Zac Getty:

Good afternoon, everyone, or morning if you're in Mountain Time or Pacific Time. Thank you all for joining us today for our Unpacking Stage IV Colorectal Cancer webinar. My name is Zac Getty, and I am the Disease Awareness Program Manager here at Fight CRC. Fight Colorectal Cancer is the leading patient empowerment and advocacy organization in the United States, providing balanced and objective information on colon and rectal cancer research, treatment, and policy. We are relentless champions of hope focused on funding promising high-impact research endeavors while equipping advocates to influence legislation and policy for the collective good.

Before we get started with today's webinar, I do have a couple of housekeeping items that I always go through. We'll have some time at the end of the webinar for general questions, but please feel free to use the Q&A panel on the right side of your screen to ask any questions that might come up along the way. We'll do our best to address them at the end. This webinar is meant to serve as kind of a high level overview of what a stage IV diagnosis might mean, but also as an opportunity for you to ask your questions. So please don't be shy.

We will have a recording of this webinar available on our site within the next few days, and you will receive that direct link via email as soon as it is available if you have registered. We will also provide a transcript of the webinar on our site for those of you that would prefer to read the information discussed today. Also, feel free to tweet along with us. You can use #CRCWebinar.

Please remember to stop by our website at fightcrc.org to check out all of our patient and caregiver resources. This includes your guide in the Fight Meetups, which are an online space to meet with other patients and caregivers that are held three times per month. They touch on a variety of topics, but are also just a great place to find a sense of community. We also have our free Community of Champions app where you can connect with other people in the colorectal cancer space and keep in touch with Fight CRC and know what we're up to.

We also offer an assortment of print and digital educational resources that are free to request and download. We are also now hosting monthly Mega Meetups, which address a specific and unique topic each month. Our next Mega Meetup will be on Thursday, May 30th, and we'll be focusing specifically on early age onset colorectal cancer. If you're interested in attending that, you can RSVP through our Community of Champions app. If you're not a member of Community of Champions, you can download that or also visit us online in a typical browser.

I do have a quick disclaimer. The information and services provided by Fight Colorectal Cancer are for general informational purposes only. The information and services are not intended to be substitutes for professional medical advice, diagnoses or treatment. If you're ill or suspect that you are ill, please see a doctor immediately. In an emergency, always call 911 or go to the nearest emergency room. Fight Colorectal Cancer never recommends or endorses any specific physicians, products or treatments for any condition.

Okay. With that all out of the way, I would like to briefly introduce our participants. Joining us today are Phuong Gallagher, our Fight CRC RATS Manager and stage IV survivor and Dr. Cathy Eng, and I'm going to try to get all your credentials here correct, Dr. Eng. She's our Fight CRC board member and Professor of Medicine, Hematology and Oncology. She's a David H. Johnson Endowed Chair of Surgical and Medical Oncology, Co-Director of GI Oncology, Co-Leader of the Gastrointestinal Cancer Research Program, Director of Strategic Relations, and Director of the Young Adults Cancers Program at the Vanderbilt Ingram Cancer Center.

Dr. Eng and Phuong, thank you so much for taking time out of your busy schedules to join us today. I'm going to give Dr. Eng here a chance to provide a little bit more on her background before we start going

over some slides. After we go through some slides, Phuong will share a bit about her story and some questions that we've received through Community of Champions from our patient survivors and caregivers there. Please, I do want to stress again that this webinar serves an opportunity to ask questions, so please don't be shy with the Q&A box. So with that, Dr. Eng, would you mind to provide just a little bit more background about who you are, what you do?

Cathy Eng, MD:

Thank you for having me here today.

Zac Getty:

Thanks for joining us.

Cathy Eng, MD:

It's my pleasure to do this webinar with Fight CRC and with Phuong. We've done some other events together as well. I am a clinical researcher that focuses on colorectal cancer and especially in early onset just because I see several of these patients in my clinic, and I focus on developing clinical trials, as well as running our Young Adult Cancers Program. Then nationally, I'm involved in a lot of different organizations that are involved in oncology in general.

Zac Getty:

Thank you so much. Okay. So we're going to start just going through some slides here. Like I said, ask some questions if you got them and we will get to them after we're done with the presentation. So first off, this is a webinar about stage IV colorectal cancer. So what is cancer staging to begin with?

Cathy Eng, MD:

So I think it's important. It's mostly important also for the providers. So cancer staging usually involves three different aspects, as noted here, a T stage, which is how far the tumor has gone through the colorectal wall, and then whether or not there's node positivity, whether pathologically or clinically, and then M does stand for metastatic disease. There's different aspects regarding M1, Ma, et cetera, but for the most part, we just really focus on just M, if it's metastatic or non-metastatic. Basically on the right is the AJCC or the American ... It's not only in the United States. It's a surgical AJCC staging system, which is basically accepted globally, and that is basically how they divide it into stages taking into account the T, N, and M stage.

Zac Getty:

So there are stages within stages it looks like based on this guide. Is that correct?

Cathy Eng, MD:

Correct, and not everybody is so specific in their physician's note, but obviously, there can be a big difference if you're stage three versus a stage one or stage two because when you have node positivity, that impacts your overall outcome, and that also impacts whether or not you would consider any additional therapy when you have node positive disease. For stage IV patients, obviously, our goal is to try to give them therapy so we can hopefully try to get them to a point of resection to make them disease-free or at least try to address it, whether it's with radiation therapy or some other directed therapy.

Zac Getty:

Thank you. So how is staging performed in colorectal cancer specifically?

