Transcript Details

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IBD and Biosimilars: What Healthcare Professionals Need to Know

Announcer:
Welcome to ReachMD. This activity, entitled “IBD and Biosimilars: What Healthcare Professionals Need to Know” is provided in partnership with The Crohn’s and Colitis Foundation in collaboration with Prova Education.

Dr. Maltz:
As new therapies such as biosimilars evolve, it's important for clinicians, patients, and caregivers to understand both the similarities and differences of the therapies, as well as their potential risks and benefits. Are you up to date on how these agents may impact the treatments of inflammatory bowel disease?

This is ReachMD, and I am Dr. Ross Maltz, a pediatric gastroenterologist. Here with me today are…

Dr. Govani:
Shail Golvani, adult gastroenterologist.

Dr. Bernasko:
Dr. Nana Bernasko, IBD nurse practitioner.

Dr. Bhat:
And Shubha Bhat, clinical pharmacy specialist in gastroenterology.

Dr. Maltz:
Let’s get started! Nana, what are biosimilars, and how do they differ from the originator biologic?

Dr. Bernasko:
So according to the US Food and Drug Administration, biosimilars are highly similar to reference product, notwithstanding minor differences in clinical and active components, with no clinical meaningful differences between the biosimilar and the reference product.

The European Medicines Agency, which is the EMA, essentially defines biosimilars as the same biologic substance, though there may be minor differences due to their complex nature and production methods. Differences will have not shown any effect on safety or effectiveness, whereas the World Health Organization defines biosimilars as in similar in terms of quality, safety, and efficacy to an already licensed reference biotherapeutic product. The exact definitions may vary, but the essential thing is that biosimilars are similar, not identical, to original biologics, but no clinically meaningful differences in safety and efficacy.

One of the key differences between biosimilars and reference biologics is how clinical trials operate during the development process. With biologics, the goal of trials is to ascertain this clinical efficacy of the product. With biosimilars, however, the goal is to demonstrate that the product is comparable to the reference biologic product in terms of its pharmacokinetics, pharmacodynamics, safety, and immunogenicity. In other words, the goal is to demonstrate that scientific concept of comparability to show that minor differences between the 2 do not have a relevant impact on the final therapeutic result.

Dr. Maltz:
And Nana, what's the difference between branded and unbranded biologics?

Dr. Bernasko:
This is a new term that has come about, but essentially an unbranded biologic is an approved biologic marketed under the biologic license application of its brand product without the propriety name on the label.

Dr. Maltz:
Thank you for that great explanation.

Now turning to you, Shubha, what are some of the key concepts clinicians should keep in mind when prescribing biosimilars for the treatment of inflammatory bowel disease, or IBD?

Dr. Bhat:
Great question. So there are about 5 key concepts to know as it pertains to the approval process and clinical studies relating to biosimilars. First is the reference or originator product. And this is the originally licensed biologic product that is used for comparison purposes. Examples of this could be infliximab or adalimumab. Another concept to know is extrapolation, which means that a biosimilar may be approved for one or more indications for which the reference product is licensed for based on totality of evidence and the scientific justification. For one example of this would be an infliximab biosimilar may be studied in patients with rheumatoid arthritis, and approval through the Food and Drug Administration, or FDA, may be granted based on that data. However, the biosimilar approval may also extend to some or all of the other FDA indications that the reference product holds, such as inflammatory bowel disease, as long as adequate clinical and scientific justification for the biosimilar is provided.

A third concept review that is becoming more prevalent, especially with the introduction of adalimumab biosimilars in 2023, is interchangeability, which is a designation granted by the FDA if the biosimilar shows that risk of switching more than once does not impact clinical outcomes or safety. Interchangeability is a designation that more biosimilar manufacturers are trying to obtain, because this actually allows pharmacists, depending on state laws, to dispense the biosimilar in place of the reference product if prescribed without needing to inform the prescriber. Switching is another important concept to know, and this applies to transitioning from reference to biosimilar, vice versa, or even biosimilar to biosimilar.

Lastly, nocebo effect is another important concept to understand as this represents new or worsening symptoms or adverse effects that occur primarily due to patients' negative perception of biosimilars, as they think that these treatments are ineffective or inferior to reference products. Thus, biosimilar education is so instrumental; it'll help combat these nocebo effects.

Dr. Maltz:
For those just tuning in, you're listening to ReachMD, and I'm Dr. Ross Maltz. And here with me today is a team of expert faculty members. We're discussing the role of biosimilars in the management of inflammatory bowel disease.

Dr. Bhat:
Shail, I would like to now get your insights. Now that we have covered some important concepts about biosimilars, why do they matter? Which biosimilars are approved, and what does this mean for our patients with IBD?

