Breaking News
In Breast And Ovarian Cancer
And What Should I Make Of It?

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Presented by:

SHARSHERET®
Your Jewish Community Facing Breast Cancer

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I. Introduction

June Mandeville: Welcome to the Sharsheret’s national webinar: Breaking News in Breast and Ovarian Cancer, What Should I Make of it? We are delighted that so many people have joined us tonight from across the United States.

My name is June Mandeville-Kamins, and I’m a Licensed Clinical Social Worker and the Senior Support Program Coordinator for Sharsheret. I am thrilled to be here moderating tonight’s webinar.

We would like to thank The Siegmund and Edith Blumenthal Memorial Fund, Clovis Oncology, MacroGenics, Merck, inventing for life, and Syndax for their ongoing support and for sponsoring tonight’s program. We would also like to thank our partners in collaboration, Breast Cancer Social Media and Holy Name Medical Center, for their ongoing partnership.

Sharsheret supports young Jewish women and families facing breast and ovarian cancer at every stage. We help you connect to our community whatever your personal background, stage of life, genetic risk, diagnosis or treatment.

Have you heard new cancer research updates in the news and you’re not sure what to make of them? Do you wonder how they apply to you? This webinar, Breaking News in Breast and Ovarian Cancer and What Should I Make of It, will highlight the latest in precision, also known as personalized medicine, new breakthroughs in immunotherapy, the hottest clinical trials and the use of chemotherapy in early stage cancer.

Dr. Deanna Attai, UCLA Health Burbank Breast Care, and Dr. Sharyn Lewin, Holy Name Medical Center, will report on the latest updates and research you need to know from the American Society of Clinical Oncology’s annual meeting. A Sharsheret volunteer will also share her personal story, and a live question-and-answer session will follow the presentation.

With the latest clinical trials in mind, Sharsheret offers the Clinical Trials in a New Age brochure designed to dispel some of the myths associated with enrollment in a trial. It helps you understand how a clinical trial works and has questions for you to ask your doctor.

With one in 40 individuals of Ashkenazi Jewish descent carrying the BRCA gene mutation, which is 10 times higher than those in the general population, Jewish women and their families, particularly those carrying a genetic mutation, may qualify and benefit from BRCA-specific trials. To order your free brochure, go to our website at Sharsheret.org or you can call us at 866-474-2774 and ask to speak to a member of our support team.

If you want to ask a question to our speakers for the evening, you can ask questions throughout the webinar by typing in the question box on your
dashboard on the right-hand side of the screen. Please get your questions broad in nature so that everyone on the call can benefit from the discussion. We will try to get through as many questions as we can after the presentation.

For those of you who are not joining us via computer, please know that you can call Sharsheret at any time with your questions, and we will be happy to discuss them with you.
II. Breaking News in Breast Cancer

So, now, it is my pleasure to introduce our first speaker. Dr. Deanna Attai is an Assistant Clinical Professor of Surgery at the David Geffen School of Medicine at the University of California Los Angeles. She's a graduate of Vassar and Georgetown University School of Medicine. She completed her general surgery residency at Georgetown University Hospital. Her surgical practice is limited to the care of patients with benign and malignant breast disease.

Dr. Attai is a past president of the American Society of Breast Surgeons. She has also served as the American Society of Breast Surgeons Treasurer, Chair of the Finance Committee and Chair of the Communications Committee. She is a Fellow of the American College of Surgeons, and she's certified by the American Society of Breast Surgeons for the performance of breast ultrasound and is an ultrasound instructor for the American College of Surgeons.

An ardent proponent for patient education and empowerment, Dr. Attai is frequently sought out by local and national media for her thoughts on breast disease, diagnosis and treatment. She is a regular contributor to social media sites and is a co-moderator for #BCSM, Breast Cancer Social Media, a popular breast cancer support community based on Twitter. So it’s now my pleasure to introduce Dr. Attai.

Deanna Attai: Thank you very much for having me here and for that invitation. You can start advancing the slides please.

I’ll be covering some of the updates in breast cancer studies from the recent American Society of Clinical Oncology meeting.

I have no financial disclosure related to any of the studies that I’ll be discussing.

I’ll cover several studies, and the take-home points will be about for early stage breast cancer: who really need chemotherapy, whether or not shortened duration of treatment for HER2/neu over-expressed breast cancer is appropriate for some patients. I’ll be covering whether or not premenopausal women should have their ovaries suppressed during as part of their treatment. I’ll cover some new options for metastatic breast cancer in estrogen receptor-positive breast cancer, and I’ll discuss preoperative chemotherapy for BRCA mutation carriers, and I know Dr. Lewin will cover these same medications, PARP inhibitors, in her discussion on ovarian cancer.

The first study that I’ll discuss is known as the TAILORx Study, and as a little bit of background, previously, we have made the decision on whether or not we treat women with early stage breast cancer with chemotherapy based on tumor stage, so the size of the breast cancer and whether or not it’s spread to the lymph nodes. But what we’ve understood in the last several years, or come to a better understanding, is that tumor biology is likely more important than the
tumor size. So the behavior of the cancer is probably more important than the actual stage or size of the cancer.

Now, patients who have what is known as triple-negative breast cancers, so estrogen, progesterone and HER2/neu-negative, or patients who have HER2/neu over-expressed or HER2-positive breast cancers routinely are treated with chemotherapy.

The challenge remains in patients with estrogen-positive and HER2-negative breast cancer is who really benefits from chemotherapy?

The Oncotype DX test is a 21-gene assay. What it does is it evaluates the genetic makeup of the tumor itself. So the BRCA test, for example, is a genetic test on the patient. The 21-gene assay, think of it as a genetic test on the cancer itself. The test is usually done on portions of the tumor taken at the time of surgery, and this study has been around since the early 2000s. It’s used in patients with estrogen receptor-positive and up to one to two positive nodes, lymph nodes, and what it can do is help predict whether or not that patient will benefit from chemotherapy.

On the right-hand side, you can see a sample report. A recurrence score result is generated, which gives us an estimate of the likelihood that this cancer will become metastatic or distant recurrence over a 10-year period. Now, it’s important to know that this test makes the assumption that the patient is being treated with endocrine therapy such as tamoxifen or an aromatase inhibitor, so it helps predict whether or not chemotherapy would provide any additional benefit.

