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Making the Right Choices for Patients with Ulcerative Colitis

Dr. Buch:
This is *GI Insights* on ReachMD. I'm Dr. Peter Buch, and today I'm joined by Dr. David Hudesman to discuss treatment options for ulcerative colitis, also known as UC. Dr. Hudesman is a Professor in the Department of Medicine at NYU Grossman School of Medicine and the Director of NYU Langone's Inflammatory Bowel Disease Center. Dr. Hudesman, welcome back to the program.

Dr. Hudesman:
Thanks for having me, Dr. Buch.

Dr. Buch:
So let's jump right in. With so many medication choices and so few head-to-head trials, how do we choose the correct medicine for the correct patient?

Dr. Hudesman:
Yeah, it's a great question, and it's great that we have so many different options. I tell patients we have 14 different options of advanced therapies or immunosuppressive therapies, but it's getting a little more complicated. And I think before I go through the therapies, the most important part is getting patients on therapy early, right? And if you get patients on drug early, they're much more likely to do well, not only in the short term, but long term, and then it probably doesn't matter as much which therapy you choose.

Saying that, with our different options, different modes of administrations, and different efficacy and safety profiles, the way I like to break it down is on the moderate-to-severe spectrum. If you're on the more moderate end, what does that mean? You're not extremely anemic; you don't have significant ulceration on colonoscopy; you haven't had multiple courses of prednisone; you're able to get through a day of work, or so forth. So on the more moderate end, not responding to mesalamine and having been on maybe one course of prednisone, I usually like to start with the more targeted therapies. Right? So, although all of our therapies are extremely safe—and I think it's very important to tell a patient that upfront—why not start with the ones that are the most targeted with the best safety profile?

So, for ulcerative colitis, I put them into three categories. That's vedolizumab or anti-integrin. That's our IL-12/23 or selective IL-23 inhibitors, which we now have three of, so ustekinumab, and then our three selective IL-23 inhibitors, risankizumab, guselkumab and mirikizumab, and then our S1P receptor modulators. And these are our oral agents, and this is etrasimod and ozanimod. So I think that's what I'm thinking on the more moderate end.

If the patients are more severe, if they were just hospitalized—or even not hospitalized—with significant ulceration or low albumin, they're not responding to prednisone or they're having trouble leaving their house, then they're either getting infliximab or upadacitinib.

Dr. Buch:
Perfect. And what should we know about the usage of steroids these days?

Dr. Hudesman:
So I think that the first point is we don't want patients, obviously, to stay on steroids long term, but sometimes there's a necessary evil. So I think the two most important things are, if an ulcerative colitis patient needs a steroid course, already you need to be thinking about an advanced therapy. If one of my patients gets a steroid course and then they're flaring again, they're not getting another steroid course. It's time to move on.

Number two, you need an exit strategy. So most of my patients I start on 20 milligrams twice a day of prednisone, and I'm looking to taper that off anywhere from four to eight weeks, depending on how the patient's doing and depending on how that advanced therapy

I'm starting is doing. And I'm adjusting that taper while I'm in close communication with the patient. And the last part about steroids, if anybody's on steroids for more than three months total, you really want to remember to screen for osteoporosis and osteopenia with a bone density scan.

Dr. Buch:
Great. And a follow-up question to that—under what circumstances do you think we can skip steroids altogether and go on to one of the more advanced therapies?

Dr. Hudesman:
Yeah, that's a great question. I think some of our current mechanisms of action and newer therapies—that, hopefully, will be approved in the next few years—might give us some options for steroid-sparing agents. So I think first, for ulcerative colitis, if somebody's flaring on the more moderate end, I use a lot of rectal therapy. So I use a lot of budesonide foam, and I use that as a bridge to advanced therapies rather than prednisone. If they're sicker, with our faster-acting medication—something like upadacitinib—a lot of times we might be able to taper off steroids more quickly or avoid steroids. That's an agent that's going to work extremely quickly.

Dr. Buch:
Thank you very much. So now let's head into the details. Could you share the pros and cons of the following groups, all of which you had mentioned: the anti-TNFs, anti-integrins, S1P modulators, interleukin-12/23, interleukin-23s, and JAK inhibitors? So a lot for you to do, but take your time.

