October 30, 2014 | Speaker: Dr. Corey Siegel TRANSCRIPT

OPERATOR:
Hello, everyone, and welcome to *What to Know About Biologic Therapy in IBD*, a free telephone/web education program. It is my pleasure to introduce your moderator Paula Dorfman, Education Program Manager for the American Gastroenterological Association.

PAULA DORFMAN:
Hello, everyone. On behalf of the American Gastroenterological Association and the Crohn's & Colitis Foundation of America, welcome, and thank you all for attending tonight's program.

This program is supported by educational grants from AbbVie and Janssen Biotech, Inc., administered by Janssen Scientific Affairs. We are also supported by a sponsorship from Takeda.

I would like to address a couple of housekeeping items before we begin. To allow full participation in today's program via the web, please be sure to disable any popup blockers on your browser. Note that this program will include interactive polling questions, which you will be prompted to answer throughout the program. Please respond when these questions appear on your screen. Note that your responses are anonymous.

For the teleconference participants listening by telephone, you will be unable to respond to the polling questions, but have the ability to hear the questions and answers.

Thanks to everyone who submitted questions in advance of the program.

After the presentation, we will open up the program for your questions. We will take as many questions as time allows from both telephone and webcast participants. If we are not able to take your question, CCFA's IBD Help Center can be reached Monday through Friday, 9 AM to 5 PM Eastern Time, by calling 888-694-8872.

Upon exiting today's program, you will be prompted to complete a brief program survey. We ask that you please take a few moments to provide your responses, as your feedback is extremely important to us as we plan for future educational activities.

I now have the pleasure of introducing our speaker for tonight's program. Dr. Siegel is an Associate Professor of Medicine for the Dartmouth Institute of Health Policy and Clinical Practice at the Geisel School of Medicine at Dartmouth. He's also Director of the Inflammatory Bowel Disease Center at Dartmouth-Hitchcock Medical Center in Lebanon, New Hampshire.

Dr. Siegel, thank you for joining us. It is now my privilege to turn the program over to you.

DR. COREY SIEGEL:
Thank you very much and thank you, everybody, for joining. I hope you find this an interesting time together where we talk about a really important topic, which is biologic therapy in IBD. And I say important topic because this class of therapy has been the really number one breakthrough we've

DR. COREY SIEGEL:
had over the past ten to fifteen years, that has really allowed us to change the natural history and the course of the disease. And I hope as we go through here, we get many of your questions answered, and then we look forward to hearing questions that you have afterwards.

The program's goals include to review the use of biologic therapy in Crohn's disease and ulcerative colitis, to help you understand the risks and benefits of therapy, to discuss the importance of adherence to treatment, and to share resources to help you monitor your disease.

We have a few polling questions as we go along. "Which best describes you? I'm a patient with Crohn's disease; I'm a patient with ulcerative colitis; I'm a friend or family member of a patient with Crohn's disease; I'm a friend or family member of a patient with ulcerative colitis; or other."

Waiting for the question to go out and the answers to come up.

Okay, the majority says they're patients with Crohn's disease, and I'm sure it's a smattering of responses of everyone else that we have out there, but thank you for joining. Really just to make sure that our polling questions are working there.

Let's start by talking about the IBD medicine cabinet. There are a number of choices that we can use when treating our patients with Crohn's disease and ulcerative colitis, and I'm sure many of you on the call have probably used some, if not all, of these. There are over-the-counter medications that we use every day, things like Imodium® or Lomotil® for diarrhea. Aminosalicylates which include the 5-ASA drugs like mesalamine and other forms of standard type of medications like sulfasalazine and there are many derivatives of these medications that fit into this class. Corticosteroids are both our friend and our hated partner. As many of you know, corticosteroids work very quickly to make everyone feel better, but comes with side effects, and one of our main goals of therapy is what we refer to as steroid-sparing therapy or keeping everybody off of corticosteroids. Immunomodulators or medications such as 6-mercaptopurine, azathioprine or methotrexate. We use antibiotics frequently for the treatment of Crohn's disease, more so than ulcerative colitis. Specifically medications like ciprofloxacin or metronidazole, which is Flagyl®. And then what we'll focus the rest of the time on together tonight is on biologic therapies and talk about the different ways we can administer biologic therapies to our patients.

Here's another polling question. "Tell us a little bit about your knowledge on biologics. Which of the following statements is false? A, biologics are grown in living cells; biologics target particular proteins, chemicals or cells; or that biologics are chemically made."

I'll wait for your responses and then we can go on.

We should be getting results coming up any second here.

It looks like most people said biologics are chemically made. All these are close statements here, although biologics are not typically grown in living cells. They can be grown in a number of ways,

DR. COREY SIEGEL:
but not typically grown in living cells. They are often chemically made and let me tell you a little bit more about biologics.

Biologics mainly include proteins or antibodies which are part of the immune defense. They're medicines made from living organisms, but not necessarily grown in cells. They're similar or identical to the actual biologic chemicals that our body makes and historically reserved for patients not responding to standard therapies, but increasingly used early in the course of disease. That's an important statement. It's actually one of the most important statements on any of these slides.

When biologics first came out they were thought to be used for failures of all other medications, meaning you had to go through all those medicines and get really sick before we would offer biologic therapy. But we've learned so much over the past few years that that's not necessarily the case. That if we wait too long, oftentimes the damage that Crohn's disease and ulcerative colitis can cause is already done. That we're now using them much earlier in the treatment course to prevent complications of the disease as opposed to always chasing the disease and treating the complications of disease. And try to keep that in mind as we go forward, that these medications, we don't want to wait until complications develop, but use these medications when they really work, which is before complications develop. An important concept that has changed over the past five to ten years.

So how do biologics work? Well, antibodies bind and eliminate infections. Molecules bind to components of the inflammatory process. The most used biologic agents are anti-TNF agents and these block a protein called tumor necrosis factor, that's where the term TNF comes from, which are made by white blood cells that promote inflammation. There are another class of biologics that have recently been developed and now being used in our patients for both Crohn's disease and ulcerative colitis, that block the interaction between receptors on white blood cells with receptors on the surface of the intestinal lining.

Think of it this way. Cells that are inflamed are circulating through the blood vessels, trying to get to the bowel to cause damage. An analogy I've heard that I think really makes a lot of sense is that these new class of drugs that are blocking this interaction between the receptors of the blood cells and the intestinal lining are like blocking an exit off a highway. If a cell is going down a highway, it wants to get off and go cause damage. But if that exit is blocked, it can't get there and it can't get to the bowel. And that's what this new class of medications, we refer to them as anti-integrin molecules, are being used for.

