

Navigating the Complicated World of Advanced Breast and Ovarian Cancer

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I. Introduction

Shera Dubitsky: Thank you for joining us this evening as Sharsheret presents “Navigating the Complicated World of Advanced Breast and Ovarian Cancer.” Tonight's webinar will focus on the unique concerns of those of you currently living with or touched by advanced cancer. We have presented prior webinars that addressed the needs of women at all stages of breast or ovarian cancer, and we encourage you to go to our website to access these transcripts and audios.

My name is Shera Dubitsky, and I'm the Director of Navigation and Support Services at Sharsheret. Much of my day is spent speaking with women, family, and friends who are living side by side with advanced cancer, and I'm excited to hear the information tonight as I imagine it will enhance my work with you and that you as well will find the information impactful and purposeful.

I'd like to begin by thanking Amgen for sponsoring tonight's webinar and for their ongoing generous support of Sharsheret. I would also like to express our gratitude to our partners: FORCE, Living Beyond Breast Cancer, Metastatic Breast Cancer Alliance, Ovarian Cancer Research Fund Alliance, and Young Survival Coalition, for their partnership and collaboration.

So, a little bit about us: Sharsheret supports women and families facing breast and ovarian cancer at every stage. Our expertise is in young women and Jewish women, though we offer support to everyone reaching out to us. We help you connect to our community whatever your personal background, stage of life, genetic risk, diagnosis or treatment, and all of our services are personalized, confidential, and free.

Increments of good news are worth sharing. There is a recent National Cancer Institute study that found that women with advanced breast cancer are surviving longer. The lead author, Angela Mariotto of NCI, called the findings favorable, because they were partly due to longer survival times resulting from better treatment, so this is indeed uplifting news and we of course hope that the trajectory continues in this direction.

As the medical landscape of advanced cancer changes and as your journey moves forward, Sharsheret is with you. Our Embrace Program for women living with advanced breast cancer and ovarian cancer is tailored to meet the needs of each woman and her family, so we offer free one to one phone support counseling as needed, as well as customized resources that meet your unique needs.

I particularly want to highlight our Survivorship Kit that you can personalize. So, in there you'll find a care plan, resources and

information, a healthy cookbook, and a pedometer. You can order this kit directly from going to our website at www.sharsheret.org.

We're also excited to announce that we will soon be launching our Sharsheret Embrace Facebook group, for those of you living with advanced breast cancer or ovarian cancer. Our goal of this closed Facebook group is to offer you a safe space to meet other women who are living side by side with metastatic breast cancer or recurrent ovarian cancer. In this group we encourage you to share your experiences knowing that other women in this community are experiencing similar challenges and hardships, moments of laughter, and really just life-changing insights, so we will share more information about when we are officially launching and how to join this Facebook community via email when we send out the transcript and recording from tonight's presentation.

We are excited to have Dr. Adam Brufsky who is joining us this evening. He is a Professor of Medicine at the University of Pittsburgh School of Medicine, and also serves as the Associate Division Chief for the Division of Hematology Oncology at the University of Pittsburgh School of Medicine's Department of Medicine. Dr. Brufsky is the Medical Director of the Women's Cancer Center at Magee-Womens Hospital of University of Pittsburgh Medical Center, and the University of Pittsburgh Cancer Institute. He is also an Associate Director for clinical investigations and Co-Director of the Comprehensive Breast Cancer Center. As an active researcher, he has published numerous abstracts and research articles in leading journals and is principal investigator on a number of research grants funded by the National Institute of Health, Susan G. Komen Foundation, and the US Army Breast Cancer Research Program. Dr. Brufsky, the proverbial floor is yours.

II. Navigating the Complicated World of Advanced Breast Cancer

Dr. Adam Brufsky: Great, thanks a lot. We can go to the next slide just to get everything started. Just a few things. First of all, I think the most important thing that was said in the last five minutes is that people with advanced breast cancer are living a lot longer, and I think it's really great. I've been doing this and I have devoted my career over the last 25 years to the treatment and research of metastatic breast cancer in particular, and it's really gratifying.

I think I started to see this on my own practice probably five or six years ago. That women really are starting to live a lot longer and that's really good, and we're going to talk a little bit tonight. I'm probably going to skip through a lot of the slides I have because I have a lot of information to go through, but basically, the fact that women are living longer, has some issues with it, which are good issues to have, but we even have better to

do and we have even more exciting new things that are coming down the pipe. With that, why don't we get started. Your next slide, please.

Breast cancer is, as we all know, the leading cancer, cause of death in women. There will be about 250,000 new cases this year, about 40,000 deaths, and the idea is that it really was one of the first diseases, the first cancers where we realized that biology was the main driver of treatment and we tried to tailor the treatment based on the biology of the cancer, in particular the receptor for estrogen and the receptor for HER2. That really has kind of guided us over the last 15 or 20 years in how we treat metastatic disease. Next slide.

What I'm going to talk about today are bones in metastatic breast cancer. Because this is a Jewish breast cancer organization, we'll talk a lot about BRCA associated breast cancer. Some very exciting things are going to happen at this year's annual ASCO meeting in a few weeks. We'll talk a little bit about Palbociclib and immunotherapy, both of which I think have the potential. Palbociclib is clearly revolutionizing the treatment of breast cancer, and immunotherapy may. Next slide.

The idea is that when women live longer with metastatic breast cancer, they are going to live longer, potentially have more side effects, and in particular those side effects are going to be in the bone. Metastatic bone disease is very prevalent. Probably between 40 and 60% of women who develop a metastatic disease will have bone metastasis, and in fact the longer women live it creeps up to 70%, and so this is a big issue. Next slide.

Because with a bone metastasis, you can get a lot of what are called skeletal related events over time. You can get a fracture of a bone, which could be devastating, the need for radiation to the bone, need for surgery to the bone, spinal cord compression where the cancer actually escapes from the vertebral body and actually compresses your spinal cord and causes paralysis. You can also get hypercalcemia malignancy where the bone secretes a lot of calcium and that causes all sorts of metabolic problems.

These bone metastases can really affect a lot of issues and really make someone's quality of life miserable. I mean, you can live six, seven, eight years now with bone metastasis if not longer, but you could be miserable if you're in pain all the time, so we really want to do things to stop that. Next slide.

The rate of these skeletal related events is quite high, as you can see here. This is actually the placebo arm of a trial long ago of a bisphosphonate, and you can see that about 50% of women develop a pathologic fracture. About 70% of women will develop some sort of skeletal related event, so this is an important issue. Even though people

may come with say one or two bone metastases, we really want to try to prevent these skeletal related events. Next slide.

So how do we do that? Next slide. The idea here again is that osteoclasts, which was shown on the bottom part of this figure, they're normal cells that chew up bone. Normally they're under control by a lot of mechanisms in the cell, but if a cancer cell comes near them, the cancer cell will secrete all sorts of growth factors that cause the osteoclast to kind of chew up more bone. The osteoclast then secretes growth factors that cause the cancer to grow, so it's a vicious cycle. The idea is to give drugs like bisphosphonate, and I think people who have advanced cancer who are on this call or know people with advanced cancer know what those are. There's a drug called Zoledronic acid which is intravenous. There's other ones called Clodronate which is oral, or Ibandronate which is oral, and the idea behind these drugs which have been used for osteoporosis for years is to kind of break this cycle by slowing down the osteoclast. That's the idea behind this. Next slide.

