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Short Report

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Changes in Biosimilar Knowledge among European Crohn's Colitis Organization [ECCO] Members: An Updated Survey

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Abstract

Background: In 2013, a ECCO survey showed that a minority of IBD specialists was aware and confident about the benefits and issues of biosimilars. We aimed to look at the evolution of IBD specialists' thinking about biosimilars one year after they had become available in the European Union.

Methods: A 14-question anonymous survey was posted on the ECCO website. Members voluntarily responded in response to ECCO office invitations to participate in their surveys. Information on gender, job position, country, and experience with biologics also were collected.

Results: Out of the 118 responders, only 17% of responders had no access to biosimilars. Most responders regarded cost-sparing [92.4%] as the main advantage of biosimilars, considered immunogenicity [69%] to be their main concern, and estimated that post-marketing pharmacovigilance, well-designed randomized clinical trials and further studies of risk profile were needed [30.5%, 27%, 32.2%, respectively, a 30–40% reduction since 2013]. Only 35% of physicians think biosimilars should carry distinct International Nonproprietary Names, as compared with 66% in 2013, and 89.8% disagreed with automatic substitution of the originator with a biosimilar by a pharmacist.The originator and biosimilar were considered interchangeable by 44.4% of responders, as compared with 6% in 2013. Only 32.2% were against the extrapolation across indications, and only 25% would not extrapolate data across IBD. Finally, only 19.5% felt little or no confidence in the use of biosimilars, as compared with 63% in 2013.

Conclusion: IBD specialists are generally well informed and educated about biosimilars. Compared with in 2013, there are now fewer concerns and more confidence about their use in clinical practice.

Key Words: Biosimilars; inflammatory bowel disease

1. Introduction

The introduction in the last 2 years of infliximab biosimilars represents a great novelty in the field of irritable bowel disease [IBD]. Since the expiration of the patent of Remicade®, the first infliximab biosimilar [known as CT-P13] has been licensed for the market in early 2015 in the European Union under two different trade names [Remsima® and Inflectra®].[1,2] The bioequivalence in terms of efficacy, safety and immunogenicity of CT-P13 has been investigated by its producer in two clinical trials,[3,4] as part of the extensive comparability exercise required to gain European Medicines Agency [EMA] approval in 2013. More clinical evidence supporting safety and effectiveness of CT-P13 came from cohort studies in the year 2015 on IBD

patients, both in Crohn's disease [CD] and ulcerative colitis [UC], across Europe.[5–8]

The state of mind of European gastroenterologists regarding biosimilars in 2013 was very conservative. We conducted an ECCO-supported web survey among the ECCO members, which showed that a majority of responders felt little or no confidence at all about the use of biosimilars.[9] Moreover, despite the cost reduction, which was considered to be the main advantage of biosimilars, the majority of ECCO members expressed concerns about their immunogenicity, safety and interchangeability, as well as about practices of extrapolation of data across indication and automatic substitution for the originator in patients already on infliximab.

Because of extensive education about biosimilars in Europe and rapid increase in use of the first infliximab biosimilar across many European countries in the year 2015, we aimed to assess how the ECCO members' views are evolving on the topic.

2. Methods

We developed a web survey, as previously described, trying to retain as many as possible of the questions used in 2013,[9] but adding or adapting questions on some new issues relevant to biosimilars in IBD. The questionnaire primarily aimed to assess the awareness and confidence of use of biosimilars among ECCO members who are considered as IBD expert gastroenterologists.

The 14-question multiple-choice anonymous web survey was conducted with the logistic support of ECCO between June 1 2015, and November 30, 2015 [Supplementary Table 1]. All ECCO members were invited via collective emails inviting them to participate in several surveys posted in the member-restricted area of the ECCO website. Responses were provided to the coauthors by the ECCO webmaster for analysis. Because we could not guarantee that the same gastroenterologists participating in 2013 would respond to the new web survey, a simple comparison of aggregate data was performed, but no statistical analyses.

3. Results

A total of 118 ECCO members replied to the online questionnaire. Of these, 60% worked in a University Hospital, 32.5% in regional hospitals or private clinics, and 15.5% in private clinics and/or hospitals or clinics. The majority of them [60%] had access to biosimilars and had already prescribed them in the previous year, whereas 22% had access to but had not yet prescribed biosimilars; 18% had no access to biosimilars.

