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Toll-Free Educational Teleconference for Women with Ovarian Cancer 2013

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Guest Speaker:
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- Completed her residency in Obstetrics and Gynecology at The New York Hospital Cornell Medical Center and her fellowship in Gynecologic Oncology at the University of Pennsylvania Medical Center.
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- Research interests include the treatment and prevention of gynecologic malignancies, specifically endometrial cancer, ovarian cancer, obesity and cancer, and survivorship.

Topics:

- Advances in treatment options in the management of recurrent disease.
- The role and promise of clinical trials.
- The latest information on personalized medicine.
- Genetics and heredity pertaining to ovarian cancer.
- Question and answer period

Robin Perlmutter: Good evening, everyone. I'd like to welcome you all to our Sixth Annual Ovarian Cancer Teleconference. My name is Robin Perlmutter. I'm the Clinical Director and a Peer Counselor here at Support Connection. Remember that Dr. Blank is sharing her expertise, and any information from tonight or the questions pertaining to individual concerns should be discussed with your physicians.

It is with my great pleasure that we have Dr. Stephanie Blank, associate professor in obstetrics and gynecology in the Division of Gynecologic Oncology at NYU School of Medicine. Dr. Blank's research interests are focused on the treatment and prevention of gynecologic malignancies, specifically, endometrial cancer, ovarian cancer, obesity, and cancer and survivorship. With a great big warm thank you in advance, Dr. Blank, for sharing your time and expertise with us tonight.

Stephanie Blank: Thank you, Robin. I appreciate the offer -- the invitation, rather, to be here this evening. I'll be speaking about advances in treatment options in the management of recurrent disease as -- disease being ovarian cancer; the role and promise of clinical trials; the latest information on personalized medicines; and genetics and heredity pertaining to ovarian cancer.

And before I begin, it is Gynecologic Cancer Awareness Month, so Happy Gynecologic Cancer Awareness Month, and thank you, Robin, for having a program like this.

So, I think first I'll start at the top here, advances in the treatment options in the management of recurrent disease. The management of recurrent disease has changed a lot since -- even since my training, where we had our frontline treatments and then we had basically two options when somebody recurred. We had our topotecan and our Doxil, as well as the Taxol [and carbo].

So, right now, in terms of recurrent disease, we do have a lot more treatment options, and people are truly living longer, living better with the disease. And I think that some of the things that have gone into

the whole concept of recurrent disease include focus on quality of life. And there's a lot that's being done to sort of best hammer out what our goals are in the management of recurrent disease.

One thing that I'll talk about in recurrent disease is bevacizumab. It's also known as the trade name is Avastin. But about a year ago or so, a large trial was presented at one of our big meetings, which is called ASCO, that looked at using bevacizumab combined with chemotherapy in the recurrent setting trial.

Now, when you have people who have recurrent disease, and I apologize for those that already know all this, but I'll just start that way. Basically, the way you decide what kind of treatment to use depends on a couple of things, one being how long it's been since your last treatment. So, if it's been a very long time since your last treatment, as in more than a year or so, there can be a role for surgery. But the other thing that's important is we stratify people frequently in terms of whether or not they're still considered to be platinum-sensitive, and that would be if platinums are -- as in carboplatin and cisplatin are the main ones that you probably are aware of -- if you would likely respond to those.

And basically, as you may know, there are some people that have this disease that live a long, long time and they maintain their sensitivity to platinums. This is associated with people that also have a genetic predisposition to ovarian cancer.

So, most of the time when we're talking about treating recurrent disease, I'm speaking about people that are not responding to platinum as much, because if you're platinum-responsive, your treatment tends to be platinum-based. And there's a little bit less mystery what to do there, because platinum generally, then, does work. And it can also have a durable response even in the recurrent setting.

In the recurring setting, there was a large study that was done in Europe. It's called the [ORALIA] trial, and it's one of those acronyms I can't even tell you what it stands for. But it basically allowed physicians to choose one of several treatments for their patients in the recurrent setting. Those could be -- I'll use the generic names, but pegylated doxorubicin, topotecan, or weekly paclitaxel, and the physician chose which of those the patient got. And they were then randomized to just that drug versus that drug plus bevacizumab (Avastin).

And I believe that something, a very good number, 20% or so had had prior antiangiogenic therapy. So, bevacizumab (Avastin), for those of you who don't know, is an antiangiogenic therapy, which means that it basically interferes with cancer's ability to sprout new blood vessels. So, it sort of gets the cancer at the feeding source. So, a little bit of a different approach than chemo, which chemo in general kills cells that are turning over quickly, and that's why some of its side effects exists. But bevacizumab is a little bit different because it really works at some of the root -- it kind of takes away some of the tools of the cancer rather than just killing it. So, the interesting thing about bevacizumab and chemotherapy is bevacizumab side effects are quite different, generally, than other chemotherapies.