Cathy Eng, MD:

So the most important thing for any newly diagnosed patient from my perspective is clinical staging, where you have diagnostic imaging completed. In this case, it usually is with a CT scan. For a colorectal cancer patient, it should be chest, abdomen, and pelvis, and then MRI is sometimes offered if the patient is allergic to contrast or if the contrast cannot be given because the patient doesn't have a good kidney function. An MRI is actually the best test to look at the liver, as well as for any potential bone involvement just in case the patient is having symptoms.

In regards to clinical staging, we also like to confirm via pathology that the patient has the malignancy that we believe it is. So usually, whether it's through endoscopy, through colonoscopy or if a surgical biopsy needs to be completed for a suspicious site of disease, a needle biopsy will be completed to confirm that the patient has colorectal cancer and it has spread to that particular organ that it appears to be an area of concern based upon diagnostic imaging.

So you have to have some type of pathology confirmed because, obviously, you want to ensure it's not another type of cancer. There are rare instances where you can have another cancer from a totally different malignancy that has metastasized to the colon. It's not common, but it does happen. Then liver and lung involvement from other cancers are very common. So you want to make sure that you have definitely colorectal carcinoma before starting therapy, but definitely, every single new patient should have full staging completed in regards to diagnostic imaging.

Patients will also ask, this always comes up, "Should I get a PET CT scan?" A PET CT scan is not necessarily needed for all patients. A PET CT scan is very helpful when you have something that's not definitive on CT or MRI, small lymph nodes, for instance, where you're questioning whether or not that they are positive or negative. They may be normal in size on a CT scan, but they may actually have activity which would be noted on a PET scan.

If you have rectal carcinoma, for metastatic disease, once again, systemic chemotherapy is going to be the most important thing regardless of whether your colon or rectum, but if you are potentially getting your rectum resected, you want to make sure you have an MRI of the pelvis. That is the best way to evaluate imaging. Prior to rectal resection, it helps the surgeon out. Obviously, not every single institution has a dedicated radiologist that knows how to read MRIs of the pelvis. So in that case, we would recommend with just a standard CT scan if that's the case, and maybe an endoscopic ultrasound for rectal carcinoma, but the true gold standard ideally would be MRI of the pelvis if you're going to have a rectal carcinoma resected.

Zac Getty:

So it's a little more complicated than just getting a CT, and you get a stage right then. It might take a little time for you to find out your actual stage from initial diagnosis to staging.

Cathy Eng, MD:

Yes, and thank you. It's extremely important. I know patients really just want to get treatment going as soon as possible, but the reality is is that if we don't have accurate staging or if we overstage you by presuming something is cancerous when it may not be, you may be receiving overtreatment. There are things called hemangiomas, which is just normal non-cancerous appearance within the liver. It's just the way the vasculature is, the blood vessels appear. On a CT scan, it may look like it's cancerous, but you

have to get an MRI in order to rule out basically a completely benign process such as hemangioma versus actual tumor.

Zac Getty:

Interesting. I also see in this pathological stage statement, it says that surgery is often involved. It's possible to get a stage IV diagnosis without the involvement of surgery.

Cathy Eng, MD:

Yes. Great point. A paper just came out in JCO, which is actually based upon three prior presentations or two prior. I can't remember how many they ended up doing their analysis, but, basically, it's literature that many of us know, but not many patients may be aware of, that you do not need to have your primary tumor resected in the colon or the rectum if you have metastatic disease unless you are having symptoms from your primary tumor because to take the time to resect your primary tumor, in fact, delays the receipt of your systemic chemotherapy and as a result, your metastatic disease may grow further. It does not improve your overall survival.

Actually, in one study it showed that if you took out the primary tumor and you thought you would receive chemotherapy afterwards, about a quarter of patients ended up not receiving any chemotherapy afterwards because they had postoperative complications.

Zac Getty:

Wow.

Cathy Eng, MD:

So do not believe you need to remove your primary tumor colon cancer or rectal cancer. It does not improve your overall survival unless you're having symptoms such as in your obstruction, potential risk of perforation, bleeding. Those are factors, obviously, that we would take into account for surgical resection. If you have a rectal tumor, we can often provide radiation therapy there to help with those symptoms locally. So do keep that in mind, and don't believe you need to resect your primary tumor. It's not like breast cancer where you have to have a resection completed.

Zac Getty:

Interesting. Thank you so much.

Cathy Eng, MD:

That's like hot off the presses. It just came out of publication.

Zac Getty:

And that's why you're here. That's so helpful to get that brand new information. I know we've touched on metastasis. So strictly speaking, what is it to receive a stage IV colorectal cancer diagnosis?

Cathy Eng, MD:

So if you have localized lymph nodes, it does not mean that you have stage IV disease. You may just have locally advanced disease. It's when the tumor has spread outside of the original primary tumor site and outside of the local regional area of involvement, and it's spread to either lymph nodes that are distant or other organs that are distant. So that is why it is considered stage IV.

As stated here, it's very complex, which it is. We fully recommend multidisciplinary management if possible if there's any potential for any type of intervention, whether it's surgery, ablation or any type of radiation therapy. Then obviously, to be diagnosed with stage IV disease, you want to make sure you know ... I think you have it in another slide going further down, which side of the tumor your tumor's on, is it left side, right side, and what type of molecular markers.

So I fully agree with the statement. There's no one size fits all treatment for stage IV colorectal cancer. They used to believe there was just kind of stage IV, everybody got the same cocktail. It is no longer with that approach. So it's really a shared decision.

Zac Getty:

Excellent. You mentioned a multidisciplinary team. Who would be part of that besides my oncologist and my surgeon?

Cathy Eng, MD:

Well, it's definitely a medical oncologist. It could involve a surgical oncologist. It could involve a radiation oncologist. So those would be the individuals that it may or may not involve or an interventional radiologist as well, depending upon what procedure is being considered.

