SPECIAL REPORT

Building stakeholder confidence in biosimilar medicines through evidence-based information sharing

Assistant Professor Gianluca Trifirò[1,2], MD, PhD

The European Commission held a stakeholder event to discuss biosimilar medicinal products in May 2017. A session on building stakeholder confidence in biosimilar medicines provided an update of the latest available clinical experiences with biosimilar medicines, focusing on switching between biological medicines and interchangeability. Assistant Professor Gianluca Trifirò from the University of Messina, Italy, discussed these issues from the perspective of physicians in Italy.

Keywords: Biosimilar, best practice, interchangeability, pharmacovigilance, switching

Introduction

As both clinical experience and real-world evidence increases, knowledge sharing and identifying best practices can support the appropriate use of biologicals, including biosimilar medicines. Gianluca Trifirò, Assistant Professor of Pharmacology at the University of Messina and a Clinical Pharmacologist in the Unit of Clinical Pharmacology of the Academic Hospital 'G. Martino' of Messina, Italy provided an update of the latest available clinical experiences with biosimilar medicines in Italy, focusing on switching between biological medicines and interchangeability. He provided clarity on the European Crohn's Colitis Organisation (ECCO) position on the use of biosimilars for inflammatory bowel disease (IBD) and discussed the challenges ahead [1, 2].

EC stakeholder event

The European Commission (EC) held a stakeholder event to discuss biosimilar medicinal products in May 2017. A session on building stakeholder confidence in biosimilar medicines at this event provided an update of the latest available clinical experiences with biosimilar medicines, focusing on switching between biological medicines and interchangeability.

Professor Trifirò discussed the issue of stakeholder confidence from the perspective of physicians in Italy. He reported the results of a survey of 816 Italian physicians including their experience with regional or national drug policies and how this has affected their prescribing behaviour.

In addition, Professor Trifirò presented the conclusions of an updated position statement from ECCO on the use of biosimilars for IBD. He concluded his presentation by looking at the future challenges facing biosimilar uptake in Italy and worldwide and how these challenges should be met.

Italian physician survey

Professor Trifirò presented the results of a survey involving 816 physicians in Italy [3] and which was coordinated by *Cittadinanzattiva* that is a non-profit organization which is aimed at promoting civic participation and protection of citizens' rights in Italy. The survey questionnaire was developed in a roundtable with representatives of several Italian scientific societies and patient and physicians organizations. The same roundtable participants distributed the survey questionnaire electronically using the web platform 'esurveypro' through a dedicated link through mailing, newsletter, Internet and participation at events and conventions.

The physicians, who worked across a range of specialties, see Table 1, were asked whether the way that they prescribe medicines was influenced by regional or national drug policies.

Physicians were asked whether they had ever prescribed a medicine that they did not consider was the best available option in order to conform to regional or national drug policies, see Figure 1, there was no response for 'Always'.

ECCO position statement on the use of biosimilars for IBD

Professor Trifirò presented a position statement on the use of biosimilars for IBD released in 2017 by ECCO [1, 2]. The statement is the result of a consensus meeting held on 15 October 2016 and is based on the current regulatory guidance from the European Medicines Agency and evidence about efficacy and safety of biosimilars in IBD patients, see Box 1.

Future challenges

Several challenges for the future of biosimilars were identified. Establishing an effective system of pharmacovigilance will be key. The first challenge highlighted by Professor Trifirò will be to explore comparative long-term safety and effectiveness of first generation biosimilars thanks to data that have been cumulated over time.

Table 1: Clinical specialties in a survey of 816 physicians in Italy

Disease area	% of physicians
Rheumatology	28.37
Nephrology	15.34
Diabetes	6.84
Endocrinology	6.51
No specialization	5.30
Gastroenterology	1.32
Oncology	0.88
Dermatology	0.66
Other	34.77

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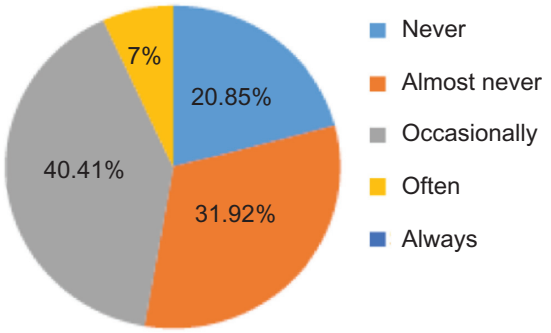
Figure 1: Physicians' views on how regional/national drug policies affect their prescribing

Q: Have you ever prescribed to your patient a medicine which you did not consider the best available option, only to be in line with regional or national drug policies?



Box 1: ECCO 2017 position statement on the use of biosimilars for inflammatory bowel (IBD) disease [2]

1. Biosimilarity is more sensitively characterized by performing suitable *in vitro* assays than clinical studies.
2. Clinical studies of equivalence in the most sensitive indication can provide the basis for extrapolation. Therefore, data for the usage of biosimilars in IBD can be extrapolated from another sensitive indication.
3. When a biosimilar product is registered in the European Union, it is considered to be as efficacious as the reference product when used in accordance with the information provided in the Summary of Product Characteristics.
4. Demonstration of safety of biosimilars requires large observational studies with long-term follow-up in IBD patients. This should be supplemented by registries supported by all involved stakeholders [manufacturer, healthcare professionals and patients' associations].
5. Adverse events and loss of response due to immunogenicity to a biological drug cannot be expected to be overcome with a biosimilar of the same molecule.
6. As for all biologicals, traceability should be based on a robust pharmacovigilance system and the manufacturing risk management plan.
7. Switching from the originator to a biosimilar in patients with IBD is acceptable. Studies of switching can provide valuable evidence for safety and efficacy. Scientific and clinical evidence is lacking regarding reverse switching, multiple switching and cross-switching among biosimilars in IBD patients.
8. Switching from originator to a biosimilar should be performed following appropriate discussion between physicians, nurses, pharmacists and patients, and according to national recommendation. The IBD nurse can play a key role in communicating the importance and equivalence of biosimilar therapy.

As experience with biosimilars grows, it will be important to evaluate clinical effects of switch between originator and biosimilars and vice versa, and between different originators.

Alongside these challenges, the secondary use of healthcare databases for post-marketing surveillance needs to be considered also for second-generation biosimilars in cancer patients.

While promoting the use of low cost biologicals, warned Professor Trifirò, prescribing biologicals wisely remains the highest priority over cost considerations. Every stakeholder (payers, healthcare professionals, patients) needs to be involved in the collection of real-world evidence about biosimilars that has to be integrated with pre-marketing evidence from randomized clinical trials [4].

Professor Trifirò concluded by noting that, given the growing number of biosimilars to be marketed in the near future across several different therapeutic areas, an international post-marketing surveillance system specifically for biosimilars must be established [5].

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