How are biologics different than other therapies? Well, biologics are more complex. They're about a thousand times larger than conventional medicines. The mechanisms of action are targeted to very particular and specific proteins, chemicals or cells. Unlike corticosteroids, biologics act very selectively. I think of them like a smart bomb, where if you have a huge fire, corticosteroid throws a blanket over the entire thing, but that suppresses all of your immune system. What biologic agents are doing are really trying to focus in on one part of the immune system that's overactive, therefore allowing the rest of your immune system to still do what it wants to do.

DR. COREY SIEGEL:
The anti-TNF drugs, as mentioned, are the ones you've probably heard the most about or they're been around the longest. In fact, infliximab or Remicade® was initially used and initially approved in 1998, so we've had quite a bit of experience with these drugs. This class of medications aren't new any more. These are really becoming very standard and part of our care.

They're all a little bit different, although they work by the same mechanism, going after anti – going after TNF and blocking TNF.

The first is adalimumab, often known as Humira®. This is taken as a subcutaneous shot under the skin. It's approved for both Crohn's disease, both adult and pediatric, and for ulcerative colitis in adults. And it's really most effective for patients where conventional therapies fail, as the package insert would say. However, as previously mentioned, again, we're using these medications much earlier in the disease course than we have in the past.

Certolizumab pegol or Cimzia® is similar. It's also taken as a subcutaneous injection. Currently it's only approved for Crohn's disease in the adult population. Certolizumab pegol is given once a month, where Humira or adalimumab is given once every two weeks in most cases.

Simponi® is one of the newer anti-TNFs that we have, often known as golimumab. And this, similar to Humira and Cimzia, is also taken as a subcutaneous injection, and right now it's indicated only for ulcerative colitis in adult patients.

Infliximab is the one that's been around the longest, or Remicade. Again, approved in 1998. This is an intravenous infusion. You start off with three infusions early on. Within six weeks you get three infusions. And then it's given typically every eight weeks, as long as you're on the medication. This one's approved for pediatrics and adults for Crohn's disease and ulcerative colitis.

There are a number of side effects that we'll talk about and address here. There're some that are common that we don't worry too much about and I say not worry too much about because although no one ever wants side effects from medications, they typically go away as soon as you stop the medication and move on to something else. And the common side effects that we think about are injection or infusion site reactions, the risk of infections, and a psoriasis-like reaction. If anybody has psoriasis or has seen somebody with psoriasis, this is a skin rash, you typically can get it on the elbows and on the knees. Sometimes it's more severe than others. It's typically very treatable and typically taking the medication away or oftentimes decreasing the dose of medication will make it go away.

The side effects that we think of a little more frequently, and not because they happen frequently, but because they're more serious, are shown on this chart here. This is something that you should be thinking about and asking your doctor about when starting these medications. The good news is that about 90% of patients who start these medications stay on them without any significant side effects, but about 10% of people have some side effect that leads to stopping an anti-TNF medication.

DR. COREY SIEGEL:
Infusion or injection site reactions aren't severe nor are they life-threatening, however, they're scary. And I bring this up to all of my patients as I start them on them. That somewhere in the range between 3 and up to 20%, depending on the medication, you can either get a rash around the site that you gave yourself a shot, or you can get a reaction when you're getting an intravenous infusion, that again will go away once we stop the infusion, and sometimes use medications to help stop that reaction. But these are very manageable and something that we can deal with every day.

About 1 per 100 people get something called a drug-related lupus-like reaction. This is a case where people can get arthritis and rashes and sometimes some abnormalities in their blood tests, that look like lupus, but it isn't exactly lupus, which is an autoimmune disease, but it's related to the medication. And the good news again is that although it is pretty rare when it occurs, when it does occur it goes away when withdrawing the medication.

The thing that I think about most when I'm talking to my patients are serious infections and then cancers.

Serious infections are defined by those infections that will end up leading to hospitalization or requiring intravenous antibiotics for treatment. Thankfully, it only occurs about 3 per 100 times, but 3% is a measurable number and it's something that I think we all have to pay attention to.

What I tell my patients about this is that they need to pay attention to this problem and although I'm not too worried about it overall, the education of both the doctors and the patients is really critically important. That having a fever and shivering under your covers for three days at home is no longer acceptable. And when you're not feeling well, particularly when you have a fever, that means calling your doctor, seeing if you need to be seen, seeing if you need antibiotics or to be treated, and getting on top of that sooner as opposed to later is what prevents infections from becoming serious infections. And that's something that is really important again, not just for all those on the call who are patients or those close with patients, but the providers need to know this as well. Even if your provider isn't a gastroenterologist who's the first person you call, you need to let your doctor know that you're on a medication that can somewhat suppress the immune system and they'll take this more seriously.

I find that the most emotional conversation we have with patients and their families in the office is around the worry about cancers related to anti-TNF drugs. When we talk about cancer, we have to think very specifically about what types of cancers have even been associated with these medications at all. And I'll tell you now that other than non-Hodgkin's lymphoma, which I'll tell you some more detail in a minute, and some small increase in skin cancers, all the other types of cancer that we hear about and worry about really haven't been shown to be associated with anti-TNF treatment. Think about lung cancer, prostate cancer, breast cancer, colon cancer, these have never been associated with these medications or really any of the medications that we use to treat Crohn's disease and ulcerative colitis. So if you hear about or read about the fact that these medications can be associated with cancer, specifically what they're talking about is non-Hodgkin's lymphoma.

DR. COREY SIEGEL:
Here it says the rate is about 6 out of 10,000 patients over the course of a year. And I'm going to show you some slides coming in just one minute that tries to put that in perspective of how often this might occur in the first place.

We have listed there some other side effects, that if you open the package insert that comes with these medications, you'll read about. Like multiple sclerosis, heart failure, serious liver injury, and believe me, as a doctor, I know how serious these sound and how scary they might sound if you don't have them in context, and what these medications really do and how often they occur. And this really comes from just case reports in our medicine literature, meaning there are a few cases reported here and there and there's really no clear association between the drug doing this or could that have happened to the patient just by bad luck. And we don't find that these are big problems related to these medications. However, if a patient has multiple sclerosis or heart failure or serious liver injury already, it might cause us to not use the medications. But this isn't used as a reason to stay off of a medication for fear of these happening because it's so incredibly unusual, we can't even put a number on how often it occurs.

This is something called a risk palette. This is to try to put in perspective this risk of cancer. I use this in the office every day, I have this up on my laptop sitting in the office because the question comes up so many times, as how often does it really occur that you can develop a cancer. In this case, as we talked about, only really referring to non-Hodgkin's lymphoma, which is a lymph node cancer.

In the background population in the United States, if you look at all-comers, not patients with just Crohn's disease and ulcerative colitis on anti-TNF drugs, but anyone in the United States, the expected rate of these cancers is about 2 people out of 10,000 over the course of one year. If you look at patients who are taking immune modulator drugs, such as 6-mercaptopurine or azathioprine, that risk is somewhere around 4 people out of 10,000, so it increases it, but it doesn't increase it that much.

