Zac Getty: Good evening, everyone. Thank you all for joining us today for our webinar focusing on treating side effects, especially skin rash and skin toxicity. My name is Zac Getty and I am the Patient Education Program Manager here at Fight Colorectal Cancer. Fight CRC 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. You are joining us today for our Dealing with Skin Rash and Other Unpleasant Side Effects webinar, so I hope you're in the right place here.

Before we get started, I do have a couple of housekeeping items. If you've ever watched a webinar with us before, these are the same every time, so enjoy. We will 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 during the webinar to ask any that might come up along the way. I'll do the best to address them as they come up if they're topic-specific, but otherwise, I will address any unanswered ones at the end. If you're watching the recording of this webinar and you have a question, feel free to reach out to patientinfo@fightcrc.org and we will do our absolute best to try to address any questions that we can.

We will have the recording of this webinar available on our site within the next couple of days. If you've registered for this, you'll receive that direct link via email as soon as it is available. Lastly, feel free to tweet along with us. You can use the hashtag #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 of Fight meetups, which are an online space to meet with other patients and caregivers, which are held about four times a month. They touch on a variety of topics. We have meetings for newly-diagnosed patients, meeting to discuss hot topics and more.

Actually, if you're watching this, we have a Guide to Fight meetup tomorrow at noon eastern time to continue this discussion about side effects. If you'd like to talk with other survivors, caregivers, people in the CRC space, that is a great opportunity. You can find a link to that meetup in our Community of Champions app. Speaking of Community of Champions app, it's our free app where you can connect with other people in the CRC space community. Keep in touch with Fight CRC and know what we're up to generally. We also offer an assortment of print and digital educational resources that are free to request and download.

A little bit of a disclaimer here. 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 and treatment. If you're ill, suspect that you're 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.

With that out of the way, I would like to briefly introduce our panelist today. We are joined by Natasha Pinheiro, Adult Nurse Practitioner at Memorial Sloan-Kettering Cancer Center. Natasha, we'd like to thank you for taking the time out of your certainly busy schedule to join us for this webinar today. I'm going to give Natasha an opportunity to give a little bit of her background and then we will start the discussion here. I'm going to stop sharing my screen and we'll just be seeing us.

Natasha Pinheir...: Thanks, Zac. Thanks so much for Fight CRC for having me here today to talk about, I hope everyone can hear me well, I'm using a little funky headphones here. I have worked at Memorial Sloan Kettering Cancer Center in solid tumor GI outpatient for 23 years. I started as a clinical nurse in the group originally working with upper GI cancers and then transitioning to working with primary liver, hepatocellular, hepatobiliary, panc, cholangio for years. I want to say about 10 years in upper GI. Obviously, we see an amalgam of all types of patients, but primary focus the first 10 years in upper GI, then about five or six years in hepatobiliary and at that time was in school, finished my nurse practitioner. There wasn't a nurse practitioner job in the group, and I wanted to stay in the group because I was so versed at that point in GI cancers, and I just wanted to do what I knew and was comfortable with and took a role as a clinical nurse specialist.

At that time, actually onboarded a lot of the nurses, the new nurses in the group, set up educational programs, worked on guidelines and formatting guidelines for practice, so a lot of the things that we're going to be talking about today, a lot of their primary initiatives were things that I worked on with CNS and nurse educator colleagues at one point. Then, probably five years in that role, and then I have been working as a nurse practitioner in the solid tumor GI group since 2018, so we're going at the beginning. January, it will be six years as a nurse practitioner in the group. I am fairly comfortable talking about GI cancers and the management of side effects based on the treatments for those cancers.

Zac Getty: Wow.

Natasha Pinheir...: In a nutshell.

Zac Getty: You've got quite the breadth of experience there, so yeah, thank you for joining us today. We're excited to talk.

Natasha Pinheir...: Yeah, not at all.

Zac Getty: I know I brought up, this is about side effects, skin toxicity, but you mentioned that you feel like you're pretty comfortable talking about side effects in general. Before we dive into skin toxicity and rash side effects specifically, I'd like to touch on just general side effects that patients undergoing CRC treatment could perhaps expect to encounter and which ones may cause the most problems for

them, and if there's any way to handle them before they start getting out of hand. I know side effects are going to be dependent on treatment, correct? Not everyone's going to experience the same side effects. Are there any specific side effects that somebody might expect to see based just if they're getting chemotherapy and this stage that they're in, will they differ?

Natasha Pinheir...: When we're talking about colorectal cancers, there's a couple of things and then you can hone in or tell me if I'm getting too broad. If we're talking to patients who are microsatellite stable or MMR proficient, we're talking about standard of care. If we're talking about people who don't have a RAS wild-type mutation, we're talking FOLFOX, FOLFIRI, CapOX, CapIRI, standards of care treatments. Those side effects, regardless of where you are in the continuum, whether you're an adjuvant post-operative for cure or whether you're a metastatic disease, the symptoms, the side effects are the side effects. Obviously, when we talk about how they manifest in one patient versus the other, it is very person-specific. It is somewhat time of diagnosis specific. We're thinking about patients who are late-stage diagnosis with pretty profuse diffuse disease, like not a single met, like if they have bone mets, if they have liver mets, lung mets, lymph nodes, they're going to have much more symptomology than a person who might be just oligometastatic with a primary liver met or something like that. That is one component.

