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Inflammatory Bowel Disease Management: Choosing the Right Therapy

Dr. Buch:
There are so many treatment options for inflammatory bowel disease, but with few head-to-head trials available, which is the best medication for my patient? Welcome to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and today we're joined by returning guest, Dr. David Hudesman, who will explore this topic. He's a Professor of Medicine at NYU Grossman School of Medicine and Director of NYU Langone Inflammatory Bowel Disease Center. Welcome back to the program, Dr. Hudesman.

Dr. Hudesman:
Thanks so much. Happy to be here.

Dr. Buch:
So, Dr. Hudesman, let's get right to the heart of the matter. Without adequate comparative studies, how do you make medication decisions?

Dr. Hudesman:
So first, I think this is a great time for patients because we have so many more different therapeutic options now than we had just five or six years ago, and each year, more therapies are coming out with newer mechanisms of action. Saying that, what's difficult is, how do you pick the right therapy for the right patient? And unfortunately, even though there's a ton of research being done—including what we're doing at NYU, trying to find some type of biomarker or companion diagnostic that could say with this therapy you're 90 percent likely to respond and with this therapy you're only 20 percent—we're just not there yet. So it's really combining the head-to-head trials we do have, which is one in ulcerative colitis and two in Crohn's and some comparative effectiveness trials, and then just our experience and real world evidence. And then, of course, talking to the patient and having that shared decision-making discussion.

Dr. Buch:
So when assessing for onset of action in Crohn's disease, which medications are the fastest acting?

Dr. Hudesman:
This is an important question when selecting therapies. How active are your patients? And some of our therapies now work very quickly where we can minimize steroids or even maybe avoid steroid use. I still think for Crohn's and with ulcerative colitis, our fasting-acting medications are infliximab and upadacitinib, so our anti-TNF infusion and our selective JAK1 inhibitor work very quickly. Within a week, you could see response with both. Also, there's always delayed responders—so patients who could take a month or two for them to respond—but as early as less than a week, you could see response with both infliximab and upadacitinib.

Dr. Buch:
And when considering serious risk of infections in Crohn's disease, which medications are the safest?

Dr. Hudesman:
So first, when you're talking about infections and other risks, there's risks of the medication, and then there's risks of not putting patients on appropriate therapy—so risks of the disease. So if you look just at the data from these large-scale clinical trials and other evidence, the higher rates of infection and the higher rates of serious adverse events are more so with ongoing inflammation than they are with actual medical therapy. So number one, you want to pick the therapy that's going to work for your patient. Now, let's say you have a handful of different options that you think are going to be efficacious. The more targeted therapies tend to have the lower infectious side effects.

Before I go into those therapies, though, I do want to emphasize the fact that when I speak to my patients, I start by saying, "All of our therapies are safe." I'm not going to talk about any therapy that's not safe. There are some that have more potential side effects than others, but these are also very small risk and very safe therapies.

Now, saying that, our most targeted therapies are vedolizumab or anti-integrin, and then our anti-IL-12/23 ustekinumab and our selective IL-23 inhibitors, which now include risankizumab, mirikizumab, and guselkumab. So in my mind, those therapies are most targeted and have the lowest infection risks.

Dr. Buch:
Now, how does disease location in Crohn's disease affect the choice of medications?

Dr. Hudesman:
So we're going to be seeing more data on this in the next few years. I think we're going to be treating Crohn's colitis more like ulcerative colitis. So what I'm saying is that small bowel Crohn's is a different beast than colonic Crohn's, and colonic Crohn's is probably more similar to ulcerative colitis. Again, if we're talking about routine moderate to severe disease, I don't think it matters significantly whether it's Crohn's colitis or Crohn's ileitis. However, if you have these deep small bowel ulcerations, if you start having penetrating or stricturing complications, that's when I'm going to lean towards an anti-TNF like infliximab or upadacitinib or start talking about surgery. So that's when I'm getting a little more concerned. Those are the more high-risk patients—those deep ileal ulceration patients.

Dr. Buch:
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 choosing the best medicine for our IBD patients.

So, if we continue with the Crohn's theme, Dr. Hudesman, what are your first-line choices in biologic-naive moderate to severe illness patients?

Dr. Hudesman:
So the way I look at this, in my bio-naive patients, without extraintestinal manifestations and without complications, I think all of our current therapies have a good chance of working. And if you actually look at the data, it's really timing of starting therapy, right? So, if you start a patient on appropriate therapy within a year or two after diagnosis, you're much more likely to have higher response and higher remission rates, than if you wait three years, five years, 10 years and cycle through steroids. Saying that, since all of our therapies would work in this situation, usually I talk about what are the most targeted to minimize risk, and then what's the most convenient for the patient. And then we talk about other factors that might be important to patients: their lifestyle, their job, and so forth. So usually, in my moderate to severe patient without complications, I'm starting now either ustekinumab or selective IL-23 inhibitor.

Dr. Buch:
And how do your recommendations differ for ulcerative colitis patients?

Dr. Hudesman:
So for ulcerative colitis, same concept. If you're on the more moderate end of the moderate-to-severe spectrum, I think all the FDA-approved therapies will work, so it's really talking with the patient and minimizing risk and choosing what's most convenient. So I think selective IL-23 inhibitors and ustekinumab are great options, and I use them a lot first-line. I think vedolizumab is a great first-line option. I do use it. Just to go back to Crohn's and Crohn's colitis, I don't use it as much in small bowel Crohn's, but for ulcerative colitis, I would use a lot of vedolizumab. And then I think this is where the S1P receptor modulator, such as ozanimod and etrasimod play as well. So, for ulcerative colitis, S1P receptor modulators, vedolizumab and IL-12/23, and selective IL-23 inhibitors first-line. For Crohn's disease, I'm mainly using the selective IL-23 inhibitors—also some ustekinumab—and if it's Crohn's colitis, I'll use some vedolizumab as well.

Dr. Buch:
Now, Dr. Hudesman, we're almost at the end of our discussion, so are there any other insights you would like to share?

Dr. Hudesman:
So even though we have multiple therapeutic options right now, it's important that we set a target. So before starting somebody on therapy, what is that target going to be? Is it going to be healing? Is this somebody that we think we could achieve that goal? And then we need to monitor them. So we're monitoring them not only based on symptoms but based on biomarkers, such as CRP or fecal calprotectin. We do intestinal ultrasound. That's another nice way. And we repeat a colonoscopy. And even though we have many different therapies, I still try to optimize therapies as best as we can before switching to something else.

And then I just want to highlight one study—we talked about first-line therapies, but for second-line therapies, there was a study relatively recently published called the SEQUENCE, which was our most recent head-to-head trial showing how risankizumab, one of our

selective IL-23 inhibitors, outperformed ustekinumab IL-12/23 inhibitor when you're using the second line after an anti-TNF. So we are starting to get some more data on how to position therapies but not only first line but second and third line.

Dr. Buch:
What great insights on choosing medicines in IBD. I want to thank my guest, Dr. David Hudesman, for joining us to share his important insights on inflammatory bowel disease. Dr. Hudesman, it was a pleasure speaking with you today.

Dr. Hudesman:
Great speaking with you as well. Thanks so much.

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 you can Be Part of the Knowledge. Thanks for listening, and looking forward to learning with you next time.