Updates from ASCO: The Latest Research on Breast Cancer, Ovarian Cancer, and High-Risk Screening

National Webinar Transcript

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Presented by:

SHARSHERET®
The Jewish Breast & Ovarian Cancer Community

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About Sharsheret

Sharsheret, Hebrew for “chain”, is an international non-profit organization that improves the lives of Jewish women and families living with, or at increased genetic risk for, breast or ovarian cancer through personalized support and saves lives through educational outreach.

With regional offices in the Midwest, Northeast, Southeast, West, and Israel, Sharsheret serves 275,000 women, families, health care professionals, community leaders, and students. Sharsheret creates a safe community for women facing breast cancer and ovarian cancer and their families at every stage of life and at every stage of cancer - from before diagnosis, during treatment and into the survivorship years. While our expertise is focused on young women and Jewish families, approximately 25% of those we serve are not Jewish. All Sharsheret programs serve all women and men.

As a premier organization for psychosocial support, Sharsheret works closely with the Centers for Disease Control and Prevention (CDC) and participates in psychosocial research studies and evaluations with major cancer centers, including Georgetown University Lombardi Comprehensive Cancer Center. Sharsheret is accredited by the Better Business Bureau and has earned a 4-star rating from Charity Navigator for four consecutive years.

Sharsheret offers the following national programs:

The Link Program

Peer Support Network, connecting women newly diagnosed or at high risk of developing breast cancer one-on-one with others who share similar diagnoses and experiences

- Embrace™, supporting women living with advanced breast cancer
- Genetics for Life®, addressing hereditary breast and ovarian cancer
- Thriving Again®, providing individualized support, education, and survivorship plans for young breast cancer survivors
- Busy Box®, for young parents facing breast cancer
- Best Face Forward®, addressing the cosmetic side effects of treatment
- Family Focus®, providing resources and support for caregivers and family members
- Ovarian Cancer Program, tailored resources and support for young Jewish women and families facing ovarian cancer
- Sharsheret Supports™, developing local support groups and programs

Education and Outreach Programs

- Health Care Symposia, on issues unique to younger women facing breast cancer
- Sharsheret on Campus, outreach and education to students on campus
- Sharsheret Educational Resource Booklet Series, culturally-relevant publications for Jewish women and their families and healthcare Professionals

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Devorah Silverman:

Okay, we're going to get started. I know more people will be joining us, but in the interest of time, we're going to dive in. So welcome to all of you. Thank you for joining us for tonight's webinar, Updates from ASCO: The Latest Research on Breast Cancer, Ovarian Cancer, and High-Risk Screening with doctors Allison DePersia, Amy Comander, and Deanna Gerber.

I'm Devorah Silverman, Sharsheret's Chief Operating Officer, and I want to begin by giving a special thank you to tonight's webinar sponsor, the Cooperative Agreement 24-0061 from the Centers for Disease Control and Prevention. And tonight's Embrace Breakout session following the webinar is sponsored by Lilly and Pfizer.

Before we begin, a few housekeeping items. Tonight's webinar is being recorded and will be posted on Sharsheret's website along with a transcript. Participants' faces and names will not be in the recording, but if you would like to remain private, you have the option to turn off your video and to rename yourself, or you can call into the webinar.

We also have closed captioning available to display live captions on the bottom bar. Click on captions, and then click on show captions. You may have noticed that you were muted upon entering the Zoom. Please stay muted during the call. We will hold a Q&A session at the end of the presentations. If you have any questions that you have not yet submitted, please type them in the chatbox and we'll get to as many of them as we can.

I want to remind you that Sharsheret is a not-for-profit cancer support and education organization, and does not provide any medical advice or perform any medical procedures. Our full medical disclaimer is in the chatbox.

Two quick program spotlights. First, Sharsheret offers monthly virtual support groups for those personally affected by breast cancer and ovarian cancer. We run one group for those in survivorship who were diagnosed stages zero through three, and one for our Embrace community, those living with metastatic breast and advanced ovarian cancer. And starting in August, we will be running a support group for those newly diagnosed with breast cancer or ovarian cancer, or in stages zero through three, or those who are in active treatment having

surgery, chemotherapy, and/or radiation. The signup link to join those support groups is also in the chat.

I want to call your attention to a webinar we're holding next Monday, July 27th, Protecting Oral Health During Cancer Care. And the link to sign up for that webinar is also in the chat. Most importantly, if you're currently facing a breast cancer or ovarian cancer diagnosis, please remember that Sharsheret is here for you and for your loved ones. We provide emotional support, mental health counseling, and other programs and resources that are designed to help you navigate the cancer experience. Everything is completely free and totally confidential. Our contact information is in the chatbox now.

And now onto tonight's webinar. At Sharsheret, we know that breast cancer and ovarian cancer are more than diagnoses. They are truly journeys. Whether you're living with breast or ovarian cancer, at elevated genetic risk, or supporting a loved one who is, tonight's webinar is designed to share the latest updates that came out of the 2026 American Society of Clinical Oncology Conference. We received many questions in advance. We invite you again to ask any that you may have in the chat, and we'll do our best to get through what we can as time permits. If you're a member of our Embrace program, someone facing metastatic breast or advanced ovarian cancer, we'll invite you to stay on at the end of the webinar following the Q&A for a more intimate breakout session with two of tonight's speakers, Dr. Amy Comander and Dr. Deanna Gerber.

So without further ado, our first speaker this evening is Dr. Allison DePersia. Dr. DePersia is Assistant Medical Director at the Neiman Center for Personalized Medicine at Endeavor Health in Chicago. She completed her clinical training at the University of Chicago, and is board certified in medical oncology and internal medicine. In clinical practice, she performs hereditary cancer genetic testing, and provides personalized cancer screening and prevention recommendations. Her research includes refining risk assessment and screening approaches for patients at elevated risk for cancer. She's part of the research team for Endeavor Health's unique population screening genetic testing initiatives, including the genetic wellness assessment and breast health assessment. Dr. DePersia will be presenting on the latest research about high-risk screening that came out of ASCO. Over to you, Dr. DePersia.