If we're talking about the patients who are metastatic versus the patients who are adjuvant who had a resection who are getting treatment for cure, it's a different mindset because they know they're in this period of time where they're getting treatment for whether it's three months or six months with the hope that they're done. The way we manage it and the way they manifest it in their brain is very different than the person who knows they are literally on this chemo indefinitely for likely the duration of their life. That was very general. Then, you're talking about chemo side effects versus immunotherapy side effects versus targeted drug side effects.

But if we're just going to talk about chemo, if we're going to talk about FOLFOX, FOLFIRI, Irinotecan, when I do teaching with patients, I always tell people that Irinotecan side effects are very much when we were growing up and you think about the person who's getting chemotherapy. You think about hair loss, you think about nausea vomiting, you think about diarrhea, you think about general fatigue, Irinotecan has very traditional chemotherapy side effects, whereas Oxaliplatin has these very strange ones that you don't necessarily think of if you're not versed in chemo. You're going to have the neuropathy, you're going to have the cold sensitivity, you're going to sometimes have that first bite sensation. It's the way you manage it.

With Irinotecan, I find, also it's where you sequence. If the person got FOLFOX already, they're not chemo naive and they've recurred or they progressed and we're giving them a second line. You're also talking about you already experienced chemo for 3 to 6 to 12 months, and then we're jumping you into another one. There's that period of your body is not getting any sort of rest

between one first line to second line to third line. That also impacts how intense your side effects are. I know it's a lot, and I'm not really being as specific, but it really does depend on where you were at diagnosis symptom-wise from the disease, whether it's metastatic, whether it's curative and/or whether it's a first line or a second line. Managing the side effects or managing the side effects with diarrhea, which you can get from any of them, but it's very specific to the Irinotecan, and then you also have increased stools with the 5-FU, which goes with it.

We always are going to start with Imodium. Once we're sure that it's treatment-based and not some underlying colitis or infectious process, we're going to start with Imodium. If Imodium is not controlling it, we're going to escalate to Lomotil. Then, if that's not working, we're going to go to tincture of opium. A lot of the times, we overlap the medications. We can overlap Lomotil with Imodium or we can overlap Lomotil with tincture of opium or tincture of opium with Imodium, depending on how much of a difficult time we have managing the diarrhea. If it's so profound, we think about dose reducing the drug that we think is causing it. We'll add supportive medications with treatment like hydration. Obviously, a lot of those patients who are having profound diarrhea, we're going to have to supplement them with potassium because they're probably depleting their potassium, so that's usually fairly routine.

With that, for the people who don't necessarily have diarrhea but have pretty profound abdominal cramping, what I do for a lot of the patients is dose with a prophylactic Imodium. We're not dosing two Imodium every three or six hours for diarrhea. We're dosing like one Imodium in the morning, one Imodium at night depending on how profound the cramping is. All that's going to do is just because that cramping is just the hyperactivity in the bowel, that's just going to slow that down. Obviously, there are other meds that we can use, but we usually start with Imodium because it's less toxic.

Zac Getty: You mentioned you do that prophylactically, so it sounds like these are things that can be predicted and at least tried to address before it becomes super disruptive.

Natasha Pinheir...: Yes. Yes. What's important is really empowering the patient to articulate the concerns. It's one of the things that I do. There's no plus in being a martyr, we're in this together. It sounds very cliche, but we do say this is a marathon not a sprint, even for the patient who have a finite period of treatment, but we really want to get them through this. We want to limit hospitalizations, obviously, at all possibility. What I tell people is, don't just push through with diarrhea. "Oh, it'll pass, it'll pass." Diarrhea left unchecked leads to a hospitalization. If we can avoid that, we will avoid that. Obviously, the thing that scares people is saying that we're holding treatment. Sometimes it is absolutely safer to hold treatment to manage the toxicity than to continue and make it get worse. There are times, depending on how profound the diarrhea is or nausea vomiting, and then we're looking at their bloods in conjunction, if we're seeing a lot of things that need to

be repleted like potassium, sodium, all of those things, we're just going to hold treatment and try to manage it again to avoid a hospitalization.

Zac Getty: Sure, thank you. For a patient that might be experiencing this who is concerned about it, do you have any tips on articulating those concerns to their healthcare team? Some of these things can be hard to talk about. Some people tend to hesitate to bring up their side effects, because one, they're afraid of treatment being discontinued, they're afraid to bring it up, they're afraid to complain, they're afraid to be the problem patient. Is there any words that patient can use, any specific ways they can bring these problems to their clinicians to their treatments team to help?

Natasha Pinheir...: It's twofold. One, you have to have a clinical team and usually, the people on the front end are the nurses. You have to have nurses that are educated in the side effects to know what to ask, because sometimes it's just pulling it out of them. They might be like, "Oh, I didn't even realize that this is not a normal thing." You have to say, "Are you having diarrhea?" You also have to know a person's baseline. If someone goes to the bathroom like three times a day or four times a day, that's their normal prior to diagnosis their whole life. If they go a fifth time, is that a diarrhea? No, that's just an extra stool.

