Top Medical Breakthroughs from the San Antonio Breast Cancer Symposium

National Webinar Transcript

January 15, 2026

Presented by:

Embrace Breakout session sponsored by:

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

Disclaimer

The information contained in this document is presented in summary form only and is intended to provide broad understanding and knowledge of the topics. The information should not be considered complete and should not be used in place of a visit, call, consultation, or advice of your physician or other health care Professional. The document does not recommend the self-management of health problems. Should you have any health care related questions, please

call or see your physician or other health care provider promptly. You should never disregard medical advice or delay in seeking it because of something you have read here.

The information contained in this document is compiled from a variety of sources (“Information Providers”). Neither Sharsheret, nor any Information Providers, shall be responsible for information provided herein under any theory of liability or indemnity. Sharsheret and Information Providers make no warranty as to the reliability, accuracy, timeliness, usefulness, or completeness of the information.

Sharsheret and Information Providers cannot and do not warrant against human and machine errors, omissions, delays, interruptions or losses, including loss of data.

Jenna Fields: Welcome everybody. Thank you so much for being here tonight for our webinar, Top Medical Breakthroughs from the San Antonio Breast Cancer Symposium with Dr. Reva Basho, who is a Breast Medical Oncologist and the Chief Medical Officer at the Ellison Medical Institute in Los Angeles. I am Jenna Fields. I'm our Chief Regional Officer of Sharsheret, and I'm based here in Los Angeles. I want to give a special thank you to tonight's EMBRACE breakout sponsor, Gilead Oncology. Now, before we begin, 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. Now, if you'd like to remain private, you have the option to turn off your video and rename yourself, or you can call into the webinar.

You may have noticed that you were muted upon entering the Zoom. Please stay muted during the call. We will hold a Q&A at the end of the presentation. If you have any questions, please type them into the chat box as we go and we'll get to as many as we can during the Q&A. I do want to remind you that Sharsheret is a not-for-profit cancer support organization and does not provide any medical advice or perform any medical procedures. And our full medical disclaimer is in the chat. And just a quick program spotlight for you, Sharsheret is launching monthly virtual support groups for those in survivorship for breast cancer and ovarian cancer. We will have one for survivorship for Stage 0 to 3, and one for the EMBRACE community, those living with metastatic breast and advanced ovarian cancer. The signup link is in the chat now and the deadline to sign up is tomorrow, so please feel free to fill it out.

I also want to make a plug for our nutrition education sessions. Sharsheret offers free 30-minute one-on-one virtual nutrition education sessions with cancer nutrition registered dietician, Tamar Rothenberg. You can get your questions answered, ideas on what to eat during treatment, and methods to meet your nutritional goals. I'm going to mute that. Okay. From our nutrition expert, you can help and learn how to meet your nutritional goals. To schedule an appointment, contact your social worker. The information is in the chat.

Most importantly, if you're currently facing an ovarian cancer diagnosis, please remember that Sharsheret is here for you and your loved ones. Sharsheret provides emotional support, mental health counseling, and other programs designed to help navigate you through the cancer experience. All are completely free and confidential, and our contact information is in the chat. If you are a member of our EMBRACE community, someone facing metastatic breast or advanced ovarian cancer, we invite you to stay on the Zoom following the Q&A for a more intimate breakout session with Dr. Basho. At Sharsheret, we know that breast cancer isn't just a diagnosis, it's a journey. And whether you're living with it or supporting someone who is, tonight's webinar is designed to give you the latest updates from one of the most esteemed oncologists on the West Coast, Dr. Reva Basho.

Dr. Basho is a breast medical oncologist and clinical investigator and is the associate professor of medicine, and currently serves as the chief medical officer at the Ellison Medical Institute. She received her undergraduate training at Rice University, and her medical degree from Baylor College of Medicine. She completed her internal medicine residency at UCLA Medical Center, and her hematology and oncology fellowship at MD Anderson Cancer Center. Alongside her clinical practice, she's a respected a nationally recognized clinical investigator and her research focuses on the development of novel therapies for the treatment of breast cancer. She served as the PI of numerous clinical trials, serves on several steering committees for international Phase 3 clinical trials, and is currently leading a SUD study of the National Cancer Institute's ComboMATCH trial. Above all, she is beloved by her patients. When one of her patients found out that Dr. Basho was our speaker tonight, she sent me this message.

She said of Dr. Basho, "She was my medical oncologist and I'm profoundly grateful for her care. Cancer can sometimes bring unexpected and odd gifts, and one of mine was Dr. Basho. She combines deep expertise with extraordinary patience and kindness, always taking the time to explain not just what she recommended, but why. Always treating me as a whole person and helping me navigate cancer with grace and dignity." Dr. Basho, we feel so fortunate to have you on tonight and know it is our pleasure for you to be here. It is now my pleasure to turn it over to you.

Dr. Reva Basho: Thank you so much for having me. I am blown away by the community here and the attendance tonight and just so touched by that message. Thank you so much for having me. I am so excited to be here today to share with you today and to start this discussion today. So let me start by sharing some slides.

So I'll start with just telling you all that 2025 was such a big year in breast cancer. It feels like so much data came out last year and really changed the management of so many different aspects of breast cancer. So to fit all of that into this short period of time, I know that I'm going to be breezing through things and I'm going to try to break it down as much as I can. And I tried to focus

on big highlights as much as I can, but stay tuned for the questions and happy to have more conversations offline.