Allison DePersia:

Good evening. Good to see everyone. I’m Allison DePersia. And as was shared, I practice high-risk cancer screening and prevention. I'm going to share my slides now, and highlight two topics that were of interest at the annual ASCO meeting. Let's see if I get this right.

Okay. So I'm going to talk about novel screening opportunities that were discussed. Primarily, there was a lot of interest and discussion around multi-cancer early detection tests, or MCED tests, which many of you may have heard of or even seen commercials for on TV, and

then talk about updated data for breast cancer risk reduction with low-dose tamoxifen.

I apologize, there's a green box around my text that is not perfectly placed, but I think everyone can probably see things. So there were a number of patients…

Devorah Silverman:

We're just missing the top line, but that's okay.

Allison DePersia:

Yeah. Sorry, that wasn't in my own formatting. So there were a number of presentations around multi-cancer early detection tests. These are just a few of the different presentations that were discussed. But first I thought to review just for patient awareness and for the audience what are we talking about here, and why are we interested in multi-cancer early detection? So I think we're all aware that cancer is common and we screen for cancers where we have effective screening modalities that show a population benefit. In the end, that means that we screen for a few common cancers in the general population, but there's many cancers that we all share a risk of that we don't screen for at this time. And that's because those cancers are less common and may not have effective screening modalities that can be available to a broad population at a reasonable cost and risk-benefit ratio.

And so this is just sort of a visual showing that the common cancers we screen for are breast cancer in women, cervical cancer, prostate cancer in men, and then colorectal cancer in men and women. And then there are lung cancer screening guidelines for smokers. Otherwise, we sometimes screen for things like pancreatic cancer in high risk individuals. We don't have effective ovarian cancer screening as I think many on this call are aware. And so there are lots of opportunities to screen for other cancers that are not as common, but certainly affect many people.

And one area of interest is, is there a blood test that we could do to screen these cancers? And that's really what multicancer early detection testing is about. So a multicancer early detection essentially uses something called a liquid biopsy to look for circulating tumor DNA. So this visual is just essentially highlighting that, in our bloodstream, there are many different types of cells that are constantly breaking down. So our blood cells are breaking down, healthy cells renewing themselves as they age. And as a healthy cell breaks down and renews itself, it releases the DNA into our bloodstream. And potentially, you can draw the blood and look at that DNA signature. So likewise, if you have an early cancer that's developing, as that cancer grows, the cancer cells are breaking down and continuing to grow and releasing pieces of DNA. And so the idea behind multicancer early detection is that you can do a simple blood draw and look at a very, very close

deep level for abnormal DNA that's in the blood that might be related to an early cancer.

Essentially, this image is just talking about where this might fall into screening modalities. So at the far left, we have cancer onset. And then shortly after that, the expectation is that the cancer, as it's developing, like I said, cells are growing and also dying, and DNA is starting to be released. And that in many instances happens before the cancer reaches what we call a clinical level of detection. So a size or growth that's reached where we might see a cancer on a screening or imaging modality or before a patient might have symptoms.

And so the idea with multi-cancer early detection tests is that you could take a blood sample, like I said, look for this abnormal DNA, and then be able to recognize that this patient may have an early cancer that they don't have symptoms of. And if it's a cancer that we don't typically screen for, this could be a signal or reason for us to do imaging to look for that type of cancer. Or if it's a cancer that we do screen for, but a patient hasn't had that screening in some time because it hasn't come due, we could even do screening before that study was due, for example, in a diagnostic way.

And so the study that was highlighted was the NHS-Galleri trial…this was a randomized control clinical utility trial. It had 142,000 participants. This was not specific to high risk, but certainly some of these patients may have been high risk, and they received three annual screening rounds of a multi-cancer early detection test. The primary endpoint of this study was to look for a decrease in stage three or four cancers, thinking that that would be a surrogate for increased overall survival. That endpoint was not reached in this study, but there were a lot of interesting secondary endpoints that were reached that I still think support the idea that multi-cancer early detection testing may have a place for cancer screening in the future. So overall, there was a reduction in stage IV cancer seen by 14% compared to the groups who are not doing this. There was an increase in stage I and II cancers, so seeing more early cancers, which are the cancers that we'd expect to be more treatable and curable.

Overall, there was just an increase in screen-detected cancers versus cancers that were presenting based on clinical symptoms. And there was a decrease in cancers that were seen through emergency presentations as well. Also, really important, notable, whenever we think about a new intervention or study is to think about the risk and benefit. And so even if you're showing benefit to screening, what could be the downsides or risks? And so there were no serious study-related adverse events from the blood collection or return of results. But even more importantly, there was an independent data monitoring committee that also looked for any concerns with the safety of follow-up testing that was done after the multicancer detection testing.

So the way that this works out in a clinical scenario is a patient goes and gets their blood drawn. They have this test done. If there is a signal for an early cancer, then like I said, they have to go on to do screening or even a biopsy. So even though the actual blood test itself

might not have risk of harm, it's really important to identify whether there are undue bad outcomes related to the additional imaging that patients did, or the diagnostic tests that were needed. And that was not seen as the case based on the independent data monitoring committee.

So thinking about how this could apply in the high-risk setting, so there wasn't any data specifically shared for that group, but there's a lot of ongoing research in this area, and I think this is going to be exciting opportunity for many high-risk patients in the future potentially. So there's probably more, but there's two opportunities that I'm aware of in North America specifically.

