Yale CANCER CENTER answers

WNPR Connecticut Public Radio

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Gastrointestinal Cancer Treatments

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Welcome to Yale Cancer Center Answers with doctors Francine Foss and Lynn Wilson. I am Bruce Barber. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Wilson is a Professor of Therapeutic Radiology and he is an expert in the use of radiation to treat lung cancers and cutaneous lymphomas. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu, and the phone number is 1-888-234-4YCC. This week, Francine and Lynn welcome Dr. Stacey Stein. Dr. Stein is Assistant Professor of Medical Oncology at Yale School of Medicine and she joins us this evening for a conversation about GI malignancies. Here is Francine Foss.

Foss Let us start off by having you tell our audience a little bit about what got you interested in this area of GI malignancies.

Stein I recently finished my fellowship and I found that some of my most challenging and rewarding patients to take care of had GI malignancies, and I also found a great mentor who does research in GI malignancies and the combination of the two led me to pursue this field.

Wilson What types of gastrointestinal tumors do you see? Tell our listeners about what GI tumors are, in general.

Stein GI tumors encompass a lot of different areas. We take care of patients with esophageal cancer, gastric cancer, liver cancer, pancreas cancer, and colorectal cancer.

Foss Can you talk a little bit about the whole issue of cancer in the GI system? I think that is one of the easiest areas to find cancer because we look in there with scopes.

Stein We have an excellent screening tool for colon cancer. There are many screening tools, but one of the most widely used is colonoscopy. All people should be getting screening colonoscopies starting at the age of 50, and sometimes younger. If they have a family history, they should talk to their primary care doctor to see if they should be getting screened sooner. It is an excellent screening tool. We are able to then diagnose people at an early stage which allows us to achieve a cure. Unfortunately though, for many of the other GI cancers, we do not have good screening tools and we are working on finding screening tools that we can use because for many cancers, like pancreatic cancer for example, unfortunately we often diagnose someone when the cancer is more advanced, and therefore not necessarily curable.

Wilson Aside from a family history, what are some other risk factors for these various cancers?

Stein We do know of a few risk factors. One is obesity, and that has now been found to be a risk factor in many cancers. Interestingly, while the rates of some cancers are going down, the rates of some cancers are on the increase in the United States because of obesity, and specifically for GI cancers, one of those is cancers of the esophagus. We are seeing more cancers at the area where the esophagus meets the stomach, which we call the GE junction, and there is an increase in those

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cancers. Part of that is due to the rise of obesity in this country. Another cancer that has been impacted by increased rates of obesity is liver cancer. Worldwide, liver cancer is most often caused by the hepatitis viruses, but in the United States, obesity is becoming a more common risk factor for liver cancer.

Foss Stacey, can you define obesity? A lot of us are a little bit overweight, but when you say obesity, are you talking about morbid obesity? At what level are you at increased risk for developing these GI cancers?

Stein The way doctors define the word 'obesity' is by something called the BMI, or body mass index, and that looks at a patient's height and weight. Basically, someone who has a BMI of over 30 is obese and that puts them at increased risk, and then even higher numbers for the BMI define morbid obesity.

Wilson And with regard to the esophagus, how about alcohol and smoking?

Stein Those are very important risk factors, especially for esophageal cancer. For colon cancer, which is the most common cancer that we treat, there probably is a small increased risk with smoking, although it is not as tightly associated as with other cancers like lung cancer, and also diet is a risk factor. Diets that are higher in fruits and vegetables and lower in red meat are diets that are associated with a lower incidence of colorectal cancer.

Foss Are there other dietary issues that we should pay attention to?

Stein There are some things potentially on the horizon that may be interesting. There is a lot of research now looking at vitamin D levels and risk of colon cancer. It is unclear now what the recommended dose should be. It might be significantly higher than what the recommendations are now, but I would say that that is still an area of research.

Foss Can you comment on the issue of barbequed foods and processed foods like hot dogs and things that may potentially have carcinogens that we are told are bad for us?

Stein There probably is an increased risk with those foods and the rate of cancers, especially in the GI tract. Fresh fruits and vegetables, you cannot get enough of those in your diet, and staying away from processed foods, food with nitrites, and overall just decreasing red meat intake, would be a healthier lifestyle.

Wilson What are some of the challenges that we face in treating these various malignancies? Presumably, GI cancers, the esophagus versus the pancreas versus the colon, tell us about prognosis, equal stage, for equal stage. Why do some areas seem to do better than other ones?

