

Anti-Angiogenic Therapy: Inhibiting Tumor Growth in Breast Cancer

Webcast

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Introduction

Andrew Schorr:

Hello and thank you for joining us once again for our live Seattle Cancer Care Alliance webcast. I'm Andrew Schorr, delighted to be a cancer survivor. Don't know if I'm cured of my leukemia, but you know what? If you can live with cancer and make cancer chronic and lead a full life, that's pretty good too. Tonight we're going to talk about that as he look at really advanced breast cancer, and are there new medications and new approaches to keep the cancer at bay even when it's spread? We'll be meeting a leading expert from the Seattle Cancer Care Alliance in a minute, but first I want you to meet Ginny, who joins us from Eugene, Oregon, down the road a ways from Seattle, I think about five hours. Ginny, when it comes to breast cancer you have known about this in your own life for about 14 years now, am I right?

Ginny:

That's correct, Andrew.

Andrew Schorr:

Tell us how it started, the terror that any woman feels, and there you know women are getting pretty good about getting mammograms, and we like to rely on it, but your story is a little different. Tell us about that.

Ginny Shares Her Story

Ginny:

Well, in June of 1994 I noticed a lump in my right breast along with some nipple retraction, and I went to my gynecologist, and the mammogram was negative. But subsequently the lesion continued to grow, and so then I had another mammogram and an ultrasound, which were both negative, but because there was obviously a lump there a biopsy was done and a diagnosis was made in October 1994.

Andrew Schorr:

All right. So you have three kids, all grown now.

Ginny:

That's correct.

Andrew Schorr:

A family and a busy professional life. What treatment did you have then to hopefully cure the breast cancer?

Ginny:

Well, initially I had some chemotherapy to help shrink the lesion because it was rather large, and then I had a mastectomy, and then I had more chemotherapy, and then I had some local radiation. And all that took almost a year, and then I was continued on tamoxifen for five years after that.

Andrew Schorr:

And the hope and the belief was, well, maybe you got it all, beat it and you could just go on with your life.

Ginny:

One always hopes for that.

Andrew Schorr:

But the awareness of course among many women is we'd like to say five years and you're clear, but after eight years it came back. How did the breast cancer show up the second time?

Ginny:

Well, in February 2002 I went back to see my oncologist. Actually he sent me a card suggesting it. And he did a blood test, which showed an elevated cancer antigen in the blood. And subsequently he did a PET scan, which showed a lesion in my right hip. And I was asymptomatic at that time, and subsequently lesions were found in my spine and liver.

Andrew Schorr:

Oh, my. All right. Now, along the way you say, what am I going to do about this? You're a very proactive patient, and although you're down in Oregon you decide to seek out a second opinion in Seattle at the Seattle Cancer Care Alliance, and that brings you to an expert we've had on our programs numerous times, Dr. Julie Gralow, who is director of breast medical oncology. I want to hear the story, before we get to Dr. Gralow, I want to hear the story from your perspective. You connected with her, and what approaches did she try and what eventually worked?

Ginny:

Well, initially when I was treated I received antihormone therapy, the three drugs were Femara then Faslodex, and Aromasin was added. And initially this seemed to halt the tumors. I went to see her first in November of 2002 and I had discussed this with my local oncologist, and he's been very supportive and said that would be a great person to see for a second opinion. And she followed me along while I was

on hormone therapy. But then in September of '04 a CT scan showed that I had lesions in my liver, and at that time I was started on chemotherapy. And she would suggest the treatments and also order what studies were needed, and then I usually got these in Eugene and then could go and consult with her about whether any change in treatment was indicated.

I tried several courses of chemotherapy between September '04 and April of '05, which did not halt of increase in size of my liver lesions. So in the spring of '05 is when she suggested the Avastin, can I use the trade name?

Andrew Schorr:

You certainly can. We're going to talk a lot about Avastin tonight, bevacizumab.

Ginny:

Okay. Avastin with a chemotherapeutic agent, and subsequently since that time, which has been almost four years there has been no progression of my liver lesions. I also had some lesions in the spine, and they have occasionally given me a problem, but I had a brief course of radiation this year and that seemed to take care of the problem with one of them. But I think that I am leading a very full life and I am living with cancer. And I really appreciate the guidance that Dr. Gralow has given in allowing this to happen.

Andrew Schorr:

Right. Amen. We're going to talk more about that, but I think I just want people to visualize this. I understand that you like to garden, and coming up before long is the marriage of your son, and you're going to have a reception in that garden. So that's your passion now. This is 2008. You were originally diagnosed in '94, I think, and then had the recurrence in 2004. Used to be a woman would have the recurrence and metastases to her liver and you'd say, You know, you're not going to make it that long, and yet you're looking forward to a reception and you're doing gardening. So we're in a new era, aren't we?

