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00:00.000 --> 00:13.700 Support for Connecticut Public Radio comes from AstraZeneca, the Global Biopharmaceutical Company behind a variety of innovative cancer medicines with a pipeline of investigational therapies. Learn more information at astrazeneca-us.com.

00:13.700 --> 00:51.600 Welcome to Yale Cancer Answers with doctors Anees Chagpar and Steven Gore. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it is a conversation about treatment options for GI cancers with Dr. Jeremy Kortmansky. Dr. Kortmansky is an Associate Professor of Clinical Medicine and Medical Oncology at the Yale School of Medicine, and Dr. Gore is a Professor of Internal Medicine and Hematology at Yale and Director of Hematologic Malignancies at Smilow Cancer Hospital.

00:51.600 --> 00:57.400 <vGore>What are cancers of the gastrointestinal tract?

00:57.400 --> 01:11.800 <vKortmansky>The gastrointestinal system is really 9 different cancers that we see -- esophageal, stomach, biliary, liver, pancreas, colon, rectal and then carcinoid tumors or neuroendocrine tumors.

01:11.800 --> 01:25.300 <vGore> That was 8, ah missed one. Well, we will have to work on that. As a gastrointestinal oncologist, do you take care of all of those?

01:25.300 --> 01:28.600 <vKortmansky>I do.

01:28.600 --> 01:30.300 <vGore>That's a lot to know about.

01:30.300 --> 01:45.900 <vKortmansky> It is a lot to know about. There is also a lot of overlap between the diseases. So, in terms of our treatment decisions, a lot of the therapies that we use are similar, hopefully as we learn more about the diseases, we will see some differences between the different types.

01:45.900 --> 01:55.900 <vGore>And, you know, I guess the one the people know most about because they tend to be screened for it is colorectal cancers, is that right?

01:55.900 --> 02:13.500 <vKortmansky>That is right, and colorectal cancer is the most common GI cancer and the third most common cancer in the United States, representing close to 180,000 cases a year.

02:13.500 --> 02:39.800 <vGore>That's a lot! And you know, we talk a lot about screening for colorectal cancers with stool, and blood - occult blood testing and of course colonoscopy, theoretically should all colorectal cancers be detected at a curable stage? Is that really the state-of-the-art right now?

02:39.800 --> 02:56.400 <vKortmansky>Well, we know that colonoscopies and colon cancer screening are very effective and lead to an increased number of cures. I would say that some of us are seeing that the cancers are being diagnosed at an earlier stage and a much more curable stage.

02:56.400 --> 03:03.200 <vGore>And mainly because of screening or are people still presenting with symptoms like bleeding, constipation or other things?

03:03.200 --> 04:06.400 <vKortmansky>Patients still present with symptoms. Those are patients that sometimes do not follow up with their screening as recommended. So, they were diagnosed later. There are some patients that just have symptoms early on. What we are seeing and what has been concerning lately is that there is an increasing number of young people that are being diagnosed with colorectal cancers. We usually consider it a disease of ageing with the majority of cases over 50, and the recommendations for screening had been around age 50. We are now seeing that about 1 out of 10 colorectal cancers that are diagnosed are in patients less than 50. Those tend to be at a later stage when they are diagnosed and so some of our guideline taskforces are recommending screening starting as early as 45 or 40 if you have a family history.

04:06.400 --> 04:15.700 <vGore>Is there any thought as to why there are these cancers showing up in younger people? I guess, the same is true in lung cancer and non-smokers, right?

04:15.700 --> 04:35.500 <vKortmansky>Right. I think that from a colorectal standpoint, it is believed that it is either lifestyle, that the American diet tends to be one that is higher in fat, lower in exercise and that may be contributing to a higher risk of colorectal cancer.

04:35.500 --> 04:48.400 <vGore>Even though it seems that the whole society has gone gluten free and exercise mania and all sorts of other Atkin's, this and trendy that right?

04:48.400 --> 05:02.000 <vKortmansky>Yeah. I would say sadly not as much of society as you think and those diets are often hard to sustain, so people go back to the old ways.

05:02.000 --> 05:19.000 <vGore>And, I mean, is there a colon cancer prevention lifestyle that people can look to? I mean, is it just a question of more fiber, less fat, just kind of a healthy Mediterranean diet.

05:19.000 --> 05:28.600 <vKortmansky>I think you hit right on it. I think that a healthy diet is the right thing to do -- low fats, 5-9 servings of fruits and vegetables a day, low in alcohol, high in exercise.