It's also one, making sure that the health team is very aware of the right verbiage and how to ask because sometimes you have to pull it out and you have to build that relationship. There's also the thing about continuity, that they're seeing a face routinely, so that they become comfortable with that person. We can't always promise that in the way that healthcare is now, but at the end of the day, the patient just has to know that it is a team effort and we can only do what we can do if they give us the information for us to make the right decisions in how to manage their care. It was a team effort. It's a team effort.

Zac Getty: Yeah, absolutely, and just really patients need to advocate for themselves and try to take this seriously.

Natasha Pinheir...: Correct. Correct.

Zac Getty: Excellent. Thank you. You mentioned Oxaliplatin and it caught my attention with some of the unusual side effects of it comes with specifically neuropathy. Can you talk a little bit more about that?

Natasha Pinheir...: Yeah. Neuropathy is very challenging because Oxaliplatin is a very effective drug, not just in colorectal cancers, in all GI cancers. It is something where we know if we're going to get benefit, we will get the benefit very quickly. We do see people respond very well to it. But keeping that in mind, we have to be mindful of the neuropathy, and the neuropathy can be lifelong. We could stop Oxali and they could have neuropathy for years and years later and a lot of patients do. One of the things, so again, now we're looking at a metastatic

patient versus someone who is getting adjuvant therapy for cure. If we're doing a 3-month CapOX, it's very limited, we're only giving four cycles. We're hoping that you're not going to have any long-term neuropathy from four cycles of Oxaliplatin every three weeks. Patients who are getting FOLFOX because maybe their surgical pathology had more risk factors than the person who's getting 3-month CapOx.

That's what decides it. It's based on the pathology post-operatively, so who has a much more profound pathology will give them a longer course of the FOLFOX every two weeks for six months, which is 12 cycles. But with doing that, routinely, we'll stop the Oxaliplatin at cycle eight because when they were originally doing this in clinical trials, they found that the risk of long-term neuropathy outweighs any benefit beyond the four-month period in a patient with adjuvant, so it's important to remember someone in adjuvant. If they're not having any neuropathy, hey, we can push through for 12 cycles, but the majority of patients will start. Like I said, if we know that we're getting the response and we're doing this for cure, we usually will stop it around cycle eight or nine with the hope that we're not going to have any long-term neuropathy. Will they have some short-term neuropathy that can last beyond finishing treatment? Absolutely.

What's very difficult for us from the clinician standpoint is that we can't give a clean answer. Usually, if we stop a certain drug, that side effect will resolve within a week or so, if not immediately. Neuropathy is not that. It actually gets significantly worse before it gets better. It is a true test of time. When patients ask me when is it going to go away and I literally answer them, "You'll have to tell me." I always say I'm not trying to be glib or sarcastic. You are the only one because we can have two patients with what looks like the same disease, what looks like the same treatment cycle, which looks like the same thing and one will say, "I've never had neuropathy. I have the cold sensitivity," which is a side effect that we expect, it isn't long-lasting, and someone will say they had neuropathy from cycle two.

It is very person-specific. We are mindful of it and like I said, when we can stop the Oxaliplatin, we do. Even for our metastatic patients, if we know we're going to be on this for an extended period of time, if we see at least two consistent scans with control of disease, we'll stop the Oxaliplatin and say, "Do maintenance 5-FU, or if it's FOLFOX and Bev, we'll do 5-FU Bev. The original thought process of that was Optimox. You pull out the Oxaliplatin while it's still effective with the thought that if you have to reintroduce it at time of progression, you can reintroduce it because you have not maximized the efficacy of it. It is still an effective drug. We play around with our metastatic patients, that way, if we're seeing the neuropathy getting too intense, we either will significantly dose reduce if they're at the max dose or if they have shown consistent stable disease from scan to scan, we then can talk about doing maintenance chemo without the Oxaliplatin.

Zac Getty: Interesting. It sounds like-

Natasha Pinheir...: Yeah, sorry. Sorry, go ahead.

Zac Getty: No, no, you're fine. I was just going to say, it sounds like as a clinician that you're very aware of trying to manage this in the best way possible to prevent these from happening.

Natasha Pinheir...: We've been using it long now and sadly, as I gave the time that I've worked here, I remember when we first started using it and we didn't know these things. I always say that the best way to learn how to manage a side effect is having the patients tell you what they're experiencing because then from person-to-person when you're hearing it enough, it's what's going on. But I remember when we first started the drug, we weren't as versed in how to manage it. Some of it is just with time and experience and it's been around for a little while now.

Zac Getty: Speaking of managing it, specifically with neuropathy, you mentioned cold sensitivity and with it being December, it's not cold where I am right now, but I'm certain it's cold in some parts of the United States at least. Any suggestions on how to manage that cold sensitivity considering the weather and the time of year?

Natasha Pinheir...: There's a couple of things With the cold sensitivity. One, it's that you shouldn't drink or eat anything cold. It's not necessarily ... there is part of a component of it that's the weather, but a big component of it is just swallowing cold. What's frustrating is in the summer, so it's twofold. In the winter, we don't want you to breathe in the cold air. In the summer when it's so hot, what's challenging for patients is not being able to drink or eat anything cold. It's usually the first four to five days post the infusion that you should not have ice cream, ices, anything directly out of the refrigerator, anything directly out of the freezer. We're talking room temperature, but then, it has to be a room that's warm and not a room that's 60 degrees because that is still cold. Swallowing that, they'll feel like a burning or a painful sensation in their throat and it's very uncomfortable. Usually, for, like I said, that first week, we tell them to have room temperature or warm.