So there's the CHARM Consortium, which is a Canadian group looking at cell-free DNA and hereditary and high-risk malignancies. And they've done some interesting preliminary work just looking at, do high-risk patients want to participate in this? What is their interest? And their publication is called I Just Wanted More: Hereditary Cancer Syndrome Patients Perspectives on the Utility of Circulating Tumor DNA Testing for Cancer Screening. And this was a qualitative interpreter description study. And what they saw is that across the board, the high-risk patients who were engaged and interviewed said that they saw the benefits of multicancer early detection, such as it being a more comprehensive screening study that could be personalized as outweighing limitations such as false positives or false negatives. Just recognizing that a positive signal in a multicancer early detection test does not always mean that there is a cancer diagnosis. So there can be false positives, and that's learned as the follow-up investigation is done. And then sometimes there can be false negatives too. And that not all early cancers are necessarily going to be picked up by these tests.

And then there's another study called the INFORM study, which is listed on clinical trials at Dana-Farber, which is also looking at high-risk patients and looking at multicancer early detection tests.

So the take-home is that multicancer early detection tests are a novel screening approach and a focus of ongoing research. More data is needed to inform clinical applications. So these tests at this time should not replace any standard screening, whether someone is an average risk patient when it comes to cancer risk, or someone who's elevated risk. But it is potentially an opportunity to do more screening, to screen for cancers we don't traditionally screen for, or to add additional screening for cancers that we're already screening for. At this time, it's not part of screening guidelines, but these tests are available on the market. And if there is an opportunity to participate in some of these tests through a research study, that's really the ideal way to approach this, because then we can continue to learn about their benefit, and where they should be in the overall approach to screening for both average and increased risk individuals.

And specifically more research is needed to see how this approach might benefit individuals who are at high risk, who might be at

increased risk for cancers that we don't have standard screening for, or can offer standard imaging modalities for.

So the other finding I wanted to comment on was risk reduction for breast cancer and updates on low-dose tamoxifen. And so just background on what is chemoprevention or tamoxifen used for. So chemoprevention is the use of medication, vitamins, or supplements to reduce the risk of breast cancer. In addition, of course, there are other options to reduce risk of breast cancer for individuals at increased risk, lifestyle modification and risk-reducing surgeries such as mastectomy if someone's at increased risk. So medications for breast cancer risk reduction or chemoprevention include selective estrogen receptor modulators such as tamoxifen and raloxifene, and then aromatase inhibitors, examples being exemestane and anastrozole.

Let me go back. Okay. So the idea of chemoprevention is actually an approach to breast cancer risk reduction, which has been available since the late '90s or early 2000s, but overall has not necessarily had great uptake among women at increased risk of breast cancer. Medications to reduce breast cancer risk are outlined by the NCCN guidelines as well as ASCO and other expert guidelines. And in general, the recommendation is to consider these medications for women who have a 10-year risk of breast cancer that is 5% or greater according to a risk model such as Tyrer-Cuzick, which is used to calculate a woman's lifetime breast cancer risk if she has personal or family risk factors, or a five-year risk using the Gail Model that is greater than 1.7%.

And with the Gail Model, I'll just mention that some of the five-year risk estimates also look at a woman's decade of life and the risk-benefit based on her specific age, too. And then chemoprevention can also be used in women who have a history of lobular carcinoma in situ or typical hyperplasia, which are high-risk breast lesions that tell us about increased future risk of breast cancer. And then there's currently limited data for mutation carriers for chemoprevention. In big part, this is because many of the studies that were done to evaluate these medications to reduce breast cancer risk actually took place before hereditary cancer genetic testing was widely available. And so presumably there were many women who had a genetic risk of breast cancer, but we didn't know their mutation status at the time of testing. And so there's a little bit of retrospective data in BRCA1 and BRCA2 cases, which primarily shows us chemoprevention benefits for BRCA2, but there's really limited data for mutation cures at this time.

That being said, many women with an inherited risk of breast cancer due to a mutation might have a five or 10-year risk that exceeds the numbers on this slide just based on the lifetime risk estimates we know for those patients.

And so specifically with tamoxifen, this is a drug that has been readily available for well over 20 years for breast cancer risk reduction, but has not seen great uptake. There are multiple data points out there, but one study had referenced that 15% of women might be eligible for chemoprevention, and less than 5% of women uptake it of all the

eligible women. So really not very good uptake. And the main reason that there's hesitation I think is because many patients don't want to take a medication unless they're told they have to. And so taking something like tamoxifen is proactive for risk reduction, but it's not a diagnosis or a setting where you're being told you have to take a medication to treat a breast cancer, because these are women who have an increased risk, but we don't know if they will actually go on to develop breast cancer. The benefit is that it offers 50% or greater breast cancer risk reduction for the populations where it's been studied. So these increased five or 10-year risk for the women who have these high-risk lesions.

But there can be adverse effects of the medication too. The most common are menopausal type symptoms, but then there also is an increased risk of DVT and an increased risk of uterine cancer. Although for the majority of high-risk women who don't have any competing comorbidities or other predisposition to DVT or uterine cancer, the benefits are thought to outweigh the risk for many of these women.

And so the question with low-dose tamoxifen, and some of this data really started coming out in around 2018, 2019, but the idea being 20 milligrams tamoxifen is the current standard dose recommended, but could we actually dose reduce and see continued benefit from a risk reduction standpoint for breast cancer, but see fewer adverse events, so the menopausal symptoms, but also some of the medical adverse events as far as risk of blood clot or uterine cancer. And so this most recent data that was shared by researchers, Jasinski and colleagues, looked at low-dose tamoxifen, which is five milligrams daily or 10 milligrams every other day, which is also called baby-tam. And it was a pulled analysis of three studies with over 10 years of follow-up, looking at baby -tam versus placebo, specifically in women who were at increased risk due to DCS or due to a high risk lesion. And they were looking at breast cancer-free interval.