Stein Some of it has to do with the ability to screen. In colon cancer, for instance, when patients are

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found to have cancer on a colonoscopy, it is usually in an early stage. The way we define it, there are four stages, and basically, the higher the number the greater the disease has spread. In stage IV cancer, that means that the cancer has spread outside of the organ that we are talking about and, unfortunately, when a cancer is diagnosed at that stage, we often cannot achieve a cure because it is not curable with surgery. The earlier we can find the tumors the better the prognosis. Unfortunately, many of the symptoms that are associated with early stages of these cancers are very nonspecific, meaning that when someone is diagnosed with advanced pancreas cancer, sometimes they will say that they just felt a little bit of bloating. Maybe they had a little bit more constipation or felt like they were full a little bit earlier before they finished their meal, but they are so nonspecific that a doctor may not necessarily do a complete screening workup when a patient has those symptoms. It would really be great if we had other tests like a blood test or something in the future that we could look at to define who is at higher risk to have some of the screenings. It is very important to know your family history because if someone has a strong family history of these cancers, then in some instances we would do more invasive tests on a routine basis. Such as if someone has a strong family history of pancreas cancer, sometimes now we do routine scopes to take a look for early stages of disease, because, unfortunately, often when it is found, it is no longer curable, and that is a much bigger challenge to treat.

Foss Can you talk about some of the other diagnostic modalities such as things like MRIs and PET scans and how they might be helpful to make the diagnosis?

Stein Usually if someone has symptoms, they will have some kind of imaging modality to find the cancer, and that often starts with a CAT scan, but we do use other modalities. Part of it also is when we are making a diagnosis, we need a biopsy, and so we then do other tests to help get the biopsy. For colon cancer, it is often a colonoscopy; for esophageal cancer, we could do an endoscopy where a scope is put down the throat and then biopsies can be obtained from that. From the pancreas, the GI doctors can do something called an ERCP where they put a scope down and it can actually get over to the pancreas to take a biopsy. Sometimes we do that just with imaging, we call it an MRCP because it is an MRI of that area of the body and we could get a better look at where the tumor is.

Foss Is it common to get a needle biopsy at the time the patient has the procedure, the diagnostic procedure like the scan, or do you oftentimes come back later because I know in breast cancer it is common that when a woman goes for an ultrasound of a lump, to get a biopsy done at that time?

Stein It depends on the test that the person is having. If it is some kind of scope, then obviously we always try to get a biopsy at the time of the procedure if they see anything abnormal, and they will take multiple biopsies to see if there is any cancer in that area. If it is an imaging test like a CAT scan, then usually the results would come back to that patient's doctor and then the biopsy will be scheduled at a later time.

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Wilson These procedures that we have discussed, the majority of these are outpatient procedures. So, the patient does not have to sleep over in the hospital. Is that correct?

Stein Correct, and I would say that in general for all of the treatments that we do, we try to make everything an outpatient procedure. When patients come and see us after they have been diagnosed and when they are receiving chemotherapy, this is pretty much all outpatient. When patients comes to us, they are able to get their blood work done, see their doctor and get their treatment all on the same floor in one day, and almost everything is done as an outpatient. We try to make it convenient.

Wilson If we are doing a biopsy on an organ, say like the liver or the pancreas, for example, where we cannot get a scope to a location where we can see something abnormal on a scan. Is that a situation where we might do something called a fine needle aspiration, and what is that procedure?

Stein We like to get as big of a biopsy as possible in general, but some areas of the body are harder to get a biopsy from. A fine needle aspiration means that a doctor, often an interventional radiologist, by using imaging, gets to the area that we are looking at that we want to biopsy with only a small needle, and we get just a little bit of tissue for the pathologist to look at, and often it is enough to make a diagnosis when we can, though in other areas we like to get a larger sample. Part of that is because the diagnosis is made by a pathologist, looking at the tissue, they make slides of the tissue that they have, but often we like to have certain staining done to give us more information, and now in the era of personalized medicine, there are often different genetic tests that we would like to perform on the sample to get a better understanding of what the mutations are that cause this cancer, and possibly direct our future treatment. When possible, we like a bigger biopsy, but sometimes because of the areas such as the liver or pancreas, we do get a fine needle aspiration.

Foss Stacey, you alluded to this earlier, but can you just take us through the process of when a patient gets a biopsy done and it shows a GI cancer, how do they actually get into your multi-modality clinic at Yale?

Stein We have a group together and their primary care doctor would contact us. We are usually able to get appointments for new patients within one or two weeks. We like to see people as soon as possible to get them information about their diagnosis and what future tests we need to complete our staging workup, and start discussing treatment as soon as possible.

Wilson We are going to take a short break for a medical minute. Please stay tuned to learn more information about GI malignancies with Dr. Stacey Stein.

