a history of breast cancer have a slightly higher risk than the general population of developing ovarian cancer.

Dr. Lauren Carcas:

So what exactly is that risk? And this is what you'll see here. What you can see on this slide is that if a person has no family history of ovarian cancer, their lifetime risk of developing ovarian cancer is 1.5%. So that's basically the general population risk. If you have one first degree relative, a first degree relative is basically siblings, mother, or children. Your risk is up to 5%. If you have two first degree relatives, it increases to 7%. And if you have a hereditary ovarian cancer syndrome, on average, we quote 40%. But with BRCA1, BRCA2, that range can be 35 to 65%. So patients often ask me why the range? What does that mean? Well, it means that there is a range. If you have the gene, it does not mean you will develop ovarian cancer.

And it's very much dependent on if you have the gene and every woman in your family has had ovarian cancer, then your risk is going to be on the higher side of that range. We call this in the world of genetics, penetrance. How likely, which penetrance means, yes, I have the gene, but how likely is it to manifest what it does? And there's variable penetrance on all of these genes. So looking more at those risk factors, we know that there are potentially treatments that can decrease the risk of developing ovarian cancer. One of those is oral contraceptive pill use, we know that that can potentially reduce the risk. Pregnancy reduces the risk, tubal ligation can reduce the risk and breastfeeding can reduce the risk. Most of these, the oral contraceptive pill use, the pregnancy and the breastfeeding is really because that has a hormonal impact. It sends our body, our ovaries into a sleep mode of almost like menopause, where they're not as active and those cells are not dividing as rapidly. So that's potentially why that might happen.

Tubal ligation, I'm not sure, we can't tell you why that's potentially helpful. So I often have patients come in, obviously after they've been diagnosed, but they tell me, "I get my pap smear." But it's really important to know that pap smears are for cervical cancer. They do not detect ovarian cancer. They don't screen for ovarian cancer, they don't screen for endometrial cancer. Really, there is no effective cancer screening for ovarian cancer. We do, however, talk about the role of ultrasound and that's either a transabdominal where it's outside of your belly or a transvaginal where it actually goes through the vagina and looks from the inside where it's a little bit closer, particularly if you're a little bit heavier or have more belly fat, it's easier to see it in greater detail, as well as a tumor marker, which is a CA 125.

These are very limited. They've been used alone and in combination, and it's never been proven to detect ovarian cancer early. But I will tell you as a physician, it makes me feel better and it makes the patients feel better to at least try. Because possibly, you might find something or it might alert you to something. What I can tell you in dealing with a lot of patients who do have gene predispositions, but are not yet done with their family planning, if you're menstruating and you develop an ovarian cyst, your CA 125 can be elevated, which is a really uncomfortable thing to find. CA 125, in fact, tumor markers in general are not specific to cancer, they're actually inflammatory markers. So in treating breast cancer,

we check other tumor markers and I've had patients who have had a gastroenteritis that they ate something bad and they had food poisoning. And they came in two days later and their tumor markers were off the charts. And they came in the following week to recheck them and they were back to normal.

So they can increase with inflammation, but they can potentially also be a surrogate. But it should not be the only thing that we rely on because harms exist. When people have an elevated tumor marker, we have sometimes submitted or subjected people to laparoscopies to look and see what's going on. And they have a surgery with anesthesia and potential complications that really showed nothing because it was a false positive result. So what can we do? And this is where we need to become empowered. You need to know your personal and your family history. You need to update your knowledge. So first, let's talk about who should get genetic testing because that's one way that we can update our knowledge. And it's exciting to know that 10 years ago, genetic testing costs $4,000 for just BRCA1 and BRCA1. Now you can get a huge panel of genes, 90 plus genes, if you were cash pay for about $300. Insurance usually covers this on almost all patients, even when they don't meet full criteria.

So we recommend that all women with ovarian cancer get genetic testing. We also recommend all women with breast cancer get genetic testing. This is a little bit more controversial because insurances don't always want to test all breast cancer patients, but the American Society of Breast Surgeons recommends that all women get tested and we might be able to better understand the biology of that person's tumor if we know whether or not they have a gene predisposition. We also know that all Ashkenazi Jewish or Caribbean women should get tested. We know that there's a higher rate of gene predispositions among the Ashkenazi Jewish population, as well as Caribbean women. And I'm in south Florida, so that's a large chunk of our population. And then patients with a family history of breast and or ovarian or uterine or colon or pancreatic cancer.