The TAILORx Study enrolled patients from 2006 to 2010. It enrolled over 10,000 patients, both men and women. Patients who had scores that fell in to the low risk category, which was about 1600 patients, did not receive chemotherapy. They received endocrine therapy alone. And, at five years, their risk or their likelihood of local or distant recurrence was less than 2%. So this confirmed that patients who score in the low risk category do not need chemotherapy. Patients who were in the high risk category did go on to receive chemotherapy.

The results that were presented in the June ASCO meeting were data of the intermediate risk group of patients, which was about 6700 patients with recurrence scores of 11 to 26. These were the patients that we didn't know if chemotherapy would benefit or not, and they were randomized to receive either chemotherapy or endocrine therapy, and what was found is that there was no difference in overall survival, invasive disease-free survival or metastatic survival regardless of whether they received chemotherapy or endocrine therapy. What was noted is that there were some benefits to chemotherapy in the group of patients that were younger than age 50 even with an intermediate risk score.
Again, the important point is for the majority of patients with intermediate risk scores, chemotherapy did not provide any additional benefit over endocrine therapy. So the take-home message is, for estrogen-positive breast cancer, genomic tumor testing - and there is the Oncotype test, there are several other genomic tumor tests as well - can help provide guidance for chemotherapy decisions, helping us better personalize the decision for chemotherapy. Low risk score does not mean that cancer won’t recur, but that chemotherapy is unlikely to provide any significant benefit.

Patients with positive lymph nodes were not included in the study, but can still benefit from the genomic testing to make a decision about chemotherapy, and again this test does not apply to patients with triple-negative or HER2-positive breast cancer.

Now, a question has been raised at the meeting and afterwards: Say you’re a patient who’s in the middle of chemotherapy and your scores is intermediate risk, should you stop chemotherapy? This is really an individualized discussion for each woman with her medical oncologist.

The next group of patients I’ll talk about is those with HER2/neu over-expressed breast cancer, also called HER2/neu or HER2-positive. That means the breast cancer has an abundance of what is known as the HER2/neu protein, and this is a protein that’s on the surface of the cell and has to do with cell growth and replication.

These patients are commonly treated with chemotherapy as well as an antibody known as trastuzumab or Herceptin, and the current recommendation is chemotherapy in addition to one year of trastuzumab therapy.

The biggest potential side effect to trastuzumab therapy is cardiac damage or heart damage, and patients who undergo this treatment are routinely monitored with an echocardiogram, essentially, an ultrasound of the heart. The cardiac damage is often reversible after treatment, but, in rare cases, it is not.

This study was done in the UK. It was a Phase III study involving 4,000 patients, and patients were randomized to receiving either the standard, which is 12 months of trastuzumab, or a shortened course, six months of trastuzumab. What was found is that the disease-free survival was equivalent at four years. And they noted that the cardiac events, and these were cardiac events that caused the medication to be stopped, were 8% in the 12-month group, but only 4% in the 6-month group.

Concerns about the study is that the follow-up has only been four years, which is relatively short, and there’s data on disease-free survival, but not overall survival. And the study has been criticized by some because the chemotherapy agents that are used, were used in the study in the UK are not always the ones that are commonly used in the United States.
A take-home point from this study is that six months of trastuzumab may be just as effective as 12 months, and, certainly, the toxicity and the cost will be lower with a shorter course of therapy.

As I mentioned, some oncologists would like longer follow-up and survival data before changing their treatment recommendations for their patients.

Now, the TEXT and SOFT trials are studies that were done in premenopausal women with estrogen-positive breast cancer, so, in these patients, tamoxifen is generally a standard part of their breast cancer treatment and usually is recommended for anywhere from five to 10 years, depending on specific factors such as the patient age, tumor factors and whether it has spread to the lymph nodes. Tamoxifen acts by blocking the effect of estrogen in the breast. It does not stop the ovaries from making estrogen.

In women after menopause, we commonly use medications called aromatase inhibitors instead of tamoxifen. And aromatase inhibitors work to actually block any residual estrogen production, and in women after menopause, they're more effective than tamoxifen. So the question raised by this study is, "Is taking premenopausal women, shutting down their ovarian function, essentially making them menopausal and using an aromatase inhibitor more effective than using tamoxifen, which has been our standard in these patients?"

There are various ways to suppress the ovaries or what we sometimes call "put them to sleep," and this is often done as part of chemotherapy treatment in young women because, if the ovaries are suppressed during chemotherapy, their function is more likely to return afterwards if the patient desires to potentially have children. So, for the study, the options to suppress the ovaries were medication, ovary removal or ovarian radiation, and the most commonly used method was the medication.

The TEXT and the SOFT trials are often reported together because there's some overlap in the groups. In the TEXT trial, they compared women who received just five years of tamoxifen, tamoxifen plus ovarian suppression, or exemestane, which is an aromatase inhibitor, plus ovarian suppression; and in the TEXT trial, patients got tamoxifen or exemestane plus ovarian suppression.

Now, I'll go through the results just by the individual column. So you can see the first column, eight-year DFS, which is disease-free survival, significantly improved in the patients who received ovarian suppression plus exemestane, the aromatase inhibitor. So the patients who were essentially put into menopause and who received the aromatase inhibitors as compared to tamoxifen had an improved disease-free survival.

The second column shows what is known as the high risk patients disease-free survival. So these are patients who also received chemotherapy as part of their treatment, and this could have been because they had more aggressive tumor...
types or spread to the lymph nodes. Ovarian suppression plus an aromatase inhibitor is also superior in this group the tamoxifen. But it's important to know, in the third column, that the overall survival was no different among the groups. And, the fourth column, the adverse events, was fairly high between 25 and 32%, and, overall, about 25% of patients discontinued therapy due to side effects.

The take-home messages is for these patients, adding ovarian suppression, so putting the ovaries to sleep, if you will, with tamoxifen resulted in a 4% improvement in disease-free survival. The addition of exemestane, the aromatase inhibitor to ovarian suppression resulted in about a 7% improvement in disease-free survival.

