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IBD & The Evolution of Targeted Therapies – How Far Have We Come?

Announcer:
Welcome to CME on ReachMD. This episode is part of our MinuteCE curriculum.

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Dr. Iroku:
Hi, my name is Dr. Ugo Iroku. I'm a Clinical Assistant Professor at Mount Sinai Hospital. And today we're going to talk about IBD & the Evolution of Targeted Therapies – How Far Have We Come?

The learning objectives are we're going to identify the benefits, risks, and clinical utility of current and emerging drug therapies for patients with IBD.

When we think about the pre biological era, we had our steroids and immunomodulator and our mesalamine-based therapies. But starting in the late 1990s with infliximab, we began to biological era. Today, however, we're going to focus in on some of the newer medications that have been available to us, ozanimod, etrasimod, risankizumab, mirikizumab, and upadacitinib.

There are broad and targeted therapy mechanisms of action. Our anti-TNF mechanism of action involves a mechanism that can be blocked with our medications that we've come to know, infliximab, adalimumab, golimumab, and certolizumab. And when it comes to the mechanism of action, it affects the dendritic cells, their activation of T cells, cytokine and chemokine release, and apoptosis in the gut lining. It's a very broad effect. But these days, we've come to be able to achieve more selective targeted therapies.

And we're going to start by looking at our S1P receptor modulators. So, our T cells are trafficked into the lymph nodes with the game plan of going to the gut to produce the inflammatory effect. However, our S1P receptor modulators blind the receptors to that S1P signaling signal, thereby trapping the T cells in the lymph nodes so they're not able to produce an inflammatory effect on the gut. These are the medications ozanimod and etrasimod. Of course, they're all targeted synthetic molecules used in moderate to severe UC. They're proven to give us, quote unquote, steroid-free remission, and durably so. There are a number of adverse effects that we talk to our patients about, especially herpes zoster, bradycardia, decreased lung function. And that affects our drug positioning; we avoid using these medications in patients with severe obstructive sleep apnea and those who are using MAO inhibitors, those who are pregnant, and those who have significant cardiac history. Ozanimod has been proven to achieve clinical remission, clinical response, clinical improvement, and mucosal healing, greater than placebo in both induction and maintenance studies. And the same has been found in the etrasimod as well.

Looking at our next mechanism of action, we're looking at the JAK-STAT inhibitors. Doing a deep dive into upadacitinib, we find that this is a medication that's beneficial because it's an oral, again, targeted synthetic molecule, FDA approved for the use of moderate to severe UC and Crohn's disease, with a rapid onset of action as quickly as 2 weeks. Mucosal healing and steroid sparing has been noted to be part of its benefits. The adverse effects that we look out for are herpes zoster, non-melanoma skin cancer in particular. And the drug positioning is that it's FDA approved to be used in bio-experienced patients not in combination therapy. And we're avoiding use in

pregnant patients. Again, found to be efficacious in both maintenance and induction studies for both Crohn's and ulcerative colitis.

And the last group that we'll be looking at today are our IL23 selective inhibitors. If you look on the left, ustekinumab affects both IL-12 and IL-23 by affecting the p40 subunit. By singling out the p19 subunit, ustekinumab gives us an IL-23 selective inhibition. The benefit again is that it's selective and that may improve its decreased side effect profile. It's used as first line, and it's efficacious in both bio-naïve and bio-experienced patients, and has been shown in head-to-head studies to have superiority over ustekinumab.

In summary, we have these new amazing treatment mechanisms of actions that are available in the treatment of both Crohn's and ulcerative colitis. These include increasingly targeted biological therapies such as IL-23 specific blockers. New and effective targeted oral small molecule treatments are available both for the treatment of ulcerative colitis and Crohn's.

Thank you.

Announcer:
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