A Satellite Symposium
at EULAR 2016
London, UK

Organised by the BIOSIMILAR MEDICINES GROUP

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Biosimilar Medicines for Rheumatologists: Understanding the Science of Extrapolation

Friday 10th June, 08:15–09:45

Capital Suite 09, ExCel London

The Biosimilar Medicines Group, a sector group of Medicines for Europe, acknowledges the financial support of the following member companies in funding this symposium:

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Dear Colleague

It is my pleasure to welcome you to London, and to this educational symposium on

Biosimilar Medicines for Rheumatologists: Understanding the Science of Extrapolation

organised by the **Biosimilar Medicines Group**, a sector group of Medicines for Europe.

Biosimilars have been available in Europe for 10 years, for use in areas such as endocrinology and supportive cancer care. Recently, the European Commission has approved biosimilar products bearing infliximab and etanercept following the European Medicines Agency's positive scientific opinion; these medicinal products are therefore now a reality in rheumatology. A clear understanding of the scientific principles of the biosimilarity concept is important for physicians to make informed treatment choices for their patients. Extrapolation of indications is a key element of the biosimilarity concept, while interchangeability is another 'hot topic' in this area. We have therefore gathered together an impressive faculty to provide you with the latest thinking, from a regulatory, scientific and clinical perspective, on these interesting and important topics. We have ensured that there is ample time in the programme for you to put questions to the faculty, and I encourage you to take advantage of our panel of experts.

Fernando de Mora
Symposium Chair

Biosimilar Medicines for Rheumatologists: Understanding the Science of Extrapolation

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Programme

Welcome and introduction — **5 mins**

Professor Fernando de Mora
Department of Pharmacology, Therapeutics and Toxicology, Autonomous University of Barcelona, Spain

Biosimilars: the science of extrapolation and interchangeability — **30 mins**

Elena Wolff-Holz, MD
Senior Medical Assessor
Paul Ehrlich Institute, Germany
Member of the European Medicines Agency's Biosimilar Medicinal Products Working Party (BMWP) and Oncology Working Party (OWP)

The EULAR position in the making — **20 mins**

Professor Ferdinand Breedveld
Head of Department of Internal Medicine and Rheumatology, Leiden University Medical Centre, The Netherlands
Past-President of EULAR

Panel discussion, Q&A — **30 mins**

Above faculty members plus
Professor Tore Kvien
Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway
Editor of Annals of Rheumatic Diseases

Summary and close — **5 mins**

Professor Fernando de Mora

Fernando de Mora

Department of Pharmacology, Therapeutics and Toxicology
Universidad Autónoma de Barcelona
Spain

Fernando de Mora is Professor of Pharmacology at the Universidad Autónoma de Barcelona, Spain, and also Research Group Leader with an interest in biosimilars and immunopharmacology. He received a first degree and then a PhD from the Universidad Autónoma de Barcelona, followed by a MBA from the University of Chicago (USA). Professor de Mora's career has also included spells at Utrecht University (The Netherlands), Southampton University Medical School (UK) and Harvard Medical School (Boston, USA). He has been heavily involved in the field of biosimilars since 2008, and has been a regular contributor (as an invited speaker/Chair) at many conferences, including the United Nations Biosimilars International Expert Meeting in 2015. His expertise has also been utilised in Scientific Advice meetings with the European Medicines Agency. In addition to his work in the field of biosimilars, Professor de Mora has a long-standing research interest in asthma, allergy and inflammation.

Notes

Elena Wolff-Holz

Paul Ehrlich Institute
Langen
Germany

Dr Elena Wolff-Holz is a Senior Medical Assessor at the Paul Ehrlich Institute. She is also a member of the Biosimilar Working Party (BMWP) of the CHMP and a national expert to the Oncology Working Party (OWP) of the CHMP, where she contributes to the development of guidelines and reflection papers. Overall, Dr Wolff-Holz has 20 years of professional experience, including 14 years in the biotech industry where she held positions in clinical development and medical marketing functions at Centocor Inc (now J&J) and Amgen in the US and Germany, before joining the German national regulatory agency. In the area of biotherapeutics, she is responsible for advising companies on drug development issues, reviewing applications for marketing authorization in the European Union and assessing clinical trial applications. Her work has resulted in several (co-)authorships in scientific journals and several presentations at (inter-)national conferences. She is also a lecturer at Institutes covering training of experts and executives from academia, regulatory bodies and the biopharmaceutical industry. Dr Wolff-Holz is a physician by training, with an M.D. degree from Heidelberg University and a postdoctoral fellowship at Harvard Medical School.

