New Findings in Gastrointestinal Cancers

Gastrointestinal (GI) cancers are the second leading cause of cancer deaths worldwide amounting to 4.5 million global deaths per year.

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According to the American Cancer Society statistics, GI cancers collectively have the highest incidence and account for 20% of estimated new cancer cases.

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GI cancers include esophageal, gastric, hepatocellular, pancreatic, small bowel, bile duct, anal, colorectal and gallbladder cancers.

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We are discussing novel agents and therapeutic approaches for the treatment of gastrointestinal cancers and how new trial findings might affect treatment of these cancers in the future with GI cancer expert Dr.

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Alan P Venook of UCSF Helen Diller Family Comprehensive Cancer Center.

Full Transcript:

Priya Menon: Good afternoon everyone. Welcome to CureTalks. I'm Priya Menon, your host. Today on cure talks we are discussing new findings in gastrointestinal cancer. The Dr. Alan P. Venook from UCSF Helen Diller Family Comprehensive Cancer Center. Talking to Dr. Venook on the patient panel, our patient advocate Danielle Ripley-Burgess, Curt Pesmen, Aki Smith and Kim Hall Jackson. To get the show started without any further delay. We have with us the Madden Family distinguished Professor of Medical Oncology and Translational Research at the University of California San Francisco. Helen Diller family Comprehensive Cancer Center, Dr. Alan P. Venook. Dr. Venook such a pleasure to have you with us today.

Dr. Alan P. Venook: Thank you very much for having me.

Priya Menon: Doctor, I'm going to start with some very basic questions and then hand over to the patient panel for their questions. So, my first question is that GI cancer umbrella includes many cancers. Can you discuss some of the novel agents and therapeutic approaches that are the standard of care for gastrointestinal cancers today?

Dr. Alan P. Venook: Well, as opposed to a lot of the cancers the way we characterize cancer these days

gastrointestinal cancers is a pretty broad brush. Now, they're related because they're all in the same, have the same part of the functional part of the body. But of course, colon cancer may be very different than stomach cancer and included in this is Pancreas cancer and Neuroendocrine cancers of the GI tract. So, there's a great deal of variety. Unfortunately, one of the overarching themes of gastrointestinal cancer is that the checkpoint inhibitors have very little activity. The immune therapies have very little activity in these cancers. As a rule, now stomach cancer and anal cancer there's a bit of activity but colon or pancreas cancer really there's very little activity in the checkpoint inhibitors. So, there is some impediment to the immune systems effect on these cancers. In terms of other therapies, obviously we do have targeted therapies, but similarly there's less targeted therapy than for example in lung cancer whether may be discreet mutations in EGFR for example that we can target with any number of new tyrosine kinase inhibitors, for GI cancer. There tends to be less specific targets less ability to target one treat one pathway and make a big impact. And so, this in many ways can't let the GI cancer to trail behind the other cancers in terms of the rapid rate of progress. There are exceptions for example, the so-called GI stromal tumor, gastrointestinal stromal tumor. Now that tends to be cancer that the used to be characterized the sarcoma and so lots of folks in the sarcoma field like to claim it as their own. This is a unique disease and again, this is the exception that makes a rule like I suppose for GI cancers because GI stromal tumor there's actually an addiction to a single pathway called the C-Kit Pathway and the drug Gleevec or Imatinib actually is dramatically effective in that disease. So that's the exception that makes rule. By and large these are complex cancers that have, don't respond to a single intervention or a single pathway and it's been daunting to try to make progress in these and another common GI cancer account for somewhere around 40% of all solid tumors and certainly cause a great deal of morbidity. So that's it in a nutshell. We again, it's a broad program and within the different diseases many things are different. So, I would you can take those searches separately as a in general not like prostate cancer, breast cancer this GI cancer is a very wide range of diseases and issues.

Priya Menon: Dr. Venook, I know you have been in this field for so long with your vast experience. I'm sure we are seeing a lot of new breakthrough treatments for cancer in the last few years, like immunotherapy, CAR T-cells, biomarkers and more. So what among these developments or diagnosis of treatment of GI cancer has impressed you in the recent years.

Dr. Alan P. Venook: Well as I said, part of most impressive things unfortunately, is that some of the things we would hope to work, we haven't been able to get to work. And so that would be that lets say the immune therapies on the other hand we've discovered that some treatments targeting amplified genes such as the HER2 gene therapies can work in stomach cancer, for example with anti-HER2 therapy. We've seen that some cancers are curable one of the unique things about GI Cancers is that as opposed to almost every other solid tumor GI cancer can still be cured even after they metastasize which we see in colon and rectal cancer, for example. So, you know, those are the things that we see that stand out as opportunities that we need to capitalize on it as well as we're looking at patients and trying to decide how best to handle them but the big missing link in the GI cancers is that more so than any other Cancers. The RAS mutation is a driving force in many of these cancers and because that's such a difficult mutation to deal with that we may very well account for our problems going forward, but I think that as well as its evolving role of multidisciplinary care the fact that as I said we can cure patients occasionally, even it would mean that disease sets us apart.