This just shows you the reduction in the risk of cellular related events with all of these drugs. Zoledronic acid is shown up at the top. It's about a 60% reduction. Some of the other bisphosphonates like Pamidronate which is intravenous, Ibandronate which is Boniva, Clodronate which is not available in the US, all can reduce the risk of skeletal related events by about 20 or 30%, but generally Zoledronic acid works the best. I think that's really until very recently has been used as the standard of care in this disease. Everybody who gets Zometa, they come in once a month to their doctor if they have metastatic disease to bone and get it. Next slide.

But recently there have been newer drugs, and the idea is that there's a protein called RANK Ligand which binds to something called RANK receptor on osteoclasts. When that happens, those osteoclasts are activated. What you can do is make this monoclonal antibody and it's a mimic of a protein called osteoprotegerin, and Denosumab or Xgeva is actually a mimic of this antibody which coats the RANK ligand receptors, and therefore they can't stimulate the osteoclasts. Next slide.

And when that happens actually, Denosumab works a little bit better than Zoledronic acid. It reduces the risk of skeletal related events by about 20% or so, and as a result it really now has become the standard of care. Everybody will likely get Xgeva or Denosumab, which is the generic name, once a month, instead of Zoledronic acid.

However, it depends on what part of the country you're in, because some insurances don't allow Denosumab because Zoledronic acid is generic and therefore theoretically at least a little bit cheaper. They both work relatively the same I think clinically, and I think it's okay to give Zometa instead of Xgeva, but on the other hand I think that most people use one

of these, one of these two to protect themselves against bone complications. Next slide.

I think the big thing that's happened in this business in the last couple of years is how often we should be giving them. Everybody generally gets the monthly, but it turns out next slide, that we can actually start giving them every three months. This is a trial called Optimize and this is patients who already were on Zoledronic acid and they were randomized to get it monthly or every three months. Next slide.

When that was done, the rate of skeletal events was exactly the same, so it turns out that what we're all starting to do now is give you your Zoledronic acid every three months instead of monthly. There's no data right now on Xgeva given every three months, although there's a Swiss trial that's going to report out in a couple of months or maybe a year or two. I think it will probably be the same result where it's likely we're going to start being given these drugs every three months instead of monthly. When we do that, one of the rare but serious complications of this was called osteonecrosis of the jaw, where your jaw doesn't heal after an invasive dental procedure like an extraction. That's actually going to probably go down if you start giving these drugs every three months instead of monthly. Next slide.

So, what's new actually in metastatic breast cancer? Next slide. This is a little bit complicated, but there have been drugs that have been developed, CDK4/6 inhibitors and Palbociclib or Ibrance is the most common one. What they do is they interfere with this pathway. It's a shame I don't have an arrow to point this out, but for cells to go through what's called a cell cycle and divide, there's a protein called retinoblastoma that controls that. It's RB, and you can see it kind of in the middle, and it's bound to another protein called E2F.

The idea is that there are these proteins called cyclins, especially in estrogen receptor positive metastatic breast cancer, that actually adds phosphate groups to the RB allowing the E2F to pop off and then start the cell cycle. If you have a CDK4/6 inhibitor, it blocks that phosphorylation, that adding a phosphate to the RB so the cell cycle can't start. These drugs apparently only work in estrogen receptor positive metastatic breast cancer. They may work actually in HER2 positive breast cancer, but the trials are not out yet. They definitely do not work in triple negative breast cancer. Next slide.

These are the ones that are actually out there. This Palbociclib which was approved, LEE001 which is Ribociclib or Kisqali, that just recently got FDA approved, and Abemaciclib actually has data that's going to be presented at our ASCO meeting and it will likely be approved over the summer. We're going to have all three of these drugs and they have

slightly different side effects, but they all tend to work basically the same way. Next slide.

For Palbociclib, there was a large straw poll polling the two, which is about 666 women who basically had metastatic breast cancer that was estrogen receptor positive and they had no prior therapy for their metastatic disease and they were randomized to Letrozole or Femara, which is a standard therapy with or without Palbociclib. Next slide. What was really dramatic is that the length of time these women lived without the cancer progressing doubled from about 15 to 16 months to about 30 months, so that's two and a half years now that a woman with estrogen receptor positive metastatic breast cancer can live without her cancer getting worse, and we believe that's going to improve people's overall survival from this disease dramatically and I think we're all looking forward to a day that either at this ASCO meeting or the San Antonio meeting in the fall or in the winter or even ASCO 2018. I think we're going to start to see some data that's going to be very, very exciting. Next slide.

The only side effect to these drugs is a reversible white count, reversible neutropenia. It's not like the neutropenia from chemotherapy. Once you stop the drug, the neutrophils recover almost within a day or two, so it's really a very well tolerated, very easy to manage drugs. Now, clearly there are rare side effects that people get like fatigue, but generally these drugs are very easy to take. Next slide.

There was another trial actually where we used these drugs and people have progressed from their disease, and this is PALOMA-3. These are women who were now in the second line, they had already had a first-line hormonal therapy, and they were given Palbociclib. They were given Fulvestrant or Faslodex, which is a standard intravenous shot that you get once a month that works pretty well with or without Palbociclib. Next slide.

Palbociclib did the same thing. It doubled the amount of time that these women did well without their cancer progressing. In fact, even though this says 9.2 months, it's more like about a year to 13 months in the latest data, and it's really a doubling or almost tripling of that time. In fact, this will likely improve people's overall survival from metastatic breast cancer as well. Next slide. Again, the only side effect that you see is a reversible neutropenia, or low white count. Most people do pretty well with these drugs. Next slide.

A few other things, and then we'll kind of turn it over to our ovarian colleague. The first one that I think is really, really interesting is that it turns out about 10% of the time now that we've learned how to do large scale DNA sequencing of cancers and we're starting to do this for a lot of people, we're finding about 10% of the time if you have estrogen receptor positive, HER2 negative metastatic breast cancer that you've acquired a mutation in HER2, and that mutation can actually be treated. This is

actually just showing you that this is one particular set of data where they found mutations in HER2 in about 7% of patients. It's actually anywhere from 7-15% of women with estrogen receptor positive HER2 negative metastatic breast cancer actually have HER2 mutations. Next slide. This just shows you again where they are. Next slide.

This is a trial called Summit, and this is some of the preliminary data from it. What this shows is that these women who have been treated with multiple, multiple level therapies and have progressed through everything, when we treat them with Neratinib, which is an oral agent that inhibits the mutated HER2 receptor, it's called a HER2 tyrosine kinase inhibitor. When we give that with Faslodex or Fulvestrant, even if these women have had Fulvestrant before, most of them either have stable disease or they respond, so if those blue bars go down it means people are responding. Really, I think this is really, really exciting, and it's one of the things that we're thinking about using large scale DNA sequencing of people to find these mutations and maybe change their therapy. Next slide.

What about triple negative breast cancer? It's about 15% of all breast cancer, and the problem with this is that we really have no therapy other than chemotherapy that's proven to work in it. That's the problem, and chemo sometimes with triple negative breast cancer doesn't even work that well. Next slide.

One thing that's interesting about triple negative breast cancer is that it has what's called homologous recombinant repair deficiency, so what that means is that the DNA has trouble repairing itself. DNA in cancer cells is continually kind of being growing. It's kind of replicating all the time, and that introduces a lot of mutations into the DNA and they have to be fixed. It turns out that if the DNA breaks in half, what's called a double stranded DNA break, that in BRCA associated breast cancer that's the problem is that you get a double stranded DNA break that you can't repair. Well, it turns out in some percentage of triple negative breast cancer, even over and above BRCA 1 or 2 mutations, which here accounts for about 15%, there's probably another 45% that may have kind of this deficiency in DNA repair. Why is that important? Next slide.

