Comment on: The Portuguese Society of Rheumatology position paper on the use of biosimilars

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Although based on very well known cellular and molecular targets in chronic inflammatory rheumatic diseases and the proven beneficial effects of the respective monoclonal therapeutic antibodies since more than a decade, antibody-based biosimilars targeting the same proinflammatory effector molecules and cells appear to become the most intensively discussed drugs amongst rheumatologists, basic scientists, health economists, patients, industry and politicians – to some extent their development even divides the discussants in heavily opposing parties[1-9].

The background of these turbulences is multifactorial, ranging from **i)** the interesting scientific question, how "similar" or "identical" a therapeutically used human(ized) therapeutic antibody can be if compared to an originator antibody, given the fact that even the batches of the originator drug vary significantly over the years due to variations in the (mostly improved) production processes, to **ii)** the "natural" expiration of the patents for the originator biologics, which –owing to their therapeutic success- must stimulate pharmaceutical companies to initiate the development of "biologic generics" as performed for chemical drugs on a routine basis, and **iii)** the painful financial restrictions of the health system of several (European) countries[10,11], which demand cheaper drugs to be able to treat more patients according to the state-of-the-art, and **iv)** the subsequently arising question for the licensing application, whether a successful clinical trial of a biosimilar for a given disease can be extrapolated to other disease entities without performing further clinical trials, to **v)** the yet unsolved problem of naming the biosimilar with a unique (international nonproprietary) name vs. "established–mab biosimilar" without creating continuous confusion[12].

After successful licensing in several countries around the world, the European licensing authority EMA has recently received the first application for an infliximab biosimilar, which resulted in a positive opinion for application in several inflammatory joint diseases that most likely will be followed by start of marketing in the upcoming year. Facing these developments, the Portuguese Society of Rheumatology has taken the chance (and challenge) to analyze all available data on biosimilars in rheumatic disease, and has formulated several statements that can be regarded pivotal for the European and rheumatologists worldwide with respect to the impact and further use of biosimilars in the daily clinical practice.

When analyzing the decisions and statements of the Portuguese colleagues, especially from a country that still has the luxury of a more or less unrestricted access to biologics, several aspects need to be mentioned and commented.

To position the patient and his or her medical needs on an individual risk-benefit profile and not solely on an economic basis underlines the value of the human being and the general task of the caring physician.

To request clear decision processes and guidelines when applying biologics and biosimilars supports the idea of a clear distinction and positioning of the drug used, even if the biosimilar shows equivalent effects (and side effects such as immunogenicity) in all relevant aspects. Here, it needs to be mentioned that in terms of interchangeability and extrapolation, non-TNF biosimilars might be a completely different story than TNF biosimilars, as could be seen in the varying outcomes of anti-CD20 and Anti-IL-6 originator antibodies in the past years.

The request for monitoring the use and effects of biosimilars in a long-term registry will improve not only the overall knowledge in the field of therapeutic an-

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tibody treatment, as has been demonstrated repeatedly by the expanding national and international databases and registries, but may also result -in favor of the biosimilars- in a decrease in the number of colleagues, who are more or less overtly opposing the use of biosimilars at present.

To conclude form the work of the Portuguese colleagues: Do the current biosimilars work? As far as we know, yes. Do they also work in diseases different from those of the licensing trials? Scientifically that's not fully proven, but given the exchangeability of the current TNF inhibitors, it's quite likely (anti-CD 20 monoclonal antibodies and others might be a completely different story). Will they be successful on the market and accepted by physicians and patients? The potential is there but it might become a long process to a substantial market share, as could be observed for the last generation TNF inhibitors in the past years. Will treatment of RA will become cheaper? As limited resources apply to all countries everybody will hope for that, but time will show how much? Do the "established" TNF--inhibitors will have to fear the biosimilars and vanish from the market (together with their producers)? Although this fear can be "felt" at meetings and symposia – history for other (including high priced drugs) tells otherwise, and may even result in pharma CEO decisions to shift resources to develop innovative novel drugs that will open up unexpected new horizons for all participants. Will rheumatologists agree on the value and position of biosimilars? Sooner or later yes, but it will be different (and sometimes painful) in each rheumatologic "society", so we do have to applaude the Portuguese colleagues for their pivotal move to create an evidence-based position paper and a review paper of all the trials on biosimilars in the field of rheumatology.

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