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IBD Immunopathogenesis: Do You Know What You're Blocking?

### Announcer:

Welcome to CE on ReachMD. This activity is provided by Prova Education and is part of our MinuteCE curriculum.

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### Ms. Orleck:

IBD is not a simple one-pathway disorder. It is fueled by parallel disruptions in genetics, immune regulation, barrier function, and microbial ecosystems, further complicated by the individual's environment and epigenome.

I'm Kim Orleck, physician assistant practicing out of Atlanta, Georgia, and this is CE on ReachMD.

### Ms. Hodnick:

And I'm Brooke Hodnick. I'm a practicing physician assistant in North Texas with GI Alliance.

With our growing number of treatment options, we now have both small molecules and biologics. Biologics are bulky proteins that have a risk of immunogenicity and are administered via subcutaneous or IV versus the small molecules, which are small oral therapies absorbed in the GI tract without immunogenicity.

Kim and I are now going to describe the current treatment classes and share some tips with each. Kim, where do you want to start?

### Ms. Orleck:

I think it makes sense, Brooke, let's start with the anti-TNFs. We've had these the longest. And as we think about how these work, the anti-TNF agents target and neutralize a pro-inflammatory cytokine, TNF, or tumor necrosis factor alpha, which is critical for amplifying immune responses and recruiting inflammatory cells to the intestinal tissue.

Brooke, again, we've used these the longest. Where do you kind of see these fitting? Any pro tips you can share?

### Ms. Hodnick:

Yeah, Kim, I still go to my TNF inhibitors when treating fistulizing or perianal Crohn's disease. I also really think of these with the acute, severe ulcerative colitis patients as well. I think we need to remind ourselves that we can have these administered via IV or subcutaneous. We also do worry about possible immunogenicity with this class as well.

### Ms. Orleck:

I agree with all those tips, Brooke. The other thing I want to add is we still turn to these a lot for our extraintestinal manifestations,

particularly the skin, but also the joints, but otherwise, totally agree.

I'm going to move next to our anti-IL-12/23s, remembering that these block the shared p40 subunit of IL-12 but also IL-23, both of which are cytokines central to mucosal inflammation. Brooke, thoughts? I know we're going to get into this. The landscape has changed with interleukins, but any big tips with IL-12/23s?

**Ms. Hodnick:**

Kim, this class has shown to have some long-term data on both safety and persistence. I think you kind of alluded there are now some head-to-head trials between the IL-23s and the IL-12/23s showing better outcomes with the IL-23s.

**Ms. Orleck:**

And maybe we'll wait and then really focus on the IL-23s. Which, again, just to hone in on the difference, these IL-23 agents target only the p19 subunit of IL-23, a cytokine implicated in Th17 cell differentiation and chronic intestinal inflammation. But again, they don't target that IL-12

So, Brooke, I think it's a really great point that you alluded to, that we have these head-to-heads now with IL-23s over IL-12/23s. So as we talk about these IL-23s, kind of what sort of tips would you give to our listeners?

**Ms. Hodnick:**

Kim, I constantly remind myself these can be used as a first-line therapy, but I also really think of them when I have more skin involvement. They are also approved for plaque psoriasis and psoriatic arthritis. There is also an option for a subcutaneous or IV induction available with one of these medications as well.

**Ms. Orleck:**

Yeah, great tips. And as you said, I think this class really has the option where we can use them in naïve patients, but we also have really good data, as you mentioned, in our exposed patient population.

Next one—our anti-integrin therapies. So these work to inhibit leukocytes from migrating from the bloodstream into the intestinal mucosa, so they actually reduce inflammation in the gut by directly targeting the integrins. Thoughts here?

**Ms. Hodnick:**

Kim, they're tremendously safe because they're gut-specific only, right? They don't have any other indications other than ulcerative colitis and Crohn's disease. So because they're so gut-specific, that also means that there is no effect on any of the extraintestinal manifestations. When I use them in my Crohn's patients, I really think more utilization of them in the inflammatory phenotype. We also remind ourselves that they have some great ulcerative colitis data as first-line therapy.

**Ms. Orleck:**

Totally agree. Brooke, you did such a good job in the beginning, really separating for us biologics versus small molecules. So as we lead into our small molecules, the first one being our JAK inhibitors. So these work by inhibiting intracellular signaling for multiple cytokines, therefore providing a broader anti-inflammatory effect. We know that these are approved as a class in both ulcerative colitis and Crohn's—one of our JAK inhibitors having coverage for both and one limited to ulcerative colitis.

Aside from that, what are kind of your tips for using these JAK inhibitors in IBD?

**Ms. Hodnick:**

Kim, thank you for mentioning that we can use these in both ulcerative colitis and Crohn's disease. I think that's important. They have a fast onset of action and great coverage for extraintestinal manifestations, especially in the rheumatological area. So I think of those patients who are very sick and I maybe need that quick onset of action or maybe some joint involvement. I think it's really key to remind ourselves that it's contraindicated in pregnancy, but that doesn't mean that we cannot use these medications in childbearing age.

**Ms. Orleck:**

I love that tip, because I see so often that everybody avoids the JAKs just because it's a young female. So I think it's so important, right? We know this—that we need to get the patient in remission before pregnancy, and if we have to use a JAK to get them there and then

transition, we don't want to take the JAK off the table there. So thank you for that.

And then our last class, our last molecule—our S1Ps. So these target the S1P receptor modulators. So by selectively binding to S1P receptors on the lymphocytes, they actually keep the lymphocytes within the lymph node, so they don't allow them to migrate to areas of inflammation, in this case, the intestine. Tips for these S1Ps?

**Ms. Hodnick:**

Again, another great oral option. They are a small molecule. We use them only in ulcerative colitis patients, and to remind ourselves that we can use these in first line, second line, third line, but they really have been shown to help more in the patients who are naive to advanced therapies. They are also contraindicated in pregnancy for females.

**Ms. Orleck:**

Thanks for that, Brooke. I really appreciate it. And then just a reminder that one of the S1Ps, we do have coverage in MS, and then one of them, we have some data for our proctitis patients.

Well, Brooke, it's always great having a conversation with you, even a bite-size discussion. So I hope, listeners, you found this information useful, and thank you for tuning in.

**Announcer:**

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