Melissa Rosen:

I want to thank everyone for joining Sharsheret today on this evening, for an important update straight from ASCO. My name is Melissa Rosen, I'm the director of training and education here, and I'm going to be moderating this evening.

Melissa Rosen:

Before we begin, I have a few housekeeping items that I would like to share. First and importantly, I want to thank our sponsors for today's webinar, which enable us to continue to offer meaningful programs. The Basser Center for BRCA, Daiichi Sankyo, GlaxoSmithKline, the Sylvester Comprehensive Cancer Center, the Siegmund and Edith Blumenthal Memorial Fund, and the cooperative agreement DP19-1906 from the Centers for Disease Control and Prevention.

Melissa Rosen:

As always, the webinar is being recorded. And it will be posted on Sharsheret's website, along with a transcript for you to use as a resource. As a reminder, participants, faces and names are not included in that recording.

Melissa Rosen:

You do also have the option to be anonymous during today's live webinar. You can turn off your camera and even change the name in your Zoom square. There are instructions in the chat box now on how to make those changes if you wish to do so.

Melissa Rosen:

We received many questions through the registration process, and I mean, many. As questions will also arise during tonight's presentation, please use the chat box, and we will address them during the Q&A at the end of the webinar. As a reminder, Sharsheret has been providing telehealth services to the breast and ovarian cancer communities for more than 20 years, because cancer is so much more than a physical experience. If you are interested in learning more about Sharsheret's free, confidential, and personalized services, please email us or visit us at our website, and that contact information is now in our chat box.

Melissa Rosen:

As we move into tonight's 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 by Sharsheret or by tonight's speaker is not a substitute for medical advice or treatment for your specific medical condition.

Melissa Rosen:

You should not use this information to diagnose or treat a health problem. As always, seek the advice of your physician or qualified healthcare provider with any questions you may have regarding a specific medical condition.

Melissa Rosen:

I am proud to say that Sharsheret continues to bring you the most up to date medical information and research from this year's American Society of Clinical Oncology conference, which took place last month. ASCO is the world's leading professional organization for physicians and oncology professionals caring for cancer patients. Throughout the years, there have been many incredible and transformative finds and advances in the cancer world in terms of how we view cancer, the technology, and how we treat it. Many patients may be hesitant or confused about what it all means and how it applies to them, so our goal for tonight is to discuss the current options before, during and after treatment, and to explore what's on the horizon in the world of breast cancer, all of which was shared at this year's ASCO conference.

Melissa Rosen:

I'm also happy to share that we will be dedicating an entire webinar on September 14th to recent updates and advances in the field of ovarian cancer, so please take a moment to mark your calendars. Tonight, we are incredibly lucky to have with us, Dr. Alisa Krill Jackson, who will help us to understand the recent advances presented at ASCO. Dr. Krill Jackson is a board certified hematologist and oncologist at Sylvester Comprehensive Cancer Center. She specializes in breast cancer, gynecologic cancers, as well as hematology, Dr. Krill Jackson believes in educating her patients about their conditions so they can work together as a team to fight their cancer. While using the most state of the art treatment and clinical trials, she believes in treating the whole patient with compassion and supporting her patient's physical and emotional needs. Now, that's why she is the perfect presenter for this evening. So, welcome Dr. Krill Jackson, and thank you so much for being here today. This information is so important for our callers to know, and to understand.

Elisa Krill Jackson:

Well, thank you for having me. It was a great conference this year at ASCO. There was a lot of very important breakthroughs. In fact, one of the papers I'm going to present got a standing ovation, which is not common in a medical conference. I'm also going to give a couple updates on the most important things that happened during the prior year that I think are important to know about in the context of ASCO.

Elisa Krill Jackson:

So, without further ado, I'm going to share my screen.

Elisa Krill Jackson:

All right. As you noted, I'm a breast medical oncologist. I'm based in Miami and Fort Lauderdale, here at University of Miami Sylvester, a comprehensive cancer center. And at this time, I see only breast cancer patients.

Elisa Krill Jackson:

I want to talk a little bit first about early breast cancer, adjuvant therapy. That means therapy after somebody is diagnosed with an early stage breast cancer involving only their breast and/or their lymph nodes. And there's a couple questions that we were able to answer a little better at ASCO this year about hormonal therapy, some add-on therapies to our therapies for breast cancer, and early detection of recurrences, which I always get questions of from my patients.