The absolute benefit, the most benefit was in patients who remained premenopausal after chemotherapy. So women who went through chemotherapy and were put into menopause did not gain as much benefit from the ovarian suppression. So it does seem that suppressing the ovaries does appear to be of benefit. We do need longer follow-up to determine whether or not there's a survival advantage to the ovarian suppression.

Sorry. I thought I had it on that slide, but it's important to note also that, again, 25% of patients overall stopped therapy early, and this just tells us that we really do need better ways to manage the side effects from both tamoxifen, aromatase inhibitors and ovarian suppression in our premenopausal patients.

The next group of agents are the CDK 4/6 Inhibitors. CDK stands for cyclin-dependent kinase. These are oral agent pills that block some of the pathways that are important in cell division, and these agents were studied in estrogen receptor-positive, HER2-negative patients with metastatic breast cancer, so breast cancer that has spread to other organs such as the lungs, the bones, the liver or the brain.

There are several agents. These are the ciclib agents, so palbociclib, ribociclib, and abemaciclib, and they're used in combination with an aromatase inhibitor or fulvestrant, which is another medication that can help block the estrogen receptor.

There were several studies that were reported at the meeting, the MONALEESA, MONARCH, and the PALOMA, using different agents, and all of them showed improvement in progression-free survival. The side effects from these agents primarily are neutropenia or low white blood count, hot flashes and nausea.

The take-home message here is that metastatic estrogen receptor-positive breast cancer does not always require chemotherapy, and the combination of an anti-estrogen agent with a CDK inhibitor was more effective than the anti-estrogen agent alone. And future use and future studies will evaluate these agents that are showing significant promise in metastatic breast cancer.
regarding whether or not they can also be used successfully in early stage estrogen-positive breast cancer to help improve outcomes.

Finally, I’ll talk about the PARP Inhibitors. So PARP stands for poly ADP ribose polymerase. This is an enzyme that is important in repairing DNA. So the BRCA1 and 2 genes code for proteins that repair DNA breaks, and when a woman has a mutation in a BRCA1 or 2 gene, that can lead to DNA breaks that then go unrepaired, which is one of the mechanisms by which cancer can develop. The PARP inhibitors prevent the DNA from being repaired, so they inhibit this PARP enzyme and don’t allow it to repair DNA breaks. This can help lead to the death of cancer cells. It seems that the effect of these agents is most intense in patients who have BRCA mutations.

These agents have been used for quite some time for ovarian cancer, and I know Dr. Lewin will cover this, and this is one example in oncology where we are going beyond the organ of origin. We’re not only looking at this as a breast cancer cell, but it is a breast cancer that may share some characteristics with ovarian cancer cells, and can we utilize some of the ovarian cancer treatment in these patients? This was a very small phase II study, only 19 patients, who received what is known as neoadjuvant therapy. Neoadjuvant means treatment before surgery. We are more often utilizing this technique, especially with larger tumors or more aggressive tumors because by treating the patient before surgery and then doing the surgery we get a better sense of did the agent actually work? Because we can evaluate that cancer after surgery and see whether or not it shrunk or if there’s even any tumor left behind.

These patients got a PARP inhibitor before surgery. 53% of them had what is known as a pathologic complete response, meaning when we took the patient to the operating room for a lumpectomy or mastectomy the pathologist found no residual cancer, it had all been killed by the agent. Typically we only see this type of response in patients who get chemotherapy before surgery. The side effects of these medications are low blood counts, and some patients reported hair loss, again, it’s a very small study. But this does show promise. And prior studies of these agents in patients with metastatic disease have shown improvement in progression free survival, so the disease didn’t progress as rapidly as expected, and improved quality of life compared to those who received chemotherapy.

The take home message from the PARP inhibitors is in addition to this being a potential breakthrough treatment for patients with BRCA gene mutations, it’s important because it shows that an oral agent may be just as effective as chemotherapy in eliciting a pathologic complete response. It’s important to note that just because we find no more cancer at the time of surgery, we’re not sure yet if that means improved long term survival rate. Certainly with a small study of only 19 patients, larger studies are needed.
My conclusions from the breast cancer studies that were presented at ASCO is we are more likely now to tailor the treatment to the individual patient's disease, whether that's a decision on chemotherapy versus endocrine therapy alone, whether it's a decision on treatment based on the genetic mutation, we're getting much better at really approaching a more precision medicine approach to breast cancer. Shorter duration of therapy may be just as effective as a longer course. Some premenopausal patients may benefit from being rendered postmenopausal as part of their treatment and oral targeted agents are showing promise in specific cancer subsets. I thank you for your attention, I'll be happy to answer questions at the end of the entire session. [25:51]

June Mandeville: Thank you so much Dr. Attai, that was a truly informative presentation. Our callers really want to know about the latest studies regarding medications and treatments, and to hear about the ways of tailoring treatment. It's really, really informative and I thank you for that.
III. Breaking News in Ovarian Cancer

Now it is our pleasure to introduce our second speaker for the evening, Dr. Sharyn Lewin. Dr. Sharyn Lewin is a graduate of the University of Kansas School of Medicine. She completed her internship and residency at Washington University School of Medicine Barnes-Jewish Hospital, St. Louis, Missouri, followed by a fellowship in gynecologic oncology at Memorial Sloan Kettering Cancer Center in New York. A board certified Gynecologic Oncologist, Dr. Lewin specializes in the diagnosis, treatment, and management of a host of gynecological cancers. Her practice employs a comprehensive, multidisciplinary team approach to care for women at high risk for ovarian cancer and other gynecologic malignancies.

Dr. Lewin serves as Medical Director of the New Jersey-based Holy Name Medical Center’s Gynecologic Oncology Division. She is Assistant Clinical Professor of Obstetrics and Gynecology in the Icahn School of Medicine Mount Sinai Hospital in New York. She is Founder and Executive Director of The Lewin Fund, whose mission is to invest in grassroots initiatives and research that directly support women who are impacted by cancer and their families. She is a longtime advocate for women and women’s health and brings more than 19 years of medical, research, and community outreach experience to her role.