Zac Getty:

Okay. Excellent. An interventional radiology, they're working on, it's not necessarily surgery as you would think of it typically, but they're using radiological imaging and stuff like that to perform procedures. Is that correct?

Cathy Eng, MD:

Correct. That's a nice way of putting it, yes.

Zac Getty:

Okay. So where are the most common sites of metastasis in colorectal cancer?

Cathy Eng, MD:

So for colon cancer, liver is the most common site of disease, and then for rectal cancer, lung cancer or lung metastasis, sorry, not lung cancer, it's lung metastasis. That is most commonly for rectal carcinoma. Then other sites of disease may involve the peritoneum, which is the abdominal cavity. Once again, you may have lymph nodes that are afar, and rare instances of bone involvement and brain involvement. Some people will say, "Well, why don't you image my brain as part of staging?" and that's just because it's not very common at all. It's probably less than 2% of our patient population.

Zac Getty:

Interesting. I want to clarify. So you say you may have distant lymph node involvement. If I have, let's say just as a hypothetical, if I had lymph node involvement in my neck, that's not necessarily stage IV cancer, it's just lymph node involvement at a distant site?

Cathy Eng, MD:

No, that would be stage IV because that's outside of the local region. So wherever your tumor is, let's say you have a rectal carcinoma, then it would not be unusual for you to have what we call perirectal

lymph nodes or lymph nodes adjacent to the rectum that are involved, but once you get past the local area of involvement and it has spread to other lymph nodes such as periaortic region, retroperitoneal lymph nodes, which are towards the back of the abdominal cavity, where you mentioned like supraclavicular lymph nodes, which are high up in the neck, that would be extremely unusual and would be consistent. Once again, it needs to be biopsied, but would be consistent with metastatic disease.

Zac Getty:

Thank you. Do we know why these are the most common sites of mets for these particular-

Cathy Eng, MD:

It's just the way the blood flow is from the primary site of involvement.

Zac Getty:

Interesting.

Cathy Eng, MD:

Yeah, it's where the lymph drainage is, et cetera.

Zac Getty:

So that all cancers are going to have their kind of most common sites of mets, and this just happens to be what it is for colon and rectal cancer.

Cathy Eng, MD:

Correct.

Zac Getty:

So we mentioned it briefly earlier. So biomarker testing and stage IV CRC, I know that we at Fight CRC really stress the importance of biomarker testing, and based on the information out there, it seems like it's of particular importance for a metastatic disease diagnosis. Is there a certain time that biomarker testing should be performed after diagnosis while it's happening? What does this look like for a patient?

Cathy Eng, MD:

So for any patient that is diagnosed with cancer, it is recommended by standard guidelines that all patients be tested for, you have listed here, microsatellite instability, which, basically, it's a defect of the mismatch repair protein or it can be inherited form of colorectal carcinoma. That's really important for all cancer patients to be tested for, especially if you're young because it may help your other family members in regards to prevention, and it also may be informative in regards to your therapy and whether or not immunotherapy may or may not have a role.

For a metastatic patient, we also recommend testing to be completed as soon as possible as soon as you've had your diagnosis. If you've not had molecular testing completed as far as you're aware of, I mean, I'm still seeing patients in my clinic that have gone through first line therapy and have no idea what their molecular testing is, and so I have to either order it or retrieve it from their outside physician because that helps the healthcare provider create a plan of what the next steps of treatment would be if the patient needed to continue therapy for second or third line therapy, for instance, if they have surgically unresectable disease or disease that is not amenable to radiation therapy.

So the reason that's important is because the molecular testing can help guide treatment because there's a lot of new molecular markers that have specific drugs that are tailored to that molecular marker. So BRAF V600E mutation is present in about 9% of our patient population, and drugs were approved many years ago in melanoma because it's more common in melanoma. We know now that the BRAF inhibitors don't work by themselves in colon cancer, but they work great in combination with anti-EGFR therapy, and now it's being explored in clinical trials for frontline therapy.

So that is just an example, but see, also identification of those molecular markers are important early on because you want to get that tissue specimen before it's sent off just to some warehouse. If it's been sitting there too long at the hospital, they need storage space, so it has to go somewhere. So they send it to a warehouse, and it may take weeks to retrieve it again or else you have to get another new biopsy. Some people will say, "You can just do testing through blood for molecular markers." Yes, that's true, but you're going to get a smaller panel.

So a tissue analysis for molecular alterations or mutations, depending on which company your hospital may be working with as a third party or whether or not they do it in-house such as MD Anderson and MSK, that will give you anywhere from three to 500 different molecular alterations, whereas a blood panel will only give you like 100 different molecular alterations. So you really want to be able to get the tissue, if possible, and utilize it for DNA and RNA analysis, which will not only look at mutations, but amplification and fusion proteins. So it's really important, ideally, to test for both tissue and blood. That's what I normally do.

Zac Getty:

That's really helpful. Honestly, that's information that I had not heard before about in terms of storage for samples or-

Cathy Eng, MD:

They run out of space, so they have to send it off to some warehouse. Every hospital has a warehouse, and at some point, it gets sent off there if they need space, and then you're going to have to track it down, and that will add just weeks onto the testing time. Keep in mind, a lot of the new clinical trials, because they have very specific drugs that they are testing, they will require your tissue, if it's not already been done, to be tested for that specific drug that they are focused on. Keep in mind, the tissue testing will take anywhere from roughly about three weeks, three to four weeks, but the blood testing, it's a faster turnaround time. It's one to two weeks, but once again, you only get 100 plus alterations evaluated versus three to 500 in tissue.