Elisa Krill Jackson:

So, just background on this, a very, very old study, ECOG 5188, randomized premenopausal women with estrogen receptor positive node positive cancer, so high risk cancers, to chemo, chemo plus goserelin, which is an endocrine blocker. It suppresses somebody's menses and periods and their ovarian function, or chemo, the goserelin and tamoxifen. And what you can see is that the triplet therapy was certainly better for all patients.

Elisa Krill Jackson:

So, the question is what patients need this triplet therapy? So, a study was presented at ASCO called the ASTRRA study this year. The ASTRRA study was a very simple study. It randomized patients one to one to either get tamoxifen alone as their adjuvant therapy after they've been treated with surgery and chemotherapy, or tamoxifen plus ovarian suppression, so putting women chemically into menopause. And what you can see here is there was a 5% improvement in prognosis in the patients who got ovarian function suppression. So, this is an effective strategy for our highest risk patients. Now, for breast cancer, unfortunately five years is not long enough to follow our patients to know how they do. More than 50% of our recurrences occur after five years of endocrine therapy. So, how can we determine which patients need longer durations of therapy? How can we personalize our recommendation? Who needs more than five years? And how can we balance that longer treatment with symptom management and adherence to therapy?

Elisa Krill Jackson:

So, looking to make our therapy more effective, there were several studies presented at ASCO, which are what we call negative trials. These trials randomized thousands of women to a drug or a placebo, and looked to see how they did. And unfortunately, we saw no benefit. So, we had high hopes that aspirin would improve prognosis after a diagnosis of breast cancer, but unfortunately this was a negative trial. There was absolutely no difference between the group who got aspirin and the group who got placebo in terms of recurrence of breast cancer. Again, Metformin. We had really high hopes for Metformin. Metformin is a diabetes drug, and what it does is it lowers insulin levels in patients and insulin growth factor, which we think of as potentially a growth factor for cancer.

Elisa Krill Jackson:

So, women were randomized to either get Metformin or to get a placebo. Again, thousands of women were randomized on this trial, and they were followed for five years, and we saw no difference in prognosis. So again, disappointing that these relatively non-toxic inexpensive therapies did not improve prognosis for women. However, we did have some significant breakthroughs at ASCO. So, we know that women who are in menopause, who are getting hormone blockers, they lose bone density and can develop osteoporosis, which can contribute to fractures. We know that if we give certain medications to help their bones, we can keep their bones healthy. Not only that, but some of these medications do appear to improve patients' prognosis. So we know that a medicine called Zoledronic acid, which you can see right here on the slide, which is given every six months for three years, improves the prognosis. It decreases the chance that the cancer will spread to the bones.

Elisa Krill Jackson:

Now, initially, we did not know that another medicine called denosumab, which is also known as Prolia, if you're familiar with that brand name, we thought that it helped the bones, but it did not help the prognosis. But at ASCO, they presented the ABCSG trial, which after long enough follow up, we found that the women who got the denosumab every six months after a diagnosis of breast cancer actually

had improved bones, but also had an improvement in prognosis. So, if you look at this, you can see that the risk of fracture in the placebo group, the blue, was much higher than the risk of having an osteoporotic fracture in the patients who got the denosumab. But if you look here at disease free survival. That's whether the cancer recurs somewhere in the body or in the breast as well in this trial.

Elisa Krill Jackson:

And what they found was there was a 17% reduction in the risk of the cancer coming back, was what we call an absolute 5% reduction in the risk of the cancer coming back. So, in the women who got the denosumab, 75% of them remained without cancer recurring, and only 69% in the women who did not get denosumab. So, taking care of our bone health is not only important for our bones, but also appears to decrease the chance that the cancer will come back now. Now, why is that? Well, breast cancer often will hide out in the bones and the bone marrow and stay dormant for years. And the thought is that these agents affect the bone environment so that it makes it kind of a hostile soil for breast cancer cells to grow. So, any patient should be asking their doctor about this. Our ASCO recommendations are anybody with early stage cancer should discuss going on a bone modifying agent with their doctor.

Elisa Krill Jackson:

So this is another new tool in our arsenal because some people can't take Zometa. And Zometa is a less expensive drug, but it is IV, and it does have a few more side effects than the denosumab. Again, it reduced bone metastases by about 5%, and it appears to improve overall survival as well. So again, this requires six doses over three years, or every three months over, two years. Now I'm going to go back a little. This was a trial that was presented before ASCO, but I think it's important to know when we're talking about big advances in the last year was the Olympia trial. And I think this is particularly important to Sharsheret members, because this is four patients who have BRCA one and two mutations. So, the Olympia trial looked at giving a medicine called olaparib, which is a medicine, an oral medication, which is particularly designed to treat cancers due to BRCA mutations.

