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2020 Crohn's & Colitis Congress: Explaining Risk to Patients

Announcer:
You're listening to ReachMD. The following episode was produced in collaboration with the Crohn's & Colitis Foundation & the American Gastroenterological Association.

Here's your host, Dr. Matt Birnholz.

Dr. Birnholz:
Welcome, everybody, to the Third Annual Crohn's & Colitis, uh, Congress in Austin, Texas. This is ReachMD. I'm Dr. Matt Birnholz, and I'm delighted to have Dr. Corey Siegel with me. He's Co-Director of the IBD Program and Section Chief of the Dartmouth-Hitchcock, uh, Medical Center. The particular department, I believe, is the digestive diseases section of...

Dr. Siegel:
Yep, Section of Gastroenterology and Hepatology, part of the Department of Medicine.

Dr. Birnholz:
Perfect, perfect. So, welcome to you. Our topic today for the "ask the expert" series is explaining risk to patient. To start, Dr. Siegel, um, I'd love to get a high-level, 30,000-foot overview of strategies that you've found to be effective and useful in practice just to help explain risk of treatments to patients and maybe just… We could start with that overview, and then we'll get into the brass tacks.

Dr. Siegel:
Sure. I've evolved overtime on this. I think I started in my career when we didn't know a lot about the risk. You know, all we had were black box warnings and no quantification of the risk. We just heard words like cancer and tuberculosis and—and dying, and—and it—it's a bad place to start when you're walking into an office visit so… You know, earlier in my career that's what actually motivated me towards the research I've done on this, is trying to recognize that, first of all, we don't even know what we're talking about as far as risk, and second, that patients are pretty scared because they don't know exactly what they're dealing with. So my initial approaches really were to be defensive about risk and try to just throw numbers out to dissuade this worry that these drugs are so risky and that they were gonna die of cancers and all sorts of bad things and—and turn that around over the past couple years to realize that that's not our intent is to have to defend these drugs but to defend the reason that we're using the drugs and really talk about the risk of their disease more than we talk about the risk of the drugs and then bring that in and give some very specific, quantitative, absolute numbers of how much risk there really is as opposed to just saying things like, "Oh, yeah, the drugs can cause lymphoma; you should talk to your doctor."

Dr. Birnholz:
And as far as that quantitative reasoning goes, what data are you drawing from typically that patients... There are many who want to take charge themselves and find whatever they can find to either rationalize or justify their fears. What data are you drawing from to help either dis—dissuade those fears or help lead them down a path that—that is right for them?

Dr. Siegel:
Sure. Well, 20 years ago we didn't have a lot of data. All we had were clinical trial data that went 6 months or 12 months, and that wasn't the right way to determine how safe these drugs were long-term, but now… You know, infliximab was approved 22 years ago, so we have... And when I tell patients that, they're amazed sometimes that we have over 20 years of data, not only from clinical trial experience but from registries that are global of tens or hundreds of thousands of patients. And even the newer drugs that are on the market now, the number of patients that are required to run these clinical trials has gone up over time, so we really learn a lot from this.

The second part, which is nice, is the rheumatologists are always a step ahead of us with our biologic drugs, so most of the drugs that we use have also been used in other fields before they're even approved for inflammatory bowel disease, so although it's a different patient population and—and different patients and different indications when you look at a safety database, it's actually pretty fair to rely on those safety data as well.

Dr. Birnholz:
And what outcome measures or, um, uh, just long-term outcomes, short-term outcomes, do you use to help translate the important data to your patients? It's the question of translation.

Dr. Siegel:
Yeah. So, you know, when you... if you open the package insert for these drugs or if you listen to the second half of every commercial about a drug that you see on TV, it's an incredibly long list of potential outcomes. Most of those are one-off outcomes that are reported truly a handful of times in the world over time of exposure to these drugs. But I find that when I ask patients what they're really worried about or I ask my colleagues what they're worried about, it's typically 2 things. It's serious infections, serious and life-threatening infections, and cancers, and those are the 2 that I really try to focus on.

Dr. Birnholz:
Now let's jump from that. Risk of infection, the patient who's gonna be moving towards a biologic—terrified of—of being immunosuppressed, being high risk for infection, how do you broach that conversation, and how do you counsel these patients?