Dr. Govani:
Thank you, Shubha. So there are currently a number of available biosimilars for infliximab. There are currently 3 available products in the United States that have been FDA-approved and are marketed. There are soon to be a number of products available for adalimumab here in the United States also that we expect to be available in 2023.

Currently, when you are interested in starting a biosimilar you could consider starting this as a brand-new medication on a patient that may be infliximab naïve. Or there may be instances where you may be asked to transition this patient to this medication from the originator product or possibly another biosimilar. If you're interested in obtaining the drug levels for their biosimilar, you can go about this in obtaining the same tests as you would have if they're on the originator product. So ordering an infliximab level will quantitate the originator product as well as the biosimilar and will also quantitate the anti-drug antibodies.

One important thing to consider is that patients who have had a failure to the originator product or biosimilar would not be expected to improve when they're switched to an alternative biosimilar or back to the originator product. So in that situation, I would recommend switching to an alternative product.

The whole reason biosimilars exist is that we hope that they would lower costs and allow greater availability of these medications for a broader range of our patients.

Dr. Bhat:
Shail, thank you for this information. It's great that there's clearly an abundance of available biosimilars, and there's more to come in the future.

Could you tell us a little bit more about some of the clinical evidence relating to the use of biosimilars in IBD?

Dr. Govani:

There are now numerous studies showing the efficacy of these medications in IBD specifically. Some of the studies that I think were worth highlighting include a multicenter study comparing Inflectra to originator infliximab in patients with active Crohn's disease. This study was published in Lancet in 2019. They randomized patients to Inflectra versus infliximab, the originator product, and among those who had a response, patients were later re-randomized to the other product at week 30. The rates of response at week 6 were not statistically different, at 69% in the Inflectra arm versus 74% in the originator Remicade arm. Side effects were similar in both arms. And a number of other observational studies have confirmed that biosimilars have similar efficacy in patients who are TNF naïve. This study also demonstrated that switching from originator to biosimilar or biosimilar to originator did not have a different efficacy outcome or safety outcomes.

The original RCT on the topic of switches called NOR-SWITCH showed that switching to Inflectra from originator infliximab was non-inferior in a wide range of conditions. An extension of this study which included more than 200 IBD patients demonstrated that switching was again non-inferior to maintenance with Inflectra. And now a number of real-world registry studies have also confirmed these findings.

In particular, there was interest in drug levels after switching. So drug levels after switching have been studied in the SECURE registry. This study compared the levels of infliximab 16 weeks after switching to the drug at the time of the switch. They found no difference in either ulcerative colitis or Crohn's disease patients. So this showed effectively that the biosimilars had good drug levels even after a switch.

And lastly, immunogenicity is a major concern with drugs switches. NOR-SWITCH and the open-label extension showed no significant difference in anti-drug level antibodies at approximately 2% or so in both maintenance and switch arms.

In conclusion, both randomized controlled data and observational studies conducted over the course of more than 5 years show that biosimilars performed similarly to the original product, and switches appear to be safe compared to maintaining the original drug.

With all this information about biosimilars, we have to remember to factor in our patients and differences in patient populations. Ross, how are you using these new agents in the pediatric population? And how do you discuss these therapies with your patients and their families?

Dr. Maltz:
As a pediatric gastroenterologist, I am very comfortable using biosimilars, and I'm not using biosimilars any bit differently than my adult colleagues. But I will point out that there is a lack of pediatric data surrounding biosimilars in the pediatric IBD population. Myself and colleagues are working on increasing that medical knowledge.

We recently had a publication in JPGN [Journal of Pediatric Gastroenterology and Nutrition] where we obtained the perspectives of pediatric patients and their caregivers on biosimilars. About 80% of the patients we asked said they were unfamiliar with biosimilars, and about 65% of the pediatric caregivers were not familiar with biosimilars. Unfortunately, if the caregivers had actually heard of biosimilars before, they actually had negative perceptions of biosimilars, which makes it really important that we need to educate our patients better about biosimilars.

Regardless, if you start the originator or the biosimilar, it's important to discuss biosimilars and educate patients on this because there's a high chance in the near future that they'll need to be on a biosimilar or they'll be switched to a biosimilar. Unfortunately, they usually find out via letter in the mail from the insurance company that really includes very little education and explanation. It will usually state that there's a formulary change and that they need to switch to a different medication.

There are useful biosimilar information for patients and providers on the Crohn's and Colitis Foundation website.

Well, this has certainly been a fascinating conversation. To summarize, we've covered biosimilars have similar safety and efficacy compared to the originator agent; we want to be aware of the risk of the nocebo effect and the importance of educating our patients prior to switching; and we are now aware that there are multiple biosimilars on the market for infliximab and multiple biosimilars being available on the market for adalimumab in 2023.

Unfortunately, that's all the time we have today. So I want to thank our audience for listening in and thank our expert panel for joining me and for sharing their valuable insights. It was great speaking with you today.

Announcer:
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