Elisa Krill Jackson:

It looked at giving this in high risk patients after their diagnosis of early breast cancer. So, what you can see here is patients were either randomized after their chemotherapy and surgery, and while they were on hormonal therapy, if they were going to take hormonal therapy to olaparib for one year or placebo. And what you can see here is a 7% improvement in whether the cancer came back over four years, or three years, in the patients who got the olaparib for only one year. And there was an improvement as well, 4% in overall survival. So, this is totally a home run for our BRCA patients. The drug does have some side effects. It can cause anemia. It can cause some fatigue, but in general, it's relatively well tolerated and patients are generally able to take it for one year. And this is a summary, a plain language summary.

Elisa Krill Jackson:

When you get the slides, if you wish, you can look at the QR code and download the information from this trial. Another big change in our treatment of breast cancer in the last year came from the Monarch-E trial. So, the Monarch-E trial used a drug called abemaciclib, which we use in metastatic breast cancer frequently, but it looked, in high risk women who had positive lymph nodes and estrogen sensitive disease, if we add a abemaciclib to their hormonal therapy for two years, when they start their hormonal therapy, does that improve their prognosis? So, half the women got abemaciclib for two years and half got just the endocrine therapy. So the abemaciclib was added to the end different therapy. So, there were 5,600 women on this study.

Elisa Krill Jackson:

And what we found was, again, there was a marked improvement in recurrence free survival, whether the cancer came back. There was about a 5% improvement after three years in whether the cancer came back. So again, this is a really, really important advance for our cancer. And I think at this point in time, we are routinely giving it to our high risk patient, patients who have multiple nodes positive, patients whose tumors have were very large, had a high KI67, were growing rapidly. This is a very important advance for our patients. Now, this drug is difficult. It's not an easy drug, and like olaparib, it's extremely expensive. But in general, we are able to get it affordable for all of our patients. I have not had to not give the drug to somebody because of affordability. We are blessed to have donors who provide grants to patients, and so we're able to get this drug for most patients affordably.

Elisa Krill Jackson:

Again, what you can see here is a marked improvement in whether the cancer comes back. So, that's enough about add-on drugs for early stage breast cancer. Now, all my patients ask me, how are you going to tell if my cancer comes back? And it's a very unsatisfying answer that I have to give my patients. I have to tell them that there's no way that we can detect the cancer early and make a change in their prognosis by detecting it early. So, we don't do a lot of studies because that gives a lot of radiation, it can contribute to other cancers. Well, we're starting to get into the era where maybe we can detect things early. Not sure we can still do anything about it, but that's just one step behind, hopefully. So, this trial is called the CHiRP trial, which looked at circulating tumor DNA in the blood in patients who had high risk breast cancer. And what they did was they took patients who had large tumors or multiple nodes positive, and they drew their blood at routine intervals and looked to see if they could find tumor DNA.

Elisa Krill Jackson:

What they found was that 10% of the patients had tumor DNA in their blood. And of the eight patients who had tumor DNA in the blood, six of them eventually develop metastatic disease. So, it looks like we can tell, with this test, who may develop metastatic disease. Now, that's an unsatisfying answer at this point, because we don't know if when we find these circulating tumor cells, whether we can do something to change people's prognosis. But in this study, it was an average of 12 months between when we found the circulating tumor DNA and when the cancer came back. So, we can detect it early. And the hope is maybe, and these trials are being done now, if we detect this and we change somebody's therapy at that time, maybe we can prevent that recurrence. So, I think we are making strides, but they're slow.

Elisa Krill Jackson:

All right, I'm going to go on to talk about metastatic disease. And I think we're making our most major strides in metastatic disease. First thing I want to talk about is what's called antibody drug conjugates. These are greatest thing to slice bread in oncology at this point in time. People often call them smart bombs, but I like calling them the Trojan horse. So, basically what we have here is our cancer cells often have a protein on their surface that we can target. So in a HER2 positive cancer, we can target that HER2 protein. So, we make an antibody. The antibody is this little blue thing right here (on the slide). That's an antibody, and we engineer an antibody to attach onto those little green proteins on the surface of a cell.

