

ADVANCES IN IBD

Current Developments in the Treatment of Inflammatory Bowel Disease

Section Editor: Stephen B. Hanauer, MD

European Experience of Infliximab Biosimilars for the Treatment of Inflammatory Bowel Disease



Peter Lakatos, MD
Associate Professor
Head of Gastroenterology/Hepatology Unit and Endoscopy
Semmelweis University
Budapest, Hungary

G&H What are biosimilars, and how long have they been in use in inflammatory bowel disease?

PL A biosimilar is a biologic drug that has been produced to closely resemble a drug whose patent has expired. Thus, a biosimilar is very similar, but not identical, to the originator drug.

As of January 14, 2016, 22 biosimilars have been approved by the European Medicines Agency. Treatment areas include diabetes (insulin; Abasaglar, Lilly), neutropenia/anemia (filgrastim; Accofil, Accord and Filgrastim Hexal, Hexal), and rheumatoid arthritis (etanercept; Benepali, Samsung). The first biosimilars for inflammatory bowel disease (IBD) in the European Union were registered in 2013, and the first use of biosimilars of infliximab (reference product Remicade, Janssen) began around the spring and summer of 2014. Currently, there are 2 infliximab biosimilars available in Europe (Remsima, Celltrion and Inflectra, Hospira).

In addition, IBD biosimilars have been in use in Korea since 2012. They are not yet being used in the United States.

G&H What makes up the approval process of a biosimilar in the European Union?

PL In Europe, each biosimilar needs to be evaluated in at least 1 therapeutic area of the registered indications and then approved by the European Medicines Agency before it can be used in clinical practice.

G&H How safe do the 2 infliximab biosimilars appear to be?

PL Thus far, we have information on the safety of these agents from the rheumatoid arthritis literature, as well as from real-life experiences in IBD patients in Korea, Norway, and Hungary in addition to limited studies from Poland. No new adverse events have been found, and the safety profiles of the infliximab biosimilars are in concordance with those that have been reported for the originator drug.

G&H What studies are currently being conducted on the infliximab biosimilars?

PL Currently, there is a study in Crohn's disease that is looking at efficacy and immunogenicity by comparing the biosimilar compound and the originator drug before and after switching. Recruitment for this study has just finished. In addition, multiple registries are ongoing in different European countries looking at real-life efficacy, immunogenicity, and switch outcomes.

G&H What are the advantages of using biosimilars?

PL Biosimilars are less costly than the originator drug. Therefore, if no dissimilarities have been shown at the regulatory level, and the originator drug and the biosimilar have been found to be comparable (which is the

case for the infliximab biosimilars currently being used in Europe), then the lower price is a clear advantage.

G&H Approximately how much is the difference in cost?

PL The expectation in Europe was that the cost of the drug would drop by at least 30% with the use of biosimilars. Naturally, there is a large variation in price among different countries in Europe, but the drop in cost has actually been more than 30% in most of the countries in the European Union. By having 2 marketing companies for biosimilar infliximab, the actual decrease in cost has been at least approximately 30% to 40% in most of the European countries. There has been a clear decrease in pricing, and this may affect not only the original formulation of infliximab, but also the price of adalimumab (reference product Humira, AbbVie) and vedolizumab (reference product Entyvio, Takeda), if competing for first-line therapy.

G&H Are these biosimilars being reimbursed by insurance companies?

PL In some European countries, copayment is still an option, but most countries in Europe include biologic agents (along with biosimilars) within the coverage of their insurance.

G&H Are there any disadvantages associated with the use of biosimilars?

PL If we accept the concept of biosimilarity and the approval of these agents by the European Medicines Agency, then we expect that the biosimilar and the originator drug are clinically similar with regard to efficacy, immunogenicity, and adverse events. Therefore, there should not be any disadvantages to the patient for taking a biosimilar.

G&H When should a doctor prescribe a biosimilar rather than the originator drug?

PL The indications are the same for the biosimilar and the originator drug. Whether a doctor recommends the use of one or the other is based on cost/reimbursement policy and availability. In the European Union, usually most of the insurances recommend the use of the lower-cost drug. Thus, cost saving is one of the main drivers of the use of biosimilars.

G&H How common is the use of biosimilars in clinical practice in Europe thus far?