05:28.600 --> 05:54.300 <vGore>Gotcha. Yeah probably not too many Americans check off all those boxes right? So, when you say family history, what is the family history that people should worry about? So, if somebody's grandmother

had colon cancer in her 90s, is that something to worry about if your father had colon cancer in his 60s, is it more than one first-degree relative?

05:54.300 --> 06:27.500 <vKortmansky> So, I think just having a first-degree relative with colon cancer does increase your risk for colon cancer. We know that there are family syndromes as well that are linked to certain genes and to identify those patients, we do look for at least three first-degree relatives, we look for one diagnosed before age 50 and at least one that is a direct offspring of the other.

06:27.500 --> 06:35.700 <vGore>And those are usually not so subtle right? I mean, oftentimes the families know that there is family history going on or not always?

06:35.700 --> 07:19.700 <vKortmansky>Not always. Sometimes you have to tease it out. Families have become more complicated these days. So, sometimes you have to tease out that information and sometimes it is not all colon cancer when you have these hereditary syndromes, they could be associated with not just colorectal but also upper GI - esophagus or stomach and sometimes uterine cancer, and when I am meeting with a patient, I will ask those questions as well, not just who has had colon cancer, has anybody had uterine cancer, and you usually find more people at risk when you ask the probing questions.

07:19.700 --> 07:47.400 <vGore>Gotcha. One thing that I think primary practitioners and patients worry about is the occasional hemorrhoidal bleeding that many middle-aged people will have, a little bit of blood on the toilet paper, is that something that needs to be investigated? I mean, it sounds like a hemorrhoid, had hemorrhoids in the past, but it is still blood.

07:47.400 --> 07:58.300 <vKortmansky> I think that blood is blood. I also think if the patient is 50 and has not had a colonoscopy, then it is a good way to get them there.

07:58.300 --> 08:03.400 <vGore>Right. But if they are 55 and they had one and it was clean when they were 50?

08:03.400 --> 08:21.700 <vKortmansky> I think if it was clean at 50 and they do not have any other symptoms of concern -- increased constipation, abdominal bloating, weight loss, if it is, I think clear that there is just blood on the tissue paper and they have had one, they may be safe.

08:21.700 --> 08:41.200 <vGore> Alright. So, that is just kind of a practical thing that I think a lot of people worry about because it is a common problem and they do not want to have a colonoscopy every day, I mean once in a while you may be fine, but every day, it is nobody's picnic right? Everyone is afraid of colonoscopies? I mean is it the thing that you hear most people complaining about?

08:41.200 --> 08:45.200 <vKortmansky>Right. It is really the cleanse that people complain about.

08:45.200 --> 09:20.200 <vGore> I mean, nowadays with the short-acting pretty good anesthesia, people wake up and it is like what happened or did anything happen or when it is going to happen. Cleaning out is never really pleasant. So, let's just walk through, with colon cancer ideally if you were being screened regularly, you would never develop colon cancer, but say somebody has a lesion - ideally things are still treated either surgically or with an endoscope right?

09:20.200 --> 09:34.500 <vKortmansky>I think that treating patients endoscopically is really pretty rare. You have to have a very early stage, shallow tumor, barely breaking that surface of the tumor lining.

09:34.500 --> 09:40.700 <vGore> More like a polyp or malignant polyp if you will, barely malignant polyp?

09:40.700 --> 10:36.300 <vKortmansky>Barely malignant. I think for most other patients, we do aim for a surgical treatment. It depends whether it started in the rectum or the colon, we do treat those 2 sites differently because tumors of the rectum have a higher risk of recurrence locally after just surgery alone, and so there is more that we need to do. All patients when they are diagnosed should have a staging study, which is usually a CAT scan to look at their abdomen, their liver, their lungs to make sure that that is all clean, at which time they can proceed to surgery for a colon cancer. For patients with rectal cancers, we tend to use more modalities of therapy and there is really a team of medical oncologists, surgeons, radiation oncologists and the GI doctors who all contribute to the patient's care.

10:36.300 --> 10:46.000 <vGore>And why is so different for the rectal cancer? Because it is a different kind of cell or is that just the location and it is harder to get a lot of tissue out because it is going to get stuck there attached to the anus?

10:46.000 --> 11:20.000 <vKortmansky>I think that both of those are correct. The pelvis is a much narrower area and so it is harder to get all of the cells out, but there does seem to be some biologic difference, and that is when you compare tumors of the rectum to tumors of the colon, stage for stage; so stage II in each, the rectal cancers do tend to have a higher risk of recurrence and so we do treat them more aggressively.

11:20.000 --> 11:23.600 <vGore>And an anal cancer would be something completely different?

11:23.600 --> 11:24.000 <vKortmansky>Anal cancer is a different disease.