It's important because we have a lot of these PARP inhibitors. What these do is that they inhibit single stranded DNA repair, and what that does it leads to a double stranded DNA break that the cell can't repair, and all of these are very, very exciting. Next slide.

You can see here are all the trials that are going on. The big one is called OlympiAD. That's the second one down. It was a trial of first-line metastatic breast cancer that's triple negative and BRCA positive. Women were randomized to Olaparib or standard chemotherapy, and this trial was very positive to the point where it is in the plenary session of ASCO.

That means it's going to be a big deal, and so we're all waiting for this. In about two and half weeks we're going to see it, and I think it's Sunday June 4th I think we're actually going to see the announcement of this particular study. I'm sure the ovarian doctor that's going to talk after we talk a little bit more about PARP inhibitors in ovarian cancer, but I think this is now going to introduce PARP inhibitors to breast cancer. Next slide.

The last thing really to talk about is the immune response, and it turns out that again, this is one of many complicated slides, but the bottom line here is that cancer cells have evolved ways of turning off the immune system. What happens is that you can have all these kind of proteins on the surface of a breast cancer cell called antigens, and your T cells can react to them and start growing and trying to attack, but there's a receptor called PD-1 that binds to a ligand called PD-L1 on the cancer cell that turns the T cells off.

These guys have it figured out an antibody that coats that PD-1 receptor and blocks that kind of break. That lets the T cells kind of start growing a lot again, and it works really well on melanoma, it works really well on lung cancer, it works really well on bladder cancer, in some lymphomas and leukemia's, and now we're trying to see whether it works in triple negative breast cancer. Next slide.

This just shows you this PD-1, PD-L1 pathway, showing you that the cancer cells can block it. PD-1 binds to PD-L1 on the cancer cell and actually turns off the immune system so it can't work. Next slide. This is pembrolizumab, which is a monoclonal antibody that binds to PD-1 and blocks the interaction, so therefore the cancer cells can't be turned off. They keep growing, next slide, or the immune cells keep growing, and this just shows you that this was again tried in triple negative breast cancer with a lot of therapies already, like three or four therapies. These are women who had gone through a lot of different things, and you can see about half of the women had either stable disease or responded to this. This is not, you know it doesn't look great, but on the other hand it is a signal and it got us all very excited and so now we're doing these big phase three trials with immunotherapy for triple negative breast cancer. Next slide.

This just shows you, this is called the IMpassion130 study. It just closed. It took women actually, it says 350. We actually ended up accruing about 650 women, all of whom got nanoparticle paclitaxel or Abraxane with or without a drug called Atezolizumab, which is a PD-1 L1 monoclonal antibody, and the whole idea is to see whether we can improve the time that women live without the oppression of their cancer. This trial accrued, it's all done. We'll know the results within about probably nine months; so again, I think it's really exciting. Next slide.

I think we'll kind of stop. The bottom line is that bone targeted agents given every three months can reduce skeletal related events, so I suspect oncologists are going to start doing this every three months. I think CDK 4/6 inhibitors are very exciting, and they show a survival benefit. I think HER2 mutations are really cool and may be another way to treat women who have gone through a lot of different hormonal therapies.

Finally, I think the big news of at least the next three or four months in metastatic breast cancer is going to be the use of PARP inhibitors in metastatic breast cancer, and maybe next year's big thing will be immunotherapy. Again, thank you all, and I think after the ovarian doctor, I'll answer questions. Thank you very much.

Shera Dubitsky: Great, Dr. Brufsky. Thank you so much. You actually covered a lot of material in 20 minutes, and I hope that the participants on the call tonight, that you'll bring some of this information back with your doctors for deeper discussion. I particularly appreciated your optimism when you were talking about not only the quantity of life that women are living longer, but I also appreciate that you were talking about the importance of quality of life, and the hopeful message that you gave around those women who are living with triple negative breast cancer, particularly in BRCA, so thank you very much.

It is now my pleasure to introduce Dr. Mira Hellmann. Dr. Hellmann specializes in gynecologic oncology. She treats all subtypes of gynecologic cancers, including uterus, cervix, fallopian tube, ovaries, primary peritoneal, vaginal, vulvar cancers. Her research focus is in clinical research, including cooperative group studies as well as industry sponsored and investigator initiated. She enjoys having the opportunity to offer patients the possibility of participating in the most cutting edge research if they are inclined to do so.

Dr. Hellmann was active in resident and student education and received several awards in resident education. She also helped spearhead a comprehensive center for minimally invasive surgeons across multiple cancer specialties. She is currently practicing at the John Theurer Cancer Center at the Hackensack University Medical Center, and in the short time since she has joined the Hackensack Medical Center, Dr. Hellmann has spearheaded an IRB approved study looking at lymph node dissection for patients with endometrial cancer. She is currently active in proposing another study to the IRB to approve patients' post-operative pain control. Dr. Hellmann?

III. Navigating the Complicated World of Advanced or Recurrent Ovarian Cancer

Mira Hellmann: Good evening. Thank you very much for allowing me this opportunity to speak to you about the topic of recurrent ovarian cancer. First of all, I'm happy that Dr. Brufsky touched on several issues that we will be touching

on tonight as well, but I'm going to go ahead and get started because our time is limited. Next slide, please.

Ovarian cancer is the fifth leading cause of cancer related mortality in women worldwide. It is the leading cause of death from gynecologic cancer. There are practically 21,000 new cases diagnosed annually, and this is from the most recent data from the 2016 SEER database. Now, as you can tell from this slide here, recurrence of ovarian cancer is directly related to the stage at presentation. Unfortunately, approximately 75% of women present in advanced stage, and if you look at the slide that will lead to about a 70-95% of recurrence for these women. Next slide.

This is a basic diagram looking at recurrent ovarian cancer. The timing and the management of recurrent ovarian cancer is directly related, and the timing of recurrence almost treats different disease processes, so if you look at this diagram the most resistant recurrence to treat is the refractory cancers. These refractory cancers are basically cancers that don't respond to initial treatment and go right through the treatments. As you go further down this diagram, you will see recurrences that are more and more sensitive to treatments. We're going to focus on two very basic different type of recurrences. One is the platinum resistant recurrence or primary resistant recurrence, and the second one is the platinum sensitive or the sensitive recurrence, and that's B and D on this diagram. Next slide, please.

This is a timeline in terms of the recurrences and where they fall. Refractory is at the onset where disease goes right through chemotherapy, then there's the platinum resistant where the recurrence occurs early on, and it's usually defined as a recurrence that occurs within the first six months after the completion of initial treatment. Platinum-sensitive recurrence on the other hand is a recurrence that occurs more than six months and some that believe the definition of a year after the completion of initial treatment. Next slide.

What are the symptoms of recurrent ovarian cancer? Bloating, constipation, pain, nausea, these are some of the most common symptoms that patients present when they develop a recurrence. As you can tell, unfortunately these are not very specific symptoms, and it really behooves both the physician and the patient to be very alert to these very subtle symptoms that can be indicative of recurrent ovarian cancer. Next slide.

Now, how do we diagnose or establish a diagnosis of recurrent ovarian cancer? It's a combination of different factors. Physical exams, sometimes there's a mass that's palpable on exam. Patients can develop recurrent ascites, pleural effusion, which is fluid around the lungs. CA 125 as I'm sure a lot of you are familiar with is a tumor marker that's used to monitor patients with ovarian cancer, and if we notice an elevation either

above baseline for the patient or above the normal range, that can be an indication of recurrent cancer.