So, anyway, let me get back to what I was saying, that patients were randomized to either having -- getting the chemotherapy alone versus chemotherapy plus bevacizumab. And some of the longest progression-free survival times were recorded in the groups here that used bevacizumab, I believe with the Taxol, I believe something like 10 months, which is a pretty good number for those of us who like numbers. I don't really, myself.

But this was fairly exciting. And another exciting thing about it was simply that a lot of these people had had Avastin before -- sorry, bevacizumab before. So, it's interesting to sort of think of it in terms of the armamentarium for recurrent disease.

There has been a lot that's been done looking at bevacizumab for frontline disease, and I think the jury is still out on that. Some people feel differently about that. But that's my opinion, basically. I do think that the role of bevacizumab in the recurrent setting has grown.

There have been some other trials in this setting. Actually, in the platinum-sensitive setting there was a large trial that has another wonderful acronym called OCEANS, which looked at carboplatin and gemcitabine plus bevacizumab in the recurrent setting, and this, too, showed an improvement in progression-free survival that was really significant.

And the other thing that is significant about some of these trials is that, for example, that trial, the OCEANS trial, when they designed it they were expecting the time people would go on without their cancer progressing to be about 18 months and it ended up being significantly longer than that, almost twice as long as that. So, it's actually very encouraging that we take our old data, we plan our new trials, and even the control arm, which should be doing the same as what you expect from the past is doing better.

So, I do think it's hard when one has cancer to be optimistic in general, but I do think even in this time that I've been practicing, I've seen people just doing longer and doing better. And I'm sure everyone is not doing better, but there are more options, and that is certainly a good thing.
I want to speak about a couple other things in the recurrent setting. One thing, and I'm basing a lot of what I'm saying on things that people ask me. So, if there's something that I don't bring up, of course, feel free to ask me, ask the whole group in a bit.

People are very interested in immunotherapy for recurrent ovarian -- actually, for all ovarian cancer. It's not exactly known when in the course of ovarian cancer immunotherapy would be best used, and sometimes people use different terms for immunotherapy. It might be also called vaccine therapy or something like that. There are different ways that people go about using immunotherapy. Sometimes they look at your actual tumor and they see if it expresses certain proteins on the surface, and if it does, then they can use therapy specifically directed to those targets. And that's sometimes done. That's been used a bit in melanoma, and at NYU we've done a study in that with people that sort of over-express a certain antigen.

There's another approach that's very intriguing, which basically entails taking a woman's tumor and growing it, or growing cells from her very blood to work for her. And that's, of course, very, very individualized. And both of these things are beautiful in the sense that they allow your immune system to do the work.

So, again, the toxicity of this type of treatment is certainly going to be less in general than those traditional chemotherapies. But it's not exactly known at this point where this belongs in our treatment. Some people thought there was a large trial a while ago where there was use of an anti-CA-125 antibody that was given to women after they've completed their frontline therapy, so they basically had no disease at all. But it did not show that people would live longer in the end. So, it is generally thought that immunotherapy is probably best for smaller volume disease, not large volume disease.

I would be remiss if I didn't mention PARP inhibitors, and I'm always excited about PARP inhibitors, and these are especially exciting in ovarian cancer and especially in the cancers that are associated with BRCA mutations. But even there are tumors that are from people that do not have these mutations but still will have excellent responses to PARP inhibitors.

So, PARP inhibitors basically are -- when somebody has a mutation, a BRCA mutation, their DNA's ability to spell-check, if you will, is sort of -- is messed up, and it is the enzymes, PARP, which basically run that spell-check. And by running that spell-check, the cancer can grow without stopping. So, a PARP inhibitor prevents that from happening. That's a very, kind of simplistic way to think about it, but I can't tell you how to -- any more differently than that.

Now, a very interesting study looking at PARP inhibitors looked at women who were platinum-sensitive, who had just had some sort of response to platinum, and then randomized them to either getting nothing, which would be what would be pretty much standard, or getting a PARP inhibitor. Now, the PARP inhibitor that was used for this was called olaparib, and it was a pill that was taken. And I shouldn't say what it was because I still have patient on this trial, so people are still taking this.

And, basically, when this was looked at, it basically showed that there was a significant improvement in the amount of time people went without the disease coming back. But when they looked longer, it did not make people live longer. And so that's something when we talk about recurrent disease, it's a never-ending debate about how to measure response to these therapies. Because is the goal going longer without the disease getting bigger or living longer? And I guess that's a philosophical discussion that I won't get into right now.

