

Emerging Advances in Ovarian and Gynecologic Cancer Care

National Webinar Transcript

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Presented by:



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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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Jenna Fields: Thank you so much for being here. I am Jenna Fields. I'm the Chief Regional Officer of Sharsheret, and thank you for joining us for Emerging Advances in Ovarian and Gynecologic Cancer Care with Dr. Beth Karlan, Professor and Vice Chair in the Department of Obstetrics and Gynecology at the David Geffen School of Medicine at UCLA.

For those of you who are not familiar with Sharsheret, we provide free, virtual personalized support, lifesaving education, financial assistance, and genetic counseling to empower those faced with or at increased genetic risk of breast cancer and ovarian cancer. For everyone on this call facing ovarian cancer and other gynecologic cancers, please know that Sharsheret is here for you during this September's Ovarian Cancer Awareness Month and throughout the year as you navigate your cancer.

As part of this month's Ovarian Cancer Awareness Month, Sharsheret is bringing you our annual marquee event, Sharsheret Summit, which runs from September 18th through October 23rd. You can join all of our national virtual symposiums on the latest hot topics in breast cancer and ovarian cancer. You can attend or host an in-person education and awareness program in your community, or you can learn about the latest screening guidelines and access the most up-to-date data and materials in our digital resource packet. And my colleagues are putting everything about Sharsheret Summit in the chat right now. Please don't forget to register for our incredible lineup of programs, including topics about AI, GLP-1s, and cancer, and more. Come to us to get your questions answered.

I'd like to thank our sponsors for tonight's program, Merck, and the sponsor of our Embrace breakout this evening, Lilly and Pfizer. Our 2026 Sharsheret Summit sponsors include AstraZeneca, Eisai, GSK, Lilly, Pfizer, Smart State, and Weill Cornell Medicine Department of Genetics and Personalized Cancer Prevention, as well as Cooperative Agreement 24-0061 of the Centers for Disease Control and Prevention. Thank you to all of our Summit national partners as well, the incredible nonprofit organizations who you saw on our opening slide. Without their support, we wouldn't be able to bring you this important educational information.

And just a few housekeeping items. Tonight's webinar is being recorded and will be posted on Sharsheret's website along with the transcript. Participants' faces and names will not be in the recording. If you would like to remain private, you have the option to turn off your video and rename yourself, or you can call into the webinar. We also have closed captioning available and you can display live captions by clicking 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 this call. We will hold a Q&A at the end of the presentation, and if you have any questions, you can just type them in the chat box as we go, and we will get to as many as we can during the Q&A. And we really do appreciate you keeping your questions as general as possible, as we cannot comment on specific medical concerns.

After the official program ends, we will continue with our Embrace breakout session that is specifically designed for those facing ovarian cancer or metastatic breast cancer. You are invited to stay on at the end of the webinar for this intimate session with Dr. Karlan and Bonnie Beckoff, our Director of Sharsheret Support Services. 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. And our full disclaimer is in the chat for you right now.

Finally, I'm happy to share that this year, Sharsheret launched our Maidenbaum endometrial cancer program, which provides tailored support to those facing endometrial cancer. You can learn more and access support through the link in the chat right now.

Before we welcome our expert speaker, Dr. Beth Karlan, we are now very thrilled to be able to invite our Sharsheret program participant, Brittany, who's here to share her story. And now, it is my pleasure to introduce Brittany.

Brittany: Hi, everybody. My name is Brittany. I'm an ovarian... Can everyone hear me? Can someone do a check?

Jenna Fields: Yes, we can hear you, Brittany, loud and clear. Thank you.

Brittany: Okay. Wonderful. Yeah. So I am an ovarian cancer survivor, and I'm just going to briefly sum up my story as quickly as possible.

So October 25th, 2022, I received a phone call that literally changed my life forever. I received a phone call that I had gynecologic cancer. Two weeks prior to that, I wasn't feeling well, my stomach was very distended, and I tried to get in with any GI doctor I could. I finally got a call back. The GI doctor, I had never been to a GI doctor before, and she brought me into her office and she said, "Yeah, your stomach looks distended. Let's do an ultrasound." They did an ultrasound, and they saw that there was fluid, ascites in there. So, they did a paracentesis to draw out the fluid.

And about three to four days later, I got a phone call on October 25th, 2022 from my GI doctor. And she said, "I'm really sorry to tell you this," and she told me over the phone that I had adenocarcinoma, they weren't sure where it was from. And drove right to the ER at a very well-known cancer hospital right outside of Philadelphia. I won't say any names, but wonderful, and right outside of Philly. Got right into the ER, they did a CT scan and I had two masses on each ovary, my left and right ovary. Seven days later, I was in for a full total hysterectomy, 11-hour surgery. It was pretty intense. Yep, 11 whole hours. I asked my [inaudible 00:06:19], I said, "Did you take a break?" She said, "No." So, I was really impressed with her, needless to say.

I found out also that I was BRCA positive during this journey, and my parents were tested. I don't have any brothers and sisters, and my father ended up being BRCA positive as well. So, I went through that. I went through chemo for about nine months afterwards, physical chemo. And then after that, I took two years of Lynparza, which is a PARP inhibitor that BRCA positive ovarian cancer patients can take, and it actually really reduces the risk of a recurrence. So, I'm just so grateful to be here with all of you. And yay, I see another Philadelphian. Hi. And yeah, so that was in 2023, all that happened, two years of Lynparza. And then in December of 2025, I had a double mastectomy, so, with expanders and then had reconstruction done after that.

