

THE EVOLVING BIOSIMILAR LANDSCAPE: APPROVAL OF THE FIRST ETANERCEPT BIOSIMILAR IN EUROPE AN INTERVIEW WITH EMILIO MARTÍN-MOLA

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ABSTRACT

On January 14th 2016, SB4 (Benepali®) received marketing authorisation application approval from the European Commission (EC). It is the first biosimilar to etanercept available in Europe as well as the first subcutaneous anti-tumour necrosis factor biosimilar. Benepali® was approved for the treatment of rheumatoid arthritis, psoriatic arthritis, axial spondyloarthritis (ankylosing spondylitis and non-radiographic spondyloarthritis), and plaque psoriasis.

SB4 adds to the available biologic armamentarium of biosimilars in rheumatology, which also includes two infliximab biosimilars; one under the brand names Remsima® and Inflectra®, and the other under the brand name Flixabi®. Unlike infliximab biosimilar, which is a chimeric monoclonal antibody, SB4 is a fusion protein.

We aimed to review the current European Medicines Agency (EMA) requirements for the approval of biosimilars and how these products can integrate into daily clinical practice in rheumatology.

To that effect, we recently discussed with Dr Emilio Martín-Mola about the European framework for approval of biosimilars and the controversies that may surround this new category of medicinal products. We discussed how the advent of biosimilars in rheumatology has the potential to truly be a game-changer for both physicians and patients.

Keywords: Biosimilars, biologics, disease-modifying anti-rheumatic drugs (DMARDs), SB4 (Benepali®), etanercept (Enbrel®), rheumatoid arthritis (RA), psoriatic arthritis (PsA), axial spondylitis, plaque psoriasis (PP), European Medicines Agency (EMA).

About Dr Emilio Martín-Mola

- Dr Emilio Martín-Mola is Head of the Rheumatology Unit at Hospital Universitario La Paz, Madrid, Spain.
- He has more than 35 years of experience in rheumatology, following a doctorate degree *cum laude* from the Faculty of Medicine of the University of Navarra, Pamplona, Spain.
- He is a member of various national and international scientific societies, including past tenures as President of the Spanish Society of Rheumatology (SER) and Executive Committee member and Treasurer of the European League Against Rheumatism (EULAR).
- Dr. Martín-Mola has authored more than 300 scientific articles for international journals and participated in EULAR consensus documents for the diagnosis and treatment of rheumatoid arthritis and osteoarthritis.



INTRODUCTION

In 2013, the European Commission (EC) approved CT-P13 (Remsima®/Inflectra®) as the first biosimilars to the reference infliximab (Remicade®). CT-P13 is the first monoclonal antibody (mAb) biosimilar approved by the EC (Table 1).^{1,2}

Likewise, on January 14th 2016, SB4 (Benepali®) received marketing authorisation application (MAA) approval from the EC following a positive opinion from the Committee for Medicinal Products for Human Use of the European Medicines Agency (EMA) in November 2015. Benepali® is the first biosimilar to etanercept available in Europe, as well as the first subcutaneous anti-tumour necrosis factor biosimilar.^{3,4}

Benepali® was approved for the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA),

axial spondyloarthritis (ankylosing spondylitis [AS] and non-radiographic axial spondyloarthritis [nr-axSpA]), and plaque psoriasis (PP). This MAA applies to all 28 European Union (EU) member states as well as Norway, Iceland, and Liechtenstein.

Since the biologic armamentarium in rheumatology is rapidly expanding with these successive approvals of biosimilars, here we aim to review the current EMA requirements for the MAA of biosimilars and how these products can integrate into daily clinical practice in rheumatology.

To that effect, we recently discussed with Dr Emilio Martín-Mola about the European framework for biosimilar approval and the controversies that may surround this new category of medicinal products. We discussed how the advent of biosimilars in rheumatology has the potential to truly be a game-changer for both physicians and patients.