The challenging part is yes, as you said, when you're in a cold environment. What we used to tell people pre-COVID and COVID changed them, and I'll explain why is we used to tell people to wear those balaclavas, so that when you breathe in the air it's warmed a little bit by the mask or the scarf. What's happened with COVID, during COVID, is that people were wearing masks. You know when we were all wearing masks that when you're breathing, you're breathing, it's warmer, you've warmed it with your breath and everything. That has helped and that's one of the things where I tell patients, at least during the time where we were all fully masked, is that that has helped with by the time the air is breathed in a bit more, it's warmed by the mask.

I just tell people around this time of year because in the northeast to definitely either wear the mask and now it's flu, cold and COVID season again, so there's

no downside to wearing your mask, wrapping a scarf around when you're outside, limiting being out in the cold if you can avoid it. Again, that cold sensitivity with breathing in the air corresponds with those days of drinking, so it's usually the first four to five days post-treatment anyway. It's just wearing masks, wearing scarves, just making sure you're fully covered so that the air is warmed a bit by the time you've breathed it in.

Zac Getty: Okay, thank you. There are a million different side effects and I'd love to cover them all today, but unfortunately, I don't think we have the time. To discuss just general side effects, what would you recommend to somebody, to a patient who's thinking about stopping or pausing their treatment due to the side effects they're experiencing?

Natasha Pinheir...: I had the conversation earlier today in clinic, it happens a lot. Again, it's a very person-specific disease, so specific how long they've been on treatment. people just get exhausted from chemo. If it's your first type of treatment and maybe it's like your third cycle, then it's a different conversation than someone who's been getting chemo for two and a half, three years and they're just beat. What we've done a lot of the times is we will offer, especially for the metastatic patients who are on chemo basically until they're not, we do offer treatment breaks especially if we're seeing consistent stable scan. Because then, the patient is comfortable saying, "Okay, things have been looking good for six months now." Again, we will offer either a chemo break and it's a short interval break. It's not that the break is short, we'll scan you in a shorter period of time than if you were on chemotherapy.

People that are metastatic, we probably will, and we've been treating them for years, we might scan them every three to four months because we are at that wall of how much we have left to offer. But the person that we've given a chemo break, we're going to scan them in two months. If everything still looks good in those two months, we continue the break for another two months until we see disease has grown again, and then we restart the chemo. I had a patient who was literally off chemo on a break for a year until we saw a small growth and then restarted. The majority of patients that we offer it to, and again, these are people who've been on chemo for years and just physically and mentally need that time off. I want to say on average when we're able to do it, it's about three to four months and then we'll go for six months with the thought of, we'll give you another short interval break if scans look that way.

Patients who are adjuvant, who are doing this for cure, it becomes more of like a coach type talk. You're getting this for either this three months or the six months, there is an end point, this is the date, so you really have to push them because we are getting to where you will be cancer-free. That's the patient that will really push, will dose-reduce obviously. A lot of the times also we'll dose-reduce. If there's not an option to break or to stop, we will dose-reduce or modify or add supportive medications, and sometimes just hydration on your treatment day or a disconnect date makes a huge amount of difference. If we can offer the breaks because radiologically and symptom-wise, you're

responding and we see that consistently, we do that. If that's not an option, we modify the dose. Sometimes we modify the schedule if we can and/or we do, we add supportive medications.

Zac Getty: Amazing, thank you. It sounds like there's some options for people at least if they're experiencing really disruptive side effects. I appreciate that. The title of this was Skin Rash and Other Unpleasant Side Effects, so I'd like to talk a little bit about one of the side effects that people we have in the community complain about the most. It's skin toxicity, skin rash, derm toxicity, it's got a bunch of different names. What is it, first of all? What is skin toxicity? We hear about it a lot. Is it treatment-specific? Is it just something that people can expect to experience? I know that you mentioned earlier most side effects are treatment-specific and stage-specific where a patient comes to you, so can you talk a little bit about that for us?

Natasha Pinheir...: Yeah. With skin toxicity, it's a little different, because certain drugs have specific types of skin toxicity, some of them we do not want to see and some of them we absolutely want to see. With immunotherapies, and I'll do the quicker ones first and then the ones that we really have to dive into. With immunotherapy, some people develop an immune rash. It's activating your immune system, and so a lot of the toxicities from immunotherapy is a hyperactivation of the immune system. One of them is that your body develops a rash because your skin is just like, "What is this drug?" Your immune system is acting on it and it manifests on the skin.

A lot of the times, we will see that and we'll add topical steroids or creams. It's something that can be managed. Sometimes it's holding, depending on how big it is or how bad it is, we can either hold the IO drug for a period of time, treat the rash with oral and/or topical steroids. Usually, it's topicals, but if it's pretty profound, they might need a course of oral steroids, hold the immunotherapy and then restart it when things have resolved. That's very straightforward. We've gotten much better also at managing immunotherapy side effects. That's very straightforward.

