Metastatic Colon Cancer: Targeting Stem Cells for Longer Life

Webcast

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Introduction

Andrew Schorr:
Hello and thank you for joining us. I’m Andrew Schorr. On this Patient Power program sponsored by the Seattle Cancer Care Alliance, we are live, and so we are looking for your questions along the way. You can send us an e-mail to patientpower@seattlecca.org. And many people already have. How come? Because we are talking about one of the deadliest cancers after lung cancer, colorectal cancer. And when colon cancer is not found early, or precancerous, let’s say those precancerous polyps if you have colonoscopy, then it may break through the wall of the colon and spread.

I know about that personally. My mother, my dear mother, Ruth, died at age 77 about 23 years ago just as I was getting married, after a four-year battle with colon cancer. And then my dad, who lived much longer, he benefited from colonoscopy, and they would find those precancerous polyps, and they would snip them out, and he lived a long life. That’s not what the died from. But then there was a fellow who worked with me a number of years ago, a man in his forties, went to the emergency room with pain. Was it a stomach ache? Well, it ended up being advanced colon cancer, and unfortunately after a year and a half Peter was gone. And so many of you know people where when cancer is spread, it's a bad deal.

But wouldn’t it be great if we could cure it, and short of that, could we find a way to control it so people even with advanced colon cancer could live better and live longer? Well, tonight during our program you are going to meet three people like that who have been helped by the team and particularly Dr. Ed Lin, a medical oncologist at the Seattle Cancer Care Alliance who specializes in helping with advanced colon cancer, and so people are not statistics. Yes, the odds are not great when you have advanced colon cancer, but more and more there are examples like the three ladies you will meet tonight who are doing better, living longer and have a lot of hope for the future based on newer approaches as are being developed by Dr. Lin and other real scientists.

Now, I love having Dr. Lin on the program. I have done a number of programs with him, and he is passionate about this, but let's start with a patient. First I
would like to introduce you to Susan Johnson. Susan lives in Longview, Washington, which is sort of down I-5, north of Portland really, and Susan was diagnosed with colon cancer after having bleeding, as people might. She is 62 years old. And she has grown children. She operates with her husband a retail furniture business. And she had this bleeding and then of course saw local doctors and then eventually was referred for surgery to the University of Washington and then with radiation and then medical oncology, Dr. Lin. It was quite a journey, wasn't it, Susan? And probably very terrifying along the way.

Susan’s Story

Susan:
Very terrifying. Having never had surgery, of course when you are told and you have to face I have cancer that is scary, but having gone to the University of Washington and had Dr. Sinanan, who did my surgery, and that helped, I mean, to give me some hope that this was going to be taken care of and that I was going to be fine. Of course I always have a positive attitude, so I do think I am going to be fine.

Andrew Schorr:
Now, you had it spread, and you had a spot on your lung I believe. You had a recurrence. So then you get into these systemic therapies with chemotherapy. So what have you been taking, and how are you doing?

Susan:
Dr. Lin has put me on, after my chemo, then I went on and had radiation, and after radiation I am on Xeloda, 500 milligrams, and I take,

Andrew Schorr:
I think Xeloda, yeah, is the way they pronounce it.

Susan:
One week on, one week off.

Andrew Schorr:
I see. And do you take any other pills as well?

Susan:
I do take Celebrex to go along with the pill, and that seems to, apparently, from Dr. Lin, stop some of the maybe possible side effects of which I really don't have any side effects. I feel great. I work. I golf. My life is as usual.

Andrew Schorr:
So here you are, and you have been through a lot, and I'm sure the people at Longview shake their heads but with a smile, that you have been through a lot and here you are enjoying life and working.
Susan:
Yes, very much so.

Andrew Schorr:
Right, and your whole family. So that's one story. So we are going to hear more from Susan, and she is a very empowered patient.

Let's move over to Oklahoma City for a minute and meet Tiffany Heigle. So Tiffany is just 41 years old, but imagine that she was diagnosed with what proved to be advanced colon cancer at age 33. She has two children, and then you had recurrences, and the therapy wasn't going so well for a while. I mean, the cancer looked like it was winning the battle, didn't it, Tiffany?

Tiffany's Battle with Colon Cancer

Tiffany:
Yeah. I had recurrences twice, both in lymph nodes, which had moved up around my kidneys. My original lymph nodes were all down around my colon. So I had recurrences a year after the original diagnosis and then another year after that. So, yeah. The second time was scary, and the third time was exceedingly scary.

Andrew Schorr:
I can imagine. Now, you formed a relationship with Dr. Lin, first when he was down in Houston at M. D. Anderson and then in Seattle. And so you then had chemotherapy as well, correct?

Tiffany:
Yes. On the second recurrence with Dr. Lin when I went to M. D. Anderson I did five and a half weeks of radiation at the same time that I took the same, the Xeloda-Celebrex therapy that Susan did. And then following that,

Andrew Schorr:
And I understand that you finished therapy in April of '05, right?

Tiffany:
Yes. I was actually rethinking, it was '06, yes. I was on that maintenance dose for three and a half years almost.

