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Decision Point IBD: Debating the Factors That Influence Patient-Centric Treatment

Announcer:
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Dr. Mahadevan:
Okay, um, so at this point, we're going to do a Clinical Countdown where we're going to go over some cases and, um, put into practice what we learned. So, Fernando -

Dr. Velayos:
We only have a certain amount of time to answer.

Dr. Mahadevan:
Yes, we only have a minute and 30 seconds.

Dr. Velayos:
We've been - Yes.

Dr. Mahadevan:
So, Fernando, the first case is for you. A 29-year-old woman with moderate to severe non-obstructive disease limited to the ileum and some arthralgias. What would you offer her?

Dr. Velayos:
Alright, so here what you have is I think you have, uh, it's important this this looks to be kind of a new diagnosis, or tends to be some extraintestinal manifestations. Um, and so we had talked about before that, you know, the TNFs do have a nice, uh, uh, um,

indication for, um, ankylosing spondylitis, rheumatoid arthritis, and so there, um, it's always important to, you know, if you can, with one therapy, address multiple symptoms, that's always preferable. Ustekinumab has an indication for psoriatic arthritis. There doesn't seem to be any indication that that's what the diagnosis is here. You have to remember that there's a certain amount of extraintestinal manifestations, arthritis and arthralgias, that are driven by bowel disease. But of course we never quite know, um, how much of that is its own independent, um, manifestation as opposed to driven exclusively by bowel disease. Um, vedolizumab, its got selective, and so, um, the thought is that, you know, it doesn't have an independent effect on, um, extraintestinal manifestations, but definitely would, um, in the sense that if it controls bowel inflammation, it could probably improve the arthritis. Surgical resection is very intriguing. Uh, there was a Liric trial that did seem to show that at least at one year, an improvement in terms of quality of life and need for anti-TNF. Um, but I think in this case it's something that's a possibility, but I don't think it's ready for primetime just yet.

Dr. Mahadevan:
Okay. Um, great. So I – I would agree. I think in this patient who has no other, um, medical issues with moderate to severe Crohn's and some arthralgias, this is a person I would probably go to anti-TNFs first because, um, it has the best data for joint pain, and we don't fully understand her joint pain. Maybe if I did, um, imaging, and the joint pain was not back or sacroiliac, in that patient, any of the other therapies would – would be fine, as well, but if I did know she had ankylosing spondylitis, sacroiliitis, or really significant joint pain, I think the TNF would be the best choice here.

Dr. Mahadevan:
Okay. So a 50-year-old man with nonspecific left-sided abdominal pain improves with bowel movement, um, occasional blood on the toilet paper, and a colonoscopy shows very mild ileitis. He denies nonsteroidal anti-inflammatory use. What would you offer him?

Dr. Velayos:
Believe it or not, this is something that actually occurs not infrequently in just routine practice. Um, and this is, um, I'm not going to call this asymptomatic ileitis, but at the same time it's highly unlikely that the patient's symptoms have anything to do with the endoscopic findings. Um, and so this patient, um, the first thing is, you know, do we call this Crohn's or not to kind of help guide the therapy. But more importantly, even if this were Crohn's, what do we know about the natural history? And here is some more where the, uh, American College of Gastroenterology's most recent guidelines would say, you know, this is probably somewhat asymptomatic or a version of asymptomatic or incidentally discovered ileitis. Um, as long as there's not, you know, prior nonsteroidal use, this is a patient probably can be followed. As a matter of fact, the most recent guidelines suggest that even diet therapy is a possibility. Um, the symptoms seem quite mild. Now, the patients who have an elevated CRP, that's something different. So I would say here that mesalamine has not shown any evidence. Ileal-released budesonide I will probably use just to kind of deal with these erosions, but again that's a short-term therapy, so we're not really using that for the long-term. But I think at this point, uh, without symptoms and very mild disease, and what we think is a very mild prognosis, we definitely don't need biologic therapy. So this is kind of the other extreme where for a small select patients, it's okay to follow them and not be significantly aggressive. But I would still do treat-to-target here. So our treatment is nothing, and our target is essentially lack of progression. And so, uh, you know there's debate, but I would rescope this patient in a year.

