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Improving the understanding of originator and biosimilar biologics among healthcare providers in Saudi Arabia



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ABSTRACT

The loss of patentability of many originator biologics has led to the rapid introduction of biosimilar agents. The anticipated economic benefit of introducing such agent has been accompanied by vagueness surrounding their biotechnology, approval requirements, positioning in treatment paradigms and potential for adverse events. The Second Symposium on Biologics and Biosimilars “Beyond Clinical Practice” was held on 24th–26th January 2020 aiming at improving the understanding of these new agents in a diverse interactive conference and to guide stakeholders how to introduce biosimilars into clinical practice. The symposium consisted of 4 tracks and 3 workshops. A total of 217 participants attended the meeting. The majority were pharmacists (78.8%) followed by physicians (18.9%) and other healthcare providers (2.3%). The workshops covered the following topics: basics of pharmacoeconomics, pharmacovigilance and patients’ perspective toward biosimilar biologics. While, the 4 main tracks included: Introduction to biosimilars, challenges in clinical practice, regulatory and pharmacoeconomic aspects and Challenges in biosimilar pharmacovigilance.

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1. Introduction

The introduction of biologics has led to a revolution in the care and outcome of diseases in different specialties in the last two decades (Baumgart et al., 2019) with a price of an increased direct cost (Sugiyama et al., 2016). The patentability of widely prescribed biologics has led to the introduction of biosimilars (Schulze-Koops and

Skapenko, 2017; Sharma, 2017). The need to introduce new technology to the healthcare system was driven mainly to reduce the cost of biologics and encourage competition among companies to enter the field of biotechnology (Tariman, 2018).

According to the Food and Drug Administration (FDA), a biosimilar is defined by the as a biological product that is highly similar to and has no clinically meaningful differences from an existing FDA-approved reference product. The FDA only allow minor differences in the clinically inactive components to be accepted.

While the European Medicine Agency (EMA) define it as a biological medicine that is highly similar to another already approved biological medicine (the reference medicine) in the European Economic Area (EEA). Similarities between the biologic and the biosimilar in terms of quality characteristics, biological activity, safety and efficacy must be established in a comparability exercise before its approval.

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On the molecular level, there is a structural difference between biosimilars and generic products. The word 'generic products' can be applied to chemical products and can never be used to describe a biosimilar medication. Generics and biosimilars are different regulatory terminologies used to define and differentiate the registrations pathway of these products. Biosimilars are approved according to different standards of pharmaceutical quality, safety and efficacy that apply to all biological medicines (Kabir et al., 2019).

Although the amino acid sequencing of an originator/reference medicine product and its biosimilar are identical, altered glycosylation and quaternary structure can occur because of different cell line origin and complex manufacturing processes. In order for a biosimilar to be approved products it must include pharmacokinetic (PK) and pharmacodynamics (PD) parameters that are relevant to the licensed use of the originator and this is a part of a step-wise approach to demonstrate its comparability with the originator.

In addition, comparability exercise covers different phases of the product. A major concern of many regulatory authorities is the immunogenicity response coming from the product itself, intrinsic protein or process-related impurities that could lead to the development of antidrug antibodies (ADAs), Companies should be provide strong evidence to provide safety measures to prevent any adverse events in the future (Scavone et al., 2017).

Once a biosimilar reaches phase III evaluation, a single successful randomized clinical trial can be is required to grant extrapolation to all approved indications of the originator. All of these facts have been overwhelming to many healthcare providers and created different opinions on the safety, effectiveness of biosimilars and the process of non-medical switching (Omair et al., 2017). A survey performed in 2015 have shown that 70.37% of rheumatologists will use biosimilar products once available (Omair et al., 2017). Recently a group of expert rheumatologist have developed some guidance on the introduction of biosimilars in Saudi Arabia (Halabi et al., 2018). The current paper describes the executive summary of the Second Symposium on Biologics and Biosimilars.

The Second Symposium on Biologics and Biosimilars "Beyond Clinical Practice" was organized by the Medication Safety Research Chair, College of Pharmacy, King Saud University and held on 24th–26th January 2020. The meeting was in partnership with the Saudi Pharmaceutical Society, Saudi Society for Rheumatology and Saudi society of Clinical Pharmacy. The Symposium aimed at improving the understanding of these new agents through a diverse interactive program. Participants were invited directly through the Medication Safety Research Chair Twitter account and emails that were sent to pharmacists and clinicians working in different governmental and private sectors. The symposium was funded by an unrestricted grant from AbbVie and Amgen.

2. Results

A total of 217 participants attended the meeting. All sessions were attended by a designated team.

2.1. Aim and objectives

The symposium consisted of 3 workshops and 2 days of lectures and panel discussion distributed in four main tracks.

The main objectives of the symposium included the following:

- 1- To gain basic knowledge about originator and biosimilar manufacturing, related technology and quality assurance.
- 2- To understand the requirements for biosimilar registration across different regional and global agencies.

- 3- To acquire basic knowledge on the pharmacoeconomic and pharmacovigilance aspects linked to biosimilar introduction.

2.2. Workshops

The first workshop tackled biologic utilization and the introduction of biosimilars and its impact on all stakeholders including healthcare providers, decision makers and patients/caregivers.

The second workshop covered basic understanding of the pharmacoeconomic methodology that was used in drug evaluation taking the originator biologic and biosimilar as a case study.

The third workshop tackled the concept of pharmacovigilance in view of infrastructure, national and global databases and pitfalls of reporting.

