Carly King:

Okay. Hi everyone and welcome for joining us today on our 2024 ASCO highlights webinar. My name is Carly King and I'm the research advocacy project manager here at Fight Colorectal Cancer. Fight Colorectal Cancer is the leading patient empowerment and advocacy organization in the US and we provide balanced and objective information on colorectal cancer research, treatment and policy. We are relentless champions of hope and focused on funding promising high impact research endeavors while equipping advocates to influence legislation and policy for the collective good. Before we get started on our webinar today, I'm just going to cover a few housekeeping items. First is just a quick disclaimer that the information and services provided by Fight Colorectal Cancer are for general informational purposes only. The information and services are not intended to be a substitute for professional medical advice, diagnoses or treatment. If you are ill or suspect that you are ill, see a doctor immediately. In an emergency 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. Second, I just wanted to let everyone know that we'll have dedicated time at the end of the webinar for a question and answer session. Please feel free to use the Q&A panel on the right side of your screen to ask any questions that come up along the way and we'll do our best to get to them at the end, and I can try to answer some throughout too. We'll have a recording of the webinar available at our website within the next few days and you'll also receive a direct link via email as soon as it's available if you've registered for this webinar. But with all that, I'm going to hand everything over to our presenter today, Dr. Dustin Deming from the University of Wisconsin Carbone Cancer Center. So thank you all, including Dr. Deming, for taking the time out of your busy schedules to join us today. So I'm going to hand it off so we can get the webinar started.

Dr. Dustin Deming:

Thank you for that introduction and allowing me the opportunity to present today. So today I'll be talking about some of the highlights from the ASCO meeting from a couple of weeks ago. Here you can see an outline of the studies that we'll be talking about. As you're probably all aware, colorectal cancer is no longer thought of as just one disease. Historically, patients with metastatic colorectal cancer were all treated in a very similar fashion, given one line of chemotherapy followed by the next without really any consideration to the molecular profile. We now know that there are many different molecular subtypes of colorectal cancer as shown here on this slide. It's very important for us to differentiate mismatch repair proficient versus mismatch repair deficient cancers, and then look at within those categories all the different molecular subtypes.

This is important because we can now offer treatment options for these individual subtypes. So it is now standard of care for patients with mismatch repair deficient metastatic colorectal cancer to receive immune therapy, whether that be anti-PD-1 therapy or the combination of anti-PD-1 therapy with anti CTLA4 therapies. For BRAF V600E mutant cancers, the combination of encorafenib with either cetuximab or panitumumab. For HER2-positive cancers there are three different regimens that we typically think about. This includes trastuzumab/pertuzumab, trastuzumab/deruxtecan, and trastuzumab/tucatinib. And we'll present an update today on the trastuzumab/tucatinib data. Additionally, one of the newest molecular subtypes is the KRAS G12C mutant subtype of metastatic colorectal cancer. And now per NCCN guidelines, the G12C inhibitors, either adagrasib or sotorasib are recommended in combination with either cetuximab or panitumumab for those patients.

Additionally, for left-sided RAS/RAF wild-type patients, cetuximab or panitumumab either as single agents or in combination with chemotherapy are recommended. And then, though rare, NTRK or other fusions do have targeted treatment options as well. In addition to the targeted options, there are also

non-targeted options and more non-targeted options than ever before. For patients with treatment refractory disease this includes trifluridine and tipiracil, also known as Lonsurf or TAS-102 in combination with bevacizumab. The recently FDA approved drug fruquintinib is also an option. And then single agent TAS-102 or single agent regorafenib are also options. It's important to think about all these options as we look at this new data that we'll be presenting as this is important to think about how the data that we see at ASCO can fit into the current standard of care treatment paradigms.

So first we'll talk about the CodeBreaK 300 study that was presented by Dr. Fakih. This is a study of sotorasib plus panitumumab versus standard of care treatments for KRAS G12C mutated metastatic colorectal cancer. KRAS G12C mutations are present in approximately 3% of colorectal cancer and there are some studies to indicate that this particular mutation could be associated with poor prognosis. Excitingly, there have been advancements now with the ability to target this specific mutation with drugs that can covalently lock this particular mutant protein in an inactive form. Recent data has demonstrated potential benefit with the addition of anti-EGFR therapies to the KRAS G12C inhibitors. And this study was presenting the final analysis from the CodeBreaK 300 study specifically focusing on the overall survival data of this study.

