Fourth and final issue of GaBI Journal's fifth volume

Professor Philip D Walson, MD

This fourth and final *GaBI Journal* issue of 2016 begins with the paper by Adjunct Professor Pekka Kurki about 'applying ancient principles in a modern society' in which he discusses a perspective recently published in our journal from Annese et al. that presented the skeptical views expressed by Italian gastroenterologists concerning extrapolation of indications for infliximab. This paper summarized resistance to extrapolation based on the quote, 'first do no harm'. In fact, some say Hippocates' actual quote was, 'As to diseases, make a habit of two things—to help, or at least to do no harm'. Perhaps another Hippocrates quote is more appropriate, 'I have clearly recorded this: for one can learn good lessons also from what has been tried but clearly has not succeeded, when it is clear why it has not succeeded. [Hippocrates On Joints, 47. Trans. R. W. Sharples. Science quotes on: Diagnosis (54)]. Both scientific studies and actual clinical experience have shown that the extrapolation that bothers these clinicians has both a solid scientific foundation and extensive and growing clinical and research data yet resistance to it continues. Such resistance is likely to be influenced by the marketing efforts of innovator companies but there are also many other possible reasons, including real concerns for patient safety, distrust of biosimilar manufacturers, regulators, insurers as well as politicians and government bureaucrats. Regardless of the causes those who want to find ways to increase patient accessibility by decreasing the costs of treatment must understand what does and what does not work and to better understand and acknowledge all barriers to the prescribing and use of generics and biosimilars. As the recent UK referendum and US election have shown, ignoring the 'will of the people' can have major unwanted consequences. More effective ways must be found to better communicate with, rather than just talk to, all 'stakeholders' including the patients who take these medications and the physicians who prescribe and monitor them.

Pharmacists are also important 'stakeholders'. Professor Philip J Schneider and Mr Michael S Reilly present data gathered using a questionnaire designed and administered by the Alliance for Safe Biologic Medicines (ASBM) to obtain pharmacists' views on the naming and labelling of biosimilars. While the validity and the ability to extrapolate such questionnaire results beyond those pharmacists who responded is always limited, these data are potentially very important and certainly deserve to be listened to and considered seriously both by those who agree with as well as those who oppose these opinions.

A paper by Khan et al. presents disturbing data collected by the authors on the poor quality control of active pharmaceutical ingredients present in generic medicines sold in Pakistan. The paper raises a significant issue, which is at least in part responsible for the mistrust of the follow-on drug industry by clinicians in both resource-poor and developed countries. Until all countries have the kind of effective regulation of generic drug products that currently exists in the EU, UK and the US, and/or until the transport and sale of poor quality drugs is stopped, such data will reinforce resistance to the more widespread use of generics as well as to the even more complicated biosimilar medicines.

The economic implications of such resistance to the use of generics is illustrated by the paper by Akku et al. who discuss the difference between potential and actual savings generated by the use of generic oncology drugs in Colombia. The need to replace brand name with less expensive generic oncology drugs is particularly important in resource limited countries such as Colombia but this is also important in resource rich countries because of the obvious life or death consequences of not having such access. However, as illustrated by the data in Colombia, the availability of less expensive but quality generic drug products on the market is necessary but not sufficient to guarantee their use. Similar problems are discussed in a paper by Fatokun et al. that appears near the end of this issue.

A paper by O'Callaghan et al. describes in some detail the structure of and significant progress made by Regulatory Science Ireland (RSI) in improving acceptance of biosimilars through efforts 'to enhance understanding of biosimilar medicines amongst stakeholders and encourage best practice in the use of these medicines'. RSI is, 'a voluntary network of interested parties from academia, the Health Products Regulatory Authority (HPRA), pharmaceutical and medical device industries and government agencies'. The authors describe a useful model for others who are attempting to increase the uptake of, and savings generated by, the availability of quality biosimilar (as well as generic) medicines.

Follow-on medicines, whether generics or biosimilars, have clear potential to reduce costs and thereby increase overall access to medicines. However, they can also have 'value added' properties for both patients and manufacturers. Dr Fereshteh Barei argues that, 'High quality, low risk, improved value-added therapeutics, and super generics/hybrids can ensure convenience, provide increasing patient adherence, efficiency, safety, sustainability, cost-effectiveness, competitiveness and innovativeness'. While not discussed by Dr Barei, similar arguments have been made that follow-on biological drugs can actually be 'biobetters'. Availability of such improved products might improve acceptance of follow-on products by all stakeholders. However, as pointed out by Dr Barei, development of such products will require, 'a team effort by innovators, entrepreneurs, regulators, payers and policymakers'.

Another possible way to increase acceptance of follow-on biotherapeutic (and generic) drug products is through the availability of improved pharmacopoeia monographs as discussed by Dr Emmanuelle Charton in a paper addressing the main challenges to developing such monographs as well as how they can be overcome. As a former, long time member of the US Pharmacopeia (USP) I can attest to how important to and yet how underappreciated they are by many clinicians. However, I agree with Dr Charton that well written pharmacopoeia monographs, 'play a major role in ensuring that medicinal products … meet the same quality standards, thereby contributing to patient safety'. I also feel that all stakeholders would be well served by a better understanding of the methods used to develop and use these monographs as described in this important paper.

Fatokun et al. summarize the data presented in a doctoral thesis that examined, 'The determinants and characteristics of generic medicines entry following the patent expiration of innovator drug products in Malaysia … The sources of data used … included 22 policy documents, a survey of 13 key informants, a cross-sectional questionnaire of 14 generic medicines manufacturing industries, and panel data analysis of the 12 best-selling single entity prescription drug products that experienced loss of patent protection and subsequent generics entry in Malaysia between January 2001 and December 2009'. The authors propose a number of as yet untested but logical actions they feel would improve the uptake of generic medicines in Malaysia.

The issue ends with a meeting report followed by four abstracted scientific papers. The meeting report is based on the presentation given by Martina Weise, MD, at the 14th Annual Biosimilar Medicines Group Conference in which Dr Weise, Head of Licensing Division at the Federal Institute for Drugs and Medical Devices (BfArM), described her personal views on how the European Medicines Agency has changed its requirements for biosimilars since approving the first biosimilars in 2006. The presentation contains important insight into this important but still evolving process.

The first abstracted scientific content is based on a paper published by Dr Tomaszewski in which a cross-sectional online survey of 781 pharmacists examined the effect of naming on pharmacists' perceptions and dispensing of biosimilars. The second is an abstract of a paper published by Alessandro Nobili, MD, Head of the Drug Information Service for the Elderly, IRCCS – Istituto di Ricerche Farmacologiche 'Mario Negri' that discusses some of the most frequent concerns raised by internists about biosimilars. The third is an abstract of a paper published by Bergman et al. describing an empirical study of the market-based purchasing policies for generic pharmaceuticals used in Sweden. The final abstracted scientific content is of a paper published by Jones et al. that discusses, 'the strategies used by brand pharmaceutical companies, often in combination, to delay market entry of affordable generic drugs in the US and other countries' and in which the authors, 'highlight 10 possible corrective measures based on US legislation that could be applied to remedy the situation in the US'.

I want to end with best wishes for a healthy and happy holiday season and New Year as well as a plea for your manuscripts and input/feedback on the *GaBI Journal*.

Professor Philip D Walson, MD
Editor-in-Chief, GaBiJournal

DOI: 10.5639/gabij.2016.0504.038