But these are the studies that we'll cover today. So we'll start first by talking about early breast cancer, the lidERA and DESTINY-Breast05 studies, and then switch gears and talk about metastatic breast cancer, focusing first on triple negative breast cancer with the TROPION-BreastO2, ASCENT-O3 studies, and then HER2+ disease with HER2CLIMB-05.

So let's talk first about early hormone receptor-positive breast cancer. So early breast cancer, meaning that's breast cancer that's limited to the breast and lymph nodes and has not spread outside of that region. It has been decades since we have seen new drugs in this space for the management of early breast cancer with anti-estrogen treatment. So we have four current options available, Tamoxifen and our three aromatase inhibitors, but since 2005, we really haven't seen new agents come into this space, and that changed in 2025. So in 2025, we saw data from our first oral SERD. So what is an oral SERD? An oral SERD is a selective estrogen receptor degrader. So estrogen, when it signals in breast cancer, it signals through the estrogen receptor that leads to downstream signaling and action of that estrogen. Sometimes, even when we block the estrogen or get rid of the estrogen, that receptor can activate itself independently.

So these selective estrogen receptor degraders actually go in and degrade that estrogen receptor, and block that downstream action, so they can be very powerful. We've seen some of these agents come into the metastatic space, but this was the first time that a study was presented in the early breast cancer space. So the drug here was Giredestrant, which is an oral SERD. The trial was lidERA. So lidERA was a study that enrolled patients with hormone receptor-positive early breast cancer, included Stage 1 through 3 disease, but in order for patients for node-negative disease, so cancer that had not spread to the lymph nodes to be included, they had to have some other high risk features, such as high-grade disease, high Ki-67, or high genomic scores like Oncotype or MammaPrint. Or they had to have node-positive disease. Patients completed all of their upfront treatments of surgery, chemo if indicated, radiation, and they were randomized one-to-one to either get Giredestrant or standard of care endocrine therapy like Tamoxifen or the aromatase inhibitors.

The primary endpoint was invasive disease-free survival. So every time I look at a trial, I like to look at who were the patients that were actually enrolled in the study so we can try to get an understanding of who was the trial evaluating. So in this study, we can see about 40% of patients in both arms, Giredestrant and endocrine therapy. Patients were premenopausal, so young patients. About 60% of patients were post-menopausal. Most of the patients had Stage 2 to 3 disease in both arms. Most of the patients had node-positive disease in both arms, and most of the patients did require prior chemotherapy. So in general, these are high-risk patients. Patients who need chemo, they have Stage 2 to 3

disease, have positive lymph nodes. They also went on to divide patients into high and medium risk categories, and the majority of patients were high risk.

And on the next slide, I sort of walked through how they defined high and medium risk, but in general, high risk was patients who had bigger tumors, more nodal involvement, high risk biology. So 70% of patients were in this high risk category. So despite those high risk features at just three years of follow-up, which for hormone-positive breast cancer is relatively short follow-up, we saw a difference in outcomes with Giredestrant versus our current standard of care. So the invasive disease-free survival was improved from 89.6% to 92.4% with Giredestrant at the 36-month time mark. This was statistically significant and very clinically meaningful for these patients. The overall survival, which is long-term survival, is immature at this time. It's very, very early for this trial, but even at three years, we're starting to see a difference in the two curves. So we can see that Giredestrant already shows signs of improved overall survival.

So it's very, very exciting data in the hormone receptor-positive space. One very important aspect of oral SERDs is, as we know, aromatase inhibitors, which are currently our backbone endocrine therapy of choice, have a lot of side effects associated with them. A lot of menopausal symptoms, joint pains, hot flashes, other things. And so we really want to know, okay, the drug is better, but is it better tolerated? Because we know that these patients are going to end up needing these drugs for a number of years. And although when we look at the side effects, they look pretty similar in incidents between the two arms. We have pretty similar rates of arthralgias, hot flashes, and other things. It is notable that there were fewer dose discontinuations due to musculoskeletal symptoms like arthralgias on the Giredestrant arm. And if you talk to physicians who have used these drugs on clinical trials, they'll tell you that in general, Giredestrant seems to be better tolerated. So that's very, very exciting. Now we have a drug that looks like it's doing better and is also better tolerated.

How does this data compare to some of the other data? So although we haven't had new endocrine therapies that have come out for hormone receptor-positive disease, in recent years, we've had CDK4/6 inhibitors that have entered this space. So we combine antiestrogen treatments with CDK4/6 inhibitors for our high risk patients in the hormone receptor-positive setting. And when we look at the data from lidARA compared to some of our CDK4/6 inhibitor studies like MonarchE or NATALEE, we see that the lidERA data is really comparable to the data that we see from CDK4/6 inhibitors. So we see about a 3% improvement in invasive disease-free survival across these trials. So this data really does keep up with CDK4/6 inhibitors, which have really transformed the management of hormone receptor-positive disease.

There are several other oral SERDs that are now in clinical trials. So Giredestrant is the first to get to the finish line, but there are several others that are being looked at either upfront, right after completion of curative treatment, or after two to five years of prior endocrine therapy switching to get an oral SERD. So a lot more data to come in this space, but the first of the data that we saw. So

conclusions from the lidERA study, this was the first improvement in adjuvant endocrine therapy that we've seen in 20 years, which is very exciting. The study showed about a 30% proportional improvement in invasive disease-free survival, as well as other endpoints with Giredestrant compared to standard of care endocrine therapy. The absolute invasive disease-free survival improvement was about 3% at three years, and that's likely to grow with time with longer follow-up.