Elisa Krill Jackson:

And then that antibody, which would be like herceptin, for instance, we put little chemo molecules and attach it to that antibody. So, what happens when it attaches to the cell? The cell takes it inside the cell, and those chemo molecules on that antibody are designed to fall off when it goes inside the cell. Those chemo molecules fall off. They're like the warriors in the Trojan war in that horse invading the city, and they can kill the cell from the inside. Not only can they kill the cell from the inside, but in some of our best antibody drug conjugates, that chemo will get outside of the cell and can kill other cancer cells in the nearby vicinity that may not have as much of this green protein around. So, this is becoming a reality; it's become a really, really important therapy in breast cancer.

Elisa Krill Jackson:

So, this was the most exciting part of ASCO this year. So, there's a drug called trastuzumab deruztecan, or T-Dxd. It's also known by the brand name HER2, which is already approved for Her-2 positive breast cancer, so breast cancers that have what we call three plus Her-2 protein on their surface. In this trial breast cancer classifications have always been we have a big pile of estrogen and progesterone repositive cancer, and then a smaller group of estrogen progesterone negative cancer. Now, some of these cancers are Her-2 neu three plus positive or FISH positive. Those are the Her-2 positive cancers. We have great, great success, treating them with herceptin and other antibodies and antibody drug conjugates. Now, this trial looked at this group of patients, Her-2 LOW cancers. So, maybe 40% of cancers are Her-2 LOW, meaning that when you stay in the surface of the cell, the Her-2 is one or two plus, not zero. Zero would be over here in this pink group.

Elisa Krill Jackson:

It's not three plus in this lavender group. It's one or two plus. So, when they stain the cells under the microscope, they see that the Her-2 is what we call one or two plus. So low, but not zero. So, basically T-DXd is that antibody drug conjugate, but instead of two or three chemo molecules on it, there's eight chemo molecules on it. This is a really, really potent antibody drug conjugate. And what you can see here is when we compare this to an older antibody drug conjugate called Kadcyla, or T-DM1, it's much more effective. You can see that patients do better for longer. The blue line is the T-DXd, the gray line, the T-DM1.

Elisa Krill Jackson:

So, we looked at this antibody in patients with Her-2 LOW cancer, and again, that might be 40% of patients with breast cancer. And what you can see here is there was a marked improvement in the cancer staying under control in the patients who got T-DXd versus the patients who got the chemo of their doctor's choice, so the chemo could have been four or five different chemos. So, this is the whole group of patients, the hormone receptor positive patients and all patients. It improved the prognosis, the time of cancer stayed in remission, for about five months, which is actually quite a lot in the breast cancer world at this point in time. But what was really exciting is if you looked at the hormone receptor negative group, so these are triple negative breast cancer patients, we know triple negative metastatic breast cancer patients don't do so well, what you can see here is the overall survival. These patients live 10 months longer if they got T-DXd versus chemotherapy.

Elisa Krill Jackson:

This is a huge, huge, huge leap for our patients. It's almost a year improvement in patients' prognosis with triple negative breast cancer that have Her-2 one or two plus on their surface if they got T-DXd versus just a plain old chemotherapy. You could see that the improvement in how many patients

responded. 50% versus 16% responded to T-DXd versus chemotherapy. So, this is a new standard of care. Again, another antibody drug conjugate called sacituzumab, which we already used for triple negative breast cancer. Sacituzumab was given the same way, sacituzumab to patients with estrogen positive cancer or the doctor's best choice of chemotherapy. So, same type of trial. And what you can see here is, again, the green arm, the sacituzumab, those patients did better for longer.

Elisa Krill Jackson:

So, we have two new therapies for our patients just based on this year at ASCO, which is really unusual to have that big a change. And within a week or two of ASCO, the NCCN guidelines, which are the guidelines that insurance companies look at to pay for medications for our patients, the NCCN guidelines added sacituzumab for ER positive patients and T-DXd or for Her-2 one or two plus patients. So, within two weeks of ASCO, we have two new therapies for most of our patients with metastatic breast cancer. All right, I want to talk a little bit about genomic testing before we finish. So, in patients with metastatic breast cancer, everybody knows, okay, my cancer is estrogen positive, or it's estrogen negative, triple negative, or Her-2 positive. Genomic testing actually looks at other mutations in the tumor.

