ED LOFTUS: Hi. I'm Ed Loftus. I'm a gastroenterologist at Mayo Clinic in Rochester, Minnesota. And I specialize in the care of patients with inflammatory bowel disease, which is Crohn's disease and ulcerative colitis. And I wanted to talk to you today about a recent development.

You may have heard that the FDA recently approved a medication, which is called a biosimilar to infliximab. And this medication is made by-- it's complicated, but it's made by a company in Korea. But it's being marketed by a US company in the US.

In any case, this biosimilar pathway is a different pathway for drug development than conventional drugs. So think of a biosimilar as sort of like a generic but not really a generic. So if you recall, these biologics are these very large protein molecules which mimic antibodies, which the biosimilar is of similar molecular construction but not exactly.

The drug development pathway for a biosimilar involves a lot of work at the cellular lower level and at sort of the pharmacokinetics level to prove that the drug is essentially similar to the originator product. So there are a variety of tests that, yeah, it does block this particular inflammation pathway, or does this, or it does that at a cellular level. And then you have to show that, if you give a certain amount, it's going to have the same pharmacokinetics properties, et cetera.

And then when you're actually getting the drug approved for clinical use, the company that makes the biosimilar basically only has to show that it's similar to the originator product in one indication for which it's approved. So for something like infliximab, which is approved for multiple indications, all they had to show was that it was equivalent to the originator infliximab in basically patients with rheumatoid arthritis. And they did that. They showed that.

And so they met all of the criteria that the FDA had set out in advance. And interestingly, that pathway was actually approved in 2010 as part of the Affordable Care Act. And so they met all the criteria of the pathway.

Now, why is this controversial, or why is this an issue? One of the reasons is that maybe not all indications for anti-TNF agents are as responsive to anti-TNF as others. And so some people would argue that Crohn's disease and ulcerative colitis of all of the indications approved for anti-TNF use are the least responsive to anti-TNF use.

And so there's a theoretical argument that, if there were small differences between the biosimilar and the originator product, that couldn't be picked up in a relatively anti-TNF responsive disease, like rheumatoid arthritis. Those differences might get magnified in a condition like Crohn's disease and ulcerative colitis. But that's theoretical. We don't know that for a fact.

Moreover, this particular biosimilar has actually been approved in multiple countries over the past year or two. And so we actually are beginning to see clinical experiences with this biosimilar, infliximab, being reported in South Korea, Norway, Hungary, and several other countries. And the bottom line is, so far it looks like it works. And so it may be that these theoretical concerns are just that-- theoretical.

I think many gastroenterologists are still feeling uncomfortable and would like to see at least some type of comparative trial, showing that these drugs are sort of in the clinical ballpark. And I don't think they're asking for like major phase III registration trials, but something to compare.

The other issue with the biosimilars is that are they as likely or more likely or less likely to generate antibodies against the drug. We know that these drugs are immunogenic-- meaning that the body's immune system can sometimes recognize that they're not completely human proteins, even in the drugs that are called fully human. And so if you develop antibodies to these drugs, then the drug levels go down, the drug stops working, or you get side effects from it.

And so one concern is, OK, what if you're on the originator drug, you switch to the biosimilar, you switch back to the originator drug, or you switch to a second biosimilar, what's that going to do to the immunogenicity of these drugs. And the bottom line is we don't know. And so it would be potentially nice to see some type of a study trying to address those issues.

And so there's a lot of heat and light around the biosimilars right now. And frankly, I think part of it is a propaganda war between the companies that make the originator products and the companies that are making the biosimilars, which ironically are also major pharmaceutical companies too. And bottom line is we just need more data.

The other confusing thing is, even though the FDA approved this biosimilar to infliximab, we don't know what's actually going to happen when that company tries to bring it to market, because technically, there is a patent on infliximab in the US that hasn't expired yet. So there's a potential patent war. So even though it's all approved, the time it actually hits the shelves of the pharmacy, so to speak, may be further off than we think. And so stay tuned, and we'll update you as needed. Thanks.