The very anticipated question is, can we combine this? We know that we have benefit now with Giredestrant. We have benefit with CDK4/6 inhibitors. Can we combine these two and give them to our high risk patients? Unfortunately, that data's not yet available, but it will come. So right now, I would say that aromatase inhibitors, CDK4/6 inhibitors are really an established treatment that have started to show long-term survival benefit. And so for our high-risk patients, this is really what we want to focus on in the first two to three years, but after that, we could certainly consider a switch to Giredestrant, and really what we need to do as a field is determine if we can give Giredestrant and CDK4/6 inhibitors together.

So with that, I'll switch to HER2+ early breast cancer. This is just sort of general management of high-risk HER2+ early breast cancer today. So for patients who have tumors that are at least two centimeters in size, or node-positive disease, so cancer that spread to the lymph nodes, our current management strategy for HER2+ early breast cancer is to treat with a combination of chemotherapy and two anti-HER2 antibodies, Trastuzumab and Pertuzumab. We call them HP, Herceptin and Perjeta. After patients get treated upfront with that combination of chemo and HP, they have curative intense surgery. And at surgery, we generally divide patients into two categories. So those who have no tumor left at the time of surgery, their treatment worked so well, there's nothing left in the breast or the lymph nodes, and these patients have a pathologic complete response or PCR. For those patients, we maintain them on the same treatment, so targeted treatment alone after surgery, so no more chemo, but HP alone to finish out one year.

And then we have those patients where treatment worked, but there's still cancer leftover. We still have something left in the breast or lymph nodes, so it didn't work as well as it did in those patients with a pathologic complete response. So for those patients, we generally switch treatment to an antibody-drug conjugate called T-DM1 for 14 cycles based on the KATHERINE study. So we're only going to focus on this group of patients, the residual disease patients. So first, what is T-DM1? T-DM1 is an antibody-drug conjugate. This is a class of agents that is getting a lot of traction, not just in breast cancer, but in cancer as a whole. A lot of our new development is in the antibody-drug conjugate space. So what exactly is an antibody-drug conjugate? It's really a way to deliver chemotherapy in a targeted fashion.

So it has three main components. It has an antibody, the blue part. This is the part of the drug that targets something specific on a tumor cell. So it hones the

drug to the tumor cell because it's targeting something specific. In this case, it's an antibody targeted to HER2. Then we have the chemo that it attaches to, the cytotoxic payload. There's different features of this payload that we can delve into, but one of the bigger things that we think about is how much of this payload can we attach to each antibody? Can we get enough payload in there so that when each of these drug molecules gets to the tumor, we're delivering enough? And then we have the linker. So we have the thing that attaches the drug to the payload. And the linker is important because we want two things to happen. We want the drug to stay attached to the antibody while it's circulating in the blood, and we don't want it to float off and cause general side effects, but when it gets to the tumor, we do want it to detach, and we want the drug to do its thing.

So that linker has to be designed in a way that it's stable in the blood, but detaches once the antibody-drug conjugate gets to the tumor. So T-DM1, which is the antibody-drug conjugate that we give today, is one that has a drug to antibody ratio of about four to one. So we can get four chemotherapy drugs onto each antibody that we give. The linker in this case is not cleavable. And what that means is that this antibody-drug conjugate has to be completely internalized and broken down in the cell in order for that payload to release. So it's very stable, so it's well tolerated, but it is a process to get that payload to release. And it doesn't have a bystander effect, meaning once that payload is released, it really only works in that cell, and it doesn't go anywhere else.

But recently, we have a new antibody-drug conjugate in the HER2+ space in the market. So this is Trastuzumab Deruxtecan or Enhertu. So how does Enhertu differ from T-DM1? Enhertu has a drug to antibody ratio of eight to one. So we can get eight chemotherapy molecules on each ADC. It has a cleavable linker, which means once it gets to the area of the tumor, the payload comes off and starts doing its job. It doesn't have to get completely internalized and broken down for that payload to release. And the payload does have a bystander effect, meaning once that payload is in a cell, it can actually migrate to neighboring cells, so it can kind of diffusely get around that tumor. So these are features that may increase the side effects a little bit because you do have more of that payload getting off of that antibody, but could increase the efficacy of the agent.

So DESTINY-Breast05 was a study that took those patients who had residual disease. So they got upfront treatment with chemo, anti-HER2 treatment, they went to surgery, and they had some cancer leftover. And then they were randomized one-to-one to receive our current standard, which is T-DM1, or the new antibody-drug conjugate T-DXd or Enhertu. And the primary endpoint was invasive disease-free survival. So again, we want to get a good understanding of who the patients were. So in this case, the majority of patients, about 70% in both arms, had hormone receptor-positive disease that's a little bit higher than our typical balance for HER2+ breast cancer. About half of patients had disease that was considered inoperable. So this is upfront when they presented, the

tumor was so big or there were so many nodes involved that they couldn't go to surgery right away. They really needed something to shrink the disease down.