Table 1: Current biosimilar landscape in Europe for the treatment of rheumatic diseases.¹⁻⁵

INN (Reference drug name)	Chemical structure	Mode of administration	Biosimilar brand name	Indications	MAA holder	EMA status
Etanercept (reference medicinal product, Enbrel®)	Human TNF receptor p75 Fc fusion protein produced by recombinant DNA technology in a CHO mammalian expression system	Subcutaneous (pre-filled syringe or pen)	Benepali® (SB4)	<ul style="list-style-type: none"> RA PsA axSpA (AS and nr-axSpA) PP 	Samsung Bioepis	Approved MAA on 14 th January 2016 ⁵
Infliximab (reference medicinal product, Remicade®)	Chimeric human-murine IgG1 mAb produced in murine myeloma cells by recombinant DNA technology	Powder for concentrate for solution for infusion	Remsima® (CT-P13)	<ul style="list-style-type: none"> RA AS CD/UC (adult and paediatric) 	Celltrion Healthcare	Approved MAA on 10 th September 2013
			Inflectra® (CT-P13)	<ul style="list-style-type: none"> PsA PP 	Hospira UK Limited	Approved MAA on 10 th September 2013
Infliximab (reference medicinal product, Remicade®)	Chimeric human-murine IgG1 mAb produced in CHO cells by recombinant DNA technology	Powder for concentrate for solution for infusion	Flixabi® (SB2)	<ul style="list-style-type: none"> RA AS CD/UC (adult and paediatric) PsA PP 	Samsung Bioepis	Approved MAA on 30 th May 2016

AS: ankylosing spondylitis; axSpA: axial spondyloarthritis; CD/UC: Crohn's disease/ulcerative colitis; CHO: chinese hamster ovary; IgG1: immunoglobulin G1; INN: international non-proprietary name; MAA: marketing authorisation application; mAb: monoclonal antibody; nr-axSpA: non-radiographic axial spondyloarthritis; PP: plaque psoriasis; PsA: psoriatic arthritis; RA: rheumatoid arthritis; TNF: tumour necrosis factor.

Box 1: How are biosimilars defined? Key characteristics of biosimilars.

- A biosimilar is a **biological medicinal product** that contains a version of the active substance of an already authorised original biological medicine (the ‘reference medicinal product’).⁶
- The World Health Organization (WHO) defines biosimilars as “**biotherapeutic products that are similar in terms of quality, safety, and efficacy to an already licensed reference biotherapeutic product.**”⁷
- After the **expiration of the patent** period (usually 20 years after filing date of the patent application) of a licensed reference medicinal product, biosimilars can be marketed following a positive assessment of a marketing application by the European Medicines Agency (EMA).
- Available biosimilars in rheumatology are administered either through **intravenous infusions** or **subcutaneous injections**, since biological disease-modifying anti-rheumatic drugs (DMARDs) cannot be administered orally. Enzymes in the stomach degrade proteins.
- Since biosimilars are biologics, they inherit the variability of any biologic. This means that even minor changes in the manufacturing process may alter their biological function and/or immunogenicity profile. EMA takes rigorous measures to guarantee this will have no meaningful clinical impact.
- Post-translational alterations can occur in both reference medicinal products and biosimilars due to the use of different cell lines and manufacturing processes, resulting in products that are highly similar, but not identical.⁸
- As per EMA guidelines, a biosimilar must demonstrate **biosimilarity** based on a comprehensive comparability analysis to the reference medicinal product for the following criteria: quality characteristics, biological activity, safety, and efficacy.⁹
- The pre-authorisation procedures ensure that **the differences between the reference medicinal product and the biosimilar have no relevant impact on safety or clinical efficacy.**⁹

Box 2: How do biosimilars differ from generics?

- Due to their complexity in production and the nature of the products, biosimilars cannot be compared to generic drugs.
- Indeed, a generic drug is usually a chemical compound that is very easy to synthesise by pharmaceutical companies. On the contrary, a biosimilar is a biological product, usually a protein with a much **higher molecular weight** (200–1,000 times the size of a chemical compound).¹⁰
- As opposed to chemically-synthesised medicines, biologics and biosimilars are manufactured in **living cells**, extracted, then purified, which complicates the manufacturing processes and large-scale production.^{11,12} Furthermore, the conformational structure of a protein is fragile, requiring special handling and storage to reduce the risk of adverse events and immune responses.

