

Yale CANCER
CENTER
answers

WNPR Connecticut Public Radio



Hosts

Edward Chu MD

Chief of Medical Oncology

Kenneth Miller MD

Director of Supportive Care

Treatment Advances for Pancreatic Cancer

**Guest Expert:
Wasif Saif, MD**

*Associate Professor of Medical Oncology
Co-Director of the Yale Cancer Center
Gastrointestinal Cancers Program*



Yale Cancer Center Answers

is a weekly broadcast on

WNPR Connecticut Public Radio

Sunday Evenings at 6:00 PM

Listen live online at

www.wnpr.org

OR

Listen to archived podcasts at

www.yalecancercenter.org

Hi, I am Bruce Barber and this is Yale Cancer Center Answers with Dr. Edward Chu and Dr. Ken Miller. Dr. Chu is the Deputy Director and Chief of Medical Oncology at Yale Cancer Center and an internationally known expert on colorectal cancer. Dr. Miller is a medical oncologist and the Director of the Connecticut Challenge Survivorship Clinic, Ken specializes in pain and palliative care. If you would like to submit a question about cancer, please e-mail us at canceranswers@yale.edu or you can call 1888-234-4YCC. If you are interested in listening to past editions of Yale Cancer Center Answers, each segment is posted on the Yale Cancer website at yalecancercenter.org. This evening, we will answer your questions about pancreatic cancer. About 30,000 people in the US will be diagnosed with pancreatic cancer this year and unfortunately pancreatic cancer remains very difficult to treat. The good news is that researchers are making progress. This evening, Ken and Ed will take a look at the causes of pancreatic cancer as well as how you go about treating it. You will also hear about some new treatment options and clinical trials available for pancreatic cancer patients right now. So without further introduction, here are Ed and Ken and a very special guest.

- Chu Good evening, Bruce. Tonight we are joined by Dr. Wasif Saif, Associate Professor of Medicine and Medical Oncology here at the Yale Cancer Center. Dr. Saif is the Director of the GI Cancer Program here at the Yale Cancer Center and a leading expert for the treatment of pancreatic cancer. Wasif, thanks so much for being with us this evening.
- Saif Thank you very much Ed. It is my pleasure to be here today with you.
- Miller Let us start off with a very basic question, what is pancreatic cancer?
- Saif I will define pancreatic cancer in a simple way. The pancreas is a 6 inch long, pear-shaped gland in the abdomen. There are two functions of this pancreatic gland. One function is to produce juices that help with the digestion of food and the second function is to produce hormones including insulin and glucagon that control the glucose level in the body. When the part of the pancreas that produces the juices develops cancer it is defined as exocrine tumor of the pancreas, or pancreatic cancer.
- Chu When cancer develops in the pancreas, what happens to the normal function of the pancreas?
- Saif The normal function of the pancreas gets disturbed by the formation of abnormal cells. At the same time, there are other phenomena that disturb the functioning of the normal cells that can lead to malabsorption; this means that the patient may have a difficult time absorbing food. People can also develop diabetes mellitus.
- Miller Along those lines, do the majority of patients with pancreatic cancer develop diabetes?

3:23 into mp3 file http://yalecancercenter.org/podcast/Answers_July-22-07.mp3

Saif Ken, you ask a very interesting question. About 10 years ago we believed that people with a history of chronic diabetes mellitus, which means people who have diabetes mellitus for more than 10 years, may be at an increased risk of developing pancreatic cancer. However, most recent research has shown that people with no known risk factors for diabetes, such as people who are not obese or patients who do not have a family history of diabetes, that develop diabetes mellitus in one or two years' time, may develop pancreatic cancer. So in summary, I would say that the relationship between diabetes and the pancreas is like a chicken and egg.

Chu Wasif, for listeners out there can you give us a sense as to how significant a problem pancreatic cancer is?

Saif This is a major challenge. I think this is one of the major challenges that humanity is facing at this time. We see more than 30,000 cases in the United States alone which makes it the fourth leading cause of cancer deaths in the USA. We lose about 98% of these cases by December 31 and unfortunately, less than 5% of the cases live beyond five years' time. This is a major public problem.

Miller So it is common, but it sounds like a very difficult cancer to diagnose and treat.