3.1. Advantages and issues with biosimilars

Compared with the previous results [Figure 1], cost-sparing [92.4%] was still considered to be the main advantage of biosimilars [89.5% in 2013], while the main issue remained the lack of data derived from clinical trials for all indications [42.4%]. In the later survey, a much lower percentage of responders estimated that there would be a higher immunogenicity for biosimilars than for the originator, or a different action than the originator [27.1 and 16.9%, compared with 67.1% and 43.1% in 2013]. However, 21.2% of responders to the later survey were concerned about patients' rights to know which drug was being administered to them. This issue emerged as a new topic not revealed in 2013. Half of the responders thought that there were no differences between monoclonal antibody biosimilars and the other licensed biosimilars [such as erythropoietin or biosimilars to growth factors]. Only 32% thought, in contrast, that monoclonal antibody biosimilars were more complex, with an eventual higher immunogenicity [62.5% in 2013], and only 30.5% and 27% of them, respectively, thought that more post-marketing pharmacovigilance, well-designed randomized clinical trials [RCTs] and further studies of risk profile were needed [54.2% and 65.4%, respectively, in 2013].

3.2. Interchangeability and automatic substitution

Only 35% of physicians agreed that biosimilars should carry distinct International Nonproprietary Names, as compared with 66% in 2013. Regarding prescription, 89.8% disagreed with automatic substitution of the originator with a biosimilar by a pharmacist, although 12.7% would support such substitution for new prescriptions, and 12.7% in all patients. This is generally in line with the previous survey, in which 84.8% disagreed with automatic substitution of the originator with a biosimilar by a pharmacist in 2013. Moreover, when participants were asked whether they would switch a patient in sustained remission from the originator to a biosimilar, 44.4% responded that the two molecules were interchangeable

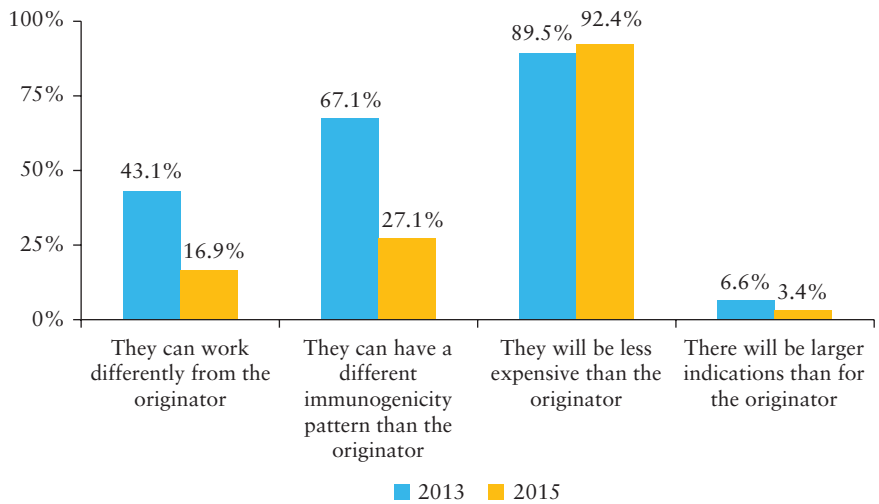

Figure 1. Comparison of responses to the question "What could be issues or advantages of a mAb biosimilar?" between the ECCO survey in 2013 and 2015 [more than one answer possible].

[5.9% in 2013]. An additional 27.4% responded that they were in favour of the substitution, but that they would inform the patient in detail [22% in 2013], while 39.9% would not do it, because of insufficient data to support switching [72.3% in 2013].

3.3. Extrapolation across indications

To explore this issue, the participants were asked to consider some hypothetical clinical scenarios that included an extrapolation across indications based on the potential availability of results from RCTs. In the theoretical case of two RCTs for rheumatology patients and one for CD patients showing no differences between a biosimilar and its originator, 50.8% thought the biosimilar should be approved for all the indications of the originator [24.2% in 2013]. In that situation, 32.2% thought that the extrapolation should not be based on clinical trials, but on preclinical data only; 29.7% thought the biosimilar should be approved only in the tested indications and only in new patients, whereas 25% thought the biosimilar should be approved only in the tested indications for both naïve and anti-TNF-experienced patients.

In the case of one RCT showing no differences between a biosimilar and the originator in Crohn's disease, 35.3% would use the biosimilar in other IBD indications as well as for off-label uses [e.g. refractory pouchitis or microscopic colitis], 31% would use the biosimilar in CD and UC [16.3% in 2013], 25% would use it only in CD [52.3% in 2013], and 8.6% would still wait for more evidence in IBD [30.4% in 2013].

Most clinicians still believed that medical societies should promote information about biosimilars [75%], but fewer felt the need for a collaboration with health institutions to develop rules on the use of biosimilars [47%], to promote guidelines [26%], or to create multispecialty safety registries [52%]. The originator and the biosimilar monoclonal antibody drug were considered interchangeable by 44.4% of the responders, as compared with 6% in 2013. An additional 27.4% of the physicians would switch to a biosimilar after patient information. Only 32.2% were against an extrapolation across other specialty indications; 25% would not even extrapolate data across IBD indications.