Biosimilars: the science of extrapolation and interchangeability

In Europe, biosimilars have to demonstrate comparability in an extensive biosimilarity exercise including analytical, preclinical and comparative clinical studies. By successfully completing the biosimilarity exercise, the biosimilar shows that all aspects considered relevant for the clinical activity of the product fall within the same range as observed for the innovator.

Various learned societies have taken the position that extrapolation of indications should never be allowed and that clinical data should be required for all indications. Distrust in biosimilars is voiced especially in therapeutic indications for which no specific clinical trials with the biosimilar have been performed and which have been licensed based on extrapolation of efficacy and safety data from other indications.

However, from a scientific and regulatory point of view, the active substance of the biosimilar is just another version of the active substance of the originator product. This is important to state because the same scientific principles that underlie the comparability exercise for the purpose of demonstrating similarity of a product before and after a change in manufacturing process also apply to the comparability exercise for the purpose of demonstrating biosimilarity.

In understanding the development and availability of information on biosimilars, physicians must accept a paradigm shift: whereas with newly approved drugs (new biological entities [NBE], originators), all clinical data resulting from the drug development are presented in the Summary of Product Characteristics (SmPC), the development modalities of biosimilars emphasize the sameness of the products on a quality level, complemented by preclinical work (mostly binding and functional assays), with clinical data aimed at only reconfirming the already observed similarity. Therefore, all new information on the development history of a biosimilar, all nonproprietary product information and scientific and regulatory decision making can be found in the European Public Assessment Report (EPARs) of each product, which is openly available on the internet, and not in the SmPC. The SmPC of a biosimilar is a copy of the SmPC of the originator and does not provide further data.

In the last 10 years, clinical and regulatory experience with 20 approved biosimilars in the EU has been obtained and has not necessitated any SmPC label changes for biosimilars. This lends credibility to the scientific basis and quality of current regulatory decision-making in the European Union.

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Ferdinand Breedveld

Department of Internal Medicine and Rheumatology
Leiden University Medical Centre
The Netherlands

Ferdinand Breedveld is Professor of Medicine at Leiden University, a position he has held since 1989. He received his medical training at Leiden University Medical School, and training in internal medicine and rheumatology at the University Hospital Leiden. On completion of his training, Professor Breedveld spent 2 years as a junior faculty member at Harvard Medical School, Boston, USA. From 2006–2015, he was Chair of the board of directors of Leiden University Medical Centre.

Professor Breedveld has authored more than 900 peer-reviewed scientific papers, and is a past and present member of editorial boards of numerous journals: Arthritis & Rheumatism, Annals of Rheumatic Diseases, The EULAR Journal, Journal of Rheumatology, Clinical and Experimental Rheumatology, Clinical Rheumatology, Nature, and Rheumatology. He is a member of several national and international professional societies, and was President of EULAR from 2007–2009.

Biosimilars: the science of extrapolation and interchangeability

Biologic drugs are improving therapeutic options for many diseases but access to these therapies is being held back by costs. This problem is likely to aggravate as growing numbers of biologic therapies enter the market. Biosimilars offer a low-cost alternative to the corresponding Original protein with a comparable quality, safety and efficacy. With the recent introduction of several biosimilars that inhibit TNF, stakeholders are beginning to understand better the basis of biosimilar development on the one hand and the reasons for concern on the other. Rheumatologists will be at the forefront of the use of biosimilars in term of recommendations for use and therefore should understand the difference in development strategies between biosimilars and the original product. Of particular interest to rheumatologists is the policy to allow extrapolation of a biosimilar of infliximab to all indications for which the reference drug is approved despite the fact that clinical studies were not conducted in all indications.

Many European countries and EULAR have published position papers for the use of biosimilars in rheumatological practice. The most prevalent recommendations are:

- Evidence-based information is needed to inform choices. EULAR concluded that there is no difference in the efficacy and toxicity between the presently available TNF antagonists including biosimilars that allow certain preferences
- The patient should be kept informed about which product they are receiving
- Safety and immunogenicity data should be collected following introduction of biosimilars in clinical practice
- Although the concerns regarding extrapolation are hypothetical, several position papers state extrapolation to completely different disease states (IBD, pediatric diseases) should not be performed
- Medical societies and physicians should be in the lead to make therapeutic choices.