Saif There is no question about that. The challenges are really multifactorial. The challenge is that this is a tumor which is not diagnosed at an early stage and when patients come to you they have a lot of symptoms and complications caused by the tumor. At the same time, the current therapies that we have available are really not very efficacious.

Chu What are some of the symptoms that patients who have pancreatic cancer will present with?

Saif The most common symptom that a patient will notice when they develop pancreatic cancer is pain. About 70% to 80% of the cases will start with pain. The second most common symptom that occurs in about 40% to 50% of the cases is weight loss. The third most common symptom is jaundice. Jaundice is the yellowish discoloration of the eyes as well as the skin due to obstruction of the bile duct that carries the bile from the gallbladder to the small intestine. In addition to these, there are some other interesting symptoms. One of the most interesting findings is that depression can also be a complication of pancreatic cancer in a person without any known reasons for it.

Chu Just to be a bit more specific, where does the pain occur? Is it abdominal pain or pain all over the body?

Saif Pain can occur in different areas. The most common presentation of pain is a

central pain in the lower part of the abdomen that can radiate to the back of the body.

- Chu Are there certain groups of people who are at a higher risk of developing it than others? For example, are women more at risk than men? People with a family history of certain types of cancer?
- Saif There are three main causes of pancreatic cancer. 80% of cases are the sporadic cases. Sporadic cases means that these patients develop pancreatic cancer without any identified risk factors. About 10% of cases are people who have a family history of pancreatic cancer and about 5% of cases are those who have some genetic abnormalities where they carry genes that can lead to pancreatic cancer.
- Miller There is research being conducted to suggest that the genes that are associated with breast cancer and ovarian cancer may, in fact, also lead to the development of pancreatic cancer.
- Saif That is exactly true. There are two genes which are of intense interest to us as investigators, BRCA1 and BRCA2, which are breast cancer gene 1 and breast cancer gene 2. There is a 4% to 8% lifetime risk of developing pancreatic cancer in a patient who carries a breast cancer gene. We have our own Yale Cancer Center Department focusing on researching this. Recently we have collected data on patients who have a family history of BRCA1 and BRCA2 breast cancer, ovarian cancer and patients who have a family history of these cancers and also pancreatic cancer. We are developing research that looks at the development of diabetes in these patients and trying to develop tools to screen those families.
- Chu Are there genes that have been specifically identified as abnormal or mutated in patients with pancreatic cancer?
- Saif Yes, there are multiple genes that are involved in the formation of pancreatic cancer. There are some genes which are involved at the earlier stages of the disease; one of these genes is p16. This gene is also found to be abnormal in patients who develop melanoma. We call this syndrome FAMMM syndrome (familial atypical multiple mole melanoma) and these patients can also develop pancreatic cancer. K-ras is another gene that is also present in pancreatic cancer. Another gene found to be of interest to us as investigators is the gene HNPCC. This is an abnormality in patients who also develop colon cancer before the age of 50.
- Chu Is there testing for some of these various genes that you just described?
- Saif There are tests available at different levels for these genes. These genes can be tested on the tumor level or they can also be detected in the juice that is obtained

from the pancreas. Few genes, such as the K-ras, can also be detected in the stool of some patients.

- Chu You at least have a clue for some of these patients as to which genes may be involved. What happens next in terms of translating that into treatment or detection?
- Saif This is a two-fold road. First of all we have to identify special tools and methods to identify and find those genes in screening of these patients. Then we have to find out how to develop therapies that can target those genes and prevent the development of pancreatic cancer in those people.
- Miller Are there any blood tests similar to the PSA screening for prostate cancer that can determine whether or not an individual may, in fact, have pancreatic cancer?
- Saif There are two tests that we can do. One is called CA 19-9 which stands for carbohydrate antigen 19-9, and the second marker is called CEA, which is carcinoembryonic antigen. These are the two markers which can be tested for in the blood. People who have an elevated CA 19-9 that have been tested in screening of pancreatic cancer patients, unfortunately was not found to be of much significance. However, if this number is high, it can help us identify the patient's response to chemotherapy, particularly patients who have received surgical removal of the tumor of the pancreas. We can follow that number very closely. About 10% of patients may not have a high CA 19-9 number but they could have a higher level of the CEA to follow.
- Chu I wanted to talk about treatment because obviously that is of interest to our audience. For people with early stage pancreatic cancer where you have detected it early, what happens in terms of therapy?
- Saif Those are the lucky folks who come to us at an early stage. When patients come to us with early stage disease, the best way to cure these patients, or at least give them a chance for potential cure, is to remove the tumor of the pancreas by surgery.
- Miller Is that what is known as the Whipple procedure?
- Saif The Whipple procedure is a surgical procedure that involves the removal of the head of the pancreas, gallbladder, a portion of the stomach, a portion of the small intestine and the bile duct, leaving behind enough of the pancreas so that the patient can produce enough enzymes to help the digestion and control of the glucose level.