Ginny:

That's right. I'm thinking now of cancer as a chronic disease.

Andrew Schorr:

Let's hope that's for everybody. I'm delighted it's that way for you. Let's meet your doctor, Dr. Julie Gralow, who as I mentioned is director of breast medical oncology at Seattle Cancer Care Alliance. She's a leading clinician and breast cancer researcher known worldwide. Dr. Gralow, welcome back to Patient Power. I know it's very gratifying to hear Jenny's story. I know it doesn't always work out this way, but it sounds like more women have the hope even with advanced breast cancer of keeping the cancer at bay for extended times and going on with their life with the benefit of newer medicines that we're going to talk about tonight.

Excitement Over the Approval of Avastin

Dr. Galow:

Right. Hi, Andrew and hi Ginny and thanks for having me back on Patient Power. I think Ginny's story is an excellent example of why this is a really exciting time in cancer research. We have a whole new class of drugs. I know we're going to spend some time talking about Avastin and the general class of drugs it's in. It was a drug that really wouldn't have been available much before we were able to try it in Ginny, and her tumor was progressing through other standard breast cancer therapies. We were kind of starting to run out of options a little bit, and then a new drug, we get some new clinical trial results, and we decided to try it and look at where we are several years later. It's really very gratifying that research led us to get this drug approved and that we could use it in patients like Ginny.

Andrew Schorr:

Right. And let's explain Avastin in this case, or, as I said, the longer scientific name is bevacizumab, and we'll learn what the "mab" means as we go on. It was approved in colon cancer I think first, is that right, is how it first came on the market?

Dr. Galow:

Colon and then lung, and it's been approved in those areas for several years now.

How Avastin is Controlling Tumor Growth

Andrew Schorr:

And just recently, in late February of 2008, in breast cancer, but happily you were able to get it approved and paid for even before it was officially approved by the FDA in the case of Ginny to help her. So that was sort of an off label or experimental use that made all the difference, and now it's an approved medicine for breast cancer by the FDA. Help us understand how Avastin works and this class we're going to discuss tonight and how this has made a big difference in controlling the tumor growth.

Dr. Galow:

So our new strategies in the treatment of breast cancer include not just treating the cancer cell itself, which is what most chemotherapy and endocrine therapy target, they target the cancer cell, but we also know that the cancer can't exist by itself. It needs to bring the body, it's the environment around it, into the picture in order for it to be able to spread and survive. So we're also now investigating, and we have some drugs approved that manipulate the area around the cancer cell, and the cancer cell's interaction with what we call its environment.

So while we have chemotherapy that would impact the cancer cell, a drug like Avastin impacts the tumor cell's ability to bring nutrients and oxygen into it. It impacts the blood vessels. The tumor sends out signals to the blood vessels and says, kind of, Grow in this area, help feed me, which is not a good thing for the

patient, that the tumor cell can bring in all kinds of extra blood vessels that bring in protein and sugar and oxygen. And by blocking the interaction between the tumor cell and the blood vessel we now have a new class of therapies. We call them antiangiogenic therapy. "Angio" is a blood vessel, and "genesis" would be the birth of. So it's anti the birth of blood vessels. So we're preventing the tumor from bringing blood vessels into it. And these drugs seem to work best when you hit the tumor cell with some chemo and then prevent the tumor cell from trying to grow back and bring more blood vessels in to feed it.

Andrew Schorr:

You know, I have this weird analogy I've used. It's helped me understand it, but I'll share with other people. So, Julie, you go to a lot of conventions and I do too, or anybody who has ever been to a business meeting or convention. So you know that the people who serve the meals and come in and the people who work in the hotels and conventions, they have other hallways and elevators that they're using beyond the ones that the visitors are using, sort of back passageways. And I have image that these cancer cells develop their own back passageways, and you can have drugs that try to stop those passageways from either happening or growing but yet you don't affect the good passageways, if you will. That's always been interesting to me. It's like the cancer cells have their own supply, and even though you have drugs that affect that you don't affect the healthy tissue. That's fascinating. Did I get it right?

Dr. Galow:

I think that that's a good analogy. If we used drugs that knocked out all of our blood vessels we'd be in big trouble, right? So what Avastin will do and drugs in this class is it's a bit more specific to tumors, and it's more specific to newly growing blood vessels. So Avastin all by itself has some activity in cancer, but not a whole lot. What we need to do is knock the cancer down, prevent the new blood vessels from growing, and drugs that prevent new blood vessel growth for the most part don't affect our normal blood vessels. So it's kind of like it's affecting the back passageways that the tumors have, the new blood vessels it's trying to bring in, but the already established, the main passageways that the rest of the body is using aren't really affected by any significant degree. A little bit, but not to a significant degree.

Andrew Schorr:

We're going to learn lot more as we continue our discussion.

