Advances in the Treatment of Pancreatic Cancer
Webcast
March 4, 2008
Douglas Evans, M.D.
Robert Wolff, M.D.

Please remember the opinions expressed on Patient Power are not necessarily the views of M. D. Anderson Cancer Center, 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.

Introduction

Andrew Schorr:
Hello and welcome once again to Patient Power. I'm Andrew Schorr on mdanderson.org. We do our Patient Power programs every two weeks.

So there are cancers, and there are cancers, I have leukemia, and it's a chronic leukemia. People live many, many years with it. There are a small percentage of patients with chronic lymphocytic leukemia and they never need treatment. There are other cancers where it turns your life upside down, I guess all cancer diagnoses do, and then it's a question of what do you do pretty rapidly because it could be a very fatal condition very fast. But there's always hope for newer and better treatments, and there are people who survive.

Today we're going to talk about one of those very devastating diagnoses but yet the story of hope and the story of advancement, and that is pancreatic cancer. Pancreatic cancer affects more than 30,000 Americans each year, but in the vast majority of people they don't survive very long. But there are people, and you're about to meet one, who do survive for an extended time, hopefully for a normal, long life. I want you to meet Mary Sharkey. Mary lives in Houston. She's 56 years old, and she is one of those examples of someone who has been treated successfully. It wasn't easy. She's needed different approaches, but she's needed some leading edge medicine that's been provided at M. D. Anderson.

Mary, you were diagnosed in December of 2001. It turned your life upside down didn't it?

Mary:
Yes it did, and my family's.
Pancreatic Cancer Diagnosis

Andrew Schorr:
Yes. And one of your three children is a doctor so they all must have been terrified for you. And there was sort of an uncertainty. First everybody was telling you, Well, there's something going on with your pancreas but we don't at all believe it's a cancer, right?

Mary:
Yes, that was before they did the biopsy, and up till that point I was basically told that it was probably 99.9 percent benign, that I wouldn't have to worry and I could go on with my life, until December 3rd, 2001.

Andrew Schorr:
And then they said, Well, we didn't think it would turn out this way, but you've been diagnosed with pancreatic cancer. Now, years before you had been a social worker who worked with an oncology practice. So did you know how terrible a diagnosis this could be?

Mary:
The particular doctor that I worked with actually his specialty was more around the line of melanoma, breast cancer. I really never encountered pancreatic cancer. But along the road you do hear about the pancreatic cancer and what a delicate organ it is and you don't mess with the pancreas, that type of thing. But I never really was exposed to pancreatic cancer.

Andrew Schorr:
So you're diagnosed, and when they look at your pancreas they found out that where the tumor is is near an artery, and the question was could you at all be a candidate for a surgery we'll talk about along the way, the Whipple procedure, a very extensive surgery, but could be successful in removing the pancreatic cancer, but they were saying initially it was not operable, is that right?

Mary:
Yes, that's correct.

Andrew Schorr:
But they thought referring you to M. D. Anderson there in Houston was the right way to go because you were a difficult case.

Mary:
Yes, that is correct. Absolutely.

Andrew Schorr:
So, Mary, you meet a medical oncologist, Dr. Robert Wolff.
Mary:
Yes.

Determining the Need for Surgery

Andrew Schorr:
Who we have on today's program who specializes in pancreatic cancer, and also you were also connected with a leading surgeon eventually, Dr. Evans. But we're going to talk about surgery in a minute. First let's meet Dr. Wolff. Dr. Wolff, Robert Wolff is an associate professor of gastrointestinal medical oncology. He's a specialist in pancreatic cancer at M. D. Anderson.

Dr. Wolff, when Mary Sharkey came to you the thought was is that she was not candidate for surgery. How do you evaluate people to see is surgery possible? And what would be the benefit of surgery? For people I talked to the idea of being able to cut the pancreatic cancer out would seem like it could be life-saving, it would be very desirable, but I know at M. D. Anderson you're very selective on who you think is a candidate for surgery.

Dr. Wolff:
So what you've just said is correct. And the first thing I would say is that pancreatic cancer is a cancer that is extremely prone to spread early in its development. And even when patients undergo surgery we know the cancer can relapse, and this is a critical problem that we face with pancreatic cancer for many of our patients. We also know that the other treatments that we have, whether they be chemotherapy or radiation to include some new medications that we call molecular targeted agents, are not able in and of themselves to cure or eradicate pancreatic cancer from the body. The best single treatment to get pancreatic cancer out of the body is with surgery. Chemotherapy can help kill the tumor, radiation can help kill the tumor, but the best single way and the only way we know to cure somebody with pancreatic cancer is with surgery.

What I need to emphasize is that surgery needs to be complete, meaning one hundred percent of the tumor has got to be removed, that all visible tumor is removed based on what the surgeon can tell with his naked eye, but importantly under a microscope all the knife edges that are examined after the tumor has been removed from the body need to be completely free of cancer along the edges. Years of experience have told us that complete removal of the tumor, what I call one hundred percent removal of the tumor, is critical to offer the patient a meaningful chance of long-term survival, meaning surviving five years or greater or being cured of the cancer.

The additional treatments is we have, chemotherapy and radiation, can help attack the tumor but they are not sufficiently powerful in our day and age to eradicate the
tumor, and this is why patients whenever possible want to have surgery for their pancreatic cancer. The bias or the institutional perspective on this at M. D. Anderson, however, is that surgery does not have to be the initial treatment for a tumor that appears operable or resectable. That's one option, but another option is to treat the tumor for a while and then to think about removal.