Dr. Hudesman:
All right, sounds great. So let's start by going back to that moderate to severe. So we'll start on the more moderate end, and we could start with the S1P receptor modulators. So, if you look at their clinical trial data, it's very nice efficacy data. However, over 70 percent of the patients included in these trials are bio-naive. So the patients I'm really using the S1P receptor modulators are really moderate patients that are bio-naive. What are the benefits? They work well, and they're oral, right? And they're also a safe class. And I think people get concerned about all the testing you need to do before or right when you start, but these are very safe therapies.

Saying that, what are the negatives? There is some baggage to get things started. You need an EKG, right? You want them to see a dermatologist and ophthalmologist around the time of starting. You have to see what other oral medications they're on. So there's a little more testing that, as GI doctors, we're probably not used to, but I think it's a very effective therapy.

Then you have our other anti-trafficking mechanism, vedolizumab. This has been approved for ulcerative colitis since 2014, and it's a very effective agent for moderate-to-severe ulcerative colitis. Again, I think it does work best first line or early in the disease course—so a second line or third line, if they haven't had a disease for too long of a time. It's very effective and very safe.

Moving on to ustekinumab and our selective IL-23 inhibitors. So, first, to talk about this class in general, this is also an extremely safe class. It's also a very effective class. And if you look at the efficacy data and the endoscopic data, it does a very good job on the more moderate patient, but also in that moderate-to-severe range. So these medications I use not only if you're just moderate, but if you're getting closer to that more severe phenotype. Also, depending on which one you use—whether it's ustekinumab or a selective IL-23 inhibitor—with ustekinumab, there's one initial infusion. With the selective IL-23 inhibitors, there's three infusions. And then the maintenance are injections. So with ustekinumab, it's an injection once every two months, and with our selective IL-23 inhibitors, it's once a month to once every two months.

Now, which IL-23 inhibitor to choose from? Again, we have three: risankizumab, mirikizumab, and guselkumab. We don't have any head-to-head comparisons, and we don't have as much data in ulcerative colitis, but practically, what I'm doing is I'm using more and more guselkumab. And the reason is is there's a subcutaneous induction option. So, as I mentioned in this class, most of the therapies you need an initial IV infusion, whether it's one with ustekinumab or three with the selective IL-23 inhibitors. With guselkumab, you just need to do once monthly injections.

Moving now to, let's say, you're passing that moderate-to-severe and moving to that severe category. That's where anti-TNFs play. And, still a very effective therapy for ulcerative colitis, but really, when I'm talking ulcerative colitis and anti-TNFs, I'm primarily talking about infliximab. I don't think adalimumab works very well. And if you remember from the VARSITY trial, which was head-to-head vedolizumab versus adalimumab, vedolizumab outperformed it. So, when I'm talking TNF, I'm talking infliximab. I think it's a very effective therapy. It is a very safe therapy, but it does have that higher infection risk compared to 23s and vedolizumab, and has that very low risk of lymphoma.

Lastly, we have our JAK inhibitor. We have both tofacitinib and upadacitinib. Pretty much, when I'm using a JAK inhibitor, I'm almost primarily using upadacitinib, and we have some real world data showing that that outperforms tofa. And just in our clinical practice, we

think that works better. And I think this is a very effective agent as well. It's a pill. It heals very well. It works quickly. There is an increased risk of infection, so you do need to vaccinate for shingles especially—that's very important. And then there's this baggage around the cardiac risk.

Dr. Buch:
Very good. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. David Hudesman, about ulcerative colitis care.

So, Dr. Hudesman, what should we know about rescue therapies in ulcerative colitis?

Dr. Hudesman:
So, when we say rescue therapy, what that means to me is somebody is flaring; they're sick. Right? What can we do to get them out of this acute flare, right? And we touched on prednisone a little bit earlier, but here, we're sort of moving past that. And again, this is where infliximab and upadacitinib play. And I think in these scenarios, with how quick you could get somebody an oral pill, I'm using upadacitinib more and more in these patients. So it could be steroid-sparing. It's oral. It works well in the more moderate patient. It also works well in the more severe patient that fail multiple medications and does a great job healing. So, when I hear rescue therapies, I'm thinking upadacitinib or infliximab.

