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COMMENTARY

Biosimilars for Rheumatoid Arthritis: Riding the 2023 Wave [Podcast]

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Abstract: This article discusses some of the queries and concerns that patients may have about initiating or switching to treatment with a biosimilar for rheumatoid arthritis following the US 2023 release of several biosimilars of the adalimumab reference product, also known by the brand name, Humira. The article also covers the difference between a generic medicine and a biosimilar, and the clinical evidence to support the safety and efficacy of adalimumab biosimilars in patients with rheumatoid arthritis.

Keywords: biosimilars, interchangeability, rheumatoid arthritis

Podcast Speakers

This podcast is brought to you by Boehringer Ingelheim
Guests: Stanley B Cohen, Mariah Z Leach

Dr. Stanley Cohen: [00:00:00.330] Hello and welcome to this podcast entitled Biosimilars for Rheumatoid Arthritis: Riding the 2023 Wave. This podcast is intended to discuss some of the concerns that patients may have about initiating treatment with a biosimilar or switching from their current medicine to a biosimilar for rheumatoid arthritis. My name is Dr. Stanley Cohen and I'm a clinical professor of internal medicine and rheumatology at the University of Texas Southwestern Medical School in Dallas and co-medical director of Metroplex Clinical Research Center, also in Dallas. Today we're going to discuss the use of biosimilars for rheumatoid arthritis in view of the multiple adalimumab biosimilars recently released to the market in July of this year. And we'll also discuss the originator, Humira. I'm happy to be joined by Mariah today, a patient advocate and founder of Mamas Facing Forward, a site dedicated to providing information to, and a community for, mothers living with chronic illness. Mariah, welcome.

Mariah Z. Leach: [00:00:56.710] Hi, thank you for having me. As you said, I'm a patient advocate, I'm a writer, and I'm a mom of three, and I've been living with rheumatoid arthritis since I was 25 years old. I'm passionate about empowering patients to live well with their chronic illness, which to me means having the information necessary to make informed decisions about treatments. So, I'm excited to be here today to talk about biosimilars for rheumatoid arthritis.

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Dr. Stanley Cohen: [00:01:19.630] Great. Happy to have you here. To get us started, let's begin with describing what biologics are and what is a biosimilar? Biologics are large molecular medications that are made inside living cells. They can be expensive to produce and, compared with other medications, it can be difficult to scale up production effectively. All of which translates into increased cost that can make them hard for some patients to afford. A biosimilar is a biologic medication developed to be highly similar to an originator biologic medication, which is also called the reference biologic or reference product. Biosimilars are biologics and we've had biologics in rheumatology for over 24 years now. The US Food and Drug Administration requires a rigorous research process to assure that approved biosimilars meet the same high standards for efficacy, safety, and quality and have no clinically meaningful differences from the reference product.[1]

Mariah Z. Leach: [00:02:15.050] So, if there's no clinically meaningful difference between the reference biologic and the biosimilar, does that mean that biosimilars are like generics?

Dr. Stanley Cohen: [00:02:23.950] Well, biosimilars and generics do share a lot of similarities, but it should be noted that generics can be made as an exact copy of the original drug because their simple chemical structure is easy to replicate. By contrast, biologics are large protein molecules derived from living sources. The process to replicate these complicated molecules is not as easy as a simple chemical compound. So, while a biosimilar is still a copy of the reference product, there may be slight differences from the reference product due to differences in the manufacturing process. Thus, they may not be 100% exact copies as implied by the name, bio for biological drugs, and similar.

Mariah Z. Leach: [00:03:03.580] I think many patients might be worried about what those slight differences could mean for them. Could it affect how well the treatment works or the side effects they might experience?

Dr. Stanley Cohen: [00:03:13.390] As we've discussed, biologics are large, complicated molecules made inside living cells. This means that even when a manufacturer produces the same reference biologic in more than one location, it's possible in reality that there are minor but clinically insignificant differences between different batches of the reference biologic. The important thing is that the manufacturer tests each batch to ensure it's highly similar and meets the appropriate standards before it's released for use. In the case of a biosimilar, a different manufacturer is producing the biologic. However, as I mentioned, to be approved as a biosimilar by the US Food and Drug Administration, a biologic has to have no clinically meaningful differences from the reference product.[1] If there were any differences in terms of efficacy or safety outcomes, then it would not be approved as a biosimilar.

