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Letters to the Editor

Biosimilar therapy for inflammatory bowel disease

Key words: Inflammatory bowel disease. Biosimilar. EMA. SEPD.

Dear Editor,

We refer to the position statement of the Spanish Society of Gastroenterology (SEPD) and the Spanish Society of Pharmacology (SEF) published in your journal by Argüelles-Arias et al. (1). The SEPD/SEF position paper contains nine final statements. Most of them can be fully endorsed, since they just echo the current standard regulatory recommendations for the development of biosimilars (BS) in the European Union (EU) (Statements 1-3 and 8) (2-7) and the Spanish legal framework for the prescription and dispensing of this type of drugs, which explicitly impedes any automatic substitution strategy for all biological medicinal products, including BS (Statements 5 and 7) (8). Indeed, and regarding statement 6, it is worth to mention that recently the EU law (9) has established that biological medicinal products must be prescribed by brand name, with the intention to impede substitution practices and ensure traceability.

The undersigned would like however to express our disagreement and our concern with the statement number 4: *As with originals, in order to obtain a given indication a biosimilar should be tested in a clinical trial specifically designed to that end.*

The aim of a BS development program is to establish similarity between the reference product (RP) and the BS, and not to demonstrate the clinical benefit of the biosimilar, since this has already been established for the RP. Regulatory requirements for the development of a BS demand a comprehensive and stepwise comparability exercise including physicochemical characterisation, biological activity, pharmacokinetics, safety and drug effect (2,5). This demonstration requires the use of the most sensitive studies and variables for each comparison. In terms of clinical data, it is widely accepted that pharmacodynamics/pharmacokinetics evaluations using biomarkers are much more sensitive approaches to detect differences between a BS and its RP that any clinical study aiming at therapeutic equivalence (10). In this regard, it is hard to conceive that two biological products showing similarity across a comprehensive non-clinical and clinical data-package will behave dissimilarly in an insensitive therapeutic clinical study aiming to show therapeutic equivalence. This line of thinking is the cornerstone behind the revision of the BS regulatory background that is taking place worldwide and that has lead to an in depth revision of the EU regulatory recommendations (2-7). The key idea underlining the assessment of biosimilarity is based on the evaluation of the totality of data, non-clinical and clinical, guarantying an acceptable level of similarity between BS and RP. Indeed, and since validated biomarker may not be available for some clinical conditions, EU requirements establish as a rule that at least one clinical study aiming to show equivalence between the BS and the RP should be conducted. Changing the regulatory requirements by demanding further therapeutic equivalence in all indications is considered today at best inefficient and at worst ethically questionable.

Questioning the marketing authorization conditions of an approved drug based on non-scientifically driven concerns is not considered the right strategy to protect patients, but rather a way to introduce alarm and confusion. BSs can be prescribed by the physicians with full confidence in all the approved indications and according to their labeling.

We would like to emphasize however, in line with the authors of the Position Statement, that BSs are entirely different from chemical generics. BS medicinal products are obliged to develop a full pharmacovigilance and risk management programs in order to ensure a proper safety signal detection system for each of them individually considered. These measures require full traceability and are not compatible with substitution policies without medical supervision. This must be our primary concern as physicians responsible for the consequences of our therapeutic decisions.

Supporting the current legal framework that impedes substitution policies is much more efficient to protect patients rather than questioning regulatory decisions.

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