5-FU and Capecitabine, which are the base of all the treatments for almost all of the colorectal regimens, they have a couple of skin issues. With 5-FU, you can get hyperpigmentation. People, I have freckles, I have moles. If I was to get 5-FU, they would become more pronounced. People who are fairer, who have freckles, they become more pronounced. 5-FU causes something called hyperpigmentation. Wherever your pigment is and people have freckles or moles, that's pigment, they will develop more of them. There's nothing you can do about it. It's fairly benign. It's just annoying for people. They're like, "Oh, I have more freckles. Oh, I have more age spots." But it's just like, the minute you stop the drug, usually that will dissipate over time.

It can also cause you dry skin. Some people get a dry skin rash, moisturize well hydrate well. Again, 5-FU skin stuff is fairly, it's not really problematic, more it's just that people are like, "Oh, I noticed this." What does happen is people that

are darker skin, darker tone, can actually get darker. The lines that we have in our hands, they can get darker, your face can get darker, and again, it's the darker you are, so obviously, the more melanin, you become more melanated. For some people, it's like they can actually become a shade or two darker. That does resolve once we stop 5-FU. Again, it's more of an annoyance than anything else.

With Capecitabine, which is the oral form of 5-FU, you can get something called hand-foot syndrome. That is usually dose-specific. What it is, is it's pretty profound. It can be dryness, cracking to the palms and the soles of your feet, you can get cracks, you can get redness, you can get swelling, you can just have skin peeling. Usually, it starts with just like a peeling and a dryness to the skin, and usually, what we tell people prior to starting this, if we can do it in advance, is that they should do a pedicure, just do a buffing of to get the dead skin off, do soaks and really, really good skin management with, and I'm not selling a product here, but these are what we recommend. CeraVe, Aquaphor, Eucerin, really good heavy creams. Bag balm, utterly smooth urea creams. Those are usually what we recommend. We talk about soaks for your hands and your feet. You really just have to reapply the creams constantly.

We expect the dryness, we expect a little bit of peeling. It can get red, it can get swollen, you can get cracks. If it goes anywhere beyond a little bit of peeling and the dryness, we will automatically usually hold the drug, the symptoms resolve, and then we usually dose-reduce the Capecitabine. Capecitabine hand-foot syndrome is very dose-specific. Those are how we manage that. Those are much more straightforward.

Then, if we're talking about, which I think is more of what we talk about when we think about skin toxicity, is the anti-EGFR drugs, which is Cetuximab, Panitumumab, and this is where it's different. We want to see that rash. We want to see that rash on your face, on your scalp, on your chest, because that usually means that we're getting benefit from the drug. That's what's hard to tell people because we're telling them the side effect is that you have this rash, it's a very dry acne-looking rash and everyone is like, "I am 30, I'm 40, I'm 27, I don't want acne again." But we are like, "No, we want to see that rash, because then we know that it's working on that receptor because this is the response we want to see."

Again, having used a drug for so long, we now have a better sense of how to manage it earlier on. The minute we know we're starting either one of those drugs, we automatically prescribe an oral antibiotic. Doxycycline, a hundred milligrams, either once a day or twice a day. We start with a topical of Triamcinolone cream and they would apply that to the affected area. Usually, when it presents, it presents in this area on your cheeks, around your nose, sometimes on your forehead.

The other thing that was helpful for a lot of people during COVID was that they said they had a mask on, so people didn't see the rash. They weren't as self-

conscious of it because they wore a mask. A lot of men will grow their beards in because again, this is the area where we tend to see the rash. It can develop in your scalp too, which is annoying, and you scratch and you want to scratch, but we don't want you to scratch it. You can't control when you're feeling itchy at night, because you don't even know that you're scratching. But that's one of the reasons why we start you on the antibiotic because if you're scratching and it opens, it can become infected and become super infected.

We didn't know all of these things at first. We didn't know to start you on an antibiotic. We didn't know to start the topicals immediately. We were lucky to have one of the dermatologists who actually came up with most of the strategies for managing these drugs was someone that worked at where I work at, Memorial Sloan Kettering. He's recently left and he's working at another hospital now, but he actually set up the guidelines on how to manage this, and so in the beginning, we would send people to him immediately. A lot of the times now, we know what's done, so again, like I said, we start with a Doxycycline, we start with Triamcinolone ointment. Sometimes we'll add Mupirocin, which is an antibiotic. Triamcinolone is a steroid cream, Mupirocin is an antibiotic. If we're seeing that they're opening a little bit and we'll tell them to put it on the ones where they've scratched or things like that.

There are times where all of these interventions are not enough and the rash is much more profound. We do still then send them to dermatology at that point. Sometimes they will change the antibiotic to Minocycline, which is a different dosing and a different mechanism. Sometimes it's even beyond the Doxycycline and/or the Minocycline. We've had patients who've had such a profound rash that they've put them on a Bactrim, which is a broader spectrum, a larger spectrum antibiotic and they will add a ton more of topicals. They'll do a Benzoyl Peroxide. The other thing is, for the patients who have it in their scalp, we now know we prescribe low-prox shampoo, so as opposed to using any of the scented things, which is just going to irritate it.

