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Addressing Hesitancy on Biosimilars: From Development to Clinical Practice

Announcer Introduction:
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This medical industry feature, titled "Addressing Hesitancy on Biosimilars: From Development to Clinical Practice" is sponsored by Amgen. Here's your host, Dr. Charles Turck.

Dr. Turck:
Since the introduction of the first biosimilar to the U.S. marketplace in 2015 in the oncology space, over 22 biosimilars have been launched[1] for a number of therapeutic areas, including for cancer, inflammatory disorders, and multiple sclerosis,[2] to name a few. But despite the potential benefits of these agents – such as decreased costs for patients, healthcare systems, and payers[2,3] – their uptake in U.S. clinical practice has lagged behind that of the E.U.[3] So how can we work to ensure that biosimilars are utilized to their full potential?

Welcome to ReachMD. I'm Dr. Charles Turck and joining me to address common misconceptions surrounding biosimilars and examine key points in their development, manufacturing, and approval process is Dr. Jerome Goldschmidt. Dr. Goldschmidt is a medical oncology specialist practicing at Blue Ridge Cancer Care, and he's also affiliated with the U.S. Oncology Network in Blacksburg, Virginia. Dr. Goldschmidt, thank you for joining us today.

Dr. Goldschmidt:
Thanks for having me here, Dr. Turck.

Dr. Turck:
To start us off, Dr. Goldschmidt, I think a lot of hesitation surrounding biosimilar usage is due to questions regarding the development process. So how do we know that biosimilars can be safe and effective treatment options for our patients?

Dr. Goldschmidt:
That's a great point to start from, Dr. Turck.

Let's begin with the FDA's definition of a biosimilar. A biosimilar is a biological product that is highly similar to a U.S. licensed reference biological product for which there is no clinically meaningful difference in safety, purity, or potency.[4]

So, we can see why development and manufacturing standards are critical to uphold so that there are no clinically meaningful differences between biosimilars and their respective reference biological product.

The first step in manufacturing a biosimilar is developing a molecule that has the same amino acid sequence as the reference product. Once this molecule is made, that new biosimilar has to endure extensive analysis and comparison back to the reference product to ensure both agents have the same *analytical characteristics*, including purity, pharmacokinetics, and stability.[4,5]

Now, during development, the product defines the process. So, starting from choosing the correct cell line to creating the optimal development process to maximize similarity, it's a constant process of testing and checking back with the reference compound.[5]

Dr. Turck:
Now another concern for clinicians may be the approval process for these therapeutic agents. After all, we know that the originator

biologics have a highly regulated approval process, but what about biosimilars? Do they have a stringent path to approval as well?

Dr. Goldschmidt:
Yes. Biosimilars also have a highly regulated set of requirements and approval process.

Biosimilars require a quality profile, which is based on the total evidence package obtained from comparative analytical characterization and comparative preclinical and clinical studies.[5]

Establishing analytical similarity is the first step. After this step, preclinical studies help determine the product's potential toxicology for similarity, followed by pharmacokinetic equivalence. The final step is demonstrating that there is no clinically meaningful difference between the originator or reference biologic through confirmatory clinical testing.[4]

Now analytical characterization is a critical part of the process for biosimilars and must be identical to the originator.[4]

However, analytical characterization is not as important for the originator biologic because it doesn't really matter what the characteristics are of that compound as long as it works. But for biosimilars, on the other hand, analytical characterization is essential because as I mentioned earlier, it has to be almost identical to the originator.[4,5]

Dr. Turck:
Thank you for breaking all of that down for us, Dr. Goldschmidt. Now biosimilars have been in the U.S. market for a little under 10 years at this point. So, what can you tell us about the real-world utilization of these agents, and in particular, how significant this is?

Dr. Goldschmidt:
Real-world evidence, or RWE for short, is becoming increasingly important to evaluate the safety and efficacy of therapeutic agents given that randomized controlled trials have more homogenous populations. As a result, randomized controlled trials may not provide a complete picture of the effectiveness, impact, and tolerability of an agent if the results aren't generalizable to other real-world populations. [6,7]

RWE studies, on the other hand, can tell us a lot about the different patient types and clinical settings where a product is being used. We can identify differences or disparities in care, and we can even see when, where, and how a biosimilar is being incorporated, such as whether it's used in new patients or in patients who have been previously exposed to the reference product. And so, RWE, in my opinion, plays a very important role in the adoption of biosimilars.[6,7]

Dr. Turck:
For those just tuning in, you're listening to ReachMD. I'm Dr. Charles Turck, and today I'm speaking with Dr. Jerome Goldschmidt about implementing biosimilars into clinical practice.

So, Dr. Goldschmidt, now that we've reviewed the processes and standards in place that help ensure the safety and efficacy of biosimilars, what challenges might still persist when it comes to their integration into clinical practice?

Dr. Goldschmidt:
From my vantage point, there's still a general lack of awareness of biosimilars among providers and patients. But I think that's changing.

Education for clinicians and patients is key. Getting the conversation going between you and your clinical colleagues, particularly the treatment decision makers like health system pharmacists, and between you and your patients during their therapeutic management brings familiarity and, by default, comfort in adopting these agents.[8,9]

Dr. Turck:
And what can clinicians anticipate looking forward to when it comes to the biosimilar pipeline?

Dr. Goldschmidt:
For rare diseases, the orphan class of biological products deserves special attention for biosimilar development as they provide a vital niche to patients and society as a whole. And while they're currently minimally investigated, biosimilar orphans would afford the only opportunity for treatment of numerous new patients worldwide due to reduced price and better accessibility.[10]

Other developments in emerging biosimilars are focusing on ophthalmology, such as wet age-related macular degeneration, neurology, such as multiple sclerosis, and again, rare disorders such as paroxysmal nocturnal hemoglobinuria.[11,12,13] So, the expansion into non-oncologic and non-inflammatory therapeutic areas continues to be an important and exciting phase of development.

Dr. Turck:
Well, we're almost out of time, Dr. Goldschmidt, so before we close, what key takeaways would you like to leave with our audience?

Dr. Goldschmidt:
So first, I'd like to reiterate that we know these agents are proven to be as safe and effective as the originator products because biosimilars must meet and maintain robust scientific standards before and after approval, including the manufacturing and real-world evidence processes that we discussed today. And despite the fact that adoption of these agents has been slow, improving awareness and education surrounding biosimilars can help clinicians utilize them to their full potential, which in turn can help our patients.

Dr. Turck:
Thank you, Dr. Goldschmidt, for sharing those key takeaways. And as that brings us to the end of today's program, I want to thank my guest, Dr. Jerome Goldschmidt, for sharing this comprehensive background on biosimilars. Dr. Goldschmidt, thank you so much for your time and insights today.

Dr. Goldschmidt:
Oh, you're welcome. And thanks for having me.

Announcer:
This program was sponsored by Amgen. If you missed any part of this discussion, visit ReachMD.com/Industry-Feature. This is ReachMD. Be Part of the Knowledge.

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