Elisa Krill Jackson:

So, just like COVID can mutate and become resistant to our antibodies, the cancer cells can mutate and they can express different proteins due to changes in their DNA. Now, we can send blood, or we can send tissue from the cancer to look to see if your particular tumor has a particular mutation. So, you can say, this is one of my patients. My patient has what's called a PIK3CA mutation. So, if this patient has this PIK3CA mutation, we have a drug approved for it for breast cancer, drug called alpelisib. So, if we didn't do this test, we wouldn't know that patient could benefit from that drug. We can also do this on the bloodstream. And what we can see in the bloodstream is this patient has a PIK3CA mutation, but they also have an FGFR mutation.

Elisa Krill Jackson:

Now, an FGFR mutation is not something we see all that commonly in breast cancer, and we don't have an approved drug in breast cancer for it, but we have an approved drug in bladder cancer for it. And if we find out that a patient has an FGFR mutation, we can use that bladder cancer drug and often see a good response in the patient. So, it's really important to do genomic testing on our patients. Now, so this is a trial at ASCO that looked at genomic testing in patients, and it gave a particular drug called capivasertib with their hormonal therapy. And what it looked at is whether the patients had mutations in a pathway called the PI3 kinase/AKT/PTEN pathway. And it gave the drug to everybody, or 50% of the patients got the capivasertib and 50% got placebo with their hormonal therapy. And what you can see here is there was a modest improvement in the patients who got capivasertib with the fulvestrant.

Elisa Krill Jackson:

But if we look at the patients' genomic testing, what you can see here is these patients who didn't have any mutations in that pathway, they didn't get any benefit from that drug, but the patients who had a mutation in that pathway, they had a lot of benefit. That red line is much higher than, than the blue line. They lived longer if they got this drug, because we knew that they had a mutation in that pathway. So again, it's really, really important for us to do genomic testing on our patients so that we can tailor the best therapy for them. And one more item. Now, when I'm treating patients with metastatic disease with a drug called the CDK46 inhibitor, like ribociclib, a lot of times their counts will be low, or they

won't be feeling well on it, and I'll tell them I want to lower the dose. And they panic and tell me, "Oh my God, I'm not going to do as well if you lower the dose."

Elisa Krill Jackson:

Well, they presented a trial at ASCO that showed whether patients had lower doses or not. And what they found was, you see all these three lines on how patients did are identical. These are patients who stayed on the same dose, patients who went one dose level down, patients who went to dose levels down. They all did the same. So, I don't think our patients have to be afraid if we lower the dose of their medication. So, just a reassurance for our patients when we have to lower the dose of those medications, we can tell them, in the large clinical trial, looking at this agent, there was no decrease in your prognosis if we had to lower your dose. Everybody metabolizes differently, and we're just finding the right dose for them. One last study that was disappointing, but I think everybody needs to know about it, was the SBR RT study.

Elisa Krill Jackson:

So, SBR RT study looked at patients with metastatic disease with what we call oligometastatic disease, only a few tumors in their body, and then looked to see, can we radiate these tumors and improve patient's prognosis? Can we get rid of all their disease with radiation, along with their standard therapy? We know that in other cancers, that does improve the prognosis, but does have significant toxicity, but we didn't have data in breast cancer. So, this trial randomized patients to getting their regular therapy, or getting their regular therapy plus radiating the areas where they had tumor to get rid of them. Most of the patients were estrogen positive on this trial. What you can see here is unfortunately there was no improvement in prognosis.

Elisa Krill Jackson:

And in fact, maybe the patients who got the radiation did a little bit worse. So, I would say that we can say, in estrogen receptor positive patients, that there really is no role for getting rid of all the disease with radiation. I talk about this all the time with my patients. I only have one or two tumors, should we radiate them? This trial sort of tells us that is not a good way to go about this, unfortunately. Now I don't think this pertains necessarily to Her-2 positive patients. There were very few Her-2 positive patients on this trial. But for estrogen positive Her-2 negative patients, I don't think we want to do this strategy. Lots of new medications at ASCO, so there's, I think, a lot of hope for our patients. So T-DXd, is it practice changing? Yes. Sacituzumab and estrogen positive disease? Yes. Ablation of oligometastatic disease? No, doesn't look like that that's helpful. And are there lots of new drugs on the horizon? For sure. So, our destiny's not written for us, but by us, and thank you very much for your attention.

Melissa Rosen:

That was a lot of very intense information that you made accessible to our callers. Thank you. And it sounds like overall, it was very much an exciting year, particularly exciting year. We have a lot of questions.