Andrew Schorr:
So today, Tiffany, you have had recurrences, advanced colon cancer. What cancer medicines do you take, and how is your quality of life?
Tiffany:
I have taken no drugs of any kind since April of '06 and had clean scans in August up in Seattle with Dr. Lin. No signs of anything.

Andrew Schorr:
Wow. I want to report more of these stories. Okay. Let's meet this famous, passionate Dr. Edward Lin. Dr. Lin is a true researcher in colon cancer, and as you heard he has moved around the country, and now for the last couple of years has been at the Seattle Cancer Care Alliance. He is an associate professor of medicine with the University of the Washington, and then of course one of the leaders in medical oncology and colon cancer in the Pacific Northwest and at the Seattle Cancer Care Alliance.

Dr. Lin, so here are examples of people alive today, and we are going to meet one more along the way a little later in the show, where normally people feel the statistics are bleak. What's going on? How are you able to accomplish this?

Targeting Stem Cells

Dr. Lin:
Andrew, thanks for the honor, and thank you for the patients who are equally passionate about the disease and taking their time to participate in the program, which I think, is very valuable for the general audience.

We noted a phenomenon back in 2000 when a 76-year-old woman from Texas came in with almost 200 metastases in her lung, and came into my clinic, and she said, well, I don't really want any IV chemotherapy. And as you know at the time she has, they only had Xeloda at the time, and she definitely has debilitating arthritis, so she was taking celecoxib at the same time. And so after just really one cycle, literally, there may be about three or four lesions left with the oral chemotherapy, which almost rarely seen with just the single agent capecitabine, or Xeloda.

So we at that time noted that phenomenon and really took it to heart. And also we had noted that it appears the cape patients who are taking combination for longer period, they tend to have less what we call the hand and foot syndrome caused by the Xeloda. And the hand and foot syndrome basically is a redness, swelling, peeling of the skin, if the patient were taking it at too high of a dose or too long of a term of the drug. So we noted that if you were to take the drug together, it appears to mitigate some of the side effects. In fact this leads to one of the phase III trials that are currently still ongoing in the community at various sites. And so we will touch upon that in just a second. So that's actually the very earliest phenomenon that we have seen.
Andrew Schorr:
Okay. I want to help people understand this. So you had a lady with arthritis who took celecoxib.

Dr. Lin:
Celecoxib, right.

Andrew Schorr:
Right, also known as Celebrex.

Dr. Lin:
Right.

Andrew Schorr:
For pain management, and you had her on an oral chemotherapy, capecitabine, or Xeloda.

Dr. Lin:
Right.

Andrew Schorr:
And so she was taking her arthritis medicine as well, and you saw a benefit that you hadn't seen before synergistically.

Dr. Lin:
Very dramatic response, yes.

Andrew Schorr:
Wow. Wow. Okay. And I know that a lot of things in medical science happen just like a revelation sometimes. And then you go back with the science and try to figure out why is this happening. So I am sure you spent, I know you have spent years on that. What do you think is going on where you are getting a response like that where you didn't get it before?

Dr. Lin:
Yes. So after that we have obviously treated a fairly large group of patients, you know, off the protocol at the M. D. Anderson Cancer Center, and subsequently since I have moved here. One of the phenomena we have seen is not only the patients have, and we have reported this years ago, that for those patients who are taking the combinations it appears that they have fairly, almost seven or eight months better than the, quote/unquote, historical control chemotherapy in average.

Furthermore about almost 28 percent the patients if they were to integrate the multimodality care could reach complete response. And in those patients who reach the complete response, we have noted that in Tiffany's case, and if they were to take the maintenance chemotherapy, we almost have 90 percent of the patients
stay in a complete response and never recurred in this setting. And we are in the process of finishing up this scientific publication. Part of reason for holding off of the publication is that we, because of the small number of patients, only 19 at the time that we reported, now we have close to 40 or 50 patients who have been reaching the kind of level of complete remission, even in those cases like Susan with multifocal disease, and we will probably even be able to make a big difference in those cases.

**Andrew Schorr:**
Wow. A lot to talk about. I want to get into the science more, Dr. Lin, as we continue. We are going to go all through the hour and invite people’s calls. We are going to get another of your patients, one from Alaska, shortly and understand what's embedded in our title, "Metastatic Colon Cancer: Targeting Stem Cells For Longer Life," and understand that whole concept too. Give us a little science class as we go, but the bottom line is there are two ladies and then a third is going to join us who are doing well and maybe with more standard therapy before, who knows. So we are glad to have them here. Much more on Patient Power coming up as we continue our discussion sponsored by the Seattle Cancer Care Alliance.

**Andrew Schorr:**
Welcome back to our live webcast. Andrew Schorr here. Just a moment ago our announcer, Tracy, was mentioning about mammography, which women need to think about too, and I just want to remind listeners on behalf of the SCCA that October is Breast Cancer Awareness Month, and they recommend that women over 40 get a mammogram every year. And there will be experts in breast imaging, you know, helping people use digital technology. They have the MammoVan that goes around, and it will be visiting many locations including UW Medicine neighborhood clinics and local Safeway stores. So if you call the SCCA at 206-288-7800 you can schedule your mammogram. And I would urge people to have that.