We're going to take a brief break. I want to tell people how you can submit questions for Dr. Julie Galow. We'll also hear from Ginny on her story. She has a lot to say about being a powerful patient advocate as a breast cancer survivor too, because it can make a difference in the approval of therapies and how quickly they can be available for you.

Send us an e-mail right now to patientpower@seattlecca.org. We'll be back with Dr. Julie Gralow and our discussion on antiangiogenic therapy, inhibiting tumor growth in breast cancer right after this.

How is Avastin Being Used?

Andrew Schorr:

Thanks for joining us tonight as we continue our live webcast which is specially of interest to women who are concerned about or may have advanced breast cancer as we learn about the new medicines that are what we call antiangiogenic therapy and inhibit the tumor growth in breast cancer even after it's spread. We have with us a leading expert in this, not just a leading expert in the Seattle area but really known around the world, Dr. Julie Gralow, who has been with us on Patient Power many times. Happily, for the Seattle Cancer Care Alliance, University of Washington, she is the director of breast medical oncology right here.

And that was so important to Ginny who even though she lives five hours down the road in Eugene, Oregon, she knew that as her breast cancer recurred that when she got a second opinion she wanted to see Dr. Gralow, and it made all the difference. And it allowed her to get access to Avastin, which had been approved for other cancers but not yet for breast cancer, but Dr. Gralow could make the case with the insurance companies that it could really help Ginny, and it did, so she's living with breast cancer that spread to her liver and her spine but it's being controlled with medicines including Avastin, and we're learning about this antiangiogenesis approach.

So it was approved, Dr. Gralow, in February. So what's going on now around the country? People may be listening worldwide but certainly in the US. Is Avastin being combined with chemotherapy typically? How is it being used to have the greatest effect?

Dr. Gralow:

Using it most commonly with chemotherapy, and we're allowing it most commonly in what we call first-line chemotherapy regimen, so shortly after a recurrence has been detected. That's where it's used. It was actually, interestingly, Avastin was approved in Europe and many other parts of the world well before it was approved in breast cancer in the United States, and there's a variety of reasons. It had already been approved in colon cancer and lung cancer in the United States, and because we had good data from a big clinical trial in breast cancer the insurance companies were allowing us to use it before its FDA approval. But many parts of the world are actually now using this drug in breast cancer as well as colon and lung cancer. It has some activity in ovarian and kidney cancer and some other cancers as well.

Andrew Schorr:

Now, this class of medicine, the idea of trying to stop the further growth or even the initial growth of blood supply to tumor cells no matter where they may be when

they've spread, are there other drugs that do this as well that you're trying out in breast cancer or even if they have some approval in breast cancer as well?

Dr. Galow:

So the whole concept of interfering with the tumor cell's ability to grow its own set of blood vessels was really hypothesized, it was first spoken about a couple decades by Dr. Judah Folkman, a real pioneer in this field. He was a surgical oncologist in Boston, and he for years said this has to be important. It looks important in the lab. And he devoted his life to this, and the first couple of drugs that were picked and looked good in the lab he kept saying, we can cure mice all the time, but when they tried them in humans they weren't terribly successful. So it took about probably two decades after Dr. Folkman came up with this hypothesis, this idea that they should work before they could actually find an agent that worked.

So Avastin was the first drug approved in the antiangiogenic class, the class of drugs that blocks of tumor's involvement with blood vessels, but we have two agents that are also approved that are kind of first cousins of Avastin. Whereas Avastin is intravenous. It's given every week, two weeks, three weeks, depending on the dose. These other two agents, which have somewhat similar generic names are oral, they're pills. And they are sorafenib, which is also known as Nexavar, and sunitinib, which is also known as Sutent, and none of those names are easy to say. But sorafenib has been approved in liver cancer. Sunitinib, or Sutent, has been approved in kidney cancer and a special kind of gastrointestinal cancer. And both of them have shown some activity in breast cancer, and much bigger trials are going on in breast cancer and other cancers with these other agents.

And they work a bit differently. I told you Avastin is intravenous. Sorafenib and sunitinib are oral, but they work on the whole blood vessel-tumor interaction slightly differently, similar pathways but slightly differently. So it's even possible, just like if a tumor starts progressing on one chemo agent you can hit with it a little differently with another chemo agent and see response, it might be that we'll have several subtypes of drugs in the class of blood vessel blockers or angiogenesis inhibitors, and even after a tumor has figured out how to get around one you could switch to another one and regenerate this activity.

Side Effects Associated with Avastin

Andrew Schorr:

Okay. We have a question we received by e-mail from Alma in Seattle, and it's exactly about that switching. She said that her mom has had ten cycles of Sutent and now she's being switched to Nexavar. So she asks, "What's the usual response and side effects associated with Nexavar?"