So this study was a 160 patient study. Patients were randomized one to one to one to sotorasib, the KRAS G12CR inhibitor with panitumumab at two different doses, and then also investigator's choice of trifluridine-tipiracil as a single agent or regorafenib as a single agent. Patients in this study had to have had greater than one prior line of therapy, must have had a KRAS G12C mutation identified centrally, and also had measurable disease and no prior G12C inhibitor. The baseline characteristics across the treatment groups are very well-balanced. And looking at the overall survival data, what you can see here is that the median overall survival was not reached in the sotorasib 960 milligram cohort in combination with panitumumab compared to 10.3 months in the standard of care investigators choice cohort. Also at the 960 milligram dose, which is the standard dose, the objective response rate was 30% with this combination compared to 2% with the standard of care investigator's choice.

And for those patients who did develop a response, the duration of response was 10.1 months. The overall median progression-free survival was 5.8 months with the 960 milligram containing regimen compared to two months with the standard of care investigator's choice, which is very similar to what was seen in the phase three studies investigating either TAS-102 or regorafenib alone. So in conclusion, these data indicate that sotorasib at 960 milligrams in combination with panitumumab is an exciting new option for patients, not only because of its improvement in response for these patients and duration of response for those patients, but now with overall survival data indicating improvement over standard of care. And so all patients with KRAS G12C mutated metastatic colorectal cancer should be considered for KRAS G12C directed therapy in combination with anti-EGFR therapy at some line of therapy.

Right now it would be at least third line of therapy, but as we'll talk about in a little bit there's also clinical trials looking at should we move these inhibitors into the earlier lines of therapy for this subtype of colorectal cancer. Next, we'll move on to the MOUNTAINEER data. So the MOUNTAINEER study evaluated tucatinib and trastuzumab for HER2-positive metastatic colorectal cancer. Just to remind everybody, HER2-positive cancer is seen in 3% of metastatic colorectal cancer. Previously, data did describe an improvement or a significant response rate and duration of response for patients treated on this single arm study, and here we get the final data from the MOUNTAINEER trial. Just to remind everybody, the MOUNTAINEER trial was a phase two study that enrolled patients in the second line or greater setting. This study enrolled HER2-positive RAS wild-type patients that had prior therapy as listed here in the orange box.

This analysis focuses specifically on cohorts A and cohorts B here, looking at the combination of tucatinib with trastuzumab. In the final analysis, the objective response rate was 39.3% with a median duration of response of 15.2 months, which is very exciting for this cohort of patients, and a median progression-free survival of 8.1 months. In general, this regimen appears to be tolerable, though there are significant toxicities with 40% of patients having greater than or equal to a grade three toxicity, which tends to be a pretty significant toxicity. Specifically for this regimen diarrhea was a significant adverse event specifically related to tucatinib. So here you can see that the most common side effects included diarrhea at 66.3% of patients with a small fraction having grade three or higher diarrhea, but then also a significant proportion of patients also having fatigue and nausea.

So in conclusion, trastuzumab and tucatinib is a very reasonable treatment option for patients with HER2-positive metastatic colorectal cancer. There are also reasonable options including trastuzumab/pertuzumab and trastuzumab/deruxtecan. I think all of these options are very reasonable options for patients to consider with this subtype of colorectal cancer. The challenging thing when thinking about which one to use for patients is that they've never been studied head to head and have been studied in different populations such that it's challenging to compare these regimens against each other. The trastuzumab and tucatinib does have exciting median progression-free survival, however it was largely studied in an earlier line setting than the other two regimens have been studied so we would expect it to potentially do better just because of that.