But obviously our ladies tonight who were diagnosed with advanced colon cancer, that's top of mind for them. Let's go back, and we will hear from them as we continue, but I want to go to their doctor, Dr. Ed Lin, who is now going to help us a little bit with the science.

Dr. Lin, so there has been various chemotherapies, infused chemotherapies around for quite a while. I think 5-FU, and also leucovorin, these different drugs that people have had. A friend of mine, Mike, had it not long ago as well as surgery. So what are we doing now that's different? So what's standard therapy then, and what are we doing now that's different that seems to be making a difference?

**Dr. Lin:**
We have been making incremental progresses with the chemotherapy, but the chemotherapy generally does not seem to eliminate the root of the cause, which is the newer concept of the cancer stem cells that has been shown in, not just in colon cancer but a variety of other tumors. These cells represent a very small population
of the tumors. We have some markers to narrow them down, but they were able to propagate in vitro, in cultures, as well as the propagation in mice. And when you inject in mice they will recapitulate the same phenotype as seen in patients, and only those tumor cells appear to be able to generate a phenotype. It's a continually evolving field, but the concept is that these are the seed, and obviously in the appropriate soluble environments, these seeds will germinate.

**Andrew Schorr:**
I want to go over that with you. I want to, you know, it's like I'm like Columbo, used to be on TV, kind of thinking of the facts of a crime and going back and kind of trying to put it together in his head. Let's see if I get it right. So we have this image, and I'm a leukemia survivor, that all the cancer cells are the same. They just keep cloning themselves, and they don't die, and they form tumors, and they affect organs.

**Dr. Lin:**
It mutates.

**Andrew Schorr:**
Right. But this stem cell idea is, now, I know there are good stem cells that create all kinds of cells that we need for our body, but are these stem cells that go awry, kind of like queen bees that can control the colony, and they are the leaders of the pact, if you will? They are sending the orders to other cancer cells?

**Understanding the Role of Stem Cells**

**Dr. Lin:**
Right. So there is believed there is essentially a hierarchy models where the stem cells the scientists have generally come to embrace, is that these cells are, obviously has gone awry and so then they pick up these stem cell characteristics as we all normal, as a normal stem cells capability of doing, and as you can see we all came from one cell, and we have to accept that fact. And so the cancers must have also come from somewhere, and there has got to be sort of a mastermind behind the pack that drives the progressions, metastases, these evasions that lead to poor treatment outcomes. And there is evolving data that shows that these cells can be induced with the presence of the systemic chemotherapy, and they fail to eliminate them, and they require these stem cell characteristics, therefore making some of the best chemotherapy, including the bevacizumab or the Erbitux, have short-lived success, and ultimately it leads to disease progression.

**Andrew Schorr:**
Okay. Now let me spit that one back to you. Ladies, as you know, help me. We are all learning the science here. So, and you mentioned bevacizumab, I think Avastin, which was seen as helping people with more advanced cancer. But these drugs, kind of as good as they can be and the latest in biotech, kind of poop out, if you will. The cancer seems smarter. So if I get it right, whether you call it
resistance or I always see these cells as kind of wily cells that can, you know, put up power shields or something to survive these drugs that are otherwise targeting them. So since these stem cells then they just have their power, so with these therapies that you have used together with the ladies, is it the idea that you think they are having some effectiveness against these stem cells?

**Dr. Lin:**
Well, when we saw the phenomenon, we actually had done two parallel research work. One is actually in the patient with colon cancer where we have published this finding in cancers about a year ago showing that if you have elevated stem cell activities in the peripheral blood of cancer patients, and if you have meeting certain levels, you are at much higher risk of recurrence, almost about 17-fold higher risk, or the odds ratio we call it in scientific terms, of recurrence compared to those patients who were below the certain level.

And on that note, we have begun over the last year or so to work in the laboratories looking at effect of the celecoxib or the Celebrex stem cells in colon cancer. We are on the petri dishes level. And we, not to elaborate this too much because we are still in the process of getting the publication finalized along with the clinical picture, is that we do see a very dramatic effect on the stem cells or the colon cancer stem cells, functionally as well as . And so that's really kind of where we are today.

**Andrew Schorr:**
Okay. So, Tiffany, tell me if you think this is a good analogy. So I gave you that queen bee analogy. So somehow these drugs, you are going to document it scientifically as you expand your study, Dr. Lin. So we are knocking off the queen bee, and then if that's happening, the other cancer cells, they are either not forming or don't have a leader, and so somebody like you can then go with no therapy for a while it seems and go on with your life. You think that's what happened, the queen bee got knocked off?

**Tiffany:**
I think so. I mean, I have had recurrences both, I mean, at the year mark those first two times, having done you know the three to six months of chemotherapy and then only being off treatment for six months and had the cancer come back. I have now been off any kind of treatment for three and a half years. Three and a half years, and I am not seeing any kind of regrowth.