So during this entire journey, I actually met a representative from Sharsheret at, it was an event at a local synagogue and they were outside. And they said, "Did you know," I had no hair, I had no eyebrows, I had nothing. And they said, "We can make a wig for you. We can get your eyebrows done." And you don't think about the vain portion of it, right? But I still wanted to feel normal. I really wanted to feel like myself.

And Sharsheret paid for myself to get a human hair wig, which is unbelievable because I couldn't afford it. I mean, they're like thousands of dollars. They also paid for me to get my eyebrows microbladed. And I know to some people it's not a big deal, but to me, it made me feel more human. It made me feel like I can be somewhat myself. And they're an incredible organization. I mean, I can't say enough good things about them. I mean, really, they made me feel really, really good in a time where I was in a deep, dark hole, so. But I've not had a recurrence, knock on wood. I'm feeling really good. I've been through five surgeries since 2022, and that is my story.

So I know there's no Q&A, but all I can say is be an advocate for yourself, especially with your physicians. If you don't feel well, tell them. Tell them every symptom, be an over-sharer, that's how I am. That's how I was with my physicians, I had to be. I'm still like that four years later. So they all know me well, all my whole team. That's really it.

So, thank you for having me tonight, and I wish best of luck to anyone enduring this awful, God-awful disease, breast cancer and ovarian cancer.

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Jenna Fields: Thank you, Brittany. Thank you so much for sharing so much with us and for really inspiring us through your journey. We're so glad you were here tonight.

Brittany: Thank you so much for having me, and I wish you all the best.

Jenna Fields: Thank you, same to you.

It's now my pleasure and honor to welcome tonight's expert speaker, Dr. Beth Karlan, who is Professor and Vice chair in the Department of Obstetrics and Gynecology at the David Geffen School of Medicine at UCLA. She holds the Nancy Marks Endowed Chair in Women's Health Research, and is the Director of Cancer Population Genetics at the UCLA Johnson Comprehensive Cancer Center.

Her research focuses on improving outcomes for women with ovarian and other gynecologic malignancies, as well as better characterizing inherited cancer susceptibility syndromes. She has authored over 500 peer-reviewed research publications. She also sits on Sharsheret's medical advisory board. Among her countless achievements, she received a Lifetime Achievement Award from the International Society of Gynecologic Cancer, a Director Service Award from National Cancer Institute, and a Giant of Cancer Care and Gynecologic Malignancies from OncLive.

But more than anything, Dr. Karlan, you are beloved by your patients and widely respected by everyone in the field, and it is such an honor to have you tonight. So, thank you for being here.

Dr. Beth Karlan: Jenna, thank you for that too kind introduction. I'm sorry it took so long, guys, because I know you're not here to hear about me. I'm here to be here for you.

Brittany, thank you for sharing your inspiring story. I almost don't need slides. I could just talk about you and your story and provide talk from there, but it is one that's too common for all of us. It is truly an honor for me to be here tonight, once again, to share updates with you.

Dr. Beth Karlan: Okay. I'll just say it at the outset, there's a lot of exciting news in ovarian cancer in 2026. A lot of new treatments, new prevention, new targets, and we'll go through it. I do want to leave time for your questions because I know how important that is to all of us, so I told Jenna, I'll send over my slides at the end of the presentation. Feel free to take a look and I hope that they can provide you some additional information. Okay, so now why is this... Let's just see here. There's always something.

Okay, so just an outline, the coming attractions here. We'll go over some numbers just because I think it's helpful to give some of that perspective, some of the headlines about the pathology and the fact that it's really ovarian cancers. Not only is everyone's journey and everyone's specific ovarian cancer her own, there's actually specific subtypes that are getting more clearly defined

so we can have better than just one-size-fits-all therapy. If everyone gets platinum and taxanes and we just go about our business, then we can actually start to really hone in to the right treatment for the right patient at the right time.

We'll go over the current standard of care, and we're really doing much better in that. Some of the new advances that are becoming a standard of care, we heard about some of it now from Brittany with the PARP inhibitors. But what's on the horizon? Is chemotherapy actually going to become obsolete? I mean, there are ways to think about that.

And then some time, I really want us to focus on survivorship, survivorship care, how do we continue to be our best selves for those years after we finish the treatment, and some comments about prevention. So hold onto your seats, and as I say, you'll get copies of these slides, so I hope we'll be able to get through all this.

These are just the numbers, they haven't changed very significantly. They bounce around these numbers of 21,000 new cases and 12,000 deaths. Ovarian cancer is still considered a high mortality cancer because of that new case to mortality ratio, but the numbers are actually coming down. With improved treatments, more and more women are living with ovarian cancer. There's now almost a quarter million women alive with ovarian cancer, and those numbers continue to increase as women are living longer and better lives despite having ovarian cancer. That you really can live a full, purposeful life that is meaningful for you and your family, and we just keep ovarian cancer and hopefully down, I always like to say, "I like to keep the ovarian cancer in eight font italics and living in 40 font bold." So, that's what we're going to be talking about.

And this is really the good news. When we look over these decades, the actual number of cases of ovarian cancer has continued to decrease, as has the death rate. It's still way too high, don't get me wrong, and every case is one too many, but we are making some progress. So the incidence seems to be going down in part because of the increased use of birth control pills that we know do reduce the risk of ovarian cancer by up to 50%. If birth control pills have used cumulatively from period time to menopause, for about 10 years, you can reduce your ovarian cancer risk by about half. Genetic testing and acting on that and doing risk-reducing surgeries reduced risk. And we'll talk more about the increased role of opportunistic salpingectomy, of removing the fallopian tubes before anything else can happen. Death rates are down because we've got treatments.