Dr. Lauren Carcas:

But what else can you do? You should work with your OB/GYN to maintain an appropriate level of suspicion when potentially relevant signs and symptoms of ovarian cancer are present. We just heard from Lynette that, that's not easy because a lot of those symptoms do mimic things that are far more common. The number of women who develop acid reflux or early satiety is really, really high, especially with our diets, especially with the obesity epidemic in our country, there are so many reasons that these are hard to diagnose. But a lot of these Lynette did already touch on, the recommendation is if you have more than 12 days per month of new onset symptoms. So over the course of three to six months of increasing abdominal size. So patients always say, "Well, I just thought I was gaining weight." This is a very specific type of weight gain or growth. It's really your pants get tight in the belly, but not in the buns, not in the thighs, not anywhere else, your breasts, aren't getting bigger. It's a very specific centralized weight gain.

Bloating, and the bloating can lead to that early satiety. So difficulty eating and feeling full really quickly, pelvic or abdominal pain and urinary urgency or frequency. And like Lynette said, even incontinence can occur. So let's going back, what can we do? We already know all of the things that we've reviewed, but the most important thing you can do is to be your own advocate. Nobody knows you better than you. So be persistent. And I appreciate it when my tell my patients, tell me, "Listen, I've been feeling this, I'm nervous about it. I just need the study to know that I'm okay." Now insurance should never know that we order studies just for patient comfort, but we are doctors at the end of the day and the brain and the mind is part of your wellbeing. It's a cheap thing to do to make sure that we know that everything has been addressed and it's been addressed appropriately.

Dr. Lauren Carcas:

So, I've been diagnosed with ovarian cancer, now what?. So we know that first, anybody diagnosed obligatory should get genetic testing. This is going to be really important because BRCA1, BRCA2 mutations account for about 15% of all women with ovarian cancer. And then somewhere between three and 8% of ovarian cancer, patients have mutations in other high risk genes. And that's important because it could impact their treatment. The next thing that we always do, if it wasn't already done at diagnosis is we do staging. The staging is really important. What this tells us is, where has the disease gone? Is it widespread? Is it localized? And even scans, don't always tell us this. They can potentially tell us this, sometimes surgery needs to tell us this. But CT scans or an MRI or a PET scan, but sometimes even that laparoscopy, where they're going in and they're taking a little peak to see, is this person a candidate for surgery up front? Or do we need to treat them a little bit differently?

Dr. Lauren Carcas:

This next slide just shows you a little bit of a schematic of what the stages of ovarian cancer are. Stage one is where the two, the tumors or the tumor cells are localized to the ovaries. Stage two is when they have spread from the ovaries to other parts of the pelvis, so that might be the fallopian tubes or the uterus, but the disease is maintained in the pelvis. It's really as if there's an imaginary line drawn, and the disease is below that. Stage three means that those cells have spread outside of the pelvis, which is remember the belly and my simple mind, I think of the belly as like a fish bowl, a gold fish bowl. And basically if you're drawing the pelvis, you're drawing just above the rocks. But if you're talking about a stage three, it means that it's spread up to where the water line is. So it's still part of the same bowl, but a little bit further up. Stage four means that it has spread into the tissue of a distant organ. That might be the liver. It might be the lungs.

Dr. Lauren Carcas:

So what is the initial management? Typically, the initial management is what we call cytoreductive surgery or a debulking procedure. The intention of that is to remove all of the tumor down to less than one centimeter, because we know that, that's associated with the best overall survival. If a woman is at high risk of complication or a low likelihood, because there's too much tumor of removing it all to less than one centimeter, we actually recommend something called neoadjuvant chemotherapy. Basically what that means is, chemotherapy before surgery. That way it can reduce the tumor burden and make surgery more successful. It can also mean that your surgery is less invasive. Another thing that we always recommend is genomic testing on the tumor specimen that's removed during surgery. Genomic testing is actually genetic testing of the tumor, which can actually be predictive of whether or not there's a role for maintenance therapy.

Dr. Lauren Carcas:

So why do we do that? It may impact the postsurgical treatment. Should we add bevacizumab? Which is a medication. It's a monoclonal antibody that is given through the vein sometimes with chemotherapy, sometimes after chemotherapy with a PARP inhibitor. And what it actually does is one of the earliest things that a tumor cell does. Remember tumor cells are parasitic, they have to get their energy and their nutrients from us, from the host. So how do they do that? They release this hormone that allows them to make more blood vessels so that they can steal the nutrition from your blood. Bevacizumab, prevents them from being able to do that as easily. It might also impact whether or not a PARP inhibitor is offered in which PARP inhibitor is recommended.

So the traditional chemotherapy includes carboplatin paclitaxel, that's usually for six cycles. We sometimes add bevacizumab, if you got surgery up front on the later cycles, and that might continue for

maintenance therapy. But what about if you're not a candidate for surgery upfront? So, these pictures, I don't like a lot of surgical pictures, I'm not a surgeon. So I don't like a lot of surgical pictures, but I thought that this picture was really helpful because you can see on the left hand side, there's a lot of unusual looking structures. That's not what the inside of the body looks like. All of those little bubbly looking things are tumor. And sometimes if you give chemotherapy first, it really reduces that tumor burden and then you need a less radical surgery. You can see on the right, that's that same patient after chemotherapy and a lot of that tumor has been removed by chemotherapy, meaning that the surgery will be less effective.