11:24.000 --> 11:26.900 <vGore>Would that be #9 or is that still in somebody else's purview?

11:26.900 --> 12:16.000 <vKortmansky>No, I think that would be #9. You could argue small bowel was #10, but that is treated very similarly to our colon cancer paradigms. But anal cancer is a different disease, most colorectal cancers are adenocarcinomas or glandular cancers, whereas anal cancer is a squamous

cancer, so it is more similar to the mouth as you had mentioned before or the skin and tends to have different risk factors for development including smoking, infections with HPV, HIV and other similar risk factors.

12:16.000 --> 12:35.900 <vGore>And so, one would hope then I guess that as the papilloma vaccine becomes more and more utilized in both men and women, boys and girls I guess, at least one sort of anal cancer proclivity might decrease?

12:35.900 --> 12:38.200 <vKortmansky>We would like to think so.

12:38.200 --> 12:46.600 <vGore>Is it the same papilloma viruses which were once associated with sexual activity and so on?

12:46.600 --> 12:46.800 <vKortmansky>Exactly.

12:46.800 --> 13:00.100 <vGore> Well, we have covered a little bit of the lower GI tract and I am going to want to move a little higher up, but first we are going to need to take a short break for a medical minute.

13:00.100--> 13:15.600 Medical Minute Support for Yale Cancer Answers comes from Astra Zeneca, a biopharmaceutical business with a deep-rooted heritage in oncology and a commitment to developing cancer medicines for patients. Learn more at astrazeneca-us.com.

13:15.600 --> 14:01.200 This is a medical minute about survivorship. Completing treatment for cancer is a very exciting milestone, but cancer and its treatment can be a life-changing experience. For cancer survivors, the return to normal activities and relationships can be difficult and some survivors face long-term side effects resulting from their treatment, including heart problems, osteoporosis, fertility issues and an increased risk of second cancer. Resources are available to help keep cancer survivors well and focused on healthy living. More information is available at YaleCancerCenter.org. You are listening to Connecticut Public Radio.

14:01.200 --> 14:26.900 <vGore> Welcome back to Yale Cancer Answers. This is Dr. Steven Gore. I am joined tonight by my guest Dr. Jeremy Kortmansky to discuss treatment and clinical trials for gastrointestinal cancers. Jeremy, before we get to the esophagus, one thing we did not talk about much or really at all for either the colon or the anus is, sometimes chemotherapy is actually involved even when the cancer has not spread, is that right still?

14:26.900 --> 15:16.700 <vKortmansky> Right. So, for patients with colon cancer, colorectal cancers, chemotherapy is often part of their treatments, especially for patients that have more advanced disease, primarily stage III, which means that the lymph nodes in the area are involved, but sometimes patients that have what we view as higher risk, stage II, we would also offer chemotherapy. We are trying to learn who gets chemotherapy, but also how much and for how long. It used to be everybody got 6 months, we are now learning that there are perhaps some patients that can get less than that and that helps us avoid some of the long-term toxicities that could be associated with the treatment.

15:16.700 --> 15:28.300 <vGore> And we hear a lot about precision medicine and personalized medicine, and is there anything going on there where certain patients with colon cancer could have certain mutations that could be treated specifically or anything like that?

15:28.300 --> 15:56.900 <vKortmansky> Yeah, I think that our understanding of the biology of colon cancer is really blossoming. I think at the most basic level, we have learned that it is not just colon anymore, there is left colon and right colon and those are biologically different types of cancers in terms of the genes that might be activated. There is a lot of interest in patients with microsatellite instability.

15:56.900 --> 15:57.100 <vGore>That sounds fancy.

15:57.100 --> 16:55.500 <vKortmansky> Microsatellite instability is a product of abnormalities in genes that effect how our bodies repair our DNA, and so, we know that is associated with some of the hereditary colon cancers that we see. But sometimes it happens sporadically and so these tumors are seen to be exquisitely sensitive to the new immunotherapy drugs that are out there and several of them are now approved for patients with colon cancer that have this microsatellite instability, and it is important because this is a marker that we could easily test for in all patients, and while the drugs are still approved for patients that have already had chemotherapy, there are now studies going on that are looking at it as in place of chemotherapy.

16:55.500 --> 17:07.300 <vGore> Very cool. Even in patients in whom the cancer has not yet recurred?

17:07.300 --> 17:34.400 <vKortmansky>So, that is also being looked at in clinical trials and that is a national study. What is difficult is that patients with this microsatellite instability actually only represent a small population of patients with the disease, and so when we look at patients with metastatic disease where it has already spread to other places, it is probably less than 10%.