Then often times we use imaging so as a CAT scan, a CT scan, or a PET CT to help diagnose or identify lesions and establish a recurrence. Now, when looking at recurrent ovarian cancer, the question is a biopsy necessary, and this is really very individual and it depends on the specific clinical scenario. Once a diagnosis of recurrent cancer is made, the question is when to start treatment and what to use in terms of treatment. Next slide.

Here's just a slide basically looking at imaging modalities and ovarian cancer. On the left hand side, you have a plain CT scan. If you look at the top image you'll notice, there's basically no evidence of disease and the area that's lit up really is bladder. If you look at the bottom image, there is a central mass that looks like a very dark black spot in the middle image. The middle image is the PET scan, and on the far right hand side is a PET scan superimposed onto a CAT scan, so you combine the two images on the left. Next slide.

When looking at recurrence, one has to bear in mind, what is the goals of treatment for recurrent ovarian cancer? Prolonged survival, controlled disease related symptoms, delay times of progression, minimize treatment related symptoms, and improve or maintain quality of life. It's important to be very clear and specific, both on part of the physician and on part of the patient as to what are the goals, because this will definitely help tailor treatment. Next slide.

A couple of slides or two slides ago, when to start treatment. With evidence of recurrence with the absence of symptoms, does not necessarily mean that that treatment needs to start immediately. Now, a lot of people in the audience may feel very uncomfortable with this, and a lot of patients may feel very uncomfortable with this, But studies have shown that initiating especially chemotherapy treatment, before the symptoms or significant disease burden, all it really does is subject patients to the unfortunate side effects of chemotherapy without necessarily improving outcome. So, it's very important to have this open discussion with the physician regarding exact timing of treatment of recurrence to cancer. Next slide, please.

Now looking at the two different subtypes I said we would focus on, there is the platinum sensitive recurrent ovarian cancer, and the main stay of treatments in this disease is surgery in very limited clinical situations, chemotherapy, targeted therapies and clinical trials. The platinum resistance recurrence surgery unfortunately is not an option as not been shown to be beneficial. So we focus mainly on chemotherapy. We are trying to develop more and more targeted therapies. Enrollment in clinical trial is of utmost importance in platinum resistant disease given that our

therapeutic options are so limited, and palliative care is something that is across underutilized and management of recurrent disease and recurrent cancer in general, specifically in terms of recurrent platinum resistant ovarian cancer. Next slide.

The role of surgery in recurrent disease is like I stated earlier, somewhat limited. All of the data to date is retrospective in nature, meaning all the trials have looked back at patients who have had surgery to determine whether or not it's helpful. There are currently three major trials that are open, looking prospectively at the utility of this surgery but the data is not in yet. One of them is BOG213 and there are two international European trials that are currently being conducted called Desktop and SOCA but the results of these are not out yet. But this surgery is really limited to patients who have very limited disease, have no evidence of ascites, plural infusions or something called carcinomatosis which is a fine spread of cancer throughout the peritoneal cavity. It's really not thought to be beneficial in these patients.

Another surgical modality that has been looked at in ovarian cancer is something called HIPEC, which is hyperthermic intraperitoneal chemotherapy, and actually Dr. Brufsky who was at Pittsburgh does a big HIPEC over there that some have been used to pursue treatment in other cancers. Now this mode of treatment really is basically, taking patients to the operating room, removing tumor and administering heated chemotherapy directly into the peritoneal cavity at the time of surgery. It's associated with a significant amount of morbidity, and therefore it needs to be used very, very cautiously.

There was actually a statement that was put out last year from the European National Group of Gynecological Malignancies, very clearly stating that today there is not enough evidence to support the routine use of this surgical modality and management of recurrent ovarian cancer, and really only to be limited to clinical trials due to the significant toxicity. Next slide. This is just a basic diagram. Next slide.

This is the diagram of the HIPEC and as you see here, there is a chemotherapy that's heated and it's instilled into the peritoneal cavity into the abdomen and then drained out of the abdomen, reheated again and recycled. Next slide.

Once surgery is performed is either performed or not performed depending on the clinical situation, the next part of treatment is chemotherapy. And plan of sensitive disease we have very effective chemotherapeutic agents and I try to highlight here the important trials that have come out over the past decade or decade and a half. One of the most important trials was the ICON4 trials which basically established that we should be really using at least two medications to treat platinum

sensitive recurrent ovarian cancers, and that has shown to significantly improve survival.

These other studies looked at other different regimens looking to decrease toxicity, the CALYPSO trial looked at the different combinations of the chemotherapies. I was shown to have different outcomes as what was at that time established chemotherapy regimen but less toxicity. The OCEANS trial was a trial that looks at standard chemotherapies for Platinum-Sensitive Recurrence adding and the agent called Bevacizumab or Avastin, which would improve survival, and has most recently hot off the press as of March of 2017, the NOVA trials came out, looking at the addition of what's called pro inhibitors which Dr. Brufsky had done, as maintenance for Platinum-Sensitive Recurrence.

Now the idea of maintenance and recurrence is maintenance basically means giving additional treatment after chemotherapies help prevent recurrence is a basically new concept. And this is the first time that actually there is the FDA approval for one of these agents. Next Slide, I'm going to skip this diagram.

Anti-angiogenesis agents have been studied and used extensively. I just want to touch on to the use of very frequently in ovarian cancer. As many of you may be familiar with Avastin a Bevacizumab, is an anti-angiogenesis agent that has been used in primary and recurrent ovarian cancer, and has been shown to increase survival both in platinum sensitive and in platinum resistant recurrent disease. So during the angiokinase inhibitor and that's actually currently undergoing investigation in Europe though it has been approved for maintenance therapy, in women with ovarian cancer in ICON6 trial. Most recently it has been looked at in terms of combining it with a Olaparib which is a PARP inhibitor with promising outcomes. Next slide.

So, what's the mechanism of PARP inhibitors? I'm not going to repeat what Dr. Brufsky said. He basically went over this very clearly. But in ovarian cancer it's particularly important as stated in patients who have a BRCA mutation, because this just adds to the damage that the BRCA mutation is unable to fix and cause this cell death which results in treatment of the cancer. Next slide.

Now PARP inhibitors, there are three currently that have been approved in the treatment for ovarian cancer. The first PARP inhibitor that has been approved was Olaparib and that was approved for the treatment of patients who have received at least three previous chemotherapy agents but were still in the platinum sensitive range. But it's only approved for patients who are BRCA mutation carriers, specifically diagnosed with their BRCA Analysis CDx testing, and it was in 2014.

In 2017, Olaparib was approved after the results of the NOVA trials which I talked to you about in the previous slide with maintenance in Platinum-Sensitive Recurrence in BRCA mutation carriers and in non BRCA mutation carriers. So, even though this is a PARP inhibitor, the approval for this was not limited only to patients who have a BRCA mutation but also to patients who do not have a BRCA mutation. It does not improve survival as much but it was definitely extremely effective in improving survival verses patients who did not have PARP inhibitors at all. Next slide.

Rucaparib is the third PARP inhibitor to recently achieve approval, and it's approved for the use after two prior chemotherapy agents as opposed to Olaparib which we saw in the previous slide was approved for the use and this after three previous treatments. This was approved in December of 2016. The important difference is this was approved for patients who have BRCA mutations or something called loss of heterozygosity, and patients who have these abnormalities that are diagnosed with the use of the foundation focus, BRCA testing. So, what's interesting is that the foundation focus of BRCA testing looks for both germline mutations or inherited of BRCA as well as systematic or acquired mutations of BRCA. Next slide.