11:43 into mp3 file http://yalecancercenter.org/podcast/Answers_July-22-07.mp3

Chu Wasif, you have played a key role in developing the multidisciplinary team here at Yale that works together to evaluate and make treatment decisions whenever you see a patient with early stage pancreatic cancer. Can you briefly review with our listeners what is involved in that multidisciplinary team?

Saif One thing that everyone has to keep in mind is that this is a very devastating disease. At the same time, this is a very complex disease. To deal with the complex problem you always need multiple minds with different specialties. I always encourage and stress the point that anybody who has pancreatic cancer should be seen by multiple modalities. These people should include; a medical oncologist, a surgical oncologist, a gastroenterologist, a pathologist, a radiologist and finally a radiation oncologist. The reason for all of these people is because it is very important that we have the biopsy performed to confirm the cancer cells, and we need a gastroenterologist to do special testing. Secondly, a medical oncologist, a surgical oncologist and a radiation oncologist, need to sit down and discuss whether this patient can receive surgical removal of that tumor. Then further treatment decisions should be made by consulting all of these people. At the Yale Cancer Center, luckily, we have specialists who are world renowned and their research is known nationally and internationally for these tumor types that are involved in the care and decision making for these patients. We not only see these patients in the clinics, but we also have a special tumor board where we discuss these cases with a panel of specialists from all modalities.

Miller We would like to remind you to e-mail your questions to us at canceranswers@yale.edu. We are going to take a short break for a medical minute. Please stay tuned to learn more information about the treatment of pancreatic cancer with Dr. Wasif Saif

Medical minute

Breast cancer is the second most common cancer in women. In Connecticut alone approximately 3,000 women will be diagnosed with breast cancer this year. But there is new hope. Earlier detection, noninvasive treatments and novel therapies provide more options for patients to fight breast cancer. In 2007, more women are learning to live with this disease than ever before. Women should schedule an annual mammogram beginning at age 40 or earlier if they have risk factors associated with the disease. With screening, early detection and a healthy lifestyle, breast cancer can be defeated. Clinical trials are currently underway at federally designated comprehensive cancer centers such as Yale Cancer Center to make innovative new treatments, which have not yet been approved by the Food and Drug Administration available to the patients. More information is available at yalecancercenter.org.

Miller Welcome back to Yale Cancer Center Answers. This is Dr. Ken Miller. I am here with my co-host, Dr. Edward Chu and our guest today, Dr. Wasif Saif who is

14:46 into mp3 file http://yalecancercenter.org/podcast/Answers_July-22-07.mp3

discussing the latest information on pancreatic cancer.