In general, when I'm seeing a patient with HER2-positive metastatic colorectal cancer, I favor either trastuzumab/tucatinib or trastuzumab/pertuzumab in the first line, or I'm sorry, not the first line, but in the typically second or third line setting. And I do either one of those regimens first and then I think about trastuzumab/deruxtecan in a later line setting. The benefit of that approach is trastuzumab/deruxtecan has shown activity after patients have received a prior trastuzumab containing regimen, and so you can get additional benefit by doing both of those regimens for patients. Next, we'll move on to the ARC-9 study. This is a study looking at an immune therapy combination with FOLFOX in the third line setting, largely in the third line setting. So this looks at etrumadenant which is an adenosine receptor inhibitor. It prevents the negative effects of adenosine on the immune response, and this is given in combination with an anti-PD-1 therapy, Zim, as it's referred to here on this slide.

This looked at patients who had prior oxaliplatin and irinotecan, but a very important factor in understanding the results of this study is that these patients did not necessarily have progression on that prior oxaliplatin containing regimen. So it's very common for patients to receive oxaliplatin in the adjuvant setting and then later have recurrent disease or patients even in the first line metastatic setting can receive FOLFOX chemotherapy, do that therapy for typically four to six months, stop it because of the development of peripheral neuropathy and then not reintroduce that oxaliplatin until a later line of therapy. What that means is that the benefit in this study is going to be complicated to understand because we know some patients when we retreat with oxaliplatin after we previously stopped, not for progression but because of side effects, when we use it again patients can see significant benefit from doing so. Regardless, I think this study has some interesting results which we'll talk about.

So looking at the baseline characteristics between this immunotherapy plus FOLFOX regimen compared to regorafenib, the baseline characteristics of these two groups are very similar as you can see here. When we look at the prior lines of therapy, they are also very similar between the two groups. Looking at the primary endpoint of progression-free survival, what we see is that the median progression-free survival for the immunotherapy plus FOLFOX regimen was 6.2 months compared to two months with regorafenib alone, as we would expect with that agent. What we see is, when we look at the different characteristics of these patients, really all of these patients seem to benefit from this regimen compared to regorafenib alone. And there was also an overall survival advantage seen in these cohorts of patients

with a median overall survival of 19.68 with the immunotherapy plus chemotherapy arm versus 9.49 months with the regorafenib arm alone.

If the study had been done in the treatment refractory setting where patients had already progressed on oxaliplatin, this would be really amazing data. However, given that this was done in the setting of not having progressed on prior oxaliplatin, it makes it really challenging to understand how much the immunotherapy is benefiting these patients. When we look at toxicities of this regimen, there were significant toxicities including neutropenia, nausea, also as you would expect with immune therapies significant immune-mediated events with 16% of patients having some degree of immune-mediated toxicity. These included hypothyroidism, adrenal insufficiency, pneumonitis, rash, among others. So in the conclusion from the study, investigators, they're very excited about this as a potential option for patients in the future and feel that this demonstrated potential for significant benefit for these patients.

However, while I am excited about this as a potential option for patients, given how this was studied with these patients not largely being resistant to prior oxaliplatin, it's very challenging to understand what benefit the immunotherapy has in the setting in addition to the chemotherapy. And so again, I think this is a promising regimen, but something that clearly needs further studies before we can get a better readout about how much patients are likely to benefit from this regimen. Next, let's talk about the TRANSMET study. So this is a study looking at liver transplantation and chemotherapy versus chemotherapy alone for patients with unresectable colorectal cancer liver mets. So there's a lot of data demonstrating that patients who undergo liver resection with potential for cure do better. Unfortunately, patients who are not able to have their cancer resected, the standard of care right now is chemotherapy of some sort for life.

And this study looked at for these patients who have liver metastases but no metastatic disease elsewhere, would liver transplantation actually help prolong their survival? And so this study enrolled a very restrict patient population. Patients were under 65 years of age, had a very good performance status or activity level, they were confirmed not to have resectable disease but did have no extrahepatic disease, meaning they didn't have any metastatic disease outside of the liver. Did not have BRAF mutations, since these mutations are associated with a very poor prognosis. And these patients had to have had either a partial response or at least stability with prior chemotherapy. They needed to have at least three months of chemotherapy but no more than three lines of chemotherapy. Patients also had to have a relatively low CEA and adequate cell counts. The patients, once determined to be eligible, were randomized to chemotherapy plus the liver transplant versus chemotherapy alone.