Priya Menon: Could you give us, please give us some suggestions on preventing it. Are there some risk factors that have been identified? I'm talking about GI cancers as a broad group and probably some methods for early detection of these cancers. Yeah.

Dr. Alan P. Venook: Well, so we of course have screening programs, for example for colon cancer because 85% of colon cancers evolve from polyps and it takes between three to 10 years for a polyp to turn into a malignancy. By intervening with a colonoscopy, you can almost you can prevent many of these cancers if you find them early enough that's the basis upon which we do screening colonoscopy. And we start doing that at age 50, unfortunately as we'll talk about in a bit. Colon cancer has evolved over the last decade to seem to be affecting younger people much more so than the average at used to be mostly disease of older folks. But so that's a screening opportunity for example. Gastric stomach cancer what used to be the most

common cancer of a hundred years ago and it all but it was decreased dramatically with the advent of the refrigerator because used to be that meat and other items that were perishable were cured with nitrates and bad chemicals, which tended to lead to kick patients at people being at risk for upper GI cancer. So, we change that by getting refrigeration. Although now probably lifestyle sort of type A personality is associated with the increased incidence of upper GI Cancers. And then one of the most dominant cancers around the world liver cancer occurs in folks who have had a diseased livers which as you know around the world is has historically been caused mostly by hepatitis with endemic hepatitis let's say in hepatitis B in Africa and Asia, hepatitis C in Japan and in the US and now that we're getting rid of hepatitis C we tried to be changing places with what's called the metabolic syndrome not alcoholic fatty liver disease which predisposes to liver cancer. So obviously if you can prevent if you prevent liver damage, if you do colonoscopy screening certainly people who adhere to non western diets have a great lesser risk of all of these cancers generally. Smoking of course is associated with the root cancer risk in almost every group including GI cancers. So certainly those factors are important factors, although there's no absolutes people who are vegetarians or who don't drink alcohol can get any of these cancers. So as we know in other diseases, there are no absolutes, but that's a general theme those are the kinds of things we think about for GI cancer.

Priya Menon: Thank you. Dr. Venook. Well then, I'm going to hand over to the patient panel. The first member on the panel today Danielle Ripley-Burgess. Daniel is a two-time colon cancer survivor. First diagnosed at the age 17, an award-winning communication professional and the author of Blush: How I barely survived 17, so she writes and speaks to encourage others that faith can survive. Daniel all yours.

Danielle Ripley-Burgess: Hello. Thank you for having me today. I have a question. Actually, I'm a survivor. I have survived for about 20 years. I have a close friend who was recently diagnosed with Stage 4 Colorectal cancer and its having me re-live some of that with her. So, the moment of her diagnosis has been so over-whelming and I found she was in more of a local hospital and just getting rushed into care, especially in the season of Covid. So, just a question like what would your advice be to someone in her situation if there are more of a local medical center that doesn't do research or trials, like what should she do?

Dr. Alan P. Venook: That's a good question. So, for the most part no cancer diagnosis, very rarely a cancer diagnosis is a cause to panic and to do something emergent. There are the exceptions let's say somebody with a colon cancer who has a bowel obstruction can't eat or has intense abdominal pain that may require immediate intervention, but for the most part these GI cancers that you're much wiser to wait get, you know get round up of extend of of the disease make sure you've been fully staged and I do think now this is a bias, of course in coming from me at a major Center may seem like it's self-serving but I do believe that every patient should solicit an opinion from experts at a major center. More and more I think imagining that a primary oncologist out in the community can have enough expertise across the range of diseases, to make sure they're pulling pushing the right buttons is it's really asking a lot. So a patient who's newly diagnosed these days and if it's not emergent, you know, I think getting another opinion over than of the week or two or three is probably well worth it as opposed to jumping into a treatment that they said make sure they've set up obstacles going forward. Very much as we as we evolve we know that in many cases with GI cancer chemotherapy or radiation is where we start as opposed to surgery, so I think that's very important for folks who are newly diagnosed to take a deep breath and pause and try to you know, get other opinions. Now in the Covid era this is a different totally different extend of last few weeks helping to develop guidelines for oncologists for the NCCN about how they treat patients in the era of the pandemic which is to say what don't we do? what can we get away without? Sort of what compromises and that's sort of always been anathema to me that that is our current era. So, to a patient newly diagnosed these days many centers can't do surgery because elective surgery which is what this is most GI cancer is elective surgery with the outset most places are not doing them or scaling back on that. That's a whole level of complexity that we never anticipated but in that instance in any instance I think patients should take a deep breath and listen to the second opinion. We're doing a lot of video opinion these days which I was never a big fan of but actually worked very well in the current system that we probably will go much more to that in the future because it's much more efficient for patients and actually for doctors as well. For example, your friend for example could certainly call in depending on where they live. They could call in to a local place and get a video visit. There's technically speaking we can't do video visits across state lines. This is bizarre but got to do with it