Elisa Krill Jackson:

All right.

Melissa Rosen:

So, I'm going to just jump right in. So, one of the questions is, 10 years seems to be still the standard amount of time for taking aromatase inhibitors for ER positive, Her-2 negative survivors. Has that number changed... Is 10 years... Because I'm hearing... The question was 10 years of standard, but I hear from women, 5, 7, 10. So, what is the current recommendation?

Elisa Krill Jackson:

So, I would say we always started five years. There was a trial recently called the ideal trial, which looked at seven years and thought seven years may be the sweet spot. We know that 10 years of tamoxifen is better than five. We know five years of an aromatase inhibitor after five years of tamoxifen is better. But I think again, the answer is genomic testing. So, we actually have tests that your doctor can do to test the tumor and get a result that tells us what is the risk of the cancer coming back after five years? And will continuing hormonal therapy help? So, I think it really depends on the stage. It depends on the side effects you're having, and it also depends on that test. There's also an online calculator one can use based on the size and the lymph nodes and the tumor and the grade that one can use to get an idea whether 10 years is going to be better than five. But I always start at five with my patients. And at five years, we discuss the risks and benefits of going longer.

Melissa Rosen:

Okay. One thing I notice you didn't talk about, which likely means it wasn't addressed, is vaccine development. Can you shed any light on where we are for breast cancer vaccine?

Elisa Krill Jackson:

So yeah, there are some vaccines that are being tested to prevent recurrence in Her-2 positive disease and in triple negative disease. They're still in the testing process. At this point, we don't have any great data that they prevent recurrences. There's some data that some may be effective in late stage disease. And again, they're being tested. There really was no major breakthrough at ASCO about vaccines at this point in time. Unfortunately, breast cancer isn't the world's most immunogenic cancer. Unlike melanoma where you can give immune therapy and it will dissolve away, breast cancer's not like that. So, that is moving slowly, but I think is a promising outlet.

Melissa Rosen:

Okay. Any thoughts about vaccinations for people who know they're at high risk prior to a diagnosis?

Elisa Krill Jackson:

I am not aware at this point, but for high risk patients, we have a lot of other strategies, anti-estrogen strategies that we know do work.

Melissa Rosen:

Thank you. So, when you were talking about new drugs that are on the market or being added to NCCN guidelines or things like that, you did indicate that some of them are difficult drugs. So, we have a question here about work on treatments, creation of treatments without such daunting side effects, extra cancers, blood clots, severe neuropathy, things like that.

Elisa Krill Jackson:

Yeah. That's the golden ticket, isn't it?

Melissa Rosen:

Okay. We had to ask.

Elisa Krill Jackson:

We would love that. I think we're getting better at managing side effects, but yeah, there always our side effects to our drugs. Everything has some sort of side effect, but no, between side effects and the cost of drugs, we're in a difficult spot sometimes with our patients. But unfortunately, cancer's a difficult problem, so we're often willing to tolerate significant side effects and significant cost to cure more patients, make more patients live longer, make more patients live better. I would tell you the T-DXd drug, that is a phenomenal drug, and most people don't have tons of side effects on. And it does have some side effects. Some people feel tired. It can rarely cause some serious lung problems, but most patients actually feel pretty darn good on that drug, especially when it's making their cancer better. So, I think slowly, we're getting to that place where we can keep people feeling well while treating their cancer.

Melissa Rosen:

Okay. Hopefully next year's ASCO will offer something else.

Elisa Krill Jackson:

There's a lot of quality of life data going on right now, a lot of studies on quality of life, so we are paying attention to it.

Melissa Rosen:

Right. Absolutely. That's important to remember, that although some of the drugs we're given do have difficult side effects, our doctors know there are quality of life issues and continue to work on them. You mentioned that cancers can change over time and that genomic testing should be done in metastatic breast cancer to check for changes. How often do you recommend that genomic testing be done for someone living with metastatic disease?

Elisa Krill Jackson:

So, in patients with estrogen positive disease, I usually do my first genomic testing when they're relapsing from their first therapy, because that lets me know if they have a PIK3CA mutation or if they have a mutation in the estrogen receptor gene, which tells me what therapies they can and can't go on in the future, and if they have any unusual mutations. And then sometimes I will do, if they have relapses in the future, sometimes I will do genomic testing at that point in time. Again, it's often an insurance issue because these are expensive tests, and getting insurance to pay for it. And in breast cancer, we don't often see people developing what we call actionable mutations, mutations that we have a drug for over time. If somebody's cancer is starting to act more aggressively, it had been growing slowly, and then it's acting more aggressively, then I'll often do a genomic test, but I don't do them on a routine basis.