Dr. Galow:

So not majorly different from Sutent, and a lot of the side effects depend on if they're being given with chemo because most of the side effects are chemo. It can cause, both of them can cause a bit more fatigue, and both of them have a rare

but possible chance of a little bit of toxicity to the liver. Both of them can increase the affect of chemo on the blood counts, so if they're being given with chemo they can lower the blood counts a little bit more.

But overall, compared to chemotherapy these drugs are fairly well-tolerated. We always worry a little bit about bleeding and clotting when we're using drugs that can affect the blood vessels. As I said they don't affect the normal blood vessels a whole lot, but they can affect them a little bit so we sometimes see a little bleeding. Most of my patients would say when they blow their nose in the morning they might see a few specks of blood. I have occasional patients who will get a nose bleed. With Avastin now, and this isn't directly answering the question, one of the main side effects is high blood pressure can happen in some patients, so we always carefully check the blood pressure before we give each dose.

Andrew Schorr:

Ginny, let's ask you. So you've been taking Avastin. Tell us what it's like. Now, you're taking several medicines, but how do you feel while you're on this therapy to keep your advanced breast cancer chronic?

Ginny:

I have had some increase in blood pressure, which is being treated with medications. And it does interfere somewhat with wound healing, so I do have a chronic wound that I have to take care of.

Andrew Schorr:

Okay. And just, high blood pressure you can't feel. How do you feel, like working in the garden getting ready for that big wedding reception? How is your energy? How do you feel?

Ginny:

Like with the Avastin I have no problems at all. The other chemotherapy agent that I get, the Gemzar, I usually get that in the morning and by the afternoon of the same day I'm ready for a nap, but then I'm usually better by the next day. And so it's really I get the Gemzar two weeks out of three, and so I just schedule nap time on those days.

Andrew Schorr:

Dr. Galow, I suggested that this is a really big deal in the change of the quality of life, I hope also the survival for women who are diagnosed with advanced breast cancer. What do we know about that now? How much of a difference is it making statistically, or even in your own practice, what are you noticing?

Dr. Galow:

I think that the main things that we've proven in clinical trials and that I see in my practice is that when I add Avastin to standard breast cancer chemotherapy I have a higher chance of the tumor shrinking, and patients can stay on the same regimen, the same chemo-Avastin combination for much of longer when we add

the Avastin. So that's been proven in clinical trials, that on average Avastin doubles of tumor response rate, meaning about a 50 percent shrinkage in the size of the tumor. And Avastin doubles the time that you can stay on a given regimen before the tumor starts growing again.

Andrew Schorr:

Now, when the FDA looks at all this data it would seem to me that That's all good news, the people with this condition are really sick, we want them to be able to live as long as they can and as well as they can, let's approve that. It was approved in Europe. Why did it take a while in the US?

Dr. Galow:

Well, this gets down to the whole drug approval process, and it's complicated because the FDA is charged with protecting patients, and that's appropriate, and they also want to make sure that a drug they approve has documented effect, efficacy, benefit. In breast cancer and in most cancers the FDA to date has really demanded that the studies not just show an increase response rate in tumor shrinkage and increase in what we call the time to progression, meaning how long you stay on a regimen before the tumor starts growing, they have when you use a drug at the first recurrence also demanded that you show that you statistically lengthen survival or the life span.

Now, if you only have one or two kinds of treatments once cancer has recurred then that is a very realistic end point, an important end point, and you would hope that an agent that works well would not just cause more tumor shrinkage and more time, a longer time until the tumor grows but also would lengthen survival. What's happened in breast cancer is that we have a multitude of treatments for metastatic breast cancer. We've got three major classes of antiestrogen therapy. Ginny has been on most of those. We have on the order of a dozen different chemotherapy agents that have been approved or have shown real activity, and we also have some other biologic agents.

And so the first agents that you give to a metastatic or recurrent breast cancer patient have much less likelihood of being the major determinant of survival when you know that you are going to be able to get second line regimen and a third line regimen and a seventh and eighth line regimen, all of which will extend survival to some degree. So when you're getting eight treatments, the chance that the first treatment will be the major treatment that impacts your survival becomes less. So with other cancers where there are only a couple of treatments I think overall survival is still a reasonable end point.

With breast cancer where we use so many drugs and our patients live so long now with metastatic disease in many cases, overall survival, we argued to the FDA, isn't as fair an end point. There was no question about whether this drug worked, whether it caused effects on the tumor in breast cancer. We had a very nice trial showing that, backed by some other trials, but the argument was that the FDA up until February of 2008 insisted that we show that we prolong life, which was not proven in this case. So there was a lot of controversy about that, and really the

FDA for this drug in this case made an exception, and so now there is a precedent set that, yes, we believe the drug works, yes, we believe patients should get access to it even if we didn't meet our own now much harder to achieve end point.