I've oftentime asked my patients when they tell me they're worried about cancers, how often they think these drugs might cause cancer. And the numbers that I get are this incredible variation from anywhere from 1% up to even 50% that these drugs might cause non-Hodgkin's lymphoma. But in reality, as you saw in the last slide, the amount of patients who develop non-Hodgkin's lymphoma with Crohn's disease or ulcerative colitis, on anti-TNF drugs, is about 6 people out of 10,000. And I don't mean to say that that's not important for those six people, of course it is, but if you look at it in perspective, compared to either two or four, either on no medications or other medications, that increase I think is pretty small and tolerable if you're talking about medications that really could change the natural history of your disease and incredibly increase your quality of life.

I've had some patients who say six is still too many and they understand it and they looked at these charts and they still say that they don't want to take it and that's fine. But I think it's important to understand how small these risks really are and how infrequently these side effects, that are very scary, actually happen.

DR. COREY SIEGEL:
Here are the other types of biologics that we mentioned. These are the anti-integrin drugs. These are the drugs that are blocking the exit of those inflamed blood cells, trying to cause damage to your colon. You may have heard of one or both of these.

If you've heard of any of them, you've probably heard of Tysabri® because it's been around the longest. Tysabri is used as an intravenous injection and it's approved for adult patients with Crohn's disease.

The newest kid on the block, just approved this past May, is Entyvio®, also called vedolizumab. This is also used as an intravenous medication and approved now for both patients with Crohn's disease and with ulcerative colitis.

What we've seen with these drugs is they're a little bit slower in onset than the anti-TNF drugs. Anti-TNF drugs, some people tell us they start feeling better after the first infusion or the injection, where these drugs may sometimes take four to six weeks to really start kicking in, if not a little bit longer than others.

But the real benefit we're seeing with these drugs is they appear to have a very nice and durable response, meaning once you respond to them the chance of staying on the drug and continuing that response, really seems to be very nice.

The other message with these drugs is they appear to be safe drugs, at least in the experience that we've had so far.

One of the drugs is much more concerning, we're not really using much these days, which is called Tysabri or natalizumab. You may have heard of this drug, but it's important to distinguish from Entyvio, which is the new one, and let me make that distinction for you.

Tysabri is very good at crossing into the brain and suppressing the immune system that helps out the brain. The reason that's important is two-fold. One, it's a very good drug for multiple sclerosis, which affects the brain and the central nervous system. So if you think of this way, that for multiple sclerosis you need the drug to get into the brain for it to work, it's a very good drug for MS. However, the downside is that there's a certain infection called JC virus or the John Cunningham virus, that when this drug is used, it causes that virus to expand and it can lead to this very devastating problem called PML, which is progressive multifocal leukoencephalopathy, which is not something any of us even want to think about.

Tysabri got some good use over the past number of years and I've had a number of patients who've had great success in using it. The trouble is, this worry about PML really has led to almost the abandonment of using it routinely. There's still some cases where it might be useful, but it's mostly been replaced now by Entyvio or vedolizumab, the new kid on the block here.

DR. COREY SIEGEL:
The reason this is different is vedolizumab really is focused on the gut and the only receptors that are known in the body for this drug are in the bowel and along the bowel wall. Again, think about those exits that we're trying to block and the only place these are active are around the bowel. It appears to be very gut-specific. And what that does is not only get rid of the risk of PML, but also seems to get rid of most of the risk of the serious infections that we're seeing with some of the other medications.

Listed here, there's a slight increased risk of colds, also nasopharyngitis. That kind of makes sense because where you get colds, which is in the nasopharynx, the back of your throat, is also the first part of the GI tract, so that wasn't a huge surprise. But just to realize that this isn't a huge, huge problem, in the clinical trials where they gave some patients this drug Entyvio, and some patients placebo, which is essentially a sugar-water infusion, the patients who received placebo had colds about 8% of the time and the patients who received this drug Entyvio had colds about 13% of the time. So although it was slightly increased and it's worth mentioning, it's not something that I think we worry about too much and certainly not a reason to stay away from these medications.

There's a lot of enthusiasm and hope about Entyvio, that this is not necessarily hugely better than any of the other medications that we have, but another choice for our patients and another way to attack the disease and thus far the experience has been very good, both in the clinical trials and clinically, as many of us have started using these medications really fairly frequently with our patients.

It's worth taking a break and referring to pregnancy. And not necessarily that so many of you on the call might be pregnant right now, but we know that these diseases affect men and women equally and when half of our patients are female, it's something we certainly need to think about. And as you also probably know, one of the most common times to get diagnosed with Crohn's disease or ulcerative colitis are in the late teens or early 20s, so we're always thinking about this when we have young women coming into the office who are either on medications or about to start on medications in the future.

I think there's some really good news here. You have to think about this in two different ways, what's been written by the FDA and listed on the package with these medications, and now our vast clinical experience with these medications, because they're somewhat different.

What we know now is that the anti-TNF drugs, specifically certolizumab pegol or Cimzia, adalimumab or Humira, infliximab-Remicade, and golimumab, really have very similar safety profiles and appear to be safe in pregnancy. What do I mean by appear to be safe? Well, we've now followed many, many kids across the country and the United States and really across the world, looking to see if there are any significant adverse effects that either happen to the mom or the baby in development or after being born. And the really good news is it's very hard to find any evidence at all that these medications cause any trouble for newborns, which is fantastic news.

DR. COREY SIEGEL:
I'll make one specific note here, that Cimzia or certolizumab pegol happens to have a little special quality to it when it comes to pregnancy because it's a very big molecule that has a hard time crossing the placenta at all. And because of that it doesn't even cross into the baby. And when babies are born and you look for Cimzia or certolizumab levels, it's essentially zero.

The good news is that although babies born with some Humira or some Remicade or some Simponi onboard, it just doesn't seem to affect them. We're not seeing infections, we're not seeing any developmental delay. In fact, they seem to be healthy babies that really don't have any significant adverse effects, which is great.

We are a little bit more worried about Tysabri, as I mentioned earlier, there are some worries about Tysabri in the first place. But thus far, from what we know about Entyvio or vedolizumab, this seems to be safe during pregnancy. Again, great news.

Although under breastfeeding it says limited human data and that's what the FDA's required to say because it's true, academically and clinically we have a lot of data now on these medications and only a very tiny bit of the medicine gets into breast milk at all. And if you think about the fact that the reason we give these medications intravenously, it's because they don't get absorbed as oral medications. Even if the babies are getting a tiny bit of this medication when they're getting breast milk, almost none of it is getting into them or none of it is getting into them and it's not something that we recommend staying away from and consider breastfeeding to be safe when using anti-TNF drugs and thus far Entyvio.