with transiting across state borders regarding payments. So, it's kind of crazy, but that's a technicality, they may change that in this era because of the need to go to video visits, but that's the reality is what one thing we face believe it or not.

Danielle Ripley-Burgess: Interesting. Thank you. That's super helpful. Does the latest research support any naturopathic therapies in addition to traditional therapies for the GI cancers?

Dr. Alan P. Venook: Well, so certainly there's evidence that diet, but there are a number of studies that have suggested diet exercise matters. This is mostly done back in the 90s and early 2000's in a big study looking at the role of chemotherapy in patients with stage 3 colon cancer. We invented a questionnaire that looked at many lifestyle decisions the patients had. So, ranging from do they smoke, do they exercise, to how many portions of nuts do they have during the course of the week, do they eat to fish, what kind of fish, what diet etc. and through all of those questionnaires, we've developed a dataset that really suggests that food and exercise all these things do matter in terms of survival and even curability of colon cancer mechanisms we can speculate to how that why that would be but so the classic recommendation we make to patient is a non-western diet. So, avoid in-and-out burger kind of, you go to you have to eat a lot of good portion of nuts, these are tree nuts not peanuts. Peanuts are legumes. Tree nuts would be what seems to help and then you've got as I said, you know, fish is good is better than not incredibly enough sugar beverages are bad, watching too much TV is bad and I probably because people don't exercise much. So those are the lifestyle factors we know of in terms of other naturopathic things. Well harder to say I'm a big believer in vitamin D. 80% of us are insufficient in vitamin D because we tend to shield ourselves from the Sun. So, vitamin D I'm a Believer in supplementing and patients trying to get their levels to normal and then aspirin is not exactly naturopathic. Although it's a natural substance that also as appears to prepare a little bit protective about developing colon cancer.

Danielle Ripley-Burgess: That's really helpful. Thank you. So, my last question is something I'm facing so, you know in the era of Covid, you know, there's clinical trials are closing I mean also like scans I think you mentioned it a few minutes ago. So, if a patient like me need a follow-up scan every year for example, but it's been put on hold and so for survivors a lot of our follow-ups are on hold which is causing extra anxiety. So just curious what's your advice to patients right now kind of in this crazy era.

Dr. Alan P. Venook: Well, you know, it may take my advice today may change tomorrow. We are so for what it's worth in San Francisco. We are starting to open up again. We're very carefully bringing people back in, we're testing patient's when they come in the door. I mean, obviously the reason not to get scans is for the most part if you don't know somebody's in the status of the virus and they happen to be shedding virus and they lay in a CT scan or MRI for half hour then that space is contaminated and there's a great risk of disseminating the virus and not to mention that patients with cancer or survivors you'd like to not exposed to the virus because intuitively worried that they may do less well with the virus, although that's not actually certain. I think what I would predict is that well, this will be a new normal I think waiting a month or two by and large is not a big problem for certainly patients who are survivors and I do understand that it increases anxiety, but I just think that it's a trade-off of anxiety I suppose. This Covid year has forced all of us to rethink how we do things and I'm not comfortable with some of the decisions we've had to make but then, but it is what it is. So, I would trust them that we are pushing back and starting to get back towards our normal behavior. I would just hold out over the next month or two you should be able to get back at least to the approximately normal schedule you were on before.

Danielle Ripley-Burgess: Got it. Thank you. Thank those are all my questions.

Dr. Alan P. Venook: Sure

Priya Menon: Thank you, Danielle. Thank you very much, Daniel. And Dr. Venook the next in the panel is a patient of yours Curt Pesmen. Curt is a seven-time author, documentary producer, colon cancer survivor, and an award-winning writer who has published with Esquire, GQ, Men's Health, CURE, as well as in The New York Times. Curt, you're on.

Dr. Alan P. Venook: I have to be careful what he asks me here. He knows too much about me. Hi Curt, how are you?

Curt Pesmen: Thank you everyone especially Dr. Venook who in my book is noted as one of the seven people, although there are probably more including nurses who did save my life. So, an extra special thank you there. I wanted to start today with again what I learned way back in 2001, but it's still an increasingly important question. Can you explain that to the listeners why the treatment regimens are so different for colon cancer and rectal cancer when it seems like the micro-biomes or the tissues would be pretty similar.