17:34.400--> 17:39.200 <vGore> But if you are in that 10%, it is good to have an option right?

17:39.200 --> 17:53.300 <vKortmansky>And I think that the field of oncology is moving towards more specific treatments for smaller populations of patients.

17:53.300 --> 18:38.300 <vGore>But as you pointed out, while we total out of these treatments that are for very specific genetic abnormalities, acquired mutations and so on, the ones for which we have treatment really often represent a small subset, and that is a little dirty secret that nobody talks about, at least in many cancers right? The esophagus, that is at the upper end of the body as we might say and the esophagus has got different kinds of cells depending on where in the esophagus it is, right?

18:38.300 --> 19:10.000 <vKortmansky>Right. Primarily the cancers that we see in the esophagus are either adenocarcinoma, which are the glandular forms

that tend to form lower down in the esophagus and are associated with diet for the most part, so high-fat diets and there is one thing that I want to stress today, which is reflux, and that is actually becoming much more common in the patients that we see.

19:10.000 --> 19:14.000 <vGore>Reflux being acid reflux?

19:14.000 --> 19:15.100 <vKortmansky>Acid coming back into the esophagus.

19:15.100 --> 19:17.600 <vGore>We used to call it indigestion.

19:17.600 --> 19:34.500 <vKortmansky>It used to be that squamous cell cancers were much more common, which is a cancer that is higher up in the esophagus that is often associated with smoking and alcohol, but we have been seeing a shift over the last 20 years or so.

19:34.500 --> 19:37.600 <vGore> Is that because fewer people are smoking and drinking?

19:37.600 --> 19:43.800 <vKortmansky> I think that there are less people smoking and more dietary indiscretion.

19:43.800 --> 20:02.500 <vGore»Gotcha. And in particular, as I recall, this adenocarcinoma thing can be associated with a benign precursor that we used to call Barrett's esophagus, I do not know if we still call it that?

20:02.500 --> 20:22.100 <vKortmansky>We still call it Barrett's esophagus. I think that patients who have this frequent heartburn are encouraged to talk with their doctor, talk with their GI doctor to be screened for Barrett's esophagus, it is done through endoscopy.

20:22.100 --> 20:25.300 <vGore> Upper endoscopy and not a colonoscopy, you do not need to clean yourself out for that one.

20:25.300 --> 20:25.400 <vKortmansky> You do not need to clean yourself out for that one.

20:25.400 --> 20:29.100 <vGore> So, do not be afraid guys.

20:29.100 --> 20:57.000 <vKortmansky> I think the majority of esophageal cancers that we see are still caught with symptoms rather than screening with patients presenting either with pain, with eating or difficulty swallowing, weight loss, and so anytime that there is difficulty swallowing or you feel like there is food getting stuck in your chest, that should definitely be checked out.

20:57.000 --> 20:58.000 <vGore>Although it does not mean that you have cancer?

20:58.000 --> 21:03.900 <vKortmansky>It does not mean that you have cancer, but swallowing should be a simple task.

21:03.900 --> 22:22.700 <vGore> Yeah, interesting. I have to tell you a little anecdote, as is my want, but when I was 50 and I was really great about signing

up for my colonoscopy at my 50th birthday plus 1 day or whatever, and I went to my friendly gastroenterology colleague, I was living in Baltimore at that time, a guy that I really like and respect and he was asking me the usual questions that the GI doctor would ask, and he asked me about reflux symptoms and I said, well you know I keep a bottle of Maalox at my desk. He said really? I said yeah, well I mean so what, like you know once in a while you take a swig right? He says, well then we should do an upper endoscopy. I said, come on, I do not have routine GERD, but he said, you know I do not think it is normal to do that and you do not want to have Barrett's esophagus and not know about it and so, I did not fortunately and in fact I think I was right that I do not really have unusual symptoms. So, with esophageal cancer, the esophagus tends to be in kind of a funny place anatomically right in terms of causing symptoms or not?

22:22.700 --> 22:33.800 <vKortmansky>It is. It is the connection between our mouths and our stomach, and so the symptoms that people have are this difficulty swallowing.

22:33.800--> 22:38.600 <vGore> But you have to have a pretty big tumor to get to that point, right?

22:38.600 --> 23:30.800 <vKortmansky>Well, that is the problem, that by the time patients do have difficulty swallowing, the tumor can be more advanced and so it is a trickier one to diagnose earlier. We are not yet recommending a routine endoscopy in the same way that we recommend colonoscopies and to be fair, these tumors are much less common than colon cancer, and so we do not see as many of them per year as we do colon or even pancreas. And so, I do not want to over-react either, but they can be caught at a later stage, which makes treatment for them more complicated and really warrants a team approach again through GI doctors, surgeons, medical oncologists and radiation oncologists, all working together.