**Dr. Lin:**
In Tiffany's case actually she had surgery, and two months later she came to see us, and I think two to four months after she had a recurrence, and the tumor already was three or four centimeters in the peritoneum.
Tiffany:
Right. And they removed every lymph node they could find, infected or not, in October, and in January I was seeing recurrence again.

Andrew Schorr:
So obviously all this needs to be documented in larger studies, reproduced and figure out what's going on, and so I don't want to create false hope for people. But, Dr. Lin, so here, you know, sometimes people feel they are at the end of the line, and Tiffany may have felt that too with these recurrence, very despondent I am sure. So it sounds like though if you can, you know, attack what's going on at the molecular level and you find the right button to push, there can be a dramatic change. It seems like that's what happened in her case.

Dr. Lin:
Yeah. The chemotherapy had made a difference, but if you were to look at all the historical data with a conventional chemotherapy, the general complete response rate is about five percent now with across the board or chemotherapy that is currently FDA approved. In fact the addition of bevacizumab or the Avastin or Erbitux has not yet shown to improve the complete response rate, which is really, ought to be the key defining standard hopefully for the future. We obviously have integrated in some patients and in Tiffany's case, some radiation therapy, but the radiation therapy, it's more of considered a local treatment, so systemically she should still need to have the coverage where we have covered her with the, quote/unquote, maintenance concept. And it has been shown at least in one study, more of a randomized phase II study, that maintenance treatments appear to improve survival than patients who were taking intermittent therapy.

What really differs, our current retrospective series is larger studies is that we have added another molecular targeted agent. Now, this agent happened to also relieve arthritis and really has be been shown to regress colon polyps, which might also represent a precursor of the colon cancer stem cells. Nonetheless, our median survival in a group of patients that we have treated has not reached, we don't have a median in those patients who had reached a complete response.

Andrew Schorr:
Wow.

Dr. Lin:
And in those patients who have included a surgical series, we have a median about 70 months. So with the historical, complete responders with chemotherapy that has been published in JCO with the small numbers, it's about 44 months to 46 months. So we are confident that with some of the laboratory support and the additional patients cohorts collected from M. D. Anderson and also the Seattle Cancer Care Alliance, we are hoping to really complete a very nice report very soon.
Andrew Schorr:
Wow. Dr. Lin, so there two words that come up in cancer a lot when you use the letter C. C for cancer, and C for cure. Now that's a very powerful word, and Tiffany and Susan, you may approach this the same way I do with my leukemia. I don't think I am cured. The leukemia cells are not detectable with me now, and, Tiffany, for you and Susan, you are going about your business and living a full life. We would like to be cured for sure, but can you foresee that, Dr. Lin? Or are you saying, well, let's just control it and let people live lives? I mean, it's still a goal, right? Could these just, could this lead to a cure?

Dr. Lin:
I don't know. Obviously time will tell. My feeling is that at least we have achieved the very initial objective, which at the time was to reduce their toxicity of the drug. And so we have achieved reduction of the hand and foot syndrome. Furthermore we got a very pleasant surprise. What is really important in the current webcast, and I want to emphasize this, is that we have made a clinical observation, and now we have come back to look at the petri dishes and say well, does this make sense? And we are going to soon be reporting this, very soon. We already have an abstract submitted to a very important scientific conference then to talk about the targeting of these so-called, quote/unquote, colon cancer stem cells.

And the bottom line is that more work is needed. More support from the patients are needed, and we hope to validate not just from my own experiences, but also from various communities who, you know, do the daily battles with this metastatic disease, and I think the education is really very important. And a program like this could make a big difference for patients who are listening and perhaps pass on the word to other people.

Andrew Schorr:
Well, I am sure people are listening worldwide, and they are saying, you know, should I beat a path to the SCCA? Now, you are a researcher, and as you said you are teaming with other researchers at your alma mater at M. D. Anderson and other institutions, and you are all trying to work together obviously.

Dr. Lin:
Right.

Andrew Schorr:
Because we are talking about I think close to 150,000 people diagnosed with colon cancer in the US, and I know it's the second leading cause of cancer death, as I recall, the colorectal cancer.

Dr. Lin:
Yes.
Andrew Schorr:
So we want to make a big difference.

Susan, I have had you sitting on the sideline there for a minute. What would you say to people to urge them to really get the best care because, you know, had you just stayed where you were, maybe you wouldn't have had the advantage of being part of this leading edge of fighting colon cancer.

Susan:
Absolutely not. I do think that I, it was suggested to me by my next-door neighbor, who happens to be a physician and an oncologist and deals with breast cancer. Her first thing to me was yes, I think you do need a second opinion, and I've got your second opinion. And having gone in and got the second opinion, it got me in to the University of Washington which then led because of further, when my cancer went to my lung, I needed to get chemotherapy, which then I was introduced to Dr. Lin and his treatment. And I do think, having been from a small town, I'm not saying our doctors aren't wonderful doctors, because I think they are, but when you are dealing with something like cancer I really feel like people should go to people, to doctors that see this every single day. This is what their field of expertise is. It reassures the patient. I mean, you get a higher level of treatment.

