

Bringing Biosimilars to the Clinic: What's the Fuss?

One of the aspects I really like about my editorial job is the opportunity to learn about things that are outside my wheelhouse, which, as it turns out, is a pretty small wheelhouse! I admit, I sometimes face writer's block when I sit down to write these editorials, so I keep a list of things that I should learn more about.

One of the things on my list was biosimilar agents. I knew there was controversy about these drugs, but that was about where my investigation had stopped. What are these drugs? What's the fuss about? I figured it was time for me to learn more.

It turns out the Affordable Care Act (ACA) had biosimilars embedded in it. We've become accustomed to generic drugs, which can be mimicked because the chemical structures and means of synthesis are known. Biologic agents are different. They are derived from living things, usually cells, but even from more complex organisms. And until the ACA, we didn't have a law that allowed for the manufacturing and adoption of biosimilars as a "generic" replacement for existing biologic agents.

The ACA amended the Public Health Service Act to create an abbreviated licensure path for FDA approval of biosimilars. Obviously the ACA required that the products be similar to the reference product and that they be safe and effective. And just as obvious was the need to have available, less-expensive versions of high-priced biologic agents. Because of evolving technologies or subtle differences in cell line clones or growth medium, biosimilars may not be identical to their reference agents. For this reason, safety testing of these drugs is more extensive than what is required for routine generic drugs.

So what was controversial about this? Was it the efficacy issue? Try as I might, I couldn't find the rules for what evidence the FDA requires to show equivalency of a biosimilar. The FDA has only approved one biosimilar in oncology—Zarxio, a copycat filgrastim. It was approved based on a single randomized trial, the PIONEER trial, conducted by the sponsor Sandoz. I searched PubMed but was unable to find this trial, so I couldn't read about the design. I trust the FDA, and I know it was reviewed by the Oncologic Drugs Advisory Committee (ODAC), so I have to assume that the results were pretty convincing, but it did seem odd to me that there was no publication. As a health care provider, I'd like a little more information before assuming a new product functions just as well as the reference agent. Having to dig into FDA transcripts to find this information just doesn't seem right.

Surprisingly, though, that hasn't been the controversy. Instead, most of the controversy has been around naming these drugs! Instead of using the generic or nonproprietary names, companies with reference agents wanted the FDA to name biosimilars differently, arguing, perhaps correctly, that they are not necessarily the identical compounds. Presumably, this would force the biosimilar companies to put more money into marketing these drugs and then there wouldn't be such a price differential. The FDA compromised by adding 4 letters to the nonproprietary name of the new agent. So Zarxio is filgrastim-sndz, which distinguishes it, a little, from the reference agent manufactured by Amgen.

Biologics are a relatively new class of agents, especially monoclonal antibodies, but patents of many of these drugs will be expiring soon, and I predict the FDA will be presented with many biosimilar applications in the future. Let's keep the debate on safety and efficacy where it belongs. And let's ask for more transparency about the clinical development of these drugs. Our patients deserve the real deal and it's our responsibility to make sure they get it.



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