Another option in the management of recurrent cancer is sometimes not treating if you do not have symptoms from disease. So, sometimes a marker can be elevated and probably never not going to be elevated, but if you, the woman with this marker feels fine, there is an option not to treat for some time. And a large study done in Europe actually showed that treating people based on CA-125 alone did not make people live longer. So, there is also another advancement in the care of women with ovarian cancer is that we have much better non-cancer-directed treatment to give people.

I will move on now to the role and promise of clinical trials, and I feel a little bit like I'm giving a public service announcement here, because I think clinical trials are wonderful.

Now, when I present a clinical trial to a woman and her family, everyone has a preconceived notion about what a clinical trial is. And people think they're going to get a placebo or that they're going to be used as a guinea pig. The main thing about making the decision to participate in a clinical trial is there probably will be more involved on your part than you would be if you are not in the trial, if you are on the trial. For example, if you're getting chemotherapy off trial and you want to go away for a week, not really a big deal; but if you're on trial, it's a lot harder to go away for that week. Or you have to have scans at certain points, labs at certain points, that type of thing.

In terms of trials that you probably have heard about phases of trials. There's Phase 1, Phase 2, Phase 3, etc., and a lot of times people are told, and this is actually accurate, you want to be in the highest phase trial that you can be in. So, basically, a Phase 1 trial is looking at the safety of whatever treatment it's studying. A Phase 2 trial is seeing if it works at all, and it has to meet certain standards on the Phase 2 trial to see if it can move to a Phase 3 trial. And a Phase 3 trial, it's randomized against a standard treatment.

So, people most of the time for, say, for frontline therapy and such, most of the time those are Phase 3 trials, and those are good because you know you're getting something -- you're getting either the new thing or the old standard thing that's good. There could be randomization that involves a placebo, but it would usually have other treatment with it as well.

So, the thing that I tell people about trials, because some people think they're great and some people think they're terrible. But people that think they're great only want to get treatment on trials, and just because something's new, despite the fact that I've been saying new things are great this whole conversation, doesn't necessarily mean it's better.

I think one thing that you can say if you are to go on a trial, it can give you access to drugs that you might not otherwise have access to. For example, the drugs I mentioned before, the PARP inhibitors, no one can write you a prescription for those because they're not available as yet, but those can be obtainable on trial. So, you can get these drugs that you might not be able to get otherwise.

But what I really tell people is that the only thing you know for sure once you're doing a clinical trial is that you are contributing personally to the advancement of the treatment of ovarian cancer. Because it's women participating in clinical trials that made Taxol a standard of care for us, and made now bevacizumab a standard of care for us. So, people are contributing. That's the only thing you know. You cannot be guaranteed that you're getting better treatment. That's the whole purpose of the trial, to figure that out.

I do think that when people are in trials, you do know that you're getting the newest, and you can be generally associated with a place that has more care. But if you don't have access to trials, it doesn't mean that you're not getting the care. As I say, you're getting a standard of care, we have a very good standard of care that is based upon trials.

I will move forward now about personalized medicine. And I guess the first thing, everyone -- it's one of those buzz words of the past couple of years, personalized medicine, and I guess what exactly is that? Because I would say ovarian cancer in general is treated in a fairly personalized way, meaning that it's not cookie-cutter treatment for ovarian cancer. And part of the reason for that is because every woman is different and we have a number of different options and different things work for different people.

But why personalized medicine is so important for ovarian cancer, even on a molecular level, it's been shown that ovarian cancers are very, very different. Sometimes they do gene analysis of certain kinds of cancers and they all look similar in some way. When they do ovarian cancers, they look extremely different across-the-board, and you can't make a lot of generalizations even about, well, this is the way it looks if you get when you're 45, and this is the way it looks if you're from Eastern Europe. There is nothing that has been very consistent in terms of the gene expression profiling of ovarian cancers.

And so what that means is that probably in order to make use of a lot of the information that we're learning in the human genome project and all that, it might be important for everybody to get their tumor molecularly characterized. Now, what that means at this point in time is that generally there's a couple different places where you can get it, and what you get is a report that basically tells you what type of proteins your tumor over-expresses and such. And you usually get a 10-page report, and it's based on the genetic makeup of your tumor.

Now, there is a foundation that exists in California that has been very helpful for a lot of people to get this information. It's called the Clearity Foundation, and you can send your tumor to them and they actually help with financially with getting that done.