I'm sorry guys, I decided to come on home to be able to have dinner after, and my dogs are being a little noisy here. I'm sorry.

Jenna Fields:

We actually can't hear you, Beth, for what it's worth. We can't hear the dogs.

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Dr. Beth Karlan: Thank you, Jenny. You make me feel much better.

Jenna Fields: We got good sound, we got good sound.

Dr. Beth Karlan: You made me feel better. Okay. And then really the idea of individualized approaches, looking at each woman not just as an ovarian cancer, but as who you are, whether you're mothers, spouses, sisters, parts of your communities and friends, to really individualize those approaches in the way and the options you have.

So, this was the headline the last time the National Academies of Medicine met to review the status of ovarian cancer. And I was on the panel, and I think one of the biggest headlines was, ovarian cancer is not one disease. We can't just treat them all the same, we can't study them all the same, we can't give grants for them all the same. We need to think about each type because they're very different in terms of their biology, their genetics, their sensitivities to chemo, their risk factors. And to be honest, most of them don't start in the ovary. The most common ovarian cancer, of course, is the high-grade serous ovarian cancer, the one you see at top, and that we believe starts most likely at the end of the fallopian tube. I think you can probably see my pointer, but I'll give you some prettier pictures later. Oops, okay.

Low-grade serous cancer, which is a unique type. It's not just you go from low-grade to high-grade, they're completely different biologies. They just have the same last name. They probably begin on the ovary, they're probably the one that begins there. But clear cell cancer and endometrial cancer likely begin in endometriosis. And mucinous cancer, we see unknown, may begin in the appendix though. Again, so we call them all ovarian cancer, they have different risk factors. Birth control pills protect to different extents, and we need to think about them differently and treat them differently.

We're not there yet. There's a lot of good studies and we are starting to have trials that look at just clear cell or just mucinous and looking at them differently, and low-grade and high-grade. But the current standard of care remains, chemotherapy and surgery, and is usually the combination of two. Whether you do debulking surgery first and then chemo, or start with chemo, and I always think that's chemically debulking, you're using the chemotherapy to debulk the tumor chemically, or that you're doing it with the scalpel surgically, but you begin with chemotherapy, then have your surgery, and then finished with chemo. We need to individualize based on the patient and a specific tumor, how healthy she is, whether the tumor has spread to, whether you might have a pleural effusion as well. The goal of the surgery, no matter when you do it, is to have absolutely no visible disease left to the abdomen, and that's what we're going after. After that, after you make the decision of primary debulking surgery or neoadjuvant chemotherapy, you then go on to consolidation.

Now, a couple of things here. The decisions really should be made by someone who has the experience of which one is going to be best for the given patient.

There's clearly fewer surgical complications if you begin with chemical debulking with neoadjuvant chemotherapy and then go on to surgery, because again, you've gotten most of the tumor to dry up with the chemo, so there's less likelihood that you'll need a colostomy, need to be in the ICU, need multiple units of blood transfusion, and the outcome's the same in terms of overall survival. HIPEC, which is a hyperthermic, so a heated chemotherapy that you put in the abdomen at the time of surgery, should be considered at the time of your surgery because it has been shown to provide significant improvement in survival, and I'll show you that in a moment.

But other things we have to remember is, everyone should be getting genetic testing. That should be universally offered to every [inaudible 00:19:56]. Genetic testing for, did you inherit the genes or what's in your tumor, in terms of using that PARP inhibitor that we heard Brittany tell us about? The standard chemotherapy is carboplatin and paclitaxel, intravenously, and bevacizumab, or Avastin, can be given as well. And then the PARP inhibitors, again, this is all the standard. This is what should be done wherever you are living, for everyone on the call, this is what's in the NCCN guidelines with level one, phase three randomized trials to show that this stuff works.

Okay, a few things. Again, HIPEC, hyperthermic intraperitoneal chemotherapy, hot chemo placed in the tummy so that whatever tumors right after you take it out, all those tumor beds perhaps are raw, the blood vessels are there. Can we get higher doses at a high temperature so that when the cells are heated up, just like when you have a fever, they reproduce more quickly, and the chemotherapy's even more effective. And by that one course, it adds about three hours to your surgery, but this was a randomized trial. All women got chemo and then went to the operating room, the HIPEC in the red, led... those extra three hours we stood on our feet, like Brittany said, her surgeon was there for 11 hours. We all have really comfortable OR shoes. Those three hours can transfer into over a year of someone's life. So, seems to be worth it. It's not a cure, but it does, as we say, shift that survival curve. This is what we call Kaplan-Meier survival curve. Every time we shift it rightward, it means you're living longer. So, this is a pretty good increment.

Okay. These are just standard of care, so I'm going pretty fast, guys. I hope you're with me here. So again, about 20% of women with ovarian cancer will carry a genetic predisposition. Most of them are due to the BRCA genes. There's a number of other genes you see listed here that can also be inherited. They're also involved in DNA repair, and that's the way they work to increase, excuse me, the risk of ovarian cancer.