I told Dr. Lin when we were going to do my chemotherapy, I said, Doctor, I want everything you can give me. I want it as hard as you can give me. I want to beat this, and I am going to beat this. I know I am going to beat this. And I then went on and had some radiation, and I am now on Xeloda, but it's, you know, it's wonderful. I mean, I feel like you need to get to the best. There is not, my life is worth everything. I have got lots to live for so why wouldn't I go to the very best?

Andrew Schorr:
All right. Well, we are going to take a break. So well said. And I did the same with my leukemia. See people who specialize in it. When it comes to really research one of the people who is really writing the articles and doing the studies, one of them is Dr. Edward Lin who is our guest.

We want your questions. Send us an e-mail to patientpower@seattlecca.org. You are listening to our discussion on "Metastatic Colon Cancer: Targeting Stem Cells for Longer Life." This is Patient Power sponsored by the Seattle Cancer Care Alliance. We will be right back.

Andrew Schorr:
Welcome back to our live webcast. Andrew Schorr here as we discuss advanced or metastatic colon cancer. We have been hearing from Susan Johnson, who has been living in that situation but doing well after a lot of therapy, from Longview, Washington, and also Tiffany Heigle who joins us from Oklahoma City. She and I were talking before the program. We are down on Oklahoma City because they stole our Seattle basketball team, but we won't talk about that now, Tiffany.
Anyway, let's go on and talk about more significant things, and that is living well even with an advanced colon cancer diagnosis. So, Dr. Lin, during the break there we played one of the Patient Power minutes you and I have done together, and we mentioned two of those drugs, Erbitux and Avastin, and they were seen as a big deal out of biotech, but as you say, so cancer kind of gets acclimated to them, and we would like it to help people live longer and live better, but you are seeing some more exciting results now early on with using Xeloda, or capecitabine, and celecoxib, or Celebrex.

So it this one of these deals, you know, I am trying to remember out of medical history, wasn't like the discovery of penicillin like an oh, my God, they found, what, the blue stuff on rye bread or something, and it turned out to be a big deal. I mean, is this one of these Eureka kind of things, or we just don't know yet?

**Dr. Lin:**
Well, the chemotherapy is a very important armamentarium for colon cancer management, and so the, and I think we will, soon we will know like in the Erbitux story we already know that if you harbor specific mutation in KRAS, then you are very unlikely to even benefit from the chemotherapy of the Erbitux. So there is a movement to personalize medicine based on even the very molecular makeup of the cancer before we even give chemotherapy. It probably won't take very long for us to even figure out, you know, what group of patients would then benefit from taking a drug like Avastin, and then obviously Avastin has a lot more wider net coverages in a cancer blood vessel formation.

And one of the critical things understanding these so-called, quote/unquote, targeting agents is that they are not very different from the chemotherapy. It has its own side effects, like Erbitux is a skin rash; Avastin, targeted vasculature has cardiovascular toxicities, and so very rare patients in the population will even have bowel perforations.

In Susan's case she had about six cycles' worth of the Avastin up front for reductions and then subsequently we were able to remove her fairly large lung metastasis that had shrunk significantly down. But we would not attempt to do surgery for a big polyp recurrence. So then she had radiation, and then she had eight maintenance treatments to maintain her from recurrence in the lung as well as elsewhere in the body.

So the critical thing here is that to understand this, this is a systemic disease. We need all the drugs that we have, but obviously we need to individualize the patients' care as they come through in consultation and figure out what would be the best time to opt to offer surgical care or the radiation care. We didn't cover the aspect of liver-directed therapy, which is also a big field in colorectal cancers as well.
Andrew Schorr:
Well, I want to get to that in a minute because my mom, that's what happened, is it broke through the wall of the colon, and when it was discovered in my mom, you know, she had bleeding and other things. She didn't tell anybody, didn't talk about it, and then when it was discovered it had spread to her liver and then continued. So we will talk, but that again was 23 years ago. I would love to hear if there is some progress.

I want to introduce another one of your patients, and that is Kay Bartlett who joins us from, this is a political year, the great state of Alaska, Anchorage, Alaska. Kay, I know you have been a medical technician in your career, and you are 69 years old now with two grown children. So you were going in for a physical and asked for a blood test that, you know, sort of a marker to see if something is going on because you had a friend who had had cancer discovered. That was elevated, and there was a lot of detective work that went on, but I understand that that led to a tennis-ball-sized tumor being found in your colon, right?

Kay:
That's correct.

Andrew Schorr:
Okay. Played reporter here. Now, I should mention, Dr. Lin, and I am sure you are well familiar with Kay's story, she had had a colonoscopy in 2000, yet you were diagnosed in 2002, two years later. In 2000, there was nothing seen. Right, Kay?

Kay:
Correct.

Andrew Schorr:
On the colonoscopy, physically looking.

Can we rely, you know, we preach colonoscopy, colonoscopy, colonoscopy. Are there certain areas of the colon that they have trouble getting to and so it's not a sure thing that there is nothing there? Or how should we, I mean, I don't want to discourage people from having a colonoscopy, and with my family history, believe me I do, but in her case it was in a place where it was hard to see.