Dr. Siegel:
Yeah, first I try to get a sense of how worried the patient really is about this. And it's not that we don't want to not inform patients who weren't worried, but sometimes you actually create more concern than you're trying to alleve by being defensive, as I mentioned earlier, so I simply ask them, "How much do you know about these medications?" "Have you looked things up?" "Have you talked to family or friends?" And you get a really good sense pretty quickly of how they shift in the chair and how they make eye contact with you if it's something that they're really nervous about. And what's amazing is, if you ask patients, their responses are not typically in line with the reality of the risk. For example, I've asked a number of patients what they're most worried about, and—and… In the region where I am in Northern New England, I see a lot of patients who are second or third opinions who—who could be because they're very complicated but could be because their doctor sent them to me to "talk some sense into them" because they're not gonna take any—they said they're not taking any drugs, and I start with, "Tell me what you're so worried about the drugs," and almost always the answer is, "Cancer." And I say, "Okay, what kind of cancer?" And they say, "Well, I don't know, you know, cancer-cancer." And I say, "Well, first of all, there are only very specific types of cancer that can occur with these drugs," and we talk about skin cancers and we talk about lymphomas. And I say, "How often have you heard that these might cause cancer?" And we did this... Not only did we do this in the clinic, but we did this as a survey as well that we published, and patients say anywhere from, you know, 1 in a million, which is wrong to 5%, 10%, 20%, and up to 50%. So some of these patients are coming in, and we as providers have a hard time understanding why are they being so unreasonable about this. Well, it's because they think there might be a 50% chance risk of cancer. And of course they should be scared of that. We would never use a medication with that sort of risk. But it's a great way to start the conversation and asking what they know so that you could then play off of that and alleviate some of those concerns. And once you start explaining the absolute risks, which are, again, how many patients out of a set denominator—I use the denominator of 10,000 when we talk about lymphoma—then all of a sudden people start getting more relaxed.

Dr. Birnholz:
Interesting. And you're speaking to a broader issue that I want to ask you about, which is the possible care gaps or disparities in communication between specialists or professionals before they even walk in your door, so patients who come to you and they've been in a situation where maybe some of their—their concerns were not only unalleviated but, uh, compounded based on some communicative issues. What are some care coordination improvements that can help take that down?

Dr. Siegel:
Yeah, I think partly it's educating our colleagues. And if you're taking care of IBD patients and you don't know these risks, you better learn them and have a way to communicate with them, because if you're fearful of them and if you pose the answer of, "Well, they're kind of these drugs that have some risks associated with them, and we're gonna have to test you for TB and do some other genetic testing, and we're gonna check your labs every couple weeks, and if you get lymphoma, give me a call," you know, they're gonna be really put off by it. And I think our patients put so much trust in their providers, and if their providers are showing hesitance or worry about it, then they're never gonna take them. So I'm not saying that they shouldn't be concerned, and I'm also not saying to cover up any risk, because there are some real risks that we have to talk to them about, but I think we have to present them with confidence that we have a lot of data—again, we have over 20 years of data about biologic therapy now, shorter on some of the newer biologics but learning more all the time—and to be very fair that we're balancing this against the risk of their disease. And the alternative of not taking

some of these immunosuppressant therapies are the riskiest drugs without question that we have in our armamentarium, which is prednisone and corticosteroids, because they're cheap, because they're easy, because they make people feel better—are really something that many gravitate to because it's an easy, quick fix, but the risks of exposure to corticosteroids actually far outweigh any of the risks that we can even come up with with the biologic therapies.

Dr. Birnholz:
Let's take an opposite situation. You've spoken on this before, I believe. It's a patient who's in remission—comes in and saying, "Well, I very much wanna just stop all my medications." Um, "Obviously, I don't need it anymore. I'm doing fine." How do you counsel these patients?

Dr. Siegel:
Yeah, these are tricky conversations. You know, uh, a number of years ago the answer was, "Absolutely not, that's crazy;" uh, "We will lose the one drug that's working for you, and it's never gonna work if you restart it again;" and it wouldn't even be a conversation that we would entertain. But we've learned a little bit more, and now that we have a number of biologics, I entertain the question with really explaining what the risks of doing this are and what the benefits might be of coming off. So, the typical situation is just what you described, but I'll add a little more specifics to it, which is we've got them on combination therapy, which is a combination of a biologic drug and an immune modulator, our best treatment regimen, and patients come in and say, "I'm doing great." You did a colonoscopy, they're doing great, and they say they wanna come off of 1 or both of the medications.

And it has been studied somewhat, not in a great prospective way or in a randomized way yet, but just recently in Europe, they completed a trial called SPARE that they randomized patients who were on combination therapy, and they had 1 arm stay on 2 drugs, another arm where they withdrew infliximab, and a third arm where they kept them on infliximab but withdraw azathioprine. And we don't know the results of this yet, but it's looking at outcomes that are both around relapse of disease and side effects and safety. And what's interesting is we were part of this, our research group at Dartmouth-Hitchcock, and part of this European actually now global study where we surveyed patients and providers to see if they would want to stop therapy, and the perception is that they always would want to stop therapy because it's a better thing for them or, you know, less exposure to drugs, but, uh, interestingly many patients didn't want to stop therapy at all. They were finally happy that they were better and in remission. And I think it's a reasonable thing to consider and in many cases… In the patient that I just described, we would consider stopping azathioprine, which I consider the riskier of the drugs if you're using them long-term as compared to biologics. But I was, you know, sort of pleasantly surprised to see that many patients wanted to stay on medication because they recognize that it made them better and they didn't want to stop.

Dr. Birnholz:
Any other research ongoing either through your group or—or some of your colleagues out there, nationally and globally, that are also looking into how to better manage, better counsel those about risk?