When you have this information now, it's not exactly known what to do with it, so I don't mean to imply that you must have this done because we don't know everything to do with it. But what it might be able to tell us is some out-of-the-box ways of thinking to treat the ovarian cancer. For example, there are drugs that get at different types of proteins that are used for other things… you've probably heard of Cox-2 inhibitors. They've been around for a little bit, but there are tumors that over-express Cox-2. It used to be used for arthritis and that type of thing. But if your tumor over-expresses Cox-2, you can maybe use a Cox-2 inhibitor and it might have some therapeutic benefit, when that is certainly a drug that is a lot easier to tolerate than a traditional chemotherapy.

So, yes, we don't know 100% what works for personalized medicine. It's still at the very, very early stages. It's not covered by all insurances, meaning the actual testing.

Sometimes people think about the personalized medicine being taking your tumor and testing if it responds to different chemotherapies in a Petri dish, especially. That's called chemo-sensitivity assay. It's not really personalized medicine, but sometimes people confuse those two. That, as far as I'm concerned, has not really been shown to be perfectly translatable to what is actually going to work in practice.

So, you can have your tumor tested against different chemotherapies and, again, you get another nice long report that says your tumor responds to this, your tumor does not respond to this. But it has not been shown that making your treatment decisions based on that information necessarily results in better care or more effective care, or anything like that.

So, again, a lot of what is done in personalized medicine is still being done on a research level. So, it's probably something that we're still learning more about, the cancers in general, than you're necessarily able to access on a day-to-day basis. What I mentioned before is sort of the most clinically applicable use of personalized medicine.

I will now speak about genetics and heredity pertaining to ovarian cancer, and this is a topic that is near and dear to my heart. And actually, this is a topic that is very important for women with ovarian cancer to know about, because you can really have an impact on family members with this.

So, it has been shown, basically, that any woman with ovarian cancer has an indication to have genetic testing, meaning genetic testing right now, it's changing a little bit. But it's going to a genetic counselor, they go through your family history with you, and they usually give you a likelihood that you might have a mutation, which is a change in your DNA that might have made you more susceptible to get ovarian cancer. And there are some of these that are especially common in certain populations. So, if you have breast cancer and you're 80, that doesn't mean that you would necessarily qualify for this type of testing, but any woman with ovarian cancer does, because ovarian cancer is rarer.

Now, most cancers, even ovarian cancers are not genetic or at least at this point we don't know that they're genetic. But if you have an ovarian cancer and you see a genetic counselor and you have a mutation that is predisposing you to this cancer, it can be very important information for other people in your family, because they can get tested for the same mutation. And if they're negative it will be a true negative, they will know they do not have the same risk; and if they're positive, there are preventative measures that they can take.

The other thing about a woman with ovarian cancer getting genetic testing done for herself is it does seem that that may inform some of her treatment decisions. For example, when I have a patient that has a BRCA mutation within a new recurrence of ovarian cancer, we will go to ends of the earth to try to get her on one of those PARP inhibitor trials. It might make you really want to pursue a specific avenue of treatment, because there are advances in this specific field.

There are other things that we know about BRCA-associated tumors. I mean, there was a study that was done just really looking back at women who had what we call interperitoneal treatment that were received straight into the belly, and those people with mutations that had that treatment did even better than people that did not. So, I think that that might also help you make a decision about what treatment you would like to pursue.

Now, when people talk about genetics, sometimes people say, well, there's nobody in my family that has any cancer, it can't be genetic. It's not always that simple. I mean, a couple of things that people sometimes are confused about is, one that the cancer can come from either your mother or your father's side of the family. It doesn't only have to come from your mother's side of the family. There might be no one had cancer in the family because everyone died young from the war, or because there are no women in a whole generation. And sometimes there could be something going on that we really don't know about, and sometimes people didn't talk about that so much.

So, basically, if you do have ovarian cancer, it is something worth pursuing, and I, personally, think I'm a nag because every patient, if I don't have it written down that she's positive, I said, "Did we talk about this? Did you have testing?" And we have them go for that.

I can speak a lot longer about this. Sometimes women don't want to hear this because they don't want to hear about prevention, because they say I already have cancer, I don't want to hear about how to prevent cancer. But basically if you have a mutation that predisposes you to cancer, any child you have or any sister, your mother or father has a 50% chance of having that same mutation. And if you have that mutation, then you have a 40% chance, lifetime chance of having ovarian cancer, and an over 70% chance of having breast cancer. And I'm speaking now about BRCA mutations, which are the ones you probably heard about, as they are the ones that we know the most about.

