

Yale CANCER CENTER *answers*

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Options for Patients with GI Cancers

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Welcome to Yale Cancer Center Answers with your hosts doctors Francine Foss, Anees Chagpar and Dr. Steven Gore. Dr. Foss is a Professor of Medicine in the Section of Medical Oncology at Yale Cancer Center, Dr. Chagpar is Associate Professor of Surgical Oncology and Director of the Breast Center at Smilow Cancer Hospital and Dr. Gore is Director of Hematological Malignancies at Smilow. Yale Cancer Center Answers features weekly conversations about the research diagnosis and treatment of cancer and if you would like to join the conversation, you can submit questions and comments to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC. This week you will hear a conversation about Gastrointestinal Cancer with Dr. Stacey Stein. Dr. Stein is an Assistant Professor of Medical Oncology at Yale School of Medicine. Here is Steven Gore.

Gore Let's start off by having you tell me a little bit about what you do and what cancers your practice includes?

Stein We actually see patients with cancers spanning the entire GI tract, so it is actually several different diseases, and that includes patients with cancer of the esophagus, the stomach, the pancreas, the liver, the biliary system, colon cancer, rectal cancer and anal cancer, so it is several different diseases.

Gore Wow, that is a lot of territory to cover, are all those cancers very similar or are there differences between them?

Stein There is some commonality, but there are quite a few differences, obviously anatomically there are different options for radiation therapy and those things are often dictated by anatomy, but a lot of the differences are also at the molecular level where we are able to offer different therapies based on the mutations of the different cancers that we treat.

Gore How do patients find out they have a cancer in their GI tract?

Stein Often this may come to the attention of the patient and then to their primary care physician first. Sometimes it can be because either they are having difficulty swallowing, having pain in the abdomen, maybe having difficulty with going to the bathroom or noticing blood somewhere in the GI tract and then usually the patient may either be referred for imaging or to a gastroenterologist that can perform a scope that would visualize the cancer and then usually after there is evidence of a tumor being somewhere in the GI tract, then they are referred to us for evaluation.

Gore And would they be referred to you as a medical oncologist or are they usually referred to a surgeon, how does that work?

Stein It depends on who saw the patient first and what they think treatment may encompass, but whether the patient was referred to us first or to surgery, we all work together in a multidisciplinary fashion, and we actually do have multidisciplinary clinics where we try to have the patient come

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and see us and the surgeon. I also treat a lot of patients with liver cancer. We also have a multidisciplinary clinic where the patient sees me and a liver doctor at the same time, so we try to make it as easy and as comprehensive as possible on the initial visit.

Gore If I were a patient referred to one of these multidisciplinary clinics, I might see more than one physician, both the surgeon and the medical oncologist?

Stein Yes, sometimes it does not always happen on the same day, but if we can we try to do that because I think it gives people more information at the same time and we are able to make decisions quicker and expedite a treatment plan quicker.

Gore And would I come out that same day with the treatment plan?

Stein Sometimes, yes, depending on whether someone has their workup here at Yale or at another place, we have all the information together, we meet together at conferences where it is not just surgeons, but the gastroenterologists are present, the radiologists, the radiation oncologists, the pathologists and we look at all of the imaging, if there are any biopsies and review the history together and try to come up with a plan, based on everyone's input and the information that we have.

Gore And I guess depending on the kind of surgery that is going to be performed, if there is surgery, depending on whether you are taking out part of the esophagus or losing some of your intestine, there may be adjunctive supportive care that might be needed help with swallowing or ostomy bags and things like that, is that part of it?