Dr. Alan P. Venook: That's a great question. So that actually they're less different now than they were years ago as we understand more about the cancer. Certainly, when you were treated with rectal cancer. We viewed it very differently. There's a mechanical reason why we treat rectal cancer differently than colon cancer not it is the limited ability of surgeon to get into the pelvis to do a complete rectal operation and that was much more the case 20 years ago than it is today with newer technology, newer equipment, newer stapling devices with robotic surgery surgeons can now do a better job down the pelvis but used to be very difficult to get all round the cancer and giving adequate margin in rectal cancers. So, back in you know, three or four decades ago, we started doing radiation to the pelvis and that was really to augment the ability to get a clean surgical margin. Surgery by large being the definitive treatment for most cancers and certainly that was the basic aids for colon cancer. So, when you were treated we did focus on radiation. More and more these days with more effective chemotherapy and better surgery we're doing less radiation. Infact, we just completed a very large study in selected patients randomly assigning patients with high rectal cancer to actually see if we can get away without radiation at all. And that so-called Prospect trial we are waiting for results on. Similarly, rectal cancer these days were also treated with chemotherapy before we do anything as opposed to chemo radiation, which is how we used to start. And again, the field is evolving for colon cancer as well. So the differences may be much less today than they were years ago but I should say that today in fact as we think about colon cancer or rectal cancer, we have now evolved to believing that rectal cancer, which is defined for purposes of studies and understanding and talking same language, the last 12 centimeters of the large intestine is called the rectum and from there to the rest of the local around to the appendix that would be called the colon. We used to think there's a bigger difference between the colon and the rectum and now we actually think there's a much bigger difference biologically and behavior of the cancer for cancers that originate on the proximal side of the colon that would be between the appendix and the liver the hepatic flexure and then cancers that originated beyond the hepatic flexure the so-called those are left sided cancers and the cancers down before the hepatic flexure called the right side cancers. Patients appear to do very differently if you bifurcate it at that point as opposed to rectum and colon. Colon and rectum by large are molecularly very same. It turns out the biome the microbiome is different on the right side of the colon than the left. There is a sort of a gradual change in bacteria that populate the different parts of the colon that may explain why there's a difference in the outcome. From an embryologic perspective, it's not shouldn't be that surprising because the right side of the colon originates from what's called the mid gut and the left side of the colon from the hind gut in the embryo and then as the embryo evolves those two parts of the of the embryo join up to form the colon. So, again, we've sort of figured out rectum is not so different than the colon. Although years ago, we thought they were very different.

Curt Pesmen: That's great. I didn't I didn't know you just caught us up on a lot of probably the last 10 years about the diagnosis being more similar than they were even in the last era. My next question actually has to do with testing. We had a recent Patient Advocate and Research Advocate seminar in which a researcher talked about measuring breath volatile organic compounds to try to get at an early look at it. Another way to diagnose or pre-diagnose cancers in the same way, you know, we used to think about liquid biopsies or blood might be able to tell us what's going on even without a biopsy and now they're trying to look at for GI cancers to look at VOCs-Volatile Organic Compounds. My question is even though it's turned out to be very helpful in early studies to measure breath, again. it may seem out of the box strange, but do you know any doctors or researchers who have ever thought to mention to measure flatulence or gas to even get closer to the VOCs to try to guess what's going on in the GI tract. Sounds strange. But you never know.

Dr. Alan P. Venook: Well, I expect strange from you. So now that was a really great question and a really great question. So, the issue turns out that there's even something called volatile mix which is studying the toxins that come out in our breath and basically these volatile organic compounds are the breakdown products of our cellular death. Our cells are always turning over, hair cells, mucus membrane cells, things like that. And so we do expire some of these compounds. It's very hard to measure, you literally need liquid chromatography. So, if you think the Covid virus testing is difficult, this would be extraordinarily difficult and very meticulous and so these VOCs are best characterized in lung cancer patients I'd say they're much less characterized in GI cancer. It's been very difficult to do that. So, we there's interest in that but I wouldn't say we've gotten very far.

Curt Pesmen: I just think it's nothing like a breath analyser that's way too simple.