INTERVIEW WITH DR EMILIO MARTÍN-MOLA

Caroline Charles (CC): Good afternoon Dr Martín-Mola, let us talk on the advent of biosimilars in rheumatology. First, can you elaborate on the process of the clinical development programme of a biosimilar in the European context?

Emilio Martín-Mola (EMM): The clinical development programme of a biosimilar is different from that of a reference medicinal product (Table 2). Specific evaluation pathways for biosimilars have been developed by the EMA.

The EMA defines biosimilars as: “Biological medicinal products that contain a version of the

active substance of an already authorised, original biological medicinal product (reference medicinal product). A biosimilar agent is similar to the reference medicinal product in terms of quality characteristics, biological activity, safety, and efficacy based on a comprehensive comparability exercise.”⁶

EMA guidance documents contain both non-clinical and clinical requirements and all translate into one single objective: to ensure that the biosimilar has no clinically meaningful differences from the originator.

At the inception of biosimilar development is an extensive analytical comparability exercise and characterisation to demonstrate that the biosimilar

is highly similar for all critical quality attributes, for example, in terms of physicochemical attributes and mode of action/non-mode of action-related biological activity. Analytical data are key to establishing biosimilarity, since the conformational structure of a protein influences its binding affinity to the target, thus potentially impacting clinical efficacy and safety.

Manufacturing a biosimilar mainly comprises circular iterations based on non-clinical physicochemical and biological characterisation to refine such structural considerations (Figure 1). The *in vitro* testing steps are usually more extensive than those required for the development of a reference medicinal product, so as to compare the results of receptor binding, cell proliferation, and cell potency assays with the targeted reference medicinal product.

Then, non-clinical animal testing (if needed) can be conducted in order to establish a comparative pharmacokinetics profile, though the latter is usually ascertained in clinical Phase I studies in healthy volunteers or patients. Finally, clinical comparative Phase III studies, namely equivalence design trials, are conducted to establish efficacy and safety comparability with the reference medicinal product in one sensitive indication that has been agreed with the EMA.

Following MAA, pharmacovigilance plans and post-marketing studies are required as they are for the reference medicinal product. These steps aim to detect any late developing adverse events (AEs) and additional immunogenicity aspects.

CC: What evidence is needed for the EMA to grant approval of an advanced biosimilar medicine such as a monoclonal antibody or fusion protein?

EMM: The EMA has published several general and specific guidelines for the development of biosimilars (Table 3). The criteria and processes can be applicable to all biosimilars in development or to a specific therapeutic class (e.g. mAbs). Such a framework is essential to provide manufacturers with guidance to establish similarity in terms of quality, safety, and efficacy. These regulatory pathways and processes are, in my opinion, absolutely acceptable as they are now.

CC: Certain clinicians have expressed some fears over the approval and use of biosimilars in Europe. Why is that and what is your personal opinion on the matter?

EMM: Biosimilars can be confused with what we call 'intended copies' or 'biomimics' that exist in countries with less stringent regulation (i.e. some Latin American countries, India, China).

Table 2: Is the development programme of a biosimilar different from that of its reference biologic? Overview of European Medicines Agency biosimilar regulatory guidelines.¹³⁻¹⁵