European regulators and rheumatological societies were the first to encounter biosimilars and countries worldwide are looking for guidance. Biosimilars offer great advantages to health care but arriving at the best solution for patients will need improved communication between regulators and health professionals.

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Tore Kvien

Department of Rheumatology
Diakonhjemmet Hospital
Oslo
Norway

Tore K Kvien has been Professor of Rheumatology at the University of Oslo since 1997 and Head of the Department of Rheumatology at Diakonhjemmet Hospital, Oslo, Norway since 1994. His current major research activities include epidemiological and health service research, with a focus on frequently occurring diseases such as rheumatoid arthritis, osteoarthritis and spondyloarthritis. Special focus is also directed on complications of rheumatic diseases, for example osteoporosis and cardiovascular morbidity.

Professor Kvien initiated a collaborative project in Norway on very early arthritis and is the leader of the Norwegian NOR-DMARD registry, an observational study of prescriptions of DMARDs and biological agents in Norway. He has published more than 450 original research publications in international peer-reviewed journals, was President of the European League Against Rheumatism (EULAR) from 2005 to 2007 and has been the Editor-in-Chief of *Annals of Rheumatic Diseases* since 2008. He is the principle investigator of the government financed NOR-SWITCH study which started enrolment in October 2014 and completed enrolment in June 2015. The NOR-SWITCH study examines the safety, efficacy and immunogenicity of switching from originator infliximab to biosimilar infliximab in patients with rheumatoid arthritis, spondyloarthritis, psoriatic arthritis, ulcerative colitis, Crohn's disease and chronic plaque psoriasis.

Professor Kvien was awarded ACR Master in 2015 and is honorary member of the Norwegian, Czech and Finnish rheumatology societies.

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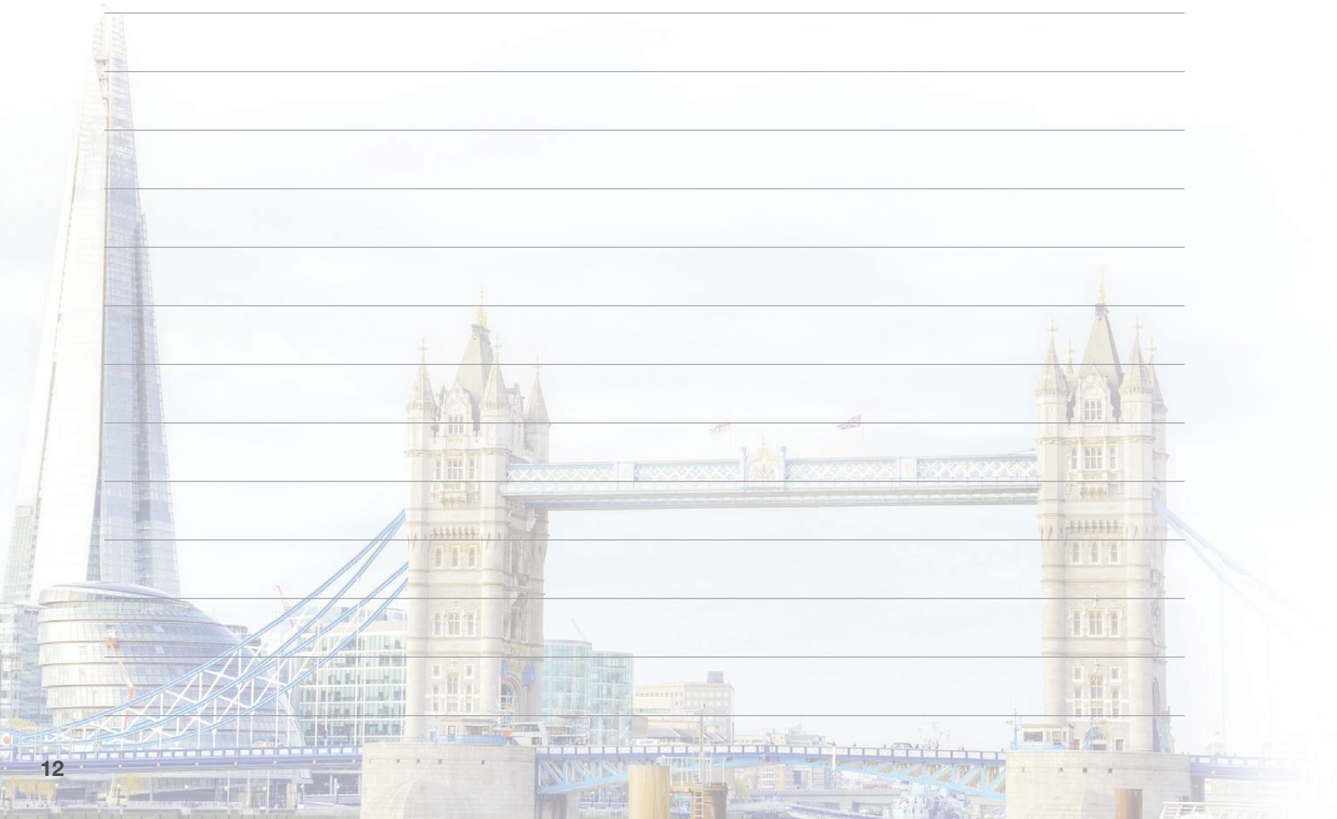