Dr. Lauren Carcas:

One of the other treatment options that exist is something called HIPEC. This is not done everywhere because not all hospitals have the capability of doing it. My understanding is, the hospitals that have the capability also have to have bypass capability because it's a similar type team that would come in to make sure that this works. What HIPEC is, it's a hyperthermic intraperitoneal chemotherapy. So the surgeon basically fills the belly with saline, warmed saline. Chemotherapy is added into that, and it is circulated through the belly for up to an hour and a half. And that can reduce, it shows benefit in reducing the risk of recurrence. It is most often used after a patient has received neoadjuvant chemotherapy. So they get their three cycles of chemotherapy of the carboplatin and Taxol, they go onto the interval surgery. If the hospital has capability of HIPEC, they can do HIPEC during that time and then three cycles of chemotherapy after.

We know that despite our best efforts, ovarian cancer still carries a high risk of recurrent disease, but we have these newer maintenance therapy options that have reduced that risk. And those include bevacizumab and PARP inhibitors. I think PARP inhibitors are arguably one of the more exciting things that we have seen come out of BRCA mutations, whether it's inherited in the blood or if it's in the tumor itself. So let's talk about what a PARP inhibitor is. It's a poly ADP-ribose polymerase inhibitor. What do these things actually do? Most people know that double stranded DNA, that DNA that looks like that spiral staircase makes up all of our body. Every cell in our body has DNA. And on a routine basis, we develop breaks in that DNA. And we have these proteins that are great spell checkers, and they go fix those breaks.

BRCA1 and BRCA2 are genes that do that. They're excellent spell checkers. And a lot of the genes that are similar to BRCA do the same thing. They go and fix those DNA breaks in our normal cells. When it's deficient, when BRCA is mutated or deficient, then you can have these abnormal breaks in our normal cells. But our cancer cells don't have a good backup system to fix that. PARP, when BRCA is deficient is what the backup system is. It goes, and it fix one strand at a time. So inhibiting PARP in a tumor cell means that that tumor cell cannot fix its DNA and it has an increased risk of dying, it leads to cell death. And that's exactly the way that it works. It's hard to understand if you don't know science or you don't have a good science mind, I try to explain it the best that I can. But it's basically we inhibit the repair mechanisms on tumor cells. So there are currently three FDA approved PARP inhibitors, they're Olaparib, Rucaparib and Niraparib. And they're indicated in different ways and at different lines of therapy.

Dr. Lauren Carcas:

But I think it's important to understand what a gene mutation actually means. Before we jump into PARP, we need to know this little bit of vocab lesson. What is the difference between having a gene mutation that you inherit from mom and dad and the tumor, having a gene mutation? So we call germline mutations, mutations that we inherit from mom or dad. Our body is made up of those little

chromosomes, those little Xs. We get one side from mom, one side from dad. So if mom let's say, this is mom, mom has an X and one is broken, one doesn't work. There's a 50% chance that mom's child gets this gene, but there's also a 50% chance that mom's child gets this gene. That's why this is inherited in a 50/50 pattern, but it's directly from your DNA. Somatic mutations means that both genes are normal, both of the sides of the chromosomes are normal and they passed on the baby completely normal, but there was a mutation in one part of the baby. That it's hard to know what type. But this is usually the part that leads to cancer.

Because we often have BRCA mutations in the tumor, but not in the person. But this allows for treatment, regardless, we call those somatic mutations. We like to do tumor testing to see what those somatic mutations and honestly, that's the most exciting part of future cancer treatment is we will be able to target those, to be able to offer personalized medicine. So among those PARP inhibitors, this is talking about in recurrent or metastatic disease, they are all approved in different indications and some of those approvals are changing and coming back, and we can talk about it. I know that there was a question about leukemia with PARP inhibitors, and we can talk about that as well. But, PARP inhibitors have been approved in the metastatic setting or the recurrent setting for a long time. However, there is now first line maintenance setting. And what is that indicated for? For a long time in the breast cancer world, about 70% of breast cancers are driven by hormones. We have put women on a pill to block hormones for at least five years, sometimes up to 10 years.