And so one of the outcomes that was of interest, and I think notable was in premenopausal women they saw a decreased contralateral breast cancer risk. And so this idea really supports the possibility of low-dose tamoxifen being appropriate for primary prevention for breast cancer in premenopausal women. We already had data to support this in postmenopausal women. This is more data to support it in premenopausal women. And when a lower dose of tamoxifen was given, what they saw is, compared to a population who did not take a medication that is, so not comparing 20 milligrams to five, but comparing five milligrams to no medication, they saw no increase in serious adverse events. So they did not see an increase in menopausal symptoms, or statistically significant increased risk in blood clots or uterine cancer, but they did see a significant benefit as far as decreased incidence of a new breast cancer in patients who were taking this medication.

And so the take-home here is that baby-tam may be adequate for primary prevention in premenopausal women. This is already a practice I think for some, but really more additional data to support this

approach in premenopausal women in addition to postmenopausal women. Further research is needed to understand if this approach could also be appropriate for women at increased risk based on family history or pathogenic variants, because this population really focused on women who had high-risk lesions. But exciting data nonetheless.

Devorah Silverman:

Thank you so much, Dr. DePersia. There's a lot to be excited about in what you've shared. Great. Okay. So we'll move on to our next speaker. Dr. Amy Comander, fellow of the American College of Lifestyle Medicine, is a breast oncologist and medical director of the Mass General Brigham Center Institute in Waltham, Massachusetts, Director of the Lifestyle Medicine Program at the Mass General Brigham Cancer Institute, and an instructor in medicine at the Harvard Medical School. As a breast oncologist, Dr. Comander has witnessed the struggles her patients face during and following completion of primary cancer treatment, and she's passionate about improving the overall health and wellbeing of breast cancer survivors through lifestyle interventions. In collaboration with Dr. Beth Fritz, she launched the PAVING the Path to Wellness Program: Lifestyle Medicine Program for Breast Cancer Survivors. She has co-authored PAVING Your Path Through Breast Cancer and Beyond, which focuses on the role of evidence-based lifestyle interventions for cancer survivors. It's my pleasure to turn the floor over to Dr. Comander, who notably serves on Sharsheret's medical advisory board. Dr. Comander.

Amy Comander:

Hi. Thank you so much for that very kind introduction. I'm so honored to join you all tonight, and I really enjoyed that presentation. So I'm going to bring up my slides, and just give me a second here. So funny, we practiced this before, and now where did they just go? One second. Go to browser tabs. Oh, here we go. Somehow everything else on my screen decided to appear just now except for my slides. Okay, we're getting there. Are we seeing them okay? Do I need to change the view?

Devorah Silverman:

You need to change the view.

Amy Comander:

Okay. We're good now, right? Okay, perfect.

Devorah Silverman:

There you go.

Amy Comander:

So thank you for your patience, everybody. I'm so honored to share with you some highlights from this year's ASCO, specifically focused on breast cancer. And I'm going to try to limit this to 12 minutes, which was the assignment.

So I just thought I'd start off with a reminder that when we think about breast cancer, we know there are many subtypes of breast cancer, and how we think about the treatment really depends on the subtype and the biology of the tumor. So we know that the majority of breast cancers diagnosed in the United States are what we call hormone receptor positive, as shown in this green panel. And that means they often overexpress receptors for estrogen and progesterone, and can be what we call HER2-negative. We also know that there's a subset of breast cancers that are HER2-positive, which means they overexpress a gene that encodes this receptor called HER2, and that comprises about 15 to 20% of breast cancers in this country.

And then finally, the third subtype I will focus on are what we call triple negative breast cancers, which comprise approximately 15% of breast cancers in this country, and they do not express the estrogen or progesterone receptors or HER2.

So in the purpose of tonight’s event, I'm going to discuss two studies related to early-stage breast cancer, and then one study related to advanced breast cancer, and certainly we'll have time for questions at the end.

So the first study I wanted to highlight, which was a really interesting study presented called the Optima phase III randomized trial, which is really trying to, it was what we call a non-inferiority trial, looking at the role of using this test, which I'm going to get to in a second, to determine which patients really need chemotherapy, and can we refine who we are actually giving chemotherapy to. And so the background, as many of you are familiar with tumor gene expression assays, I'm sure many here who have a history of breast cancer are familiar with the Oncotype test or the MammaPrint test. So increasingly, we're using these gene expression assays in our clinic every single day with our patients to determine who should get chemo or who would not benefit from chemo.

And the majority of the time early on, these were studied primarily in postmenopausal women, but increasingly now we have data for the use of these tests in premenopausal women. But interestingly, the data thus far really has been for individuals with breast cancer that may involve one to three involved lymph nodes. In general, we don't have data using these genomic assays in patients with more than three lymph nodes. And that's why this trial was particularly interesting, because they hypothesized, the researchers, that the number of involved lymph nodes should not affect the chemotherapy response if the tumor has a low-risk biology, as determined by one of these gene expression assays. And so in this particular study, they did use a test that many of us are now learning about. It's called the Prosigna test, which uses 50 genes, and it's now available in the US since the ASCO meeting. So we'll be hearing more about this. And tumors which had a

score greater than 60 were considered a high-risk tumor. And so let's look at the data a little bit more and how they did this study.

So this is a slide from the ASCO presentation, which shows who was eligible for this study. So women and men, aged greater than 40, who had their breast cancer excised, it had to be estrogen receptor positive, HER2-negative, and individuals could have zero to nine positive lymph nodes. And so I think that's a really important thing to focus on for this study, that it involved patients with multiple positive lymph nodes. And so patients were consented, if you look at the bottom panel here, and then they were randomized. And so if they were randomized to the test-directed arm, then their tumor was sent for this gene assay called Prosigna, and the result was determined. And if it was a low score, namely under 60, they received endocrine therapy or anti-estrogen therapy alone. And if it was a high score greater than 60, the patients received chemo and endocrine therapy.