In Mary's case her tumor was considered inoperable because the fear was if we tried to remove it entirely at the time she first came to M. D. Anderson chances were fair to good she would be left with a microscopic amount of cancer around where the tumor was removed, meaning not all the knife edges would be clean of tumor. And this is why we took the approach in her to give her treatment first with chemotherapy and subsequently with chemotherapy and radiation before trying to remove the tumor.

Andrew Schorr:
Okay. I want to put this in perspective. This is a very important point, and I know people are living around the world. So, yes, Mary is with us and we'll tell more of your story along the way, Mary, but Mary did have chemo and chemo and radiation and then did qualify for surgery and then had some chemo afterwards as well, and now, more than six years later, she appears to be cancer-free and she has her yearly checkups. And, Mary, you're one of those examples who can get up in front of a room to people who are shocked with the diagnosis of pancreatic cancer and say there is hope. And I know you do that all the time, and we'll talk more about that.

But the point that Dr. Evans was making, and I'm just going to sort of spit it back to you because I want to understand and make sure our audience who I'm sure tuning in around the world. As you were saying there is a bias to have surgery because it can be cured of, but if I heard you right you're saying if someone goes straight to surgery that the likelihood of then being able to follow up with chemo and radiation and get those clear margins is reduced. And so the way you look at it is first decide is somebody going to be a candidate for surgery right off the bat or maybe do they fit in sort of a borderline category where chemo and radiation first could make a very substantial difference if you do it first.

Dr. Wolff:
That's correct. We believe that currently too many patients undergo surgery as the first step. That's a very emotionally charged time in someone's life. Most patients with minimal reading quickly understand that surgery is the only way to cure the cancer, and therefore their sense is, As soon as it can be removed from my body please do so. But we also know from years of reports in the medical literature that even when the tumor appears to be operable based on CAT scans or other tests that the tumor is not always removed a hundred percent, and that leads to a very difficult situation because by and large if somebody has surgery that is not one hundred percent successful, meaning the tumor is not removed in its entirety, it
does not appear that chemotherapy or radiation have the same level of effectiveness after that type of surgery. We think there's too much scar tissue, blood flow in that area may be compromised, that those treatments just don't work as well under those circumstances.

Andrew Schorr:
There's a phrase that I've heard numerous times among leading cancer organizations. We try to remind the public that your first shot is your best shot, and it seems to really apply in pancreatic cancer. So at M. D. Anderson you're amassing this data. You have lots of experience. You have super subspecialists like yourself. So if somebody was diagnosed with pancreatic cancer it would seem like this decision of what to do first needs to be a very considered decision with people who specialize in the disease.

Dr. Wolff:
We believe that's very true. I will also tell you I think, and it's very hard to control one's emotions when this diagnosis confronts them, but panic is a terrible response to a diagnosis of pancreatic cancer because what panic does is make you seek care in a much more urgent way than is necessary, and the first person you meet who says, I'll deal with this with a blade is usually the person you'll go with. There's growing evidence that going to a center of excellence, meaning a place that sees a lot of patients with pancreatic cancer, what we call high volume tertiary centers for pancreatic cancer should evaluate patients, particularly when there is some question that surgery is a possibility.

There are certainly patients who when they are first diagnosed with pancreatic cancer have evidence for metastatic disease, meaning cancer spread. Those patients are not going to be considered for surgery at any point in the future based on our current understanding of this disease. Whether those patients should always go to a center of excellence for care, I think many people could debate. But certainly patients where surgery is being considered as one of the options that is being entertained, I really believe patients should go to a center of excellence to be considered for surgery, even if it takes a week or two to arrange for that.

I think many patients are told by their surgeons in their local communities, It will take too long to arrange for a second opinion. You must have this tumor removed as soon as is humanly possible, and I will book you for the OR the day after tomorrow. And sadly too many patients will take the surgeon up on that offer and have surgery when it is not necessarily the correct initial step as an approach to their pancreatic cancer.
Time Between Diagnosis and Treatment

Andrew Schorr:
Wow. We've been receiving some e-mail questions, Dr. Wolff. So Beth from Evanston, Illinois wrote in exactly about that. I'll just share a little bit of her question. She said, "My mom was diagnosed with stage IV pancreatic cancer. It would be just about three weeks ago. We have seen two oncologists for consultations and have been referred to a university center. Right now she can't get an appointment at that center for a month. That would be about a month and a half after diagnosis before starting treatment. Any thoughts on that? The last oncologist said we had time to explore treatment and should start treatment about a month from now. So besides being agonizing, is it a safe idea?"

So they're just on pins and needles and terrified and maybe a little panicked and wonder about this delay as to whether that shoots themselves in the foot while they wait.

Dr. Wolff:
Let me put it this way, and I can appreciate very much the concern, particularly with someone having stage IV disease. So what we've tried to do at our institution is to let people know it could be two or three weeks before they're seen, and as a general rule that interval of time, and I do think a month cut-off is a reasonable one to use with patients in terms of trying to get started on treatment or more importantly having a plan for treatment.

Many people need to understand that when these cancers develop they do not develop overnight. These are tumors that were, quote/unquote, born typically a year, two, three years before they're detectable in their body, and is it does take time to get to the point where they become metastatic. They do not spread in the body overnight. So when someone is diagnosed with stage IV pancreatic cancer that cancer spread has been in there for some period of time. And if you say, well, does a week make a difference, does two weeks make a difference? Certainly a couple of months we would not be comfortable having a patient go without treatment for that kind of time, but what I'm just going to say is generally a few weeks is an acceptable time frame.