2.3. Track 1 (introduction to biosimilars)

The definition of biosimilars and how they differ from generic drugs in view of structural and manufacturing complexity was the main focus of this track. Unlike generics, biosimilars are never identical to the reference medicine product because changes to the manufacturing process can result in differences in quality, safety, and efficacy. The session covered the world experience of switching from originator to biosimilar and the pros and cons of a full switch compared to a staged switch. The session was concluded by describing unmet needs in the region in view of the goal to improve the understanding of biosimilar structure and biotechnology, which the currently described educational activity is targeting.

2.4. Track 2 (clinical challenges in practice)

In this track clinicians from different specialties discussed the impact of the introduction of biologics and other biotherapeutics on patient care and outcome. This included rheumatology, hematology, oncology, neurology and gastroenterology. Also, speakers have highlighted the economic challenges of biologic use in the context of expanding populations and rising costs of treatment with pressures to contain cost in health care systems. All specialties agreed that non-medical switching should be adopted. The discussion was ended by underscoring the importance of strategies that may reduce the use of biologics, assesses the cost-effectiveness of biosimilar by comparing the costs and outcomes of a medicine with those of a relevant originator, involvement of all stakeholders and evidence-based decision-makers in the process of introducing biosimilars into their respective institutions.

2.5. Track 3 (regulatory and pharmacoeconomic aspects)

This track discussed the similarities and differences between registration requirements for Biosimilars in the US-FDA, EMA and the reflection by the Saudi Food and Drug Authority (SFDA). Speakers covered the important difference of PK, PD and clinical trial requirements between an originator biologic and its biosimilar. This was a major part of the discussion with the attendees as healthcare providers are used to looking at an adequate number of clinical trials/observational studies that prove the safety and effectiveness of a newly introduced biologic before they can prescribe it. In contrast, biosimilar approval heavily relies on PK and PD studies with only one to two phases III clinical trials required for approval and extrapolation for all indications that have not been evaluated. Published data have shown that the current healthcare in GCC is projected to reach 104.6 billion USD in 2022, compared to 76.1 billion USD in 2017 (Alpen Capital Group).

There is a need to introduce a medication cost effectiveness role in institutions in order to enable providers to manage healthcare

budgets, shortage of medications, available medicines despising through the national healthcare transformation strategies from the Ministry of Health (MOH) coming from 2030 Saudi Arabia's vision.

2.6. Track 4 (challenges in biosimilars pharmacovigilance)

The last track started by stating the definition, importance and discussing the importance of introducing Pharmacovigilance programs of different products including biologics by agencies from around the world. Speakers introduced the different global databases including the Saudi vigilance system "Taiqaqth". They also discussed different strategies adopted by US-FDA and EMA in naming the biological product in clinical use and during reporting of adverse events. The discussion concluded by highlighting the need for training healthcare providers and encouraging them to report AEs in addition to improving the infrastructure of Pharmacovigilance. Implement policies and practices that may improve the fidelity of safety signaling reporting of biosimilars by increased use of barcodes to improve traceability. Speakers unanimously expressed their belief that all of the above mentioned interventions can lead to a higher reporting rate and more efficient detection of safety signals in the Saudi Healthcare.

3. Discussion

The current paper describes an educational activity that has targeted a diverse audience aiming at improving the understanding of the challenges and added value of introducing biosimilars into the Saudi healthcare system. EMA was the pioneer and the first in developing regulatory guidelines on biosimilars since 2005. This was followed by other agencies such as the US FDA and SFDA in 2010. (Kabir et al., 2019). The strategies of introducing biosimilars differs from one country to another.

EMA long expertise in the field of biosimilars had led to the establishment of well-defined step-wise approach that made it easier for other regulatory authorities to follow them. They have published many guidelines specific and general to help companies to reduce the uncertainties and improve their products (Scavone et al., 2017).

Many societal activities have been undertaken globally but few were reported. Some were targeting the general concept of biosimilars such as The American Pharmacists Association in 2016 (Crespi-Lofton and Skelton, 2017) and the Parenteral Drug Association in 2018 (Krause et al., 2019). Others were specialty specific like the International Society of Oncology Pharmacy Practitioners in 2019 (Tan et al., 2019) and the National Kidney Foundation (Wish et al., 2016). While, few were challenge specific such as the International Society for Pharmacoeconomics (Ingrasciotta et al., 2019) in 2019. All of these activities were characterized by involving important stakeholders such as regulators, healthcare providers and industry representative. Also they focused on economic challenges, priorities, data sources and strategies in both registration and surveillance. Our symposium is unique as it partnered with 3 societies (2 pharmaceutical and rheumatology). The first symposium that we have organized in October 2018 had partnered with 3 societies (rheumatology, hematology and pharmaceutical). Additionally, 3 unrestricted grants were announced by the Medication Safety Research Chair, College Pharmacy, King Saud University in order to encourage research that explore important

questions relation to biosimilars. It is also important to mention the fundamental role of pharmaceutical industries in supporting such events without influencing the content. As in our conference, many speakers were SFDA employees and all other speakers had disclosed any conflict of interest prior to presenting their educational material.

In conclusion, despite of many challenges and ambiguities, the introduction of biosimilars into the Saudi Healthcare system will hopefully lead to substantial cost-savings. Educational activities related to this topic are important to be organized and reported.

Declaration of Competing Interest

Mohammed A. Omair has received speaker's fees/grants from Abbvie, Actelion, Amgen, Bristol Myers Squibb, Glaxo-Smith-Kline, Hekma, Janssen, New Bridge, Novartis, Pfizer, and Roche.

Mahmoud Mosli has received speaker's fees/grants from Pfizer, Abbvie, Janssen, Takeda, and Hekma.

Hanan Al Rayes has received speaker's fees from Abbvie, Amgen, Bristol Myers Squibb, New Bridge, Pfizer, Novartis and Roche.

All other authors declare no conflict of interest.

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