Those patients were who were randomized to the transplant arm were put on a transplant waiting list and then underwent prioritization prior to receiving that transplant. The primary endpoint of the study was overall survival. Looking at the baseline characteristics of these two cohorts of patients, these patients were relatively young with median age of 52 and 55 as you can see here. In general, the treatment groups were fairly balanced. One thing that you will notice though is that there was a... if you look here at the tumor response group... what we can see is that there was about a 10% higher rate of the patient's cancer actually responding to chemotherapy. In the liver transplant cohort, though that is a mild difference, it could actually help favor outcomes for that liver transplant group at least to some degree. 47 patients were randomized to liver transplant, 47 patients were randomized to the chemotherapy alone cohort.

In the liver transplant group there was no liver transplant done on nine of the patients because the cancers progressed while waiting for the liver transplant. And one patient received a liver transplant despite progressive disease such that only 36 patients were included in the analysis for that cohort. In the chemotherapy arm, there were seven patients who were able to go on to liver resection and additionally two patients who had liver transplant outside of protocol. So those were excluded from the

analysis such that there were 38 patients included in the per protocol analysis. So just to note, these patients that were excluded here are not included in this analysis. So this wasn't done in an intention to treat analysis where we typically think it's best to continue to keep all of these patients in the analysis regardless of what happened to them over time.

Excitingly, there was an improvement in five-year overall survival for those patients who were able to undergo liver transplant as shown in the graph here. I'm sorry, and this is the intention to treat group and then this is the per protocol group here, so if you take out those patients who are excluded where 73% of patients were still alive five years later compared to 9% in the chemotherapy alone cohort. Just because these patients were alive doesn't mean that their patients didn't recur. In fact, the majority of patients who had a liver transplant still had recurrent disease with the lungs being the most commonplace for that recurrence. These patients underwent a high rate of surgery or ablation. Excitingly though, despite this intensive therapy, even after the liver transplant, 15 patients in follow-up remained without evidence of disease while only one patient who was in the chemotherapy group did not have evidence of disease.

Of note, it does appear that there is quite an imbalance between these groups with the use of additional procedures. So it's hard to know how much of the difference between these cohorts here is due to the liver transplant or due to the types of therapies that these patients received after initially being enrolled and having their liver transplant. Here you can see the progression-free survival for the per protocol analysis. Again, this is with the exclusion of those patients that we outlined earlier. And what we can see is that there's about 20% of patients who did do quite well without having recurrence of their cancer following liver transplantation. So the conclusions from the authors are that based on this analysis, liver transplant is a reasonable new standard of care option for patients with liver only unresectable colorectal cancer. I do think that these results are very promising and exciting and I do think that for a highly select few patients with metastatic colorectal cancer this might be a reasonable option.

I think as we think about this for patients, we really need better data on which patients are the patients who did the best in this and other studies, and we need further information outlining exactly what happened to these patients after their liver transplant because I think that could be playing a big role in their overall survival especially. When patients are considering liver transplant I think it's important for them to understand that it is extremely unlikely that liver transplant is actually going to be curative and that really what we're hoping with this liver transplant is that we're doing a significant de-bulking of the cancer and that it is extremely likely that further anti-cancer therapy is going to be needed down the road. Also, it's important to understand that when we knock down someone's immune system to be able to accept a liver transplant, that would make them ineligible for immunotherapies and immunotherapy clinical trials, and there's a lot of exciting immunotherapy clinical trials going now that these patients would not be candidates for.

Also getting a liver can be a very long and challenging process. As you saw, there's a significant proportion of patients whose cancer progressed while they were waiting for transplantation and thus were not eligible. It can be very nerve wracking for patients to be on a waiting list and see if they're going to get a liver transplant or not. All this being said, it's still something that is an exciting option if the right patient is there and the disease biology for that patient is cooperative with all the things that have to go into getting a transplant done. Next, we'll talk about the anti-PD-1 one study for mismatch repair deficient locally advanced rectal cancer. Many of you may remember that a couple of years ago there was some very exciting data about using immunotherapies for mismatch repair deficient locally advanced rectal cancer with the ability to cure these patients potentially without the need for surgery or radiation.