Dr. Lewin is national educator on hereditary genetics, cancer survivorship, and state-of-the-art treatment for advanced ovarian cancer. She has authored or co-authored over 100 articles abstracts, book chapters, and made many presentations at scholarly conferences. She is a recipient of the President’s Award from the Society of Gynecologic Oncology and NYP’s prestigious Physician of the Year Award. Now it is my pleasure to introduce Dr. Lewin. Over to you.

Sharyn Lewin:

Thank you so much for that nice introduction. It's really an honor and a pleasure to participate tonight in this important webinar. In the next few minutes I would like to talk about some of the updates from the ASCO meeting regarding gynecologic oncology. It was really interesting to hear about the highlights in breast cancer, which certainly received a lot of press. Just want to talk about some of the potentially practice changing and thought provoking abstracts surrounding ovarian cancer and gynecologic cancers that were presented this year.

As I mentioned, we'll spend most of the time talking about ovarian cancers. I do want to mention very briefly some of the ASCO data that was presented on endometrial and uterine cancers as well as cervical cancers. Then we will talk about quickly PARP inhibitors and the new FDA indication of endometrial cancer, just to talk about something that is hot off the press. New slide please.

Beginning with ovarian cancer. This was a national randomized study known as GOG-213. GOG stands for the Gynecologic Oncology Group. They are the major
national cooperative that runs clinical trials. It's now sort of emerged into what's
called the NRG, but essentially the same national cooperative that runs the
majority of gynecologic cancer trials in the United States.

The first study was actually presented by Dr. Robert Coleman from the
University of Texas MD Anderson Cancer Center, GOG-213. This study was
already presented and published. I just want to talk about the schema in this slide a little bit. This year Dr. Coleman presented one of the surgical objectives.
Just to talk to you about the study in a little bit of detail. The first objective of
this study was to look at Avastin, which is also known as bevacizumab, in
addition to carboplatin and Taxol, and then followed by Avastin maintenance in
women who have had a recurrence of ovarian cancer, which is known as
platinum sensitive recurrent ovarian cancer. Platinum sensitive recurrent
ovarian cancer is when a cancer has recurred at least six months following a
platinum based regimen.

These women, once they recurred and they were deemed platinum sensitive,
they were determined to be surgical candidates or not. If they were surgical
candidates at that point they were randomized to surgery or no surgery. The surgery arm in the results were actually presented this year at ASCO. What we
did learn from the non-surgery arm, because that had been previously published
and presented, is that there was certainly an improvement by adding Avastin to
Taxol and carboplatin followed by Avastin maintenance in women with platinum
sensitive recurrent ovarian cancer.

What was interesting about the abstract presented or the presentation this year
is that we were looking at the surgical objective and to evaluate whether or not
what's called a secondary site of reduction, or a secondary surgery when cancer
has recurred, to see whether or not that would be effective in improving what's
called progression free survival, or the amount of time that women remain
cancer free.

In this particular trial or this surgical arm, there were 485 women that had been
deemed to have resectable or removable recurrent ovarian cancer. They were
randomly assigned to either surgery followed by chemotherapy, which included
a platinum based chemotherapy, and there were 240 patients in that arm, or to
go straight to chemotherapy alone, 245 women were in that arm, and not have
surgery. The conclusion of this portion of the study was that there was really no
difference in the overall survival for the women who underwent a secondary
surgery. That was a little bit interesting to us. The overall survival is the amount
of time that women live.

What's interesting about that is there had been other presentations in the past,
namely DESKTOP III, which was presented actually at ASCO last year, which
actually did show an improvement in the amount of time that women remained
progression free who underwent surgery. We think that the overall survival data
from this DESKTOP III trial are not yet ready to be presented, they’re not quite
mature. But we did see an improvement in the amount of time that women remained progression free.

It's a little bit interesting that GOG-213 did not show a benefit from surgery then followed by chemotherapy, whereas DESKTOP III, which was a similar surgical trial that was presented last year did show an improvement. The only difference majorly between the two studies was that women in the DESKTOP III trial did not receive Avastin, whereas they did in GOG-213. It makes us wonder, is the addition of Avastin, or bevacizumab, too part of the chemotherapy regimen potentially alleviating the need for further surgery. It's really a thought provoking clinical trial. There was a lot of data that we found in this particular meeting regarding Avastin which we will talk about, which actually led to some exciting new FDA approvals for Avastin in women with ovarian cancer.

The next potentially practice-changing presentation was from a group in Italy. These particular authors were, again, looking at Avastin, or bevacizumab. Avastin is what's known as an angiogenesis inhibitor. In preclinical models we think it blocks blood vessels in tumors potentially, which helps tumors shrink. This particular Italian group looked at a randomized trial, evaluating whether or not adding bevacizumab or Avastin to some type of platinum based chemotherapy, whether or not it would improve the amount of time that women remained progression free for patients who had recurrent disease and who had already received Avastin, or bevacizumab, with their first line or their initial treatment.

It's a very interesting trial design there. It was a large study, about 405 patients with recurrent ovarian cancer who had recurrent disease at least six months after their last dose of platinum, so still platinum sensitive. These women had to have Avastin during their initial treatment and then they were randomized to six cycles of platinum based chemotherapy with or without Avastin, then following that, Avastin as a maintenance therapy until any evidence of disease progression.

Essentially what the authors concluded is that women who had Avastin in the second line setting and had received Avastin in the front line setting still had a significant improvement in the amount of time they were being cancer free compared to women that did not have Avastin. We certainly saw benefit from the addition of Avastin, or bevacizumab, in the second line setting or the second setting with chemotherapy, even if they had Avastin in the front line therapy. That was definitely one very interesting improvement in the amount of time that women could remain cancer free.

Unfortunately we did not see a benefit in the overall survival or the amount of time that women would live with the addition of Avastin or not. Unfortunately in a lot of ovarian cancer trials we don't find that overall survival or the amount of time that women can live is a meaningful endpoint. According to the FDA and a lot of the thought leaders in ovarian cancer research and treatment, that
looking at the progression free survival or the amount of time that women live cancer free is actually a much better endpoint in studying this disease. Once again, adding Avastin in the second line setting to women that have platinum sensitive disease, even if they had Avastin in the front line setting still seemed to benefit them.