And we've seen that it reduces the risk of cancer ever coming back in those women by at least 50%, if not more. And that's what we're trying to emulate. We're trying to see if we can do that in the ovarian cancer world. We know that if there is no BRCA mutation, either germline inherited by mom and dad or somatic in the tumor itself, Niraparib is approved. If there is a germline or somatic mutation, either BRCA1 or BRCA2 or one of the other genes that could potentially reduce DNA fixing, Olaparib or Niraparib can be used. But Olaparib with bevacizumab is used in those patients that do have that genomic instability, that inability to spell check. And we what's exciting with that combination for the people that qualify is their progression free survival. So that means, time from completing treatment to the time they have a recurrence is more than double that of people who do not have that maintenance therapy. 3.1 years is a huge, huge difference in ovarian cancer survival, because we know that there are high risks of disease recurrence.

Dr. Lauren Carcas:

A lot of people think that immunotherapy is the silver bullet of cancer treatment. And unfortunately that has not been proven in the ovarian cancer world. There is no clear role, there's a low predicted benefit, but it is indicated for any tumor. It doesn't matter if it's ovarian, it doesn't matter if it's skin, it doesn't matter if it's colon. Whatever type of tumor, if they have something that we call a high mutational burden, MSI high, which is micro-satellite instability, these are tests that we do on the actual tumor or mismatch repair deficient. For ovarian cancer, those are very rare findings for those tumors to have that type of a target. The response rate is low only about seven to 10%, but for that seven to 10% that respond, they can potentially respond for a good while. So it might be very helpful, but in a very small subset of women. The role of surgery, we know that there's that primary benefit of surgery upfront, that's very well established.

And despite the excellent response rates, we know that unfortunately, most of our patients with advanced disease will develop recurrent disease. So the question is, is there a role of cytoreduction in recurrent disease? And that's less clear. But what we know is secondary cytoreduction, which means interval surgery. So you treat with chemo first, the neoadjuvant chemo, then surgery, and then finish your chemo after, has really showed excellent results and it's been able to decrease the duration of

surgery and how invasive that surgery needs to be. So risk reduction. What can we do? What do we have control over? And this is a really important thing because when people are diagnosed with cancer and the majority of my patients will tell me this, is they feel like they have no control. And that's the hard part, cancer happens to you. But what can you do to happen to cancer? What can you potentially do to further reduce your risks of cancer recurrence?

Dr. Lauren Carcas:

Majority of this is lifestyle modifications. We know that diet can impact risk of recurrence. In general, higher sugar diets are a good, they set up a good [inaudible 00:44:08] for tumor growth in general. High alcohol consumption has been associated with cancer recurrence in all cancer recurrence, as well as tobacco use. We know that exercise is really healthy, it's super important. The more fit your body is, the more likely you are to do well with the treatments, or be able to stay on the treatments at a dose that is effective, as long as your body stays fit. We want you to avoid environmental toxins. That's alcohol, that's tobacco, that's drugs. Sleep, sleep is super important. I try to tell my kids this all the time, because they're in a big hurry to grow up, even though I'm not in a hurry for them to grow up. But I tell them you have to sleep. Our bodies heal and our bodies grow when we're sleeping. And if you've gotten chemotherapy, you're growing new cells, you need to repair your body. Your body needs rest.

Most people want to show that it's not getting them down, that treatment's not getting them down, that they're stronger than the treatment. And that's a really important mindset, but you also can't go about your life without any adjustment because your body doesn't have the time to repair. You need more time to repair before, during and after chemotherapy. Once you've recovered from chemotherapy, get back, do all of the things, run the marathons. But I think that it's important to give your body that rest. Stress reduction, this is so hard because cancer diagnosis is stressful, but stress reduction is really helpful. If you can find ways to reduce stress, whether it's, when friends want to help you friends always want to help. Tell them that instead of recommending that you take scorpion venom to help fight your cancer. Say, "What would really help me is if you hired somebody to come clean my house next Thursday. If you brought me meals on Wednesdays after chemotherapy."

If you tell your friends what to do, they will be so eternally grateful because they're really just looking at some way to help you, but that can reduce your stress also. And accept practical and emotional support. That's exactly what I'm saying. Let people help, but tell them what you want them to do to help. So let's look more at risk reduction. We know that in gene mutations, there is a clear role of removing the ovaries and the tubes. If you look at NCCN guidelines, which is where we get our guidelines for recommendations in cancer care for patients who have a BRCA1 or a BRCA mutation, it is not a consider, it is not a recommend or think of, it is a, you should have a prophylactic removal of your ovaries and your tubes when you are done having children. The timing of that is different. It's variable, it could be early if it was early in your family history that people were getting ovarian cancer. Sometimes it can be up to age 45.