Dr. Alan P. Venook: Correct, because these compounds are in infinitesimal amount that may be enough to give you a heads up what you really need to do amazingly complex into and you know detailed analysis of the breath. So right now, it's just not it's not ready for prime-time great thought but I think we had work to do. That the issue that you raised about the flatulence is a very smart issue because we have a lot of effort of course flatulence and gas is related to the microbiome. What would inhabit of microbiome clearly, different people have different features. Microbiome for the for people listening who aren't familiar with that term that's sort of the community of bacteria and fungi and everything else that live in our you know guts it is said I don't know who counted them and it said there are more microbiome elements in our body then cells in our body. And so we're just a walking zoo of these weird little creatures and clearly they have a lot to do with our ability to digest foods, with many things. We think it's really a big important in interacting with the immune system. And the reason is if you can imagine this the GI tract, the gut is full of these bacteria and these elements that you know, there must be a sort of a mutual non-aggression pact between the human body and these bacterial elements or fungal elements because we let them coexist. And so, we think that may explain why the GI tract cancers don't respond to immune therapies because somehow or the other the immune system is not does not do its normal work in the GI tract because of its the ability to leave these bacteria and these other items alone. Now irregularities in the microbiome are incredibly important in all sorts of colitis and inflammatory bowel disease and probably in different GI Cancers and we're studying that aggressively. We have a huge effort in that a few centers around the country are doing this looking at younger people to see if there's a difference in microbiome and their risks of cancer, to see if people who let's say have a non-western diet do they change the microbiome. These are all things that are very difficult to know because first of all, if you sample the microbiome you change it right because even introducing a tube or taking an antibiotic or anything you do will change the makeup of that community of organisms. So that's one thing but also there's so many of these organisms even figuring out which end is up requires an immense computer technology and only recently have we do we have enough computer power. So, the microbiome is a very big area and that is in the flatulence issues that that's an example of the kinds of things were looking at. There's a company called second genome in the area around here in the Bay Area, which is very interesting very cool. They're looking at things that you find in our stool that these elements that may in fact be markers of cancer, not the so-called Cologuard which is looking for KRAS mutations in cells. But looking at the kinds of you know ailments you're asking about, but it is the problems are so much in there so much there and again just as with the breath collecting these tissues and analyzing them is not so easy, sounds easy but isn't.

Curt Pesmen: Well last real quick question because I know time is tight. You probably have forgotten this Dr. Venook, but about 17 years ago I read a study in asked you about Aspirin because it seemed very promising and for a long-range survivor question and as you were leaving a meeting hall you looked back at me when I said would you advise somebody like me to take Aspirin because it was early, but it was very encouraging and you actually looked back at me and you said well, I wouldn't advise against it, that was quite cautious, but it was a good answer I guess all these years later. Thanks very much.

Dr. Alan P. Venook: Sure. You're welcome. I still take Aspirin to this day.

Curt Pesmen: Okay.

Priya Menon: Thank you Curt. Dr. Venook our next patient panel guest is Aki Smith. Aki is a caregiver and patient advocate for her father, who was diagnosed with advanced stomach cancer. She's also Founder and Executive Director of Hope for Stomach Cancer, a nonprofit organization that provides resources to patients, caregivers, and loved ones facing stomach cancer. Aki please ask your questions.

Aki Smith: Hi, thank you so much for having me on today. I really appreciate it. I wanted to know so gastric cancer is devastating, and survival is measured in months as opposed to years. What's currently being done to give hope to stage four patients and what steps do we need to take in order to start treating that this is a chronic disease.

Dr. Alan P. Venook: Well, that's asking a lot in a few minutes. The problem with many cancers is if we could find them early enough, we could probably impact their outcomes much better. In Asia, for example, there's routine upper endoscopy done because stomach and esophageal cancers are so common, not done in much of the rest of the world. And if you don't find these diseases till they are advanced it's hard to say that you can make much impact in any of them. Stomach cancer, esophageal cancer these cancers don't usually cause symptoms until they damage the cusp of quite a lot of turmoil in the organ. The stomach is like a is like a muscular bag and it basically there to hold food and propel it through the body. You know to move it on to the GI tract and Cancers have to be really extensive to impact the ability of the stomach to work. So, you rarely get enough of advance warning, sometimes a little bleeding or something you might catch a break but short of finding ways of really diagnosis, I think our ability to change to really make a big impact in this diseases is really difficult. We do know from the tumor cancer Genome Atlas studies, which basically have analyzed primary cancers for molecular features. We hope that there's some features that may give us a little handle on how we can treat Stomach cancer better, but in fact because we don't usually know about until it's too late. We don't routinely do screening. It's a bad disease as you said.

Aki Smith: Yeah, so follow up to that question, then you know it appear to me that metastases is a very common and it's really difficult to treat. I mean I saw that you've written some studies on IP chemotherapy. What are some of your take on PIPAC, HIPEC and some Cold IP therapy?