Since 2010, for over 15 years, it has been a national recommendation paid for by chemotherapy that everyone with ovarian cancer should get genetic testing, yet less than half of the patients are getting it done. This has many, many implications both for the patient, the woman, and her family. We can only get PARP inhibitors paid for by insurance and they're wicked expensive, but if you have the genetic predisposition to be able to have it approved. And also, it's

only because the PARP inhibitors really only work and work best in those women who have this susceptibility, and that's the mechanism by which the PARP inhibitors work, is in conjunction with those DNA repair genes. It leaves that second hit that when you knock out different repair pathways, the cells with cancer just die.

Also, I mean, Brittany went ahead and had her prophylactic mastectomies, but if you didn't know you had a BRCA gene a few years after you finished your chemotherapy for your ovarian cancer, you might get breast cancer. So again, it provides opportunities for secondary cancer prevention, and then an opportunity for your family members, your blood relatives, to also find out if they carry that same gene and are at risk. So, you can actually have a significant role in saving the lives of those you love the most.

So genetics really can improve ovarian cancer survival. It's actually over half of ovarian cancer patients will be susceptible and eligible to get a PARP inhibitor. It really has transformed, and I'll show you just one slide to that effect, but really has transformed how we treat ovarian cancer and really allowed women to live longer. There's other immunotherapies, especially if you have one of these mismatch repair genes, MMR, that's associated with the Lynch syndrome, and then there's a whole growing list of other targeted agents, that we'll talk about a whole bunch of them.

One slide about PARP inhibitors. I mean, for someone who's been treating women with ovarian cancer now for over three decades, this is the nicest survival curve I think I've ever seen. Here, these are all women with stage three and four advanced ovarian cancer who had chemotherapy and surgery, and they were then randomized to either get olaparib, which is Lynparza, or placebo. Those women that get olaparib, you can all read this curve, they lived a hell of a lot longer. And this has been taken out even over now seven years. Olaparib really is allowing patients to live significantly longer, and I'm optimistic even allowing us to have some cures by the chronic treatment here. So, it really has been transformative. I mean, it's the first maintenance therapy in ovarian cancer that's really shown benefit.

It's not easy. It may just be a pill, but there are clearly side effects from taking a PARP inhibitor. But hey, I think I know what I would do, and I know from my patients, being able to live those extra years and enjoy life is clearly worthwhile. So genetic testing really can improve survival. And we need to, as Brittany said, be an advocate, talk to your own communities, and make sure that happens.

But in this era, molecular testing is really the basis for precision oncology. Now, BRCA and those things we're talking about, inherited genes, but a cancer cell itself has a lot of different mutations and a lot of different breaks. 30... It depends on the given cancer in terms of how many breaks. Over 17,000 genes, I did this literature research just recently, have been associated with some cancer diagnosis, and we only have 20,000 genes in our whole body that make us who we are. Hair color, eye color, your personalities, and everything else. Most of

them are involved in some kind of cancer. So, how do we know what to target, what's the driver? So that's really where we're getting into this precision oncology.

So I just want us to remember, differentiate, a somatic change is basically a tumor change. It's a change that defines the cancer. Testing that may have been done by many of the companies, Tempus, Caris, Foundation. They're going to do a profile of your cancer cells and they give you two or 300 genes they're testing, sometimes they can test up to 1,000 genes that could be a target for a new treatment. There's only about 50 genes that are associated that are inherited, so they're different. Now, the inherited genes are in every cell of your body, which is why you're at risk for breast cancer or pancreas cancer if you have a BRCA gene. You can pass it on, your siblings may have it, and that's the area for prevention, can also be a target for treatment. But they really are different than they're tested differently.

The other thing I want us to have an awareness of, because I think this is something very exciting, and you guys have been hearing lots about it, is this idea of liquid biopsies. So again, all of our taxes we've been paying all these years, a lot of it's going to the NIH, and we're giving grants, they're doing some of the most cutting edge research to allow us to have these discoveries.

So tumor cells, as they're growing, some die, the DNA breaks out of the cells, or they break off from the tumor, maybe going to metastasize or not, but they go through the blood. And in a tube of blood, you'll have lots of cells, white cells and red cells. You can find one cancer cell among a million normal cells, and these traces we call circulating tumor DNA, ctDNA, and this can be used to test for mutation. Did your BRCA mutation revert to normal? Do you have a RAS mutation? Do you have a CC... You can look at it in the biopsy. So if your cancer occurs, and I hope... I mean, many of you probably have had that happen, and those that haven't yet, I hope you don't, but you can't get a biopsy. Let's say on your CT scan, it's too hard to get a biopsy. Often you can do a liquid biopsy, take a tube of blood, and you can look for your circulating tumor DNA.

There's also tests that can look better than a CA 125 to see whether you have a recurrence called minimal residual disease. Tests like the Signatera test do something like that. They're very different. You're not looking for a specific target. You're looking at how big are the little pieces, and those tests are based on your initial tumor and can be looked at, in your case, did the tumor come back? And I think we've all heard in the news lately things like the Galleri test that is also based on circulating tumor DNA. Again, perhaps not quite ready for prime time, but it's coming. So, this new technology of being able to take a snippet of DNA and amplify it that we can analyze it, has really meaningful information for patients, for us, for drug developers, for everyone to treat women better.

Okay. I think I said earlier that maybe chemotherapy will become obsolete, and I mean the way we currently give chemotherapy. So, antibody drug conjugates

are a way to have a secret smart bomb way to send the chemotherapy just to the cells that have the cancer.