Melissa Rosen:

Interesting. You mentioned it's often an insurance issue. I saw somebody just recently put in the chat, does Medicare cover this genomic testing?

Elisa Krill Jackson:

Yeah, medicare does cover genomic testing. And I don't know if they have a limit on how many you can get in a course of a disease, but again, there are high copays for these sort of things, and I haven't found much utility to repeating it over and over and over, so I tend to do it once at the beginning, and then again if somebody's cancer is acting differently than I would expect. Then I'll do another genomic test to see if I can find something different. I think now, for our patients with metastatic disease, it's really important to go back to their first pathology and see... A lot of us just mentioned their Her-2 negative. Now, it's important to know if you're Her-2 one or two plus, because that gives you that other therapy, the T-DXd. And sometimes it may be worth doing another biopsy to see if the tumor has developed Her-2 one or two plus.

Elisa Krill Jackson:

There's a blood test called define MBC that actually looks for estrogen receptor and Her-2 on the circulating tumor cells. So, I think that's really important for patients now with metastatic disease to know whether their tumor has any Her-2 on it at this point.

Melissa Rosen:

Okay, great. Thank you. So, the denosumab, the bone modifying agent you talked about, so I just want to ask you to clarify who is a candidate. Does the person have to be in menopause, whether surgical or natural menopause? And if they are, can they still be... Are they qualified for this, if they're on an aromatase inhibitor or tamoxifen?

Elisa Krill Jackson:

So, they can be on any hormonal therapy, but in the studies, the studies only found a benefit in women who were in menopause. So, young women who aren't in menopause who are tamoxifen alone, not with ovarian suppression. If you have ovarian suppression, you're considered menopausal. But if you're not in either a chemical or a natural menopause, we don't have any benefit to these bone modifying agents.

Melissa Rosen:

And what if someone has metastatic disease? Is an agent like that also used to help reduce the growth of bone metastases or the occurrence of bone metastases?

Elisa Krill Jackson:

Yes. And we use these medicines routinely in patients with metastatic disease. We know that it decreases bone pain, it decreases fractures, it decreases the need for radiation in the bones. So, we use these routinely in those patients, but again, we're finding a role in early breast cancer to even prevent metastases.

Melissa Rosen:

That's very good information. Okay, some of the next questions are a little more specific. Someone wanted to know about the benefits of Boniva for osteoporosis with early stage hormone receptor positive cancer.

Elisa Krill Jackson:

So, oral Boniva has not been shown to improve prognosis. I mean, it certainly will help your bone density, but it has not been shown to improve prognosis. So, if we're looking to improve prognosis, the agents that we would use as an oral agent called Clodronate, which is actually not approved in the US. That's used in Europe. Or, we tend to use Zometa and denosumab. So, those are the two agents in the US that we will use routinely after diagnosis of breast cancer to improve bone health and prevent metastases now.

Melissa Rosen:

Great. Thank you. Another question has to do with someone who had a complete hysterectomy due to complications from a different medicine and is wondering why she would need an aromatase inhibitor after her ovaries were removed. So, can you explain why we do that, even if somebody has had an oopherectomy?

Elisa Krill Jackson:

Okay. So, if you go back to the very first slide that I showed, there was a clinical trial many, many years ago that looked at giving chemo, chemo, plus ovarian suppression, or chemo plus ovarian suppression plus tamoxifen, so three things, and the Tamoxifen won. So, all menopausal women in menopause, their ovaries aren't functioning, right? They're not making a lot of estrogen, and they still get breast cancer and their breast cancer can still come back. We know that either giving tamoxifen or an aromatase inhibitor will decrease the risk of it coming back. And I like to describe how these drugs work as an ignition and a key. So, if an estrogen receptor on a cell is like your car ignition, if the estrogen receptor is stimulated, it turns on that car, so it turns on that breast cancer cell.