So it was very interesting to observe, and of course very frustrating when you have patients who you want to give the drug to, and in some cases insurance companies won't always pay for a drug that's not approved in breast cancer even though there might be good data to support it.

Patient Advocacy and Persistence

Andrew Schorr:

Right. Well, it's a complicated but interesting story. The point I also want to make here is, Ginny, patient advocacy, patients speaking out, lobbying FDA, that may have helped. And you wrote a letter, didn't you?

Ginny:

I wrote a letter to the FDA saying that I really think other women should be given the opportunity to be on Avastin if their physician thinks it's appropriate for metastatic breast cancer.

Andrew Schorr:

Well, we're going to take a break because I believe, I know Dr. Julie Gralow knows from all her caucuses with scientists around the world, that there will be new drugs yet to come. So there's really a partnership between researchers, clinicians and people living with a condition like this to make sure that we work together, get the research done and then tell the story, yes, to the government regularities and then if something really deserves its day in the sun that it can get it expeditiously and help save lives, lengthen lives and improve the quality of life. We'll talk more about that.

We invite your questions. Send them to patientpower@seattlecca.org. We'll be right back with more of our live webcast, Patient Power, right after this.

Can Avastin Treat Other Cancers?

Andrew Schorr:

Andrew Schorr here again live on April 9, we're doing our live webcast. I have to make just a couple of comments that are meaningful to me but I think are symbolic for other people too. So April 9th, if you heard that little promo that I recorded a little while ago that says I'm an 11-year leukemia survivor, well, today it makes it 12 years. So I don't think I'm cured, but I'm living well, yay, for 12 years. It's also my third child's 11th birthday, and we had the confidence to conceive of that child when we felt, well, we had a good fighting chance to beat or at least knock back the leukemia for me, and I hope that's a real hope for you if you're dealing with cancer, whatever cancer that may be.

Let's go back to our discussion with Dr. Julie Gralow, who is director of breast medical oncology at the Seattle Cancer Care Alliance and her patient, Ginny, who joins us from Eugene, Oregon. You know, many people who are affected by breast cancer may have a spouse or a friend who is affected by another cancer, and it could be prostate cancer.

Tell us, Dr. Gralow, what your colleagues in other cancers are saying about Avastin. For instance, Margaret wrote in from Marion, Ohio, she's been listening, and she said, "Do you think that Avastin will be effective against prostate cancer? Have you heard anything about that? Because I know that I've been talking about ovarian cancer doctors, and they have some hope there."

Dr. Gralow:

Right. So I will say that I don't know of any data at this point on Avastin and prostate cancer, and I am so specialized in breast cancer that I don't know. I'm sure that there are trials that are going on. I just don't know if we've seen positive results from them yet. But there's no reason to think that Avastin should be terribly tumor specific to the kind of cancer. We've talked about how it's approved in lung cancer, colon cancer, breast cancer, we've seen activity in several others, so if I had to guess even though I haven't seen any data to date, I would bet that the trials that are going on in prostate will probably show some benefit. The whole idea of bringing blood vessels into the cancer is something that most cancers do.

Andrew Schorr:

Right. And I know I have had some discussions with experts where they I think there's some thought about whether it can be tried and effective in ovarian cancer too.

Dr. Gralow:

We've seen some very good interesting results in ovarian cancer, a bit early, but we've seen some good responses there too.

Andrew Schorr:

All right. Here's a question that just came in from Claire in San Francisco. I think you spoke about this a little. She says, "Do we have solid numbers of the survival figures of women with metastatic breast cancer who are being treated with Avastin particularly in the trials?"

Dr. Gralow:

So I'm not quite sure what that means. If it means how many women are living for how long. In the trials we clearly know when somebody started treatment, when they went off treatment, when they have disease progression, and when they die, so I would call that very solid. It's very different, in the trial that led to Avastin approval in breast cancer, the E 2100 trial, some of the women had progressed and had died quickly whereas others are still alive and doing well many, many years later. So I'm not quite sure exactly what the question is. The data is solid, but for any one woman we can't quote the averages. The averages for the whole trial are wrong for everybody essentially.

Role of Statistics

Andrew Schorr:

Right. And I want to actually talk about that for a minute. So the FDA wants hard numbers, statistics, etc., and I know you have women who come see you with advanced breast cancer and they say, What are my odds of living this long and this being effective, but it really comes down to their individual situation and not always the big statistics, right? Maybe you could talk about that for a minute, Dr. Galow. And, Ginny, I want to hear from you, your perspective on it too, because it's really about you, the individual patient.

But, Dr. Galow, how do you speak to people about statistics?