Mariah Z. Leach: [00:04:01.460] So, I'm thinking about some recently published survey data that have shown that patients with rheumatoid arthritis and other chronic illnesses have concerns about the safety and efficacy of biosimilars.[2] In fact, potential side effects and long-term safety were the most frequently reported patient concerns overall. One recent survey found that side effects, in particular, were identified as a really big concern by a big proportion of patients with rheumatoid arthritis, more than with other indications such as inflammatory bowel disease or psoriasis.[2] So, this is kind of a concern of mine as well. What evidence is there to show that biosimilars are as safe and effective as the reference product in patients with rheumatoid arthritis?

Dr. Stanley Cohen: [00:04:41.470] In the case of adalimumab, a biologic commonly used to treat rheumatoid arthritis, the good news is that most of the biosimilar studies were conducted in patients with rheumatoid arthritis, so there's really quite a lot of direct clinical evidence for the equivalent safety and efficacy. Studies have also looked at interchangeability. That is to say, the impact, if any, of switching between the reference product and a biosimilar has demonstrated similar efficacy between patients who switched and those who did not. For example, in VOLTAIRE-RA, a study that compared the safety and efficacy of the adalimumab biosimilar Cyltezo to adalimumab reference product, there was no reduction in effectiveness or safety in patients who switched from adalimumab reference product to Cyltezo at week 24, compared with patients who remained on either treatment throughout.[3] A systematic literature review of eight adalimumab biosimilars looked at a number of clinical trials where patients with rheumatoid arthritis were switched from reference product to the biosimilar, and found similar efficacy and safety with all biosimilars compared with the reference product.[4] It's also notable that many biosimilars and biologics have been approved and widely used in Europe for a number of years, providing us with clinical data from real-world use that consistently supports their efficacy and safety.[5–7]

Mariah Z. Leach: [00:06:03.640] For myself and for many of the patients that I work with. I find the lack of information on biosimilars in pregnancy to be a major concern. Can you speak to that a little?

Dr. Stanley Cohen: [00:06:14.840] The safety of using biosimilars in pregnancy and breastfeeding is certainly an important issue, and while there are not any studies on this specifically, there is ample evidence on the safety of many biologics in pregnancy.[8] The estimated background risk of major birth defects and miscarriage for indicated populations, including patients with rheumatoid arthritis, is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. Treatment with a biologic or biosimilar during pregnancy should be a risk–benefit discussion between the patient and healthcare provider to make a decision that's right for them. One review of electronic health records of patients with inflammatory mediated immune disorders who were pregnant while using a biosimilar did not find a link between biosimilar use during pregnancy and concerns such as congenital abnormalities or preterm birth. Additionally, there was no clinically meaningful evidence that biosimilars caused antibodies to cross the placenta, causing significant immune suppression in babies.[9] Stopping the biosimilar, however, in pregnancy was associated with childbirth at an early gestation, as well as a flare of inflammatory disease in pregnancy or postpartum. Ultimately, while patients should have informed conversations with their providers about the risk and benefits of using biosimilars during pregnancy, there is evidence that biosimilars can be used safely and with increasing confidence during pregnancy.

Mariah Z. Leach: [00:07:37.650] Thank you for explaining that. A little bit ago you mentioned interchangeability studies, and I've heard some biosimilars are described as being interchangeable with the reference product. Can you explain what that means?

Dr. Stanley Cohen: [00:07:49.750] Firstly, interchangeability is a regulatory designation in the United States. For a biosimilar to be classified as interchangeable with a reference product, additional studies are needed to demonstrate that if a patient is switched to and from the interchangeable biosimilar, the efficacy and safety remain the same as it would be in a patient who had remained on the reference product throughout. This means that requirements to be designated an interchangeable biosimilar are more stringent than those for a biosimilar, as it has to meet

this additional standard. To date, only three biologics have been granted this interchangeable designation. This includes insulin glargine [Semglee, insulin glargine-yfgn and Rezvoglar, insulin glargine-aglr], an adalimumab biosimilar, Cyltezo [adalimumab-adbm], and a ranibizumab biosimilar, Cimerli [ranibizumab-eqrn]. A biosimilar that has been approved as interchangeable is considered similar enough that it can be substituted for its reference product by a pharmacist without the need for a new prescription from a provider.