The other thing that's very important is, it looks like acne and it's dry, so we do not want them to put acne medication on it because that's going to dry it out more and make it look worse. Again, things that we've learned through the years and we've learned from our dermatology partners. That's one of the things. Yes, we always start on the oral antibiotic, we always start with at least the Triamcinolone. Then, for the areas that aren't as bad, again, I'm back to my Eucerin, Aquaphor, CeraVe, usually things without a scent. Also, we tell people just like you would for if you had any sort of eczema-type thing, you don't take hot showers, you take lukewarm showers, you don't use scented soaps, you don't use scented lotions. You put the creams on while you're still a little wet from the shower so that your skin will absorb it. Those are the ways to manage it. But again, what's a little odd for the patients is that we want to see the rash.

But having said that, there are times where the rash is so profound, even with our interventions, initial interventions and dermatology interventions where we have had to hold the drug because it was so profound for some people. There

was an abstract presented at ASCO in, I want to say 2022, that Wade giving the Panitumumab or the Cetuximab, the anti-EGFR, the RAS wild-type drugs for eight cycles indefinitely until time of progression versus eight cycles while the person was still responding. Stopping it at eight cycles and reintroducing it when a scan showed that disease progressed and to any extent, and then you reintroduce the drug. But in that time you've given, it's the same thing, like I mentioned earlier, with pulling out the Oxali while it was still beneficial and putting it back in.

One, you've given them a break from the skin toxicity while still having the efficacy of the drug in place that you can then put it back. That's an option too for people who have very, very profound rashes that is not necessarily responding to all the interventions. If they are clinically responding, radiographically responding, we can stop the drug and reintroduce that at a later time if progression is happening.

Zac Getty: Thank you. I've got a two-part question about this.

Natasha Pinheir...: Sure.

Zac Getty: Talk about how you starting somebody on an EGFR and you just want to immediately start on oral antibiotics, that thing. Is that standard of care? If a patient is beginning an EGFR and their physician or their clinician hasn't started them on those drugs, how would you recommend a patient go about discussing this and bringing up that, "I know I'm going to get this rash. How do I make it as manageable as possible?"

Natasha Pinheir...: I want to say, and this I wish I could definitively say, it is mostly standard of care. That's the safest way for me to say it, and we have patients who have come from the community and come to us, and I can't think of anyone who, and from smaller centers, similar types size centers, local oncologists, I cannot think of anyone who ... they might not be on the oral antibiotics, but they're absolutely getting the topicals. I can't think of anyone who I have seen, and definitely, within our institution this is standard, but I can't think of anyone who I've seen from the community that wasn't getting, if not both the oral and the topical and/or one of at least the topicals.

Zac Getty: Okay, excellent. If a patient feels that this rash is unmanageable, if it's becoming so impactful and they don't feel like enough has been done, can they go to their physician and discuss with them other options and treatments?

Natasha Pinheir...: Right. The thing that's tricky about that is that we have, like I said, the physician who created these guidelines on how to manage it was at our institution and was here from when we started using these drugs, so it grew together. We have dermatology in place that know how to deal with these treatment-induced rashes. That's what's tricky. If you're looking in the community and you just go to a regular dermatologist, do they always know how to manage the rash or the

skin toxicity from chemotherapeutic or cancer type agents? That's what can be tricky. I think everyone has gotten a bit better about it. I think because so many people are treated in the community, dermatologists have gotten better about it. It does sometimes get out of the oncologist hands as the best way because they aren't derm. Yes, I think it's important to have a dermatology partner, whether it's in your institution or for that patient or that local oncologist to have a derm that they work with, especially if they are prescribing this family of drugs.

Zac Getty: Perfect. Thank you. I do just want to say, I have plenty more questions, but if anybody watching has questions, please feel free to type them in the Q&A box. Otherwise, I'm just going to keep going. You mentioned that you want to be seeing this rash when patients start this treatment, does no rash, is that indicative that treatment may not be working as you prefer?

Natasha Pinheir...: No rash has a tendency to mean that they are not going to get the benefit from the drug. A small rash doesn't mean it's less efficacious. For the most part, if you are a RAS wild type, we should see that rash because you have the receptor that we're targeting. But are there patients that didn't have a very significant profound rash? Yeah. Then, you have the people that it's florid where it's just out of control.

Zac Getty: How does a patient know if they're RAS wild type?

Natasha Pinheir...: This has now become more standard of care. We are doing, for the majority of patients now, and I am going to say across the spectrum in GI, not just colorectal, we're looking at the mutation of the tumor we're testing at the majority of patients a lot of the time are diagnosed sometimes from a colonoscopy. That sample, we're always looking for microsatellite MSS, which is microsatellite stable, MSI high or the other nomenclature is MMR deficient or MMR proficient. We're always testing the tumor to look for possible genetic tumor mutations. RAS and MSI tend to be done, can be done on that sample. Then you have a larger panel.

Institutionally where I am, we have our internal panel, but there are tons of companies that do oncogene testing. I think there's a company called Oncotype, there's Garden, so there's all of these places that can either test the tumor itself or do liquid tumor testing. I want to say it's definitively standard of care because now we want to see whether there are targets that we can treat.

Zac Getty: Tumor testing, biomarker testing, we [inaudible 00:41:57].