About 80% had positive lymph nodes after upfront treatment. So not only did they have residual disease or cancer leftover, but cancer was in the lymph nodes as well. And the majority of patients did get both anti-HER2 antibodies H and P in the upfront setting. That's standard in the US, but when we go to the rest of the world, sometimes these drugs are not available.

So here is the primary endpoint, invasive disease-free survival. And you can see at 36 months of follow-up, the difference in invasive disease-free survival between the TDM-1 versus the T-DXd treated patients was at 8.7%. So again, very clinically meaningful, statistically significant hazard ratio of 0.47. So this is very exciting data for patients with HER2-positive disease and residual disease at the time of surgery. If we look at the disease-free survival events, we can see that the majority in both arms, so both T-DXd in the blue and T-DM1 in the gray were distant recurrence events. So the things that were impacting really are distant recurrence. And what's really notable here in HER2+ breast cancer, one of the things we worry about is brain metastases, and we can see that T-DXd not only did it reduce distant recurrences, it reduced CNS or brain recurrences, and that was really very meaningful.

For HER2+ breast cancer, this is likely a new standard of care. So HER2+ high-risk early breast cancer, standard treatment is neoadjuvant or upfront chemo with dual HER2-targeted therapy, H and P. For patients who have a pathologic complete response, we continue the HP, but for residual disease, T-DXd is really the new standard of care. And with T-DXd, brain metastases were numerically fewer compared to T-DM1. So with that, we'll switch now to metastatic breast cancer. We're going to continue on with antibody-drug conjugates though. So antibody-drug conjugates are disrupting many different spaces in breast cancer. And one of the other spaces that we see a lot of interesting data is metastatic triple-negative breast cancer. So today, how do we manage metastatic triple-negative breast cancer? So this is upfront management. This is the first line of disease in the metastatic setting. So when patients first present with metastatic disease.

We typically break patients into two categories. So those who are PD-L1 positive, which we define as a combined positive score of at least 10%, and those who are PD-L1 negative, so have a score of less than 10. What is PD-L1? PD-L1 is a marker for immune checkpoint inhibition, and for those patients who are PD-L1 positive, our standard treatment is to combine chemotherapy with an immune checkpoint inhibitor Pembrolizumab. And we'll get more into the nitty-gritty. But patients who are PD-L1 negative, our standard treatment today is single-agent chemotherapy, and this treatment really has not changed, despite all of our advances in breast cancer for many, many years. So approximately 70% of patients with upfront metastatic triple-negative breast cancer are not candidates for immunotherapy, so they're PD-L1 negative, or they have other reasons, other medical comorbidities because of which they wouldn't qualify for

immunotherapy. So the majority of our patients are not candidates for immunotherapy in the frontline setting.

And again, for these patients, chemotherapy is really what we have given for years and years, and that has not changed. And if we look at the data, approximately 50% of patients who get treatment in the frontline setting do not go on to get treatment in the second line setting. And that's just a testament to how big of an unmet need we have in triple negative breast cancer. So the antibody-drug conjugates that have entered this space and are making an impact here are TROP-2 antibodies. So when we think of that antibody in Enhertu, it was an antibody targeting HER2. In this case, it's an antibody that's targeting TROP-2, which is a membrane protein that signals inside the cell and results in cell growth. And in breast cancer, we have a very high expression of TROP-2. So about 80% of breast cancers have high expression of TROP-2, and generally these are triple-negative breast cancers and hormone receptor-positive breast cancer.

So that's where we've seen data from TROP-2 ADCs. There are two TROP-2 ADCs that are currently available, and both of these have had some data in triple-negative breast cancer now. So first is Sacituzumab Govitecan. Sacituzumab Govitecan has an SN-38 payload, which is a Topoisomerase 1 inhibitor and prevents DNA damage repair. It has a high drug to antibody ratio, about eight to one, and like Enhertu has a cleavable linker. So once it gets into the tumor microenvironment, that linker can be cleaved. And then the other one is Datopotamab Deruxtecan or Dato-DXd.

Dato-DXd has the same payload as Enhertu, but a different antibody. So the antibody is TROP-2. It has a moderate drug to antibody ratio, four to one. And again, it also has a cleavable linker. So once it gets to the tumor microenvironment, it can dissociate from the antibody. So in 2025, we first saw data with TROP-2 ADCs in the PD-L1 positive group. So this was data that came out actually at ASCO last year, so I'll breeze through it very quickly. Just a quick refresher on Pembrolizumab. So Pembrolizumab is an immune therapy. The PD-L1 PD-1 signaling access actually emits the immune system from acting on the tumor. So when we use an antibody to block that interaction, we actually activate the immune system to attack the tumor cell. So it is immune therapy that stimulates the immune system to attack tumor cells. Its benefit is limited to patients who do have PD-L1 expression, so we need to have the target there for the treatment to work, but when that is there, Pembrolizumab can bind and stimulate the immune system.

So at ASCO, we saw data looking at Sacituzumab Govitecan in combination with Pembrolizumab for frontline PD-L1 positive metastatic triple-negative breast cancer. So patients who presented had PD-L1 positive disease, were randomized to Sacituzumab or standard of care chemo in combination with Pembro. And this study showed us a statistically significant and clinically meaningful improvement in median progression-free survival from 7.8 to 11.2 months with Sacituzumab Govitecan instead of chemotherapy in combination with

Pembrolizumab. So this really became a new standard of care for PD-L1 positive patients. So we already saw antibody-drug conjugates sort of enter this early space in PD-L1 positive patients. But towards the end of the year, we saw now the TROP-2 antibody-drug conjugates in the PD-L1 negative patients. So this is the group of patients where we would have given single-agent chemotherapy. These agents went head-to-head with chemotherapy in that setting.