So, what is an antibody drug conjugate? It's an antibody which has the specificity to bind its target. And we know about this through our whole lives of getting an infection. Antibodies lop on those, gather up those antigens, those things that may be causing the infection. In this case, the antibody's been engineered with what we call a linker that links the honing antibody, so the smart bond that's going to get it, there to a drug. And the drug may be like a chemotherapy drug, but rather than going to every cell, to causing your hair to fall out, to giving you the nausea and other effects, it delivers the chemotherapy-like agent directly to the cancer cell. So, that's what the idea is here, that you have an antibody, a linker that joins it, and the drug. And each one of them is a bit different, so you need a specific target, and that's what we're going to go to next.

Okay, so these are ovarian cancer antibodies. Some are FDA approved already, some are in clinical trials. We'll talk about the folate receptor alpha, things like mirvetuximab, HER2, things like trastuzumab, and then this whole list of other ones that we have actively now in clinical trials. All of them have the same idea. The names here that I list is the target on the ovarian cancer cell. The payload, the drug, can be different. There's about 10 folate receptor alpha ADCs in clinical trial, even though mirvetuximab exists, to try to make things better, have less toxicities, have more drug delivered for every single antibody. So there's lots of ways to keep iterating and improving the difference here.

So mirvetuximab, many of you may have already know about Elahere. The antibody targets the folate receptor alpha that's in about 80% of ovarian cancer cells. It has a linker, and it's linked to a drug called DM4, which it doesn't allow the cells to split and undergo mitosis. It's one of the molecules that pull the DNA apart every time a cell divides. And we've had to learn a lot about these drugs. It was thrown out years ago. We were doing clinical trials with this exact agent almost 15 years ago, and they didn't work because we didn't analyze the studies correctly.

And I just bring this up, because when you participate in a clinical trial, there's lots of science that goes into it. Here, they tried to give it to everybody rather than just those who had high levels of folate alpha expression, and they threw out the whole drug because they said, "Oh no, it doesn't work." Same thing happened with Herceptin, which we've heard about for breast cancer. You had to have a bunch of the HER2 expression, over-expression to allow to show that the drug works. So it really is a science in and of itself. But here were these curves for, the trial was called MIRASOL, the drug is Elahere, showing again, women who got this drug lived a lot longer, and this led the FDA to give this drug an accelerated approval.

This trial is called DESTINY. This is using an antibody drug conjugate to HER2. This was done across many different cancers, and it actually has an approval

that says all these cancers, if they have a high expression of the HER2 antigen, that they can get this drug and show efficacy. And here, you just see here's the ovary, if you overexpress a two plus or three plus, you had a very high likelihood of having benefit, similarly with endometrial cancer and cervical cancer as well.

Okay. These are some of the ADC trials that are ongoing in ovarian cancer, many different targets, some first line is actually one we are enrolling on now using mirvetuximab and carboplatin. Forget the Taxol, don't lose your hair. It's still a randomized trial. You may not get in that arm, but trying to say, "Hey, look, it's worked so well when we have recurrent ovarian cancer. Why not try it from the start?" There's other drugs like that that are being looked at in the first line setting, including in HER2 that I mentioned before that goes against the HER2, something called sacituzumab we'll talk about in a moment. But many of these looking at platinum-sensitive recurrences, platinum-resistant recurrences, and there's a very, very long list.

But the FDA in setting up its oncology branch really has had a focus on cancer drugs. And over the last 20 years, 385 unique indications for medicines to treat solid tumors, novel drugs, and then supplemental new indications. But chemotherapy is this light blue, way down here. Not many new chemotherapies are being approved. Most of them are targeted therapies, yeah, that are going specifically small molecules, going after one specific gene. I think the biggest one we've heard about recently is for pancreatic cancer that's going after KRAS, but similar things like that. Immunotherapies, antibody drug conjugates are just starting to pick up. But I expect to see this overtake many of these in the coming years. The pipeline is just really at very, very high pressure right now.

Let's talk about the things that matter to us for a moment, ovarian cancer. It's really been uneven. Prior to 2014, there was nothing very exciting. Taxol came on the scene in the early 2000s. We got bevacizumab or Avastin, but then since then, it's really been accelerating. We had PARPs, with three PARP inhibitors approved for ovarian cancer during these years. Then we start to see a few [inaudible 00:36:26] there as the PARP inhibitors had to be narrowed because we had more data seeing they really only worked in those with these DNA alterations. And then we started to look at new targets. FR alpha, we talked about Elahere in low-grade serous tumors. There's other genetic alterations and new drugs came out there, and it continues to increase and increase.

So, I'll go through quickly two FDA approvals that happened in this last year, and it continues to go ahead. And I really do think it is a great path ahead for better treatments. And the better you can live, the longer you're alive, the better treatments you're going to have in the coming months and years to come.

So this was a new 2026 approval for platinum-resistant ovarian cancer. Again, when your tumor has recurred and the last time within six months of having had a platinum chemotherapy. This trial looked at a cousin of Taxol that many of you had, where it's bound to a nanoparticle of albumin, it's called... And that binding allows it to get into the cell better. Nab-paclitaxel or... it's blanking on me for a

quick second, sorry guys. And it's combined with recorilant. So, recorilant inhibits the glucocorticoid receptors. That's a steroid, that's cortisone. It's a cortisone receptor on basically 95% of ovarian cancer cells. And when you combine this Taxol derivative with this glucocorticoid receptor inhibitor, you start to see again, improvements in survival. A year improvement here and even overall survival was better with this combination.