Zac Getty:

Sure. Well, thank you. That's really good information to have.

Cathy Eng, MD:

It really helps providers.

Zac Getty:

Absolutely. I want as much information as you possibly can get.

Cathy Eng, MD:

I mean, as soon as they come in, I want everything immediately available to me and then I have to track it down. So the more information you bring to the provider, the easier your first visit will be.

Zac Getty:

Sure. So touching on the treatment options available, and I know that in stage IV it quickly explodes, and there's a lot of different treatment regimes and steps you take, first line, second line. Can you speak a little bit about immunotherapy and what that is in the context of stage IV cancer?

Cathy Eng, MD:

I mean, I think in simple terms, immunotherapy now is the standard of care we know in GU cancers or bladder cancer, renal cell carcinoma, lung cancer, and melanoma. In colorectal cancer, it's a smaller subset of patients. It's less than 5% of our patient population. It is being evaluated for earlier stage colon carcinoma just so people are aware, but the trial has finished enrollment. We don't have any results yet.

We basically provide you ... These are the various companies that have PD-L1 agents or PD-1 agents that basically allow you to utilize your own immune system to help fight the cancer and have ... That's just a very simple way of putting it in order for you to have a better outcome. The one thing that's very unique about the setting the metastatic disease is that we know that pembrolizumab, for instance, is already approved as a single agent. There's phase two data with nivolumab as well, but there's recent data that shows combined therapy, which is very early with the results, we don't have the final results of nivo and ipi in combination. All of these are better than chemotherapy alone.

Historically, we would always give chemotherapy to these patients because that was our only option. So the fact that you may be a candidate for immunotherapy is of critical importance. In fact, once again, I don't want to advocate for the combo data because we don't have enough information yet. There's phase two data that has been with more long-term followup, but the big phase three data, the data is very early on in development. It was a three-arm study, and it only compared the doublet of nivo-ipi versus chemotherapy alone, which was no surprise, it was superior. We don't have the overall survival results though, but only for progression-free survival, but is nivo-ipi better than nivo? We don't have any of that data yet.

So as a patient and as a healthcare provider, I would only recommend pembrolizumab at this time because we have long-term data for single-agent treatment. Nivo-ipi is being also evaluated in upper GI cancers as well, and then some people will say, "Well, I saw that report at Memorial Sloan Kettering where it cured all those patients." The original data is from a single institution. It is being validated at this time because there's been other data from other institutions which are not as high of a cure rate. There's a national trial that's ongoing for both early stage colon and rectal, but for the metastatic setting, pembrolizumab is a single agent, is FDA-approved with long-term followup, and we should be getting updates for nivo-ipi combination hopefully this year, as well as next year with more longer term followup.

I want to kindly remind everybody that immunotherapy is not a walk in the park. People think because of all these advertisements it looks like it's very easy and they won't have any toxicity. That is not true. There's just different side effects, and I think that's really important to keep in mind.

Zac Getty:

Appreciate that insight.

Cathy Eng, MD:

And there's long-term side effects.

Zac Getty:

Sure. Appreciate the insight and the insight especially that this is kind of an ongoing study is happening now. So this is changing, this landscape is changing. I think that also applies to this next slide, discussing targeted therapy. Looking at the bottom here where I've listed out drugs that have been used in colorectal cancer, I think you've got a lot of options with targeted therapy. What generally is targeted therapy? What qualifies for targeted therapy? How is it different than other options you might receive?

Cathy Eng, MD:

Well, chemotherapy such as 5FU or oxaliplatin or irinotecan, they're not so much focused on any particular mutation or any type of molecular alteration. Even with the long-term use of bevacizumab, we have never identified a good molecular marker for anti-VEGF therapy. What does VEGF mean? Vascular Endothelial Growth Factor. Why do we give it? It's because it's focused on blood vessel growth. In order for a tumor to metastasize, it needs a blood supply. So bevacizumab, which is longstanding, ramucirumab, aflibercept, those are all approved, but bevacizumab is the more common one utilized in that setting. Then fruquintinib is the most recent drug that's been approved, which is an oral agent, but it's specific to VEGF receptors 1, 2, 3. Bevacizumab historically requires use in combination with chemotherapy. Fruquintinib is an oral agent by itself, and then you start looking at all these other agents.

So historically, the one mutation that everyone knows is the RAS mutation, so I'll utilize that as an example. So KRAS mutation is present in 30 to 60% of all of our colorectal carcinoma patients. Previously, if you had received cetuximab, which is an anti-EGFR therapy or anti-epidermal growth factor receptor therapy, if you have a RAS mutation, you don't benefit from this class of drugs at all, and that class of drugs has side effects such as potential allergic hypersensitivity reaction and a rash. So nobody wants to receive a drug that they may not benefit and may have potential side effects.

So that was the first drug and the first molecular alteration that showed if you have a mutation, you don't want to receive that class of drugs, but also, if you have a mutation, there are certain drugs you do want to receive. So for instance, I mentioned BRAF earlier, but HER2, that's the most recent drug approval in January of last year, tucatinib, which is an oral tyrosine kinase inhibitor of HER2. That is specific for HER2 ImmunoHistoChemistry 3+, where it has the most benefit, and it's given in combination with trastuzumab or Herceptin.

Many people are familiar with that class of drugs because of breast cancer and gastric carcinoma, but now it's in 4% of colorectal cancers and it has significant benefit. So this is why you want to make sure molecular testing is completed. So you can learn what you should not receive, but also what you can potentially receive, and that's how you kind of create your sequence of therapy.

Zac Getty:

You really just took the words out of my mouth. I was going to say, so this really kind of underscores the importance of knowing your biomarkers, knowing what specifically subset of cancer you have and what treatments it may or may not respond to.

