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Navigating the Therapeutic Landscape for IBD

Dr. Buch:
The treatment landscape for inflammatory bowel disease, or IBD, has rapidly grown with the development of new therapeutics, but there are still many questions to be answered.

Welcome to *GI Insights* on ReachMD. I'm your host, Dr. Peter Buch. Joining us today to take a look at current and emerging medication is Dr. Aline Charabaty. Dr. Charabaty is Clinical Director of Gastroenterology, Sibley Memorial Hospital, and Director of the Inflammatory Bowel Disease Center at Sibley. She's also Assistant Professor of Medicine at Johns Hopkins.

Welcome to the program, Dr. Charabaty.

Dr. Charabaty:
Thank you, Dr. Buch. Thank you for having me today.

Dr. Buch:
So, Aline, let's start out with anti-TNFs. Since there have been so very few comparative side-by-side studies, how can we possibly compare effectiveness?

Dr. Charabaty:
Well, Pete, you bring out a great point. However, I'd like to start by saying that anti-TNF have really changed how we treat moderate to severe inflammatory bowel disease. Before these drugs were available, all we had were nonspecific immunosuppressive therapies, like steroid and thiopurine, will have many potential side effects and/or surgery. Many patients had to undergo multiple surgery in Crohn's disease or colectomy in ulcerative colitis. So, with anti-TNF, we really started targeting pathway involved in the pathogenesis of IBD, and we have therapies that now can achieve not only clinical remission but also endoscopic healing and fistula closure in Crohn's disease. So these therapies really have changed how we approach the treatment of IBD, and they have been very effective in treating both Crohn's and ulcerative colitis and treating extraintestinal manifestation of IBD. But you're correct. We don't have comparative trials between different anti-TNF to really draw a firm conclusion which one is more effective than the other. But in general, the approach has been that infliximab is truly the first choice to treat acute severe UC, hospitalized patients with severe UC, and also have been the first choice for perianal Crohn's disease as well for patient with severe extensive and very symptomatic disease.

Dr. Buch:
Thank you. And moving on to this very important topic, are you concerned at all about biosimilars?

Dr. Charabaty:
So, to be honest initially, both physicians, clinicians, patients were really concerned about biosimilars. But at this point, Pete, we have really solid data showing that biosimilar are truly similar to the original product in terms of inducing and maintaining remission and in terms of safety.

What we do not know is what happens if a patient undergoes multiple switches, you know, whether because the patient's insurance decide to approve one biosimilar one year and another one the next year or whether the patient changed insurance and that new insurance favors a different biosimilar to the one that the patient was originally on. So this data we don't know, and hopefully, we will have real-world data as we follow closely our patients who are now being switched to a biosimilar.

Dr. Buch:
Thank you for that clarification. And now let's discuss some of the newer medications. Where does risankizumab fit in the treatment

algorithm of Crohn's disease?

Dr. Charabaty:
So we are all very excited about risankizumab. It's the first anti-IL-23 antibody type of biologic that has been approved for Crohn's disease. And the reason we're excited about it is that it's really very effective in terms of inducing and maintaining clinical remission and endoscopic healing and in both patients who are bio-naïve, and also patients who have been exposed to anti-TNF. It also has a very good safety profile and can treat potentially associated conditions that are present in the patient. So, if your patient has Crohn's disease but also psoriasis or psoriatic arthritis, we have now a drug available to us that can treat both conditions.
So, in reality, probably what we're going to do is first use risa as a second-line therapy. Right? So, typically, when a new drug comes to the market, we are using it in patients who have lost response or have not responded to other effective therapy, but hopefully, with time, we'll be able to use it as a first-line in patients with luminal Crohn's disease that requires a biologic.

Dr. Buch:
Is there any data yet to show that it is appropriate as a first-line therapy?

Dr. Charabaty:
So the randomized controlled trials show that it's effective as a first-line, and it's also effective in people who have been exposed to anti-TNF, and it is approved for use in bio-naive as well as in patients with prior exposure to biologics.

Dr. Buch:
Thank you. For those just tuning in, you're listening to *GI Insights* on ReachMD. I'm Dr. Peter Buch, and I'm speaking with Dr. Aline Charabaty about medication placement in inflammatory bowel disease.

So, Aline, where does ozanimod fit in the treatment of ulcerative colitis?

Dr. Charabaty:
So, with ozanimod, the exciting thing about ozanimod is that it's convenient. It's a pill, and however, the randomized controlled trials show that it's mainly mostly effective actually in patients who have not been on a biologic therapy. So the way I see it is really as an excellent option in patient with mild to moderate UC who have not responded to mesalamine or who have a reaction to mesalamine but also in patient with moderate to severe UC who have not yet been on a biologic, so I would use it before using biologic. It's a great option for people with UC who have mainly luminal ulcerative colitis.