When people find out that they have mutations, the term that some use is a previvor as opposed to a survivor, but a previvor, and previvors basically can be followed much more closely in terms of their breast cancer screening. Ovarian cancer screening has been less effective, but frequently birth control pills or something that we can put people on that actually do reduce the risk of ovarian cancer. And, of course, people have preventative surgery, such as Angelina Jolie, who needs to have her ovaries out, but preventative surgery to prevent both breast and ovarian cancers.

An important thing about genetic predisposition cancers is these cancers not always, but frequently, come earlier in subsequent generations, so it is important. I do like for people that have mutations, I give them quite a talk about, you know, don't wait until you're 40 to start having your children, do it sooner. Additionally, they have a shorter reproductive life associated with BRCA mutations, so there's just a lot that goes into that. I think that's maybe a little off topic for what we want to talk about here. I would like now to have no more monologue, if that's all right with you, Robin.

Robin Perlmutter: That is perfectly fine. You did a great job. Let's take some questions.

Unidentified Participant: I have a two-part question. Can you hear me?

Stephanie Blank: Yes.

Unidentified Participant: Okay. You had indicated that immunotherapy is best used for small volume disease. Is immunotherapy indicated if your recurrence is in the lymph gland area? And then the second part of that is, for those of us with recurrent disease, you talked about needing -- I think you need a tumor sample to get molecularly profiled or with some of the vaccines, etc. Do you recommend having surgery if it's not indicated for your treatment plan?

Stephanie Blank: Great questions. Really great questions, and I'll go through that and if I forget something, please let me know. So, your first question was about immunotherapy being most for small volume disease. That's just a supposition. That's not an absolute at this point in time. It does make sense, as you mentioned, that maybe disease that's only in the lymph nodes might do -- because the lymph nodes are so involved in our immune response that that might be -- those might be a good cancers, if you will, for immunotherapy. I don't know that that's been shown as yet. But I don't think that would rule it out. I think if you are interested in immunotherapy, again, it's only done on a trial basis right now, meaning that you can't just ask anyone to do it. There are certain centers where it's done. I would certainly investigate to see if you are a candidate as yet.

Now, I think I'm forgetting the second part of it, but I do know your third part of it, so I'll answer the third part and then you'll ask me the second again. Your third part is, do I recommend surgery to obtain tumor specimens if you wouldn't otherwise need it? And I cannot say that I recommend that. I mean, that is obviously putting yourself at risk. They can be done in different ways. Sometimes they can be done through a radiologist, or something like that.

Sometimes, not often, though, sometimes you can use a historic sample, meaning they can look at an old sample, but not usually for the immunotherapy. If they're looking for whether your tumor expresses a specific antigen, that's kind of the first way that I was talking about with immunotherapy, sometimes they

can use sort of a tumor that they have in the pathology lab. Now, what did you ask me something in the middle that I think I forgot.

Unidentified Participant: I think that was basically it. So, if you're not having surgery and you can't use pathology slides, then it really kind of rules you out of immunotherapy at this point in time, or immunotherapy trials?

Stephanie Blank: Well, it depends-- If you have ascites, sometimes ascites can be used. Hopefully, you don't. I think that there are some places where when you do have a surgery even upfront some people will bank a tumor then, so that it's properly processed so that you can use it. There are commercial venues that -- there's one called something like Store My Tumor, Bank My Tumor, something like that. I mean, these things exist now. I'm not advocating them because I think that at this point they're a lot like cord blood, meaning that these things are designed to make money for companies more so than we know what to do with them as yet. So, I don't mean to say that, but sometimes, yes, you will need to have some tumors that the doctor or the scientist can look at to, I guess, if you will, construct the proper immunotherapy for you.

Unidentified Participant: Thank you.

Stephanie Blank: Sure.

Unidentified Participant: I have a question.

Stephanie Blank: Yes.

Unidentified Participant: My cousin lost their daughter two months ago to ovarian cancer. She was 22 years old.

Stephanie Blank: Oh, I'm so sorry.

Unidentified Participant: Horrible situation, thank you. She has a surviving brother, who is 19. I have known that in breast cancer they test for the BRCA in males for prostate and other things. Would they test in a male sibling in this kind of situation?

Stephanie Blank: First of all, do you happen to know if the 22-year-old had a mutation?

Unidentified Participant: No, I don't know the answer to that.

Stephanie Blank: That would be the most helpful, if they knew if she did, or if anyone else in the family with cancer. You generally test the person with cancer first, because if the person with cancer is negative, then the people that don't have cancer, there's no point in them being tested, because you won't know if a negative really means anything.