Dr. Galow:

Well, when somebody has metastatic breast cancer at that point we generally say that it is incurable, meaning it is unlikely that we will be able to get rid of all the cancer, that you will live out a normal life span and die of something else, that would be incurable, but that we think it's highly treatable. That we will have agents that can cause the tumor to shrink, hopefully give you a good quality of life, and hopefully you can live a long time. So that's an important kind of distinction going for a cure versus going for treatment and good quality of life. So we make sure we set that goal.

When patients say, how long do you think I have to live, my response is I hope a long time, and we don't have a crystal ball, and there's nothing right now that is really defining it, so let's plan on it being a long time and a good time. And when treatment starts if you're having a response then your life expectancy goes up. And there will be progression occasionally. Ginny has been through it all. My patients with metastatic disease have been through the disappointment of finding out the tumor has grown somewhere, but then we try a new agent.

And every time you try a new agent, whether there's a response or whether there's a lack of response, that also kind of helps add to the picture of how long a patient will live. So those numbers, those estimates are always changing. We always try to be optimistic but realistic as well and just have frank discussions about how the numbers are always averages and they're never the exact right number for any one patient.

Andrew Schorr:

Let's look at the pipeline of potential new drugs for a minute. So if cancer were to be chronic and you have drugs that work for a while, sometimes at extended times but it might kind of peter out after a while, but you hope that, well, there's something new to hit it with. So where are we now in the progression of drugs? What's in the lab? What's in research that could be yet new therapies for women who have Avastin or these other drugs you mention then at some point need something else?

Dr. Galow:

Well, to carry on the theme of having some of the therapy targeting the cancer's environment instead of the cancer directly, you and I have talked in the past about my main focus of research interest, which is the treatment of bone metastases, and how we have some drugs that impact the bone, which the cancer is trying to stimulate. So a breast cancer cell gets into the bone and metastasizes there. It sends out signals to the bone and says, Chew up some bone, make space for me. And as the bone is destroyed to make room for the cancer, then there are signals from the bone that stimulate the breast cancer.

And there's this cycle set up where the cancer feeds the bone, the bone feeds the cancer, and by using drugs that inhibit the bone, the bone cells that chew up the bone, we call them osteoclasts, we can see a reduction in complications from bone metastases, and we're looking at these drugs and whether they can prevent the bone metastasis from happening in the first place. So another way, just like inhibiting blood vessels from growing that the tumor is stimulating, we can inhibit the bone from helping feedback the tumor, too. I think that's a fascinating area of interest. And although the main drugs we use for this right now that we're exploring to prevent bone mets are in the class we call bisphosphonates to treat bone metastases.

We've got lots of other targets. The more we understand about what allows a cancer cell to survive and progress and live through chemotherapy, the more pathways we understand to distinguish it from a normal cell, the more drugs that we are able to make and test. We're getting smart, Andrew and Ginny. We're getting smart. Through the human genome project and a better understanding of cancer we're developing drugs that would at least in the lab seem to be selective to cancers and inhibit pathways that allow them to survive, and we'll have them approved in the very new future, probably in breast cancer because some very exciting agents there.

Andrew Schorr:

Okay. Well, I'm looking forward to that.

Here's a question we got in from my hometown, Mercer Island, Washington. Carol writes in, "I'm confused about the delivery protocols for Avastin. Some say twice a month, week-long infusion. What does this mean? And then we're told that my wife is losing her hair, and I am guessing Avastin may be contributing to this. Is this something you've heard it of?"

So the complication of losing hair, is Avastin playing a role? And also, what is the delivery protocol for Avastin.

Dr. Galow:

So Avastin doesn't generally cause hair loss. I'm not sure if this patient is on any other drugs that might do that, but Avastin doesn't usually cause that.

As far as how it's delivered, it's an antibody that can stay around in the system for many weeks. So that gives us the luxury of being able to give it in different ways because it stays in the blood a long time. In breast cancer the two most common ways of giving Avastin are every other week, where you get an infusion that goes in over about an hour, or every three weeks. And we vary the dose a little bit so that over the course of a month, whether you get it every two weeks or every three weeks, you're getting the same total amount of drug. If you're getting it every three weeks you get another 50 percent more each time.

In colorectal cancer they have some regimens where you get it weekly as well, but again it's at a lower dose every week compared to what you'd get every two weeks. So because it sticks around in the blood for a long time you can give it, depending on whatever other chemotherapy you're giving, for example weekly, every two weeks, and every three weeks. In breast cancer we frequently give it every two weeks or every three weeks.

Andrew Schorr:

And Carol's husband worries about her losing her hair. Is Avastin the bad guy in that?

Dr. Gralow:

No, not a known side effect of Avastin, so I would wonder about maybe any other drugs that would be being given.

Andrew Schorr:

Okay. We're going to take more questions when we continue after a short break.