So the first study was TROPION-Breast02. This study looked at Dato-DXd for frontline PD-L1 negative patients. These were patients who had had no prior treatment for metastatic disease. Immunotherapy was not an option. Either they were PD-L1 negative, or they had already received immunotherapy in the curative setting and had progressed, or they had a comorbidity for which they could not get it. What was interesting about this trial is that it did enroll patients who had no minimum disease-free interval. So what does that mean? That's patients who presented, let's say, initially with curative breast cancer, cancer that was limited to the breast and lymph nodes. They started on curative chemo, in combination with immunotherapy and progressed. And progressed and became metastatic and needed to switch course of treatment, and they were included in this trial. So that tells you that these patients, they've been given our best chemo immunotherapy and they're progressing through it. This is a very, very high risk group of patients, and they were included in this study.

Patients were randomized one-to-one to Dato-DXd or investigator's choice chemotherapy. The And there were dual primary endpoints of both progression-free survival and overall survival in this study. So looking at the patients, about 34% of patients, about a third were De novo metastatic. So that means they never got treatment in the curative setting. They've never seen any treatment, they presented with metastatic disease that had been untreated. About 20% had received chemo in the curative setting and progressed within 12 months. And about 15% of them progressed within six months. So these are those early progressing patients that we talked about. And then about half of patients progressed after curative treatment, but progressed greater than a year later. The majority of patients could not get immunotherapy because they were PD-L1 negative, but there were about 10% of patients in both arms who were actually PD-L1 positive.

Most of the patients had visceral metastasis, so cancer in organs like the liver, the lungs, the brain, so these are high-risk patients. One sort of critical thing that's been brought up about this trial is that despite the fact that about two-thirds of patients had received chemo in the curative setting, and we know in general we give Taxanes to those patients. The choice of chemo that was given in the investigator's choice standard chemo arm was generally Taxane therapy. So you're re-exposing patients to something they've already sort of maybe been resistant to in the past. So that was something to think about in the control arm. So here's the first endpoint, progression-free survival. We can see that progression-free survival was improved. Again, clinically significant and statistically significant, 5.6 to 10.8 months with a hazard ratio of 0.57. That's a relative risk reduction of 43%. Here's overall survival, also statistically

significant, 18.7 to 23.7 months with Dato-DXd compared to standard chemo. Hazard ratio of 0.79. So very exciting data. We've made some progress in the standard chemo treatment.

Here's another very interesting endpoint in the study. So this is overall response. This is how much did the tumors that exist, how much did they shrink? And we can't call it response when there's at least 30% shrinkage. And you can see that in the standard arms, the standard chemo, the response rate was about 30%, but in the data-DXd arm, the response rate was doubled to 63%. So very exciting. We're actually shrinking those tumors about double the time. And the complete response rate is, which is we totally shrunk everything to a point where nothing was visible on scan anymore, 2.5% of patients in the standard arm compared to 9%. So we tripled the complete response rate with Dato-DXd. So exciting data compared to standard chemo. Dato-DXd does have some notable side effects. It's an antibody-drug conjugate. We hope that the side effects are less, but it does cause some ocular issues.

We do have to have patients see optometry or ophthalmology through the course of treatment. For a lot of patients, it also causes mouth sores. We generally use steroid mouthwash to help prevent some of those mouth sores. And then it does cause some of the other things we see with chemo, so nausea and low blood counts as well. So things to watch out for with dato DXD.

So we're switching gears now and talking about the other antibody-drug conjugates, Acituzumab, Govitecan. So back to back, we saw presentations from both of these drugs in the frontline triple negative breast cancer population. So ASCENT-O3 was a study that looked at Sacituzumab in frontline, PD-L1 negative metastatic triple-negative breast cancer. So similar to the TROPION-Breast02, there are some differences. So this trial did not include those very early progressors. Patients had to have at least six months between their curative treatment and metastatic recurrence. So it eliminated those very high, high risk patients. It did randomize patients one-to-one to get Sacituzumab versus standard chemo. But here in this study, those patients who progressed were allowed to go on to Sacituzumab second line. So they were offered on study the opportunity to get sacituzumab second line. And so you can imagine that that may have an impact on our long-term survival outcomes because if everybody on the trial has seen the study drug, it sort of takes away that opportunity to evaluate the long-term effect.

So here's the baseline characteristics. Again, about a third of patients, de novo metastatic, no prior treatment they presented upfront with metastatic disease. The rest are all recurrent. Half are recurrent after more than 12 months and about 20% within that six to 12 month period. In this trial, almost nobody had PD-L1 positive disease, so most of them qualified because they have PD-L1 negative disease. And here we have a little bit of a better balance between the chemotherapy options. So about half-and-half got taxane, which they likely saw in the curative setting before, and the other half got probably new chemotherapy, a combination of gemcitabine and carboplatin.