I think the biggest issue that we have with some of our patients with stage IV disease is that how they're feeling can be declining as they're waiting to see an oncologist. Primary care physicians and medical oncologists who are not at tertiary centers should be trying to help people in terms of their appetite, in terms of pain management even before they see an oncologist or an experienced oncologist in pancreatic cancer. So there are some things that I think the oncologist can be doing in the local area to try to help support somebody.
But as a general rule, a few weeks after diagnosis, and I would say three or four, somebody should be able to have a plan of action developed for them.

**Andrew Schorr:**
I'll just mention, I have a family member from Los Angeles who was on a cruise in South America, and she was jaundiced. And she didn't get a clear diagnosis there. Maybe the doctor on the ship suspected it, but they were told to continue with the cruise and manage her diet, etc. She got back to Los Angeles and eventually had the diagnosis, but it was a couple of weeks. And then she did have consultations. She eventually had surgery.

I want to ask you about the surgery. Now, Mary, you went through this Whipple procedure, it's called, and it worked for you. You had chemo and radiation to shrink the tumor and then were subsequently able to have the surgery. The surgery is a big deal, isn't it, Mary?

**Mary:**
Yes, it is.

**Andrew Schorr:**
But you're glad you had it, of course.

**Mary:**
I was very, very grateful when Dr. Wolff informed me that I was able to have the Whipple.

**The Whipple Procedure**

**Andrew Schorr:**
Dr. Wolff, we've had some e-mail questions about people. They've heard this term "the Whipple procedure." What is it?

**Dr. Wolff:**
The issue is where tumors are located in the pancreas requires that not only the pancreas is removed to take care of the tumor, about 75 to 80 percent of patients who develop pancreatic cancer developed it in what we call the head of the pancreas. And the head of the pancreas is at a tremendous intersection within the body that involves the bile duct and the upper part of the intestine called the duodenum. And so to remove the tumor requires removal of these surrounding structures in an end block way in addition to the tumor in the head of the pancreas.

So roughly one-third of the head of the pancreas is removed with the Whipple procedure. The very lower part of the stomach and the first portion of the small intestine is also removed, and a substantial segment of the bile duct is also removed. That requires that the bile duct is reattached to another segment of
intestine, and the bottom part of the stomach which is sewed shut needs to have a new opening created to allow food to pass from the stomach downstream into the small intestine. So this is not just removal of a portion of the pancreas, but the lower part of the stomach, the first portion of the small intestine and the bile duct are also removed, and the bile duct and the flow of food from the stomach into the small intestine has to be reconstructed.

And this is what makes it a complex operation. It commonly takes on the short end, six or seven hours, on the long end, 10 to 12 hours. It often requires seven to ten days in the hospital afterwards. Many patients need to have nutritional support after surgery with either a feeding tube or on occasion artificial nutrition through their bloodstream. And usually after hospitalization there would be, I guess I would say a full month before people are really starting to get back on their feet and a full three months before people are having good emptying of their stomach through their new intestinal route and their pain has subsided and their energy is coming back.

So it's a major operation. Back when it was first being performed there was about a ten percent chance or higher of dying in the immediate postoperative situation. In many small volume centers the risk of death is still over five percent. In high volume centers that have a lot of experience with the Whipple procedure the risk of dying is less than one percent. But it is not a trivial operation. The length of stay after surgery, meaning the length of stay in the hospital, is routinely higher than that for open heart surgery for a bypass procedure, etc. So we think of this as one of the most complicated GI surgeries or surgeries of any type that can be performed on someone.

**Andrew Schorr:**
Yeah, it certainly sounds that way to me. Now, Mary, for people who are listening, you've come out the other side of this. What comment would you make on the Whipple procedure? You've had those tubes and drains. You're an extremely positive person. You had wonderful family support. But what would you say to people about going through that?

**Mary:**
I talk to a lot of candidates for Whipple surgery and people who are newly diagnosed with pancreatic cancer, and as I tell them, it is a doable surgery. I mean, you've got to look at what your options are, and when you look at those options you realize that your option is you have to do the surgery. If somebody came to me having experienced the surgery, knowing what it's about, and said you will have to have a Whipple tomorrow, I wouldn't shake in my boots or boo-hoo or anything. It is doable. It's not a great ride or anything, but you do make it through, and there is a light at the end of the tunnel.
And you have to, through the whole thing, follow through with what your surgeon says, what your oncologist says, your nurses tell you, and do what they tell you to do. And I think that, you know, I look back on it now and it almost seems like a dream, but going through it I just decided I was going to keep a stiff upper lip and I was going to fight it all the way and that included dealing with whatever the Whipple had to show me or, you know, whatever I had to deal with.

**Andrew Schorr:**
Mary, let's just recap what you went through. So you were diagnosed in December of 2001, right?

**Mary:**
Yes.

**Andrew Schorr:**
You had the surgery early the next year, 2002. Excuse me, no. I'm wrong. You had chemo and then chemo and radiation to shrink the tumor.

**Mary:**
Yes.

**Andrew Schorr:**
And then when did you eventually have the Whipple procedure?

**Mary:**
It was May, 2002.

**Andrew Schorr:**
Oh, okay. And then after you recovered from that you and Dr. Wolff spoke about having some additional chemo afterwards. Now, what was the--let's start with you, Mary. You advocated for that. How come?

**Mary:**
I just felt that I knew I had a tough fight and I had been through the majority of my treatment and if I wasn't going to pull through I wanted to know in my heart and to be able to tell my family everything was done that could have been done in my particular case. Each case is so different. And so I just felt that when I went to Dr. Wolff, who I have to add other than my family was absolutely my strongest advocate, I just told him, I need to know that I have done everything, everything possible to try to beat this disease. And fortunately Dr. Wolff worked with me, supported me and did some research and came up with a protocol that I began.