So that's what the test-directed arm did. Really, how does this assay help us? And then the control arm, these patients got chemo and endocrine therapy. And just to highlight the results, which is indicated on the next slide, really the goal was to say, can we potentially eliminate use of chemotherapy for individuals where it's not providing a benefit? So this trial was very impressive. They had well over 4,000 patients enrolled over nine years from multiple countries. And essentially, they found that for those individuals who did have a score under 60, even with multiple positive lymph nodes, that they did not derive a benefit from the chemotherapy. And that included women who are premenopausal, who are over age 40, but again, with multiple positive nodes.

So I look at this trial as showing us another gene expression assay that we can use in our clinic now in the US as part of our toolkit to determine who really needs chemotherapy, because certainly we don't want to over-treat our patients with chemotherapy. So that's the Optima test, and happy to talk about that Optima trial more later.

Another hot topic at the ASCO meeting is this drug giredestrant, which many of you have heard about and perhaps are asking your doctors about it. I know I get many questions from my own patients about this study. So this is called the lidERA trial, which was presented at another major meeting many months ago, but this was an update of this trial looking at this exciting drug, giredestrant, specifically looking at results based on the menopausal status of the participants.

And I included this slide because I think sometimes it's very confusing to think about the mechanism of all these different drugs. So in the presentation we just heard, we learned about tamoxifen or baby-tam, as I like to call it. So if you look at this panel, how is tamoxifen working? So the little pink circle is estrogen. Tamoxifen is the arm circle, and basically tamoxifen is what we call a selective estrogen receptor modulator. So it's competing with the woman's endogenous estrogen to bind to this estrogen receptor. And so if the tamoxifen binds to and changes the confirmation of the receptor, and basically

prevents it from going into the nucleus to do all the things that estrogen can do in the cell. So that's how tamoxifen's working.

Aromatase inhibitors work differently. We know that aromatase inhibitors end up reducing the production of estrogen in the body. So if we go to this panel where I hope you see my little cursor here, so how do selective estrogen receptor degraders like giredestrant work? So giredestrant's the little green ball, and pink is estrogen. So basically, again, the giredestrant is hoping to bind to the receptor before the estrogen, and then it causes degradation of the receptor through this very complicated process, which I won't get into all that, but basically it's going into sort of like a trash can in the cell and degrading the estrogen receptor. So that's how this drug giredestrant and other selective estrogen receptor degraders work.

So let's talk about this drug, which is very exciting. So basically in this particular study, the lidERA study, patients did have to have early stage estrogen sensitive HER2-negative breast cancer, stage I through III. If they were stage I, the tumor had to have some adverse features. For example, if it was greater than one centimeters, if they had to have a grade III tumor, or an elevated KS67 score, or a high score on a genomic assay, MammaPrint, Oncotype, or they could have a node positive tumor, they could be pre or postmenopausal. And essentially over 4,000 women were in this study, and they were randomized to either get this drug, giredestrant, estrogen receptor degrader versus standard of care, which could be tamoxifen or an aromatase inhibitor. I do want to make the point that the premenopausal women on this study also received ovarian suppression. In addition, men on this study received ovarian suppression. So I think that's an important thing to keep in mind as we interpret the study.

The primary endpoint was something called invasive disease-free survival, looking at time if there's going to be a recurrence, and then there were additional endpoints noted below. And so I think what's really important about this drug, and why there's a lot of excitement, is the lidERA breast cancer trial demonstrated a statistically significant and clinically meaningful invasive disease-free survival improvement with giredestrant over the standard of care endocrine therapy. So if you go out to three years, which is what the follow-up was that was reported, the invasive disease-free survival, meaning a time to a recurrence, was 92.4% versus 89.6%. So basically the individuals who were taking the giredestrant had a lower likelihood of reduction in terms of developing some type of recurrence.

So that is exciting. And I should note, they of course highlighted the common adverse events that were noted for folks. So the purple is giredestrant, the gray is standard of care. We know that in standard of care endocrine therapy, arthralgias or joint pains and hot flashes are very common. So those were certainly seen in the standard of care arm. They were also seen in the arm of patients who were receiving arthralgias, hot flashes, headache. So they were actually comparable. But what is interesting is that fewer individuals discontinue the giredestrant compared to standard of care regardless of menopausal

status. So that does suggest to me that I hope it's better tolerated so our patients could comply with their endocrine therapy and feel better and have improved quality of life.

So this lidERA trial is a very important study to be aware of. And it does suggest that for the higher risk tumors, there is a benefit to being on this medication compared to standard of care endocrine therapy, but also acknowledging that the premenopausal individuals on this study did receive ovarian suppression, which we know does add additional side effects and toxicity. So something to keep in mind, it is possible this drug will be FDA approved. I see perhaps November, that's what I've read most recently, so stay tuned. But right now we would not prescribe this medication since it's not yet FDA approved for early-stage breast cancer.

In my last few minutes, I'm going to give one quick highlight about a study that was presented for advanced breast cancer. There were many studies I could have chosen, but I decided to focus on one related to triple negative breast cancer. And I also just wanted to show one of these helpful figures highlighting another very exciting class of drugs in the field of breast oncology, namely antibody drug conjugates. These are so exciting. Take a picture of the slide if you really want to look at it later and understand how these really cool drugs work. But basically, the green part here is showing that this is an antibody that's targeting an antigen or a little signal on the surface of the cancer cell. And what I love about these drugs is that they're bringing along with them a cytotoxic agent, the actual chemo, and targeting it to the cancer cell, which is pretty cool.