3.4. Education about biosimilars

The majority of responders [56%] judged the educational activities that they were exposed to about biosimilars was fair and adequate, whereas 16% of them found it unnecessary. On the other hand, 15.3% of clinicians thought the education was confusing. Finally, 12.7% found the education was too optimistic about efficacy and safety. The need to promote and inform on biosimilars increased in 2015 [75.2%] as compared with 2013 [65.7%], whereas the collaboration within scientific societies and institutions to develop rules in this sector, the development of multispecialty practice guidelines, and the creation of multispecialty registries to monitor safety was felt less needed in 2015 than in 2013 [47.9% vs. 77.5%, 26.5% vs. 57.2%, and 52.1% vs. 80.7%, respectively].

3.5. Confidence on use of biosimilars

Finally, the majority of participants felt more confident to prescribe and use biosimilars [28.8% totally confident, 17.8% very confident, 33.9% confident enough] as compared with 2013 [5.0% totally confident, 7.6% very confident, and 26.4% confident enough, Figure 2].

4. Discussion

The introduction of biosimilars in the IBD field generated a series of concerns, probably due to the novelty of the topic and the development of a knowledge gap between experts close to the institutions and practicing physicians. Furthermore, the concerns about immunogenicity and safety, as well as about the concept of extrapolation across indications generated quite conservative positions among scientific societies.[10–13]

The introduction of the first infliximab biosimilars on the European market, leading to a hand-on experience, rapidly followed by the publication of a clinical practice series in IBD dramatically modified the state of mind of European IBD physicians, as shown by our survey of ECCO members. Generally, compared with 2013, we found that almost double the proportion of responders were in favour of increasing the use of biosimilars, with limited concerns about their safety. This evaluation represents a complete reversal of the physicians' position since 2013. However, IBD specialists still do not consider biosimilars as 'generic drugs' that can be automatically substituted by non-physicians. They also consider educational activities on biosimilars fundamental, although they consider the need for guidelines, rules, and registries has dramatically decreased in the last 2 years, revealing again more confidence in the use of biosimilars.

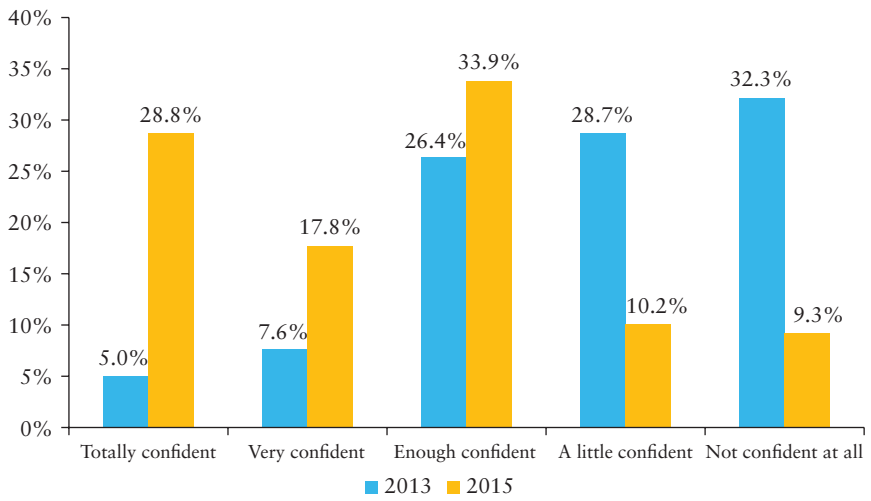

Figure 2. Differences in confidence rates in 2013 and 2015.

We conclude that, in two years, the opinion of IBD experts on the use of biosimilars has dramatically changed to a favourable and confident position. Increased knowledge from postgraduate education and published evidence from clinical practice are probably the main reasons for this change of mind.

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Conflict of Interest

Silvio Danese: Schering-Plough, Abbott Laboratories, Merck, UCB-pharma, Ferring, Cellerix, Millenium Takeda, Nycomed, Pharmacosmos, Actelion, Danone, Alpha Wasserman, Genentech, Grunenthal, Pfizer, Astra Zeneca, Novo Nordisk, Cosmo Pharmaceuticals, Vifor, and Johnson & Johnson; Gionata Fiorino: MSD, AbbVie, Takeda, Janssen, Mundipharma, Sandoz, Pfizer; Pierre Michetti: AbbVie, AstraZeneca, Calypso, Diagnoplex, MSD, Takeda, UCB, and Vifor.

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Author Contributions

Silvio Danese and Pierre Michetti designed the study and collected the data; Gionata Fiorino analysed the data and drafted the manuscript; Silvio Danese and Pierre Michetti critically revised the manuscript; all authors approved the final version of the manuscript.

Supplementary Data

Supplementary data to this article can be found at *ECCO-JCC* online.

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