Dr. Lauren Carcas:

So a prophylactic bilateral salpingo-oophorectomy, that's the surgery. Is recommended if a gene carrier with or without a family history of ovarian cancer. It's a very, very clear recommendation. Occult ovarian cancer, meaning undiagnosed ovarian cancer is found in about three and a half to 5% of patients as they're undergoing their prophylactic procedure. So I think that, that's an important tidbit of information. Fortunately, those are usually found early, right? Because those patients undergo imaging studies, they're on some type of screening. Even though we know screening is not highly effective, but this proves to you how it's not that effective. And that once you're done, it's a good consideration. I

think it's also really important that if a gynecologic oncology surgeon is available to you in your area, you should go to that type of surgeon. I am not poo pooing on any OB/GYNs, they do excellent work. They were trained to do what they do and a basic hysterectomy is great. And they can do that in people who are not at risk.

But when you have a risk of 3.5 to 5% of patients having incidental cancer at the time of their prophylactic surgery, you need a cancer specialist to be able to do the appropriate surgery. The lymph node samplings, the pelvic washings that are part of that prophylactic surgery. What about just removing the tubes? The benefits are still not yet proven. And the question also is, why would you consider just removing the tubes? Some people are fearful of an early menopause, and we know that there are harmful outcomes to early menopause. There's an increased risk of decreased bone density and changes to cardiovascular health. But hormone replacement therapy is generally safe after an early prophylactic menopause. And I think that, that's an important thing to know.

Dr. Lauren Carcas:

And in fact, there's actually a lot of a discussion right now in the breast cancer world that whether or not hormone replacement therapy is as big of a risk to breast cancer, as we thought it was, that's still evolving. We in general, don't recommend it to breast cancer patients, but for your young patients that are getting a prophylactic surgery, there's no reason that you need to be post-menopausal at age 35 if you can take hormone replacement therapy until an age of normal menopause. Survivorship care, it's important after a diagnosis of ovarian cancer, to follow up with the exams in the studies, get your other age appropriate screenings. For BRCA mutations in much of the other hereditary genes, that might include skin checks every six months. Also dilated eye exams, you can get melanoma in your eye and melanoma from your eye can spread to other parts of your body, really important.

Vaginal exams, you're going to your gynecologist, but if anybody ever went to a tanning bed, they're at risk for vaginal melanoma. So there're really important things that we need to be looking at that we don't always think of, we think breast cancer, ovarian cancer. Following the late and long term side effects of treatment. And this is where I wanted to talk about the leukemia for PARP inhibitors. It's a little bit confounding because we can't tell you for sure that it's from PARP inhibitors. We know that our chemotherapy drugs impact good and bad cells. We kill cancer cells with chemotherapy, but we damage good cells. Our bone marrow is highly impacted by chemotherapy. That's why our white blood cells drop low, you have an increased risk for infection because we're damaging bone marrow. But we do it at a cost of very low risk of future developing leukemia. One of the drugs that does that are the platinum agents. Carboplatin, which is a backbone in ovarian cancer treatment.

Dr. Lauren Carcas:

Parp inhibitors mimic the same function as carboplatin. So is there a potential increased risk of leukemia? Yes, there is a potential increased risk. But the risk of developing leukemia is significantly about, I would say 60 fold lower than the risk of developing recurrent disease. So just like anything in medicine, it's a risk benefit analysis. Unfortunately, almost any treatment we have has an adverse side effect. And then it's important to have a primary care doctor. I am the patient's cancer, primary doctor, but I have to tell you, it's been a long time since I have done appropriate cholesterol management, diabetes care. You need to make sure that you have somebody doing all of the other things, because if we've cured your ovarian cancer, we don't want you to have a bad outcome from something else that is more common in this world.

And seek mental health because it's really, really important to make sure that you're coping. So in conclusion, the best defense is a good offense. And it's really true. Talk about your history, cancer is not

taboo. Talk about it with your family. Be aware of your body, know how your body changes. If you feel something, think something, bring it to your doctor and if that doctor doesn't listen to you go to a different doctor. Because you deserve to be proven that it's nothing. I feel that when a patient comes to me and says, "Oh, I have this lump in my breast." I might think that it's just a cyst, but my eyes are not Superman eyes and I can do an ultrasound to look at it. And then I can prove to the patient that it's not something that they need to be concerned about. Because otherwise they're going to feel that cyst every time they shower, every time they dry off, every time they put on deodorant and they're going to think it's cancer.

Let us prove to you or make us prove to you that it's nothing. Seek evaluation for any concerns, be proactive and think prevention. And I put think prevention, because it's so important that if you have a gene mutation and you have a strong family history of something, let's do preventative measures, surgeries to prevent ever having to deal with cancer. I'm not underestimating what it is to lose your ovaries, your tubes, your uterus, your breast. I'm not underestimating that, but I can tell you that it's much easier to say goodbye to those things without cancer than it is with cancer. We know that ovarian cancer's aggressive, but it's rare. 25% are due to the hereditary predispositions. An additional 25% have targetable somatic mutations. And despite the high risk of disease recurrence, we're making advances in progression free survival with maintenance therapy and PARP inhibitors.