We need to think about kids a little bit differently and of course not one size fits all with children, and we always need to think about safety first when it comes to kids. So although there are limited data in pediatric IBD compared to the adult population, we don't expect that things will be all that much different. Treatment is sometimes extrapolated from the adult studies, but again it's probably fair to say that we're going to see similar things in kids as in adults. In fact, I was part of an academic publication looking at this and kids appear to have even fewer infections and fewer, thankfully, fewer malignancies such as lymphomas, compared to adults. So anything you heard from the adult presentation, if you thought that was reassuring, and I hope you do, it's even more reassuring when it comes to kids.

I want to spend a few minutes on this topic of therapeutic monitoring. This is something that we didn't even have a word for about five or certainly ten years ago. But therapeutic monitoring refers to the idea that we don't just start these medications at a certain drug dose and then say good luck, come back and tell us if you get better. We're understanding now that we can measure drug concentrations and antibody levels. Currently we're only able to measure them for infliximab and adalimumab because these are commercially available and your doctor can order these today, but the others are coming and they'll be out soon.

DR. COREY SIEGEL:
What it helps us understand is are they getting the right dose and is your body trying to reject this medication. We now know what the amount of drug in your body is associated with people getting better. And if we can slightly increase or in some cases decrease the dose to get right in that window of the right dose, we know that we're able to get more patients into remission, more patients off of steroids, and if it's not too high of a dose, prevent any unnecessary side effects.

The other thing that can happen with these biologic drugs is that you can develop antibodies against the drug. Why does that happen? We talked about this earlier, that they're really being developed from proteins that are essentially the same human proteins that we get. But just as you can have an allergic reaction to anything that you get exposed to in life, you also can develop antibodies against this drug. What antibodies do are, number one, cause allergic reactions to the drug, which would cause you to stop it; but number two, the antibodies bind or grab onto the drug, so the drug doesn't work.

So we need to be very careful in the way we use these medications now. And in my practice, we're really careful about measuring drug concentrations and antibody levels to make sure that we're getting it right. Because I feel that if we're going to use these medications, why not get it right now that we have the ability to understand how to increase or decrease the drug dose.

When we get those results, they can guide decisions that optimize the medications that are working or tell us when to move on. If you have Crohn's disease and your symptoms are increased or you're flaring and you're already on one of these biologic drugs and you come to see your doctor and they check your blood level and the blood levels are low, then they know to increase the dose. However, if you come in and that same patient has a flare of their illness and you check drug levels and they have perfect drug levels of one of the anti-TNF drugs, that probably tells us that for that particular person, anti-TNF drugs aren't going to work. And instead of going through all four of our anti-TNF drugs, we might move on to one of these newer drugs such as Entyvio. And this way your doctor can personalize treatment by monitoring biologic therapy. And this is really one of the few places in inflammatory bowel disease that we can personalize therapy and be very careful about getting it right, which is really, really important early on, not waiting until you're sick and we have to chase and find why you're sick, but let's prevent it from happening in the first place.

This is something called an option grid. If you can't see it too clearly on the screen here, if you go to the website listed there you can find this and you can print it out. I developed this option grid with some colleagues. And what this is is just a one page summary of many of the things that we just talked about, comparing the different types of drugs that we have, such as immunomodulators, which are azathioprine or 6-mercaptopurine or methotrexate, to the anti-TNF drugs that we just discussed, and then something referred to as combination therapy, which is a very frequent way that we use these medications and it's not one or the other, but using the medications together. And if you look at this option grid, this is meant to be really a one page summary of what types of medications they are, how they're given, how often we can expect people to get better, and then a review of those side effects that we just talked about.

DR. COREY SIEGEL:
Another resource that I've been very proud to be a part of are developing some video decision aids. Decision aids are not meant to be an educational program about a certain drug, but really a display of both the benefits and risks of different treatment options to help engage our patient, so that you can weigh in what your preferences are for treatment.

As I mentioned earlier, if the side effects still worry you and there are other medication choices that appeal more, well, we need to hear that as your doctors. We need to hear what your preferences are. And decision aids are meant to help guide you towards what the right decision is for you, based on your personal beliefs and preferences, based on the severity of your disease, and based on your prior experiences.

The great partnership that we've created with the Crohn's & Colitis Foundation around this work is that this video, which is put out by a company in Chicago called Emmi Solutions, is available to all professional members of the Crohn's & Colitis Foundation for their patients. That means your doctors, if they're members of the CCFA, can get you access to the videos for both Crohn's disease and I'm happy to say that the one for ulcerative colitis has just been completed over the past couple of weeks and will be available any day now. And if you ask your doctor if they're a member of the CCFA, they have access to these videos. I would argue to say that if you ask your doctor and they're not a member of the CCFA, you should tell them they should be, not just because of these videos, but of all the great other resources they can help you find by being part of this organization.

These are just little screen shots of what the videos are like. But first we go through the benefits of the medications, some of which I went through with you already, and how the medications work. We carefully talk about all the risks of the medications. And then focus on this concept of early therapy. Let's not wait until you're too sick, let's use these medications early on before you get into trouble, and a concept that as I've mentioned a number of times now, I think is really important.

How do you know if a treatment's working? If you start on one of these biologic therapies, what are the questions that you should be asking yourself and talking with your doctor about? How do I know if my treatment is working? Well, your symptoms will really be the way to guide you, but also looking at blood tests, X-ray studies such as MRIs or CT scans or colonoscopy are ways to work.

A question that comes up all the time, if I am in remission, should I stop my treatment? Something really important to know. At the current time, this is not something we do. If you were sick enough to get on the medications, we think it's important to stay on the medications. There are some circumstances where we might stop one of your medications if you're on two or three medications. But almost never do we stop all medications that are working, assuming that you're not having any side effects and that you're doing well.

How much time should I allow before trying a new medication? Again, very important. You might remember my saying that the anti-TNF drugs start working even within one or two infusions or shots.

DR. COREY SIEGEL:
That's just within a few days or a few weeks. Where Entyvio or Tysabri, the anti-integrin drugs, might take four to six weeks to really start showing effect.

We don't try to change medications too frequently. If you're quickly cycling through all your medications, you're going to lose the benefit of giving it a good shot and once you use one of these medications and go off of it, because of the antibodies I talked about before, it might be hard to get back on that medication later. So in my practice, and I know many of my colleagues who do what I do for a living's practice, we try very hard to get everything we can out of a medication and really make sure that we've optimized it, increased the dose, are getting it right before moving on to something else.

Let's briefly talk about adherence. Adherence to therapy essentially means staying on your medication. And we completely understand there are a lot of reasons why people have to stop their medications. It's not as simple as you don't want to take it, although that in itself is important. And if you're feeling like you don't want to take your medications for one reason or other, please talk to your doctor about it. There might be ways to change the dosing, change you to a different medication or really work through what your worries might be. But I'm always worried when I hear my patients stop medications on their own because of all the risks we just mentioned about stopping medications and about the disease leading to further complications. So please, please, talk to your doctor if you're worried about your medication. I promise he or she will be willing to listen and work with you about different options, or to talk with you through your concerns, to make it better.

