



Viewpoint: Knowledge and viewpoints on biosimilar monoclonal antibodies among members of the European Crohn's and Colitis Organization



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Abstract

Background: Recently, two infliximab biosimilar monoclonal antibodies (mAb) have been approved by the European Medical Agency for all immune-mediated inflammatory diseases (IMID), including inflammatory bowel disease (IBD). Current knowledge regarding biosimilars among gastroenterologists and in particular among IBD specialists is unknown. Therefore we developed a web survey to evaluate the awareness of biosimilar mAb among IBD specialists and their readiness to use these therapies.

Methods: A 15-question multiple choice anonymous web survey was conducted with the logistic support of ECCO, with questions covering the most relevant aspects on biosimilars. Randomly selected ECCO members were invited by e-mail to participate. A descriptive analysis of responses was performed and analyzed.

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1 . Introduction

Recently, two infliximab biosimilar monoclonal antibodies (mAb) have been approved by the European Medical Agency for all immune-mediated inflammatory diseases (IMID),

including inflammatory bowel disease (IBD).^{1,2} Current knowledge regarding biosimilars among gastroenterologists and in particular among IBD specialists is unknown. Therefore we developed a web survey to evaluate the awareness of biosimilar mAb among IBD specialists and their readiness to use these therapies.

A 15-question multiple choice anonymous web survey was conducted with the logistic support of ECCO, with questions covering the most relevant aspects on biosimilars, between October 20th and November 30th, 2013 (Supplementary Table 1). One thousand randomly selected ECCO members

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were invited by e-mail to participate. A descriptive analysis of responses was performed and analyzed.

A total of 307 IBD specialist responded to the survey, of whom 87% autonomously prescribed mAb for >2 years.

2. General aspects of biosimilars

The majority of respondents (70%) were aware that a biosimilar is a similar copy, but not equal to the originator, 19% responded that it is a copy of a biological agent, identical to the originator (like a generic), with a further 8% confusing a biosimilar with a different anti-TNF agent, like adalimumab to infliximab.

Most responders regarded cost-sparing (89%) as the main advantage of biosimilars. When questioned regarding the impact of biosimilars on healthcare costs, 50% agreed that biosimilars can significantly reduce them, whereas 27% expected biosimilars to have only a marginal impact, 6% expected the additional costs of introduction, regulation and pharmacovigilance to offset any potential savings, with 16% conceding they did not know.

The responders ranked as the main issue of biosimilars a different immunogenicity pattern than the originator (67%), while only 6% of respondents stated that there are no additional issues.

Responding whether biosimilars can present differences as compared to other biosimilars (such as erythropoietin and growth factors), 62% agreed that mAbs are more complex than other biosimilars, thus with higher risks of them not being similar enough, 54% noted a requirement for more accurate postmarketing pharmacovigilance, and 65% for well-designed trials with validated endpoints in each medical specialty.

3. Traceability and regulatory issues

Concerning traceability, 67% agreed that biosimilars should carry distinct International Nonproprietary Names (INN). An overwhelming majority was against autonomous replacement of the originator with a biosimilar (64%) by a pharmacist, while 18% would agree on such substitution only for new prescriptions.

Most clinicians believed that medical societies should promote information about biosimilars (66%), collaborate with health institutions on the development of rules on the use of biosimilars (78%), verify and disseminate data regarding the registration process for biosimilars (61%), develop multi-specialty practice guidelines (57%), and create multi-specialty international safety registries to monitor safety and effectiveness (81%).

Most responders (73%) thought that patient organizations should be involved in these processes and 40% of respondents said that there should be joint position statements by physicians and patients' associations to regulators. However, 22% believed that this was a matter for expert physicians and regulatory agencies only.