Non-clinical aspects	<ul style="list-style-type: none"> • Target binding, signal transduction, functional activity/viability of cells of relevance must be evaluated • If <i>in vitro</i> comparability is satisfactory, animal studies may not be required • Potency must be the same as the reference medicinal product • Route of administration (galenics) must be the same as the reference medicinal product • Higher-order structures, post-translational modifications must be as similar as possible, and demonstrate no impact on the clinical efficacy and safety
Clinical aspects	<p>Comparability confirmed by a stepwise process:</p> <ul style="list-style-type: none"> • Pharmacokinetics: the biosimilar should be used at the same dose as the reference product (Phase II studies are not needed because dose-response was established for the reference product) • Pharmacodynamics (if feasible) • Clinical efficacy and safety (Phase I/III) (in a sensitive indication and sensitive population)
Naming	<ul style="list-style-type: none"> • Commercial name, appearance, and packaging should differ from reference product • INN should be the same for related reference medicinal product
Pharmacovigilance	<ul style="list-style-type: none"> • Risk management pharmacovigilance plan (as for any biologic, i.e. reference medicinal products or biosimilars) must be submitted • Clinical safety monitored closely after MAA approval

INN: international non-proprietary name; **MAA:** market authorisation approval.

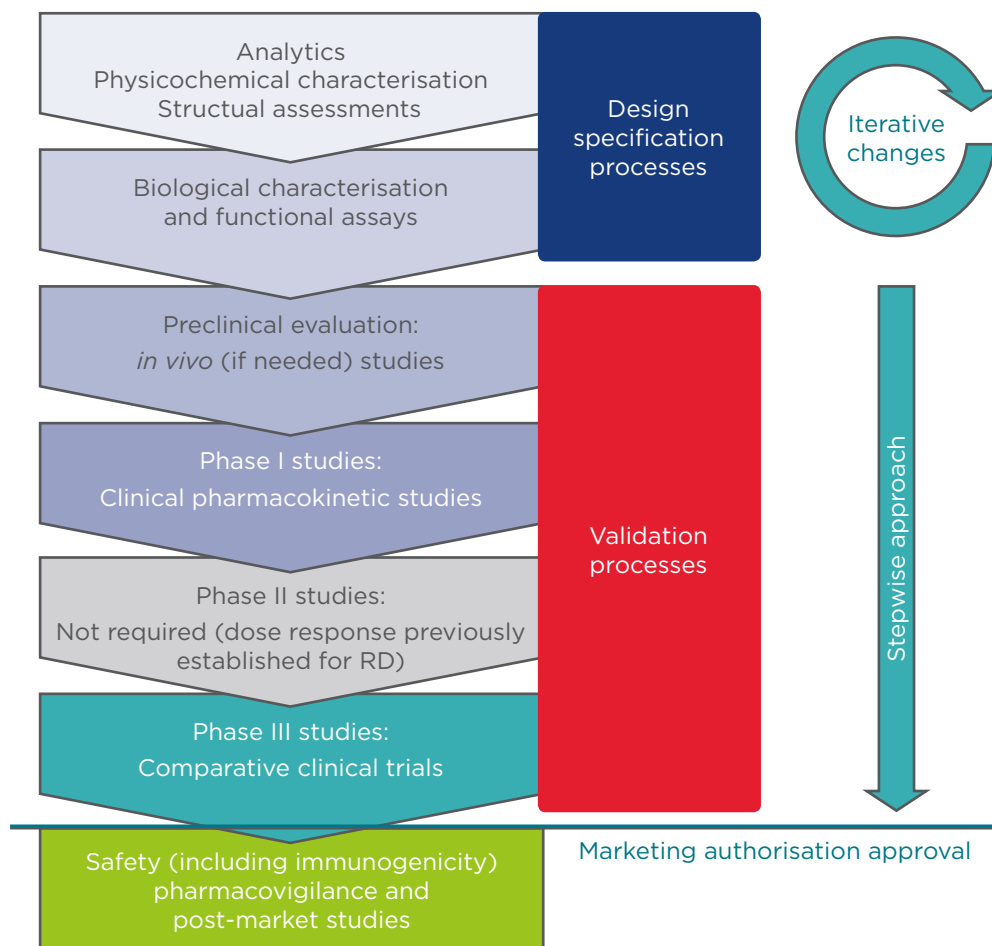


Figure 1: General development steps for biosimilars in Europe.

RD: rheumatic disease.