And once it gets inside the cancer cell, the antibody is essentially, the cytotoxic agent is kind of getting released into the cell, and therefore damaging the cell, or into the microenvironment around where the tumor is and causing the tumor to die. So very, very cool class of drugs. Many of you maybe have heard of sacituzumab-govitecan, also known as Trodelvy, trastuzumab-deruxtecan, also known as Enhertu, and there's more and more on the horizon. So very exciting. And I love sharing this figure because I think it explains it quite well.

So this study, which was highlighted at ASCO this past year, was called the ASCENT-04 study, looking at the role of this regimen, sacituzumab-govitecan, an antibody drug conjugate, along with pembrolizumab, which is immunotherapy, again, harnessing our immune system to fight the cancer, versus chemotherapy and pembrolizumab in patients with previously untreated PD-L1 positive metastatic triple-negative breast cancer.

So what does that mean? That means these are individuals newly diagnosed with triple-negative breast cancer that their tumors do overexpress this marker called PD-L1, which suggests that the tumor will respond to the immunotherapy. So this combination is now a very novel combination that we can use to treat individuals with advanced triple-negative breast cancer. And very exciting, because it’s really showing how much the field is changing even over these recent years.

So in this particular study, we know that this particular combination of sacituzumab-govitecan and pembrolizumab versus chemo plus pembrolizumab is beneficial in the first-line setting. But specifically the researchers are trying to uncover, are there certain subtypes within triple-negative breast cancer that may or may not derive benefit from this regimen? So they analyzed the tumor specimens for the individuals in the trial looking at something called Trop-2 expression, which is the antigen that the sacituzumab-govitecan is targeting, or BRCA expression, or HER2 biology. So they were looking at these various biomarkers within the triple-negative breast cancer to see, could they see any associations here.

And I think, just to go through this quickly, again, they did this analysis. And I think what's important to note is that this combination was meaningful in the individuals with all the different biologic subtypes. So for individuals with advanced triple-negative breast cancer that overexpress this marker called PD-L1 positive, PD-L1, which means it would respond to immunotherapy, all the different subgroups, whether they had BRCA expression, HER2 expression, Trop-2 expression, all derived benefit from this regimen. So I think that's very exciting and just shows that this is another really powerful drug combination that we can use to make a difference for individuals with advanced triple-negative breast cancer.

I know I spoke really fast. I wanted to stay within 12 minutes, but happy to take questions later. So thank you.

Devorah Silverman:

Thank you so much, Dr. Comander.

Okay, our final speaker for this evening is Dr. Deanna Gerber, a gynecologic oncologist at NewYork-Presbyterian/Weill Cornell. Dr. Gerber specializes in the treatment, prevention, and management of cancers of the female reproductive tract. She's passionate about raising awareness about the complex needs of cancer survivorship, and advocating and educating survivors and caregivers so that they can feel informed and empowered. Dr. Gerber.

Deanna Gerber:

All right, let me pull up my slides. Thank you for that lovely intro. You can see my slides?

Devorah Silverman:

Yes. Perfect.

Deanna Gerber:

So ASCO this year was very exciting. Everyone on this call, and probably Sharsheret, knows that breast cancer, there's always a lot of new practice-changing things that come out. And every few months we're adding new medications that are FDA approved for breast

cancer. But ovarian cancer doesn't get as much research, and there's not really as much that's changing the practice. But ASCO this year really gave a lot of food for thought about what the future of ovarian cancer treatment might look like.

So when we think about the spectrum of ovarian cancer treatment, we have upfront, so we have women who are newly diagnosed. And in that setting, we have to decide if you get neoadjuvant chemotherapy or surgery. There's two trials I'm going to present that are in this upfront setting in women who are receiving neoadjuvant chemotherapy, meaning they're getting chemo first followed by surgery eventually.

So the CHRONO trial looked at the question, when is the best time to have surgery in women who are undergoing neoadjuvant chemotherapy? What we typically do now is three cycles of chemotherapy, surgery, then additional chemotherapy, and that's how the initial trials were designed. And so the authors of this study thought, "Is it beneficial to give you more chemo first and then do surgery?" And so women in this study were advanced ovarian cancer who were getting neoadjuvant chemotherapy. The control arm was women who had three cycles of chemotherapy, and then had surgery followed by five cycles. That's the controller and the standard arm. Then experimental arm, arm E, was they got three cycles of chemotherapy that were randomized into the trial, and then got an additional three cycles of chemo followed by surgery and then two cycles. So that's more than we normally give neoadjuvant chemo.

The primary endpoint they were looking for was disease-free survival. And so what they found was that there is no significant difference in disease-free survival. They were approximately the same, 20 months versus 23 months. It was not statistically significant. But they did find that both were safe, both yielded essentially same oncologic results, but that social functioning, insomnia, and sexual health were better in the experimental arm. So women who were getting chemo first. So while we didn't see a true result in the disease-free survival, there was some benefit, and this did yield a lot of information for the gynecologic cancer community.

Another trial that I think is fascinating was investigating the effects of short-term fasting compared to normal diet in ovarian cancer patients. Again, this was in women receiving neoadjuvant chemotherapy. The study question was, could short-term fasting help chemotherapy work better? This was a pilot study, only 18 participants in each arm. It's just really to see if this is feasible. So the control arm, the standard arm was the free diet. So women had normal eating habits leading into chemotherapy before, the day of, and afterwards. In the experimental arm, women fasted for 36 hours prior to each chemotherapy, and then again afterwards. During the fasting window, women were allowed to consume a maximum of 350 calories and were restricted to herbal tea, water, vegetable juice. And so it was a very standard diet of fasting.

What they found in this study was that in the fasting group, there was lower insulin levels, which we think helps fight cancer better. And that translated, they saw an improved pathologic response rate. So in the

fasting group, 60% of women had a complete pathologic response compared to just 17% in the control group. And this is at the time of surgery, which is usually after three cycles of chemotherapy. And so they also found an improved progression-free survival in the fasting group. Side effects were similar. And so the bottom line here is that short-term fasting may help chemotherapy work better, but this was just a pilot study, and there's a lot more research that needs to be done before this becomes standard of care.