What we see is that mismatch repair deficient rectal cancer is about 5 to 10% of all rectal cancers and these patients have been shown to be less sensitive to chemotherapy and in the preliminary data potentially very responsive to immune therapy. And so this study led by Dr. Cercek, is looking at dostarlimab and if patients have a complete clinical response following them without radiation or surgery. And they're looking for, when determining a complete clinical response, that on an endoscopic exam like a colonoscopy or flexible sigmoidoscopy, that there's no visual appearance of the cancer remaining and that there's a normal rectal exam. Also, on a MRI there's evidence of a great response and no evidence of growing cancer. They've now enrolled 48 patients in this study. You can see the characteristics of these patients with many of these patients having very advanced disease including node positive disease and T4 disease, meaning that the cancer is invading, in many instances, adjacent organs.

And here you can see the swimmer's plot looking at these 48 patients and how they've been doing on study. There's now a median follow-up of 17.9 months for these patients. And to date all of these patients, 100% of them have had a complete clinical response and remain without evidence of their cancer recurring. Of note, you can see that, based on the gold circles here, the timing of when that complete clinical response occurs. In the initial cohort everyone had a complete clinical response by six months. In the additional cohort here, there's some patients that took longer to have a complete clinical response, but overall it's extremely exciting that all of these patients have had a complete clinical response. These patients are actually doing extremely well from a toxicity standpoint. In many aspects the patients on the study appear to be having less toxicities than we would typically expect with anti-PD-1 immune therapy. And so the investigator's conclusions from this study were that excitingly all of the patients who've completed the dostarlimab therapy have had a complete clinical response and that these responses are very durable with no patients requiring chemotherapy, radiation or surgery.

And from my own side of things, this has now been added to the NCCN guidelines as a standard treatment option for these patients and very exciting that at our own center we're seeing similar results with all of our patients having a great benefit. So we'll finish up now by talking about where the field is heading and what clinical trials we're looking forward to getting results on. In the mismatch repair deficient metastatic setting, the Checkmate 8HW study is looking at the combination of anti-PD-1 therapy pembrolizumab with anti-CTLA4 therapy ipilimumab. And excitingly, this study is demonstrating that at two years out from initiation of therapy, 72% of the patients are without evidence of progression. This appears to be much higher than we would expect with anti-PD-1 therapy alone, which is the current standard of care. This Checkmate 8HW study, the data continues to mature and we look forward to getting further results from the study in the future.

Additionally, the COMMIT phase three clinical trial is evaluating the combination of FOLFOX chemotherapy with bevacizumab and atezolizumab versus atezolizumab alone in this setting. I think there's a high likelihood that that chemotherapy plus immunotherapy regimen will do better than the anti-PD-1 one therapy alone. Additionally, the SEAMARK study is looking at the BRAF V600E mutant mismatch repair deficient population in the first line setting and looking at does the combination of encorafenib and cetuximab in combination with pembrolizumab, is that better than just doing pembrolizumab alone in the first line setting? In addition to the immune therapy being used in the first line setting, there's also excitement about trying to do targeted therapies in earlier lines of therapy for metastatic colorectal cancer. This first has been seen in those patients with RAS/RAF wild-type metastatic colorectal cancer who also have left-sided primary tumors.

The FIRE-3, CALGB 80405, and PARADIGM studies have all shown improved survival for patients who have done anti-EGFR therapy in combination with chemotherapy. Expanding on this data to the BRAF mutant population, the phase three BREAKWATER study is looking at should we be adding encorafenib and cetuximab to chemotherapy in the first line setting for BRAF V600E mutant colorectal cancer. In the

safety lead-in study, which is a portion of the study which has already been reported, excitingly these regimens have been shown to be reasonably well tolerated and there appears to be an improvement in response rate and progression-free survival compared to what we would expect with standard of care therapy alone and so we're really looking forward to those results in the future. In addition to the BREAKWATER study for HER2-positive metastatic colorectal cancer, the MOUNTAINEER 3 study is also looking at should we add tucatinib and trastuzumab to FOLFOX in the first line setting for that subtype of colorectal cancer?