Financial barriers are a huge problem. Again most practices are able to help you manage this. At big institutions like mine at Dartmouth, we have case managers and social workers to help. The pharmaceutical industry is very generous when it comes to helping provide free medication for many people going through application programs. And there are oftentimes ways to get therapy even if your insurance company is saying they won't pay for it, or if you don't have any insurance. So please, please talk to your doctor about this as there are many ways to get you on medication and to keep you on medication.

I'm going to change the topic a little bit and bring something up that I'll really tell you is on the leading edge of knowledge. I don't know that even all gastroenterologists know about biosimilars and you should be happy to know that you're going to learn a little bit about this term because it's something that will certainly be in the vocabulary of doctors and patients coming over the next few years.

Just to get a sense of what you know about biosimilars, let me just ask this true-false question. "Which of the following is true? A, generic biologic medications are currently available; B, biosimilars are identical to biologics; or C, biosimilars are not generic biologics." Which one of these is true, A, B or C?

Just going to give you a few moments there to respond and get the answers.

DR. COREY SIEGEL:
Okay, excellent. Many of you know a lot about biosimilars already and that's really fantastic, to see how much reading and learning you've done. That biologics [sic] are not generic biologics. Let me tell you a little bit about biosimilars.

Biosimilars are products that are highly similar, but not exactly copies of the biologic medications. And as part of the Affordable Care Act or Obamacare, the Food and Drug Administration will review and approve biosimilar versions of already FDA approved drugs. The FDA has given guidance on this, but I'll tell you has not initiated formal rule-making, so this is still in evolution and we as doctors aren't exactly sure how these drugs are going to roll out to our patients. But as of now, there are no USA FDA approved biosimilars, but we do expect this is going to change in the very near future.

Biosimilars really are an effort to develop something like a generic for biologics, but there are no generics for biologics, as the majority of you already knew. They're very similar to a particular drug, but they're not exactly the same. And all biosimilars differ from biologics and from each other.

Biologic medications can have generic versions, but the active ingredients can only resemble at best what the biologic original was and not exactly the same thing.

An analogy that I like that we show here is that different – identical twins, although similar in so many ways, don't have the same exact fingerprint. And therefore they're similar, but not necessarily exact copies.

Things to consider about biosimilars that we're all thinking about very carefully and we're not exactly sure how this is going to roll out, so collectively you our patients and all the providers are going to have to think about the interchangeability of biosimilars. Let's say a biosimilar of Remicade is available, which is available in other parts of the country. Can we just switch you from Remicade to the biosimilar? Does it need the same rigorous testing or can we say it's close enough that it's probably safe and probably effective? We have to be thoughtful about the names and not get confused about the drugs that we know and about these new biosimilar drugs. And being very careful about substitution and notification. Is it fair that you might go to your infusion suite, having gotten Remicade for ten years, and now all of a sudden getting a biosimilar? Or getting something that looks like Humira or Cimzia or Simponi or vedolizumab, that's not exactly the same thing, but that your insurance company has decided that because it's cheaper they might switch you to something else.

These are things that we're going to have to work through, but pay attention to this as it's definitely going to be part of our vocabulary and our day to day work.

Here's our next polling question. "Which of these is your biggest concern about biologic therapy? A, the risks and side effects of biologics; B, insurance benefits and costs; C, the effectiveness of the treatment; D, deciding which treatment to choose; and E, which is other."

I'll give you a moment and then I'll let you know what the majority of you said.

DR. COREY SIEGEL:
Okay, well, the majority said the risks and side effects of biologics. So I'm curious to hear more about that. I hope we address many of your concerns. I would like to hear if there're more. Again, I'm not trying to tell you not to be thoughtful about side effects of medications and I'm not telling you at all to say it's not a problem, don't worry about it. But really my message is these are manageable and these are side effects that we pay attention to, we know how to prevent them, we know how to watch for them. And the ones that scare us the most, such as cancer, specifically lymphoma, we think are really vanishingly small. But again, of course, we pay attention to this and I think it's very fair for you to still be concerned about it.

Just a couple of final messages. Talk to your healthcare team. You need to communicate with your doctor. If you don't tell your doctor what you're worried about, what you're feeling, what you want in your treatment, you're not going to get it. You need to be an advocate for yourself and you need to stand up for yourself. You can look and print off the CCFA's IBD Doctor Discussion Guide, which goes through questions such as which treatment options might be right for you, what are the benefits and risks of these options, how long might it take before we see an improvement, these are the type of questions that you need to ask if you don't have the answers, and you should be asking your doctor so they can help prescribe a personalized treatment plan, not just what your doctor thinks is best.

This is my last slide in summary of the key points that we tried to touch on here and then we're going to take some time for questions.

Let's remember, biologic drugs are made from living organisms and resemble chemicals in the body, that are different than the standard conventional therapies that we've used. It's always important to consider the risks versus the benefits, but when you're thinking about the risks of the treatment, please remember that the biggest risk to you as a patient with Crohn's disease or ulcerative colitis is the risk of the disease itself. Whether it's causing you symptoms and leading to complications requiring surgery, whether it's when a woman is pregnant and we're worried about pre-term labor and very sick neonates or very sick moms, or whether you're thinking about ten years of untreated disease, even without big symptoms, but constantly causing damage to the intestines that are irreversible, you have to think about the risk of the disease first, and then think about your treatment options and weigh the risk of the disease and what might happen without treatment versus the benefits and risks of those drugs.

We need to remember that response to biologics definitely differ from person to person. Some patients do great on anti-TNF therapy and others don't. And if you don't, let's make sure we optimize those drug concentrations, make sure you don't have antibodies, make sure that we understand why the drug's not working, and if it's simply that that drug type is not going to work for you, well, then it's time to move on to something else. You should not be going six or twelve months suffering on a medication that isn't working. After three or four months you should be talking to your doctor about figuring out if this drug's working for you and if it's not, move on to something else.

DR. COREY SIEGEL:
We talked briefly about biosimilars that resemble biologics, but they're not generic versions.

And I hope you get this point and I already hope you're doing this, and if not, please try to do it more, is you absolutely need to communicate with your healthcare team to get the treatment that you deserve, to help improve the quality of your life.

So with that I say thank you so much for paying attention and listening in. I look forward to your questions and I hope this has been helpful thus far.

PAULA DORFMAN:
Thank you very much, Dr. Siegel, for your informative presentation.

Now it is time for the question and answer part of our program. For everyone's benefit, please keep your questions general without personal details, so Dr. Siegel can provide an answer that is general in nature. In the interest of time, I also ask that you keep your questions related to the topic. You are always welcomed to contact the IBD Help Center if you have other questions.

Operator, can you please give instructions to the telephone and webcast audience?