Here's another one. First time an immunotherapy with Taxol with or without Avastin or bevacizumab, also improves survival. And it's the first time we actually have a biomarker. This is your tumor cells have to have a score that shows they're sensitive to chemotherapy. Again, I'd love these curves to look like the one I showed you for PARP inhibitors, but each one is another option that keeps buying you more and more time that you can kick the can down the road and live your life. I know you're on chemo. I know it may not always be the same, but with the right supports, we have patients who travel globally and can still lead full lives.

Lots more coming down the pike. This one is called NaPi2B. It's another transport protein on ovarian cancer cells that's looking good. When the cells go down, these are the people who responded. These are the different doses, but many, many more people responded than didn't respond. This is another one coming down, this is an immunotherapy. So it is bright. I want to leave time, so I'm going to move on, but there's a lot of new novel treatments coming along with less toxicities. We're trying to deescalate treatments that we realize we don't need as much. There's trials saying rather than needing two years or three years of PARP inhibitors, one year just as much. So, there's a lot of ways we're trying to look at benefit and toxicity to help women live longer. And we recognize this continuum, previvorship, survivorship, and really the big arrow here is long-term survivorship. How do we have women, after they've been diagnosed and finished with chemotherapy, live their best lives?

Shout out to Sharsheret. Part of survivorship is having community, having exercise, living healthy, eating well. And upcoming in next month, I guess October's in this week, so very soon, four weeks is the Sharsheret 5th Annual West Coast Dash down in Playa Del Rey. I'll be down there, I'm sure many of you may show up. Do a 1K walk, just come in to have some hot dogs. I don't know. No, not hot dogs, I'm only teasing you. But be with friends and share the empowerment.

Okay. Survivorship plans are key, and it's really part of the national standards to have a survivorship plan to help you manage things like menopausal symptoms, hot flashes, your sexual health, an important part of being alive, the ongoing chronic fatigue, neuropathy, lymphedema, cognitive complaints, anxiety. There's real PTSD that hits you really when you finish and you get to process it. Aspects that may be accelerated aging and financial toxicities, what this has meant to you.

Lots of actions, healthy lifestyle, eating better, exercise, Tai Chi, yoga. All these have been shown in randomized controlled trials to really help. I'm advocating that we have a new subspecialty of survivor clinicians that actually have a fellowship training like we do in many other things, specifically looking at cancer survivorship. So, that's one of my little soapboxes. But I'll just give a shout-out here. We just published, I've gotten lots of praise from it from my colleagues, but I think an excellent review on ovarian cancer survivorship and what should be considered.

So, I think it's a science. It can't be left as an afterthought. Survival, the easiest thing for us to measure as clinicians is how long you're alive, right? But how well you live is a lot harder, and I think it's at least as important for us to focus on this. Rachel Frankenthal is one of our PAs that I work with who's very interested in this. She actually is a certified yoga instructor, and she will provide free GYN cancer yoga classes for survivorship to really just help you get back into the swing of things, of being alive. And this is open to any of our patients here.

Lastly, I'm going to quickly touch on an ounce of prevention is worth a pound of cure. I think we now know that most ovarian cancers begin in the fallopian tube, and that risk reducing surgery is the best way to reduce mortality. We have to look carefully to find these pre-invasive lesions, but when you find a pre-invasive lesion even, you're still at a risk to get cancer later on, so you want to get these tubes out at the right time.

Indeed, we now have population-based data from British Columbia, and these are women who don't have a BRCA gene, this is just looking at the whole population. If you remove the tubes either instead of a tubal ligation or at the time of a hysterectomy, you reduce the risk of getting ovarian cancer by 80%. That's pretty darn powerful. We still don't have a screening test, we're not giving up on it. But the thing you could do now for many patients is to have your tubes out.

In fact, there's new guidelines. American College of Obstetrics and Gynecology just issued a practice update that's been endorsed by the American Cancer Society, Society of GYN Oncology, and the European Society of Medical Oncology, saying that OBGYNs should remove the fallopian tube at time of hysterectomies. Don't leave that fallopian tube in there, it comes out with the uterus. If you've completed childbearing, you shouldn't be offering tubal ligations, you should remove the fallopian tube. OS is opportunistic salpingectomy. OBGYNs at the time of any other surgery, so you're moving a cyst and the woman's completed her childbearing, remove the fallopian tubes. If you're having an appendectomy, a gallbladder out, bariatric surgery, you're having another surgery and they're in the abdomen, you've completed your childbearing, consider having an opportunistic salpingectomy. 80% reduction in the number of cases of ovarian cancer.

I'm actually chairing again for the National Academy's conference in a few weeks on how do we make this a new standard of care? What are the steps we

need to get it reimbursed, to get the consents? I mean, there's many different aspects of this to make it happen, but I think it's a very exciting new initiative.

What does it take to prevent ovarian cancer, outsmart ovarian cancer? Basically, broader awareness. Most of my physician colleagues who are not in OBGYN still don't know that ovarian cancer begins in the fallopian tube. We need more women to ask about it, so we need to educate women, residents, medical students all the way through that that's where the ovarian cancer begins for most of the ovarian cancers.

We've talked a lot about BRCA. I think you know that men and women who have a BRCA gene have a significant increased risk in these cancers, breast, ovary, pancreas, and prostate, we see the numbers here. And that the standards for ovarian cancer risk reduction are to remove the tubes and ovaries at 35 to 40 for BRCA1, or 40 to 45 for BRCA2. Unfortunately, we still don't have a good screening test, but the salpingectomy and then delaying the oophorectomy should be discussed.