Stein There are a lot of people that are involved in the care of our patients and often the treatments, even when it is surgery, we are often giving other treatments prior to the surgery to help prevent recurrences in the future, so for diseases like esophageal cancer or rectal cancer that may mean giving chemotherapy and radiation prior to the surgery. For certain other cancers like stomach cancer it may involve just chemotherapy prior to the surgery and actually we are looking at a clinical trial now of giving chemotherapy for patients with pancreatic cancer before their surgery to try to decrease the rate of recurrence. Then we also have a lot of other people involved in our patient's care, as you mentioned. So we have dieticians, social workers, care coordinators, there may be people involved in care of if someone needs an ostomy or if they have any drains or those kind of things. So, there are a lot that go into the care of these patients. Sometimes patients need nursing services at home that we set up and a big goal of our care is always to try to decrease the inconvenience that all these treatments cause and the side effects. The pain associated with it. Wherever the cancer is in the GI tract there is often difficulty with eating and digesting food and so it is a big part of the care of our patients to work on optimizing their nutrition and making things as easy as possible.

Gore It sounds like it could be easily very overwhelming for patients and their families.

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- Stein It is overwhelming. A cancer diagnosis is always overwhelming and so while it is always frustrating when people get that information, we try to expedite a care plan because that initial period of time is very anxiety provoking until a plan is in place and even then dealing with the uncertainty of the diagnosis and how it impacts peoples' ability to work or the symptoms that they have, impacts a whole family and it is very important to be aware of that and try to address it as best as we can.
- Gore So are there psychological services offered as well?
- Stein Yes, we have social workers and care coordinators, there are therapists available and actually, Smilow will have a psycho-oncology division soon as well, which I think will be very helpful. We also have support groups for our patients.
- Gore You had mentioned clinical trials in pancreas cancer. I think you said where you are giving chemotherapy upfront. I know pancreas cancer certainly has a reputation of being the worst cancer, or one of the worst cancers, and I think people hear those words with a lot of trepidation, are there reasons to start being more optimistic about pancreas cancers?
- Stein There have been a couple of regimens recently that have extended the lives of people with pancreatic cancer and while it has been incremental progress, I am very hopeful that we are going to continue to see more progress. There are a couple of different areas that we have been focusing on. One is a clinical trial that Dr. Jill Lacy is running of giving chemotherapy called the FOLFIRINOX regimen, which is aggressive chemotherapy that we give to patients with metastatic disease before and after surgery when they have curable disease and we are hoping that by doing that we can decrease the risk of recurrence. But also we are looking at molecular targeted therapy as well. We know even though it is only a small subset of patients, there are some patients with pancreatic cancer that have a BRCA mutation and if people are familiar with that term, usually you hear it.
- Gore It sounds like a vegetable.
- Stein It is BRCA and most people know about that in relation to breast cancer.
- Gore That's why I am familiar with BRCA.
- Stein Right, so it is very well known that some women with breast cancer carry this gene and that it could be something that is passed on in a family, but actually, there is also an association with pancreatic cancer and so we will be opening a trial here giving patients Olaparib which is a PARP inhibitor, which has been used in other patients that carry this and we are hoping that this will help benefit that group of patients with pancreatic cancer as well.

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Gore I am guessing our audience has no clue what a PARP inhibitor is.

Stein There is so much molecular therapy right now looking at the specific mutations that are in our patients' cancers and what we are looking at is really at the molecular level to say what proteins are not functioning well in this cancer. What proteins are supposed to be there and are not because of the cancer. What proteins are supposed to be there at low levels and are at very high levels that should not be there in the cancer and we are trying to target therapy directed at those specific proteins to try to increase or decrease their levels to make them more like a normal cell, and this drug is just one example of a drug like it that may help to kill these cancer cells.

Gore That is given with chemotherapy, is that right?

Stein Right.

Gore I guess with the BRCA mutation, it has something to do with the way the cells repair the damage, to the DNA that the chemo does.

Stein Correct.

Gore And the PARP inhibitor impacts that?

Stein Right and so there is a reason to believe that at least for the patients with a BRCA mutation that this may benefit them more than just chemotherapy alone.

Gore So will that trial be restricted to patients with that mutation?

Stein Correct, yes.

Gore Wow, we are really getting very specific now compared to the days when anybody with pancreas cancer or whatever cancer could all be enrolled in the same trial.