OPERATOR:
To participate in the call by asking a question, please dial star-1 on your keypad. If you are joining us by web, simply click on the Ask a Question, type your question, and then hit Submit. We will take your questions in the order they are received. We only take one question per person. Once your question has been voiced, the Operator will transfer you back into the audience line. Again, to ask a question, please dial star-1 on your keypad or click on Ask a Question, type your question, and then hit Submit.

PAULA DORFMAN:
We will take our first question from our webcast audience. "Should people with mild to moderate disease consider using biologics for symptom control or are they better left for people with severe disease that can't be controlled with other medications?"

DR. COREY SIEGEL:
Well, thanks for that question, that's really important. And it gives me an opportunity to reiterate a point that we made earlier about not waiting too long to get on these medications.

I'll say that from an FDA standpoint and the way that these drugs have package labels on them, they talk about using them in moderate to severely active disease. We have to remember, though, that when we say moderate to severely active disease, that doesn't necessarily mean how you feel today. People could have mild symptoms, but have moderate to severely active disease because there's so much inflammation going on in their bowels. So we have to think about what we mean by mild, moderate and severe disease.

DR. COREY SIEGEL:
The way that I think about it and I try to get my patients to think with me about it is not is it mild, moderate or severe today, but where is it going in the future? If we think that you have mild disease and it's always going to stay mild disease and you're never going to have complications and your biggest problems are going to be an occasional loose bowel movement or cramps, then no, biologic therapy isn't right for you. But if we think that over time you can progress to moderate or severely active disease, then absolutely regardless of the symptoms that you're having today, you should be thinking of biologic medications, as they are the most effective medications to prevent these disease complications from occurring.

PAULA DORFMAN:
Thank you. Our next question from the webcast audience, "Can you just stay on biologics your entire life if they are currently working to keep Crohn's in remission?"

DR. COREY SIEGEL:
Well, I'm glad somebody asked that, thank you. This comes up all the time and I have so many patients come and say to me, well, I don't want to start biologic medications because I heard I need to stay on them for my entire life. Well, think of it this way. When we have other diseases that we take care of as providers or many of you may have trouble with these, such as high blood pressure or diabetes, you don't go on your insulin for a short period of time and then stop it. You don't go on your blood pressure medications or your blood pressure's better and then stop it, you stay on them forever. You may not stay on that medication forever, but you'll stay on the most effective medication as long as you can, as long as you're not having any adverse events to it. So I think forever is a really long time and I never would say you're going to be on this drug forever. In fact, ten to fifteen years ago, before we had biologic drugs, we had no idea how we'd be treating inflammatory disease. And I promise you that in another ten to fifteen years, we're going to be doing things differently.

Look at the explosion of new medications we've had over the past few years and it's only increasing as we go over the next five, ten, fifteen and twenty years. We're going to be treating these diseases in much more broad ways and have many more options.

So my answer to that question is let's take it year by year, let's get you better, keep you better. As long as you're better and as long as there're no side effects to the medications, I would say that's fantastic news, stay on the medication as long as you can until either something comes out that we think is even more effective and even safer, or for some reason or other you have to come off the medication. But I wouldn't think of this as a lifetime burden that you have to stay on forever. I would say you're very lucky the medications are working for you and continue to work and let's accept that luck and go with it as long as we can.

PAULA DORFMAN:
Our next question, "When a biologic drug is initially effective at achieving remission, how long does it remain effective in your experience? Months, years, decades?"

DR. COREY SIEGEL:
Yeah, that's a very good question and we're getting better at this. This is the good news. So going back to the portion of this discussion about optimization or monitoring of our drugs, one of the main reasons biologic drugs would stop working over time is because your body starts getting used to the drug and maybe even needs more drug, or you develop antibodies against the drug.

We had no idea how to prevent antibodies from occurring a number of years ago. But now we know that by checking drug concentration levels, always keeping the drug at a high enough level so your body never runs out of drug. I've used the analogy of you never want to go into the red on your gas tank. You always want to fill up before it gets too low because when your body gets into that red level of the biologics, that's when you start developing antibodies against the drug.

So if we can optimize the drug dose and in many cases add a second drug, such as 6-mercaptopurine, azathioprine or methotrexate, that also helps prolong the durability of these medications.

I feel that if we can get patients through six to twelve months on a biologic drug with good drug concentrations and without antibodies, that these medications can work for years for sure.

PAULA DORFMAN:
Thank you. Let's take the next question from our telephone audience. Operator, could you put a question from the phone line, please?

OPERATOR:
Our first telephone question comes from Jane in Ohio. Jane, please state your question.

JANE:
Yes, my question was on the Remicade. My son has been on it for three and a half years and he's doing quite well. Wanted to know how long he should be staying on it, the longest amount of time anyone's been on it, and will it lose its effectiveness in time?

DR. COREY SIEGEL:
Great. Hi, Jane, thanks for your question, and I'm glad to hear your son's doing so well, that's great news.

I think at this point I wouldn't have any plans on changing his therapy. I think checking drug concentrations, as we mentioned, might be important, to make sure that he gets the same dose and the right dose for him. Something really important, I'm not sure how old your son is, but if he's a growing boy, he's going to gain weight and get bigger over time and many of these drugs, the right dose is based on

DR. COREY SIEGEL:
your weight. So it's probably important to check those drug concentrations of Remicade, make sure that it's keeping up with his weight, so that you never get into that red area on the gas tank, going empty there. So for him, I would stay on it.

The longest duration of anybody on these drugs is probably somewhere between, you know, fifteen and twenty years, depending on if patients were on these drugs when they were being used in clinical trials. But practically speaking, most people have been on these drugs, you know, the longest that we see in practice is somewhere between ten and fifteen years.

And it's a fair question to say, well, we don't know what happens after twenty or thirty years. But as I mentioned already, I don't expect that in twenty or thirty years we're going to even be using these drugs or drugs that resemble these drugs. I hope for all of us on this call that we'll have cured Crohn's disease and ulcerative colitis by then. But for now, let's use what we have.

PAULA DORFMAN:
Our next question, "What is the best way to plan a family when you have Crohn's and are on biologic therapy?"

DR. COREY SIEGEL:
Well, thanks, another great question. I think the number one thing to think about is to get healthy. And whether you're a male or a female, the most important thing to planning a family is getting yourself well, that a sick mom or dad is of no benefit to trying to start a family. And particularly when we're thinking about women who are looking to get pregnant, we need to get you healthy before we think about the fine-tuning that we need to do on your medications.

All of the biologics we've mentioned, except possibly Tysabri, is believed to be safe and I feel confident that they're safe during pregnancy and in breastfeeding. And stopping your medications without talking to your doctor is not the right answer. If you have worries about it and there are some cases where we'll transiently stop the medications, meaning in the third trimester, we might hold the medication until the baby's born and then restart it, but that's something that you really have to carefully plan with your doctor and make sure that you're getting it right. Because the worst thing for a developing fetus and a newborn baby is a sick mom. And those are the things that we need to prevent.