I would say, you said 18 or 19, he's a teenager, a teenage boy like that, I don't know that I would certainly put him through testing at this time. It might be still information that might be of use to him for future, be it for his own health or health of his family. The BRCA2 mutation, for one, is associated with male breast cancer, and that's a very rare disease, but when it occurs you think a lot about it being part of the BRCA spectrum of cancers.

In terms of other things that men can get, you mentioned prostate young, also pancreatic cancer can tend to run in families as well. We do not have screening for all those cancers right now, so I guess if an 18-year-old man, boy, finds out he has a BRCA mutation, I don't know how that will affect him on a day-to-day basis in terms of, I wouldn't necessarily recommend anyone changes their health practices or their lifestyle based on that. But certainly that will be information that will be of use in the future, probably.

But it also might be a lot cheaper in five years and easier to get that done, so I don't think he needs to rush to have that done.

Unidentified Participant: Okay, thank you.

Unidentified Participant: Dr. Blank, thank you very much for your time. I hope you can hear me.

Stephanie Blank: I can.

Unidentified Participant: I have a quick question, I hope. I was diagnosed last year, in February, with Stage II ovarian, and I've been very fortunate to have come through it very well. Having gone through the tough chemo, I have been on Avastin for a year and a half. And my surgeon told me last week that it could be conceivable that I would be on Avastin for the rest of my life. I was wondering, it's very difficult to find any information on this. I trust my oncologist very much, as well as my surgeon, but I wanted to ask you in your own studies and the information that you get, is that a reality, that one would take Avastin for the rest of one's life?

Stephanie Blank: Again, I don't mean to just be cliché and say that's a great question, but it is a great question. When Avastin was studied in the frontline setting and in the recurrent setting, the times where it had benefit was when the Avastin continued after completing the chemotherapy, such as what you are talking about right now. Now, in the upfront setting, it generally did not continue forever; it generally had about an 18-month time period over which it was given, but in the recurrent setting it was continued until progression.

Now, you having Stage II disease, or having had Stage II disease, your prognosis is potentially very good. You may or may not -- you may not recur even without the Avastin, so that's one thing to know about. But I certainly understand what your doctors are telling you, that some of the compelling evidence for Avastin involves continuing it on after sort of the initial treatment is done.

One of the thoughts about continuing Avastin indefinitely is there was a thought that if you stop Avastin the tumor is going to suddenly grow very quickly, which has not in fact proved to be accurate. I think sometimes people are afraid to stop Avastin for fear of that.

In terms of what we know about the side effects of Avastin with time, it doesn't seem that it gets -- that they get worse or that things develop more. I think it's very hard, I haven't been in a situation with somebody with a Stage II disease that I put on anything for the rest of her life. If it's something that you are not uncomfortable with and you can get covered, it seems like it is working at this point in time, but I guess that's just not an automatic to be on treatment for the rest of her life.

I would say sometimes more that may be in a recurrent or doubling, tripling recurrent setting that one may have that, but a little bit less so upfront. Not to say I disagree, I just think that it surprises me a little bit, but I understand why that's being done. I just think that the words probably were a little shocking.

Unidentified Participant: Yes, and thank you so much for answering. God bless.

Stephanie Blank: Sure.

Unidentified Participant: Yes, I have a question, can you hear me?

Stephanie Blank: Yes.

Unidentified Participant: When you talk about immunotherapy, is that appropriate for people who are BRCA-positive?

Stephanie Blank: I believe it probably has not been studied relative to the mutation, so I think that that would probably be reasonable either way. I don't think it is especially appropriate or especially inappropriate based on that.

Unidentified Participant: Okay, thank you.

Stephanie Blank: Sure.

Unidentified Participant: I have a question about PARP inhibitors.

Stephanie Blank: Yes.

Unidentified Participant: I have the BRCA2 mutation and I was on one of the PARP inhibitor trials and did recur. Actually, the trial doctor did say that everybody will recur, it's just a question of when. But is there any indication that it might be useful if there was a trial, perhaps a Phase 1, for a different PARP inhibitor, that switching PARP inhibitors would be indicated or helpful at all?

Stephanie Blank: That's a great question, too. I think that we don't have those data as yet. I think there is a new one out -- there's always a new one that's coming out, and I think unfortunately most of the time the trials prohibit you from having had PARP inhibitors before, but I definitely read some trials where you can have them. And I do think that certainly I wouldn't rule it out for future once they're available. For now it's going to be a little bit hard to get them.