The next abstract that was actually a poster discussion was actually, again, surrounding Avastin. You can see that there were many presentations and posters that talked about the use Avastin, or bevacizumab, in ovarian cancer treatment. Another study from the Gynecologic Oncology Group known as 218 actually was previously presented and published. This is looking at patients who received Avastin with and following chemotherapy, compared to chemotherapy alone. We did see a significant improvement in the amount of time that women remained cancer free if they received Avastin with chemotherapy followed by chemotherapy alone.

What was presented at this meeting with extended followup was a final overall survival data. Even though we did see a significant improvement in the progression free survival, unfortunately we did not see a difference in the overall survival, the amount of time that women lived with the addition of Avastin, compared to chemotherapy alone. When we looked at some of the different subgroups that were actually studied in this particular paper, we did see a possible benefit for women with stave IV ovarian cancer who certainly would benefit from treatment with Avastin followed by Avastin maintenance.

What's interesting is that Avastin most recently has been approved by the FDA with first leg chemotherapy based on this trial. Now Avastin, or bevacizumab, is FDA approved for patients with newly diagnosed ovarian cancer who have undergone surgery and now are receiving chemotherapy in the front line or first line setting. That's very interesting, it was really based on the initial improvement and progression free survival from GOG-218. The survival data, as I mentioned, was presented this year at ASCO.

There were two studies that actually looked at surgery for women with ovarian cancer. One of the trials was known as the SCORPION trial and the other trial was known as JCOG0602. The results for these two studies were fairly consistent. These studies were both looking at what's called primary debulking surgery or initial surgery versus what's called neoadjuvant chemotherapy, which means giving chemotherapy first followed by surgery. The two trial designs were a little bit different.

The SCORPION trial looked at neoadjuvant chemotherapy versus primary debulking or primary surgery in patients with what they called a high tumor load. To test whether or not neoadjuvant chemotherapy was better in these women that had a high tumor load or a high tumor score. And they concluded that neoadjuvant chemotherapy was not superior but the surgical complication rates were actually lower in the patients that received chemotherapy first. The
second study, the JCOG0602 study showed that primary debulking surgery or surgery first was not inferior to neoadjuvant chemotherapy.

The bottom line is that there is a lot of data looking at the order in which things should be done. It’s a very tailored discussion between a patient and her physician. Overall if a patient is medically fit to undergo a big surgery and have a disease that can be completely removed, the data overall does really support surgery first followed by chemotherapy. We do see that the women who have the best outcomes and live the longest are really ones that are able to undergo surgery first. Sometimes it can be a very big surgery because they really need to remove all the disease followed by chemotherapy. The type of chemotherapy that can be utilized can either be a combination of intraperitoneal and IV chemotherapy or IV chemotherapy alone on a weekly basis. There’s definitely good data to support both of those strategies.

I do want to say just very quickly, there were two other very interesting studies that had to do with other gynecologic tumor types. Dr. Hensley from Sloan Kettering presented some results of a rare type of uterine cancer called a leiomyosarcoma. These were early stage women who were randomized to, following surgery, either observation or chemotherapy. Essentially the study found that there was no improvement in how the patients did if they were treated with chemotherapy or not. Really the standard of care for women with early stage leiomyosarcoma should be observation rather than chemotherapy.

Very quickly, an important topic on cervical cancer was the results of a study called KEYNOTE-158. This was a phase II study in women with advanced or recurrent cervical cancer who were treated with an immunotherapy drug called Keytruda, also known as pembrolizumab. This was for women that had advanced or recurrent disease who had already had a prior type of chemotherapy. Of note, the response rate was actually much higher than what we would see with systemic chemotherapy, and the progression free survival or the amount of time that women remained cancer free with this novel immunotherapy agent was quite impressive. Pembro, or Keytruda, has now been FDA approved for women with advanced cervical cancer.

Just a few more points. We did speak a little bit about PARP inhibitors already. There was some exciting data in the breast population as well as the Olympiad trial, which was also in the breast population, which did look at women who had a suspected or a germline B or C mutation. This was a breast cancer trial that was actually looking at patients that had HER2 negative metastatic breast cancer. They could be either triple negative or ER/PR positive, estrogen receptor or progesterone receptor positive, who were treated with chemotherapy or olaparib, which is known as Lynparza. There was actually a significant benefit in the time that the patients remain cancer free by using the PARP inhibitor olaparib.
In terms of ovarian cancer we do know that there are three PARP inhibitors that have now been FDA approved as maintenance treatment for women with recurrent ovarian cancer who are at least partially platinum sensitive. This means that women ideally will undergo a surgery to remove all of their disease, followed by chemotherapy, and that does include a platinum based regimen whether it’s carboplatin or cisplatin. Then they will hopefully go into a very long remission.

With the majority of women, unfortunately, at some point, may have a recurrence. And then if they are treated more than six months from their initial platinum based regimen or are considered platinum sensitive, could go on either to surgery or to chemotherapy. They should have a platinum based sublet again, which means carboplatin with another type of chemotherapy agent. And following that treatment should then go on to maintenance treatment with a PARP inhibitor. And there’s excellent data on the various PARP inhibitors and has really shown an improvement in really all women with recurrent ovarian cancer who receive PARP as maintenance therapy. If you have any questions about this I would be happy to take that at the end.

So there was definitely some educational sessions that were presented at ASCO for the clinicians there about the use of PARP inhibitors in the maintenance setting, which definitely is very exciting and a targeted agent for women with recurrent ovarian cancer.

And the last point I’d like to say is just recently there was some data about Keytruda, which is also known as pembrolizumab, which is a PD-1 inhibitor, and a novel agent that’s called Lenvima for women with advanced or metastatic endometrial cancer who have progressed on one prior line of chemotherapy. These are specifically for women that have what's called proficient MMR endometrial cancer. So the genes within the tumor itself are proficient, they don't have any mismatch repair deficiencies. So this novel combination has really been shown to improve the length of time that women remain cancer free.

