

Transcript Details

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Diving into the Details of Upadacitinib for UC and Crohn's Disease

Announcer Intro:

You're listening to *GI Insights* on ReachMD. On today's episode, we'll hear from Dr. Andres Yarur, who's an Associate Professor of Medicine at Cedars Sinai Medical Center in Los Angeles, California, and the 2023 Sherman Emerging Leader Prize Recipient. He's also the lead author of a study that looked at upadacitinib for patients with moderately to severely active ulcerative colitis and Crohn's disease, which he presented at Digestive Disease Week 2024. Let's hear from him now.

So before we get into the details of this study, can you tell us why obesity is an important consideration to evaluate with administration of biologics?

Dr. Yarur:

Well, obesity has surfaced as an important topic in patients with inflammatory bowel diseases. Historically, people with IBD, Crohn's, and ulcerative colitis, especially Crohn's, have been underweight. But as therapies get better and the number of surgeries go down—with that I mean bowel resections and development of complications, such as short gut—there has been a raise in the prevalence of obesity in the IBD population, just as the global population.

We have studied the role of obesity and very specifically, the role of visceral adipose tissue in their response to biologic therapy in patients with IBD. Because visceral adipose tissue is an endocrine organ that secretes a lot of hormones that are proinflammatory, there might be an important role in how these drugs that we use in a day-to-day basis work.

A previous study that we did a couple of years ago that was published in *Gastroenterology* showed very nicely that a high visceral adipose tissue burden significantly affects the efficacy of three biologics: infliximab, vedolizumab and ustekinumab. The microbiome was not really explaining this lower efficacy rate even though we did find that very specific cytokines, TNF and IL-6, were correlated, and overexpressed in patients with a high visceral adipose tissue burden and nonresponse to therapies. So obviously, the natural question is well, how about the other drugs? And specifically, this new generation of small molecules that are currently available for both Crohn's disease and ulcerative colitis.

Announcer:

So now turning to your study, can you tell us about the objectives, the design, and your patient population here?

Dr. Yarur:

In a recent analysis, we looked at baseline BMI in patients entering the phase III pivotal trials for upadacitinib in ulcerative colitis and Crohn's disease and how that baseline BMI affected the efficacy. BMI is not a perfect index to assess visceral adipose tissue burden, but it does have a correlation with obesity, at least in most patients. So in this trial patients with moderate to severe ulcerative colitis or Crohn's disease, they were randomized to receive placebo or upadacitinib at different doses.

In this specific post-hoc analysis, the efficacy endpoint at week eight to 12 was for the induction studies, and week 52 was for the maintenance trials. BMI was stratified by less than 18, 18 to 25, 25 to 30, and more than 30. The endpoint in ulcerative colitis included the Adapted Mayo score, and for Crohn's disease used the Crohn's Disease Activity Index, which are pretty standard for these clinical trials. We also looked at endoscopic improvement in UC and endoscopic response in Crohn's disease and other endoscopic outcomes, including endoscopic remission. Ultimately, we also looked at steroid-free clinical remission in both UC and Crohn's disease.

So what did we find? Well, overall, in the induction studies, 988 patients were included in the UC analysis, and 1,021 patients were included in the Crohn's disease analysis. They received upadacitinib 45 milligrams or placebo for this induction period. For the

maintenance studies, a total of 451 patients were included in the UC maintenance trial, and 502 were included in the Crohn's disease maintenance trials.

So in terms of efficacy regardless of baseline BMI, patients that received upadacitinib in both UC or Crohn's disease had significantly higher rates of the outcomes when compared to placebo. So in other words, baseline BMI did not influence the efficacy of the drug. And this was true not only for induction but also for maintenance. So this is important. And even though, as I said, the BMI may not be a perfect marker for visceral adipose tissue or potentially even obesity, it does give a hint that these small molecules, this new generation of small molecules may not have the influence on efficacy or may not be influenced by BMI versus other drugs, such as biologics.

Announcer:

So, Dr. Yarur, based on these results, how can clinicians use these findings when treating patients with UC or Crohn's?

Dr. Yarur:

Overall, we do need more studies looking specifically at visceral adipose tissue for small molecules, not only JAK inhibitors but also S1P modulators. It is tempting to say that patients with a high BMI may be well served using a small molecule, but I think it's still very early, and this is just a beginning a journey, and we need to look more into more specific studies.

Announcer:

And what advice do you have for your peers in approaching treating patients given the changing landscape?

Dr. Yarur:

Well, we have a variety of drugs for ulcerative colitis and Crohn's disease. Some drugs even we have the option of IV versus subcutaneous. I think that it's important to assess the patient's characteristics when choosing a drug, specifically a first-line drug; and again, maybe small molecules would be a better option for patients with a high BMI. And also, at the same time, I think we need to recommend our patients with obesity to try and lose weight to improve their response to these drugs.

Announcer:

Any final thoughts that you'd like to leave with our audience?

Dr. Yarur:

Overall, it's very interesting what we have seen in terms of the influence of obesity in the efficacy of the drugs that we now have. Sometimes, we have thought about IBD as every patient being malnourished, but I think that we need to switch our thinking and really think different about how we approach IBD nowadays in 2024.

Announcer Close:

That was Dr. Andres Yarur discussing his recent research on improving clinical and endoscopic outcomes in patients with moderate to severe UC and Crohn's regardless of body mass index. To access this and other episodes in our series, visit *GI Insights* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!