Before we move on, I want to just give a quick reminder about how we think about treatment of recurrent ovarian cancer. It's this paradigm called platinum resistance. And so women who have their recurrence of their cancer within six months are considered platinum resistant, and women who recur after six months and on are considered platinum sensitive. And that is how all of our trials are designed. That's how we as oncologists also think about which phase and which treatments to use.

And so I'm going to review a few platinum-sensitive trials and a few platinum-resistant. Dr. Comander already went through what an antibody drug conjugate is, so I don't have to go through this slide, but it's very exciting for all oncologists, this new technology. And I'm going to review some ADC, some antibody-drug conjugates.

So MIROVA is a trial. Many people on this call may have heard of mirvetuximab-soravtansine, affectionately called MIRV, also known as Elahere. And so this drug has been FDA approved in the treatment of platinum-resistant ovarian cancer, was FDA approved in 2023 with a groundbreaking trial that showed improved overall survival and progression-free survival in platinum-resistant patients.

The study question in this case was, can MIRV be used earlier in treatment? So women were randomized to receive... So this is platinum sensitive, meaning they received platinum-based treatment, carboplatin. With MIRV, they were either MIRV plus carboplatin followed by MIRV maintenance, or carboplatin plus another standard agent, paclitaxel, gemcitabine, doxil, and then a different maintenance medication. They did not find a difference in progression-free survival in this study. And so they didn't find a progression-free survival difference, but they did find a difference in objective response rate, which means that the cancer went away, but it still recurred in the same time despite the arms. And so the conclusion of this arm is it didn't really yield a progression-free survival difference. And so for this point, MIRV will likely be only used in the platinum-resistant setting.

Another trial that I thought was really exciting was the Tedova trial. It's a vaccine approach to ovarian cancer. And so back to something Dr. Comander was saying is that immunotherapy and the immune system is really, really important for treating cancers. Ovarian cancers are technically considered cold tumors, meaning they don't have a robust immune response. So the immune system doesn't really work to help fight ovarian cancer generally, but this vaccine turns a cold tumor, so a non-immunogenic tumor, into a hot tumor, which means that immunotherapy may work to treat. And so the way this study was set

up is that women with platinum-sensitive ovarian cancer were randomized either to get their standard treatment for at least four cycles with platinum-based chemo. And then after were randomized to either best supportive care, so whatever the oncologist would do in a normal setting versus the vaccine alone in arm B, or arm C, was vaccine alone plus pembrolizumab, Keytruda, which is one of our best used immunotherapies.

And so what they found was that in the experimental arm in women who received the vaccine plus the pembrolizumab had a longer progression-free survival, so it did have a benefit. And so this is exciting from my standpoint, as this is one of the first studies that showed that a vaccine is beneficial in women with recurrent ovarian cancer. Again, not at all standard of care, but it's just proof of concept and really exciting for, again, for someone like me who we don't really have groundbreaking studies like this in gynecologic cancer often.

Another target I think that was really exciting is this study called NAPISTAR 1-01. NaPi2b is an antigen - it’s a signal that's overexpressed on many tumor types, especially in high-grade ovarian cancer. TUB-040 is an antibody drug conjugate that targets this specific antibody and provides chemo into the cells. So this study was really just looking at the optimal dose of this ADC and when to give it. And so what they found was, with the use of this ADC, the progression-free survival was 11 months. This was not a comparison, it wasn't comparing two different treatments, but they found that progression-free survival was 11 months. And that over three quarters of women remained in response for more than six months, which in ovarian cancer is a very great response. It was well tolerated. I just want to present this one, because it just shows that things are evolving. We're looking at new targets, new ways to treat ovarian cancer beyond just the ones we know of. And this is really exciting.

Another study that you may have heard of is the ROSELLA study. The ROSELLA trial was presented several months ago at a different meeting. It uses two medications, one that's novel to ovarian cancer. Relacorilant is an oral drug that increases tumor sensitivity to cell death. So it causes tumors to shrink more. Used in combination with nab-paclitaxel, or Abraxane. So this combination, which was presented previously, was presented mainly just for the progression-free survival benefits, and it was shown to have a significant improvement in progression-free survival. And so this combination a few months ago was FDA-approved for treatment of platinum-resistant ovarian cancer.

And what was presented at ASCO this year was the final overall survival analysis. And it showed that this treatment had a statistically and clinically significant improvement in overall survival. Improvements in overall survival in a platinum-resistant cohort, it's really meaningful, it's really profound, and so this is very exciting. We were very excited to see this final overall survival readout. And so the overall survival was improved by over four months.

And so this combination, you will hear about it. It's the newest big thing in platinum-resistant ovarian cancer treatment, the relacorilant plus Abraxane, nab-paclitaxel. And then how much time do we have?

Devorah Silverman:

Another minute or two.

Deanna Gerber:

Okay. I have two quick trials. I'm not going to go through the details of them, but PRESERVE-004 was a study that looked at two non-chemotherapy options. So this medication, Gotistobart, which is a next-gen immunotherapy combined with pembrolizumab again, which is not usually helpful in ovarian cancer, because ovarian cancer, again, isn't immunogenic. But they looked at combining these two medications, finding the optimal dose, and it importantly provided a chemo-free, so no cytotoxic chemo without the cytotoxic chemo side effects. And what this study found is they figured out the optimal dose of this experimental drug, and they also showed a meaningful improvement in overall survival with the lower dose. It was relatively well tolerated. And so this is not yet on the market, but it's another meaningful result in platinum-resistant ovarian cancer.