Modified from McCamish and Woollett.¹⁶

I think that apprehension might stand in some cases for the confusion between copies and biosimilars. But intended copies have nothing to do with biosimilars: copies have been used in Latin American countries for several years prior to the establishment of regulatory guidelines, thus without robust clinical trials and thorough evaluation as we see now for European MAA of biosimilars. Some of the copies are still on the market in some Latin American countries as well as in India and China, and unsurprisingly, local rheumatologists have observed some safety issues.^{14,17}

I believe these fears also come from the fact that studies for biosimilars are often conducted in only one indication, i.e. RA. I can understand how gastroenterologists could be sceptical about the use of a biosimilar in Crohn's disease (CD) when the equivalence studies have been conducted only in RA. On one hand, determination of the key disease in which to conduct a clinical equivalence

or non-inferiority Phase III trial for the development of a biosimilar is a difficult and challenging decision that should be discussed and agreed with the EMA. On the other hand, for a biologic that has several different indications, it is absolutely impossible to conduct many different clinical trials simultaneously.

Extrapolation is a concept adopted by the EMA as part of their biosimilar approval process to respond to this impossibility of conducting, as an example, eight Phase III trials for the approval of an infliximab biosimilar. The rationale set forth by the EMA is that a reference indication can be extrapolated if the mechanism of action for all indications is the same, among several other considerations.⁶ In rheumatology, the reference disease to conduct such studies so far has been RA, but some authors have claimed that other rheumatologic diseases or even plaque psoriasis should be the reference disease for Phase III biosimilar studies.

Table 3: European Medicines Agency Guidelines relevant for biosimilar approval processes in rheumatology.

<p>Overarching biosimilar guidelines (all biosimilar products)</p>	<p>Guideline on similar biological medicinal products⁶ CHMP/437/04 Rev 1 (30 April 2015) http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003517.pdf</p> <p>Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substances: non-clinical and clinical issues¹³ EMEA/CHMP/BMWP/42832/2005 Rev1 (1 July 2015) http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/01/WC500180219.pdf</p> <p>Guideline on similar biological medicinal products containing biotechnology-derived proteins as active substance: quality issues EMA/CHMP/BWP/247713/2012 Rev.1 (1 December 2014) www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2014/06/WC500167838.pdf</p>
<p>Product-specific guidelines</p>	<p>Guideline on similar biological medicinal products containing monoclonal antibodies: non-clinical and clinical issues EMA/CHMP/BMWP/403543/2010 (1 December 2012) www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/11/WC500099361.pdf</p>
<p>Other guidelines relevant for biosimilars</p>	<p>Comparability of biotechnological/biological products ICH Topic Q 5 E CPMP/ICH/5721/03 (June 2005) www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002805.pdf</p> <p>Comparability of biotechnology-derived medicinal products after a change in the manufacturing process: non-clinical and clinical issues EMEA/CHMP/BMWP/101695/2006 (1 November 2007) www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003935.pdf</p> <p>Immunogenicity assessment of biotechnology-derived therapeutic proteins EMEA/CHMP/BMWP/14327/2006 (April 2008) www.emea.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003946.pdf</p> <p>Immunogenicity assessment of monoclonal antibodies intended for <i>in vivo</i> clinical use EMEA/CHMP/BMWP/86289/2010 (1 December 2012) www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/11/WC500099362.pdf</p>
<p>Draft guidelines (under public consultation) relevant for biosimilars</p>	<p>Draft guideline on immunogenicity assessment of biotechnology-derived therapeutic proteins EMEA/CHMP/BMWP/14327/2006 Rev. 1 www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/10/WC500194507.pdf</p> <p>Draft concept paper on the need for a reflection paper on statistical methodology for the comparative assessment of quality attributes in drug development EMA/297149/2013 www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2013/06/WC500144945.pdf</p>

CHMP: Committee for Medicinal Products for Human Use; EMEA: European Agency for the Evaluation of Medicinal Products; BMWP: Biosimilar Medicinal Products Working Party; EMA: European Medicines Agency; CPMP: Committee for Medicinal Products; ICH: International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.

CC: Can you elaborate on the topic of extrapolation?