So before we move on to questions, I think in the future we're going to see a lot more data about the combination of PARP inhibitors with other noncytotoxic drugs like checkpoint inhibitors. I think we'll hopefully see some biomarker research that really helps us guide appropriate therapy for these targeted agents with our patients. Right now we do see that a lot of the clinical trials that are ongoing in women with newly diagnosed ovarian cancer include carboplatin and Taxol, and then either Avastin or a PARP inhibitor or some type of checkpoint inhibitor. We will have more surgical studies that will come about in the future and we’re all anxiously awaiting the results of SOLO-1 trial and its impact on clinical care. And SOLO-1 was actually looking at Lynparza, which is a PARP inhibitor, as maintenance therapy for women with a germ line B or C mutations following their initial chemotherapy. So the whole landscape is
potentially changing and certainly growing with all the new data that's emerging constantly.

Of note, my last little bit before I stop speaking is that if anyone on the phone has a history, a personal history, of ovarian cancer or a family history, please do have genetic testing. It's very important that you have a panel genetic test to rule out some type of a genetic mutation, like a BRCA or other mutation, for example. And thank you for your attention.

June Mandeville: Oh thank you so much, Dr. Lewin, for your truly informative presentation. Thanks for pronouncing all the medications. We have problems with that in the office that was really good to hear them pronounced correctly. Anyway, that was really informative and thought provoking so I thank you very much.
IV. Personal Story

For many women undergoing chemotherapy, hair loss is a traumatic reminder of a frightening diagnosis. But some studies have shown promising results for using cold caps as a way of significantly reducing hair loss caused by chemotherapy. With that in mind, it is my pleasure to introduce our last speaker of the evening, Rachel, a breast cancer survivor and one of our amazing peer supporters. She will share her story and her experience with cold caps while undergoing chemotherapy. So over to you Rachel.

Rachel: Hi. Good evening. It's a great honor and also great privilege for me to be speaking to this wonderful group. When Sharsheret had asked me to speak I jumped at it, I was really happy to be able to give back to such a wonderful organization. Generally I'm a really private person, but I felt it was important to raise awareness of breast and ovarian cancer. In addition, as someone who unfortunately is going through cancer, I can gain from my experience and somehow my pain wasn't for naught. I hope that by sharing my story I can inspire others just as so many have inspired me.

On November 24, 2014 my doctor told me the words that everyone dreads and no one wants to hear. It was an ordinary Monday and I went for a routine mammogram but it turned into a day that I will never forget. I was petrified. All I can remember saying was that I don't wanna lose my hair. I had thick, gorgeous, long auburn hair. The next two days were a blur. I don't think I stopped crying. When the doctors called to confirm I did have breast cancer I just sat there. My husband and siblings cried. I don't think a person can ever be prepared to hear those words they have cancer. I was so young. When did I become so grown up to make such big decisions?

Unfortunately for me cancer was too advanced and chemo was a must. The treatment plan was rough. There are no words to explain what chemo can do to a person. Nor can one understand it unless they have been through it. I think the hardest part for me was not being able to take care of myself, my kids, and my house. Not being able to remember things, not being able to focus on simple tasks. In addition to all of this was the realization of how little control I actually had over my situation.

I made the decision not to tell people I was sick, I didn't want anyone's pity or to be labeled differently. I told my siblings, a few close friends and my work. I didn't even tell my children. I felt they were too young.

One of the most difficult things for any woman who undergoes chemo is the inevitability of losing her hair. Hair is how a woman defines her appearance and then suddenly it's gone. My fear about going through chemo was losing my hair.

I was so attached to my hair I didn't want to look sick. I heard about cold caps and decided to do the research and find out more. I googled it and found that
Penguin Cold Caps is the one that is most used in the States and discussed it with my oncologist. While some hospitals and doctors are not really for it, it's becoming much more popular today. My oncologist explained to me the risks were very low and he was comfortable with me using cold caps.

For me the decision was easy. I was too afraid to lose my hair. So I decided to go for it not realizing all the details. Cold caps are caps that are negative 32 degrees and it freezes the scalp in order to prevent hair loss. Although shedding and losing some hair occurs. These cold caps are wrapped around the patient's head during treatment and are changed every 30 minutes in order to keep the freezing temperature of the scalp.

The process starts 30 minutes before chemo and needs to continue for four hours after chemo making the day at the hospital much longer. There's also another type of cold cap called DigniCap which works the same way however it's attached to machines and always keeps its cold temperature so that a person doesn't have to keep switching the cap.

There are also rules how to comb the hair and what to do with the hair, for example no heat to the hair. Meaning no hot showers, you could only shower on certain days like not on the chemo day, not after the chemo day. You have to use a certain brush. And then you can't color your hair, you can't cut your hair. And cold caps also must be started at your first treatment, if not it won't work.

For me, even though there is some hair loss with cold caps, one still has hair during chemo. For most people it works, but unfortunately for some patients it doesn't work. Personally for me I was grateful that it worked, even though I lost a decent amount of hair, but to the outside people no one really noticed. Every time my hair shed I cried, I cried like a baby. My hair became dry and so brittle, it still wasn't the same as it was before. But when I looked in the mirror, I had hair. And the just the fact of me seeing that I had hair helped me emotionally go through the rough treatment plan. Even though my days at the hospital were longer and my hair didn't look the same.

It does cost to use cold caps, but most insurances cover it and some hospitals pay for it as well. Some hospitals even have the freezers and the DigniCap for patients to use. When the hospital that I was at saw that the chemo worked for me even though my chemo was AC, and AC is, like, it's supposed to have the worst results, they saw that it worked for me, so they started telling patients about cold caps and then they created a separate room with chairs and a freezer for patients who are using cold caps.

I have spoken to many other patients who use cold caps, most were pretty happy with their decision, while others say it was too complicated with all the restrictions and the rules. But I really think it's a very personal decision.
It’s been a little over three and a half years since I was diagnosed, and I’m thankful to God that I have finished my treatments. Of course fear of recurrence is always in the back of my mind, but I’m healthy today and I’m very grateful for that.

They say God brings the healing before the illness and I can see true that statement really is. My help and strength came from the most unexpected people. Sharsheret and the peer support network are on the top of the list. My life will never go back to the way it was before cancer. But I believe that everything happens for a reason. I have fully come to accept and appreciate the new normal that I have. There is no doubt I have become stronger, and oddly more comfortable in my own skin. I am no longer afraid to meet others or to feel uncomfortable. I have become less judgmental and less critical. I have learned to see the good in things and appreciate the small wonders of everyday life.