We need to recognize that regardless of the stage, we have options. Hope is the most important, just peace of care. You have to have hope and you need to see a doctor who has hope for you. The future of ovarian cancer is very hopeful. We're learning how to evaluate tumors for hundreds of gene mutations and targets. And although right now we're not proficient enough to know how to treat them, we know that they're there and that's the future of care to create a future of personalized and targeted treatment for each individual based on their specific tumor profile. I think I might have gone a little bit over, but I appreciate your patience. I kept talking, I'm sorry, interjecting. But if you have questions, I'm happy to address them.

Melissa Rosen:

So first of all, thank you so much. I learned a lot and I would guess that the people who have stayed on this webinar, that we have very little drop off, even though we're running a little late, also learned a lot. Do you have a couple of minutes to answer some questions?

Dr. Lauren Carcas:

Absolutely. It was my fault for going over, so I apologize. So yes, I'll answer whatever question.

Melissa Rosen:

Well I will say that we sent you a list of questions ahead of time and you managed to get a lot of those answers in. So hopefully you heard your answers if you asked a question. But there are still more questions and so we're going to ask a couple more. First of all, a couple of people have asked if you've already had a prophylactic hysterectomy, and no cancer was found at the time, can you still be diagnosed with ovarian cancer? And what would the symptoms be?

Dr. Lauren Carcas:

So the answer is yes. And I'm assuming when you're saying hysterectomy, you're also talking about the ovaries and tubes. The take it all out.

Melissa Rosen:

Take it all out.

Dr. Lauren Carcas:

Okay. So yes. And that's because we cannot remove the peritoneum that lining around the entire fishbowl, we can't remove that. It is less common to develop primary peritoneal cancer. That's a very, very rare entity, but it is possible. The symptoms are the same, abdominal bloating, all of those same exact features are the symptoms. It's much less common though, which is why we recommend the prophylactic procedures, because it really reduces the incidence of cancer.

Melissa Rosen:

You know what? I'm going to take a break. Some people may need to leave at nine o'clock. I've been watching my colleagues put in certain links into the chat box. So I'm going to explain what those links are and then we'll go back for anybody who has the ability to stay and will answer some questions. So of course, again, thank you for your expertise in sharing it. There are some upcoming programs I want to share with everybody this evening. Of special interest to those who came tonight. Sharsheret is part of a program geared to those who have recently been diagnosed with ovarian or other gynecologic cancers. We're having to partner with many other organizations and cancer centers, including some of our program partners tonight to bring you this. If there is a link that went into the chat box so that you can register, this will be on the 20th at 6:00 PM Eastern, 3:00 PM Pacific, navigating a gynecological cancer diagnosis.

I also mentioned something about the Sharsheret Summit earlier this evening. We have during this annual summit, several amazing national webinars and over 100 and counting programs across the country as we commit to raising awareness about breast and ovarian cancers and higher diagnostic risk. The link to that special summit website is in the chat box now and I encourage you to take a look at the program offerings and keep checking back because new ones are added every day. There might be a program right around the corner from you. I also encourage you to consider joining the summit by helping to arrange a program in your community and we are here to help you with that.

As we conclude this evening, there is an evaluation link that is in the survey. So please take a moment to fill that out. You can still listen to the answers to the questions while you're filling out the survey and a quick, thank you once more for all of our sponsors and partners. The Basser Center for BRCA, the Siegmund and Edith Blumenthal Memorial fund, Daiichi Sankyo, Merck and the Miami cancer Institute and tonight's program partners, The Amy Krouse Rosenthal Foundation, Oneinforty, Woman to Woman and Judy's Mission. Okay, let's go back for anybody who can stay for a little bit to answer some questions, let's go back to do that. Are there any new updates on low-grade serous ovarian cancer specifically?

Dr. Lauren Carcas:

So that type of ovarian cancer has a less malignant potential. The faster the tumor cells are growing high grade, the more likely it is to spread wildly. Low-grade tends to be found at an earlier stage. But in general low-grade tumors and we're talking all types of tumors that are low-grade outside of surgery often are not responsive to chemotherapy, because they're not growing fast enough to be killed by the chemotherapy, which chemotherapy kills fast growing cells. So usually if it's found, it has not often spread. Sometimes if it has spread the outcome or the treatment of that is not much different that we

would still treat, but it might not respond as well. So I don't have any good update on it. But fortunately it's a little bit less common.

Melissa Rosen:

Thank you for that. Several people have just recently asked tonight if somebody has hetero ovarian cancer, do you also recommend prophylactic mastectomy with a mutation and also without a mutation?