Most of the things that we talked about up to now where in Platinum-Sensitive Recurrence have Platinum-Resistance Recurrence are unfortunately much more difficult to treat. There is limited treatment options that chemotherapy agents all over there is a long list of chemotherapy agents that are effective, the utility of them is limited and often times patients end up going from chemotherapy agent to chemotherapy agent over a short period of time. To date, when selecting agents the focus needs to be on limiting toxicity and obtaining the best outcome.

The AURELIA trial was one of the few trials that showed improved in outcome, even with patients with Platinum-Resistance disease and that was with the addition of the Avastin a Bevacizumab, you can see that not it's in the middle of the slide. Integration of palliative care is extremely important in this situation for these patients as we stated earlier surgery has a very limited role but consideration really needs to be given to molecular profiling and enrollment of clinical trials. Next slide.

Now, targeted therapies is something that is a major focus amongst many cancer specialties. When you look at the NCCN guidelines for treatment of ovarian cancer, there is a very exhausted list of different chemotherapies that are approved. Literally it's like a couple of pages. But when you look at targeted therapies that are approved, there are only three targeted therapies that are currently approved for treatment of ovarian cancer and that's Bevacizumab, Olaparib and Rucaparib. I think

these were put out before Niraparib was approved. But that's pretty much it. Next slide.

Why is this important? Dr. Brufsky talked about different receptors and that's also applicable to ovarian cancer in terms of using this to tailor treatments specifically, two patients who have specific mutations or specific predisposition to these agents. I included here a little slide that explains it but I don't think we have time to show this little slide so, but basically it just focuses on different receptors that are present in ovarian cancer cells and why these targeted therapies are useful in the management of ovarian cancer. Next slide.

Here is a diagram of different mutations that are present in ovarian cancer in different areas that are potential targets for targeted therapy. Next slide. Some of the agents that have been studied are as we said earlier, anti-angiogenesis, which are receptor inhibitors, Bevacizumab otherwise known as Avastin which a lot of you are familiar with angiokinase inhibitors inhibit PDGFR. Cedinarib, Pazopanib and Iniparib.

PARP inhibitors, we talked about extensively. Veliparib is still being investigated and it's been promising. So the top three here have really been studied extensively and currently approved for you to use in recurrent ovarian cancer. The bottom three are a little bit more limited fully receptor and targeted since it was supposed to be promising but really did not prove to be that beneficial. Herceptin, as much as it's used in breast cancer unfortunately, it has not been a very good contender in treatment of primary or recurrent ovarian cancer.

Hormone Therapy is of limited use also in ovarian cancer but sometimes can be specifically for patients who are positive for a hormone receptor status, or patients who have just an elevated CA-125 as a clear evidence of cancer. But it is a really of very limited use. Immunotherapy is currently being studied extensively. Specifically, checkpoint inhibitors PD-1 and PD-L1, and there is a phase one and some phase two data that look promising and so the treatment of ovarian cancer currently is actually being studied in trials looking at combining PD-1 and inhibitors in combination with other agents to try to increase efficacy. Next slide.

Precision medicine is basically trying to tailor chemotherapies to patient's specific cancer. Currently most of it is not FDA approved. Foundation Testing is just one company that basically what they do is they take tumor, they analyze it for the molecular profile or for the mutation that is driving the development that is driving this particular cancer. Not everybody's ovarian cancer, but this specific particular cancer, to help tailor chemotherapies to address this specific to underline mutations.

The only testing that is currently FDA approved is what we talked about earlier, which is a foundation focused on CDxBRCA testing which is used

to determine whether or not patients will benefit from treatment with Rucaparib. What I found is interesting is the foundation aspect, actually a serum blood test trying to identify molecular mutations and specific cancers. But as I said, all of this is pretty much on a trial basis, and it's currently has not achieved FDA approval. I know there was some data out in ASCO last year. It is something that is helpful especially in patients with Platinum-Resistance Recurrent disease where the treatment options are limited. But please bear in mind that it's not a non-approved test for management. Next slide

We covered a lot of information in these slides. First of all, when going to talk to someone about management of recurrent of ovarian cancer, it is very important to insure that your doctor is specifically focusing the treatment on you with this specific condition clinical situation that is present. The American Cancer Society actually advises to obtain second opinions especially in recurrences where treatment recommendations may vary.

When someone presents the platinum sensitive recurrence right off the bat the management is pretty directed. But once we are talking about second and third line recurrences or recurrence in the platinum resistance in a category, a second opinion may be of help. It's important to insure appropriate genetic testing to be helpful both to you, and your family. I really want to drive the point home that please I want to emphasize that palliative very important management of recurrent disease. It can really enhance quality of life without detracting quantity of life. I also want to encourage strongly to consider clinical trials because this will not only offer treatments that are not currently approved but also allow for the possibility of advancement of the field. Next slide.

The next slide is the list of websites that can be helpful to obtain further information. Thank you for allowing me to present tonight and I hope that this was a helpful presentation to you and please feel free to just ask any question. Thank you.

Shera Dubitsky:

Great. Thank you, Dr. Hellmann. This was indeed very comprehensive and I appreciate your discussion of precision medicine and targeted therapies. I particularly appreciated both you and Dr. Brufsky sort of sharing the hot off the presses. Research and treatments that are really on the horizons because that leaves us feeling very hopeful, and as you said many of these things are becoming more and more promising. All these slides will be on our website so if you are interested in checking any of these out we will have that on our website when we post our transcripts.

I would like to now introduce Dikla Benzeevi. Dikla will share her personal story about navigating metastatic breast cancer. She has touched the lives of many, many women across the country, providing information

inside guidance, and really operates on uplifting message and we are honored to have Dikla on our Sharsheret LA Regional Office Committee. Dikla, go ahead.

IV. Personal Story

Dikla Benzeevi: Hi Shera, thank you. I want to start by thanking Dr. Brufsky and Dr. Hellmann for their insightful presentation. It's always good to see in a concise manner what the latest and greatest is happening out there for all of us with metastatic disease. Also thank you to Sharsheret and your partners FORCE and Ovarian Cancer Research Fund Alliance. LBBC, YSC and MBC Alliance for collaborating and making this webinar possible, and for everyone listening in, you've made it to 50 minutes and I appreciate you hanging in there to listen to me as well, so I appreciate that thank you.

Again, my name is Dikla Benzeevi and I've been living with metastatic breast cancer for almost 15 years. It's been a long journey with lots of challenges and definitely not something I could have done all by myself. Navigating this difficult, difficult road is not easy.

My specific breast cancer is what's considered triple positive, HER2-positive, ER-positive and PR-positive. My metastasis was in lung and bone, so my bone metastasis has resolved and my lung metastasis, I have been dealing with that for 10 years now. I have been in continuous treatment for 15 years. I was originally diagnosed at the age of 32. I have changed therapies due to progression nearly every two years or sooner, and I've been on over 10 cancer therapies, in fact maybe half of the therapies I've been on were not around when I was initially diagnosed.

It's very hopeful hearing the stories about what's up and coming and what's existing because we never know what comes up in the future that will benefit us and give us some extra years that we are seeking. My spine alignment metastases have caused issues. Back when I had the bone metastasis it was in my spine and I did have one of those fractures Dr. Brufsky mentioned as a skeletal related event and it almost paralyzed me but thankfully my spinal cord was preserved even though the tumor ate up most of the vertebra in my spine. I needed spine surgery, I was in a back brace, it was a very very difficult time, I was fully disabled.