It's important though to remember that this is a drug that is not approved in pregnancy. And it's also important to screen patient for arrhythmia of the heart, so severe bradycardia that are not controlled with a pacemaker, and for recent cardiovascular events.

Dr. Buch:
Thank you so much. And continuing this theme, where does upadacitinib fit in the treatment of ulcerative colitis?

Dr. Charabaty:
So upa has a different story. So it's a JAK inhibitor, and JAK inhibitors at this point are approved after anti-TNF. So, if your patient have lost response or did not respond to anti-TNF, then this patient with ulcerative colitis could be a candidate for upa. The advantage of upa is that it's a pill, so it's convenient for patient. It also act very quickly, and it's been shown to be very effective in patients with moderate to severe UC who have not responded or lost response to anti-TNF.

The few things about upa is that it's important to provide patients with the shingle vaccine. JAK inhibitor have been associated with a higher risk of shingles. And this is a vaccine with two dose. The patient does not have to complete both doses before starting upa.

The other thing to do with JAK inhibitors, we have data with tofacitinib, which is another JAK inhibitor, where there is an increased risk of cardiovascular event and thromboembolic event in patient using tofa, for rheumatoid arthritis and who are above age 50 and with an additional risk factor for a thromboembolic event. So in this particular patient population, there was a higher risk of cardiovascular and thromboembolic event. We don't see this in the randomized controlled trial of using JAK inhibitor in patients with UC, but it's, I think, important at this point to be cautious, so screen your patient for potential cardiovascular risk factor or VTE factor. So it's important to screen patient for these potential factor because these might be a contraindication to using upa. On the other hand, upa has the advantage of also being effective for psoriatic arthritis, rheumatoid arthritis and ankylosing spondylitis, so that might be a good choice for patient with UC and these associated condition.

Dr. Buch:
That's great. Shifting focus for a moment, which patients with IBD should receive anticoagulation?

Dr. Charabaty:

Pete, I am so happy you are addressing this question because this is often an overlooked issue in particular in patients being admitted with an IBD flare. So it's important to remember that patients with IBD who have active disease are actually in a hypercoagulable state, and their risk of a venous thrombotic event is increased by two-fold compared to the general population, and they are also at increased risk of arterial thrombotic event. And it's important also to remember that anticoagulation does not increase the risk of GI bleeding in patients with IBD. So often there's a reluctance in patients with active disease who are bleeding to start them on anticoagulation because we're concerned that that might induce more bleeding, and the reality is that this is not the case. So, at this point, absolutely any patient with active IBD being admitted to the hospital needs to be on anticoagulation. Any patient with IBD admitted for IBD-related surgery, a colectomy, a stricture resection, etc., should get anticoagulation. And, actually, a recent consensus recommend anticoagulation for patients with IBD admitted for any reason, even for non-IBD-related reason. And what we favor are low molecular weight heparin or fondaparinux over the low-dose unfractionated heparin.

The question that is still being debated is whether or not patients with IBD benefit from anticoagulation after being discharged from the hospital, and if so, for how long. So, at this point, the consensus is maybe to extend anticoagulation after discharge from the hospital in patients with IBD who also have additional risk factor for thromboembolic event and extend that for up to six to eight weeks.

Dr. Buch:
Really appreciate that insight. So, before we conclude, are there any other thoughts you would like to share with our audience?

Dr. Charabaty:
Well, one, I'm very excited to be here and very excited that people are listening to us. The key points here are: use the therapy that you think is most effective for your patient based on the disease activity, the disease severity, the presence or absence of extraintestinal manifestation whether or not there are comorbidities that can preclude certain therapies or associated condition that can actually benefit also from the specific therapy that you're using. The key is really to start treatment early in patient with moderate to severe inflammatory bowel disease to really avoid recurrent use of steroids. It's very important to control the disease quickly in order to put the patient in clinical remission, prevent further flare, prevent disability, prevent hospitalization, needing for surgery and needing for recurrent steroid use and, like you mentioned, Pete, putting the patient at higher risk of thromboembolic events.

As we are moving forward in the field of IBD, hopefully we can really have objective criteria on how to position different therapies and how to choose the right therapy for the right patient. And always, always don't forget to ask the patient what are their preferences, what are their life events that they're planning. Are they planning trips, traveling, going to college, going abroad, starting a family? This will also affect the choice of therapy.

So it's always important to really have this discussion with the patient and achieve a shared decision.

Dr. Buch:
This was a really great discussion on therapeutic challenges in inflammatory bowel disease. I want to thank my guest, Dr. Aline Charabaty, for sharing insights on the treatment landscape. Thanks for a great discussion.

Dr. Charabaty:
Thank you for having me, Pete.

Dr. Buch:
For ReachMD, I'm Dr. Peter Buch. To access this and other episodes in this series, visit ReachMD.com/GIInsights where you can be Part of the Knowledge. Thanks for listening, and see you next time.