Here is the progression-free survival. So again, clinically meaningful, statistically significant improvement from 6.9 to 9.7 months with sacituzumab govitecan hazard ratio of 0.62. And you can see at the six and 12 month points that there's clearly an improvement in the sacituzumab govitecan treated patients. So exciting improvement on our current standard of care. In this trial, our overall survival events were really exactly the same between the two arms. There was no survival benefit, but again, all of the patients in the chemo arm were offered Sacituzumab Govitecan second line, so it makes survival a little bit difficult to interpret. One thing they did highlight was progression-free survival two, which is when they went on to the second line therapy, those patients who had seen Sacituzumab in the front line still did better in the second line. So maybe there's a lasting effect of having gotten it in the frontline setting.

Tumor response in this study was pretty similar. So unlike TROPION-Breast02 where we saw a difference in the response rate about a doubling of the response rates, we really saw very similar response rate 46%, 48% in the two arms on this study, but the duration of response. So once the tumor shrank, how long did they stay small was longer in the Sacituzumab arm. So improved from 7.2 to 12.2 months. So some differences in the two studies. Here's the most common side effects really consistent with what we've seen with Sacituzumab in the past. So this is not a new drug for us. It does cause low blood counts, nausea, diarrhea, hair loss tend to be big side effects, fatigue with this drug. So nothing new. It's really what we have seen before with Sacituzumab.

So frontline metastatic triple negative breast cancer, as we talked about in the PD-L1 positive groups, so those patients who are eligible for Immunotherapy, sacituzumab And Pembrolizumab is really our new standard of care based on the ASCENT-04 trial.

And in the PD-L1 negative group for patients who don't qualify for immune checkpoint inhibitors, we now have two monotherapy options. We have DATO-DXd based on the TROPION-BreastO2 study and Sacituzumab Govitecan based on the ASCENT-03 study. So big strides in the management of triple-negative breast cancer. So we'll switch gears now to HER2+ metastatic breast cancer. This is another space where we haven't seen a lot of change for a number of years, and then all of a sudden we have multiple studies coming out that are shifting the gear. So for many, many years, our standard of care was established in 2012 based on the Cleopatra study. This was a study that took patients with upfront HER2+ metastatic breast cancer. Patients were randomized to get docetaxel chemotherapy with Herceptin or Trastuzumab, which is one of our anti HER2 antibodies, plus or minus a second HER2 antibody, so PERJETA or Pertuzumab.

So they either got Docetaxel, Herceptin alone or Docetaxel, Herceptin and PERJETA. And this study showed us that dual HER2 targeted therapy, so two HER2 antibodies was better than one, but it really showed us how impressive our outcomes were. So this is frontline treatment, HER2+ metastatic breast cancer. We have a median progression-free survival of 18.7 months, so a year and a half. We have a median overall survival of about five years, 57.1 months.

But you can see this tail of the curve, which is there are some patients with HER2-positive disease with this treatment who we were able to get durable control or potentially cure. So these are patients who, a number of these patients, about 16% of the patients at the time of the final analysis, about 10 years out, were still on that frontline treatment. Patients would get Docetaxel just for six to eight cycles and then go on to maintenance HER2 target therapy alone, and they were on that maintenance throughout the course of that trial.

So until very recently, this has been our standard, frontline HER2-positive breast cancer. This is what we gave. And then ASCO last year, we saw the frontline treatment change. And in fact, in December of last year, we just got FDA approval for this combination. So the DESTINY-Breast09 study looked at our standard treatment, THP versus INHER2 in combination with pertuzumab. So now we've replaced the docetaxel chemotherapy and Herceptin with Enhertu and combined it with a second Enhertu antibody pertuzumab. There's a third arm that hasn't reported out, so we'll ignore that light blue arm for now. So this study reported a very meaningful improvement in progression-free survival with T-DXd plus Pertuzumab from 26.9 to 40.7 months. So this is frontline therapy, median progression-free survival of 40.7 months in HER2-positive metastatic breast cancer with T-DXd plus pertuzumab. So this just got FDA approved and is really now one of our very promising and available options.

The challenge and why many of us have struggled with this is when we give THP, like I said, we give the chemo for six to eight cycles, we stop and then we transition to HP maintenance. And we know there's a number of people who have very durable control, whether that's cure or not, it's hard to say, but really stay on maintenance therapy for decades. But now we have a treatment where you don't stop after six to eight cycles. So here, patients get Enhertu for that 40.7 months. And we know that Enhertu does cause a number of side effects. So this is a more toxic treatment, but one where the numbers are clearly much, much improved.

And then we saw some more data in the HER2 positive frontline space. So we saw at the end of 2024 data from the PITTINA study, which was now looking at maintenance therapy. So this is a little bit different. This is patients who get treated with our CLIOPETRA regimen, our standards, so chemotherapy and two HER2-target therapies. This is before the era of the INHERTU data. They got their six to eight cycles. They transitioned to HP maintenance, and now we're looking at adding things to that HP maintenance. Can we make maintenance better and improve the long-term control? So this was a study that involved patients who were HER2 positive and hormone receptor positive. And in the maintenance phase, they got either HP plus an antiestrogen treatment, or they got HP plus an antiestrogen treatment and Palbociclib. So this was a little bit different than our initial studies because our initial studies, nobody got endocrine therapy at all, but now we're putting everyone on endocrine therapy if they're hormone receptor positive, and we're also adding a CDK4/6 inhibitor or Palbociclib for half of those patients.