Dr. Lin:
Yes. There is dead angles because the colon is kind of like, rather like a little square, and the colonoscopist has to go through, navigate, and depending on how big the fold is, and you have to retroflex, sort of like looking at the tumor in your rearview mirror as you are driving instead of forward looking, so that sometimes there is a dead angle, and the colon moves, and then, you know, depending on other circumstances, the op prep, and there are multiple other factors that could potentially mask the lesion. And the polyp could have started off small, and they could be flat so you might not be able to discern it. And obviously that's only the,
sort of the top view. The bottom part of the view where it's really the invasive cancer component will be completely hidden under the colonoscopy, so you can't see what's deeply inside, so there is going to be some hit and miss on the colonoscopy.

**Andrew Schorr:**
Okay. Well, of course, folks, get your colonoscopy. We don't want to discourage that at all, but it's like mammography, you know. There is maybe ten percent of the time that it doesn't show.

And you knew your body, Kay, and it got investigated further. What treatment did you end up having after that tennis-ball-sized tumor was discovered, Kay?

**Kay:**
I did have the standard 5-FU leucovorin regimen.

**Andrew Schorr:**
And you had surgery of course. And more? Did you have radiation?

**Kay:**
Yes. I had a colon resection first, and then I had the chemo second.

**Andrew Schorr:**
Okay.

**Dr. Lin:**
She was on a trial, a national trial, and she was randomized to the 5-FU leucovorin, I believe.

**Andrew Schorr:**
Okay. How are you doing, Kay?

**Kay:**
I am doing just great, thanks to Dr. Lin.

**Andrew Schorr:**
Okay. Now, did you also receive the Xeloda and Celebrex?

**Kay:**
Yes, I did. Yes, I did.

**Andrew Schorr:**
Okay. Let's understand this about trials, Dr. Lin. So you try and answer a question of whether this approach can improve outcomes, and it's still a research question.
At the SCCA you have trials, and at other major academic medical centers. If someone is diagnosed with metastatic colon cancer, is this a discussion they should have with their doctor to say what are trials that I should consider?

**Getting Involved in Clinical Trials**

**Dr. Lin:**
Yes. So we, trial takes time, and so we have taken almost three years of efforts to get one of the phase III studies ongoing with the combining capecitabine and Celebrex, and actually in both breast cancer patients as well as the colorectal cancer patients. And it's actually open through the M. D. Anderson community cooperative group. And I believe even Puerto Rico is participating in the trial. But as we painstakingly in taking the effort of developing the trials, the trials are actually not accruing very well across the nation for reasons is that because, I don't know the exact reasons. And sometimes there are reasons, you know, the patients probably don't like the randomizations, and I hate to mention that perhaps after the program, you know, half of the patients who feel like if they could take the medications, they probably don't want them to be randomized. And the trial endpoint was to look at the hand and foot syndrome reductions, and not exactly the maintenance questions.

The maintenance questions came about when we saw Kay and, you now, Tiffany and many other patients that have done well over this long period of time, and we have our patients that are crossing the eight years mark since they started their treatments in 2000 and have been off therapy for at least the last three years. So then we began to develop a very different therapeutic program, and that's actually something we are working hopefully with NCI and hopefully patients to get support for our program so that more patients can benefit from therapy.

**Andrew Schorr:**
It's a partnership.

**Dr. Lin:**
Yes. And in Susan's case, in fact, she is actually buying some of the medications from Canada because it's cheaper, and so she can afford to continue to receive the maintenance treatments.

**Andrew Schorr:**
I want to talk about the liver. So you mentioned that just a minute ago about the liver. So as I said my mom's cancer spread to her liver. What are some approaches going on there?

**Dr. Lin:**
Liver, successfully can be managed with liver resections. Dr. Yeung here at UW, and Dr. Park and also the liver directed experts. And I have worked with Dr. Currie, who is also a world-renowned expert in liver directed surgeries for colorectal
metastases. And some of these tumors in best-selected cases it has been reported previously you can get a median survival of 70 months for liver metastases. And keep in mind these patients are the patients who were rejected by the surgeons because they are not considered surgical operative candidates at the time when we saw them. And they were extrahepatic metastasis. That means they have metastasis outside the liver. So for some reasons in some of the liver metastasis patients, if we select them well, under surgery you could potentially get a long-term remission. A ten-year survival has been seen in that group.

Andrew Schorr:
Wow. Well, I want to get them, I have my three ladies as my kind of cancer reporters here. Susan, you are pretty fiery as a patient advocate. It sounds to me, wouldn't you agree, that people need to really talk turkey with very smart doctors about their personal cancer situation? It's not at all a one-size-fits-all, is it?

Susan:
No, it's not. Absolutely not. And Dr. Lin has been very good about just telling me exactly what kind of treatment we needed to do to go forward and to keep me in remission and to hopefully cure me down the line. It's, and, you know, this is not only just, which he is good with too, is the fact that you have to consider the family, the husband, the children, etc. This cancer affects everyone. And yes, it's the patient, but I almost think sometimes it's harder on the children and the husband than it is the patient that's going through it.