EMM: The argument that states that the behaviour of the drug should be similar in all the indications is very simple. Extrapolation of safety and efficacy has emerged as an important way to simplify biosimilar development. However, a few issues happened with the biosimilar for infliximab. It was shown that CT-P13 had a lower *in vitro* antibody-

dependent cell-mediated cytotoxicity (ADCC). That was the only difference between the reference product and this biosimilar.

The EMA did not consider this difference relevant and extrapolated the indications of this biosimilar to inflammatory intestinal diseases. However, the EMA required that the company perform a randomised double-blind study in patients with CD

and a prospective observational study to assess the effectiveness and safety of this drug in CD and ulcerative colitis (UC).

Initially, Health Canada, the regulatory agency from Canada, based on these *in vitro* studies, did not approve the extrapolation for inflammatory intestinal diseases. However, following a review of additional data, Health Canada very recently approved the infliximab biosimilar Inflectra in three extra indications, namely CD, fistulising CD, and UC.¹⁸

Furthermore, both the US Food and Drug Administration (FDA) and the Australian regulatory agency, the Therapeutic Goods Administration (TGA), recently approved the extrapolation for the same diseases that the EMA did.^{19,20}

CC: How do you see this evolving?

EMM: Eventually, clinicians will overcome these unfounded concerns. Once a drug has been approved by the EMA as a biosimilar, there is no reason not to be confident with it, because the steps and the regulatory processes are both

numerous and stringent, and ensure security of use. I think those fears stem from a lack of education in the process of biosimilar approval: specialists in Europe should be better informed about the processes and the numerous steps and checkpoints set in place to ensure biosimilar quality, efficacy, and safety.

Of course, we also have to keep in mind that over time pharmaceutical companies have gained the trust of physicians due to their solid history with the patented originator drug. Some physicians may want to rely on the reference medicinal product, but I think medical education on biosimilars is crucial to making physicians more confident about using biosimilars.

CC: Are there any other topics of discussion on biosimilars?

EMM: Some patients generate an immune response to biologics (characterised by the production of anti-drug antibodies [ADAs]), which can potentially limit clinical efficacy and increase the risk of AEs.

Box 3: Main SB4 clinical and safety data from equivalence study with Enbrel®.

- The clinical and safety outcomes of SB4 were evaluated in a Phase III, randomised, double-blind, parallel-group, multicentre equivalence study,²⁵ which included 596 patients with moderate-to-severe active rheumatoid arthritis (RA) despite methotrexate therapy, randomised 1:1 to receive a weekly dose of 50 mg SB4 subcutaneously (n=299) or etanercept reference medicinal product (n=297).²³
- SB4 resulted in equivalent primary endpoint American College of Rheumatology ACR20 response rates at Week 24 compared to Enbrel®.
- The ACR20 was 78.1% for SB4 and 80.3% for the reference medicinal product (per-protocol patient set from the final analysis set). The 95% confidence interval of the adjusted treatment difference was -9.41% to 4.98%, which was well contained within the predefined equivalence margin of -15% to +15%, indicating therapeutic equivalence between both products. Other efficacy endpoints and pharmacokinetic endpoints were comparable.
- The incidence of treatment emergent adverse events at Week 24 was comparable between both arms (55.2% in SB4 versus 58.2% in Enbrel®). Both drugs were well tolerated.
- The immunogenicity profiles appeared to be significantly different (incidence of anti-drug antibody development up to Week 24 was 0.7% versus 13.1% in SB4 compared with etanercept), but according to the European Public Assessment Report (EPAR), this was considered to have minimal clinical significance.⁴
- After a 52-week follow-up, the ACR20 response rate was 80.8% in the SB4 arm and 81.5% in the reference medicinal product arm.²⁶ The safety and efficacy of continuing SB4 and transitioning from reference etanercept to SB4 was evaluated in an open-label, 48-week extension study period. The results were reported at EULAR 2016.²⁷ Data showed comparable safety, immunogenicity, and efficacy between patients who continued receiving SB4 and those who transitioned from the reference product to SB4. SB4 was well-tolerated and effective over the 2-year period in patients with moderate-to-severe RA. This 48-week extension transition study provided clear evidence that switching from reference etanercept to SB4 produced no new treatment emergent issues, such as an increase in adverse events, an increase in immunogenicity, or loss of efficacy. These and other coming data will further increase our knowledge and confidence of switching patients from reference products to biosimilars.^{27,28}