Dr. Lauren Carcas:

So with a mutation we can do high risk screening. High risk screening means that you're getting imaging every six months. Usually alternating between mammogram and ultrasound six months later, bilateral breast MRI. Because if we look more frequently, we're more likely to find something when something grows. But you need to remember that, that is not prevention, that is early diagnosis. The only prevention of breast cancer is mastectomy. But I understand that's a hard thing to do. I'm not for a moment underestimating what that actually means, entails and the psychologic impact. I think it's important also to address that it appears that there is no data that tells us that we cannot do nipple sparing mastectomies, which is really important for our young women who are doing this prophylactically. If you're doing a mastectomy because you have a diagnosis of cancer and your cancer is right below the nipple, we can't save your nipple.

But if you're doing this for prophylaxis, your risk of developing breast cancer with a prophylactic nipple sparing mastectomy is no different than if you would've done a non nipple sparing. So I think that, that's one important feature that some women, it might move them one way or the other. Yes, I recommend it. I have the conversations with my patients, but I respect their decision because they're the owners of their body and I'll support what they decide.

Melissa Rosen:

Let me ask sort of a related question. If somebody's taking a PARP inhibitor, does that reduce risk of breast cancer diagnosis?

Dr. Lauren Carcas:

So it should. No studies have looked at that. No studies have looked at that, but we do have PARP inhibitors indicated for breast cancer. We use them in the maintenance setting for BRCA mutated high risk breast cancer patients. We also use it in stage four, breast cancer for BRCA mutations. So yes, it should decrease the incidence of BRCA associated breast cancer. But there have been no studies that look at that.

Melissa Rosen:

Interesting. Okay. Somebody asked a question, I had never even thought of it's a great question. Are treatment protocols different if the cancer is found in the tubes versus the ovaries or? No, it's all the same.

Dr. Lauren Carcas:

It's the spectrum. Remember, it's that umbrella term. That umbrella kind of houses all of them and really the treatment's more or less the same.

Melissa Rosen:

Thank you. Any updates on rarer ovarian cancers, such as carcinosarcoma?

Dr. Lauren Carcas:

So carcinosarcoma is more rare. It's not unheard of, we see it enough, but the treatment more or less is the same. I think that as carcinosarcoma and those other kind of, I would argue more difficult tumors. This is where the genomic analysis is going to be so beneficial because I would argue that those are the patients that are more likely to have that high mutational burden or might potentially be candidates for immunotherapy or other targeted therapies.

Melissa Rosen:

Thank you. Okay. Here's another interesting question. It's not necessarily about advances, but I think it's fascinating. If there are no proven screening methods for ovarian cancer that have a significant success rate, how is most ovarian cancer diagnosed?

Dr. Lauren Carcas:

When they're symptomatic. Exactly like the story we heard from Lynette. People go to the emergency room, they go to the emergency room, or they go for their annual visit with their gynecologist and on the bimanual exam, when one hand is in the vagina, you've got fingers in the vagina and you're pressing down on the belly, that can potentially lead to, "Oh, I feel something enlarged." And lead to a workup, an ultrasound or something. But it's usually symptomatic. Patients are symptomatic and by ultimately they get a scan and it shows something.

Melissa Rosen:

So that also means that based on symptoms, it's probably more than one doctor a patient goes to before they get, one specialty before they-

Dr. Lauren Carcas:

Oh, absolutely. Yeah. Yeah.

Melissa Rosen:

Somebody had a question. You had said, you can get ovarian cancer after an oophorectomy because you can't remove the peritoneum. But somebody said they heard that they do remove that and confine cancer cells there. Does that mean they only remove part of it or is that a misunderstanding?

Dr. Lauren Carcas:

They do brushings, but they don't remove the whole thing. You can't, it's like, I don't know how to explain it. Almost like saran wrap that lines it all, but it's not easily removed. You can't. But you can develop cancer of that. It can be sampled, you can have samplings of the peritoneum, but routinely it's not. But it wouldn't necessarily be called ovarian cancer, but remember the umbrella term, primary peritoneal cancer is the same as ovarian cancer, is the same as fallopian tube cancer. It's the same spectrum of disease.

Melissa Rosen:

Okay. I have another question. What is your opinion on dog sniffing or artificial nose successfully becoming the screening method? There have been a couple of articles in the news lately about that.

Dr. Lauren Carcas:

I don't think that I know, but I will tell you I've had patients never with ovarian cancer, but I've had patients with breast cancer tell me that their dog diagnosed it, I think it's fascinating. I don't see why not. I mean, dogs can detect seizures before they happen. So listen, I won't put it past anything, I think science is fascinating.

Melissa Rosen:

Yeah, absolutely. Okay. There are some more questions here. So you mentioned a lot of different mutations. We speak a lot about BRCA mutations, but can you share any insights into what to make of the ever-changing guidance on other mutations? Whether it be PALB2, whatever it is for ovarian.