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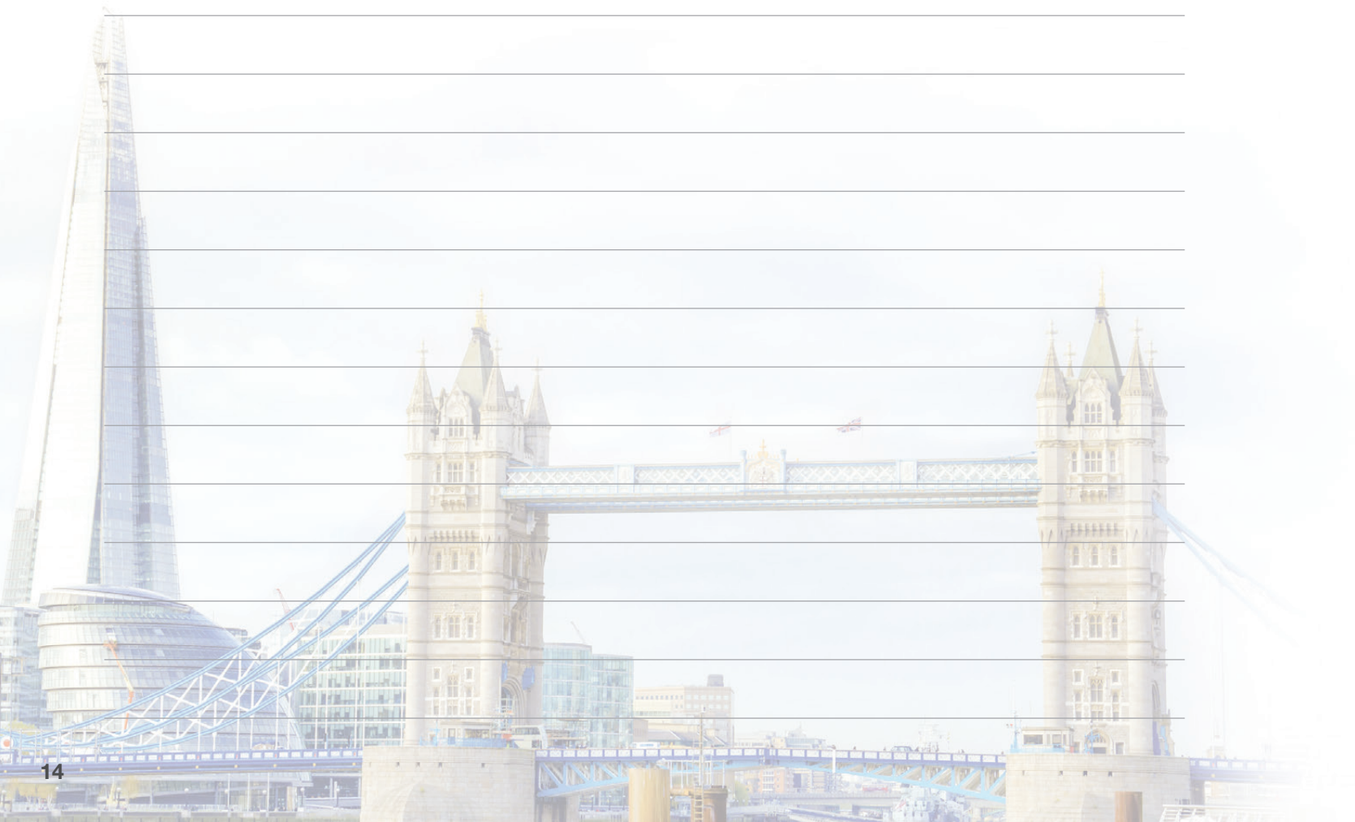

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