Dr. Siegel:
Yes, so work... The other work that we have done… And, you know, we've tried to take a broad look about managing risk, and as I mentioned earlier, most of my research career early was focused on figuring out how much risk these medications really brought and how do we accurately communicate that to patients, and we developed videos, we developed 1-page risk pallets of how many patients out of 10,000 might develop lymphoma. The number, by the way, that I use is up to 9 patients out of 10,000 is the highest risk estimate we've really ever seen in the literature of developing lymphoma whether you're on biologic monotherapy, azathioprine monotherapy or combination therapy.

And after I worked on those, the next place I turned my attention was to trying to understand the patient's risk of their disease. So, if you're seeing a patient who's relatively recently diagnosed and you're trying to figure out if this is somebody you can just watch and see how they do for a while or do we need to jump in and use our very best treatment regimen, which in some cases would be combination therapy, some cases would be one of the newer biologics as monotherapy, wouldn't it be nice to know which of the patients are at high risk of progressing their disease and how quickly they'll get there versus patients where you might actually be able to watch them for a year or 2 or 3 and treat them symptomatically and repeat and endoscopy in a year and see how things look?

So, uh, with efforts from a great group, we developed a tool called PROSPECT, which is a program that patients come in, we take blood from them and check their genetics and some serologic markers in addition to looking at their disease distribution, so where their Crohn's disease is, and we're fairly accurately able to predict over the next 3 years what their chance of having a complication of their disease is, a complication meaning a stricture or penetrating disease or needing an abdominal surgery. And it's a very pretty graphical tool that's printed out for patients so that you can look at it as a shared decision-making tool with your patients. And when patients see that they're actually at pretty high risk of needing a surgery over 2 or 3 years, the whole conversation changes. It turns away from, "Oh, I'm too scared of these drugs" to "Doctor, what can we do to prevent these complications?" So, to me, a lot of our effort, again, has to

go toward making sure our patients understand the implications of undertreated or untreated disease as opposed to just trying to defend the safety of these medications.

Dr. Birnholz:
Nice. Now, before, uh, I scale back again just in case there's any other questions that come around I want to pose it to you, put the question-talking opportunity into your camp to address anything that we haven't talked about that you think is particularly important, something that—whether it's, you know, an ongoing issue a continuing challenge or just an opportunity to be able to, uh, speak to our audience about an area that you're particularly passionate about in this field.

Dr. Siegel:
I think the one thing I'd like to add—and many, you know, at this meeting and many in the audience know this—but the risk of these drugs is—is time-dependent, so the biggest risk… Again, time and time again when patients come in, I could almost assure you that what they're worried about, whether they vocalize it or not, is worried about cancer, and I urge you to take a few minutes to explain to them that we're dealing with really only 2 specific types of cancers. We're talking about skin cancers, which we could manage and we understand how to prevent, and lymphomas, which are more unpredictable but have a very definitive risk profile that we can predict for them—again numbers of about 9 out of 10,000 patients, which is a pretty low number, but you can show that and display it to them in a number of different ways. But the important message I want to add to that that we haven't covered is it's based on how long you've been on therapy.

So the scariest type of the cancers that we deal with both as adult and pediatric gastroenterologists are these what are called hepatosplenic T-cell lymphomas, these very aggressive, very hard-to-treat lymphomas that happen mostly in young people, mostly in young men but could happen with anybody. If you look at the world's literature of who's ever developed hepatosplenic T-cell lymphoma, almost every single one of them have occurred after 2 years of therapy, so you have this window of opportunity within the first 1 or 2 years of treating patients that it is really a very safe environment to use almost any treatment or combination of treatments that we have.

And the question you asked before about withdrawing therapy, that's the appeal, is we have 1 great shot to get our patients into remission. It's that golden time when they come in and they're recently diagnosed; they haven't failed 3 biologics and had 6 surgeries, but they're a relatively new diagnosis. We might predict their risk is high and want to treat them aggressively with our best drug combination, that that risk of cancer, although you need to have it with your patients, is truly near negligible in the first 1 to 2 years of therapy. So my practice has been let's use our very best treatment regimen, whether it's 1 drug or 2 drugs, carefully evaluate things over 6–12 months, look for an opportunity to withdraw the drug that we think is most implicated in these long-term cancer risks, which are the immunomodulator drugs, and then thinking about pulling that away. And once you say that to patients, it really changes it, because if you can help alleviate their concern about these cancers, help alleviate our concern—totally backed up by data—that we're doing something that's safe and effective with a plan to take away the drug that you and the patient might be worried about, I think it's really the best strategy. So I'd urge our—our colleagues to really make sure your patients understand that this isn't something that happens after a week or 2 or a month or 2 or even a year of therapy. It's something that really happens after 18, 24 months of exposure.

Dr. Birnholz:
Those are sage words. And I have to tell you right up front, Dr. Siegel, you are one of the best color commentators in your IBD sportscaster setup I could ask for.

Dr. Siegel:
Oh, well thank you.

Dr. Birnholz:
So I really appreciate your time. Uh, from all of us at ReachMD and, uh, over here at the, uh, Crohn's & Colitis Congress, I really thank you for sharing your insights today.

Dr. Siegel:
Great. Thank you for having me.

Announcer:
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