Cathy Eng, MD:

On the right, you listed all those new drugs. Now, it's not just KRAS. We narrow it down. Is it KRAS G12C? So now, there's drugs specific to G12C.

Zac Getty:

Wow. So chemotherapy, we've mentioned a couple times. So I know there are multiple chemotherapy combinations that may be prescribed for stage IV. Do these differ from what might be prescribed from earlier stages like two and three or are these unique to stage IV treatment?

Cathy Eng, MD:

These are all specifically for stage IV. For stage II chemotherapy, the role of chemotherapy is questionable, and for stage III, it's still only oxaliplatin-based therapy with 5FU or capecitabine.

Zac Getty:

Okay. So these are just all options they may run through or are they going to try these first line or these generally superior or inferior to other options?

Cathy Eng, MD:

I mean, for the metastatic setting, these are first, second, third line potential therapies. Sometimes they are combined. As mentioned, they're in bullet four with an EGFR inhibitor if you're RAS wild type. If you're not, as if anything would be utilized in front line. I don't see it being utilized as second or third line just because it is a tough regimen, but it's got very high response rate.

Zac Getty:

So speaking to something being a tough regimen, I know that if you can't tolerate certain chemotherapy regimens, there are maybe some additional options. Are these as effective as what you would typically be using or are these something that you only would need to use if you absolutely cannot tolerate the side effects from-

Cathy Eng, MD:

These are for patients maybe with poor performance status. Maybe they're very far along in regards to their disease evolving and they don't have enough energy in order to sustain chemotherapy. So in this setting, these would be kind of a lower dose chemotherapy setting. Then obviously, our elderly patients or multiple comorbidities, you would have to consider starting up with a more gentle chemotherapy regimen.

Zac Getty:

Sure. So I know that Lonsurf specifically is not indicated as a first line treatment. That's something you would try further down the line if you're not able to tolerate other medications. Is that correct?

Cathy Eng, MD:

Correct.

Zac Getty:

Okay, and is that considered chemotherapy or is it a different class of-

Cathy Eng, MD:

No. Lonsurf or trifluridine or tipiracil, it is chemotherapy and it's given with bevacizumab, which is an anti-VEGF therapy, but yes, it is part of the 5FU-based family.

Zac Getty:

Thank you. So those are just some of the medication options. I did want to touch on surgery briefly, and I know that there's a lot of information here.

Cathy Eng, MD:

And I'm not a surgeon.

Zac Getty:

Yeah, Dr. Eng is not a surgeon. So I know that there are approaches for meds to different organs are going to differ. Can you speak at all to that? I know that you are not a surgeon, so-

Cathy Eng, MD:

Yeah, I mean, I think once again, I just like to emphasize this is where multidisciplinary engagement is important. Patients always ask me, "Well, what would you do?" and I say, "I'm not a surgeon." I always, always refer to my surgical colleagues for a informed decision and a team approach so that we can discuss after their consultation with the patient. Sometimes it's due to anatomy. Sometimes it's due to the liver function test. Sometimes it's due to a history of cirrhosis or maybe there's been too much damage to the liver from too much chemotherapy or sometimes you have patients that have a fatty liver just due to their dietary habits. Then there's other times where ... I do want to bring this up because this actually happened to me yesterday. Be very careful with your dietary supplements. A lot of them are metabolized through the liver. So you may end up compromising your own care without realizing it. So please talk to your physician, once again, multidisciplinary management. Work with your PharmD or work with your integrative medicine program to make sure that you are choosing the right supplements that don't interfere with your treatment.

Zac Getty:

Helpful, thank you, especially with the liver. So with lung meds, is there anything else that you might need to just specifically be aware of that you may be impacting your treatment by taking supplements, something like that or-

Cathy Eng, MD:

Once again, it's the same discussion. I always refer my patients to a thoracic surgeon first before referring them to a radiation oncologist because I think we want the expertise of the thoracic surgeon. Honestly, a CT scan may be read very basic, and then you send the patient to the thoracic surgeon and they will identify much more disease sometimes, and don't be alarmed, it's just that this is what they do. They're very focused on the lungs and they catch up very, very tiny sites of potential disease, which impacts their surgical approach, but you want the insight of the surgeon first and foremost before considering any kind of resection or directed therapy.

Zac Getty:

Okay, and again, that's going to apply as well for meds to the abdomen.

Cathy Eng, MD:

So this one I highly recommend. No one proceed with any of this without speaking to an expert in the field of peritoneal disease. There's been multiple studies. The largest study was the French study, which showed there was no additional benefit for heated intraperitoneal chemotherapy for metastatic colorectal carcinoma patients. There may be a role for cytoreductive surgery. This does not apply to other malignancies that use HIPEC. There may be a role in stomach cancer and ovarian cancer, et cetera, but for colorectal carcinoma, it is a rare case where we would ever utilize HIPEC unless there's very few sites of disease. Once again, that's not a decision for the medical oncologist, that's for a surgical specialist.

I would highly recommend if there's not a surgical specialist at your institution, go get a second opinion. This should not be done without great thought. These are significantly morbid procedures with a high mortality of up to 20%. These procedures take anywhere from six to 14 hours. So do not go in lightly. You can have a surgical recovery time as well, anywhere from one week to three weeks. So do not do these procedures without getting a expert opinion.