Immunogenicity is a crucial issue for all biologics; any therapeutic protein injected in the body can be immunogenic. These ADAs can be neutralising (i.e. suppress the drug's activity by competing with the binding site for tumour necrosis factor or other targets and lead to a clinical non-response) or non-neutralising (not affecting the drug's efficacy). One of the requirements of the EMA for biosimilar approval is that the biosimilar must have the same or lower immunogenicity profile as the reference medicinal product. Both the etanercept reference medicinal product and SB4 have a low immunogenicity profile with non-neutralising ADAs.

We also have to be careful with interchangeability issues. When a biosimilar is available, patients may be switched from a reference medicinal product to a biosimilar or the other way around. In this context, when a patient is started on a biologic therapy, it would be wise to treat from the beginning either with a biosimilar or a reference medicinal product, because if we interchange therapies and AEs occur, it might be difficult or impossible to establish which of both drugs is responsible. We need safety data of interchangeability and at present, in Norway and Denmark, studies are being conducted on interchangeability safety. Until these data are available to guide us, it could be wise to keep giving the same drug that the patient received since the beginning of treatment. Of note, the Spanish Society of Rheumatology (SER) stated that until pharmacovigilance practices improve, we should be prudent in all decisions related to interchangeability concerns.²¹

I anticipate biosimilars to be integrated into current treatment algorithms just as well as reference medicinal products, and as first-line treatment choices in treatment-naïve patients due to healthcare costs, so as to 'bypass' switching issues right from the start.

CC: Benepali® (SB4) has recently been approved as a biosimilar of etanercept. What data are available to show equivalence to the reference etanercept (Enbrel®)?

EMM: SB4 (Benepali®) is a biosimilar to etanercept reference medicinal product (trade name, Enbrel®) and is produced by recombinant DNA technology in a Chinese hamster ovary mammalian cell expression system. Pharmacokinetic equivalence

was demonstrated in a Phase I study conducted in healthy male subjects.²²

SB4 exhibits similar structural, physicochemical (except for a single amino acid), and biologic properties and has demonstrated therapeutic equivalence to etanercept reference medicinal product.^{4,23,24} The clinical outcomes of SB4 were demonstrated as equivalent to its reference medicinal product, Enbrel®, in a Phase III clinical trial (Box 3).

CC: How will biosimilars, such as Benepali®, be used in rheumatology clinical practice?

EMM: Since etanercept is an excellent drug for RA with a very good track record and is well known by physicians, I think its biosimilar, Benepali®, will be a success and, because of the reduced prices, it will drive down healthcare costs for both patients and healthcare payers. This will undoubtedly increase patient access to biologics and the number of patients receiving a biotherapy in rheumatology will be expanded. This drug should increase the access to biologics in countries where, for economic reasons, there are restrictions to receive biologics.

CC: What benefits will biosimilars bring to rheumatologists? Do you anticipate biosimilars to change the treatment landscape for patients with rheumatic diseases?

EMM: As of now, in Europe, three advanced biosimilars have been approved, but physicians can expect several other biosimilars on the market in the next few years due to the expiration of many patents for biologics, including some used in rheumatic diseases.

I think biosimilars will change the landscape of the management of rheumatic diseases, since these drugs are disease-modifying anti-rheumatic drugs. The introduction of high-quality, well-tolerated, and effective biosimilars has the potential to increase access to biotherapies and, as patients from a wider demographic will receive proper treatment, stringent regulatory pathways will ensure continuity without reducing the quality of care. Since patients with rheumatic diseases are prescribed long-term treatment with individualised drug regimes, biosimilars will undoubtedly change the clinical landscape and help close the affordability gaps of biologics access.

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