PAULA DORFMAN:
Our next question, "Are you finding that patients doing vedolizumab also see further benefit from the addition of the immunomodulators as the Remicade-Humira patients have?"

DR. COREY SIEGEL:
Yeah, thank you for that really great question. This is really on the cutting edge because we're just learning this now.

DR. COREY SIEGEL:
I do think that adding a second drug to vedolizumab, which is Entyvio, is probably just as beneficial as it is with the other biologics, the other anti-TNF drugs. This somewhat remains to be proven, but you also can develop antibodies against vedolizumab, although it seems to be a little less often than some of the other biologics. We do want to prevent those antibodies from developing and we expect that the response rate will probably be higher or maybe even be longer term or more durable when you have a second drug onboard.

I'm proud to have been part of a – what I think was a really important research project that we just presented last week in Philadelphia at the American College of Gastroenterology meeting, and we had looked at all of the patients in the clinical trials who got vedolizumab or Entyvio with or without a second drug. And we looked at safety, specifically around infections. And I'm really happy to report to everybody that the infection rate was the same and very low, whether you used vedolizumab on its one or vedolizumab combined with a second drug, such as 6-mercaptopurine, azathioprine or methotrexate. So good news on that front, that you get some benefit and not necessarily any added risk.

How about some further questions?

PAULA DORFMAN:
Our next question from the webcast audience, "Are biologics safe to take if the patient is allergic to penicillin and other related antibiotics?"

DR. COREY SIEGEL:
Thanks for that question. Yes, biologics should be safe, whether you have a penicillin allergy or potentially other antibiotic allergies.

There are some questions if you develop an allergy to a biologic drug such as Remicade, would you be more prone to develop an allergy or antibodies against the other medications such as Humira, Entyvio, Cimzia or Simponi. They don't necessarily cross-react, meaning if you had an allergy to Remicade you don't necessarily have an allergy to Humira, but it does point out the fact that you're more at risk to develop allergies.

We have strategies to help prevent that. We oftentimes give something called premedications before giving it to help prevent antibodies from forming, and we also think very carefully about using a second medication like we just talked about with Entyvio, of 6-mercaptopurine, azathioprine or methotrexate, which seems to help prevent allergic reactions to the biologic drugs.

PAULA DORFMAN:
Okay, Operator, can we go ahead and take another question from the phone lines, please?

OPERATOR:
Our next question comes from Mike in Maryland. Mike, please state your question.

MIKE:
Yes, thanks for taking the call. My question is I was doing some reading and one area of concern was using these biologic medications, is that – this website said that multiple patients had been reported to develop a rare T-cell lymphoma when treated with that dual therapy, such as 6-MP and anti-TNF inhibitor. It actually mentioned that all the reported cases were actually in adolescents and young adults, and I think it even went on even further to say that it was in all boys except for one case. So I was a little confused because I believe you mentioned that it's very rare with children, but yet this thing seemed to indicate that it happened in maybe young adults, teenagers and adults.

DR. COREY SIEGEL:
Right, thanks, Mike, that's a really important question, I'm glad you brought it up. I was hoping somebody would ask about the specific subtype of lymphoma.

What Mike's talking about is something called hepatosplenic T-cell lymphoma. We call this HSTLC, hepatosplenic T-cell lymphoma. And this is a subtype of the non-Hodgkin's lymphoma that we talked about earlier. But actually an even more rare subtype than we heard.

But you're absolutely right, that it seems to affect particularly young males. And although that sounds scary because, you know, half of the patients may be male and a big subgroup of those may be young, the good news is that the frequency of occurrence is probably even less than I showed you for the standard non-Hodgkin's lymphomas earlier. You might remember that the highest number that we looked at, was out of 10,000 people, about 6 patients developed those non-Hodgkin's lymphomas.

These lymphomas are particularly occurring in people who have been on drugs specifically of 6-mercaptopurine and azathioprine, while using biologic drugs.

There's another important point here, too. Is it's not the short-term use of 6-mercaptopurine or azathioprine, it's the long-term use, meaning two years or more.

So my approach to this has been even in young males, who I think need treatment, and I might be worried about hepatosplenic T-cell lymphoma, I'm not hesitant to use 6-mercaptopurine or azathioprine, but for a short period of time, meaning one or two years.

I think the number one goal is getting everybody better, getting you off prednisone, getting you feeling better, and then once we do that you can stop the 6-mercaptopurine or azathioprine. Although I said earlier I rarely stop the biologic drugs, and that's true. But it is safe to stop 6-mercaptopurine or azathioprine when you're doing well, and then ultimately manage your patients on just the biologic drug or the biologic drug plus methotrexate.

Many IBD experts around the country and around the world are not using 6-mercaptopurine and azathioprine along with biologic drugs in young males, but using methotrexate instead, and we think that might be a safer approach.

DR. COREY SIEGEL:
So I appreciate you asking this. I hope that this clarifies the fact that it is true, but the numbers are really tiny and we can manage it by using these medications short-term. And if we don't want to use those medications even at all, we have the option of using methotrexate along with a biologic drug.

PAULA DORFMAN:
Thank you, Dr. Siegel.

Our next question from the webcast, "What do you classify as an injection site reaction? Could you please describe?"

DR. COREY SIEGEL:
Oh, sure. I'm sorry I wasn't specific about that. These typically occur with the injectable drugs like Humira, Cimzia and Simponi. And what that means is a rash or like a welt, like a big hive that you might get around the site you gave your shot, whether it's in your body or in your leg.

There're some ways to prevent that and there're some ways to treat them if they occur. Specifically, taking medications like antihistamines before taking a shot can help, putting ice on the site afterwards if it develops. Curiously, they seem to go away on their own over time and I'm not sure that any of us really understand why that happens. But if you're getting these reactions, say, with Humira, we find that over a period of time your body seems to get used to it and they seem to go away.

But they're not a reason in itself to stop using these medications. And again, if you're having that problem or worried about that you might be having that problem, you should talk to your doctor because there're typically things that you can do to make it go away or prevent them.

PAULA DORFMAN:
Thank you. Our next question, "Is it safe to take vaccinations or booster shots while on anti-TNF meds, be that flu shot, etc."

DR. COREY SIEGEL:
Yeah, fantastic question, thank you. This is the perfect time to ask the question as well since it's flu shot season coming up. It is not only safe to use vaccinations, but it is critically important to use vaccinations when you're on any immune-suppressive drugs, not just biologics, but immune modulators or prednisone as well.

The right vaccinations to get are the injectable flu vaccine, the shot. The reason that is is there's an inhaled flu vaccine that sounds appealing because you don't need a shot, but it's a live virus and that can lead to getting the flu when you're immune-suppressed with drugs like biologics or immune modulators or prednisone.