For myself and for thousands of other women who are facing cancer, and other life threatening illnesses, I pray that God will continue to give us strength that we need to fight and be healthy. So that we can give back to others who are so bravely fighting. Sharsheret, thank you for ensuring that no woman going through breast or ovarian cancer can do this alone. Thank you.

June Mandeville: Thank you so much, Rachel, for sharing your experience. That was very brave and it takes a lot of courage to stand up and talk about your story so I really do appreciate that you did that. And I know a lot of women participating in our webinar are very interested about cold caps, you’ve really given them some good information. So thank you thank you thank you so much.
V. Question & Answer

So now we have about five-six minutes to start our question and answer period. You can type your questions in the text box located in the dash port at the right of your screen. We already have a few questions, so I'd like to begin with those. And this one is for Dr. Attai. What are the side effects that have caused women to stop the tamoxifen treatment or the AI’s [Aromatase Inhibitors]?

Deanna Attai: So the side effects from the endocrine therapy are essentially some of the side effects of menopause: Hot flashes, sometimes sleep disturbance because of the hot flashes, in addition tamoxifen specifically it acts as a blocker in the breast, but it can act as a stimulant in a way to the ovaries and the uterus. So some patients develop ovarian cysts; if patients have endometriosis - that can flare up; some patients have a significant amount of vaginal discharge that's annoying or uncomfortable. Some patients may have abnormal periods or abnormal uterine bleeding, and occasionally, it's not very common but there's a slight incidence higher than average, of uterine cancer that can develop form tamoxifen as well. So patients on the medication should be monitored. The aromatase inhibitors can also cause menopausal type symptoms such as hot flashes and bone pain, joint pain as well almost like anarthritis, but they are not generally associated with the ovarian or the uterine symptoms like tamoxifen is. And both sets of medications can be associated with a type of chemo brain, what we call cognitive dysfunction, which is a little bit of a mental fog that we typically associate with chemotherapy but can happen with the endocrine agents as well.

June Mandeville: Great thank you, that was very interesting. Dr. Lewin, how long is it beneficial to stay on Avastin to prolong recurrence free survival for ovarian cancer? Is it possible to continue the treatment indefinitely if tolerated relatively well?

Sharyn Lewin: That's a very excellent question. So the literature, the data that we have, supports keeping women on Avastin maintenance until there is some type of an unacceptable toxicity or there's any evidence of disease progressions. So yes, a woman can stay on it sort of indefinitely as maintenance therapy until, as long as she's not having any side effects or any evidence of disease progression.

June Mandeville: Thank you. Dr. Attai, what can be done to help with hair thinning while on aromatase inhibitors or PARP inhibitors? Is it safe to take Rogaine?

Deanna Attai: That's an excellent question and I don't think we really have the answer to that. I know a lot of oncologists are a little hesitant to recommend any agent that might stimulate cell growth such as Rogaine. It's a theoretical concern, I don't think there's really any data in patients with cancer, but we're all a little hesitant to recommend something that might promote cell growth. So honestly the real answer is there's not a lot of good options for these patients. And as you just heard, hair loss or hair thinning is sometimes something that's extremely important to patients, they're very self-conscious about it at times. So this is...
sometimes something that causes quite a bit of distress. I think as far as using Rogaine, I think that's something for a patient to discuss with her individual oncologist because I believe opinions vary.

June Mandeville: Thank you. Dr. Lewin, are PARP inhibitors used for first line ovarian cancer?

Sharyn Lewin: At the present time they're only being used on a clinical study or a clinical trial as first line. As I mentioned, the SOLO-1 trial has closed, this is for women that had a BRCA mutation in ovarian cancer who did receive a PARP inhibitor, Lynparza, as a maintenance therapy. That study we are anxiously awaiting the results, it hopefully will be released either this Fall or Spring. But that'll be really interesting data to look at PARP inhibitors in the first line setting. So Avastin is approved as maintenance therapy as well as PARP inhibitors, so it's an interesting discussion to speak individually with your physician about which one would be best for you, because there is very good data surrounding both.

June Mandeville: Thank you. This question's for Rachel. Do you have any tips or advice for someone preparing to use cold caps during treatment?

Rachel: Yeah, I think the first thing is to read all the facts, make sure you understand what you're getting yourself into. Also I think there's some rule: my hair was very long and in hindsight, had I been a little bit more prepared, there's a certain amount of time you need before that you're able to cut your hair before you start treatment. And I would have cut my hair just a little bit, at least, so it would have made it a little bit easier that my hair wasn't gonna be so tangled. And then, I guess, just be prepared that it's not gonna be easy. It [cold caps] makes it [treatment] a little bit harder. But it also brings comfort when you're looking in the mirror and you're able to see that you have hair on your head. And then I think the last tip is that, I found when I coached other women, is drink as much water as you can. It helps with chemo in general, but with using cold caps and for your hair, the more water you drink, I felt, the less hair you ended up losing.

June Mandeville: Thank you Rachel.
VI. Conclusion

So unfortunately we're out of time for questions, but your feedback is important to us. And we are committed to staying relevant by enhancing our programs to reflect the growing and changing needs of the women and families of our Sharsheret community. So with that in mind you'll be receiving an evaluation in your email box in the next couple of days. So if you could just take a few minutes to complete the survey that would be wonderful.

There will be a video and transcript from tonight’s presentation available on Sharsheret’s website in the coming weeks. You can access it by going to www.Sharsheret.org.

And I wanted to share one additional resource with you before we close for the evening. If you want to continue learning more about this and other research, Facing Our Risk of Cancer Empowered – FORCE – is a great program called XRAYS, which provides plain language summaries on new breast cancer research.

I would like to thank the Siegmund and Edith Blumenthal Memorial Fund, Clovis Oncology, Macrogenics, Merck Inventing for Life and Syndax for their ongoing support and for sponsoring tonight’s programs. And to all our partners in collaboration. I would like to give a huge thank you to Dr. Deanna Attai and Dr. Sharyn Lewin and last but certainly not least to our caller Rachel for taking the time to share their expertise, research, wisdom and insight for us. And to giving us some ideas about the importance of new research. So thank you thank you so much.