Zac Getty:

Wow. Thank you for that insight. I think I just have one more treatment modality that we haven't covered, radiation therapy, specifically, and I know you're not a radiologist or a radiation oncologist, but-

Cathy Eng, MD:

So collective internal radiation therapy, also not very commonly done now in colorectal cancer. It does have a role in other malignancies. It's just that two big international trials completed in front line and second line setting did not demonstrate any improvement in overall survival, and that's done by interventional radiology. Stereotactic radiation therapy is different. That is selective radiation therapy to focal site. Once again, we don't offer radiation therapy if you have multiple tumors. If you have a limited number of tumors, then we would consider selective, I'm sorry, stereotactic radiation therapy potentially. Once again, I don't make that decision without my surgeon and without my radiation oncologist, but we cannot radiate the entire liver because you have to remember, if we radiate something, you're going to have scar tissue. So we cannot radiate your entire lung, you won't be able to breathe.

So we only radiate select sites of disease. It may be the size that may impact the decision. It may be the anatomic location which may impact the decision and the number of sites. So it is very much an informed decision making process with the entire team and a shared decision with the patient.

Zac Getty:

Thank you. So next is just general takeaways. I think if there's one thing that I can pull from what you've had to say so far in this webinar is that this is complicated. There are a lot of different options.

Cathy Eng, MD:

Yeah, it is very complicated. I think it's very important to keep in mind people find these numbers on the internet and they're like, "Oh, my god, I was told that I only have this much time," or, "The median survival is this." The reality is that is a median. Keep in mind, that is the hump in the road, and there's a lot of people, 50% of patients surpass that. So I mean, I have patients, several patients that are past three years. So that doesn't mean that everybody is three years. So don't read everything on the internet and believe in what you read.

Zac Getty:

Thank you so much. I really appreciate your insight, and that's honestly a really nice segue, I think, into Phuong Gallagher's story, who has joined us and has volunteered to kind of give a little bit of her background and her experience and share with people on this webinar. Then we do have some questions coming in, Dr. Eng. So after Phuong has a chance to share, I'm going to go ahead and relay some of those to you and we can move forward with that. So thank you so much, Dr. Eng. Phuong, thank you so much for sharing as well.

Phuong Gallagher:

Yeah, no, thank you so much. Actually, I always appreciate the opportunity to share my story because I think my story is unusual. One of the things that happens when you first hear the word stage IV is there is this huge loss of hope for a lot of people. They automatically think, "Oh, my gosh, I'm going to have to get my affairs in order," and that's it. I am 17 years into my journey. I'm stage IV. I was diagnosed originally when I was stage III. I was borderline stage II and III. Treatments back then were very, very different from what it is now. Back then, it was basically FOLFOX, FOLFIRI, and then good luck. There was a lot of clinical trials and a lot of research being done, but it was prior to all these options of targeted therapy and precision oncology.

So things are a very different view now from what it was back then. We've gone through so many of these options that have been discussed, and I'm sitting here thinking, "I've done that, I've done that, I've done that," and it's not all at the same time. Different things happened at different points in my journey.

So I was only 29 when I was first diagnosed. It was the typical story of I was young, I was misdiagnosed about a year and a half delayed into my diagnosis because my primary at the time literally said when I asked for a colonoscopy, "You're too young to have cancer," because I didn't look sick. I mean, aside from the fact that I was down to 85 pounds, which should have been a sign, although I presented with a checklist of symptoms, I had the extreme stomach pains, extreme weight loss, changes in my bowels, I had blood in my stool, I really didn't know what's happening to my body. When I asked, that was lesson number one for me in hindsight is don't accept the answer of, "You're fine. You're imagining things," or something like that. If you really feel like something's wrong, go check it out.

Anyhow, I was diagnosed at stage three. I went through my initial radiation, and then I went through FOLFOX. At the time, things looked good. Went into monitoring every three years, three months with scans, and I was fine for about a year, and then I had my metastasis. So I have had metastasis to my liver, to my lung. Each time that it shows up, we had to decide what's next, and what's next really was dependent on what was available.

For quite a while, it was FOLFOX and FOLFIRI, and then we had to go to surgical and radiological interventions. So the thing about surgical resections was I was able to have multiple resections to my liver because when you resect, it does grow back in size. There's the scarring, of course. That is to be considered, as Dr. Eng said, with both radiation and the surgeries. So that was something we were watchful for, but then as we progressed, FOLFOX failed me, FOLFIRI failed me, and then at the time, regorafenib had just come out as being approved as the next line.

This speaks to the importance of patient forums. I was on the colon clubs, colon talk forum where there was somebody who was actually on regorafenib as a part of the clinical trial, and they were sharing, "Here's what I'm going through, here's what the effects are." So I was able to follow along, and I decided along with my doctor it was not for me. The side effects at the time of what presented versus what it could possibly do for me was not worth the trade off. So this is where it's really important, as Dr. Eng said, the multidisciplinary team. It's just as important for you as a patient to have that relationship with

your doctor, to find out about your disease, to learn about what can you do, what does this mean for me, and to make these decisions together.

The other thing that I've really learned since in these 17 years is clinical trials is super important as an option. Don't discount it. Don't write it off. Don't think that, "Oh, this is my last ditch effort before I give up on all my options." It should not be like that. Clinical trials, it's not like you can say, "Okay. Well, I've decided I want to do a clinical trial, now I'm going to go do it," and jump into one. There's a lot of preparation that goes into it. You have to know your biomarkers so that you can find out what is the right clinical trial for you. You have to know so much of your history and everything needs to be gathered, and then you have to find out, "Is there space for me on that clinical trial?"

So you have to have all your things together. You have to be prepared because when that spot opens, it's a short window. If you don't take it, somebody else is going to be able to take that spot. So that's the importance of getting all these tests and all these scans and all these things gathered. So I think that those are some of the big things that I would say as a stage IV patient that you should be aware of. Be open to the options. Talk to your doctors about your options because just because something's not right for you now doesn't mean that it won't be right for you later.