Dr. Mahadevan:
Okay. So I would agree. I think this is something that we see sometimes when you're doing a screening colonoscopy on a 50-year-old and you tip into the ileum and you see some inflammation. And in this case, his symptoms absolutely don't match. I think this person needs to go on a high-fiber diet and, uh, do some, uh, lifestyle modification, and that would be the best thing. However, because he does have some ileitis, if there was chronicity on the biopsy, by the guidelines, I would give him budesonide for eight weeks. If that completely improved his symptoms, you'd have to think about whether, uh – and you stop it and his symptoms come back, whether you need to step up therapy, but it's highly unlikely that his left-sided symptoms match at all with that very mild ileal inflammation.

Dr. Velayos:
Alright, so moving on to ulcerative colitis. This is a 45-year-old woman with pancolonic disease for 10 years and reports feeding –

feeling well taking mesalamine 2.4 grams a day, and has three to five bowel movements per day with some urgency, some bleeding, fecal calprotectin has been elevated, did two colonoscopies during that time point that show friability, erosions, kind of a Mayo subscore 2. Um, what would you recommend? You know, kind of active symptoms despite being on mesalamine.

Dr. Mahadevan:
So, so this, um – so in this situation, she still has moderate disease. She has three to five bowel movements per day, so I would do – I would increase to 4.8 grams of mesalamine because that would be the easiest thing to do. I would repeat a flexible sigmoidoscopy at eight weeks, and if she still has active disease at that point, I would offer her biologic therapy. Um, in somebody who says she's feeling absolutely fine, and we all have these patients, she feels fine but her endoscopy shows disease, uh, in that patient, you're going to have a hard time convincing them to go to a biologic, but the argument is that this is going to increase your risk of having a complication down the line, whether it's a severe flare or whether it's an increased risk of dysplasia and cancer. So, uh, she will likely agree to 4.8 grams because that's not really changing the type of therapy, but if that's ineffective, I would strongly recommend biologic therapy in this patient.

Dr. Velayos:
I think this is where the – the beauty of kind of treat-to-target really comes out in that, um, you know, the fact is that this patient very well may be a biologic or small molecule therapy or, you know, some escalation of therapy in the future. Um, but you know, there – you haven't proven that an increase in mesalamine wouldn't work, but the point is that it – even if you decide that's your next, um, decision, um, the fact is that you're talking to the patient. You're saying this is what we need to see on this next treatment. We are going to reassess at a certain period of time. And if not, then we're going to change you to another therapy. So it really helps to map things out, uh, for yourself and for the patient. Um, and so the fact is that when I think about treat-to-target, like I said, it's kind of treatment agnostic. And it's okay, even if this patient goes on a biologic in the future or even flares, um, if after discussing you feel like that's the next best therapy, that's okay. Um, you don't necessarily need to go to the endpoint, um, as long as you're reassessing. Now, clearly she has active symptoms so with her I would say that timeframe is shortened for reassessing, but I think that's the beauty of the kind of a treat-to-target strategy.

Dr. Mahadevan:
Okay. So the next case is a 25-year-old man with severe ulcerative colitis, hospitalized. He has been in remission on mesalamine therapy for two years, but was noncompliant and is currently flaring after returning from Burning Man. How would you manage his therapy? And what would be the diagnostic and therapeutic steps?

Dr. Velayos:
So for the hospitalized patient, um, I'd say probably over the last 10 years, there's been a kind of a nonproven, but uh, a certain algorithmic approach which kind of the peak principles are, uh, day one of admission they're essentially preparing the patient. You know, this patient is admitted, uh, on I.V. steroids, um, you're going to make that first kind of decision about three to five days after admission, which at that point you are going to decide if they responded to I.V. steroids or not, whether they need a biologic or not. This patient has never been on a biologic before. Um, and then in terms of the testing, preparing for that timepoint, getting a PPD on admission, getting hepatitis serologies, um, getting a flexible sigmoidoscopy, getting stool tests. And then after that first colonoscopy, that flex sig you can assess severity along with the symptoms. Um, critical here then is, um, three to five days you're going to start, uh, typically an anti-TNF if they have refractory disease, reassess them about five to seven days after, and decide whether to continue or go to surgery. Um, here I would say that the hospital-specific recommendations in addition that we don't often think about is avoiding narcotics, which can complicate the situation and can precipitate toxic megacolon, as well as, uh, thromboembolic prophylaxis. And the treat-to-target measures again not really shown, but we do know that a reduction at – getting a CRP on admission and following it over time, if you can see a reduction after starting the anti-TNF or the steroids, that tends to be a very favorable prognostic factor, and the, um, that's how I would go.