Also, if you're listening with us, thanks for your e-mails, sending them to seattlecca.org. But we'd love to hear your voice. You can call the studio just like you would call Larry King or something like that. We'll be right back as we continue our discussion with a true breast cancer expert, Dr. Julie Gralow, director of breast medical oncology at the Seattle Cancer Care Alliance. We're learning about the newer therapies that are helping women live better, even with advanced breast cancer. We'll get also some inspiring words from Ginny in Eugene as she sought out the best care and is living every day to the fullest. We'll be right back with more Patient Power sponsored by the Seattle Cancer Care Alliance.

Andrew Schorr:

We've got about ten minutes more in our live webcast. Andrew Schorr here. We welcome your questions, Patient Power at seattlecca.org.

Dr. Gralow, just one question about cost. So you were able to talk to Ginny's insurance company and Avastin was already approved for some cancers, and you made the case they should pay for it in her case for breast cancer. And of course now as of February 2008 it's approved in advanced breast cancer and insurance should be paying for it. But we do have some listeners in Canada, and Kathy wrote

in from Toronto, and she says Avastin is quite expensive. She says, "In Toronto it costs \$2700 per treatment. What is being done to reduce these costs?"

So what do you do about costs? These are expensive medicines, and are you aware of what's going on to help more people have access to it?

Reducing the Costs of Treatments

Dr. Galow:

So cost is a huge issue for us as we develop all these new drugs, and it's a complicated issue because for every drug that gets approved for a company that may have had 20 other drugs that they spent years in the laboratory testing in humans that never make it to approval. And it is fair that some of the cost of all those other agents is somehow compensated.

Now that being said, we would like everybody in the country, in the world to be able to get access to exciting drugs that have efficacy, but we haven't figured out how to do this with drugs that are a lot cheaper than Avastin. Avastin is an expensive drug. Many other cancer drugs are in this range. So I think that what we need to do to help control costs across the population is work much harder than we have done to date to figure out which cancers are most likely to benefit and respond to Avastin and which patients are more likely to respond to Avastin so that we're not giving the drug to all patients. Maybe we're going the drug to 20 to 25 percent of patients who would have a profile or their tumor would have a profile that would show that Avastin would work particularly well in that group.

By doing that we're not giving drugs that don't work, and we're only giving these expensive drugs to a quarter of the population as opposed to the whole population. I think we really need to focus on this. In breast cancer we know how to find the estrogen receptor and we know that drugs that target the estrogen receptor, the antiestrogen drugs, only work in those patients. Same thing with HER-2 and breast cancer. Only about 20 to 25 percent of breast cancer expresses HER-2. We've got some excellent drugs that work in that population.

With Avastin we have collected tumor blocks and blood samples and we're trying to define it but haven't yet. And I think that we are really be obligated to do the same for any new agent that is approved in cancer is to find the population who will benefit most so that we can use some of these more expensive agents more sparingly but more directly and specifically.

Andrew Schorr:

Well, we're increasingly in the area of targeted medicine, and I understand how you need those tests to say who will this work for. So I wish you well with that.

Let's talk for minute about clinical trials. So a drug like Avastin is developed after a lot of research and ultimately women who have it as part of their experimental therapy. At the Seattle Cancer Care Alliance what would you say as far as women

considering with advanced breast cancer being in trials, how it might give them access to tomorrow's medicine today and how it will also move research along for anyone affected with these conditions?

Dr. Galow:

Well, I think you've just said it for me, Andrew. I think that the only way that we will ever understand whether drugs work and which cancers they work in is to do it in a setting of a clinical trial. So all new drugs that are being investigated are first tested in clinical trials, and we at the Seattle Cancer Care Alliance at any given time have a variety of different clinical trials for breast cancer patients at different stages, different types of breast cancer and cancers of all types. And we do them in a controlled fashion with proper statistics and controls and patient safety. This is always our big concern when there's a new drug and you're not sure what it will cause. And then if it looks promising it makes it through the next step where it might be moved to a bigger national trial, and we then start to try to meet the mandates for what the FDA would need to get a drug approved.

So joining a clinical trial, helping to answer questions for people who follow you, sometimes getting access so drugs that you wouldn't have access to otherwise, this is always something that we offer. And we like to have a variety of trials for all of our patients who are seen here because we really think it's part of our job to take not just good care of our patients but to make sure that we're part of what's moving research ahead, and that's what clinical trials are all about. No drug will ever get approved without patients enrolling in clinical trials.

Andrew Schorr:

I'm going to make my pitch for it because I was in a phase II clinical trial, and what I was treated with in that for my chronic lymphocytic leukemia is what most people get now. And as we heard and I can celebrate today, I'm a 12-year survivor. So I would definitely invite women and some men if you're affected by the recurrence of breast cancer, advanced breast cancer, please consider that.