And I think that's a lot of the battle, too, is having doctors that work with you, that deal with you, you're emotions, your feelings, whatever it might be, stubbornness, which I'm very stubborn. And just knowing that they're for you, they're your
advocate, they're behind you just as much as your family really, really, really helps in this battle. And Dr. Wolff absolutely walked the walk with me.

**Chemotherapy Treatment**

**Andrew Schorr:**
Dr. Wolff, help us understand now related to chemo after Whipple procedure. So we heard about the effort to shrink the tumor and help more people be candidates for surgery where you can feel much more confident that you're going to contain the tumor and then remove it and where that can be curative, but this whole idea of chemo after, does that always apply? How do you decide what to do and what drugs?

**Dr. Wolff:**
So it's an excellent question. The first thing I would tell you is that right now with what we call operable tumors there are two approaches being taken. One is to do surgery first and then after surgery and adequate recovery to give patients usually about six months of additional treatment. For many doctors that's chemotherapy alone for six months. For other doctors it's a combination of chemo treatments and some chemotherapy with radiation. There's no consensus right now on what the best strategy is after surgery. Our approach at M. D. Anderson, by and large, is to do chemotherapy and chemo with radiation treatments first, operate second.

Now, for most of our patients after surgery we have not delivered more chemotherapy. We don't have any evidence one way or the other that additional chemotherapy after surgery would be beneficial, which in Mary's situation led to a choice. We don't know what's best if people take treatment before surgery if more treatment after surgery will help increase the chances of cure. Mary, because she's Mary and because she did come through the prior chemotherapy and the prior radiation and the prior surgery very well, we felt that she was strong enough, I felt that she was strong enough to have the option of more chemotherapy after surgery, and that was what I would call a shared decision.

And this is an important concept that Mary is raising is that in today's world doctors shouldn't be as paternalistic as in this old days when we would say you should do this or you should do that. I think increasingly what we try to do is say your options are this or this or that and go over the pros and cons of those different choices with patients. And so Mary and I sat down and we talked about additional treatment with chemotherapy or to follow very closely and just keep repeating the testing with CAT scans and blood work to try to be sure that the tumor wasn't coming back.

Because she was very aggressive in approaching her tumor before surgery and with surgery, Mary clearly expressed an interest in being aggressive with more treatment after surgery. Now, as a general rule in patients with stage IV pancreatic
cancer we know that if you give them a particular chemotherapy or chemotherapy combination it can work to attack tumor cells for a while but then there will be tumor cells remaining that are resistant to that treatment. And so it was my idea that we had used a certain regimen before surgery that if there were still microscopic amounts of tumor in her body after her surgery they would probably be resistant to the initial treatment that we gave.

So we gave her a different cocktail of chemotherapy drugs to try to continue to combat any microscopic seeds that may have been left in her body after surgery, which is in fact a risk for all patients, whether they have surgery first or surgery as a next step. So we gave her a different regimen of chemotherapy based on some work at Virginia Mason University which used a specific regimen of chemotherapy in patients with relatively good success in their hands. That treatment I think was more fatiguing for Mary, particularly after all she had been through, but she's still standing and it looks like it was the right thing to do for her.

Andrew Schorr:
Right. Well, we're going to talk more about your medical oncology area and the various tools you have now to work with surgery when we continue our discussion about advances in the treatment which pancreatic cancer. I know people hang on every word and I think the advice and the guidance and the perspective we've given them so far in this program is critical, and we'll get into more of the research work and the pioneering work you continue to do at M. D. Anderson in just a minute.

You're listening to Patient Power on mdanderson.org. We're visiting with Dr. Robert Wolff, who is a specialist in pancreatic cancer and associate professor of gastrointestinal medical oncology and also his patient now more than a six-year survive of pancreatic cancer, Mary Sharkey. We'll be back with more Patient Power in just a minute brought to you by M. D. Anderson Cancer Center.

Hope and Progress Through Research

Andrew Schorr:
Welcome back to Patient Power on mdanderson.org. This is what we do every two weeks is connect you with inspiring patients, Mary Sharkey, our guest today, certainly is that. We're going to hear more from her now as a six-year, over six-year pancreatic cancer survivor. There are not many, but fortunately with the latest care there are people who are examples of that, and we'll learn more about that. And hopefully you can be one too if that's the diagnosis that you've received. And also Dr. Robert Wolff who is a specialist in pancreatic cancer at M. D. Anderson.

Dr. Wolff, we started to talk about the various drug therapies and what to do when. Mary was treated initially like six years ago. My hope is that things continue to
change. I know you do a tremendous amount of research. There are many labs and specialists, molecular biologists, just buildings full of people working on cancer at M. D. Anderson. Where are we with the leading edge of where things are headed? Is there hope as research progresses?

**Dr. Wolff:**
I think there is a lot of evidence that we have lots to be hopeful for. I will have to admit that the progress is quite slow, but what I would say is that for many years the focus of our research has been on what I will describe as brute force approaches to this cancer. And what I mean by brute force are things like the Whipple procedure, things like chemotherapy or what I'll describe as conventional chemotherapy and radiation. And all of those treatments, surgery, radiation and conventional chemotherapy, have side effects.

Radiation can damage the normal tissues that surround the target of tumor that we hit with the radiation. We can lead to ulceration. We can lead to fibrotic changes. You can have long-term consequences of radiation.