And what we saw was our numbers just keep getting better and better. Frontline therapy, the standard arm, which is just HP and endocrine therapy, median progression pre-survival of 29.1 months. And for those patients who got Palbociclib, we've improved our progression-free survival to 44.3 months. So very impressive maintenance data. So the study that was presented at San Antonio was another maintenance trial. It was HER2-CLIME-05. So this was a study. Again, patients got docetaxel chemotherapy, dual HER2-targeted therapy, H and P, six to eight cycles of chemo, or sorry, four to eight cycles of chemo here. And then they got randomized one-to-one to just continue the HP and they could get endocrine therapy if they were hormone receptor positive or get HP plus this new drug, Tucatinib. So Tucatinib is a drug that we've had available for our metastatic patients for some time, but now we're seeing it in the frontline maintenance setting.

Primary endpoint was progression-free survival. So just briefly, what is Tucatinib? HER2 is a protein that has a component outside of the cell and a component inside of the cell. Outside of the cell is where the antibodies and antibody-drug conjugates bind. Inside the cell is what we call the tyrosine kinase domain. That's the part that actually does all the downstream signaling. And drugs like Tucatinib are small. They can diffuse into the cell and they attach and bind to that intracellular domain and block that downstream signaling. So we're looking at adding this drug to our maintenance phase. So here's our baseline characteristics. About half of patients were hormone receptor positive. A little over 10% had brain metastases, which are very common in our HER2-positive metastatic breast cancer patients. About 70% have a De novo metastatic disease. So they haven't gotten any prior treatment. They just presented with metastatic disease.

And here's the primary endpoint. Investigator-assessed progression-free survival, improved from 16.3 to 24.9 months, a change about 8.6 months with a hazard ratio of 0.64. So adding Tucatinib to frontline maintenance therapy extended the median progression-free survival to over two years in patients with HER2-positive metastatic breast cancer. And when we break it down by subgroups, we see that there was maybe a greater benefit in the hormone receptor negative patients compared to the hormone receptor positive patients with Tucatinib. And one of the questions that always comes up with Tucatinib is brain efficacy because we know that it is a drug that is able to penetrate the blood-brain barrier and get to the brain. And we've seen some CNS data with it. But interestingly in this study, we did not see that the addition of Tucatinib prevented brain metastases. This was a surprising finding for many of us.

We really expected to see that. But in that about 10% of patients that did have brain metastases already when they enrolled on the study, it did delay new brain metastases. So this was a surprising finding from this study. So it's a lot of data. I mean, all of a sudden we went from having one trial in 2012 to now in 2025, having four trials in the frontline metastatic HER2-positive breast cancer space, and they're competing. Whether we give patients upfront chemo or upfront Enhertu is competing and whether we give them in the maintenance

setting, Tucatinib or Palbociclib, the CDK4/6 inhibitor is competing and the field has a lot of different considerations here in terms of which patients to give what, and we're trying to make sense of what to do. And I think many of us have thoughts about when we would choose one or the other, but I can tell you that there's a lot of ongoing discussion about what is the right combination of our different options for each patient.

It's only going to get more complicated. So it's expected this year that we will see data from INAVO-122, which is an ongoing study, another maintenance study that's looking at bringing in Inavolisib, which is a PI3 kinase drug. So about 30 to 40% of HER2-positive patients have PIK3CA mutations, and this drug targets that mutation. So for those patients with mutations, it's looking at bringing this drug into the maintenance space. So it's only going to get more complicated and have more decisions to make. But in general, I can tell you for HER2+ frontline metastatic breast cancer for our upfront treatment, we do have two options now. So we have Enhertu or TDXD plus Pertuzumab. We're generally going to consider this for our very high risk patients, those who have a lot of cancer in organs like the liver, the lungs, the brain. We have our old standard, the Docetaxel for six to eight cycles followed by HP maintenance.

This is a much better tolerated treatment. We might consider this in patients who haven't gotten any prior treatment. We're hopeful they're going to have a good response. They have very high HER2 expression, and we're hoping that they're part of that tail of the curve. Once they get to maintenance, we have two options also, we have Tucatinib. The benefit of Tucatinib seemed to be greater in our hormone receptor negative patients. And then we have Palbociclib, which is limited to our hormone receptor positive patients and is given in combination with endocrine therapy. We have learned over time that adding endocrine therapy generally seems to be improving our outcome. So for those patients with hormone receptor positive disease, we do add endocrine therapy to maintenance therapy. But obviously this is now a very complicated space where there's decisions to be made for each patient. And with that, I will stop and wrap up.

Thank you all for your attention. I left our clinic's contact information up there if it can be helpful in any way. Our clinic is located in West LA and you can always get ahold of us if we can help out. Thank you so much for having me.

Jenna Fields: Thank you so much, Dr. Basho. That was excellent. I learned so much and I really appreciated the through line that you provided us between studies over the years. That was really, really excellent. We're now going to open up for Q&A and we do have time for a few questions. My request is that you keep your questions as general as possible. I know that she covered a lot, so we'll get to a few. So I just want to jump in. A question for a male breast cancer patient who's starting estrogen blockers, oncologists said Tamoxifen is the only option for them after completing radiation. Is that accurate they want to know or are there other options available?