23:30.800 --> 23:34.500 <vGore>And the surgery for esophageal cancer can be pretty complicated right?

23:34.500 --> 24:05.500 <vKortmansky>It is pretty complicated. There are some patients that we do not recommend surgery because it can be complicated or that we recommend surgery at a later point, but for many having that surgery leads to a change in lifestyle, you cannot eat the way that you once did, you know losing weight is now a much more common problem and so it can be challenging.

24:05.500 --> 24:07.200 <vGore>It is the bariatric surgery you never wanted to have?

24:07.200 --> 24:11.300 <vKortmansky> Exactly, exactly.

24:11.300 --> 24:16.400 <vGore»Wow! And then I guess people who also end up having radiation can have problems with that as well?

24:16.400 --> 24:29.900 <vKortmansky>They can. Not all the treatments that we use are walks in the park, so I have a lot of respect for the patients who go through these treatments, dealing with the side effects during their treatments and also those that come afterwards.

24:29.900 --> 24:37.800 <vGore> Is there anything exciting happening in terms of immunotherapies or targeted therapies?

24:37.800 --> 25:01.800 <vKortmansky> So, in the immunotherapy world, I think we are learning that there is a marker for patients that would benefit from immunotherapy, a protein called PDL-1 which I am sure you have touched upon in this show once before maybe, but that is showing to be a marker of response to the immunotherapy.

25:01.800 --> 25:01.900 <vGore> Predictor response?

25:01.900 --> 25:34.400 <vKortmansky> Right. A predictor response and one that may be suggested that using one of our new checkpoint inhibitor drugs might be better than a chemotherapy drug. Again, that only represents a small percentage of the population. I think the results that we have seen are still modest and there is a lot of effort to try to build on that to find newer therapies, newer immunotherapy combinations that might be better.

25:34.400 --> 26:10.200 <vGore>How can you be sure when you are having a diagnostic and/or therapeutic surgery for any of these cancers that your tissue is going to be studied for the appropriate things, it sounds like the knowledge base is changing on a regular basis and what was standard evaluation of tissue last year may no longer be adequate. 26:10.200 --> 26:43.200 <vKortmansky>Well, I think that the challenge is keeping up with these changes in the field and then talking with our colleagues in the pathology department and the laboratory department to make sure that these tests are being done. We work to try to figure out where we can make them just the standard, everybody gets tested for it; for example, the microsatellite instability in upper GI cancers, we do look at another protein called HER2 to see if that is amplified. Everybody gets tested for that.

26:43.200 --> 26:49.500 <vGore> That is the same one that is often mutated in breast cancer right or amplified in breast cancer?

26:49.500 --> 27:04.200 <vKortmansky>Correct. And similar therapies seem to have some benefit. So, the newer ones that are coming out really require a dialog between all the folks that are involved in the care.

27:04.200--> 27:23.400 <vGore> So, would it be fair to say then that it is reasonable when a patient is having surgery or plans to have surgery that they could ask their surgeon whether the pathology department with whom she works does all the state-of-the-art tests that may be appropriate?

27:23.400 --> 27:29.100 <vKortmansky>I think it is fair to ask your surgeon or your medical oncologist.

27:29.100 --> 27:32.800 <vGore> One of those should know?

27:32.800 --> 27:51.500 <vKortmansky>Right. I think that a lot of these new biomarkers that we have or tests that the medical oncologists use to try to prepare their treatment, and so they are the ones that are often acting upon the results and so I think it would be important to ask them as well.

27:51.500 --> 28:17.400 <vGore> And I guess in the short time we have left then, one thing I would ask you is in the old days, a lot of these surgeries were done by general surgeons and as a matter of fact colon cancer surgery was probably the bread and butter of general surgery, and is that still the case or should patients really be seeing surgeons with a surgical oncology expertise?

28:17.400 --> 28:47.200 <vKortmansky> I think that to the best that they can, I think not everybody has access to that degree of subspecialization. I think for surgeries of the esophagus or the pancreas, we know that high volume centers have better outcomes. I think the same is true for colorectal surgery. Many surgeons have experience with colorectal surgery, but you know, you want to know that your surgeon has done a lot of them.

28:47.200 --> 29:14.500 Dr. Jeremy Kortmansky is an Associate Professor of Clinical Medicine and Medical Oncology at the Yale School of Medicine. If you have questions, the address is canceranswers@yale.edu and past editions of the program are available in audio and written form at YaleCancerCenter.org. We hope you will join us next week to learn more about the fight against cancer here on Connecticut Public Radio.