Andrew Schorr:
Right. We've done programs on caregivers, and we will do more and talk about that. Maybe we will get some of your family members on.

I want to take a quick break. When we come back, we will hear more from you and from the other ladies, and then we have got questions from Henry and Louise and Vivian and Gary. And we will try to get you on too as we discuss really new hope for people with advanced colon cancer. We will be right back.

Andrew Schorr:
Welcome back to our live webcast. Well, I have asked my producers and hopefully Dr. Lin and the ladies will stick with us. I am going to go maybe a couple of minutes after the top of the hour because this is such a big topic and, you know, I have friends now living with advanced colon cancer that have been in therapy, young children, prime of life, and really they are hanging on every word, Dr. Lin and ladies. I am sure you can relate to that.

Here are some questions we got in. And again if you want to send us an e-mail we are live if you are listening today on September 10th, and you can send an e-mail to Patient Power at seattlecca.org.
So, Dr. Lin, we got a question from Henry in Seattle, so he says, "In what stage of the cancer would stem cells or fighting the stem cells be most beneficial? So when does this kind of stem cell approach start?"

**Dr. Lin:**
You know, in theory a stem cell starts when the cancer forms. That probably can even date it back to when you even have the polyp times developed initially, and so as you know surgery or polypectomy with simple colonoscopy would cure all those polyps. And if you left those, earliest stage possible, you can't call those cancer, but they are precancerous lesions. These patients are clearly cured, because you not only destroyed the very nests but also potentially the microenvironments.

But when the cancer forms, then it has got some of the invasive features. So even the stage I patients, up to ten percent of the patients could still have recurrence. That means the tumors are pretty much in the very first layer of the colon. At stage IV obviously the patient has already had distant metastasis. Stage III means you have lymph node metastasis. So all those cells that try to spread are the ones that perhaps are harboring the capability of taking up in new centers. And coming back to think about the stem cells is that in fact we have a lot more metastasis circulating in the body. We have an article coming out very soon, and in fact we have tried to calculate the number of circulating tumor cells in the body is, can be up to 1,400 to 700,000 circulating tumor cells that has been seen in the patient. And then if you were to calculate these, quote/unquote, stem cells that may be circulating, they could be somewhere between 14 to 7,000 of the cells. And obviously a patient doesn't have thousands of metastases. Often we only see from one to ten metastases. So obviously the cells that can set up residence are the ones that are causing the problems, and that's in Tiffany's case and in all the other patients' cases.

**Andrew Schorr:**
So you want to get those queen bees, knock them out early.

**Dr. Lin:**
Right.

**Andrew Schorr:**
And isn't this the way it usually ,

**Dr. Lin:**
And there are just worker bees there too, right? So you,

**Andrew Schorr:**
Right. Right. Right. Isn't this the way it usually goes, just so people understand. So I was in a phase II clinical trial, and I was a newly, well, not a newly diagnosed patient, but it was my initial therapy. I had synergistic drugs being used together as you are doing here and we have been discussing. But usually you start with
people with more advanced cancer and then as you gain experience and see some
efficacy, it starts moving up, right, to try to affect the cancer at an earlier stage.
Will that happen here do you think as research moves forward?

Dr. Lin:
That's what we are trying to do now is to first develop potential in vitro readouts,
and we are working with the Stem Cell Institute at the University of Washington,
Dr. Blau's lab, and try to grow these patients' tumors spheres. We have been
successful to some extent in that endeavor, and then perhaps be able to generate
some readouts. And we are actually pursuing measuring the stem cell activity in
the peripheral blood of the cancer patients. We have this circulating tumor cell
machine that we have been doing some of the work in that area.

And then really to work with pharmaceutical companies who have this same
interest to develop stem cell, quote/unquote, targeted therapies and comparing to
certain benchmarks. I think our current benchmark should be hopefully established
in comparison to some of the other standard chemotherapies.

Andrew Schorr:
Okay. Let me see if I have got this then. So we heard about Xeloda or
capcitabine, celecoxib or Celebrex, which were medicines approved to be used for
different things.

Dr. Lin:
Right.

Andrew Schorr:
Or Xeloda for advanced colon cancer, but otherwise Celebrex for pain. And you
found, so these drugs were available.

Dr. Lin:
Right.

Andrew Schorr:
But what you are, if I get it right is now as you learn maybe scientifically what's
going on, you are working with the drug companies to have drugs developed for
that purpose.

Dr. Lin:
Correct. So looking at these stem cells as their own signaling pathways, and if one
were to figure out what exactly the Celebrex is targeting, we have some preliminary
information about their signaling pathways, and hopefully we will be able to tailor
the treatments based on the patient's tumor presentation characteristic. And also
really look at the other known mutations, such as the KRAS and many other new
markers that have been developed in the colon cancer arena, and sort of combining those and make a sophisticated menu of choices when the patient comes through the door. And that's what we are hoping to achieve.

**Andrew Schorr:**
Wow. Well, you know, I'm your cheerleader, Dr. Lin, and for your colleagues and the other scientists you have mentioned both locally and around the world.