Zac Getty:

I really appreciate you sharing your story. I do just want to highlight, we went over a lot of these giant lists of medications that have been coming out, targeted therapies, differences, things are changing, and those are all pushed forward by clinical trials, and those have a real impact on you personally and other patients. That would not be happening without active participation in clinical trials. The options, I think you mentioned this right at the beginning, the options when you were initially diagnosed are much different than the options that are still around today. I think we're all happy you're still here because of these options that you have for treatment. So thank you so much for joining us. Thank you for sharing your story. I really appreciate it.

Cathy Eng, MD:

Can I elaborate on clinical trials because my other hat is for the NCI? So in full disclosure because the co-chair of the GI Care Committee, I'm the full advocate of clinical trials, but also, it's important to keep in mind, every single drug that's FDA approved went through a clinical trial. That's how drugs get approved. In the United States, we do a very poor job in regards to clinical trial enrollment relative to our European colleagues. So that's why you'll find most of the trials that have been completed are now largely being conducted overseas with a very small percentage of US participants.

So there was a paper that just came out recently, I think last month, where just historically, United States clinical trial enrollment is about 7%, but an NCI designated cancer center clinical trial enrollment is up to 20%. Once again, it's really a matter of communication between you and your provider. As Phuong stated, it's extremely important. Some people will say it's inconvenient because you have to be treated at that center, and that is true, but if you have an experimental trial, you have to be treated at that center because there's multiple blood tests, EKGs, and other tests that need to be completed appropriately in order to ensure that that clinical trial moves forward.

I just want to mention there's three stages of a clinical trial. Sorry, I don't mean to elaborate so much, but I just want to make sure because this always comes up. So phase one, it may be first in human, first in man, sorry. It may be something old combined with something new, but the combination is new, so it has to go through phase one, which means we're looking at the dose and we're looking at the side effects, and that involves all cancers. So you may be on a trial with a pancreatic cancer patient, a lung cancer patient, and a lymphoma patient, for instance.

Phase two is they found the dose, they know the side effects, but now they want to test it in a certain type of cancer. In this setting, it would be stage IV colorectal cancer. So it's going to be either a single-arm study or a randomized study depending upon the way it's been designed.

Then phase three is it seems very promising in phase two in metastatic colon cancer. So we know the dose, we know the side effects, we know which cancer we want to study it in, but now we have to compare it to the standard of care. So I'm just going to create a scenario. So drug X plus B is the investigational arm and the control arm would then be FOLFOX plus bevacizumab. Is drug X plus B superior in regards to time to tumor growth or progression-free survival or overall survival? Then if it's positive, it goes to the FDA for approval.

So ideally, you always want to try to find a phase three trial because that's obviously less experimental, but still, it gives you a new drug, but sometimes if you've had lots of therapies, so Phuong has been through several lines of therapy, for instance, and so it might be more appropriate for a phase one trial because not always a phase three trial is open. Those are very few and far between.

Zac Getty:

Thank you so much for that additional context. It's very helpful, and we talk a lot about clinical trials and the need to participate, so it's helpful to have your input on that. Phuong, again, thank you. I know we do have a list of questions that came in through Community of Champions, but I do have several live questions that have come in during the webinar that I would like to try to address first time permitting. I have one. Let's see here. This is going to be for you, Dr. Eng, and this is just a general, what would the symptoms of a brain metastasis look like?

Cathy Eng, MD:

Maybe changes in vision and maybe lightheadedness, loss of balance. Those are the more common side effects. Could be headache. Also, refractory nausea and vomiting, that's not easily treated with your standard anti-nausea medications that you would normally respond to. So whenever I have a patient that has continued nausea and vomiting despite all types of anti-nausea medications, I am concerned in that setting. Once again, it's not as common by any means. It's less than 5% of all of our patients, but any neurological symptoms, a droopy eyelid, for instance, change in speech, generalized weakness on one side versus the other side of the body, anything that may suggest a potential stroke, those things should be evaluated.

Zac Getty:

Thank you. I have one that's pretty specific here. Do you have an opinion or any research around the ability to slash or impact on treatment for stage IV disease if the patient has had a lower anterior resection to treat stage III rectal cancer?

Cathy Eng, MD:

I'm not exactly sure I understand that question, but a stage III resection would not impact therapy for stage IV. That would just be a patient that has been diagnosed with stage III and then unfortunately may have developed recurrent disease and now they're stage IV. It would not make them ineligible for any treatment.

Zac Getty:

Okay. I think that's probably-

Cathy Eng, MD:

Unless they're having issues like with their low anterior resection such as small bowel syndrome, for instance, where they just have uncontrolled diarrhea, and if they're taking oral agent, for instance, that may impact the electrolytes, but if they have good bowel motility and they recovered from their surgical resection, it should not negatively impact their enrollment.

Zac Getty:

Sure. Thank you. Here's another specific one, "My husband, age 51, has stage IV metastatic colorectal cancer with a lung mass since 2020. He did one cycle of chemo and now he will start with targeted chemotherapy." I'm assuming targeted therapy. "Taking consideration side effects, is there a typical survival rate and timeframe for this type of diagnosis?" I know that's going to depend on a lot of specifics, but-

Cathy Eng, MD:

It depends on how many sites of disease and if that's the only site of disease, lung. Sorry, I apologize. I'm recovering from a cold. Lung-only metastasis patients' survival is very, very long because lung metastasis tend to be very slow growing relative to liver metastasis and other sites of disease. So in fact, it's very favorable and, in fact, there's some data to say because the disease is so slow-growing, those are the ones that you may want to consider giving immunotherapy to as part of a clinical trial though.