So please, everybody should be getting the flu shot, but make sure that you're getting the shot and not the inhaled version.

DR. COREY SIEGEL:
The other shot that's important is pneumococcal vaccination, also known as Pneumovax®. Although this shot typically is used for people who are older than 65, it's recommended for all patients who are getting immune-suppressive therapy, including children and adolescents. So I try to have all of my patients who are on these drugs get a pneumococcal vaccination or Pneumovax. And it's something that you get once and then you get again five years later. It's not something that you get every year.

One important vaccination that you want to avoid on biologic medications is the vaccination for shingles or zoster. You may have been offered this if you're an adult patient, but talk to your doctor and remind them that you're on an immune-suppressive drug and that zoster or shingles also is a live vaccination and not known to be safe when getting anti-TNF or any biologic medication.

With that said, we might be thinking differently about this in the future and it might be safe to get zoster or shingles vaccine in the future, but right now this is unknown and our typical recommendation is to tell our patients not to get the shingles or zoster vaccine when they're on biologics.

PAULA DORFMAN:
Thank you. Our next question, "If non-Hodgkin's lymphoma runs in the patient's family, are biologics too risky to use?"

DR. COREY SIEGEL:
Thanks, that question comes up a lot. In fact, we even added a line on this in that Crohn's decision aid video that I alluded earlier, that your doctors, if they're members of the CCFA, have access to.

Thankfully, most cancers, but specifically non-Hodgkin's lymphoma, really does not seem to run in families. There's some very rare circumstances where a number of family members have had lymphomas that certainly requires investigation. But thankfully, family history is not a very strong or worrisome component about non-Hodgkin's lymphoma. There might be a very slight increase over time and this conversation comes up a lot in the office. I typically tell my patients that I would not withhold biologic therapies in those who have a family history of non-Hodgkin's lymphoma, as long as it was one member in the family and there was really no worrisome story that went along with multiple family members. So in general, it's certainly worth a discussion with your doctor, it's probably worth a discussion with the family members who had lymphoma's doctor to make sure that they're not worried about any familial problems, but in almost all cases that wouldn't hold back doctors from using these drugs in family members.

PAULA DORFMAN:
Thank you. Operator, can we go ahead and take another question from the phone lines, please?

OPERATOR:
Our next phone question comes from Alan in Massachusetts. Alan, please state your question.

ALAN:
My question is if you're on Humira every two weeks and then suddenly you have a little flare-up and you've got to be on it every week, the doctor put you on it every week, is there any sort of increased risk of side effects, if that's like a temporary situation?

DR. COREY SIEGEL:
Thanks, Alan. That's a great question. Thankfully, all of this was looked at in all the research trials that were done to get these drugs approved. In fact, all of the drugs that we've talked about had different parts of the research study where they looked at different doses. And in fact, many times they looked at doses like you just suggested, going from Humira every two weeks to Humira every week, or Remicade, giving Remicade at a higher dose than the initial dose or giving it more frequently than every eight weeks, and Cimzia and Simponi were the same way, that they gave more frequent doses. And thankfully, there didn't really seem to be much of what we call a dose response with side effects, that if you're getting a higher dose it didn't seem to lead to any higher risk of infections or other problems.

Now with that said, when you're sick, you might need a higher dose. So in the old days, we used to think that if you got sick on a drug like Humira or Remicade, well, then it was time to stop. But now that we understand that drug levels go up and down when patients are sick, meaning when you're sick, just like your car engine, it's struggling going up a hill and it's going to use more fuel, that when you're sick and your disease is active, you might need more drug. So instead of just staying on a certain dose, we might go up to a weekly dosing of Humira or a higher dose of Remicade or Cimzia or Simponi, and then once patients get better, decrease that dose back to where we were. And with talking about the point earlier regarding drug levels and looking at drug concentrations, we can even be more elegant about that now and check the level and make sure that we're giving you enough drug, but not too much and not overdosing anybody.

PAULA DORFMAN:
Thank you very much, Dr. Siegel. We have time for one more question from the webcast audience. "What are the long-term effects from taking these types of biologic drugs?"

DR. COREY SIEGEL:
Well, thanks, that's an important and good last question. So to be fair, as mentioned earlier, the longest anybody's really been on these biologic drugs is fifteen to maybe pushing twenty years if people were receiving them in clinical trials, but really ten to fifteen years. At this point we feel really confident that the side effects that we've already reviewed on this call are the side effects that we should be thinking about out to the ten or fifteen year mark. And we haven't, thankfully, seen any new things come up as patients have now been on these drugs for a long period of time.

It would be completely unfair to say that we understand what happens after twenty or thirty years of being on these drugs. And as I've said a number of times, we'll learn more as we go forward here,

DR. COREY SIEGEL:
but I really hope that in twenty or thirty years, we're going to be treating these diseases with really different, much more elegant, much more sophisticated patient-centered and individualized therapies that are going to rely on all the great research that we're doing at the CCFA and all around the world, to understand these diseases better.

PAULA DORFMAN:
Thank you very much, Dr. Siegel, for your insightful presentation and answers to our questions.

If your questions were not answered, you can call CCFA's IBD Help Center Monday through Friday, 9 AM to 5 PM Eastern Time at 888-694-8872. The recording of today's webcast will be placed on CCFA's website next month. You will receive an update once it is available.

Upon exiting today's webcast, you will be prompted to complete a brief program survey. We ask that you please take a few moments to provide your responses, as your feedback is extremely important to us as we plan for future educational activities.

And now I'd like to talk about some additional resources that can be helpful in managing Crohn's disease and ulcerative colitis. The American Gastroenterological Association offers a helpful patient center with guides on GI procedures and information on diets and medication. To access these resources, visit www.gastro.org or the link shown on this slide.

The Crohn's & Colitis Foundation of America is also available to help. The IBD Help Center is open Monday through Friday, 9 AM to 5 PM Eastern Time at 888-694-8872, by email at info@CCFA.org, or you can chat online with an Information Specialist directly via Answer Chat. Visit www.ccfa.org for more information.

If you'd like to watch other educational websites on IBD, please visit the website on the screen to explore other IBD-related topics. You can also connect with other IBD patients and engage in discussion through the CCFA Community website, support groups, and Power of Two peer-to-peer mentor program.

Another resource, GI Buddy, is a tracking tool and mobile app that has everything you need to stay on top of managing your inflammatory bowel disease. Visit www.ccfa.org for more information.

Finally, to participate in other educational events by connecting with your local chapter, visit the CCFA website for more information. If you are looking for other ways you and loved ones can be involved with CCFA, join a local Take Steps walk or a Team Challenge event. Find out more at the websites listed.

We would like to thank AbbVie, Janssen Biotech and Takeda for their support of this program.

On behalf of the American Gastroenterological Association and the Crohn's & Colitis Foundation of America, thank you very much for joining us. Goodbye.

END