Dr. Alan P. Venook: Right. I'm not a big I think there are selected patients who may benefit from HIPEC. HIPEC is heated intraperitoneal chemotherapy. The idea is that you can there's some cancers that don't invade into organs, but actually just sort of spread on the surfaces of the abdominal cavity in the what's called the peritoneal and the best example of that an ovarian cancer. In GI tract, there are some cancers that tend to do that stomach cancers one, pancreas cancer is another. So idea with HIPEC is you essentially bathe the surfaces and chemotherapy you may get better delivery of the treatment. The heated part is sort of a little bit of wishful thinking. This was started years ago. The Studies have never distinguished whether the heated part is necessary for the effect of the intraperitoneal chemotherapy and in truth, in fact, we don't know that any of those treatments matters much as when you do HIPEC the surgeons will generally going into a very extensive removal of all the cancer they can see and that then in itself may be the difference in outcomes for those patients. There have been just two large randomized studies of HIPEC in patients whose cancers appear to be confined to the peritoneal cavity and in neither case did the HIPEC improve outcome. So, I think the selected patients who'd probably get benefit, but it's just a very tough disease and unlike what you might sort of into it turns out tha0t patients with peritoneal cancer have much worse prognosis than patients with liver metastases for example, that's because peritoneal involvement tends to change the functionality of the intestines the ability for peristalsis to be normal and patients lose weight and feel much worse of the cancer. So it's a terrible problem right now and not an area where we've made a lot of headway. Studies have been done recently though, and certainly HIPEC is not an answer on average.

Aki Smith: Okay. Well, thank you. And my last question is more about clinical trials and clinical trial design. Some of these clinical trials look so similar. How do we help patients connect the dots on clinical trials that are very similar?

Dr. Alan P. Venook: Well good question. Obviously, the reason is very similar as in general reacting. You just compare comparing the old to the new standard to something different or better than standard. So, I

mean, it depends on what the circumstances are. I think with any clinical trial requesting you going to ask is when we risk benefits, what are the chances you doing better than your standard? In general, these studies have to have what's called equipoise. So, in general people have to believe this is not similarity and more likely it in outcomes that you can justify patients participating in one or the other in a random fashion. Now much of the research we do at a place like my UCSF what we're looking to develop is new treatments. Mostly in studies that are not sort of randomized but studies that look at either standard plus something or entirely different approaches. But for a given patient, you know, it's very hard. It's a hard question. You need to go see what the standards are? I would emphasize that new is not necessarily better. So many patients assume that well if this is a study looking at Drug X, that must be really good because then they would not have studied it otherwise. Well in many cases we are hoping drug X is good, but we have no idea if it is. So, patients need to take stock of what the choices are and really spend time doing the homework. I think in the community by and large the studies tend to be industry driven with your companies asking question that would if at the end of the day it will hopefully help patients, but also help their bottom line and I think, so before any patient participates in the study, whatever the disease it's probably worth getting another opinion just to make sure that other people think that the study is asking about question and that patients actually stand to benefit

Aki Smith: Great. Thank you.

Dr. Alan P. Venook: Thank you.

Priya Menon: Thank you Aki. Okay, Dr. Venook next in the panel is Kim Hall Jackson Kim is one of the nation's leading colon cancer advocates, and a strong voice extolling the need for cancer screenings. Kim please ask your questions.

Kim Hall Jackson: Yeah, and thank you. Good afternoon. Thanks for having me. I guess my initial question was in reference to your clinical trial design. The number of African-American and people of color getting access to clinical trials has always been a challenge. I do know that you guys have done something to make it more accessible in terms of financial and transportation, but I think my concern is more about people of color feeling comfortable. I'm on a Clinic trial and I just feel like they're getting a fair share based on you know, social and historical issues. We need to overcome that to increase the comfort level so more people will have accessibility and I just want to know what your organization or what you thought about that process.

Dr. Alan P. Venook: Well, I totally agree with you. I think there's a certain there's a many cases cultural and demographics bias and concern about participating in research. I think the African-American community in particular have a long memory to think back to some of the egregious things that were done to let's say study the natural history of syphilis for example, which is one the shames for our profession for many years ago. You know, we do try to increase access for people of color to participate in research trials. It's a functional whether they have access to the health system. So, level of sophistication, their means, all of these things play a role. What I would say, is that we just submitted the manuscript this week on a big study we did on Colon cancer where about 12 percent of participants were African-American. This is that upto 2,000 patients and those patients did exactly the same as patients who were not pure white or other in our group as opposed to Godly speaking we know that African-Americans how propound they were for stage two or worse with cancer and the assumption then is that that's because of access to care and have more so than inherent biology. So how do we fix that? Well, it's a daunting challenge talking about it doesn't mean we can fix it. At our place at UCSF we work very hard at trying to encourage basket-mixing participation, but it's easier to say than done. The patient need to have access to the system after know about it, so we try and I think we haven't done very well. Just looking at the Covid experience, we see a horrible example of the differential, what difference race makes, racing demographics and socioeconomic status because unfortunately, we're seeing African-Americans doing much more poorly than others with Covid for example. And that's probably related to the nature of the work, that these folks tend to do where they often are out in the front lines doing a lot of things behind the scenes, maybe not, you know, unfortunately they simply tend to be in deep jobs or copulated frequently by people of color. And so this is shines the light on inequities but

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fixing them we can talk about it, but doing it is very hard to know, how we can do that. I mean super challenge and not bad for a satisfactory progress. So far, I must say.