Stein Absolutely, and so it is very important that when we are thinking about treatment options for any of our patients that we start thinking about the specific mutations in their cancer and that often tailors the treatment to that specific patient, and I can give a couple of examples of that. There is another protein in breast cancer called HER2 and about a third of women with breast cancer have too much of that protein and the breast cancer group has already come up with several antibodies now targeting that protein, and the people in GI oncology thought that was completely unrelated to us until a couple of years ago, when we found out that about 15% to 20% of people with cancer in the esophagus and stomach also have too much of that protein and so we have had clinical trials now looking at that protein in some of our patients and have seen some benefit. So that is another

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area where we are looking at specific mutations to target therapy. It is also very important in colon cancer. We know that patients with colon cancer, about half of the tumors have mutations in something called the RAS gene and that is going to be a very important target coming up in the future and we have clinical trials for these patients as well whether they have the mutation or do not have the mutation. We are now starting to target therapy towards that type of tumor as well.

Gore That is fascinating and I am just thinking, not every patient has access to tertiary or quaternary cancer centers like Yale Cancer Center and Smilow, or one of the other great cancer centers in the North East. Do patients, who are treated at other places, do they have access to these molecular tests? What should patients be advocating for? What should they be thinking about, they are so overwhelmed with their diagnoses?

Stein It is very difficult when you are getting all this information to sort out what is the right treatment and I would say, so for some of these tests, they have been around a couple of years, they are already approved by the FDA and they are available to everyone. So, every patient that has a gastric cancer or esophageal cancer should be tested for that HER2 protein. Every patient with colon cancer and rectal cancer is now being tested for a specific RAS protein called KRAS. But as we are getting new information, we are really trying to stay on the cutting edge of doing more than just those tests that the FDA has already approved. So, we actually have larger panels here that we are testing patients based on specific disease and I think that it is a good idea at some point to be seen at a large center where you could have some of that other testing done and at least then be able to go back to the community with that information.

Gore We want to pick up on that thread right after our break. But now, we are going to take a short break for a medical minute. Please stay tuned to learn more information about treatment options for patients with gastrointestinal cancer with Dr. Stacey Stein.

*Medical
Minute*

Genetic testing can be useful for people with certain types of cancer that seem to run in their families. Genetic counseling is a process that includes collecting a detailed personal and family history, a risk assessment and a discussion of genetic testing options. Only about 5% to 10% of all cancers are inherited and genetic testing is not recommended for everyone. Resources for genetic counseling and testing are available at federally designated comprehensive cancer centers such as Yale Cancer Center and at Smilow Cancer Hospital at Yale-New Haven. The Yale Cancer Center Cancer Genetic Counseling Program is a new frontier in the fight against cancer. The program provides genetic counseling and testing to people at increased risk for hereditary cancer and helps them to make informed medical decisions based on their own personal risk assessment. This has been a medical minute brought you as a public service by Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven, more information is available at yalecancercenter.org.

Gore Welcome back to Yale Cancer Center Answers. This is Dr. Steven Gore and I am joined tonight by my guest Dr. Stacy Stein. We have been discussing treatment options for patients with

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gastrointestinal cancers. Stacey, before the break, we were talking about making sure that you had access to certain standard molecular tests performed on your tumor biopsies and you had mentioned that it is always a good idea to get a consultation at a specialized center and I certainly agree with you, in my experience it has been very important for my patients. It sounds like at least the one thing patients should feel like they can do would be ask their surgeon, will this be processed for whatever gene testing is appropriate. Something people should feel empowered to ask?