Medical Minute *Breast cancer is the most common cancer in women. In Connecticut alone, approximately 3,000 women will be diagnosed with breast cancer this year and nearly 200,000 nation-wide, but there is new hope for these women. Earlier detection, noninvasive treatments, and novel therapies provide*

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more options for patients to fight breast cancer. In 2010, more women are learning to live with this disease than ever before. Women should schedule a baseline 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 available to patients. A potential breakthrough in treating chemotherapy-resistant breast cancer is now being studied at Yale combining BSI-101, a PARP inhibitor with a chemotherapy drug, irinotecan. This has been a medical minute, brought to you as a public service by the Yale Cancer Center. More information is available at yalecancercenter.org. You are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.

Wilson Welcome back to Yale Cancer Center Answers. This is Dr. Lynn Wilson and I am joined by my co-host, Dr. Francine Foss. Today, we are joined by Dr. Stacey Stein and we are discussing GI malignancies. Stacey, in the first part of the show you had mentioned the term 'personalized medicine', go ahead and please describe that in a bit more detail.

Foss What we are finding out in GI oncology, and really across the board in all cancers, is that because a cancer comes from a certain organ, it does not necessarily mean that they are all the same. What we are trying to get at with personalized medicine is, what mutation is there in a gene that caused this person to have this cancer, and can we find a treatment then that is tailored to that mutation, to that specific pathway that is not working properly in those cells, to give targeted treatment? In GI cancer, I can give you a couple of examples of how we are doing that. There are two antibodies that are used for some patients that have colon cancer called cetuximab and panitumumab, and they both target something called the EGFR or epidermal growth factor receptor, and initially pathologists were looking to see if this receptor was expressed in tissue and then those patients were given those two drugs in a few large clinical trials. It turns out that there is a gene called KRAS that is mutated in about 40% of patients with colon cancer, and it was found looking back on all the patients in these trials that patients who had a mutation in that gene did not have any response to cetuximab or panitumumab, but the patients that had the wild-type or normal KRAS gene often did have some kind of benefit from getting those drugs. So, now we routinely look at all patients who are diagnosed with colon cancer for their KRAS gene status, whether they have a wild-type gene or mutated, and then we make treatment decisions based on that.

There is another gene called BRAF which is mutated in about 10% of patients with colon cancer, and it appears that those patients also do not respond to those drugs. Another example is that there is a protein called HER2 which has been widely used in screening breast cancer patients for use of the drug Herceptin, and in breast cancer, there have been huge strides in improving patient's response and survival with chemotherapy when they have an overexpression of the HER2 protein, and they receive the drug Herceptin. Well, a group found that about 20% of patients with gastric cancer also have an overexpression of the HER2 protein, and there was a trial done where those patients were given the drug Herceptin in combination with some of the more traditional

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chemotherapy that we use. It was found that they had a benefit in how long they lived when they received the Herceptin with the other chemotherapy. That is another example of personalized medicine where we can look at the initial biopsy someone has and check for the expression of these different proteins, and then tailor the treatment, and hopefully this is just the beginning of many advances that we will see in the future of targeting treatment to that person's tumor.

Foss Should most patients with these GI cancers nowadays expect to get those assays and are most patients treated in this personalized medicine approach?

Stein Yes, and at Yale, we are screening all of our patients for these mutations.

Foss Can you also talk a little bit about another interesting pathway in cancer, which is the angiogenesis pathway? We have heard a lot about this in the context of other kinds of tumors. Is that relevant in GI cancers and do you use angiogenesis therapies in these settings?

Stein Yes, it is very relevant. There has been a lot of interest in looking at angiogenesis in cancer development, because when a tumor gets to be beyond a certain size, it really needs its own blood supply to continue to grow, and so it has been thought for a long time, if besides just stopping the cancer cells from being able to divide and grow, if we could stop the ability for the tumor to have its own blood supply we could also target tumor growth. There is a drug called bevacizumab that targets this pathway, and it has been tested in multiple cancers and it has been found to have benefit in patients that have metastatic colon cancer, but it does provide benefit when combined with chemotherapy. Unfortunately, we also looked at the combination of bevacizumab with drugs in the adjuvant setting, meaning patients that have an earlier stage colon cancer where we give them some chemotherapy after surgery to help reduce the risk of having a recurrence of the disease in the future, and there was a large trial that people were very excited to see being done looking at the addition of that with chemotherapy in these patients. While it looked like it delayed some patients being diagnosed in the future, unfortunately, it did not seem to decrease the number of patients that eventually recurred. We are still working on figuring out what the role is for some of these drugs in our treatment.

Wilson What are some of the treatment options that are available for these various cancers and how are those coordinated together or combined?