Last one, another medication combined with weekly paclitaxel, Chiauranib, showed improvement in progression-free survival as well. Overall survival was not affected. But again, really I'm just showing that there's a lot of new targets and a lot of new exciting stuff going on in ovarian cancer research, and it's providing me with a lot of hope as a GYN oncologist, and hopefully to this audience as well.

And yeah, that's all I got.

Devorah Silverman:

Thank you so much. Really thank you to all three of you for sharing information about these exciting new treatment options. It's wonderful to hear.

We're going to move into our Q&A session, and we are very short on time, so I'm just going to ask a couple of questions and ask you to try to focus some quick responses. I'm wondering if one of you could share a little bit about hormone replacement therapy. There were a lot of questions about if there's anything new being discussed about safety, premenopausal, post-menopausal, pausing HRT during pregnancy, endocrine therapy, anything that's related to that world. Who would like to take that one?

Amy Comander:

I'm happy to jump in.

Devorah Silverman:

Great.

Amy Comander:

I know in my own clinic, my patients are asking me about this all the time. It's certainly a hot topic for anyone on social media these days. And I will say, as a breast oncologist, which I will speak to, not to ovarian cancer survivorship, I can let Dr. Gerber comment if she would like, but I will say, as a breast oncologist, when I'm talking to my patients about managing people who have a history of breast cancer, estrogen sensitive was actually showed in my slide 70%, we first are really doubling down on our non-hormonal strategies, of which we have many, of which there was an exciting drug update presented at ASCO. I didn't have time to talk about it. It's called elinzanetant, or Lynkuet, which really shows dramatic improvement in hot flashes and improvement in sleep for women with breast cancer. That's just one example of a great tool in our toolkit.

So we really try to optimize the use of these non-hormonal approaches. I will say there is certainly evolving research and interest in looking at which populations we may safely be able to give hormone replacement therapy to. For example, vaginal estrogen. Increasing research has demonstrated the safety of that, even for individuals with estrogen-sensitive breast cancers.

I just want the person who asked this question or the people that we are listening, we're aware, we are studying it, but this is definitely a work in progress. That was my quick answer.

Devorah Silverman:

Okay, great. Thank you. Dr. Gerber, any new... Sorry, go on, Dr. DePersia.

Allison DePersia:

Oh, I was just going to say, for high-risk women, if that is a question or consideration as far as hormone replacement and specifically BRCA1 and 2 carriers, this was not at ASCO, it was a few months before, I can't remember what conference, but there was some data that came out to show that hormone replacement is safe, reasonable, and appropriate for women who have inherited BRCA1 or 2 pathogenic variants who are postmenopausal, who choose to keep their breast tissue. So combined hormone replacement, they saw a neutral effect of hormone replacement on breast cancer risk for those women. And there's been support and recommendations for women to take HRT after they have first reducing removal of their tubes and ovaries or go into menopause, but then actually for estrogen only. So for women who had an increased risk of breast cancer due to BRCA and chose to have their tubes and ovaries removed and maybe had their uterus removed as well, and were taking estrogen only, there's actually a signal for decreased breast cancer risk in those patients.
I think there's a lot of awareness around that, but I still do see plenty of patients who have the risk reducing surgeries for ovarian cancer risk

due to BRCA1 and 2, and are not put on hormone replacement therapy. I think there's definitely consensus that those women should be on hormone replacement. We maybe don't have to say exactly how long that is safe or appropriate, but the study did show the average median follow-up I think was six years of women being on hormone replacement, and the average age was the early 40s. So really looking at women who are continuing hormone replacement until an average age of menopause, which I think is really meaningful for bone, cardiovascular health, neurocognitive health, and then quality of life, of course.

Devorah Silverman:

Are there any new options for those who are triple negative and PD-L1 negative?

Amy Comander:

Yes. So we shared the excitement about the antibody drug conjugates. So sacituzumab-govitecan, which is also called Trodelvy, that is an option, very exciting. And I always have a hard time pronouncing it, but datopotamab, I'm so bad at pronouncing these drugs, it's also called Datroway, that's another antibody drug conjugate that is new and hot off the press. So for individuals who are PD-L1 negative, they can consider that.

I think there was also a question, what if you're BRCA positive? We have our friends, the PARP inhibitors, which are awesome, which can be used as well for treatment of triple-negative breast cancer that's advanced. And platinum chemotherapy has certainly been shown to be beneficial.

So again, lots of new tools, depending on the biology of the tumor, which is very exciting, especially for triple-negative breast cancer.

Devorah Silverman:

Okay. I'm sorry to say that we're already at time for this part of our webinar. I want to remind everybody that you will be receiving a copy of the recording and the transcript from this webinar, and you'll be able to review and listen a little bit more slowly and perhaps repeatedly listen to these amazing presentations.

And thank you for submitting so many questions. Apologies, we couldn't get to all of them. We're so grateful to doctors DePersia, Comander and Gerber. Thank you for sharing so much and for helping us understand the new research that was presented at ASCO. And thank you for your time this evening.

I want to ask everybody, please take a moment to fill out a brief evaluation survey, the link for which is being put in the chatbox now. Your feedback really does help us shape our future programming.

And if you're a member of our Embrace community, someone who's facing metastatic breast or advanced ovarian cancer, we invite you to stay on the Zoom for a more intimate breakout session, sponsored by Lilly and Pfizer, with Doctors Amy Comander and Deanna Gerber. I'm going to ask my colleague to just one more time put Sharsheret's

contact information in the chatbox. Remember that we're here for you and for your loved ones, and the services that we provide are free and confidential, so we hope you'll reach out if we can support you.

As we come to a close, I want to thank all of you for participating in tonight's webinar. Again, here's the evaluation link in the chatbox. And in just a moment, we will turn to our Embrace Breakout Group, facilitated by my colleague, Bonnie Beckoff. Thank you all so much, and enjoy the rest of your evening.