Kim Hall Jackson: I appreciate that. I appreciate that feedback because it is a super challenge and it is easier to discuss them than it is actually to do it. So, I thank you for acknowledging it and I think any steps that your organization have begin to make. I only have two questions, I'm probably a non-traditional colorectal cancer patient, you know, I was 45 when I was diagnosed. I'm a dancer has a really great exercise. I'm a pescatarian and I was diagnosed.

Dr. Alan P. Venook: Does that mean you eat fish?

Kim Hall Jackson: Yeah, yep. Everything else is vegetarian, but I do eat fish. So at the time of my diagnosis, at 45 they were still saying that you should be tested at 50. Now we're starting to get somewhere maybe should be 45, but my bigger question is that after I went through surgery chemo radiation. I'm still dealing with my new normal, which is frequent bowel movement accompanied with painful cramping. I had a temporary ostomy that was removed and maintain this with medication. Just wanted to know if you had any thoughts on a better way to manage this process.

Dr. Alan P. Venook: Great question. So, you know a couple things we do but we and a few others around the country develop programs specifically for young people with cancer colon survivors. We have a big survivorship program in general, but with an emphasis on young people with colon and rectal cancer, especially women who have many like life altering changes related to the curative therapy. One thing that we unfortunately know is that for many patients the goal is of course not have to have an ostomy. Nobody wants an ostomy and yet in fact, sometimes the functioning of the rectum following surgery and radiation the other things you have to do to cure the disease. The function is so bad many times patients would probably be better off with an ostomy and current technology, surgeons can fashion ostomy because actually patients can evacuate at as they wish they don't necessarily need to have a bag as you go around date, you know in out in the community out in the world. They may have a Band-Aid it but over the ostomy and then evacuate as they need to. I mean that's a that's the best circumstance you can accomplish in sometimes. But we're very aware of the of the plight of the survivor and the impact on their lives and much of survivorship these days is trying to figure out what less we can do. As I mentioned about rectal cancer, for example, we now believe we don't have to radiate nearly the number of patients we graded. We think actually in some people with early-stage rectal cancer we can do watch and wait we can do chemotherapy or chemotherapy and radiation and not even do surgery, but they have to be very selective and careful about that. So as in general for cancer treatment you start out your goal is to cure the disease and you may do more than you need and then you try to dial it back and see, you know, what damage did we do? And how can we avoid some of the damage? It's a long process, but I hear you loud and clear especially in women following rectal cancer, we have a lot of quality of life issues that really we need to be much more thoughtful about what we do, what we subject those patients to.

Priya Menon: Thank you Kim. Thank you Dr. Venook. What we will do now is I'm going to read out that we have some audience questions coming. So I'll be reading those out and you can answer them briefly. The first question is what are the latest findings on treating metastatic HER 2 positive colorectal cancer that has not responded to the typical lines of chemo therapy. Particularly asking about Herceptin.

Dr. Alan P. Venook: Right. So there is a there's this trial to a couple of clinical trials that has been recently completed one called HERACLES. And in general, it is a case of patients who have an amplification of the Her 2 gene. Now that's not common cause less than 5% of patients with colon metastatic colon cancer have that genetic amplification but those patients do get some benefit on average from anti Her 2 therapy. The working right now I think most interest is in the combination of two blockers of Her 2 Trastuzumab and Pertuzumab in combination but there are other combinations that have been used. The problem is first of all, it's an uncommon finding in patients with advanced colon cancer, and the results are not so spectacular, but that's a group that we're looking at and theoretically this is your patients who might get greater benefit from treatment earlier on in the course of their disease. Right now, as on the average these patients, they start

with standard therapy and then we switch to Her 2 based therapy at the time of progression and you can imagine we might be better off moving that the Her 2 therapy of earlier, but that's a research question and we are not quite doing that yet.

Priya Menon: Thank you Doctor. The next question is that if you could comment on any new possible treatments for pNET, in particular, that metastasized to the liver, it would be great. Thank you.