Natasha Pinheir...: Biomarker testing, tumor testing. A lot of the times, if originally the tumor wasn't tested because it was just a stand, you went to your local GI, you were getting a routine colonoscopy, they may not. We might not get, and a lot of the times just getting the sample from one institution to the next is not always easy. If we're really looking at that window of time where we want to start doing

something and we want to know if you have a target to give you the best bang for the buck treatment wise and to give you the best hope of giving you the most efficacious treatment, we will do a liquid tumor ... we'll do a liquid biopsy. There are outside companies that do liquid biopsies and the turnaround with those are usually within two to three weeks versus an internal panel where we're looking for so many different possible mutations, which can take six to eight weeks, and some patients don't have that time and we really do need to get them started on something, so we will do liquid biopsies then.

Zac Getty: Okay. Thank you. I know you mentioned briefly a couple of products that you brought them in, but I'd like to just touch on it. We don't endorse products, but fact of the matter is that, as a clinician, you're going to recommend things that will help. You mentioned just heavy creams, emollient creams, urea creams, these all built equal for management of side effects or [inaudible 00:43:15]?

Natasha Pinheir...: The urea creams are specifically for hand-foot syndrome. There's a difference between a prescription urea cream and an over-The-counter urea cream. The over-the-counter urea cream is not as obviously not as strong, the percentage is less on that versus what you can do prescription. We usually tell people to start with the over-the-counter urea cream. A lot of the times we then prescribe if that's not working enough. With regards to just, again, and I'm also not just, these are the ones that we use and we tell people to use. A lot of them, it's just for really, really dry skin. The majority of the chemos that we use for colorectal cancers will dry your skin out separate and apart from any skin toxicity. It just makes your skin drier. If you're talking about people that are challenged with what they can take in orally, if you're not hydrating, if there's the discussion between whether you're eating or drinking, you can't just take in as much.

People will be like, 'Oh, I'm going to eat. I don't drink as well." Some people just don't drink as well. They're not getting into two and a half liters of fluid. All of those things, throwing chemo and a cancer diagnosis in there is just going to exacerbate it. A lot of us have dry skin. If you live in any place where there's cold weather, you're going to be drier in the winter than we're giving you drugs that dry out your skin. You're not hydrating well, you're not eating well, it's an amalgam of things. Just like I said, just really good moisturizing of your skin and hydrating separate from any of the drugs that even can cause dry skin.

Zac Getty: Is there any benefit to using fragrance-free detergents or [inaudible 00:44:59]?

Natasha Pinheir...: I don't think that's as much of the issue unless you're also on top of the dry skin, you're just sensitive. Some people are just sensitive, and so if you have sensitive skin and maybe you have an eczema or a psoriasis underneath a skin rash from a drug we're giving you, those people I would definitely say to do that. If it's just azurine result of the drug, you don't necessarily have to. But I always tell people who do have the skin toxicity to not use any fragrances in their creams and/or shower gel soap.

Zac Getty: Okay. Thank you. I am going to share my screen here just to perhaps encourage, see if anybody has any questions for you, because I don't want to monopolize this entire thing. But with it being the holidays, people are getting back together with their family, we're seeing people they may not have seen for a while, and this isn't necessarily a direct medical question, but how would you encourage people to explain what's going on with their skin if their family asks? Oftentimes rashes, stuff like that shows up on the skin. People are concerned about it being contagious, about catching something like that or just concerned about how it looks. Are there any ways, any success you've seen that patients have with [inaudible 00:46:15]?

Natasha Pinheir...: Yeah, I want to say, again, the rashes that you get or the skin toxicity that you get from these anti-EGFR drugs which is, again, Panitumumab or Cetuximab. It doesn't look like a contagious rash. It looks like pretty profound dry skin. I don't even think it looks like acne. It just looks like really dry skin. Some people present with very red skin, like it looks red and shiny. The rash, and again, I feel like I keep saying this, it's very person-specific, you know what it's going to look like, but I've had patients who say it flares right before treatment, right after treatment, it's a wax and wane. It doesn't look the same way for 30 days. I'm just pulling 30 days. Usually, around treatment, it will look its most profound, and then it levels down on your week off or your two weeks off.

Zac Getty: Okay. How about when you wear make-up?

Natasha Pinheir...: Yeah, go ahead. Make-up, no. No make-up.

Zac Getty: No make-up?

Natasha Pinheir...: No, because I've had patients who ... I did have a female patient who was a therapist. She's seeing people. She's interacting all day long, that's part of her job. She actually went to her dermatologist outside of here. She saw derm here and got fully hypo-allergenic, non-comedogenic, all makeup because she said it made her feel better to present to patients. But again, that was very cost ... she spent a lot of money to get that. That I would never tell anyone to go buy this expensive, very specifically-made makeup for you. But people have done it. I usually say not to just because if you're just buying regular makeup over the counter, wherever, you don't know what's in there that's going to possibly exacerbate or irritate the skin even more.

Zac Getty: I know a lot of skin conditions can also affect your nails. When you go to a nail salon, you [inaudible 00:48:25].

Natasha Pinheir...: Yeah. A lot of the times, if you're having any of those issues, we will likely see some nail changes with a lot of these drugs. If we're noticing that at all, we actually tell people to not go to the nail salon. Don't put polish on. If you are going to go to the nail salon, you go with your own kit. You don't use the shared kits. Most places don't do that anymore. You have individual packets with your

name or you get a new one every time you go. But yeah, we actually tell them to be very mindful. Don't cut the cuticles, don't have them shaved down the nails, anything that's going to impact the texture. Sometimes it's just a buff and a polish and some people just want to do that because it just makes them feel better about themselves just to have that done. But for the most part, we usually tell them if we're noticing nail changes just to do anything at home and not go to a salon.