I tell my patients that conventional chemotherapy is a poison. It is intended to poison the tumor cells and to kill them, but there's a lot of collateral damage. It can affect dividing cells in all parts of the body. This is why chemotherapy can lead to hair loss, because the follicular cells, the hair follicles, are also dividing and hair can fall out. People can develop mouth sores or diarrhea because the mucus membranes of the mouth or the intestines can be affected and killed and lead to significant side effects. They can lead to nausea and vomiting because they're poisons to the gut and there are poisons in the brain that the brain is reacting to with vomiting. And very importantly they are poisons on the blood-forming elements of the body in the bone marrow where your red cells, your white cells and special blood cells called platelets are made. And so chemotherapy, what I describe as conventional chemotherapy can have quite devastating affects on the blood cells. This is why people are at risk for infections, at risk for bleeding.

Now, increasingly, oncology and oncology research is refocusing from these brute force approaches to the treatment of cancer to what we call targeted approaches, where we're not trying to poison the entire tumor cell. We're trying to identify critical proteins and other molecular structures within the tumor cells that the tumor cell relies on for its survival, its growth in the body and its spread in the body. In other cancers the use of drugs that are designed not to kill the tumor cell in toto but they're designed to attack and block the function of certain proteins are yielding dividends. This has been true in breast cancer. This has been true in lung cancer and in colon cancer. And there is recent evidence that this can be true in pancreatic cancer.

So there is a protein on the surface of pancreatic tumor cells called the epidermal growth factor receptor. That is a protein, and for many patients with pancreatic
cancer this protein seems to be important for the tumor's growth and spread in the body and survival of the tumor cells. There's a drug called erlotinib, it's also called Tarceva, which when added to conventional chemotherapy in the form of Gemzar, or gemcitabine, seems to strengthen the Gemzar at least somewhat. The added benefit is quite frankly fairly modest, but it is a proof of principle that if we start to think in a targeted way to attack the tumor cell and to inhibit proteins that the tumor cells are very dependent on we will make for increasingly more sophisticated treatments for pancreatic cancer which hopefully will also not have the collateral damage.

Tarceva does have some side effects, but it does not affect the bone marrow. It does not cause hair loss. It doesn't cause a lot of nausea and vomiting. It can cause a skin rash, and in some patients it does cause some diarrhea. But compared to what I call regular chemotherapy treatments that can be quite harsh, that type of side effect is more easily managed for the patient with the doctor than some of these very harsh treatments that patients can be asked to undergo.

That is the first example of a new approach to the treatment not just of pancreatic cancer but of other cancers, and as I mentioned the progress with this approach of looking at targeted drugs is quite slow. Having said that, there are a growing number of molecular agents or targeted agents that we have available to study, and very importantly we need patients to help us conduct that clinical research, meaning we need patients who are willing to be research subjects with new drugs that we hope with improve our treatments for pancreatic cancer, and this will be critical for our success.

What is GTX?

Andrew Schorr:
A couple of comments I want to make. First of all, I was in a phase II clinical trial at M. D. Anderson. It was a single center phase II trial, and the treatment that I received is what most people receive around the country, if not often around the world, now. So I really felt that I was happy to be part of the research, and it gave me a chance at tomorrow's medicine today. So I'm grateful for that.

The other thing I would mention to people listening in is we've done another Patient Power program with Dr. Maurie Markman who is head of the clinical trial area at M. D. Anderson, and that explains clinical trials in depth and how you can be considered for one and how you should consider a clinical trial and see whether it may be right for you. So I urge you to listen to that.

Dr. Wolff, we did get a question via e-mail in from Erica in Dallas, and she asks about the exact area you were talking about. She said her husband is a 46-year-old man getting treatment now for pancreatic cancer which has spread to
his lever. He's getting Gemzar at this stage, and right now it seems to be keeping the cancer at bay. She's heard about GTX. I'm betting GTX has something to do with some of the drugs you were just discussing. What is GTX?

**Dr. Wolff:**
GTX stands for three different chemotherapy drugs. One is Gemzar, the other is Taxotere and the third is Xeloda. Now, as it turns out, all of those drugs are what I call conventional chemotherapy drugs. This regimen of GTX was designed by doctors at Columbia University in New York, and in some patients it can be quite effective to control the tumor. Now, because these drugs are what I call conventional chemotherapy drugs they do have side effects, and that is what I call a very strong program. It can be quite strong on the tumor and on the tumor cells in the liver or elsewhere, but it can also be a fairly tough regimen for a patient to tolerate, meaning that regimen is much more apt to cause some hair loss, it's much more apt to cause fatigue, mouth sores, diarrhea, and affects the blood system more so than Gemzar alone.

In my practice I have used GTX, but I haven't usually recommended it as a first treatment, and I am more inclined to recommend Gemzar or Gemzar in combination with Tarceva or other drugs, but I will consider GTX as a treatment option for my patients as their tumor shows resistance to Gemzar.

**Andrew Schorr:**
Okay. Now, guess what. We're now joined by one of the leading surgical oncologists in the country if not the world for pancreatic cancer, and that's Dr. Douglas Evans. Dr. Evans, I'm willing to bet you were in the operating room.

**Dr. Evans:**
That's correct. I'm very sorry I'm late, and I certainly apologize to you, Mary and Bob.

**Medical Oncologists and Surgical Oncologists Working Together**

**Andrew Schorr:**
No problem. No problem. Well, we're in the middle of our program, and Dr. Wolff has done a great job I think in describing the Whipple procedure. And Mary, we've heard of Mary's story. And with it our understanding too, as Dr. Wolff has described, is you at M. D. Anderson are pretty conservative about who will benefit from surgery and seeing are they an obvious candidate for surgery, are they a borderline candidate as now we view Mary and not to create false hope for people that the surgery can be curative when maybe you're not able to get all the cancer cells.