- Stein Right, absolutely, I think that one should always feels comfortable asking questions and even in your health care team.
- Gore It's hard.
- Stein It is hard, but I think people are doing it, certainly my patients always come in with good questions and they do their own research.
- Gore But you're not a very scary doctor.
- Stein Thank you. Another focus of mine is liver cancer and I would say that is another area where it is so important to have a multidisciplinary approach to look at each patient and our goal actually for our weekly liver conference is to really present every new patient, whether they are referred to a liver specialist, a medical oncologist, an interventional radiologist, to the transplant group and we all look at the patient from our own perspective and try to come up with a plan that is best for each patient.
- Gore It is a very confusing area for many lay people, I know many patients who have breast cancer and then they find that there are tumors in their liver and they think they have liver cancer, is that right?
- Stein That is a little bit confusing, there are many tumors that can spread to the liver. Just by the nature of the blood flow to the liver it is very common in several different cancers to have tumors form in the liver, but it is actually not liver cancer, it is metastatic disease from where the tumor started, whether it was in the colon or breast or somewhere else and the treatment that they get is primarily still focused as either breast cancer treatment or colon treatment. When I mention liver cancer, actually there are really two different types of cancers you can get in the liver. I think of the liver as a tree and I think of it as big vessels going into the tree like a tree trunk and then they branch out, branch out, branch out and at the end are the leaves and the leaves are doing the work. So, if there is a cancer that happens in what I called the leaves of the tree, or the hepatocytes, that is a liver cancer we call hepatocellular cancer. If it happens in the branches of the tree, anywhere from the big trunk to the main branches to the little branches that go right up

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to the leaves, that is called cholangiocarcinoma and that could actually happen in the liver or outside the liver and so that is a kind of biliary cancer.

Gore Biliary, easier to say than cholangiocarcinoma.

Stein Yes, cholangiocarcinoma is called biliary cancer. So there is hepatocellular cancer, which we call HCC or cholangiocarcinoma, which is biliary cancer and they are really treated quite differently.

Gore Just going back to that confusing point, if I have colon cancer that has spread to the liver and you were to do a biopsy, it would not look the same as one of these 8 cc's under the microscope, right?

Stein No, it would look just like colon cancer, but being taken out of the liver. So, it is very important when someone is first diagnosed that we do have a biopsy, so that we are sure where that cancer is coming from because the treatment is really dependent on that information.

Gore Are there any patients who have a particular risk of developing one of these primary liver cancers?

Stein Absolutely, it is very well known that there are groups of people that are at risk for developing HCC. Patients that get cirrhosis, which is scarring of the liver that happens over many years are at high risk for getting liver cancer and that can happen from a variety of reasons. Most commonly in the world it is from hepatitis B infection and so most of the patients are in Asia. In this country it is more common for people to get cirrhosis either from a lot of alcohol use over many years or from hepatitis C and I have to say one of the most exciting advances in this field recently is the number of new drugs for treating hepatitis C and I really hope that this impacts us to having a lower number of people diagnosed with liver cancer in the future.

Gore Is that one of the hepatitis viruses that we have vaccines for?

Stein We have a vaccine for hepatitis B, and all babies in this country are vaccinated as babies. So the rate of hepatitis B for people born here is low, but we do not have a vaccine for hepatitis C and so it has been a real problem in how to prevent people once they get infected with hepatitis C and they continue to have the virus in their liver of how to treat them.

Gore These people would know they had it because they jaundice, become yellow?

Stein So we want to prevent it from getting to that level and unfortunately, most people do not know that they have hepatitis C and it is a real epidemic in our country. Many people from the baby boomer generation, and Steve is raising his hand right now, may not realize that they are infected with hepatitis C. The recommendation now is anyone in that age group, if they have

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never been checked to at least have just one test to make sure that they do not have hepatitis C because we have treatment for it now and so we really want to identify everybody. If we wait until they have cirrhosis we have really missed an opportunity.

Gore And you think that hopefully if we can treat the hepatitis C, there will be less liver cancer?

Stein Absolutely, because that will prevent them from getting cirrhosis in the future and it is that chronic damage to the liver over many years that allows for this mutation then to happen in the cells and the liver to form cancer down the road.

Gore So all you fellow boomers who are out there make sure, at your next general physical exam, to ask if you have ever been tested for hepatitis C. It sounds like that is really good preventive care.

Stein Absolutely.

Gore You have mentioned that liver cancers also have a multidisciplinary approach. Is surgery a part of that therapy too, how can you take out the liver?