Zac Getty: Sure. Great. Thank you. I actually have had a couple of questions. The first one I have is back to our general side effects and specifically with neuropathy due to Oxaliplatin. Are you familiar with icing to manage [inaudible 00:49:41]?

Natasha Pinheir...: Yeah.

Zac Getty: Do you recommend it?

Natasha Pinheir...: I don't personally recommend it and institutionally, we don't recommend it, but I'm going to tell you that I have patients who have sworn that it has been beneficial. I've seen it on both ends. I've seen people not be able to tolerate the icing, like it's uncomfortable your hands or your feet. I want to say I've had about 60, 40, 60% of people who did the icing found it beneficial, 40% it's not that it wasn't beneficial, they couldn't tolerate it. It was just too cold for them. As an institution where I am, we don't, but patients can come in with their own and do it. We just don't give them the setup, but they can come in and do it themselves. But again, like I said, I've had more people find benefit. The ones that were able to tolerate it found it beneficial.

Zac Getty: Thank you. Do you recommend an oatmeal bath or something similar? The dry skin [inaudible 00:50:42].

Natasha Pinheir...: Yes, absolutely, because it's soothing, it's soothing. This is why I tell people just do warm soaks to your hands and your feet and with lavender oil and just let whoever give you a foot rub, whether it's your partner, whether it's your child, whether it's your grandchild, whatever. Just let them take care of you, soak your feet, do a nice rub, a massage, yeah.

Zac Getty: Excellent. Thank you. Similar to the icing question, do you have any thoughts on, we've heard about fasting prior to treatment to manage side effects. Is that something you're familiar with?

Natasha Pinheir...: Again, anecdotal. Anecdotal. I have four patients who find fasting and all of them are on FOLFIRI, so they're all getting Irinotecan. I have one patient who is now been on, she's on a chemo break, so this goes into what we were talking about earlier. She has been on FOLFIRI and I put in her orders, I number her cycles because she's been on it that long. She was on it for over two years, stable disease this whole time. She just needed a break. She was exhausted from chemo. But she initially was doing intermittent fasting for weight prior to

her diagnosis and found that fasting for the day before treatment, and then for two days after doing liquid, she was doing juices and juicing and juices.

For those three days where she was fasting from all solid foods, really decreased her side effects, because she actually tested it and ate and noticed that she had increased saliva production. She was heaving a little bit more, but with the fasting, she found benefit. I had another patient who, again, had previously intermittent fasted prior to diagnosis and fasted again on FOLFIRI, Irinotecan, fasted around treatment and felt that it did help her side effects. I have two more patients who asked about it and I said, "I have two people who've done it, who found it beneficial." They're both doing it around that same thing the day before and for the two days after, and they have found it to help with side effects.

Zac Getty: Thank you.

Natasha Pinheir...: But again, this is four. These are four people.

Zac Getty: Sure. Yeah. We are getting toward the end of our time and I do want to be respectful of your time, but I would just kind of like to provide if what I think is a summary correctly for specifically like anti-EGFR skin toxicity. It sounds like there's ways that can help address the issues but not necessarily completely prevent it and that you're actually looking for the rash as a sign of effectiveness of a drug, and that you would encourage, I would imagine, people to, if they're finding it unmanageable, can't deal with it, to talk to their physician, talk to their clinic, talk to their nurse about potential options to maybe deal with it a little bit better than it's currently being dealt with.

Natasha Pinheir...: Correct.

Zac Getty: Okay.

Natasha Pinheir...: Again, with this study that they presented at ASCO, there is, it's called the Improved Study, there is a thought process of stopping the drug, the anti-EGFR drug at eight cycles and if consistently stable disease, keeping them off and then reintroducing it and again, giving them them and the skin a break from that toxicity. We've done that with a handful of patients.

Zac Getty: Excellent. Can you repeat the name of that study just to [inaudible 00:54:15]?

Natasha Pinheir...: The Improved study?

Zac Getty: Improved Study?

Natasha Pinheir...: Yeah.

Zac Getty: Okay. Thank you so much. I haven't had any patient questions come in or viewer questions come in the past couple minutes, so I would like to take this opportunity to thank you profusely for taking time out of your busy clinic schedule to come and talk to us about this. It's been very enlightening. You obviously have the experience, you know what you're talking about and we really just appreciate you taking the time to meet with us today and discuss all these different issues.

Natasha Pinheir...: Thank you so much. It's always really nice to share with patients and families and other clinicians. I don't get to do that as much with other clinicians like I did previously, but it's important for everyone to have the knowledge so that they can be advocates.

Zac Getty: Absolutely. Well, I want to thank you again. Thank you to everyone who attended our webinar today. I would like to thank Amgen for making this webinar possible and sponsoring our efforts here. I do like to end every webinar with just our mission statement. Fight colorectal cancer's 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. Natasha, thank you so, so much. We really appreciate.

Natasha Pinheir...: Thank you guys for having me.

Zac Getty: Thank you. Take care.

Natasha Pinheir...: All right.