I've gone through long surgeries and radiation therapies, chemotherapies, targeted therapies, I think hormonal therapies, immunotherapies and I continue to undergo therapies now. In fact I've gone through all the HER2 targeted therapies and I'm about to start a clinical trial. So, clinical trials are so essential in fact I just signed up, I signed my consent form yesterday. It was a momentous occasion for me and I hope that this new trial treatment drug whether I get it or not depending on the arm will work for me.

The journey has definitely been rocky uncertain and with definite ups and downs from towns of near total disability and chaos and extreme pain to times of feeling excellence. There were years when I even almost forgot I was in treatment because I was feeling so good. Did I know back in 2002 that I'd still be here 15 years later? The answer is no. When I turned 40 I had a gigantic party because I didn't even know if I'd reach that. Will I be here in another 15 years? Well, I hope so and I do the utmost that is in my control to make it happen.

What I cannot control and I think many of us dealing with advanced stage either breast or ovarian cancer, or any type of advanced stage cancer. For what we cannot control and all that is uncertain, scary our mortality, physically and emotionally uncomfortable painful with this disease. I seek out lifestyle habits that work for me. Mind body practices and nurturing supportive connections with peers and others to quite the stormy seas in my mind, and to learn and to ease the journey not only for myself but for others as well.

I think as important as it is to deal with the physical side effects, it's just as important to deal with the emotional, spiritual and mental side effects that go with it. Some of these effects are definitely treatment induced and others are situation induced. It is a traumatic experience but we can deal with it. Many of us are living longer lives with metastatic disease. Dr. Brufsky mentioned, hallelujah, thinking that's fantastic but what I think a lot of us want is a guarantee of decades and not single digits. Something we all want for ourselves.

My story is not unique, I think some of us do better with metastatic disease, some do worse. My wish is for all of us dealing with metastatic disease to live full lives with a good quality of life. In detail my cancer journey started 15 years ago. My diagnosis was purely by surprise, I had a just regular gynecological visit, she did a breast exam, thought "Oh, I feel a cyst", go get it taken care of and that's how it all started. I went to a breast center and I had a lot of first. My first mammogram, my first ultrasound. Four biopsies later and I did diagnosis of malignant breast cancer and more firsts. First scan, first IV.

Such a chaotic time that in this short period of trying to figure out what's going on. Dealing, working and dealing with my normal life so to speak and the chaos of figuring out what to do next. It was overwhelming, it was scary, I felt like I had to become an instant expert immediately. And also, understanding the effects that the treatment might have on my fertility and how can I preserve that. Such a big issue for many of us who are diagnosed pre-menopausal.

At the time I had family's support, I had siblings. My parents had passed away many years earlier from cancer themselves and lots of issues to consider. Definitely my mortality, fertility. Could I work? Could I not work?

What are my rights at work? Insurance issues, the side effects. I was single, dating, what is that going to be like? And the stress of it all. As well as going to genetic counseling and then surgery. You can only imagine and I'm sure a lot of you have experienced this yourselves or your family members have as well.

My biggest need was for information and understanding, and help. Practical help as well as emotional help. I was looking for other young women, I went to the young women's conference back then and it just nurtured my soul to be around other women who are feeling exactly the same thing I was. Also learning through the seminars presented, what's available to us. In support, in fertility preservation or family planning options and treatment options and so on and so forth in support groups. I think it's essential for all of us to get that kind of support as well as the medical expertise.

I went along with treatment and then I had a crisis with my spine fracture, that happened in 2004 and they nearly put me in a chin to waist back brace. Very scary time, what are we doing? We changed therapies. I was on hormonal therapies, that's a bisphosphonate and HER2 therapies, and I needed my support group like you can't even imagine. Then I got my back brace, I went right to a metastatic cancer support group. I would call into the hotlines available who like Sharsheret and the LBBC, and the YSC and the other groups to get phone support, a one-on-one counseling. Trying to get through each day the best way possible, and trying to not be too hard on myself because prior to cancer, it was sort of built into me as being kind of stubborn and trying to be as independent as possible.

When the spine incident happened I was completely dependent, and how do you mentally cope with that, come to terms with that? Validate it and make it okay to ask for help. That help is essential in recovery and in dealing with the condition. As much as wanting to be as independent as possible. The years go by you keep switching therapies, the treatment works then it doesn't work so well. Lung metastasis comes up and dealing with that for 10 years. On and off, on and off. Saying it works, then doesn't work. And therapies, side effects come up. Dealing with new side effects, figuring out a new normal and then treatment not working and moving on like that.

In the meantime, I worked at my old job for several years into my diagnosis until I could no longer work, and I went on disability and I found a new passion which is supporting my peers. When I felt something that was lacking, I went out and wanted to create it. Back in the early 2000 pre-social media time I realized there wasn't a young women's support network in my community, so I created one. I just reached out to everywhere, ask everyone who knew anyone and we got together.

I enjoy helping my community, it feeds my soul as well as helping others and patient navigation, patient advocacy for young women with Mets, and for all women with metastatic disease is my passion and my calling and it's what helps me live each day, as well as my family. I have created the largest Facebook support group for people with metastatic disease so that we can all network. There are many groups out there. I think finding a group that really helps you, that makes you feel good, is important. Maybe one group doesn't do it but there is many out there and you can test them all out and find what really works for you.

I'm a peer counselor of numerous national cancer hotlines. I'm active with Sharsheret and Sharsheret's California chapter, the Young Survival Coalition, LBBC and many others. It's not that everybody needs to be so involved in advocacy, it's more finding what gives you purpose each and every day, and what you are able to do with the capabilities that you have now. If the situation improves then you change and you do whatever provides you fulfillment at this point in time. Day by day, day by day.

We come to now. May 2017, for me at 12 cancer drugs later, 47 changes in therapy later. Hundreds of chemo infusions, thousands of cancer pills. I mean I've been in chemo since 2011. I utilize complementary therapies and when a progression hits, how do I cope? How do I navigate the system again to figure out what's the best next step. Obviously, consulting with my medical professionals. Maybe getting second, third, fourth opinions. Talking to my peers on chat sites, reading articles and then sitting with all of that quietly and figuring out what I think will work for me and everyone needs to do what works for them and feels right to them.

Do I deal with side effects? Definitely, when I had this spine metastasis I had lots of pain, I could barely move and my mobility was limited and I had to deal with that. Of the years past some of the treatment, I felt great, I wanted to continue with it forever but I had progression. Currently my side effects include neuropathy, anemia fatigue and GI issues I hope that this new clinical trial will keep me going for years to come and if it ever does stop working that all these new therapies that are being tested now will be approved and showed to be very, very promising and just skipping forward, from one treatment to the next. Navigating advanced stage disease and all of its complexities is tough. There are so many struggles and obstacles and challenges along the way, Physical emotional life struggles and finances, relationships, work. It takes a village, a nurturing, actively supportive village, to get through this.

If one doesn't already exists for you, then please take the guidance, create one for yourself. It does not come at once, it takes time to build and practice, it takes support and guidance. There is guidance; there are resources and support for you out there all for free. Please seek them out; they are available on line, in person or by phone. You can learn about what's out there, and complementary therapies and new medical

therapies and peer support. It comes from many places including from Sharsheret. You go online there is this Embrace Program, free peer support. You can talk to a genetic counselor as well as many other services. There's the Young Survival Coalition, they have meet-up groups locally as well as a hotline. A metastatic navigator book list that is fantastic. My Facebook group and many other Facebook groups, FORCE, peers at high risk or dealing with a BRCA Diagnosis, Metastatic Breast Cancer Alliance. Metastatic Breast Cancer Network, LBBC. Shera has even a calling support group for young women with metastatic breast cancer.