Just remember the conversation doesn’t have to stop here. You can visit Sharsheret’s website at www.sharsheret.com or call us at 866 474 2774 to discuss tonight's topic or any other concerns you are facing. Thank you so much for joining us, enjoy the rest of your evening.
VII. Speakers’ Biographies

Deanna J. Attai, MD, FACS is an Assistant Clinical Professor of Surgery at the David Geffen School of Medicine at the University of California Los Angeles. After completing her undergraduate education at Vassar College, she graduated with honors from the Georgetown University School of Medicine, and then completed her General Surgery Residency at Georgetown University Hospital. Her surgical practice is limited to the care of patients with benign and malignant breast disease.

Dr. Attai is a Past-President of the American Society of Breast Surgeons. She has also served as ASBrS Secretary / Treasurer, Chair of the Finance Committee, and Chair of the Communications Committee. She is a Fellow of the American College of Surgeons. She is certified by the American Society of Breast Surgeons for the performance of breast ultrasound, and is an ultrasound instructor for the American College of Surgeons.

An ardent proponent for patient education and empowerment, Dr. Attai is frequently sought out by local and national media for her thoughts on breast disease, diagnosis and treatment. She is a regular contributor to social media sites and is a co-moderator for #BCSM – Breast Cancer Social Media – a popular breast cancer support community based on Twitter. A native of New York, Dr. Attai grew up in a medical family. Her father is a retired cardiac surgeon, and her mother, godmother and aunt are registered nurses. In addition to running her practice, teaching and speaking, Dr. Attai is an avid organic vegetable gardener and an enthusiastic cook.

Sharyn N. Lewin, MD, FACS, FACOG, is Founder and Executive Director of The Lewin Fund, responsible for the organization’s operations, and for setting its strategic vision. She is also the organization’s chief ambassador, responsible for advancing The Lewin Fund’s mission to invest in grassroots initiatives and research that directly support women who are afflicted with cancer and their families. She is a long-time advocate for women and women’s health and brings more than 19 years of medical, research, and community outreach experience to her role.

A board certified Gynecologic Oncologist, Dr. Lewin specializes in the diagnosis, treatment, and management of ovarian, endometrial, uterine, cervical, vulvar, and vaginal cancers. She serves as Medical Director of the New Jersey-based Holy Name Medical Center’s Gynecologic Oncology Division.

Her practice employs a comprehensive, multidisciplinary team approach to screening, treatment, and overall improvement in quality of care for women at high risk for ovarian cancer and other gynecologic malignancies. She is an Assistant Clinical Professor of Obstetrics and Gynecology in the Icahn School of Medicine Mount Sinai Hospital in New York.

Dr. Lewin’s expertise includes radical operations for ovarian cancer, including upper abdominal and extended pelvic resections. She has extensive training in minimally invasive laparoscopic procedures and robotic techniques using the da Vinci® Surgical System. She uses intraperitoneal
chemotherapy and has research interests in novel chemotherapeutic agents, including immunotherapy and hyperthermic chemotherapy (HIPEC) for recurrent ovarian cancer.

Most recently, Dr. Lewin was an Assistant Clinical Professor and a member of the Division of Gynecologic Oncology in the Department of Obstetrics and Gynecology at Columbia University Medical Cancer, New York-Presbyterian Hospital (NYP), and a member of the Herbert Irving Comprehensive Cancer Center at Columbia University College of Physicians and Surgeons. While at NYP, Dr. Lewin was the first Medical Director of the Woman to Woman Program, a cancer support initiative.

Dr. Lewin is a graduate of University of Kansas School of Medicine. She completed her internship and residency at Washington University School of Medicine/Barnes Jewish Hospital, St. Louis, MO, followed by a fellowship in gynecologic oncology at Memorial Sloan-Kettering Cancer Center, New York, NY.

A national educator on hereditary genetics, cancer survivorship and state-of-the-art treatment for advanced ovarian cancer, Dr. Lewin has authored or co-authored over 100 articles, abstracts, book chapters, and made many presentations at scholarly conferences. She is a recipient of the President’s Award from the Society of Gynecologic Oncology and NYP’s prestigious Physician of the Year Award.

A list of Dr. Lewin’s publications is available on request.
VIII. About Sharsheret

Sharsheret, Hebrew for chain, a national cancer organization with three offices (New Jersey, Florida, and California), serves 120,000 women, families, health care professionals, community leaders, and students, in all 50 states. Through 12 national programs, Sharsheret provides culturally relevant support and information to women and families facing breast and ovarian cancer. While our expertise is in young women and Jewish families, all Sharsheret programs serve all women and men of all backgrounds. In fact, more than 15% of the women who reach out to the organization for support are not Jewish.

Bringing our cause to the national platform, Sharsheret is a member of the Federal Advisory Committee on Breast Cancer in Young Women, has been awarded two multi-year grants to develop support programs from the Centers for Disease Control and Prevention (CDC) and participates in psychosocial research studies and evaluations in partnership with federal agencies and major cancer centers, including Georgetown Lombardi Cancer Center. Sharsheret is accredited by the Better Business Bureau and has earned a 4-star rating from Charity Navigator for four consecutive years.

WHAT WE DO - Sharsheret:
- Creates a safe community for women at every stage—before, during, and after diagnosis. We offer tailored resources, information, and support to caregivers, family members, and friends of women facing breast and ovarian cancer to guide them through the cancer journey.
- Services are free, confidential, and easily accessed online and by phone, email, text, and live chat. All services are individualized and provided one-to-one by skilled and trained professionals.
- Builds a strong community of “links in the chain” through education and outreach events for college students, healthcare professionals, and community organizations.

OUR NATIONAL PROGRAMS
Support Programs
- Peer Support Network, connecting women newly diagnosed or at high risk of developing cancer one-on-one with others who share similar diagnoses and experiences
- Embrace, supporting women living with advanced 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 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 active women facing breast and ovarian cancer
- Beatrice Milberg Campus Program, outreach and education to students on campus and young professionals
- Florence and Joseph Appleman Educational Resource Booklet Series, educational and supportive publications for 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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