Elisa Krill Jackson:

Tamoxifen blocks you from turning on that ignition. It's like a false key, or it doesn't let you push the button nowadays. We don't use keys anymore, I guess. But the aromatase inhibitors, they take away the keys. Okay? So as opposed to making the button not work, they take away the ability to push it at all. So, aromatase inhibitors take away the keys, tamoxifen blocks the keyhole, so they work differently. So, even women in menopause, you still make some estrogen in your fat cells, in your adrenal glands, and the aromatase inhibitors decreased that estrogen. So yeah, menopause alone is not good enough hormonal therapy.

Melissa Rosen:

Thank you for that. Somebody asked when we expect Enhertu to be approved for Her-2 LOW patients.

Elisa Krill Jackson:

So, that's what I was talking about.

Elisa Krill Jackson:

And Her-2 is T-DXd. It does not have an FDA approval for Her-2 LOW. However, it has been added to the NCCN guidelines, which I showed, which is what insurers use to pay for it. So, it should be accessible, at this point, to all patients with Her-2 LOW disease, because the NCCN guidelines have added it. So, if an insurance company denies it, you should be able to fight that and win, because again, the people who make our guidelines have said, this is strong enough evidence that we are recommending it.

Melissa Rosen:

Okay. Someone shared that they have a BRCA one mutation and had DCIS 25 years ago. Are they more or less susceptible to cancer as they age?

Elisa Krill Jackson:

You're always more susceptible to cancer as you age. I mean, your DNA just has more chances to divide and mutate. So, somebody who had DCIS 25 years ago, if they still have their breasts, they're still at risk for breast cancer, and that risk goes up with time.

Melissa Rosen:

And because I know because they carry a BRCA mutation, they're already at higher risk, but are they at higher risk because they had a previous diagnosis, or is it the same as anyone?

Elisa Krill Jackson:

Not really, no. You're not at higher... If you have the BRCA mutation, you're at higher risk, just cause of the BRCA mutation.

Melissa Rosen:

Okay. Somebody asked about treatment plans for secretory breast carcinoma.

Elisa Krill Jackson:

Well, that's a really rare type of cancer. That's something that I rarely rarely see, and unfortunately, I have to look up every time I see it, so I can't help with that tonight.

Melissa Rosen:

Okay. I appreciate your honesty. Somebody asked what is a better option in terms of efficacy and side effects, Actinol, Fosamax versus denosumab?

Elisa Krill Jackson:

Well, I mean, depends what you want. I mean, Actinol and Fosamax are really good oral agents for bone density. Again, they will not improve cancer prognosis, but they're really good oral agents for bone density. Denosumab is a great agent for bone density, but once you stop, the bone density tends to go down, so you need to add something like zoledronic acid or Fosamax or something like that to maintain the bone density.

Melissa Rosen:

Got it. Thank you so much for sharing and clarifying so much information and answering so many of our questions. I want to be aware of the time. So again, special thanks to Dr. Krill Jackson for sharing her expertise with us. I learned a lot. I am sure everyone here did. Once again, thank you to our generous sponsors, the Basser Center for BRCA, Daiichi Sankyo, GlaxoSmithKline, the Sylvester Comprehensive Cancer Center, the Siegmund and Edith Blumenthal Memorial Fund, and the cooperative agreement DP19-1906 from the Centers for Disease Control and Prevention. I see that we've posted a link to an evaluation for tonight's program a few times in the chat box. Maybe it'll go in one more time now. There it is. During the next few days, you will receive a follow up email with a link to the recording, the

transcript. I saw somebody asked if the slides will be available, they will be a part of that recording, and access to some of the resources we talked about today. So, please be on the lookout.

Melissa Rosen:

I also want to make you aware that, separate from an evaluation of tonight's program, we will shortly be sending out an evaluation of all outreach programs. That will arrive, like I said, separately, and it's going to ask you to focus on the last 18 months of programming at Sharsheret, whatever you've participated in. So, please take a few minutes to fill that out as it does, just as individual evaluations help, this is a more global one that will help us as we move forward planning our programs. And please remember that Sharsheret is here for you and your loved ones. We provide emotional support, mental health counseling, and other programs designed to help you navigate through the cancer experience. All are free, completely private, one on one, and our contact information is the chat. And finally, as we conclude, I want to remind you that we are always planning innovative webinars on a wide range of topics, including the one I mentioned earlier, focused on the advances related to ovarian cancer, which is scheduled for September 14th.

Melissa Rosen:

Check our website regularly to see what topics are coming up, and right in the chat box is a link to that, and you're also able to find recordings and transcripts from previous webinars. Thank you all for joining us, and have a wonderful evening.