Unidentified Participant: Everybody, Dr. Blank is my doctor and I'm on a PARP inhibitor trial with her, and I'd just like to clarify one thing that came up in my situation, which was though I had done the myriad testing for BRCA mutation, that didn't show a mutation. And when I went to Clearity and had them look at my actual tumor, that showed a mutation. So, you can have a sporadic mutation which just is in your tumor but does not affect your other genetic makeup in your blood.

So, it's a really good thing to get your tumor analyzed, because you may think that you don't have a mutation, but you may actually have one, and the PARP inhibitor has been shown, or at least I think I'm getting PARP inhibitor, is that it's effective against a sporadic mutation, I would think what's happening in my case. Because I've been on it for four years.

Stephanie Blank: Great point. So, the difference there is when you go to a genetic counselor they're looking for a germ line mutation, they're checking either your blood or they're swabbing the inside of your cheek, is that Clearity testing where they actually look at your tumor. And probably a lot of people that don't -- just like she said, a lot of people that do not think that they have mutations may have these other kinds -- this sporadic mutation that you can't check for in the blood and still can have a good response to PARP inhibitors.

Unidentified Participant: Doctor, can I ask you a question? I've been fighting primary peritoneal IIIc for the last 10 years, and originally I was operated on and given carboplatin and Taxol. I had nine of those and I was free for three and a half years. Then it came back and they put me on carboplatin and Taxotere, but I was toxic to it so my throat closed and they tried a slow drip and tried to medicate me but it didn't work. Then they put me on cisplatin and Taxotere and my CA-125 kept on rising. So, then I was put on topotecan for another nine sessions of it, nine months of it, and I was in remission for a year. And then it came back, and then I was put on [doxorubicol] for another nine months. And when it came back my leg, it came back in the groin and my leg was swollen and my feet -- my whole leg was swollen. So, they put in a stent and there was one nodule there and they put me on [doxorubicol]. It's three years since I had that and I'm in good shape. I go every three months for CA-125. I did go for the BRCA testing for the 1 and 2, and I don't have that. What would you -- is there anything else? Should I try to find the tumor and have that analyzed? Is there anything else that you can tell me to be proactive?

Stephanie Blank: Your course has been -- it's been a long course, a very interesting course, and I do think that if you can touch base with Clearity and find out what exactly they need for testing, that you may have a sporadic

mutation rather than one that you check in the blood. So, there is still a possibility that you could have one. And the reason why I'm saying that is when you hear somebody who has a long course such as you, that's fairly typical for BRCA mutations. So, right now you're not being treated; is that correct?

Unidentified Participant: I go every three months for CA-125. And, in fact, I have some cousins that know you and are at NYU on staff, so I just wanted to know. I'm not on the East Coast, I'm in the Midwest, so I know nothing about Clearity, but I should check into that?

Stephanie Blank: Yes, you should. C-l-e-a-r-i-t-y.

Unidentified Participant: Okay.

Stephanie Blank: Yes, anything you would find -- I've directed people there, but I haven't gone through it.

Unidentified Participant: Well, in my case they used the slides from my operation and it was several years old, but I think I read something on the site recently about wanting more up-to-date tumor because when you have chemotherapy it changes you cancer. So, I'm not sure what they're requiring, actually now, but I would call them. They're really very responsive. They have this woman named Deborah who has a long last name, like Sakowski, and she'll get back to you and she's fabulous. Very knowledgeable.

Stephanie Blank: It's worth looking into. And even if Clearity won't fund it, you can still probably have it tested, even your historic tumor.

Unidentified Participant: Even my historic tumor that's over 10 years old I could get from a teaching hospital?

Stephanie Blank: They generally save it. I mean, I can't tell you you're going to walk in and walk out with the slides that day. They're going to have to retrieve them from somewhere, and you might need to make a couple of phone calls to get it, but you should be able to get those slides still.

Unidentified Participant: Okay. You would say for me to be proactive and that's the course you would tell me to go?

Stephanie Blank: I think your situation is -- I think I'm impressed with how you're doing right now and how you've made it through a lot of different things. I think it's hard for me to tell you to do anything differently, because you've done a very good job.

Unidentified Participant: Well, you know, I'm very fortunate. I just -- so, anyhow, I haven't gone to NYU. I had been thinking, but when you're alone and you're doing this and I'm in very good shape. I'm in excellent shape considering all of the chemos that have gone into me. So, I thank you and I will definitely look into that and find out if they could get a tumor from what was done over 10 years ago.

Stephanie Blank: Absolutely. Well, good luck to you.

Unidentified Participant: Okay, thank you very much. Thank you.

Unidentified Participant: I had a question about Avastin. I've been being treated for, let's see, I'm in the second recurrence, I guess, and have been on a lot of different chemos. But I've never been on Avastin. Would a blood-clotting issue keep you from Avastin? I have Factor Five Leiden.