Mariah Z. Leach: [00:08:46.190] Thanks for that clarification, Dr. Cohen. I have a follow-up question there. So, does this mean that a patient could be switched from a biologic they're stable on to a biosimilar? And could this occur without their knowledge? Because I think that while most patients would understand why they might be switched from a treatment that isn't working, a lot of patients would probably be pretty apprehensive about switching from a treatment they're on that's currently working. The potential for this to happen without the patient being informed is pretty concerning.

Dr. Stanley Cohen: [00:09:15.350] Whether or not the patient is notified of the change depends on the state laws where the pharmacy is located. Most states do require pharmacies to notify the prescribers when a biologic was substituted with the biosimilar, but there are states that do not.[8] Depending on the state laws, pharmacies may also be required to notify the patient of the substitution.[10]

Mariah Z. Leach: [00:09:35.510] I would find it concerning if I received my medication and it contained something different than what I was expecting. Even if I was notified, there's a lot of potential anxiety surrounding starting any new biologic. It can take months to initiate a therapy and to see if it's successful and patients may need to go through this process more than once to find a biologic that works for them. Personally, I've tried six biologics, so I wouldn't want to be switched to a biosimilar without my knowledge.

Dr. Stanley Cohen: [00:10:01.630] Those are truly understandable concerns, and your anxiety about switching is something that I've seen in my practice on several occasions. The decision to switch patients like this often comes from the payer or list of medications on the formulary, and which version of biologics that are carried by a payer and available. I can see it as being uncomfortable at first for both patients and providers, and as the new biosimilars are now available and more will be coming, it will require a significant amount of education to familiarize patients with the biosimilars. In my practice, I try to address my patients' concerns the best I can, but there's not enough time in the day to cover them all. I can certainly understand when a patient receives a medication that has a different name and different packaging, it's going to be unsettling to the patient. I try to convince the patient, based on the tremendous real-world evidence that we have and the clinical trial data, that there is very little difference, if any, that's not clinically meaningful between the biosimilar and the originator reference product biologic. So, I'm very comfortable with this switch, and again, we just want our patients to be properly educated about why this is occurring and what to expect.

Dr. Stanley Cohen: [00:11:20.010] Again, with the five to ten years of experience that we have in the United States with infliximab and rituximab biosimilars, we're comforted with the switches which have occurred frequently. And again, the real-world data, the observational registry data, and clinical trials, demonstrate the safety and benefit of biosimilars.[11] So, to summarize, from the evidence we have, no major issues have arisen with switching, and patients appear to have done just as well over time when they switched biologic to the biosimilar.

Mariah Z. Leach: [00:11:48.370] So, if a patient is switched from a reference biologic to a biosimilar and they have concerns or they want more information, what should they do?

Dr. Stanley Cohen: [00:11:57.320] Well, I think a discussion with your healthcare provider is the initial thing to do, to better understand the process. If you're concerned and you're one of these very rare patients who doesn't do well after a switch to the biosimilar, at that point, you work with your provider, and you go to your insurance carrier and you let them know your concerns, and we'll be hopeful that you could go back to the reference product if that situation occurs.

Mariah Z. Leach: [00:12:28.030] Thanks, Dr. Cohen, for taking this time to speak with me today. I hope that our conversation helps other providers realize that patients may have real concerns when they're being switched to biosimilars, whether they have valid concerns, or they're simply concerns that are arising from lack of information and lack of education. So, I hope that patients feel empowered to ask the questions that they might have and learn all they can to make the best treatment decisions possible.

Dr. Stanley Cohen: [00:12:53.890] I concur with all that you've just said. I hope that our discussion will be helpful to patients who will be switching or initiating biosimilars as we move forward.

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