There's a lot out there, websites to help you with issues related to your job or employment. There is information out there dealing with fertility and family planning. I would say peer support is hugely important to navigate the system. Not just for getting practical information but in getting emotional support. It's a scary-

Shera Dubitsky: Dikla?

Dikla Benzeevi: Yeah.

Shera Dubitsky: Sorry, I'm going to jump in there because you are giving so much information and just in the interest of time I wanted to say that I think that a lot of the things that you are mentioning I hope when we launch our own Facebook page, that you will be reiterating these things because these are amazing resources. So, I want to make sure that people know how to get these. I hope on our official page that we are going to be launching, that you will be sharing this and a lot of these will be on the transcript.

I'm sorry to just sort of jump in there but-

Dikla Benzeevi: No problem, can I just say one last thing-

Shera Dubitsky: Yeah, please do.

Dikla Benzeevi: To reach out. I just want to say what I wish for us all is to thrive, to find joy and fulfillment amidst and in spite of this difficult metastatic diagnosis and to stick around as long as we can and help each other out to do well. I wish continued survivorship to everyone.

Shera Dubitsky: Thank you, and I have to say every time you said the word 15 years. I am sure that that went straight to the minds and the hearts of many of the participants on tonight's call. Dikla, thank you, thank you, thank you.

V. Question & Answer

We now have a few minutes for question and answers. To ask a question you can dial *1 address the question in the order that they are received. Dr. Brufsky, we did get a question where somebody asked that when they were originally diagnosed, they had one particular HER2 status, and then when they had a recurrence the HER2 status changed. Can you maybe address that quickly?

Dr. Adam Brufsky: Yeah, about 20% of the time it does change, and usually it changes from negative to positive although it can go the other way. I think that you've got to be very careful when you analyze the HER2 on the specimen because it can go to a positive from equivocal, and I still think equivocal is considered positive. Some of us still believe equivocals are positive. Just be very, very careful. But this is why a lot of times some people have recurrences, we as the people to get re biopsy to try and figure this out. I still would treat someone with a HER2 derived therapy, because I think the downside risk is low, and the upside risk is really high. That's kind of been the way I take care of these patients who may or may not have switched from one HER2 status to the other.

Shera Dubitsky: Okay, thank you. Dr Hellman we had a question that came in, they just wondered if you could just talk about the difference between precision medicine vs. targeted treatment.

Dr. Mira Hellmann: Well, it's not that there is a clear defined distinction precision medicine vs. targeted treatment in terms of definition. The difference is precision medicine takes a specific cancer specimen and tries to tailor Targeted Therapies to that specific cancer specimen. For example, you take a piece of tissue, from someone's particular cancer and send it for profiling or molecular analysis and then try to identify targeted therapy drug that would address this person's underlying mutation. Does that clarify it?

Shera Dubitsky: I think so.

Dr. Mira Hellmann: Okay.

Shera Dubitsky: If not we'll get a follow-up question. Okay. Dr. Brufsky we have a question that came in, It says "Is there a way to improve bone health after a metastatic diagnosis, where the metastasis is to the bone?"

Dr. Adam Brufsky: Yeah, I mean the big ways to really do it are what you do normally. Calcium, vitamin D and more importantly when metastatic disease goes to the bone, we give everybody either Xgeva or Zometa. So, it's either Denosumab a shot, or Zometa. That usually given after every 3 months, will improve bone health dramatically. Even more than any other kind of thing which you can do but we always tell people that they can do all the

normal things they do. Try to get out, move around if you can, take out or invite them indeed the same thing we tell people with osteoporosis.

But in the other hand most people are getting a bone targeted agent, so bone health really is the big thing. You really should be a bone targeted agent, if you have metastatic disease for the bone.

Shera Dubitsky: Okay. Thank you. Dikla a question came out about clinical trials. The woman said that she is so overwhelmed trying to find the right clinical trial. Do you have a quick tip in terms of how to go about finding the right clinical trial?

Dikla Benzeevi: Well, I would suggest speaking to your oncologist and even getting second, third opinions and asking them what clinical trials they would suggest and why. There is also in the breast cancer world there is a site called breastcancertrial.org that offers personalized trials searches. Living Beyond Breast Cancer as well in their site has a metastatic breast cancer trial search engine, that also will personalize it for you. There are sites out there that can help you out as well as speaking to medical professionals and then sometimes reaching out in the chatrooms and forums and asking if someone has specific type and what type of trials they are on and what they think.

Shera Dubitsky: Okay, Dr. Brufsky we had had that there is a very low percentage of women participating in clinical trials. I think the number somebody had quoted is 3%. What's your understanding of that?

Dr. Adam Brufsky: Yeah, that's about right. I think that again one of the many jobs that one of the many jobs that I do at the University of Pittsburgh is, I'm the Associate Chief of Clinical Investigations so I'm in charge of trying to get all these people on trials and the problem is A, the trials sometimes are very tightly written, so it's also very difficult to get on the trial.

Number two, the trial is a lot of work so sometimes the seminar is a very busy practice. It's kind of hard for them to do the work with someone on a trial. Three I just don't think they are explained enough to people, I think that the most important thing about any trial is you are going to get the standard of care that's really important, that's the minimum. It's the standard. Potentially it's a standard plus is the ways I always put it. And so, it shouldn't be that part of it the people being worried about the trial. If you are a patient with metastatic breast cancer, or ovarian cancer, being worried about a trial should be the least of the concerns. It's more getting more resources and physicians to make a trial approved easier. I think that's probably the biggest thing, and making the understanding of people that you are not a guinea pig, you are getting the standard of care, the minimum. I think those are the two things that we need to do. Going forward and trying to improve that number.

- Shera Dubitsky: Thank you Dr. Hellmann the question just came in, I'm sorry I'm probably going to mispronounce this. But is it unusual for someone with advanced ovarian cancer to have anaphylactic shock each time they get chemo?
- Dr. Mira Hellmann: Well, anaphylactic shock is an anaphylactic reaction maybe what the person was trying to say. Platinum agents are used very often in the treatment of ovarian cancer as a cell, and sometimes when patients are exposed to platinum agents, specifically, carboplatin and they are re-exposed to it again, they can develop severe allergic reactions to it. And also, Taxol which is used very often in the treatment of ovarian cancer does have a fair incident of hypersensitive or allergic reactions and rarely I believe that it's written 3% or so. Patients can have a anaphylactic reaction to it. So, that can occur and it's something that is fortunately rare.
- Shera Dubitsky: Okay. I guess this participant should certainly bring that up with the doctor to obviously, alert them to what the situation is and hopefully the doctor will make the appropriate adjustments. I guess this is for both the doctors. In terms of palliative care, I think it's a scary word and sometimes people associated palliative care with hospice care. Is it different and if it is, can you just briefly address them? Maybe Dr. Brufsky and then the Dr. Hellman you can jump in on that.
- Dr. Adam Brufsky: End of life care there is only one part of palliative care. I think that it's important to get people involved and helping them in symptoms and psychology and a lot of other stuff that palliative care guys do. Palliative care people are also very good at helping you focus on what your goals are if therapy, and I think that we should be getting them involved earlier mainly because I think we can kind of start talking about these goals of therapy questions before it really becomes a non-discussion, it's more of a live discussion. What do you want out of your therapy? What do you want to do? That sort of thing. I think that the more, the earlier we get people involved the sooner we can have those sorts of discussions.
- Dr. Mira Hellmann: Yeah, I absolutely agree with that and like I tried to point out in my presentation, I think it's an integral part in terms of management of recurrent cancers, where so many facets that goes into the management of the recurrent. Not just the chemotherapy agent but taking the persons whole life situation into account, and like Dr. Brufsky said, it does not ... palliative care is not equal to hospice care. Palliative care focuses on improving quality of life in all stages and it's well known in the oncology world that unfortunately is completely underutilized across all fields and it's a big drive to try to improve the use of palliative care and I think overall it will improve patient satisfaction as well as the treatment.
- Shera Dubitsky: Okay. Looks like we have one more question that came in and that was a couple of times through the presentations that I think Dr. Brufsky maybe in your, but certainly Dr. Hellman I'm sure if this is true for ovarian is that,

the discussion about treatments that are approved and year up are not necessarily here. So the question that came in is why would that be?