And the CodeBreaK 301 study is looking at should we add sotorasib and panitumumab for KRAS G12C mutant cancers to the FOLFIRI regimen that we would otherwise use, or at least consider using. And then the KRYSTAL 10 study is looking at adagrasib which is a different KRAS G12C inhibitor in combination with cetuximab versus standard of care chemotherapies in the second line setting. All these studies have significant potential to help us better understand if adding targeted therapies for these particular subtypes could be helpful in earlier lines of therapy. As we think about moving targeted therapies to earlier lines of therapy, there's a lot of caveats to trying to do that practically and so we need to think about how we can get the NGS testing done as quick as possible. For us at the University of Wisconsin, we've started looking at trying to do blood-based testing on everybody right away so that way we can get our readout of the molecular profile for these patients as soon as possible.

Now, this doesn't completely rule out the need for tissue testing because the tissue testing can still be very helpful still even if you have a blood-based test. So we try to do both for our patients. And then one of the things that we really have to think about in how we treat patients is thinking about potentially changing our therapy early in the lines of therapy depending on what those results come out. So it's not enough just to order the tests. We also need to get the tests back in a timely fashion. We need to identify which patients are most likely to benefit from particular options. We need to get patients back into clinic and talk about the different options that they have. We have to talk with them about what that might mean for insurance coverage and copays, especially as it relates to oral therapies, which unfortunately still is problematic.

And then anytime we're talking about adding something to a treatment regimen there's also the chance for enhanced toxicities. And so those all have to be discussed and the risks and benefits weighed with patients. So it does make things more complicated, but if we can really help improve outcomes for patients, obviously worth it. In addition to improvements in the treatment options for patients, we also need to think about are we selecting patients and identifying their subtypes of cancer in the best ways? So hyper selection using circulating tumor DNA has shown potential for benefit in the PARADIGM study showing that patients without these molecular alterations listed here on the left, based on a circulating tumor DNA assay, did much better with panitumumab in combination with FOLFOX in the first line setting.

Additionally, as we're thinking about these patients and the molecular profiles, what we're seeing is that the resistance mechanisms that can arise from treating with targeted therapies early, there can be a lot of them, that can be related to mutation profile, it can be related to metabolic changes in the cancers, but excitingly many of these resistance mechanisms can actually go away over time. Time off of that therapy that induced that particular resistance mechanism, which has led us to be excited about the possibility of doing re-treatment for cancers. Here I show some of the recently resulted clinical trials looking at can we re-treat patients with anti-EGFR therapy after they've received prior anti-EGFR therapy? And while we can see benefit in all patients that we consider for this re-treatment strategy, there seems to be potential for additional benefits specifically for those patients who have a circulating tumor DNA test that does not show RAS/RAF or EGFR mutations that could lead to resistance to that therapy.

There are multiple clinical trials looking at EGFR re-treatment that we're excited to see readout in the near future, including FIRE 4, PULSE, and then also I'm leading the STRATEGY study here at the University of Wisconsin. Beyond targeted therapies, there's a lot of excitement about immune therapies for patients with not only mismatch repair deficient colorectal cancer, but also mismatch repair proficient or microsatellite stable cancers. So these are the cancers that we don't think of typically these therapies working for, but it does appear that there is a subset of patients with mismatch repair proficient cancer who can do well with immune therapies. This was seen in the CheckMate 9X8 study, which looked at the first line setting combination of standard care chemotherapy with anti-PD-1 one nivolumab versus standard of care chemotherapy alone.

If you look to the far right of this curve, what you'll see is that there were about 20% of the patients who did much better on the nivolumab containing arm. Additionally, there's now been a number of clinical trials looking at different combinations of immune therapy combinations, and there are patients with microsatellite stable colorectal cancer who do respond to a lot of these regimens, including in the cabozantinib and durvalumab study, 27.6% of patients developed a response. And interestingly, if you look at the molecular profile of those patients, the patients that were RAS and RAF wild-type, the response rate was actually around 50% for those patients. Additionally, as we think about trying to figure out who are the patients that respond the best to these therapies, there's growing literature about those patients who have liver mets tend not to do as well with some of these immune therapies and those patients with lung only or at least no liver metastatic disease do better.