PL The use of these agents depends on reimbursement and insurance policies, as previously mentioned, and whether

the patients are new or already receiving biologic therapy. The use of biosimilars is recommended by most insurance companies for new IBD patients in need of biologic therapy.

As for patients who are already taking biologic therapy, at the moment in Norway, Poland, and the United Kingdom, a mandatory switch process has already been partly implemented for patients on maintenance therapy as well as patients in the induction phase.

In Hungary, there is no mandatory switch process thus far. All new patients, however, must start with biosimilar infliximab; they do not have the choice of starting with the originator drug. Similar rules apply in Norway in terms of new patients. Some of the other countries in Europe offer a choice between the biosimilar and the originator drug, and switching to the biosimilar occurs at the discretion of the specialist.

G&H Have biosimilars been accepted by the average European gastroenterologist, or is there any reluctance to prescribe these agents?

PL Around the time of the approval of the biosimilar infliximabs, the European Crohn's and Colitis Organisation (ECCO) conducted a survey among gastroenterologists in Europe. Approximately one-third did not have any concerns about using biosimilars, while the other two-thirds had moderate concerns. The survey was repeated this year, and the results are expected to be presented at the next ECCO congress, which will be held in March of this year in Amsterdam, The Netherlands.

From what I have seen, after doctors use biosimilar infliximab in clinical practice, they usually have little to no concern about the agent. However, this may depend on whether the doctor is working in a private practice or in a more academic, public environment. In my experience, high-volume academic centers use biosimilars more frequently, are more comfortable with them, and have fewer concerns regarding their use.

G&H Do you have any first-hand clinical or research experiences with biosimilars?

PL Yes. My colleagues and I collected a nationwide data sample of biosimilar infliximab use throughout Hungary. All 16 of the centers that prescribe biologics gave us all of the data from the start of biosimilar infliximab use in all IBD patients in Hungary. The findings of our study, which were recently released online in the *Journal of Crohn's and Colitis*, cover the use of biosimilar infliximab in the first 210 IBD patients. As expected, there was no difference in terms of immunogenicity or side effects between those found for the biosimilar drug and those previously published for the originator drug. In addition, the efficacy rate of biosimilar infliximab until

week 30 was also comparable with the data that were published with the originator drug.

G&H Do you have any advice for doctors considering biosimilars?

PL Doctors should take into account insurance and reimbursement policies, but if there are no restrictions, the data right now suggest that there should not be any differences between biosimilar infliximab and the originator drug. The indication and expected outcomes should be the same as those expected from the originator drug.

However, this recommendation only applies to the 2 biosimilars currently available in Europe for infliximab. This coming year, at least 1 more biosimilar option is expected to be released for infliximab. I cannot comment on this drug, as it is not yet on the market.

G&H Are any other IBD biosimilars currently in development?

PL There are multiple biosimilar infliximabs currently in development. The new version mentioned above has already been submitted for evaluation for use in Europe. In a few years, adalimumab will lose its patent, and there are already several biosimilars in development.

G&H What does the future hold for biosimilars?

PL In the future, for many different drugs and disease settings, whenever a patent expires, the next step will likely be the development of a biosimilar. I think most pharmaceutical companies will start developing biosimilar drugs after the expiration of patents for most of the biologics that are currently on the market. I predict that the use of biosimilars will also spread to more countries, including the United States.

G&H Is there a need for further research on the infliximab biosimilars that are currently available in Europe?

PL The main area of interest and concern for most clinicians involves biosimilar switch data and safety issues surrounding the switch period. These issues will be tackled at least partly by the aforementioned Crohn's disease study that just finished recruitment. In addition, studies on another area of concern, real-life immunogenicity and pharmacokinetics, will be reported early this year regarding antibody development and drug trough levels, as well as the therapeutic drug monitoring strategy for biosimilars.

Dr Lakatos has served as a speaker and/or advisory board member for AbbVie, Celltrion, EGIS, Falk Pharma GmbH, Ferring, Hospira, Kyowa Hakko Kirin Pharma, Mitsubishi Tanabe Pharma Corporation, MSD, Otsuka, Pharmacosmos, Roche, and Takeda. He has also received unrestricted research grants from AbbVie, MSD, and Hospira.

Suggested Reading

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