Dr. Adam Brufsky: Because the European authorities have a completely different mechanism, and approval process for the United States and so remember we are different that we have different areas of the world, and so what drugs are approved and what isn't depends on what the authorities of those countries allow. That's the real reason more than anything.

Shera Dubitsky: Is there anything that a woman can do if there is something that has been approved in Europe but not yet approved here, but it looks like a promising treatment. Is there anything that she can do to have access to that?

Dr. Adam Brufsky: Sometimes we get things called compassionate use, you do what's called the compassion use investigative drug application, and that will allow us to do that sort of thing. I mean we could do that potentially. It really depends on what the drug is, how available it is. I think that if it's a drug that's already commercially available for some more indication in the US, but not another country, that's one mechanism. Compassionate use is another if it's not available at all.

Dr. Mira Hellmann: I agree with him especially in the setting of recurrent ovarian cancer that's not platinum sensitive, where options are limited or specific situations where there are not really great alternatives available at often times it's easier to obtain what Dr. Brufsky is referring to as a compassionate care, target approved for use in this specific situation.

Shera Dubitsky: Okay, well thank you very much.

Dikla Benzeevi: Shera, can I make one point? It's Dikla.

Shera Dubitsky: Sure, please do Dikla.

Dikla Benzeevi: Just from the clinical trials part, just something to consider if you are looking at clinical trials, and for myself, my perspective is that clinical trials are just an additional treatment option in the whole scheme of treatment options that are available to a person at any one time. There is no like a separate window, it's like 1-2-3-4, and one or several of them might be clinical trials.

But the other thing to consider is strategic planning. If you do certain therapies now, if they are all being equal. What will keep clinical trials open for you in the next three to six to nine months? So that you are not excluding yourself from trials that are open now because you are going to go into a therapy. It's always good to discuss with your oncologist what's

a good strategic plan for the future, to keep the most options for me open now and later. As for palliative care I just consider it same to management or quality of life improvement planning. If it's just issues that are happening to my body that are affecting my quality of life then I'd go to palliative care to help with it, whether it's pain or neuropathy or any other issues that maybe they can help find solutions for.

VI. Conclusion

Shera Dubitsky: Thank you, thank you, that was incredible that you added those two pieces, so I really appreciate that. Dikla, thank you. Everything at Sharsheret is driven by the conversations and feedback that we hear from, so we will be sending out an online evaluation, so please take a few moment to complete this, about tonight's webinar because your feedback is invaluable to us.

You can also access the transcript and the audio of this webinar at www.org/resources/transcripts, and I also encourage you to check out other previous webinars and teleconference that may be helpful to you.

I would like to thank Amgen again for their support in making tonight's program possible. I would also like to thank Dr. Brufsky and Dr. Hellmann for your expertise and again I hope that many of you will use the information as a spring board to going back to your treatment team, and I also want to particularly thank you Dikla, for your expertise both in terms of the breadth and depth of your experience in taking what they spoke about and really bringing that to life, so thank you very much. I also want to give a special shout out to Shira Kravitz, Sharsheret Support Program Coordinator, for all the time and the work she put into, making this webinar such success.

And finally I want to thank all of you for joining is this evening. If you would like to continue this discussion with a member of our support staff, please feel free to connect with us by calling the office, emailing us or simply going online. I also want to invite you to follow us on Facebook and on Twitter and again to look for our email, announcing the launch of our community in Facebook group, and we are here when you need us and as you need us. So, have a good evening, take care.

VII. Speakers' Biographies

Adam Brufsky, MD, PhD, FACP, is Professor of Medicine at the University of Pittsburgh School of Medicine and also serves as the Associate Division Chief for the Division of Hematology/Oncology at the University of Pittsburgh School of Medicine's Department of Medicine. Dr. Brufsky is the Medical Director of the Women's Cancer Center at Magee-Women's Hospital of University of Pittsburgh Medical Center and the University of Pittsburgh Cancer Institute (UPCI); Associate Director for clinical investigations at UPCI; and Codirector of the Comprehensive Breast Cancer Center. An active researcher, he has published numerous abstracts and research articles in leading journals, and is principal investigator on a number of research grants funded by the National Institutes of Health, Susan G. Komen Foundation, and US Army-Breast Cancer Research Program.

Dr Mira Hellmann, MD, FACOG specializes in Gynecologic Oncology. She treats all subtypes of gynecologic cancers including uterus, cervix, fallopian tube, ovaries, primary peritoneal, vaginal and vulvar cancer. The scope of her surgical expertise includes both traditional open surgery, as well as minimally invasive surgery. She has extensive expertise in complex laparoscopic surgery as well as robotic surgery.

Her research focus is in clinical research including cooperative group studies and well and industry sponsored and investigator initiated. She enjoys having the opportunity to offer patients the possibility of participating in the most cutting edge research, if they are inclined to do so. Dr Hellmann received her MD at SUNY Downstate in Brooklyn, and is a lifelong member of AOA. She completed her residency in Long Island Jewish Medical Center, and returned to SUNY Downstate for her fellowship training. She maintained a faculty position in central New Jersey for eight years where she developed a robust practice in a short period of time. She was active in resident and student education, and received several awards in resident education. She also helped spear head a minimally invasive center which was a comprehensive center for minimally invasive surgeons across multiple cancer specialties. She transferred to the John Theurer Cancer Center at Hackensack University Medical Center, where she currently practices. In the short time since she has joined Hackensack Medical Center, Dr Hellmann has spearheaded an IRB approved study looking at sentinel lymph node dissection for patient with endometrial cancer. She is currently active in proposing another study to the IRB to improve patients post operative pain control. Aside from her research endeavors, Dr Hellmann has a robust gynecologic oncology practices that spans the entire scope of the specialty. She is also a certified proctor for Intuitive Surgical, and helps other gynecologic surgeons obtain expertise in robotic surgery.

Dr. Hellmann is board certified in both Obstetrics and Gynecology as well as Gynecologic Oncology.

VIII. About Sharsheret

Sharsheret, Hebrew for “chain”, is a national not-for-profit organization supporting young women and their families, of all Jewish backgrounds, facing breast cancer. Our mission is to offer a community of support to women diagnosed with breast cancer or at increased genetic risk, by fostering culturally-relevant individualized connections with networks of peers, health professionals, and related resources.

Since Sharsheret’s founding in 2001, we have responded to more than 67,000 breast cancer inquiries, involved more than 8,000 peer supporters, and presented over 250 educational programs nationwide annually. Sharsheret supports young Jewish women and families facing breast cancer at every stage--before, during, and after diagnosis. We help women and families connect to our community in the way that feels most comfortable, taking into consideration their stage of life, diagnosis, or treatment, as well as their connection to Judaism. We also provide educational resources, offer specialized support to those facing ovarian cancer or at high risk of developing cancer, and create programs for women and families to improve their quality of life. All Sharsheret’s programs are open to all women and men.

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

IX. 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.

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