Stephanie Blank: Yeah, and that would make it tricky. I mean, generally, in trials and such, it was something that ruled you out for being eligible for a trial having a blood-clotting issue. That said, are you being seen on blood thinners or not?

Unidentified Participant: Well, I've been on Coumadin and it wasn't well regulated, and then I had a third surgery recently and they put me on Lovenox initially after the surgery. And now I'm on Taroza.

Stephanie Blank: Yes. I mean, if you're on something counteracts your predisposition to bleeding, it may be okay. I am sure that your doctors have thought about that in making the decision for you.

Unidentified Participant: Yeah, it isn't something we talked about, so I didn't know.

Stephanie Blank: It is not the right drug for everybody. I would say that if you come to a treatment crossroads, it's not a bad thing to ask if that's even a consideration. If you're on blood thinners, would that sort of take away that part of the risk, and that is something that some people suppose, but we don't know the answer to that as yet.

Unidentified Participant: Okay, thank you.

Stephanie Blank: Sure.

Unidentified Participant: Dr. Blank, have you seen these vaccines used for -- is it used as a maintenance drug after you're put back into a remission so that your body is -- when you say low volume, so your body is sort of speaking out as it may start up again? Or is it used as a way of putting you back into remission?

Stephanie Blank: I think that studies have been done with both. I think that the ones that, right now, a lot of times when they're doing those trials they can't even -- it's too early for them even really to look at how well does this work. They're looking really to see does your body respond to the tumor, so they're really, really early on these.

I think some people believe that there's probably a bigger role for this in the setting like you mentioned, sort of the maintenance setting, and part of that may be that this is not something that is going to work instantaneously. And if you have a lot of disease it's going to be -- you may need something that's directed against the disease that works a little bit quicker than that.

Unidentified Participant: And then I think there's also different kinds of vaccines, kinds that use your particular tumor.

Stephanie Blank: Yes, yes.

Unidentified Participant: And there are kinds that are made with, I don't know, they're just not using your tumor but they're using stuff that hopefully will attack your cancer but not created from your own body.

Stephanie Blank: Right. Maybe it's something that is on, say, 30% of women's cells, you know, women with ovarian cancer tumors and they have devised something against that. So, there are a lot of different ways that immunotherapy is being used, again, all in a trial setting. And I think we're still really at the beginning of learning what the potential for that is.

Unidentified Participant: And do doctors like yourself know who is doing what? You know, like Hopkins is doing it this way and --

Stephanie Blank: Yes, a little. It changes frequently. I mean, there are certain centers that do a lot more. I think also our big group that does trials is trying to come along with some of those as well. It would -- you're absolutely right in that it probably would require willingness to potentially travel or go somewhere else to get it if it's not offered near you.

Unidentified Participant: Thank you.

Robin Perlmutter: We have time for one more question.

Unidentified Participant: Dr. Blank?

Stephanie Blank: Yes?

Unidentified Participant: Yeah, hi. I have Stage IV ovarian cancer. I was diagnosed in 2008. I've done really well. Presently I've been on Avastin since February of 2011, and coupled with Cytoxan, but I seem to be approaching another recurrence and I'm just wondering if I did get involved with a PARP inhibitor trial, would they stop the Avastin or do they continue, or how does that work?

Stephanie Blank: If you were to go on a trial for a PARP inhibitor, they would stop your Avastin.

Unidentified Participant: Oh, okay.

Stephanie Blank: I would say that if you're going to go on any trial, they're going to stop the Avastin.

Unidentified Participant: Oh, so perhaps maybe throwing in something like Doxil if the Cytoxan stops working; would that be an alternative?

Stephanie Blank: That's an alternative, a little weekly Taxol , that is an alternative.

Unidentified Participant: Or Doxil?

Stephanie Blank: Doxil is an alternative. When used with Avastin, sometimes the skin changes can be a problem, but there are good data with Doxil and Avastin.

Unidentified Participant: Okay, thank you very much.

Stephanie Blank: Sure.

Robin Perlmutter: Okay, folks. Well, Dr. Blank, thank you so much for you expertise, your time, and everybody for joining us tonight, and especially in honor of Ovarian Cancer Awareness Month. So, until our next conference, this is being recorded and the recording and the transcript will be available for you in the next couple of weeks on our website so that you can refresh the memory, take notes. And, again, Dr. Blank, thank you so much.

Stephanie Blank: Thank you. Thank you. Everyone have a good evening.

Robin Perlmutter: Have a good night, everyone.

- END OF TRANSCRIPT -