Stein At Yale we have a multidisciplinary team that meets every week. It is made up of the medical oncologists, the surgeons, radiation oncologists, radiologists and pathologists. Also, some of our social workers come, people from the High Risk Clinic, and we all get together and discuss our new cases. We can look at the pathology up on a screen together and we look at their imaging studies and we discuss the best treatment approaches for each patient, and it is really great to be able to have that as opposed to making phone calls to different people. It is nice to have everyone in the room looking at everything together and really putting their heads together. I think that that is a big benefit of coming to a large institution for treatment, and we often discuss what the

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sequence of treatment should be and what treatments are available. Often, that is determined by the stage of the disease the patient has when they are diagnosed. Whenever possible, we hope to incorporate surgery for curative treatment, but we do work in a multidisciplinary team and often discuss the patients there.

Foss And what about the role of radiation therapy in these diseases?

Stein There is a role in some of these diseases for radiation therapy. For rectal cancer, that is a large part of the treatment effect. Usually, when patients are diagnosed, if they have local disease, before we do the surgery, we often give chemotherapy and radiation together, and then the patient has surgery, and often that can allow the patients to have a smaller surgery which helps preserve their rectal function after the surgery. Also, in esophageal cancer, radiation plays a large role in the treatment, and there we often also give chemotherapy and radiation prior to the surgery.

Wilson What are some of the things that have changed in a positive way, or advancements that have taken place over the last 10 years? You mentioned some of the personalized medicine drugs that have been developed, but what is your sense of where we have been over the last decade?

Stein I would say that there have been advances in every area of GI cancer. I will give you a few examples. A couple of years ago, there was a drug approved for liver cancer, which was the first drug that really showed a survival benefit, called sorafenib, and there is a lot of active research looking at new drugs for liver cancer. It is nice that we now have a systemic treatment available when local treatments have failed for liver cancer. Also, I would say the use of targeted therapies in colon cancer, such as the antibodies, cetuximab and panitumumab, and also bevacizumab for targeting angiogenesis. In pancreatic cancer which has notoriously been a difficult cancer to treat with chemotherapy, recently, there was an advancement of using a three-drug regimen. All drugs had been used previously and are used in colon cancer, using a combination that has shown a survival benefit over a standard drug that we have been using for a while, which we still use, gemcitabine. I would say that there have been achievements in all areas of the diseases we treat, but there is certainly room for improvement, and I think that with increased research in the pathways that are involved, hopefully, we will be seeing new drugs in development.

Foss That leads me to my next question, which is, what is the role of clinical trials in this disease and do most patients actually go on a clinical trial at the beginning of their treatment or are the clinical trials usually after they fail their original treatment?

Stein That is a great question. Clinical trials are very important. They dictate all of the decisions that we make now. All the treatments that we use now are based on previous clinical trials; it is really invaluable. Often the clinical trials that we have are for later stages of disease, but I think that there are still important questions to be answered even in the curable settings, because we have, for instance, in colon cancer, we know that a certain percentage of people will eventually have a

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relapse. So, there is ongoing research in those areas too, but many of the clinical trials we have open are for what we would call second-line therapy, meaning after someone has initial treatment and has progression of their disease, then we try to have trials open in every setting for patients to be able to enroll.

Wilson Since we have had some advances in the last 10 years, are we seeing them translate into better prognosis for some of these diseases?

Stein Yes, we are. Specifically for colon cancer, which has the highest incidence of all GI cancers, we have seen a big benefit. Now, the overall survival, or how long people live even after they have been diagnosed with metastatic disease, has increased significantly over the last couple of decades. Initially, we had only one drug, 5-FU to treat patients and since then there have been other new drugs, oxaliplatin, irinotecan, cetuximab, panitumumab, bevacizumab, and hopefully newer drugs down are coming down the pipeline. All the changes have been incremental, but when you look over the span of the last few decades, you can really see that there have been stepwise improvements, and it really gives me hope that we are going to continue to see more improvements in the future.

Foss As more patients are living longer and longer with GI cancers, do you have an active program at Yale focusing on issues of long-term follow-up for these patients and survivorship issues?

Stein We do. We follow all of our patients even after they have finished receiving treatments for what we call surveillance, where we continue to do physical exams, check blood work, and sometimes do imaging at certain points. Also, one of my colleagues, Dr. Tara Sanft has started a survivorship clinic here which combines the use of nutritionists, physical therapists, and social workers and other people interested in this area to help follow our patients even after they have been technically cured of their disease to make sure that they are getting all of the other medical care that they should be, and dealing with any long-term issues that they still have, maybe side effects from the treatments that they received in the past.

Dr. Stacey Stein is Assistant Professor of Medical Oncology at Yale School of Medicine. If you have questions or would like to share your comments, visit yalecancercenter.org, where you can also subscribe to our podcast and find written transcripts of past programs. I am Bruce Barber and you are listening to the WNPR Health Forum on the Connecticut Public Broadcasting Network.