I have UCLA medical students who come to me, they found out they had a BRCA gene and say, "Look, I want to think about my training. I want to think about getting through this. I want my tubes out now. I may have assisted reproductive technologies in the future, IVF type of procedures, so I can make sure I have a BRCA-free baby in the future. So for now, I want to have my fallopian tubes out." And doing that, again, you don't go through premature menopause, you don't influence ovarian cancer function. It is a procedure, it is a surgery, but something to consider. So, and that, remember to tell your family members when you have a BRCA mutation.

So, September's Gynecologic Ovarian Cancer Awareness Month, talk, educate, advocate, live. Our call to action, we've been able to allow women to live longer, we keep pushing that survival curve rightward, as I said. But emergence of platinum-resistance is too common and we need better treatments now. We have new drug approvals, but we need better insurance coverage for them, improve access to clinical trials, and allow us to do new kinds of trials so we get answers faster. Ways we can help patients, no matter where they live, to have access to this cutting edge type of therapy. We need to really implement broader genetic testing and cascade testing and primary prevention. And please, let's all vote increase funding to ensure the pipeline of new drugs, of new scientists, really continue to help us move this forward.

So with that, I'll say thank you. I welcome your attention. I thank Sharsheret for its commitment to really helping everyone live a better life. And I hope everyone has a wonderful, joyous, healthy, and happy new year ahead, [foreign language 00:48:03], and I'm here for you guys, whatever else we can do here today.

Jenna Fields: Thank you, Dr. Karlan. That was fantastic, and just appreciate your insight and your optimism and really just your total support for all of the patients on this call. So, thank you.

I'm going to dive right into the chat with questions, starting with the first one that came in. So Dana asked, "In clinical trials, how can patients balance trial efficacy with toxicity when it leaves only a handful of days of feeling okay and functioning between treatments, especially their limits on the number of prior lines of therapy if needing to switch trials?"

Dr. Beth Karlan: Yeah, great question, Dana, thank you. And I think clinical trial matching is really important. Depending on the institution, looking at the NIH, there are some AI type of chatbots that you can use to help you match to the clinical trial. What are the preliminary... They're just questions you can ask. Remember that the clinical trial is a contract, but you can say no. You can say, "I've had enough. I want to try something else." So, just like we heard at the beginning from Brittany, be your own advocate and weigh that. What are the options? If I don't go on this trial, is there another one?

I have to tell you, the portfolio, there are really hundreds of trials available, and I always make the comment with my patients, "I'm not going to put you in a trial if I think the likelihood of helping you." And there's a real difference as a clinical trialist, and I'll move ahead, is between what they want to say is a response, a drop in CA 125 or a half centimeter shrinkage in your tumor and clinical benefit. Clinical benefit is what it means to you, and clinical response is what it means to the FDA. And I'd always advocate for my patient, and no one's going to hold it against you if you say, "No, I've had enough of this. I need to go on something else," or, "I just want to take a break for a while, and I need to think things through."

Jenna Fields: Yeah. Roger asked in the chat, "One you often hear is that early detection of ovarian cancer is rare due to not great screening. Can you share any updates on progress regarding screening for ovarian cancer?"

Dr. Beth Karlan: Roger, thank you for that. I started my career looking at screening, dedicated my career to screening for decades. So, well, we do not have a ovarian cancer screening test on the horizon. For years, I gave this lecture and said, "Oh, sure, it's going to come out within the next five years, don't worry." Part of it is we were looking at ovarian cancer as one disease, and the screening test for clear cell cancer is likely going to be different than for high-grade serous cancer than for low-grade serous cancer. So, we're beginning to look at clinical trials for early detection using those tests.

I mentioned Galleri just briefly, but I'll bring it up again. Finding more cancers is not the same as screening for early cancers. Again, screening wants to find cancers that are stage one or pre-cancers, so that we can affect cures. With most ovarian cancers presenting at advanced stage, we don't have a sense of those early markers that are the earliest to appear when it's just starting to

grow. There are many new screening modalities, including circulating tumor DNAs, exosomes, and a whole list of analytes, things to look at that are in progress, that I'm excited about them and on advisory boards for. I'm still committed to it, but I'm not going to promise you anything is going to be here in the next few years. I hope so, but I've stopped promising that.

Jenna Fields: So, that's the first time I've heard that articulated the way that you did, this idea that we don't have a good idea of the screening markers for early stage ovarian cancer. So for something like a liquid biopsy, they're still only screening for later stage markers. Is that part of the issue?

Dr. Beth Karlan: There's screening for markers that indicate ovarian cancer, period. Okay? They're hoping that if they find them in women who are not yet symptomatic, that it will be a benefit.

So, the largest trial done with that was done in England with 200,000 women. They did the whole National Health Service, and they looked at it, and they found ovarian cancers. There were fewer stage four, but there weren't a lot of stage one. They group them all as stage one and two. Well, stage two is a little cheating with ovarian cancer because it's already spread some. And so, they did not show any survival benefit, and that's really what we want. I mean, finding stage three versus stage four cancer, you're not going to show a true survival benefit, so that's really what we're going after.

Jenna Fields: Understood. Amanda asked, "Help me understand adding Avastin to maintenance with Lynparza. Never had it during frontline due to ostomy healing." Just a few personal details. So, what is the goal with adding Avastin? I want to make sure-

Dr. Beth Karlan: Avastin or bevacizumab is what-

Jenna Fields: To maintenance with lynparza. What's the goal there?