4. Extrapolation across indications

Based on the demonstration of equivalence between a biosimilar and its originator in one randomized trial in RA, in terms of safety and efficacy, 24% of responding ECCO

members agreed that the tested biosimilar mAb could then be approved for all indications for which the originator is approved, 19% agreed that the tested biosimilar mAb could then be approved for all rheumatologic indications, 14% for RA only, 3% stated that all biosimilars could be approved for all indications of the given originator, with 39% disagreeing with all of the above. In particular, concerning IBD, if one RCT showing equivalence between a biosimilar and originator mAb is available for induction and maintenance of remission in CD, 53% would use it only in CD, 16% would also use it in UC for induction and maintenance, with 30% answering that they would wait for more evidence of biosimilarity in both diseases.

5. Interchangeability

Only 6% of responders thought that the originator and biosimilar mAb were interchangeable, although 28% would consider replacing scheduled originator therapy with a biosimilar. Though, when clinicians were asked, in the case of an IBD patient in prolonged remission under an originator mAb, to continue the scheduled therapy with a biosimilar, 63% disagreed due to a lack of disease-specific evidence of interchangeability, 22% agreed but stated that they would provide detailed information to their patient regarding the limited data on the safety of the biosimilar, 8% disagreed based on the results of the SWITCH study between infliximab and adalimumab, and 6% said the two molecules are interchangeable.

Finally, when asked if they would feel confident in prescribing biosimilars to their patients, most (61%) felt little or no confidence in using biosimilars in their everyday clinical practice, 26% felt confident enough to use biosimilars, 8% were very confident, and 5% were totally confident.

6. Discussion

Our survey showed that most IBD experts have a good understanding of the definition of biosimilars. However, there is still a proportion of IBD specialists with a misconception of these molecules, viewing them as "generic" copies of original biological agents, or as additional follow-on agents of the class of their originators.

Biosimilars are expected to be cost-sparing for 90% of respondents, but only half of them believe in a significant reduction in healthcare costs, and 15% remain dubious on this aim. Immunogenicity remains the major concern for the majority of respondents, who claim due to this reason for pharmacovigilance and postmarketing measures to monitor equivalence in terms of safety of biosimilars compared with originator. This monitoring demand that the nomenclature allows for each biosimilar to be distinguished from its originator, by carrying distinct International Nonproprietary Names, by an accurate postmarketing pharmacovigilance for each product, and by well-designed trials with validated endpoints in each medical specialty is also required. The majority of responders expect a primary role for medical societies to improve knowledge, to develop appropriate guidelines and pharmacovigilance registries, and to collaborate with

patients' association to clarify unmet needs in the use of biosimilars.

Extrapolation of data across indications and interchangeability between biosimilar and originator remain key issues.³ The majority of respondents are reluctant to accept data from clinical trials conducted in rheumatologic indications^{4,5} as valid for IBD and wish to base their opinion on disease-specific evidence. Similarly, less than 10% would replace the originator with a biosimilar for a patient already under treatment, while 25% would consider interchangeability only for new prescriptions. At the moment, confidence in prescribing biosimilars in IBD remains low among clinicians, although they seem to be adequately informed. IBD-specific data on the comparison for efficacy, safety, and immunogenicity are thus urgently needed.

Contributor

All authors have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and (3) final approval of the version to be submitted. The manuscript, including related data and tables, has not been previously published and is not under consideration elsewhere.

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Conflict of interest

Silvio Danese has served as a speaker, consultant and advisory board member for Schering-Plough, Abbott Laboratories, Merck

& Co., UCB Pharma, Ferring, Cellerix, Millenium Takeda, Nycomed, Pharmacosmos, Actelion, Alpha Wasserman, Genentech, Grunenthal, Pfizer, Astra Zeneca, Novo Nordisk, and Johnson & Johnson; I.O. has received advisory/speaker honoraria from AbbVie, Roche, MSD, Novartis, and Pfizer; Gionata Fiorino served as a consultant and a member of Advisory Boards for MSD, Takeda Pharmaceuticals, AbbVie, and Janssen Pharmaceuticals; and Pierre Michetti received consulting fees and was a member of the speaker bureau for AbbVie, MSD, and UCB. He received unrestricted research grants from MSD and UCB.

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