Stein Well there are a couple of ways we do that. One is that if the cancer in the person's liver function are within certain criteria, they may be eligible for a liver transplant.

Gore A transplant for cancer?

Stein A transplant for cancer, and it is not for every patient with liver cancer. They have very strict guidelines for this, but for some patients absolutely, yes.

Gore Does that work?

Stein It does, if they are within certain criteria they have a very high cure rate and then also you remove that person's diseased liver because they usually also have cirrhosis. So, it is very important that anyone with a new diagnosis of liver cancer really be evaluated for all these options to make sure that they are not being passed over on any potential options, especially because this is a curative one.

Gore Yeah, I am sure you cannot get that kind of treatment at every hospital.

Stein No, that is only in tertiary centers. Fortunately, Yale does have a liver transplant program that is very active and they are part of an evaluation for all new patients that we bring to conference and they do a very comprehensive evaluation to see if someone is potentially eligible for that.

Gore So, what about people who cannot get the liver transplant?

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- Stein Sometimes they may still be eligible for surgery where just part of their liver gets removed and we try to offer that for anybody who may be eligible because that can also be potentially a cure of removing the cancer.
- Gore And for people that can't have that?
- Stein It depends if the tumor is still only in the liver or if it has spread outside. If it is only in the liver and the person has pretty good liver function, the cirrhosis is not too advanced, they may also be eligible for treatments that we call local regional treatments and those are done usually by an interventional radiologist. They are a very specialized kind of physician and what they do is they actually look to see where the tumor is in the liver or sometimes multiple tumors, where the blood supply is to those tumors and they are able to go in, they actually put a needle into someone's groin, thread it up into their liver and are able to sometimes direct either heat or chemotherapy directly into the tumors and there is another option also, something called Y90, which is where radioactive beads are distributed into parts of the liver to help control the disease as well.
- Gore Wow, it sounds very hi-tech, and that heat sounds kind of painful, I do not know?
- Stein We try to be very careful about how these procedures are done and who they are offered to, to make sure that we are not damaging the liver further, but often these treatments are usually not curative, but they usually help and so it is an important part of the full evaluation to offer these treatments as well.
- Gore And are there any new molecular therapies for liver cancer or other chemotherapies that can be helpful?
- Stein Right now, there is one chemotherapy that is approved by the FDA for liver cancer and that is sorafenib, but we are always looking for new drugs also for liver cancer. Unfortunately some of the more recent clinical trials have not shown a benefit, but we are always looking for new drugs, we are starting to work on molecular studies for liver cancer. A lot of people right now when they have liver cancer they get diagnosed just by their MRI and without a biopsy, but I am always interested in getting a biopsy on patients because I think that just helps us to advance the field further to have a better understanding of what mutations are happening in this cancer and what we can offer, but I have to go back and say, I think the most important thing is prevention and to really start further back and try to prevent the cirrhosis because we really know that that is the main risk factor for liver cancer.
- Gore And are things different for this other biliary cancer that you talked about?
- Stein That is a little bit different and the treatments unfortunately are very experimental, doing a transplant for those type of patients and most transplant centers do not offer liver transplant for

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cholangiocarcinomas, but it is sometimes possible to do surgery and remove the tumor, so we always have a surgeon involved in our planning and for patient's that are not eligible for surgery we do have different chemotherapy options. We have standard chemotherapy that we use and we are also participating in a trial that is through a large cooperative group in this country looking at something called a MEK inhibitor for patients with this type of cancer and that is just another type of drug that is targeting a certain protein that seems to not be regulated well in this type of cancer.

Dr. Stacey Stein is Assistant Professor of Medical Oncology at Yale School of Medicine. We invite you to share your questions and comments, you can send them to canceranswers@yale.edu or you can leave a voicemail message at 888-234-4YCC. As an additional resource, archive programs are available in both audio and written form at yalecancercenter.org. I am Bruce Barber and hoping you will join us again next Sunday evening at 6:00 for another addition of Yale Cancer Center Answers here on WNPR Connecticut's Public Media Source for news and ideas.