It sounds to me like there has to be a lot of teamwork between you on the surgery side and folks like Dr. Evans on the medical oncology side to work together,
whether radiation and chemo come first, targeted procedures that Dr. Wolff was just speaking about, but how it can all work together in sort of an interdisciplinary team.

**Dr. Evans:**
Oh, I think that's absolutely correct, and Bob has certainly been one of the leaders in that effort here. I think hopefully one aspect of the care of patients with pancreas cancer that we would like to think is exportable to almost any medical center in the world would be the ability to interpret CT scans and then to classify patients' tumors as to whether they're removable and, as Dr. Wolff has already discussed, borderline removable or resectable and then locally advanced. I think certainly here at our center a patient could enter into the institution through virtually any department, whether it be medical oncology, surgery, radiation oncology or gastroenterology, and they should receive the same initial evaluation, and their case will be discussed at our weekly multidisciplinary conference.

But certainly the initial importance of accurate cross-sectional imaging with good quality CT scan or MRI cannot be overemphasized. It's hard to do anything beyond that if that is not done well.

**Andrew Schorr:**
I want to go back to that because, you know, we hear on the news, etc., about all these new imaging modalities, and then I've interviewed some people who have been treated for pancreatic cancer, had surgery and finds that the surgeon finds a different story maybe when they get in there. It would seem to me, just to underscore what you said, how critical it is to know what you're dealing with.

**Dr. Evans:**
Absolutely. There always will be the situation where the preoperative imaging studies will not be able to see a small metastasis to the liver or to the lining of the tummy that may only measure one, two millimeters in size. That's visible with magnification in the operating room, whether it be with laparoscopy or after opening the abdomen, and it's not going to be seen on an a CT scan, MRI, PET scan or anything else. That happens relatively infrequently, and at our institution it probably is no more than 10 percent. And that's because we know pretty much exactly who will benefit from surgery and who won't with respect to the primary tumor.

If your analysis of the primary tumor is less sophisticated then you will probably be taking more patients to the operating room, many of whom stand little chance of benefit, and in those patients you're likely to have a higher incidence of finding small metastases to the liver or to the lining of the tummy. So the frequency of that is much smaller if you are more refined in your analysis of the primary tumor itself.
Long Term Progress

Andrew Schorr:
Dr. Evans, you've been at this quite a while. After all, you're the chief of endocrine and pancreatic surgery there and you've been there for a number of years. For people who are listening to us, the shock of diagnosis of pancreatic cancer, your perspective makes a difference. Dr. Wolff was saying he wishes the progress was a lot faster, but do you see progress? What hope could you give people as you've observed it now, surgery, working with medical oncology and radiation oncology to try to make an impact on what's been a very difficult disease?

Dr. Evans:
I agree with you. It certainly is a difficult and challenging disease, but I think I would divide it into progress that is immediately applicable to patients with pancreas cancer and then progress that is probably within the short term, within the next five to maybe ten years. And I think there are a number of reasons to be optimistic. Number one, through institutions like M. D. Anderson and some others we have certainly refined and understood how best to combine chemotherapy, surgery and in some patients radiation. That really was not as well understood, certainly ten years ago it wasn't anywhere near as well understood as it is now. What you have already discussed, the importance of accurately staging patients and applying the correct treatment to the correct patient is now much more refined than it was before.

And the entire research community and to some degree the lay community now has an awareness about pancreas cancer that previously didn't exist. And the amount of money and the amount of attention that is being directed toward pancreas cancer research is really orders of magnitude greater than it was before. I spent the weekend reviewing the PanCAN grant applications, which is administered by the American Association of Cancer Research, and I think they had about 170 applications. They're only going to award four grants, but just the number of applications attests to the fact that this disease has received the attention of a lot of really smart people. And there's no question that there will be a series of small to moderate breakthroughs that will certainly occur over our lifetime.

Andrew Schorr:
Well, that will certainly be great. I wanted to also underscore, you mentioned the patient advocacy group PanCAN, based in Los Angeles. It's just been an outstanding example of patients and researchers and clinicians working together. And I know, Mary, you're involved in it, and I know my relative who was treated for pancreatic cancer is very involved, and I'd commend that to someone, family touched by pancreatic cancer to get in touch with PanCAN.
Now, Mary, so here are two doctors who touched your life at M. D. Anderson. What comment would you make to people about the care you got that I think made a difference in you being with us now, six years post diagnosis?

Mary:
Well, first of all I had what is called the dream team, and also added to that is Dr. Christopher Crane, who is my radiation oncologist, who also is just the top of the top. And I just feel as though I was so incredibly blessed to have Dr. Evans, Dr. Wolff and Dr. Crane on my team working for me. Because as I stated earlier and as Dr. Wolff pointed out it wasn't just do this do that, there was a team approach. We shared opinions. We consulted. I felt as though I was part of what is going on with my care, with my healthcare.

And I'm a proactive person, and as all the people I speak with I do tell them, be proactive in your healthcare. I talk to a lot of people who don't have a clue what chemotherapy they're on. They can't remember their oncologist's name. They just have no knowledge of where their healthcare or their treatment plan is going, and I think it's very, very, very important to stay on top of what is going on in the field of where you're disease is. And it's like I point out, I may make stupid comments about a drug or whatever, but at least my doctors always treated my as though good question or let me answer that question. I always felt as though I was being active and an active participant in my healthcare. And I knew I was in the best hands I could be in, and M. D. Anderson is just that, a cancer hospital, a cutting edge cancer hospital, and I'm very grateful that I was able to be treated there.