Zac Getty:

Interesting. Enroll in a clinical trial. All right. Thank you. So here's a question about ablation. I know you're not a surgeon, but generally, can ablation be repeated several times if it initially does not destroy the tumor?

Cathy Eng, MD:

Once again, it has to be evaluated anatomically to make sure it's safe, but yes, you can potentially re-ablate a lesion. It depends upon the interval from the last ablation, but yes, that can happen more than two times not, I don't know if I've ever had a lesion ablated more than two times, unless there's a very long timeframe in between.

Zac Getty:

Thank you.

Cathy Eng, MD:

But it's possible.

Zac Getty:

Possible. I think a lot of these are it depends. Phuong, I have a question for you, actually. Which of your treatments or surgeries was hardest on your body and recovery since you've been through more than just a few?

Phuong Gallagher:

That's a great question. This one is actually related to a metastasis. I had a tumor that actually sat on my bladder. It didn't penetrate. It was just very bizarre that that would happen, very unusual. Anyway, that

resulted in a very major surgery. At the same time, I had the removal of that tumor. They did a hysterectomy. I got a stoma. All of this happened at the same time. Believe it or not, the surgery itself was not the hardest to recover from. It was the radiation that followed because they couldn't get clear margins. Generally, you only radiate the pelvic region once because toxicities, dose limitations and all that, but because this was about a decade after my initial radiation, the team felt that they could safely break up the doses in a manner that they could do a second.

Well, that ended up not being a problem itself during the radiation, but the fallout following has been tremendous for me. It has caused a lot of nerve, what is it, radiculopathy I think is the term. So it's caused all sorts of issues with my nerve roots. So it's affected much of my life. I'm still dealing with that. It's caused a lot of pain because of that associated difficulty. So I would say that radiation is like sneaky because it has the lasting late effects that a lot of people don't realize.

Zac Getty:

Thank you. I've got another one.

Cathy Eng, MD:

I think it's important to keep in mind there's acute and chronic side effects of radiation therapy, and that needs to be discussed with your radiation therapist.

Zac Getty:

Sure. Dr. Eng, I've got another one for you here. I am aware of the time. We've got about a couple minutes left before we need to let people go. I have seen it's very common nowadays many oncologists are using fruquintinib for the refractory colon cancer, which is FDA-approved, who failed FOLFOX or CAPOX therapies. How is the survival rate for this?

Cathy Eng, MD:

So fruquintinib, it was approved in the third line plus setting. So patients may have received prior oxaliplatin-based therapy or irinotecan-based therapy or just 5FU-based therapy alone or they may be intolerant of that drug, but basically, there was definitely an improved overall survival based upon the third line data from China, as well as the large international study that we conducted after median of four prior lines of therapy. So it has shown a benefit of overall survival when compared to placebo.

Some people say, "Well, why placebo?" Well, unfortunately in the fourth or fifth line setting, there is no standard of care. The trial allowed patients to have received prior, well, our trial here, not the original one in China, but the extended FRESCO-II study allowed patients to receive prior TAS-I or II or prior regorafenib. So we allowed all prior lines of therapy. So there is nothing that you could put in the control arm because there is nothing that is considered standard of care after that. So it was improved overall survival and improved progression-free survival as well, and it appears to be tolerated well.

Zac Getty:

Thank you. I've got two more here. I think we can get through them before the end. One is more general. I'm going to go in the specific one here. So wife was diagnosed with stage IV CRC with liver mets. CTs have shown reduction in the tumor, repeat colonoscopy, so the colon is free from lesions. PET scan shows all lesions including liver are inactive. What tests should be done in order to guide treatment. Wife has been on FOLFIRI plus Panitumumab for 30 cycles.

Cathy Eng, MD:

I'm sorry. What was the question?

Zac Getty:

What tests can we do in order to guide treatment from this spot? So lesions are inactive, no lesions in the colon. PET scan showed all lesions including liver are inactive. Is there anything specific they should be doing to guide their treatment from here?

Cathy Eng, MD:

Once again, I don't know enough information because I have no idea how they've been on therapy, et cetera, how well she's tolerating it. She's been on FOLFIRI plus panitumumab for prolonged period. It may be worthwhile doing some maintenance chemotherapy to allow the patient some time to recover. It sounds like clinically they have had what's called a clinical complete response, but you should keep in mind that doesn't mean that all the disease is gone in regards to microscopic disease. You still need additional therapy, but obviously, everything sounds like it's going in the right direction. I just don't know if you necessarily need the full systemic chemotherapy combination for quality of life.

You may want to consider maintenance therapy, and an MRI is the best test for the liver. It's nice that they looked at the PET scan for avidity, but that would not be my only scan for followup, an MRI of the liver if that's really the only side of disease.

Zac Getty:

All right. Thank you. So I've responded to the prior question via text, so I do not want to hold anybody after what they've already committed to for us. So I do want to take a second to thank Dr. Eng and Phuong both for sharing their time and carving out some time for us in their very busy schedules. Thank you so much. I think this has been really enlightening. We really appreciate your participation here.

I do like to end all webinars with our mission statement. Fight Colorectal Cancer mission is we fight to cure colorectal cancer and serve as relentless champions of hope for all affected by this disease through informed patient support, impactful policy change, and breakthrough research endeavors. I would also like to take a second to thank Taiho Oncology for sponsoring this webinar. We appreciate their support. Again, Phuong, Dr. Eng, thank you so much for taking your time out of your day to day to join us. We really appreciate it.

Cathy Eng, MD:

Thank you so much for inviting us.

Zac Getty:

Absolutely.

Phuong Gallagher:

Thank you, everybody.

Zac Getty:

Everyone, take care. Thank you so much.

Cathy Eng, MD:

Have a great day.