Dr. Beth Karlan: Sure. So bev, I'm going to just call it so we use the generic name. There was one study called PAOLA, that looked at getting carbo-taxel and bev during your treatment, and then adding Lynparza and continuing the bevacizumab or Avastin. That's the only combination that's been shown in a clinical trial to offer any benefit. It's unclear how much the bev adds, especially if you're a BRCA carrier, because Lynparza works so well. And I think, as you said in your specific case, you really do need to individualize. The clinical trials are based on hundreds of patients. If you needed the stoma, the bowel resection and it wasn't right for you, it may not be right. Bevacizumab, remember, has a lot of complications or can, including bowel perforations, kidney failure, stroke, high blood. So we use it very carefully, we try to choose the patients. But don't feel like you missed out on something, that you did something wrong. It wasn't right for you. And you may get it in the future because we often use it when tumors come back to work with the chemo, but in maintenance, it's less common.

Emerging Advances in Ovarian and Gynecologic Cancer Care

Jenna Fields: Can you touch on endometrial cancer, Dr. Karlan? What's the standard of care for endometrial cancer right now?

Dr. Beth Karlan: So, endometrial cancer also needs a lot more work. So endometrial cancer is one of the few cancers that has had an increasing number of new cases and an increasing death rate. We don't completely understand why, we don't understand what's in the environment. The whole shifting of the microbiome and more cancers in younger women, endometrial cancer is one of those that we're really seeing more cases, younger women, and unfortunately, more deaths.

The standard of care is early diagnosis. Again, most endometrial cancers are diagnosed at stage one because there's bleeding. So, be aware of changes in your period if you're premenopausal or any bleeding post, after menopause. Even if it's some pink staining, go and have it worked up. Workup usually entails a biopsy. It can be done in the office, an endometrial biopsy. I've had them done, so when I say it's not that painful, I say from personal experience, but there's lots of things that can be done in the office to give you some anesthesia. And if that doesn't work for you, you can have a regular D&C. The benefit of doing it in the office is you get your answer faster.

That tissue is then analyzed. There's lots of kinds of endometrial cancer, each one of those need to be treated differently. Endometrial cancer is one where the science-based treatments, personalized treatments have gone through the ceiling. They too are not one disease. They either have over expressed P53. There's many different molecular patterns, and the clinical trials have gotten very, very specific. So it's, make your diagnosis. Since most of the cases are early, it is a hysterectomy. Most of those can be done minimally invasively either by robotics or laparoscopy, so almost as an... you come in the morning, go home the same day. It's important to do a sentinel lymph node biopsy to sample the lymph nodes that drain the uterus to see if there's been any spread. And then we decide what the appropriate next step is, whether it's radiation, whether it's chemotherapy, whether it's different types of radiation, based on different factors. How deeply it's invaded into the uterus. Has it been in any lymph vascular spaces, and what the genetic profile is.

Lots of different aspects that are hard to describe without some slides. And another talk or next year, I will try to give more time. It's just, I know we had this ovarian cancer community and I wanted to... Not as much time, so we pushed it there.

Jenna Fields: Yes. No, absolutely. Thank you. Okay, last question. I'm going to squeeze one more in around hormone replacement therapy. Are you currently recommending it for people who are postmenopausal, including those who've had a total hysterectomy?

Dr. Beth Karlan: Yes. So, again-

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Jenna Fields: Great.

Dr. Beth Karlan: Okay. So again, have you had breast cancer? Was there breast cancer? I mean, we have to look at each [inaudible 00:58:15]-

Jenna Fields: For ovarian cancer patients. I'm sorry, that's what [inaudible 00:58:17].

Dr. Beth Karlan: No, it's okay, but many of them have already had a breast cancer. Right? So a BRCA patient may have had breast cancer years ago. So again, we need to look, again, the total patient. But the current data say that women with high-grade serous cancer actually live better and live longer if they get hormone replacement therapy. There's less risks of osteoporosis. There's better sexual functioning, cognitive functioning, and they actually have better quality of life.

It's not everyone. Low-grade serous cancers are very responsive to hormones. In fact, one of the treatments is to use estrogen blockers. So if you have a low-grade serous cancer, I would not give you hormone replacement therapy, even though unfortunately those women are younger, so we have to find other ways to control the symptoms. But in general, to try to keep it short, as you said, I do think most women with advanced stage ovarian cancer can benefit from hormone replacement, safely.

Jenna Fields: Wonderful. Okay. Well, thank you, Dr. Karlan, for all of your expertise, and thank you to everyone on this call.

I do want to ask those who have metastatic breast or advanced gynecologic cancer to stay on. We are going to do a small breakout for our Embrace program participants. And for the rest of you, thank you so much for being here. Please take a moment to fill out our evaluation survey that's being put in the chat right now. It really does inform our future programming, and we appreciate it.

Thank you to our sponsor today's program, Merck, and the sponsors of our Embrace breakout, Lilly and Pfizer. Our 2026 Sharsheret Summit sponsors are AstraZeneca, Eisai, GSK, Lilly, Pfizer, Smart State, Weill Cornell Medicine Department of Genetics and Personalized Cancer Prevention, and a cooperative agreement 24-0061 of the Centers for Disease Control and Prevention.

Our Sharsheret Summit is running from September 18th to 23rd, and you can register for all of our upcoming webinars in the chat. Please don't hesitate to reach out to us with any questions or support. Sharsheret has two genetic counselors on staff that are available for free consultations, as well as all of our supportive mental health programming. My colleagues are putting our contact information in the chat as well. Thank you again everyone for joining.