I do want to mention one thing about PanCAN. March 9th through March 11th of this month is Raise Your Voice on Capitol Hill. It's the Second Annual Pancreatic Cancer Advocacy Day. And you can go to www.pancan.org and find out information on it. And they want to know, they need voices to come out to help fund research for this disease, and it sorely is needed. We need to get pancreatic cancer out into the forefront.

Genetics and Cancer

Andrew Schorr:
Good point. Now, I wanted to ask Dr. Wolff a question. Maybe you wondered about it, I'm sure, Mary, you've got three kids. Dr. Wolff, when somebody is diagnosed with pancreatic cancer is it then more likely in their family? Do they have to worry that they were diagnosed with it and then maybe a child or some offspring will be more likely to be at risk?

Dr. Wolff:
That's an excellent question, and we think the answer to that is yes. There are certain ethnic groups or certain ancestries that is we do take very seriously. We think, we currently estimate that five to seven percent of all patients who develop
pancreatic cancer have a family history of pancreatic cancer or other tumors that put their family members at risk. There is increasing evidence that a mutation in a gene called BRCA2 can be an important driver for pancreatic cancer. In that situation with a BRCA2 mutation there is often a family history of other cancers to include breast cancer or ovarian cancer, sometimes a history of prostate cancer in men. And it's often been associated with people who have Ashkenazi Jewish ancestry or come from Eastern European regions in terms of their family origins. Right now it may be that BRCA2 mutations are more common in other populations. I have a patient, I have two patients who are African-Americans who also have been found to have a BRCA2 mutation. So I think it's important to emphasize pancreatic cancer can be a genetically driven disease. There are other mutations that are not so common, something called Peutz-Jeghers syndrome and other genetic syndromes that put people at increased risk.

But I also want to emphasize that pancreatic cancer can be preventable. The number one way to prevent it is to stop smoking. Smoking is clearly a risk factor for pancreatic cancer, and we encourage all our patients, not just to reduce their risk of pancreatic cancer but other tumors and heart disease, to stop smoking. There is growing evidence that patients who are overweight or have what I would describe as unhealthy lifestyles, meaning they don't get enough exercise, they're not eating a particularly healthy diet or they have obesity, particularly patients who are at risk for type II diabetes, these factors also put people at risk for pancreatic cancer.

So as a general health concept we think patients should eat better, less fat in their diet, more fresh fruits and vegetables, more exercise are all critical not just to a healthy lifestyle but to reduce the risk not just to pancreatic cancer but a number of other cancers.

Andrew Schorr: You touched on one thing I need to follow up on because certainly I've done programs on cancer hereditary risk. We've talked about BRCA1, BRCA2 testing for women with breast cancer and in their families if there are a lot of first-degree relatives, and then they're monitored for earlier detection of ovarian cancer. So if someone like that, and my family happens to be Ashkenazi Jewish, if it turned out somebody had let's say the genetic test and they were being evaluated for ovarian cancer or family members were, should they also be screened somehow for pancreatic cancer? And how would you do that, because I don't think you have a blood test yet? How do you try to have early detection for that?

Dr. Wolff: That's an excellent question, and right now that's a major research initiative in some centers around the country and in Europe. Right now I guess I would say our screening for pancreatic cancer is still fairly crude in part because the pancreas is deeply seeded within the body itself. So it's not particularly accessible to
visualization with a colonoscope like you would to screen people for colon cancer. It's not on the surface of the body and is not palpable, like a breast exam allows a doctor or a woman to palpate or examine her breast or undergo mammography.

And currently there are I guess I would say two approaches to try to screen for pancreatic cancer, and in my opinion these really are going to be applicable to patients that we identify at risk, and generally that means genetically at risk for pancreatic cancer. Currently the approaches are predominantly looking for anatomic abnormalities in the pancreas using combination of CT scans, CAT scans to look at good detail of the pancreas and by using a modality we call endoscopic ultrasound, which is an ultrasound probe at the end of an upper endoscope. That's a scope that's introduced through the mouth into the esophagus and stomach and down into the first portion of the duodenum where the endoscope probe is situated, and then a very detailed ultrasound of the pancreas can be obtained. And those are anatomic things. The CAT scan and the endoscope with ultrasound are looking for abnormalities anatomic.

Now, the other approach that is going to be looked at with increasing interest--and again this is a research question, is to sample juice from the pancreatic gland. The pancreas is a gland. It secretes insulin, but it also secretes digestive juices into the intestine. Increasingly, researches are interested in sampling this juice and looking for molecular abnormalities, very specific problems at the molecular level within that pancreatic juice. We believe the day will come where either a single protein or a single fragment of DNA or a signature of proteins or signatures of different DNA or genetic fragments will tell us this person has gone from being at risk for pancreatic cancer to a patient who is starting to develop early evidence for pancreatic cancer.

The hardest part for us is that it's one thing to advise a woman to undergo a prophylactic mastectomy with reconstruction for cosmetic purposes of he breast tissue or to undergo removal of the ovaries. It's quite another thing to advise someone to have complete removal of their pancreas where they're going to be destined to require insulin for the rest of their life. So right now it's a research question. Can we pick up early evidence of pancreatic cancer before somebody has symptoms? By the time somebody has symptoms of pancreatic cancer for 80, 90 percent of patients it's too late to intervene with surgery, and so we know that we should not wait for symptoms.