- Chu Wasif, I want to start out with an e-mail from Ann who lives in West Hartford. She says that a family member of hers is undergoing treatment for pancreatic cancer at a local hospital. She has lost a considerable amount of weight. Do you have any advice you could share with her to help with dietary needs?
- Saif One thing we all need to understand is that the pancreas is a gland which also produces juices that involve the digestion of food. When the patient loses weight with pancreatic cancer, which is the second most common symptom of pancreatic cancer but chemotherapy can also play a role, these patients must be evaluated by a specialist in diet or nutrition. At the same time, sometimes these patients need supplements of pancreatic enzymes which can aid digestion of the food.
- Miller Do you recommend any other type of nutritional supplements to go along with those enzyme replacements?
- Saif We use multiple high protein and high calorie juices and drinks for these patients. As you may know, there are special drinks and juices with high calories content for diabetic patients as well. Definitely have them consult with a nutritionist and keep a close eye on the calorie intake.
- Chu Is there any role for either chemotherapy or radiation therapy once the pancreas that has the tumor has been removed?
- Saif The problem is that even if we remove the pancreas there is still a very high risk of the cancer coming back. This is the role of chemotherapy. Studies have shown that patients who have received chemotherapy double the timeframe during which the tumor will not come back. Historically, studies done in the USA have shown that patients, who have a tumor in the head of pancreas and receive chemotherapy with radiation therapy, have a long-term survival rate and also delay the onset of the disease coming back.
- Miller For listeners out there, this is called adjuvant chemotherapy, or adjuvant radiation therapy.
- Saif The intent of this chemotherapy or radiotherapy is to prevent the cancer from coming back.
- Miller We have another e-mail question here from Linda who lives in New London that is similar to the first one. She is talking about her father who is being treated for pancreatic cancer and has lost weight. Her question is, do you recommend high doses of vitamins or other kinds of alternative therapies?

17:33 into mp3 file http://yalecancercenter.org/podcast/Answers_July-22-07.mp3

- Saif This is a very touchy question. First of all, we have to understand that patients are given vitamins based on what we believe and that combination vitamin is the best way to go. At the same time, we have to keep in mind that certain vitamins can also aid the tumor to grow. We give chemotherapies that try to interfere with the working of those vitamins at the tumor level. We are working on these issues and looking into complimentary medicine in corporation with pancreatic cancer therapy. We are looking at special drugs, which are not cancer drugs, which we can develop and incorporate into the treatment of pancreatic cancer.
- Chu What is one of the very interesting studies that you are working on for pancreatic cancer?
- Saif I am very blessed to say that we are the pioneers in the United States who developed the drug called PHY906. This drug is a derivative from a Chinese botanical drug that has been used for the last 1500 years. At the Yale Cancer Center we were able to develop this drug into pill form. In our initial studies done for colon cancer, and also in experiments on animals, we found that this drug, which is used in China for ailments of GI such as diarrhea, can not only help make chemotherapy much more tolerable with less side effects, but also increases the efficacy of chemotherapy in terms of shrinking the tumor. At the Yale Cancer Center we are running a study that combines this PHY906 with a chemotherapy, also given by mouth, called capecitabine or Xeloda. We are running the study for patients with pancreatic cancer who have failed chemotherapy gemcitabine, which is the only chemotherapy approved by the FDA. We are seeing very promising results at this stage.
- Chu The beauty of this trial is that you have two medications that are taken orally. This obviously helps patients maintain their normal activities of daily living. It sounds like this Chinese herb actually may be able to reduce side effects and may also help boost the activity of the traditional chemotherapy.
- Saif Exactly, it is a two in one benefit. Decreasing the side effects and increasing the efficacy; it is the best combination you can ask for.
- Chu Just to emphasize to the listeners out there, this particular trial that you are conducting here at Yale is focused on patients who have metastatic disease.
- Saif Exactly, patients with metastatic disease who have failed chemotherapy gemcitabine can join the study.
- Chu And what does metastatic disease mean for those listening?
- Saif Metastatic disease, or advanced pancreatic cancer disease, means patients who are not a candidate for surgery and the tumor has spread into the distant organs such

as lymph glands, the peritoneum, which is a thin lining in the abdomen, the liver, the lungs, etc.