Tiffany, when you listen to this, now you have gotten a really good result, and I hope it lasts for a long time, for someone who is newly diagnosed, maybe a pretty young mom like you were, do you think there is reason for hope?

**Tiffany:**
Oh, definitely. I mean, I had a three-year-old when I was diagnosed. So you face pretty quickly maybe the likelihood that your children grow up without you. So, yeah. I think there is hope. Because honestly I think if you had asked my surgeon and my oncologist here in 2000, they would have told you that I wouldn't be here today. And so it's the therapy that Dr. Lin is developing. He is a hero in my mind. That's the reason I am still here.

**Andrew Schorr:**
Okay. So, Kay, do you have a comment you want to make about Dr. Lin? Go right ahead, ma'am.

**Kay:**
Pardon?

**Andrew Schorr:**
Yes. I was saying do you have a comment you want to make about Dr. Lin? Tiffany said he was her hero.

**Kay:**
I was just very excited about his last comments. I thought it gives so much hope.

**Andrew Schorr:**
Right. And Susan, what about you? So there is somebody listening, whether a family member or a patient themselves, and they have been told, A, you have got colon cancer, that's really bad news; and, B, it has spread. You are going to have surgery, you are going to have radiation, you are going to have chemo, and you say, oh, my goodness. You know, can I resume my life at some point? Now, there are no guarantees, but what encouragement would you give them?

**Susan:**
Yes, I can. Hopefully that they can get in to see Dr. Lin or one of his colleagues, get the treatment that I have gotten and other ladies have gotten, and there is hope. There is always hope. And I think positive thinking, positive feeling, positive
through your family and your ministers or whatever you would like, positive thinking is really I think key to this whole thing besides good medical treatment. And believe you me, I have had excellent medical treatment from day one.

Andrew Schorr:
I want to make a pitch, thank you for that comment, I want to make a pitch for clinical trials.

So Dr. Ed Lin is a clinician and a scientist, and you heard about petri dishes and machines that count stem cells, all this kind of stuff, and you heard him mention about clinical trials and the NCI and working with other major centers. We, patients and family members, are their partners. And so you need to ask yourself if you have a diagnosis like this, first I would urge you to have a consultation with a specialist in your cancer, in this case treating advanced colon cancer, and second of all to have discussion of clinical trials be part of what you consider. And if it seems right to you, then you can not only maybe help yourself, but you can also help many others and get these answers that we are trying to figure out.

You hear that articles are being written and studies are being extended and it's very exciting, but we need to quantify all this. So you are getting kind of an advanced look. It's going to be debated in the scientific community, but I know for people living with advanced colon cancer they are saying, well, does this apply to me?

Dr. Lin, I am going to let you get the final word here. So you are devoting your life to this. We talked about the word "cure." Can that be in the future? And can you be hopeful as people really with advanced disease wonder, you know, can this be an answer for them? Are you hopeful looking in your crystal ball and in the lab where we are headed with this?

Dr. Lin:
Obviously what you saw is the great success stories, and I have alluded to earlier about 28 percent of the patients that we treated as a whole cohort have achieved complete responses, and so even among some of those patients who did not take the maintenance therapies, actually have subsequently relapsed. And so what we are also challenging is the rest of the 70 percent of the cases and how can we make incremental progresses to make, you know, just like lymphomas and leukemias, they all have a very flat curve when you look at a survival curve. There is a flat curve, and it stays flat, and that's the real success. I would truly hope to see that in colon cancer we could raise the bar higher than what we have seen, and then maybe sustainable for long term. And so the C word applies to when we open a bottle of champagne 20 years from now, or when Tiffany become a grandmother. Or you know, so that will be the C word.

Andrew Schorr:
Right. And I think, Susan, aren't you hoping to be a grandmother someday too?
Susan:
I hope I am a grandma. I have granddogs now, but I want to be a real grandma someday. Yes.

Andrew Schorr:
Okay. Well, ladies, I want to thank you so much. I want to thank Susan Johnson from Longview, Washington for being with us; and Kay Bartlett who jointed us from Anchorage, Alaska; and Tiffany Highgold from Oklahoma City even though I am down on Oklahoma City because of the SuperSonics, now Thunder basketball team. But we will forgive you for that, Tiffany, okay? And wish you all the best and hope that, yes, you dance at the weddings of grandchildren, and we prove that when we look back on the treatment you have received you have been pioneers. And Dr. Ed Lin from the Seattle Cancer Care Alliance, Ed, I want to thank you for your passion and your dedication to patients, and I want to wish you and your colleagues all the best for the research you are doing.

Dr. Lin:
Thank you so much.

Andrew Schorr:
Yes. Thank you. We are going to get you back for an update. You always come back. This is what we do on Patient Power. And we have our programs every two weeks, and I am just bowled over with what I learn all the time. It's really inspiring, the teaming of researches who are also in the clinic there to help you, and certainly the Seattle Cancer Care Alliance has a very dedicated team. Be back with us in two weeks as we do another program with experts from the Seattle Cancer Care Alliance. I want to thank them for the sponsorship of Patient Power. And just remember, knowledge can be the best medicine of all. I am Andrew Schorr. Thanks for joining us. 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.