Dr. Mahadevan:
Okay, yeah, so to summarize, so diagnostic steps: He comes in the hospital, stool studies, rule out infection, flexible sigmoidoscopy

to determine severity of disease. Most likely this patient's going to get a CT enterography and, as Fernando said, the therapeutic steps if there's no infection, intervene with steroids, um, uh, place a PPD on day three – if by day three you've read your PPD, you would start the biologic. If he had a complete response to the I.V. steroids, you would consider seeing if he can transition to oral and go back to being compliant on mesalamine, but that's pretty rare that that can happen. And then hospital-specific recommendations, DVT prophylaxis is extremely important. Um, every patient with ulcerative colitis needs DVT prophylaxis. Even if they're bleeding, it does not increase bleeding. And that's something that you have to educate the hospitalists about. Uh, and then, um, also in terms of what's your target, if his CRP goes down in the hospital, if he's feeling better, great. But I think this is somebody who is going to need to go onto a biologic, and then at eight weeks we would rescope them to confirm that they are healed. And by day seven, if there's no response to I.V. steroids or to the biologic, which is infliximab in this setting, then usually that patient will go to colectomy.

Dr. Mahadevan:
Okay. Great. So, um, the final thoughts on collecting the – on selecting the correct therapy for IBD and treat-to-target strategies. Selecting the correct therapy involves assessment of disease severity. You heard us talk a lot about how severe the ulcers were, what were the extraintestinal manifestations, the drug efficacy, the patient comorbidities. Treat-to-target means that symptoms alone do not determine therapy; you need objective markers, whether that is endoscopy, calprotectin, uh, biomarkers, and blood. Regardless of therapy, discuss with the patient a timeline for assessing response using combination of symptoms and objective markers of mucosal healing and inflammation, as well as agreed-upon criteria for changing therapy. Okay. We're happy to take any questions. Okay, so what role will emerging therapies such as JAKs play?

Dr. Velayos:
So um, I think that, um, it's clearly I think a very interesting new class of therapies. I think that one of the attractive options, or one of the attractive features of it is that they tend to be, uh, being small molecules, they tend to be oral, which is I think a convenience for patients. Um, you know, some of the safety issues have to be addressed, but increasingly, um, those are being addressed with more kind of specific, um, JAK inhibitors that are kind of under development. And so I think that, you know, as I said our therapies are not perfect, and so I think as we get these new classes of therapies, I think those – that can only be a good thing for – for our patients There are some also some attractive features, not being a biologic, um, the issues of kind of therapeutic drug monitoring and – and anti-drug antibodies kind of get eliminated. So I think it's really an exciting new class.

Dr. Mahadevan:
Yeah, I have to say I've been very pleased with the response my ulcerative colitis patients have had to tofacitinib. It's currently only FDA approved for ulcerative colitis, and the new FDA guideline is that they have to have failed a TNF before you could go on to tofacitinib. Um, that being said, it – it really is the only drug that has shown benefit versus placebo even in patients who have failed, um, other biologic therapies. And so it's an effective agent. Um, and again men and women can have this, um, but we do – we don't use it in the pregnant woman. And then how does it fit into stride? I think it would be the same thing; you'd use the same treat-to-target measurements. Um, and when you start it eight weeks later, you would do your flex sig, confirm their remission, and you use 10 mg twice a day for eight weeks, and then you would reduce to 5 mg twice a day per the FDA guidelines. But if they didn't respond at eight weeks, you can give them an additional eight weeks of therapy per the FDA guidelines, reassess, and then drop to 5. And in the patients I've dropped to 5 twice a day who flared, again I have a very refractory practice, I do have them on 10 mg BID with them understanding there is an increased risk of being a thromboembolism and taking precautions for that. There are JAKs that are coming out – that are being studied for Crohn's disease, as well more specific JAKs that are, um, more specific that tofacitinib.

Dr. Velayos:
And just to kind of emphasize that, you know, the treat-to-target concept is really treatment agnostic. So the nice thing is that regardless of the therapy, it's going to be the same – same principles.

Dr. Mahadevan:
Yeah. And patients do like the oral, um, the oral formulation rather than I.V. and injectable. Okay. Thank you for joining us.

Dr. Velayos:
Thank you, everyone.

Dr. Mahadevan:
Enjoy the meeting.

Announcer:
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