Now, we might have had patients that have been on a TNF or been exposed to a JAK, so in those situations, we have to start thinking a little bit more outside the box, and where the field is moving is with combination therapies. And from combination TNF and thiopurine, now we're talking about combining two different biologics, or a biologic and a small molecule. And really, what that looks like most of the time is, you use a baseline safe therapy—and all of our therapies are safe—but a baseline therapy of vedolizumab or 12/23 or 23 inhibitor, and combine that with upadacitinib or infliximab. And we should have some data released, hopefully by mid-to-end of 2026, on a larger phase 2 program that could give us more insight on how these patients do with combination therapy.

Dr. Buch:
Looking forward to that. So, when treating patients with ulcerative colitis, how do you assess when it's time for surgery as opposed to going to the next medication?

Dr. Hudesman:
Great question. And I think this is one of the more difficult parts about managing inflammatory bowel disease and ulcerative colitis. So I think, first, there's never a wrong time to discuss it, right? There's obviously the acute indication. So if somebody is severe in the hospital, losing weight, having fevers, and you're worried about toxic megacolon, there's not really a choice. You're talking about surgery. If you have somebody that's exsanguinating, you're talking about surgery. If you have somebody with high-grade dysplasia or cancer that's not resectable, you're talking about surgery.

But that's a minority of our patients, which is a good thing. So what about the rest? And I think this is something where you need to build that doctor-patient relationship and see where your patient's coming from. I have some patients that are like, "Doc, I don't want a surgery. Keep giving me whatever. Combine whatever you want. We want to avoid it." But then there's others that are sick of feeling well for six to nine months, then feeling sick for six months, and being in this constant cycle. So if I have a patient now on the third therapy—and usually, that's my cutoff; you can do sooner, you can do later; again, there's not a right time point—but usually, in my practice, by that third therapy, I introduce the idea. That's not to say that's what we're doing next, it's just to get a better understanding about how patients feel about it.

Dr. Buch:
So how many therapies can you go through?

Dr. Hudesman:
If you go by class, I would put our anti-trafficking in one class, so that's our S1Ps and vedos. That's class one. You have our 23s and 12/23s as class two. You have TNFs, class three, and JAKs, class four. So you have four classes. You could combine different classes. And then we have some therapies that are not FDA approved. We use it less and less commonly now at NYU because of upadacitinib, but I still have patients that come in that we give IV cyclosporine to as an inpatient and then transition them. We could use something like Prograf as an outpatient as an induction agent. So we have these other options that we're doing less and less commonly. So we have plenty of options, and we could combine, but we also want to be thoughtful while we're doing this. I will also tell a patient at a certain point, this isn't making sense. Right? We're not getting that patient better.

And just one last point on this—I also think, yes, I mentioned how quickly some of these agents could work, but also, we want to be thoughtful, right? So we want to give that specific agent enough time, whether we optimize the dose, give it more frequently, or give a

higher dose of a JAK inhibitor longer before giving up on that class and moving on to the next class.

Dr. Buch:
We're in the last few minutes of our conversation. And do you have any additional thoughts that you'd like to share with our audience today?

Dr. Hudesman:
I want to come back to what I said originally, that the most important thing is to treat early. And if you get patients on the advanced therapy early, they're much more likely to do well not only in the short term, but have great long-term outcomes. I think the difficult part with ulcerative colitis is how do you define that right patient? It's very easy if somebody's coming into the office, going 10, 15 times a day, is extremely sick, and can't go to work. That's a no-brainer. But what about those patients in between? So things that I think about are, do I need to get this patient onto an advanced therapy early, even if they don't look so sick in my office? Are they anemic? Does the colonoscopy have significant ulceration? Have they been on multiple courses of steroids? Are they not making it to work or school? Any of those four things I'm talking about advanced therapy soon and not doing a course of prednisone on the side.

Dr. Buch:
Dr. Hudesman, we always learn so much from you. Thanks so very much for sharing this wonderful, important information.

Dr. Hudesman:
Thanks so much for having me.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit *GI Insights* on ReachMD.com, where it can Be Part of the Knowledge. Thanks for listening, and looking forward to learning with you again very soon.