Additionally, there's a growing literature about different factors in the tumor microenvironment, which is the cells around the cancer cells in the cancer. Some of those factors could really help us predict which patients are more likely to benefit from immune therapy options in this setting. In addition to the ARC9 study that we talked about earlier, the STELLAR-303 study is looking at XL092, which is a derivative of cabozantinib in that study that I talked about just a couple slides ago, in combination with atezolizumab versus regorafenib in patients with metastatic colorectal cancer. And we're also excited about the potential for the combination of bot and bal and recently completed a phase two study there that we're eagerly awaiting results.

So overall, there's a lot of excitement with how patients are treated. What you can see is that there are clearly advances happening and a lot of excitement about the results at ASCO. We're definitely getting better at treating colorectal cancer both in the metastatic and in the localized settings. There's a lot of promise for better molecular characterization of patients and then also tailoring therapies, whether it be targeted therapies for those molecular subtypes or maybe even immune therapies for those molecular subtypes. And then also there's a lot of excitement about the potential to retreat patients with therapies and giving them additional lines of therapy over time depending on how the mutation profile of their cancer changes across different sequences of chemotherapy.

So thank you everybody for your attention and happy to answer questions.

Carly King:

Sure. We do have a question in the Q&A so I'll read that for you. The question is, would stage three patients getting their biomarkers done be helpful if they ever have progression for early line targeted trials?

Dr. Dustin Deming:

So I commonly consider, with patients, having molecular testing done for stage three cancers. It in no way changes anything that we do as far as standard of care chemotherapy in that setting. But if it's a patient who has a high risk cancer, if that cancer comes back it's really helpful for us to already have that

molecular testing in hand. Especially if we're wanting tissue-based testing, it can take multiple weeks for that testing to come back. And so for patients who have a high risk cancer, I definitely would consider doing that molecular testing ahead of time just in case we need it down the road. And excitingly, a lot of the companies that offer this molecular testing have really great financial assistance programs such that if insurances don't cover it many patients can get the testing at no cost or limited cost.

Carly King:

Great. And there's another question, are there any promising vaccine trials going on for stage four colorectal cancer patients?

Dr. Dustin Deming:

So there are clinical trials ongoing. Some of these clinical trials are building on some of the COVID vaccine strategies with how those vaccines were made. It's way too early for us to know any of those results and it'll probably be years before we get readouts from those studies. But I do think that especially patient specific vaccines hold a lot of promise and I'm very hopeful about those studies going forward.

Carly King:

Okay, we're getting some questions flood in so we'll see what we can answer in the last couple minutes. Someone asked if we talked about clinical trials related to metastatic colorectal cancer with KRAS G12C mutation, so we did, and the recording will be sent out in an email so you can watch back. If you have any specific questions let us know. Someone asked in a stage two A is it protocol not to do any mutation testing except for the MSS/MSI?

Dr. Dustin Deming:

That is correct. So all patients with colon cancer should have mismatch repair testing or microsatellite instability testing done. For a stage two cancer it would be extremely uncommon circumstances for us to want to do any further testing based on what we know now about those cancers.

Carly King:

Let me find another question. So someone said, I'm going to paraphrase here a little bit, but that if you're microsatellite stable and you don't have any mutations, you go through FOLFOX plus bev with oxaliplatin. There's currently no evidence of disease but will be on treatment for life. Would potentially the prognosis be better if they had showed positive for mutations so that they could undergo targeted therapies?

Dr. Dustin Deming:

So actually the best prognosis right now is to not have those mutations. And not having KRAS, NRAS, BRAF or HER2 alterations is still a good thing. And it's not that you don't have targeted options, your targeted options are actually the anti-EGFR therapies, so cetuximab and panitumumab are targeted options that could work potentially very well for you depending on your circumstances.

Carly King:

Okay, thank you very much. There's lots of comments saying how helpful this was and great overviews. So thank you so much Dr. Deming for taking the time out of your busy schedule and everyone else for

tuning in. Like I said, the recording will be sent out by email and also on our website, hopefully by the end of this week, if not, early next week. And thank you so much for joining.