Dr. Lauren Carcas:

So I think it very much depends again, because there's variable penetrance in those genes. So I have patients who have PALB two mutations that I follow on the same high risk screening protocol as I do my BRCA patients. So I think that's why it's so, so important to get early genetic testing so that you can know your risk and you can be followed by somebody. It doesn't change what our recommendations are or our considerations are. We know that in general, the biggest clear recommendation is yes, we recommend removing ovaries and tubes for BRCA. There's no other gene mutation where we say, yes, we recommend you do it. However, if you have a PALB2 mutation and every single woman in your family has had ovarian cancer, you're going to go see the doctor and the doctors just say, "We recommend you do this."

Melissa Rosen:

Okay. A couple more questions, and then we're going to finish up. Are there any advances in early detection for recurrences specifically?

Dr. Lauren Carcas:

So in general, patients that have had ovarian cancer are getting scanned about every six months. So they're being looked at pretty often to evaluate those risk of recurrence. Statistics, and I hate to talk about statistics. So I'm not even going to mention numbers, but the majority of women who have a disease recurrence recur within three years. So if you after that three year mark, we tend to space out the frequency of the scans. But early on, you're being evaluated really often. I usually see my patients every three months for the first two years, then every six months, years three through five.

Melissa Rosen:

We're going to go with two more questions and then wrap up. One question is obviously nothing is close to being rolled out, because we would've heard about that. But do you know of any work being done on vaccines for prevention and ovarian cancer?

Dr. Lauren Carcas:

So I think that what we're really looking at is vaccines or how to prevent gene mu mutations from penetrating, from expressing. So yes, we know that you have a, BRCA mutation, but how can we prevent that BRCA mutation from doing what it does. And I think that, that's an exciting piece. We've looked at a lot of other means of doing this. It's not quite there. I wish that it was, I'm sure that your group would actually be the first that anybody goes to because you have the largest group of united people that are educated about gene mutations and would be proactive in that type of a consideration. We're not there yet, we are looking at vaccines like in breast cancer at reducing disease recurrence, but not yet in the upfront setting and nothing has panned out quite yet.

Melissa Rosen:

Thank you. The difference practically between removing ovaries and tubes or having a full hysterectomy, does the complete hysterectomy do anything to put odds in our favor?

Dr. Lauren Carcas:

Okay. So that's important. We know that there is some potential correlation with a BRCA mutation in certain types of uterine cancers, even uterine sarcomas. So some people choose to do it all. I think that just terminology wise, you can have an oophorectomy ovaries only. You can have a bilateral salpingo-oophorectomy that's ovaries and tubes. A hysterectomy is just the uterus. When people say, "Oh, I had a hysterectomy." That means they had just the uterus removed. It doesn't mean that they had the tubes and ovaries. If you have everything the complete, that actually includes the cervix up, but the real terminology for it is a complete or a total hysterectomy and bilateral salpingo-oophorectomy and BSO it's both.

Melissa Rosen:

And does that put the odds in our favor?

Dr. Lauren Carcas:

It does put the odds in your favor, but the most important is the ovaries in the tubes. The uterine is debatable because it goes back and forth. Is it related? Is it not related? We know that people with Lynch syndrome have higher risk of uterine.

Melissa Rosen:

Okay. There were two types of questions that we didn't get to tonight because we're going to address them differently. So let me just say first, there were several questions that came in that were really of a psychosocial nature, how to deal with a diagnosis and with family. And we will have, if you were one of those people that asked one of those questions, we will have somebody reach out to you specifically. The other one that was asked, actually had to do with testing negative and then testing positive for BRCA mutation and the question specifically referenced a recent interview with Chris Everett about her sister. We're going to actually do something more on that because that's just come up for our staff as well. So maybe we will have our amazing genetic counselor, Peggy Catrell write a blog about it or something like that, because it's not something that can be explained in just two minutes.

So for those of you who asked hang in there, we will get you an answer on that. Again, presentations throughout... Yes, and somebody just asked me to repeat a little bit of information. Could one of my colleagues please put the summit website back in the chat box right now? We have a summit that every

fall, that raises awareness it's in there now for breast and ovarian cancer, for heightened diagnostic risk. We have a really large handful of some amazing national webinars and local programs across the country that you can either attend or help us add to that list by reaching out and helping us do something in your community. Again, what a Testament that we lost, such a small percentage of our participants, and we're almost 20 minutes over. Dr. Carcas, thank you so much for your information tonight. And we appreciate all of you attending and we appreciate you sharing your time and your insights. Have a wonderful evening and good night.

Dr. Lauren Carcas:

Thank you. It was my pleasure.