- Chu Wasif, you are one of the leaders in this country for developing clinical trials for metastatic pancreatic cancer. What are some of the other studies that you are actively pursuing right now?
- Saif We recently finished a study with a drug called Genexol-PM. I thank my patients and their families for contributing because we did a great job in learning about that agent. We are now developing at initial stages, experiments trying to combine that drug with gemcitabine. Just two weeks ago I opened another study with a drug called AV944. This is a very interesting drug because it consists of chemo by mouth, again making the drug more convenient, and this drug is involved in the inhibition of the proteins which are required for DNA synthesis. This drug has shown activity in pancreatic cancer that has failed gemcitabine. We just started a study at Yale Cancer Center where this drug will be given in combination with gemcitabine. The two good points about this study, and I would encourage people to contact the Yale Cancer Center and my team, is that the patient will be able to get that drug, which is the standard of therapy, plus they will be able to get another drug which seems to be very beneficial in pancreatic cancer that seems to increase the efficacy of Gemzar without adding anything to the toxicity. This is available at the Yale Cancer Center.
- Miller Can you tell us a little bit about targeted therapies in pancreatic cancer. What does that mean?
- Saif Targeted therapies mean that we develop drugs which target a particular hormone receptor or some growth factor involved in the process of cancer formation. Unfortunately, this year we have multiple studies presented at the National Meeting of Cancer that we are publishing from Yale Cancer Center at different media including Medscape, and those studies have not shown any benefit at this time to the addition of gemcitabine. The only target therapy which has shown some benefit statistically, but may not be beneficial clinically, is a drug called Tarceva, or erlotinib. That is the only targeted agent approved by the FDA at this time for stage IV or advanced pancreatic cancer.
- Chu What does Tarceva specifically target?
- Saif Tarceva targets a growth factor receptor called EGFR which is an epidermal growth factor receptor. It is a tyrosine kinase inhibitor that is one of the targets involved in the growth of the tumor.
- Miller I have a somewhat unrelated question that I have been thinking about. I know that you are impassioned about fighting pancreatic cancer. Why did you choose this

disease in particular?

- Saif It is a thing of passion, and it is also a challenge. I have always enjoyed challenges and have taken the pancreas as my personal problem. I take it very personally and my aim is to focus all of my life and devote all of my energy to finding a better treatment, or a cure, for this disease. It is really a personal stand that I have taken against pancreatic cancer because somebody has to change the outcome for these patients.
- Chu As you have said in many of your lectures, progress has been slow in terms of making significant advances in treating pancreatic cancer once it is metastatic. Any thoughts as to why pancreatic cancer is so difficult to treat once it has metastasized and spread beyond the local confines?
- Saif There are three factors to it. First of all, you know the pancreas is a hidden organ and by the time the patient comes to see us, the disease has involved the vital organs. Secondly, this disease deranges the entire functioning of the body and the patient is very sick. Thirdly, there is less energy, effort and resources spent on the research of pancreatic cancer. As you may know the other name for pancreatic cancer is the orphanage tumor. A tumor, which was always an orphan, that the research, the money and the grants are not spent on the development of this tumor.
- Miller There is a great deal of research, in addition to the research that you are doing, to develop new clinical trials and new treatments, but there are a great deal of basic resources that hopefully we can eventually bring into the clinic. Can you tell us a little bit about what is going on here at Yale?
- Saif We have basic scientists who are developing special models and testing novel agents in the pancreatic cell lines. At the same time, we are developing multiple new agents which are affecting different targets in the process of cancer formation; such as heat shock protein inhibitors, also the drugs, a combination of drugs which has shown activity individually in pancreatic cancer. We are trying to improve those drugs, but understanding basic knowledge as well as trying to implement how best we can use these drugs in combination with each other or with radiation therapy is the key to improvement in pancreatic cancer.
- Chu Again, if someone out there who is listening this evening would like to find out more about your clinical trials how do they go about doing that?
- Saif People can go to www.yalecancercenter.org. I think that is the easiest way to get a hold of us. At the same time, we are only a telephone call away from you. You can give us a call and approach the cancer center or my team directly. We will be

very happy to help you in the fight against pancreatic cancer.

Miller Wasif, I want to thank you for joining us and for all the exciting work that you are doing on behalf of people with pancreatic cancer.

Saif Ken and Ed, I really appreciate you inviting me. Before I finish today's discussion I have to thank my patients, and particularly the grant that we received from the wife of one of my patient's and their support of pancreatic cancer research.

Chu This has been a great session, very informative. We look forward to having you on a future show.

Until next week, this is Dr. Edward Chu and Dr. Ken Miller from the Yale Cancer Center wishing you a safe and healthy week.

Thank you doctors. If you have questions, comments, or would like to subscribe to our podcast, go to yalecancercenter.org where you will also find past broadcasts in written form. Next week on Yale Cancer Center Answers, join us for a discussion on supportive care and pain management with our host Ken Miller.