But if we're going to do screening for pancreatic cancer in high risk groups, what will our intervention be? We hope eventually it gets to the point of what we call chemoprevention, meaning we don't operate to remove the entire pancreas, which is a fairly invasive and severe operation as I've already pointed out and I'm sure Dr. Evans could reemphasize, and it leaves patients with diabetes. So we wonder if there is some drug or drug combination that we could give people who seem to be
developing early signs of pancreatic cancer and reverse that cancer process and to protect them from the development of ever having pancreatic cancer. That I think is more like 20 years away.

I do think that Dr. Evans is correct that we are going to continue to see gradual improvements in our treatment for pancreatic cancer in the more foreseeable future, meaning the next five to ten years. But the whole idea of screening and detecting pancreatic cancer before it is more advanced is a research question right now, and what the intervention should be for those patients is still not well defined.

**Statistics**

Andrew Schorr:
I love these discussions because when I speak with you experts at M. D. Anderson I know we're really talking about the leading edge of medicine and a lot of questions about what makes the most sense to help people.

Dr. Evans, thank you for joining us. I want to get a final comment from you before we run out of time here. So there you are. You spend long hours in the operating room, and I know the hope is is that that person can be cured of pancreatic cancer. A word about statistics, sir. People see the statistics in pancreatic cancer and they don't look good, and then the whole family feels, Well, that's the way we're going too. But I know you've seen many examples in your career, and I hope you'll see more, where despite those statistics there are people like Mary who do, as I say, come out the other side and could go on to a longer and productive life. What would you say to people about statistics? Because I know you're asked about it every day.

Dr. Evans:
Well, I think Dr. Wolff may certainly be more eloquent with this and more knowledgeable on this aspect than me, but from my perspective I think the challenge for the cancer specialist regardless of whether he or she is a medical oncologist, surgeon, whatever the specialty is, is to provide honest information when asked yet also provide hope. And I think the importance of maintaining hope when someone is faced with what Mary had to deal with and what patients every day who are diagnosed with cancer have to deal with cannot be overemphasized. There clearly is an important relationship between the mind, the emotional state of the patient and their ability to physiologically fight the cancer. And that's something that we always have to pay attention to.

And then I think people have varying abilities to analyze and digest all of the potential complications that may be associated with complex cancer treatment. And for some patients a detailed discussion of all aspects of the treatment is extremely helpful. For other patients it may just promote high anxiety, and Mary can certainly give us her insight and comments on this. But I think that certainly
the mistake that we make sometimes is overemphasizing the statistics and the data regarding a specific disease and not paying enough attention to the importance of maintaining hope.

And certainly I think this was one of the many reasons why we tried to develop an institutional practice, not just an individual practitioner's practice but an institution-based practice for pancreatic cancer that was based upon the stage of disease that the patient was diagnosed with based upon high quality imaging so that we, as I think Dr. Wolff mentioned before I came on the program, we're then able to take patients who have either resectable or borderline resectable disease, and in those patients, even though many of those patients will not have the outcome that all of us want, we certainly will be treating them with curative intent, and that will be the goal of therapy.

And for those patients it's critically important that that be the number one priority in their life, that they invest all of the energy and emotion that they have in their cancer treatment program. I and I for one, even though we don't have the answers to all the science behind it, I think it really is terribly important. Right now in the last analysis of our database we--our true five-year survivorship of those patients who underwent a potentially curative operation was almost 30 percent, and that does not include the most recent five to six years, because we analyzed this data only for patients who had actually lived five years and were cancer-free at their five-year anniversary. So that certainly is a tremendous advance to what was reported even a decade ago, to have almost one-third of patients who undergo a potentially curative operation have the cancer not come back within five years.

Andrew Schorr:
Absolutely.

Dr. Evans:
So I think we're definitely making progress. As was mentioned, we just have a ways to go.

Remaining Positive

Andrew Schorr:
Well, thank you for being part of it, Dr. Douglas Evans. Thank for your devotion to the patient you were with the in operating room as well and then joining us to share your perspective. That was Dr. Douglas Evans who is chief of endocrine and pancreatic surgery at M. D. Anderson.

Dr. Robert Wolff, I want to thank you for sharing your insight and your devotion on the medical oncology side. And then of course Dr. Crane was mentioned. I know there are radiation oncologists who are specialists as well in pancreatic cancer and I thank them. I want to give the last word to Mary.
Mary Sharkey, you're that rare person, who I hope will be less rare in the future, who has survived the diagnosis and lived now way beyond the five-year mark, six, six and a half years and feeling good. What would you say to people listening as we close who their life has been turned upside down?

Mary:
Never give up hope. Always, always, facing adversity as you are always try to remain positive. Be proactive in your healthcare and do not allow negativity surround you. Definitely. And keep your faith strong.

Andrew Schorr:
Mary, thank you so much. We wish you all the best. I look to meeting you at the Anderson network event in the fall.

Mary:
Yes.

Andrew Schorr:
And this is been a very enlightening discussion. And I think again even in one of the most serious cancers, pancreatic cancer, still preserves hope and the promise of advances as we continue. And as Dr. Evans was saying, looking at how they're doing, continued improvement, but at a major center. And I urge you wherever you may be listening to have a consultation with a major center like M. D. Anderson where there are teams like this who are devoting themselves to it to give you the best care.

Our next program is going to be March 18th when we look at advances in stem cell transplants. You've been listening to Patient Power brought to you by M. D. Anderson. I'm Andrew Schorr. As always, knowledge can be some of the best medicine of all. Thank you for joining us. All the best.

Please remember the opinions expressed on Patient Power are not necessarily the views of M. D. Anderson Cancer Center, 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.