Dr. Reva Basho: Yeah. Male breast cancer is, of course, so challenging because we have such, such limited data and we don't know if we can extrapolate from female breast cancer to male breast cancer. So the drugs that are available are the same. However, the data that we have in male breast cancer is really Tamoxifen-driven. So many oncologists will focus on Tamoxifen in that space because we've seen the data. There's been some conflicting very small data with aromatase inhibitors. There's some studies that suggest it could be better, some studies suggest it could be worse. And there's now ongoing studies that are really randomizing and looking at this question. So the jury's still out. It's not to say that it can't be given, but I will say that Tamoxifen is generally the approach.

Jenna Fields: Okay. And for someone who's looking to extend adjuvant endotherapy after 10 years, is there any data about the post-10-year mark for those patients?

Dr. Reva Basho: No. So 10 years is really the longest that we have. Most of our studies are at the five-year mark, and then recently we saw some studies that looked at either seven to eight years or 10 years compared to the five years, but nothing beyond 10 years.

Jenna Fields: Great. And Clark, I did see that question in the registration, thought it was a great one, about reoccurrence of breast cancer in the lungs in relation to respiratory viral infections that came out last summer at San Antonio. Is there any more study on this since it came out last summer? Aside from vaccination and masking, it doesn't seem like there are many options to keep safe.

Dr. Reva Basho: Yeah, this is really an important question. There's so many different variations of this question that have been asked for people who get infections through the course of chemo, for patients who get infections later, and does that change the milieu or does that change the incidence of recurrence? And I'll tell you that all the data that we have is relatively small. And unfortunately, this is such a, like you say, it's such a hard thing to actually control and intervene on that it's a tough thing to even give advice on. I will say I always encourage patients to get vaccinated and if they're getting chemo to stay protected, but I can't recall any other big data that came out at San Antonio related to this. There might've been some posters.

Jenna Fields: And is there any news on vaccines to prevent recurrence of early triple negative breast cancer?

Dr. Reva Basho: Ever since the mRNA vaccines, there's definitely some momentum in this space, a momentum in triple negative breast cancer where we're starting to see some very interesting data start to come out. I think time will tell what role these vaccines will play. It's generally more of a treatment rather than prevention role that they're playing right now. In HER2+ disease, we're starting to see some very exciting. We have a vaccine in phase three trials now, looking at vaccine in the maintenance phase and prolonging the duration of control. So I do think vaccines are going to have more of an impact. It's very early days for vaccines.

Jenna Fields: That's very exciting to hear. Okay. For someone facing metastatic breast cancer eight years in, in the liver and now more active in the bone and spine, are there any oral drugs available that are effective for getting cancer in both the liver and the bone/spine?

Dr. Reva Basho: Yeah. I mean, whether a drug is oral or IV doesn't really change its potential efficacy. So whether it's oral and then systemically absorbed into the bloodstream and circulated, or given as an IV and systemically circulated, both have the potential to have profound impacts. It really depends on the subtype of breast cancer and the treatments that have been given in the past and what the features of the cancer are.

Jenna Fields: How is the duration of AI inhibitors determined between five and 10 years?

Dr. Reva Basho: So in general, what I always tell people is the impact between zero years and five years is very clinically significant. We see big changes in recurrence rates when we don't give it at all versus we give it for five years. When we look at the five to 10-year data, we're now talking about incremental benefits and we're talking about those incremental benefits coming at a cost for some people. So some of those drugs cause bone loss, cause osteoporosis, cause a lot of other side effects. And so we really have to balance the what is the benefit and what is the cost? So if someone has a pretty low-risk cancer, they already have osteoporosis, maybe that's not someone where we want to push it, but someone had a higher risk cancer, a lot of lymph nodes upfront and we're worried about that cancer and they're tolerating the treatment very well, their bone health is doing okay.

That's a patient where we want to try to push it. So it's always a nuanced discussion in terms of where do we push versus when do we stop?

Jenna Fields: Oh, we know that there's been an impact on federal funding for cancer this year and just more of a landscape question. Are you seeing breast cancer research specifically impacted by this reduction in funding?

Dr. Reva Basho: Yeah. I mean, so our NCI research is definitely affected. So we definitely saw some holds and some stops in our government-funded research. So it's very, very sad to see the tremendous years of work that have gone into that work and the tremendous number of institutions that are dependent on that funding to continue the work that they do. So I think we are as a whole, as a community, going to see some impact from it all. A lot of our research does come from pharma and in general, I would say pharma studies have carried on. And you can see in 2025, the pace of new drugs and new data being presented was very, very high. So some, hopefully that will continue, but I think some of our foundational research is definitely going to be affected.

Jenna Fields: Well, we appreciate your expertise. I know we can't get to every question here, but thank you so much, Dr. Basho, for this excellent and informative

presentation. As we wrap up, I want to remind those that are in our EMBRACE program that you can stay on. EMBRACE program is for those facing metastatic breast or advanced ovarian cancer. And we're going to have an intimate breakout session sponsored by Gilead Oncology with Dr. Basho. So please stay on and you'll be able to have that conversation in just a minute. Please remember to take our brief evaluation survey, which we're putting into the chat. It really does inform our future programming, and we appreciate you taking the time to fill it out. And then finally, just remember that Sharsheret is here for you and your loved ones. We provide emotional support, mental health counseling, and other programs designed to help navigate you through the cancer experience.

All are completely free and confidential, and our contact information is being put in the chat one last time along with that SurveyMonkey link. And as we close, I just want to thank you again.