Dr. Alan P. Venook: So, pNET is a neuroectodermal tumor. pNET is pancreatic neuroendocrine tumors. Well any of these two neuro-tumors have a propensity to puncture the liver. Any p endocrine tumor are unique as in many of them promote, produce hormones. And so they can cause clinical syndromes. The classic example is carcinoid which are tumors that arise from the intestine. Like for example, make hormones like Kinase and Serotonin which can cause flushing and blood pressure changes. Tumors in the pancreas they can make insulin and glucagon these weird hormones that have a moderate impact on day-to-day life. There's a lot of treatments for these, it used to be thought that these rare cancers now, they're happening more and more. Also, people are living much longer. We have drugs, drugs that can turn off the hormone production something called octreotide and we have a number of these newer treatments that can block their hormones released, these things called let's see drug called Lanreotide or Somatostatin that these all have some effect, and the most dramatic effect on neuroendocrine tumors is what is essentially radiation to these tumors, you can take a molecule that targets that the mechanism that lieth these cells to secrete hormones and by attaching radiation to those that molecule it's sort of like a Magic Bullet and this so called peptide related therapy. You can deliver radiation directly to neuroendocrine cells that is the most effective new treatment and very dramatically effective in most patients not available broadly because it's quite labour intensive but that's the biggest advance and most exciting thing in NET. And again, I'd say the field is evolving and we should make newer molecular ways of targeting and I think that holds out the best hope for that disease.

Priya Menon: Thank you Doctor. The next question is my husband has stage 4 metastatic rectal cancer (liver), has gone through Folfox regiment and radiation. I heard of treatment called Side Effect Free (SEF) chemo. Have you heard of this SEF? Will this treatment has potential in treating the cancer?

Dr. Alan P. Venook: I've not heard of this and I have no idea what they're talking about. Side Effect Free chemo that sort of an oxymoron. I think it's true that there's something so called targeted therapies or thought not to be so. They also have side effects. So, I'm not I don't know what they're referring to sorry.

Priya Menon: And my next question is, (interrupted) Sorry doctor you saying something?

Dr. Alan P. Venook: Go ahead I'm sorry.

Priya Menon: Yeah, So the next question is that the father of my children was diagnosed with esophageal cancer stage 3 in January 2017, died in June. He died, the person says in my opinion, because he couldn't eat. They inserted a stent that made it impossible to eat anything but soft food, then the chemo, then the radiation – everything they did made it worse. As his radiation doctor said, sometimes it's the cure that kills you. It was ironic that they had eradicated the cancer, but he died of starvation. What could have been done differently?

Dr. Alan P. Venook: Well, I'm not sure as I wasn't there. I'm not sure. It's sometimes he just can't do you can't do anything differently. We do occasionally put tubes in patients and feed them intravenously called Total Parenteral Nutrition (TPN) that may be appropriate in some cases. But you know again this is a bad disease requires aggressive treatment and sometimes it's too much and so that very unfortunate but esophageal cancer in particular as I said cancers of the GI tract can have a lot of collateral damage both from treatment and from the disease and many factors including nutrition are big problems. So that's a very bad outcome and unfortunate that sometimes you can't help that are you think we can do better than that, but we may not be able to do that necessarily.

Priya Menon: Dr. Venook, we will have just one more question before we wrap up today's discussion. Could you talk about some of the trials, clinical trials, ongoing clinical trial that folks should be keeping track of?

Dr. Alan P. Venook: Sure. Well probably the most exciting clinical trials relate to the immune therapies. And now some in many cases they have not panned out let's say colon cancer, but for in liver cancer and other cancers, the progress is this stuff is astounding. So one of the first questions to ask with a new diagnosis of GI cancer that is there a rule for immunotherapy to may not be but if there is the upside is dramatic because some people have phenomenal benefit from these therapies. As I said some of these new radiation techniques to isolate the cancer cells and treat them with radiation sparing the tissues the, surrounding tissues that those representing big advances and again, I think as we understand the microbiome, hopefully we will get we may get to the point. I would hope that we can change the microbiome and perhaps change the way the body and routes with the cancer, that's futuristic. But I think that we're hoping that that could be even steps ways of preventing cancer by doing all kind of manipulation. That's what I'm looking for. But it's you know, it's tough It's great to think about and to look forward. It's hard to know what the time frame is and what how much advance we can expect to me quick, but those are things were aiming at.

Priya Menon: Thank you. Dr. Venook. I think that was an information packed to one hour. Thank you very much for your time and all the information that you shared with us and the audience and the panel today.

Dr. Alan P. Venook: Sure.

Priya Menon: Danielle, Curt, Aki and Kim Thank you so much for participating and questions and the questions, you know, you asked to bring the patient perspective to the discussion. We also would like to thank the UCSF Helen Diller Family Comprehensive Cancer Center and our audience. As this talk will be available curetalks.com so please visit our website for details on upcoming talks. Thank you everyone. Have a great day and stay safe. Thank you.

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