The other thing I want to ask Ginny about, Ginny, you decided to go beyond your local oncologist and seek out a breast cancer subspecialist, Dr. Galow at an academic medical center, and it seems like it made a big difference for you. What would you say for people listening if they find themselves in a situation like yours?

Ginny:

Well, I think with the initial occurrence of cancer often local oncologists are able to give very good treatment. But when there's a recurrence there is more concern about which treatment to try first. And I was very happy that I could become Dr. Galow's patient because she was familiar with all the recent treatments and could find something for me that was very helpful and also advocate to my insurance company to pay for it. So I'd say yes, go for it. And also discuss it with your local oncologist. Mine was very happy with the idea and has been very cooperative, and I think most doctors would feel that way too.

Advanced Breast Cancer Patients Living Well

Andrew Schorr:

I might mention to our listeners, the way I've come to see this is a subspecialist like Dr. Julie Gralow is like an architect of a treatment plan, and it could be evolving over time. Certainly the cancer may be involving so the treatment plan involves too. And it may be that your local oncologist, who may be just in a smaller city or even here in Seattle, people coming to Seattle Cancer Care Alliance from far and wide, maybe will be part of that team and they may be helping execute the plan, but it's in consultation with someone like that research leader like Dr. Gralow. I think if you have advanced breast cancer that's a good idea, to expand your team that way. So that's my pitch.

Dr. Gralow, when we're all said and done, though, it comes down to hope. And since you've devoted your life to it how hopeful are you? With what you know you have today and what you think may come out of the lab and out of the trials and be available to women nationwide and maybe worldwide, how hopeful are you that we can continue to see people living with advanced breast cancer and hopefully living a pretty good life?

Dr. Gralow:

Well, I look back to when I started specializing in breast cancer back in the early 90s and at the limited number the drugs available and at how much shorter patients were living compared to now once they had metastatic disease. We've already come a long way. We're far from doing well enough. I know that. I spent the whole day seeing patients today, and I had to tell a couple that they were progressing. I know we have to do better. I promised one of my patients today that we would keep working to make it better because although overall patients are doing better, they're not doing well enough.

What I see on the horizon, Andrew, is that it's very bright. It's so exciting compared to back in the early 90s. We have so many different classes of drugs and they're so much smarter at targeting the tumor, less effect on the normal cells. I think a big issue will be how are we going to pay for the research to get these drugs approved, how are we going to get them approved quickly so that we can weed out which ones are the winners and which ones to not pay research money?

And then how are we going to get them into patients, as our Canadian listener is asking? In the United States many of my patients have good insurance but not all of them do, so I deal with these costs in the United States. And I travel internationally all the time and I don't know how we're going to be able to get women around the world access or patients around the world access to some of these drugs in the near future.

Andrew Schorr:

Well, I think part of the answer, I mean there are some big public policy issues in the US and nationwide, but I know that part of the formula is us working together

as a community. So if you, someone in your family is touched by breast cancer become an advocate as well. Consider being in a clinical trial and then really partner and support people like Dr. Julie Gralow in their research so that we can move this forward more quickly and hopefully for a lot more people.

Dr. Julie Gralow from the Seattle Cancer Care Alliance, thanks for being with us again, Julie. And I know we'll talk other times and continue to tell the story of this progress. All the best to you and your work.

Dr. Gralow:

Thanks, Andrew.

Andrew Schorr:

And, Ginny, keep working on at that garden for the big wedding reception, and I hope you'll have not just a wedding reception to plan for but maybe some grandchildren and special occasions in the years to come.

Ginny:

Thank you very much, Andrew. It's been a pleasure.

Andrew Schorr:

Okay. Thank you very much.

Well, this is what we do on Patient Power. We went a couple of minutes over, but I hope it's been a rewarding program for you. The replay will be posted shortly on the Seattle Cancer Care Alliance website. You can also take a look on my website which is patientpower.info. All our programs, I'm happy to say, are now shuttled right along and distributed also by new Microsoft search engine, healthvault.com, and so you can look for our programs there as well.

On April 23rd we'll have our next Seattle Cancer Care Alliance webcast. That's where I'll have a discussion on colon cancer screening, and if you can be screened and if they can identify the little precursors to colon cancer early it could save your life. We'll have Dr. Bill Grady from the Seattle Cancer Care Alliance along for that one.

As always, when you take all this together, knowledge can be the best medicine of all. And I hope we've given you some great knowledge tonight. Broadcasting from Seattle, I'm Andrew Schorr. Thanks for joining us, and thanks to the Seattle Cancer Care Alliance for making all this possible. Have a good night.

Please remember the opinions expressed on Patient Power are not necessarily the views of Seattle Cancer Care Alliance, its medical staff or Patient Power. Our discussions are not a substitute for seeking medical advice or care from your own doctor. That's how you'll get care that's most appropriate for you.